**SUPPORTING INFORMATION**

# A "click" chemistry constructed affinity system for 2-oxoglutaric acid receptors and binding proteins

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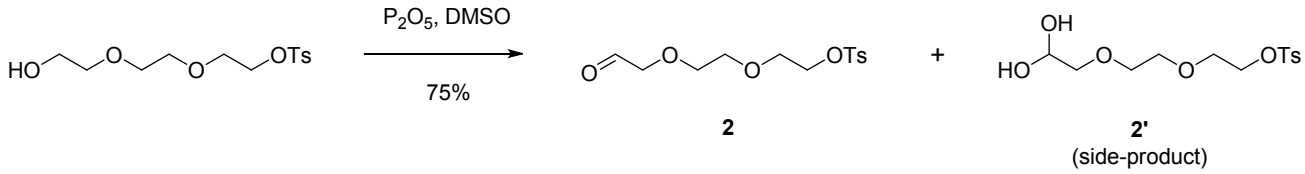
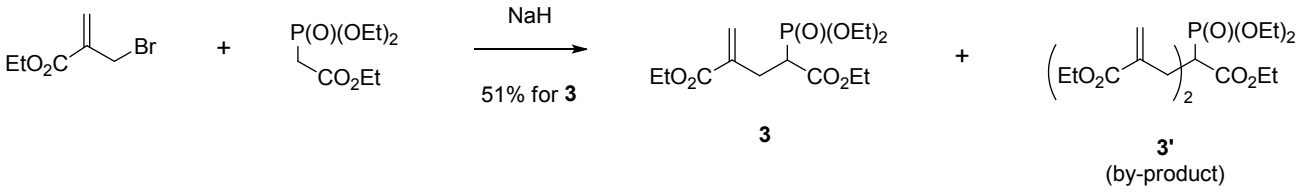
**Scheme S1:** Synthesis of the compound **2**.




