One-pot synthesis of $\alpha$-substituted acrylates

Supporting Information

Magdalini Matziari* and Yixin Xie

Xi’an Jiaotong-Liverpool University, SIP, Suzhou, Jiangsu Province, P R China

*Corresponding Author: Magdalini.Matziari@xjtlu.edu.cn

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**General considerations:** All of the compounds, for which analytical and spectroscopic data are quoted, were homogenous by TLC. TLC analyses were performed using silica gel plates (E. Merck silica gel 60 F-254) and components were visualized by the following methods: UV light absorbance, iodine vapour and charring after stained by phosphomolybdic acid (PMA), using as eluents (A) PE 30-60 °C/AcOEt=95/5, and (B) Hexanes/DCM=2/1, unless otherwise stated. Column chromatography was carried out on silica gel (0.060-0.200mm 40A). All the compounds were characterized by $^1$H and $^{13}$C-NMR spectroscopy. $^1$H and $^{13}$C and were recorded in CDCl$_3$ on a Bruker Avance III 400 spectrometer at room temperature. Chemical shifts (δ) are reported in parts per million (ppm) using residual CHCl$_3$ as internal reference (7.26 ppm in $^1$H spectra and 77.36 ppm in $^{13}$C spectra) and J values are given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), and multiplet (m). Splitting patterns that could not be easily interpreted were designated as multiplet (m). HRMS were obtained on a Bruker Daltonics – micrOTOF - Q II – ESI – Qq - TOF mass spectrometer. All commercially available reagents, solvents and starting materials were used without further purification.
General method for the synthesis of ethyl ester acrylates:

Triethyl phosphonoacetate (5 mmol) and KOTBu (1.5 equiv, 7.5 mmol) were dissolved in dry DMF (25 mL) in a round-bottom flask and stirred at 100 °C for 10 min under Ar. The alkylation agent (1.5 equiv, 7.5 mmol) was added slowly into the flask, and the reaction mixture was stirred for 3 h at 100 °C (except for low b.p. alkylating agents where heating 15-20 °C below the b.p. was applied). Then K₂CO₃ (3 equiv, 15 mmol) and 37 wt.% aqueous HCHO (3 equiv, 15 mmol) were added and the resulting mixture was stirred for another 3 h at 100 °C. The reaction was quenched with HCl 0.5 M to pH~5 and the mixture was extracted with Et₂O (2 x 40 mL). The combined extracts were washed with water (50 mL), dried over Na₂SO₄, filtered and concentrated. Target acrylates were obtained as colourless liquids by flash column chromatography purification using hexanes/DCM as eluent.

4-tert-butyl 1-ethyl 2-methylenesuccinate (4)

Alkylation agent: t-butyl chloroacetate
Yield: 68%
TLC: Rₜ (A) = 0.40, Rₜ (B) = 0.11
¹H NMR (400 MHz, CDCl₃): δ 6.28 (s, 1H), 5.63 (s, 1H), 4.21 (q, J = 7.12 Hz, 2H), 3.24 (s, 2H), 1.44 (s, 9H), 1.29 (t, J = 7.12 Hz, 3H)
¹³C NMR (100 MHz, CDCl₃): δ 169.98, 166.37, 134.64, 127.62, 80.94, 60.91, 39.05, 27.99, 14.16
HRMS ([M+1]⁺) calcd for C₁₁H₁₉O₄ 215.1205, found 215.1264

5-tert-butyl 1-ethyl 2-methylenepentanedioate (6)

Alkylation agent: t-butyl-3-bromopropionate
Yield: 65%
TLC: Rₜ (A) = 0.38, Rₜ (B) = 0.10
¹H NMR (400 MHz, CDCl₃): δ 6.17 (s, 1H), 5.56 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 2.59 (t, J = 7.5 Hz, 2H), 2.42 (t, J = 7.5 Hz, 2H), 1.43 (s, 9H), 1.30 (t, J = 7.2 Hz, 3H)
¹³C NMR (100 MHz, CDCl₃): δ 172.10, 166.80, 139.38, 125.27, 80.42, 60.72, 34.24, 28.11, 27.42, 14.21
HRMS ([M+1]⁺) calcd for C₁₂H₂₁O₄ 229.1362, found 229.1350
Ethyl 3-methyl-2-methylenepentanoate (10)

Alkylation agent: 2-bromobutane
Yield: 53%

TLC: R_f (A) = 0.62, R_f (B) = 0.35

^1H NMR (400 MHz, CDCl_3): δ 6.15 (s, 1H), 5.48 (s, 1H), 4.20 (q, J = 7.12 Hz, 2H), 2.68-2.56 (m, 1H), 1.50-1.35 (m, 2H), 1.38 (t, J = 7.12 Hz, 3H), 1.08 (d, J = 6.92 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H)

^13C NMR (100 MHz, CDCl_3): δ 167.60, 146.15, 122.45, 60.49, 36.13, 28.66, 19.32, 14.22, 11.65

HRMS ([M+H]^+) calcd for C_9H_{17}O_2 157.1150, found 157.1106

Ethyl 4-methyl-2-methylenepentanoate (11)

Alkylation agent: 1-bromo-2-methylpropane
Yield: 67%

TLC: R_f (A) = 0.60, R_f (B) = 0.32

^1H NMR (400 MHz, CDCl_3): δ 6.15 (s, 1H), 5.47 (s, 1H), 4.18 (q, J = 7.12 Hz, 2H), 2.16 (d, J = 7.0 Hz, 2H), 1.86-1.72 (m, 1H), 1.30 (t, J = 7.12 Hz, 3H), 0.89 (d, J = 7.2 Hz, 6H)

^13C NMR (100 MHz, CDCl_3): δ 167.60, 139.99, 125.45, 60.52, 41.31, 27.20, 22.27, 14.20

HRMS ([M+H]^+) calcd for C_9H_{17}O_2 157.1150, found 157.1200

Ethyl 2-methylenehexanoate (14)

Alkylation agent: 1-bromobutane
Yield: 84%

TLC: R_f (A) = 0.75, R_f (B) = 0.42

^1H NMR (400 MHz, CDCl_3): δ 6.12 (s, 1H), 5.50 (s, 1H), 4.20 (q, J = 7.12 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 1.50-1.41 (m, 2H), 1.39-1.28 (m, 2H), 1.30 (t, J = 7.12 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H)

^13C NMR (100 MHz, CDCl_3): δ 167.45, 141.17, 124.09, 60.53, 31.55, 30.59, 22.30, 14.22, 13.89

HRMS ([M+H]^+) calcd for C_9H_{17}O_2 157.1150, found 157.1124
Ethyl 5-((tert-butoxycarbonyl) amino)-2-methylenepentanoate (15)

Alkylation agent: t-butyl (3-bromopropyl) carbamate. This reaction was performed at rt, 10 h for each step.

Yield: 43%

TLC: Rf (A) = 0.33, Rf (B) = 0.05

\(^1\)H NMR (400 MHz, CDCl₃): δ 6.16 (s, 1H), 5.56 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.15-3.10 (m, 2H), 2.38-2.27 (m, 2H), 1.75-1.62 (m, 2H), 1.44 (s, 9H), 1.29 (s, J = 7.2 Hz, 3H)

\(^{13}\)C NMR (100 MHz, CDCl₃): δ 167.12, 155.98, 140.02, 125.06, 79.13, 60.67, 40.04, 29.01, 28.92, 28.39, 14.17

HRMS ([M+1]^+) calcd for C\(_{13}\)H\(_{23}\)NO\(_4\) 258.1627, found 258.1624

Ethyl 2-benzylacrylate (16)

Alkylation agent: Benzyl bromide

Yield: 73%

TLC: Rf (A) = 0.57, Rf (B) = 0.23

\(^1\)H NMR (400 MHz, CDCl₃): δ 7.34-7.17 (m, 5H), 6.23 (s, 1H), 5.45 (s, 1H), 4.18 (q, J = 7.12 Hz, 2H), 3.63 (s, 2H), 1.26 (t, J = 7.12 Hz, 3H)

\(^{13}\)C NMR (100 MHz, CDCl₃): δ 166.94, 140.42, 138.82, 129.06, 128.39, 126.30, 125.96, 60.74, 38.08, 14.14

HRMS ([M+1]^+) calcd for C\(_{13}\)H\(_{15}\)O\(_2\) 191.0994, found 191.1028

Tert-butyl 3-(2-(ethoxycarbonyl)allyl)-1H-indole-1-carboxylate (20)

Alkylation agent: t-Butyl 3-bromomethylindole-1-carboxylate. This reaction was performed at rt, 10 h for each step.