**Scheme S2:** Synthesis of the compound **3**.




**Scheme S3:** Synthesis of the resin **6**.

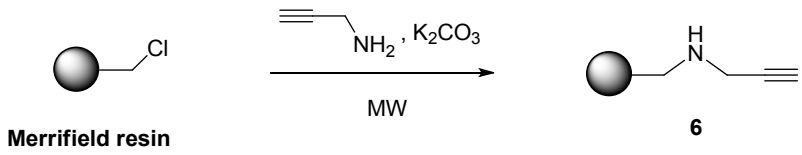


**Figure S1:** Conversion of **6** to **7** followed by IR spectroscopic analysis.

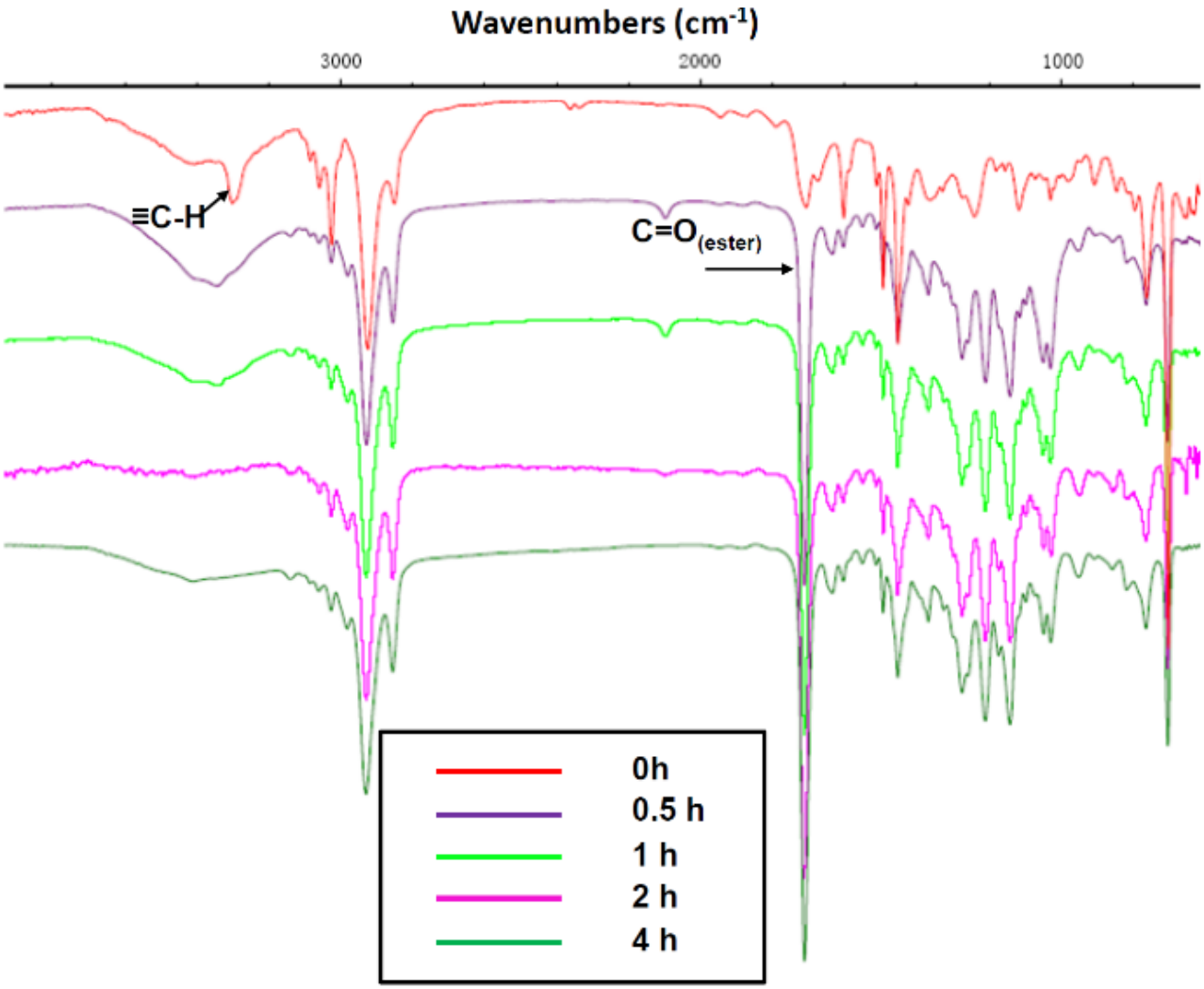


**Figure S2:** Protein revelation of resin **1** capturing and eluting NtcA from a pure NtcA solution. Lane 1: protein molecular weight marker; Lane 2: NtcA as reference; Lane 3: supernatant from the incubation buffer; Lane 4 and 5: elution with PBS; Lane 6: elution with 2-OG solution (0.5 M) in PBS buffer; Lane7: elution with PBS; Lane 8: elution with NaCl solution; Lane 9: elution with PBS. The pH of PBS and 2-OG elution was controlled at pH=7.5.