Yield: 78%

TLC: Rf (A) = 0.37, Rf (B) = 0.19
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**1H NMR** (400 MHz, CDCl₃): δ 7.50-7.18 (m, 5H), 6.24 (s, 1H), 5.50 (s, 1H), 4.23 (q, J = 7.12 Hz, 2H), 3.71 (s, 2H), 1.67 (s, 9H), 1.31 (t, J = 7.12 Hz, 3H)

**13C NMR** (100 MHz, CDCl₃): δ 166.99, 149.70, 138.68, 130.31, 126.56, 125.91, 124.33, 124.04, 122.41, 119.30, 117.65, 115.26, 83.50, 60.84, 28.24, 27.29, 14.20

**HRMS** ([M+1]⁺) calcd for C₁₉H₂₆NO₄ 330.1627, found 330.1682

**Ethyl 2-(4-methoxybenzyl) acrylate (21)**

Alkylation agent: 1-(chloromethyl)-4-methoxybenzene

Yield: 84%

TLC: Rf (A) = 0.53, Rf (B) = 0.22

**1H NMR** (400 MHz, CDCl₃): δ 7.10 (d, J = 8.54 Hz, 2H), 6.82 (d, J = 8.54 Hz, 2H), 6.19 (s, 1H), 5.42 (s, 1H), 4.17 (q, J = 7.12 Hz, 2H), 3.78 (s, 3H), 3.56 (s, 2H), 1.26 (t, J = 7.12 Hz, 3H)

**13C NMR** (100 MHz, CDCl₃): δ 167.01, 158.15, 140.83, 130.84, 128.89, 125.60, 113.83, 63.79, 60.70, 55.28, 37.24, 27.75, 14.17

**HRMS** ([M+1]⁺) calcd for C₁₃H₁₇O₃ 221.1099, found 221.1089

**Ethyl 3-methyl-2-methylenebutanoate (22)**

Alkylation agent: 2-bromopropane

Yield: 76%

TLC: Rf (A) = 0.58, Rf (B) = 0.39

**1H NMR** (400 MHz, CDCl₃): δ 6.10 (s, 1H), 5.49 (s, 1H), 4.21 (q, J = 7.12 Hz, 2H), 2.85-2.80 (m, 2H), 1.29 (t, J = 7.12 Hz, 3H), 0.88 (d, J = 7.2 Hz, 6H)

**13C NMR** (100 MHz, CDCl₃): δ 167.22, 147.37, 121.18, 60.31, 31.56, 22.60, 21.67, 14.06

**HRMS** ([M+1]⁺) calcd for C₈H₁₄O₂ 143.0994, found 143.0894
Ethyl 2-methylene-5-phenylpentoanoate (23)

Alkylation agent: 1-bromo-3-phenylpropane

Yield: 89%

TLC: Rf (A) = 0.72, Rf (B) = 0.33

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.32-7.14 (m, 5H), 6.14 (s, 1H), 5.51 (s, 1H), 4.19 (q, \(J = 7.12\) Hz, 2H), 2.64 (t, \(J = 7.66\) Hz, 2H), 2.34 (t, \(J = 7.66\) Hz, 2H), 1.84-1.76 (m, 2H), 1.29 (t, \(J = 7.12\) Hz, 3H)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 167.29, 142.14, 140.73, 128.43, 128.32, 125.78, 124.54, 60.60, 35.43, 31.54, 30.10, 14.22

HRMS ([M+1] \(^+\)) calcd for C\(_{14}\)H\(_{18}\)O\(_2\) 219.1307, found 219.1335

Ethyl 2-methylenepent-4-ynoate (24)

Alkylation agent: 3-bromopropyne

Yield: 64%

TLC: Rf (A) = 0.61, Rf (B) = 0.39

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 6.34 (s, 1H), 6.04 (s, 1H), 4.22 (q, \(J = 7.12\) Hz, 2H), 3.24 (s, 2H), 2.20 (s, 1H), 1.31 (t, \(J = 7.12\) Hz, 3H)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 166.05, 135.23, 126.07, 80.18, 71.92, 61.01, 21.51, 14.18

HRMS ([M+1] \(^+\)) calcd for C\(_8\)H\(_{12}\)O\(_2\) 139.0681, found 139.0642
**General method for the synthesis of tert-butyl ester acrylates:**

_Tert_-butyl diethylphosphonoacetate (5 mmol) and KOTBu (1.5 equiv, 7.5 mmol) were dissolved in dry DMF (25 mL) in a round-bottom flask and stirred at 100 °C for 10 min under Ar. The alkylation agent (1.5 equiv, 7.5 mmol) was added slowly into the flask, and the reaction mixture was stirred for 3 h at 100 °C (except for low b.p. alkylation agents where heating 15-20 °C below the b.p. was applied). Then K2CO3 (3 equiv, 15 mmol) and 37 wt.% aqueous HCHO (3 equiv, 15 mmol) were added and the resulting mixture was stirred for another 3 h at 100 °C. The reaction was quenched with HCl 0.5 M to pH~5 and the mixture was extracted with Et2O (2 x 40 mL). The combined extracts were washed with water (50 mL), dried over Na2SO4, filtered and concentrated. Target acrylates were obtained as colourless liquids by flash column chromatography purification using hexanes/DCM as eluent.