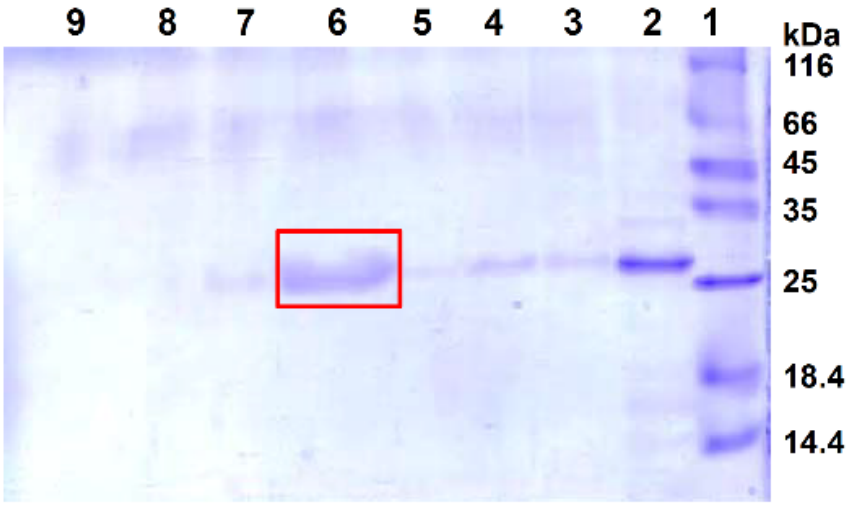
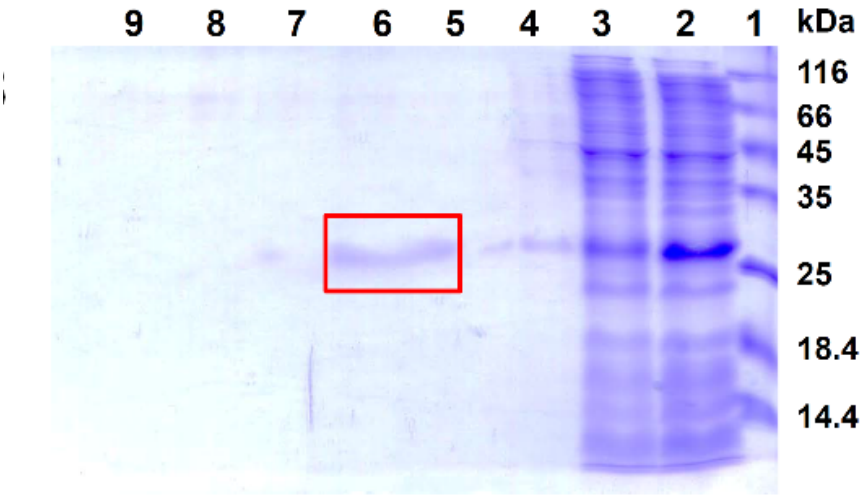


**Figure S3:** Protein revelation of resin **1** capturing and eluting NtcA from *E. coli* cell lysate. Lane 1: protein molecular weight marker; Lane 2: *E. coli* cell lysate as reference; Lane 3: supernatant from the incubation buffer; Lane 4 and 5: elution with PBS; Lane 6: elution with 2-OG solution (0.5 M) in PBS buffer; Lane7: elution with PBS; Lane 8: elution with NaCl solution; Lane 9: elution with PBS. The pH of PBS and 2-OG elution was controlled at pH=7.5.



**2:** To a mixture of $P_2O_5$ (1.08 g, 7.60 mmol) in freshly distilled $CH_2Cl_2$ (10.0 mL) at 0 °C was added a solution of anhydrous DMSO (0.590 mL, 7.60 mmol) in freshly distilled $CH_2Cl_2$ (5.00 mL) over a period of 5 min. To this mixture, a solution of monotosylated triethylene glycol (1.22 g, 4.00 mmol) in freshly distilled $CH_2Cl_2$ (10.0 mL) was then added at 0 °C over a period of 15 min. The obtained reaction mixture was then allowed to warm up to room temperature and stirred for 30 min before quenching with triethylamine (4.27 mL, 30.8 mmol). Water (15.00 mL) was added and the mixture was stirred at room temperature for another 30 min. The organic layer was separated, washed successively with 3.0 M HCl (15.0 mL), water (15.0 mL), saturated $NaHCO_3$ solution (15.0 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography using a gradient of petroleum ether/ethyl acetate, (2:1, 1:1 to 1:4, v/v), yielding a mixture of the desired aldehyde product **2** and its corresponding hydrate **2'** as a pale yellow oil (**2**/**2'** =1/2, 782 mg, 65%). $^1$H NMR (300 MHz, $CDCl_3$) δ 9.69 (s, 1H, C*H*O), 7.80 (d, *J* = 7.5 Hz, 2H, *Ph*$CH_3$), 7.35 (d, *J* = 7.50 Hz, 2H, *Ph*$CH_3$), 5.25-5.00 (m, br, 1H, C*H*$(OH)_2$), 4.16-4.14 (m, 2H, -C$H_2$CH$(OH)_2$, TsOC$H_2$), 3.72-3.58 (m, 9H, -OC$H_2$, CH(O*H*$)_2$), 2.45 (s, 3H, PhC$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 200.8, 145.2, 133.0, 130.1 (2C), 128.1 (2C), 93.3, 73.6, 71.2-68.4, 21.8; HRMS for **2** calcd. for $C_{13}H_{18}O_6SNa^+$, 325.0716, found 325.0716.