1-(tert-butyl) 4-ethyl 2-methylenesuccinate (4a)

**Alkylation agent:** ethyl bromooacetate

**Yield:** 72%

**TLC:** Rf (A) = 0.45, Rf (B) = 0.16

_1H NMR_ (400 MHz, CDCl3): δ 6.25 (s, 1H), 5.62 (s, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.30 (s, 2H), 1.50 (s, 9H), 1.28 (t, J = 7.2 Hz, 3H)

_13C NMR_ (100 MHz, CDCl3): δ 170.87, 165.33, 135.53, 127.21, 81.08, 60.79, 38.07, 27.96, 14.16

HRMS ([M+1]+) calcd for C_{11}H_{20}O_{4} 215.1205, found 215.1198

_Tert_-butyl 3-methyl-2-methylenepentanoate (10a)

**Alkylation agent:** 2-bromobutane

**Yield:** 58%

**TLC:** Rf (A) = 0.73, Rf (B) = 0.58

_1H NMR_ (400 MHz, CDCl3): δ 6.06 (s, 1H), 5.40 (s, 1H), 2.60-2.55 (m, 1H), 1.58-1.31 (m, 11H), 1.06 (d, J = 7.00 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H)

_13C NMR_ (100 MHz, CDCl3): δ 166.93, 147.57, 121.39, 80.28, 36.09, 28.79, 27.42, 19.21, 11.71

HRMS ([M+1]+) calcd for C_{11}H_{22}O_{2} 185.1463, found 185.1502
**Tert-butyl 4-methyl-2-methylenepentanoate (11a)**

**Alkylation agent:** 1-bromo-2-methylpropane

**Yield:** 63%

**TLC:** \( R_f (A) = 0.70, R_f (B) = 0.42 \)

\[ ^1H \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3): \delta 6.06 \text{ (s, 1H)}, 5.40 \text{ (s, 1H)}, 2.14 \text{ (d, } J = 6.9 \text{ Hz, 2H)}, 1.80-1.75 \text{ (m, 1H)}, 1.49 \text{ (s, 9H)}, 0.89 \text{ (d, } J = 7.0 \text{ Hz, 6H)} \]

\[ ^{13}C \text{NMR} \ (100 \text{ MHz}, \text{CDCl}_3): \delta 166.78, 141.38, 124.54, 80.23, 41.38, 28.03, 27.37, 22.28 \]

**HRMS ([M+1]⁺) calcd for C₁₁H₂₁O₂ 185.1463, found 185.1422**

**Tert-butyl 2-methylenehexanoate (14a)**

**Alkylation agent:** 1-bromobutane

**Yield:** 78%

**TLC:** \( R_f (A) = 0.73, R_f (B) = 0.54 \)

\[ ^1H \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3): \delta 6.03 \text{ (s, 1H)}, 5.43 \text{ (s, 1H)}, 2.26 \text{ (t, } J = 7.4 \text{ Hz, 2H)}, 1.44 \text{ (s, 9H)}, 1.37-1.35 \text{ (m, 2H)}, 1.34-1.31 \text{ (m, 2H)}, 0.92 \text{ (t, } J = 7.3 \text{ Hz, 3H)} \]

\[ ^{13}C \text{NMR} \ (100 \text{ MHz}, \text{CDCl}_3): \delta 166.72, 142.58, 123.17, 80.27, 31.63, 30.71, 28.04, 22.35, 13.89 \]

**HRMS ([M+1]⁺) calcd for C₁₁H₂₁O₂ 185.1463, found 185.1478**

**Tert-butyl 2-benzylacrylate (16a)**

**Alkylation agent:** Benzyl bromide

**Yield:** 78%

**TLC:** \( R_f (A) = 0.68, R_f (B) = 0.31 \)

\[ ^1H \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3): \delta 7.33-7.22 \text{ (m, 5H)}, 6.19 \text{ (s, 1H)}, 5.41 \text{ (s, 1H)}, 3.63 \text{ (s, 2H)}, 1.48 \text{ (s, 9H)} \]

\[ ^{13}C \text{NMR} \ (100 \text{ MHz}, \text{CDCl}_3): \delta 166.22, 141.78, 139.14, 129.00, 128.34, 126.21, 125.19, 80.70, 38.24, 28.00 \]

**HRMS ([M+1]⁺) calcd for C₁₄H₁₉O₂ 219.1307, found 219.1350**
**Tert-butyl 2-(4-methoxybenzyl) acrylate (21a)**

Alkylation agent: 1-(chloromethyl)-4-methoxybenzene  
Yield: 89%  
TLC: $R_f$ (A) = 0.65, $R_f$ (B) = 0.28  
$^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ 7.13 (d, $J$ = 8.48 Hz, 2H), 6.86 (d, $J$ = 8.48 Hz, 2H), 6.14 (s, 1H), 5.37 (s, 1H), 3.81 (s, 3H), 3.56 (s, 2H), 1.47 (s, 9H)  
$^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ 166.30, 158.07, 142.16, 131.14, 129.96, 124.79, 113.75, 80.62, 55.22, 37.34, 28.02  
HRMS ([M+1]$^+$) calcd for C$_{15}$H$_{20}$O$_3$ 249.1412, found 249.1450

**Tert-butyl 2-methylene-5-phenylpentanoate (23a)**

Alkylation agent: 1-bromo-3-phenylpropane  
Yield: 84%  
TLC: $R_f$ (A) = 0.84, $R_f$ (B) = 0.43  
$^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ 7.28-7.22 (m, 5H), 6.08 (s, 1H), 5.47 (s, 1H), 2.66 (t, $J$ = 7.76 Hz, 2H), 2.34 (t, $J$ = 7.56 Hz, 2H), 1.78-1.83 (m, 2H), 1.51 (s, 9H)  
$^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ 166.59, 142.25, 142.15, 128.43, 128.31, 125.75, 123.64, 80.45, 35.54, 31.66, 30.28, 28.08  
HRMS ([M+1]$^+$) calcd for C$_{16}$H$_{22}$O$_2$ 247.1620, found 247.1688

**Tert-butyl 2-methylenepent-4-ynoate (24a)**

Alkylation agent: 3-bromopropyne  
Yield: 62%  
TLC: $R_f$ (A) = 0.72, $R_f$ (B) = 0.50  
$^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ 6.24 (s, 1H), 5.96 (s, 1H), 3.19 (s, 2H), 2.19 (s, 1H), 1.49 (s, 9H)  
$^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ 165.19, 136.55, 125.14, 81.06, 80.43, 71.72, 27.99, 21.48  
HRMS ([M+1]$^+$) calcd for C$_{10}$H$_{15}$O$_2$ 167.0994, found 167.0903
Synthesis of Ethyl 5-acetoxy cyclopent-1-ene-1-carboxylate 17

A solution of 2,5-dimethoxytetrahydrofuran (1.06 g, 8 mmol) and HCl 0.6 M (6.5 ml) was heated to 70 °C for 2.5 h under vigorous stirring. After cooling to 0 °C, the mixture was neutralised with KHCO₃ 10% (4.5 ml), and triethyl phosphonoacetate (1.8 g, 8.1 mmol) and K₂CO₃ 6.4 M (3.5 mL) were added. The reaction mixture was stirred for 24 h at rt. Extraction with AcOEt (3 x 20 mL), washing with brine (10 ml), drying over Na₂SO₄, filtration and concentration, and purification by column chromatography using hexane/AcOEt=3/1 as eluent afforded ethyl 5-hydroxycyclopent-1-ene-1-carboxylate (1gr, 6.4 mmol, 80%) as colourless liquid.

In a solution of ethyl 5-hydroxycyclopent-1-ene-1-carboxylate (1gr, 6.4 mmol) and pyridine (3.04 gr, 38.4 mmol) in DCM (3 mL) acetyl chloride (3.02 gr, 38.4 mmol) was added dropwise at 0 °C. The reaction mixture was stirred overnight at rt. Solvent removal, solution in AcOEt (50ml), washing with HCl 1M to pH~3, washing with NaHCO₃ 5% (30 mL) , brine (20 mL) drying over Na₂SO₄, filtration and concentration, and purification by column chromatography using DCM as eluent afforded the product as pale yellow liquid.

Yield (over 2 steps): 68%

TLC: Rf (hexanes/AcOEt=3/1) = 0.55

¹H NMR (400 MHz, CDCl₃): δ 7.06 (s, 1H), 5.97-5.92 (m, 1H), 4.20-4.13 (m, 2H), 2.68-2.61 (m, 1H), 2.48-2.33 (m, 2H), 1.99 (s, 3H), 1.90-1.84 (m, 1H), 1.26-1.22 (m, 3H)

¹³C NMR (100 MHz, CDCl₃): δ 170.47, 163.52, 149.63, 135.10, 77.21, 60.28, 31.20, 31.05, 21.11, 14.15

HRMS ([M+1]+) calcd for C₁₀H₁₅O₄ 199.0892, found 199.0924
Phenylpropyl
Propargyl