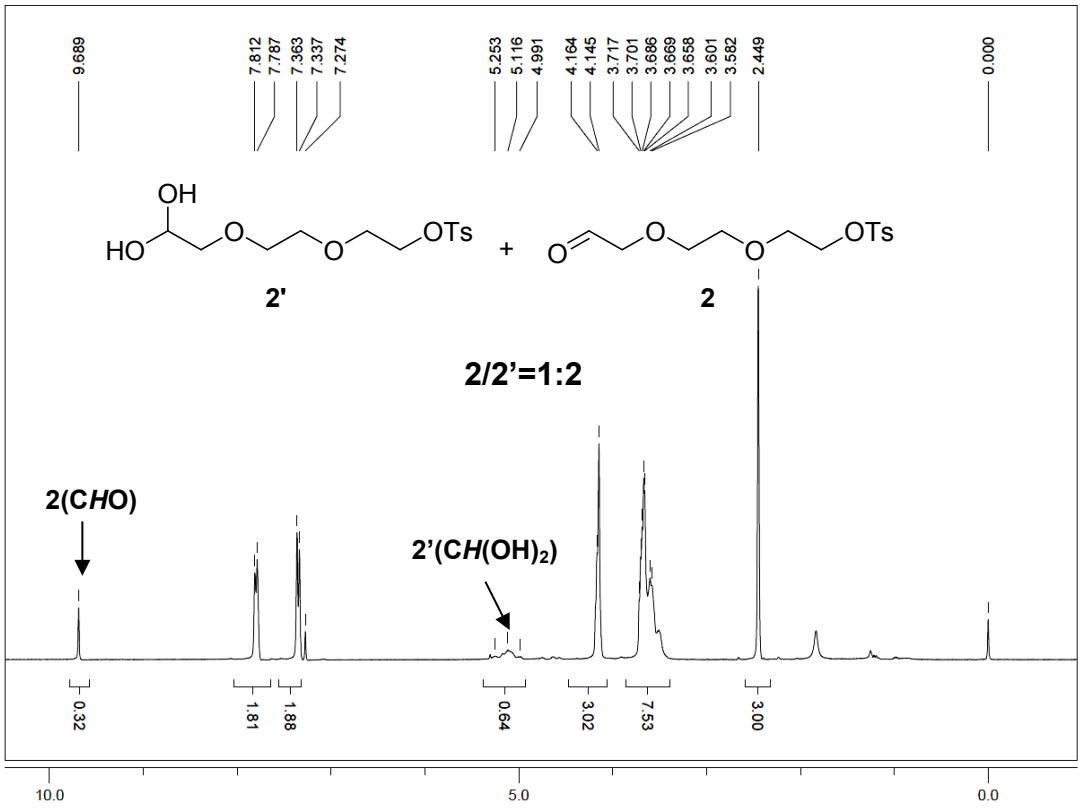
**3**: To a mixture of 85% NaH (568 mg, 20.1 mmol) in freshly distilled DME (50.0 mL) was added a solution of triethyl phosphonoacetate (4.62 mL, 23.2 mmol) in freshly distilled DME (80.0 mL) over a period of 30 min. The reaction mixture was stirred at room temperature for 2 h. After complete disappearance of powdered NaH, a solution of ethyl 2-(bromomethyl)acrylate (3.94 g, 20.4 mmol) in freshly distilled DME (10.0 mL) was added to the reaction mixture over a period of 10 min at -40 °C. The resulting mixture was allowed to warm up to room temperature and stirred for 30 min before quenching by addition of a saturated $NH_4Cl$ (30.0 mL), followed by extraction with ethyl acetate (3×30.0 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography using a gradient of petroleum ether/ethyl acetate, (4:1-1:1, v/v), yielding a mixture of **3** and the corresponding byproduct **3'** as a pale yellow oil (**3**/**3'**= 19/1, 3.80 g, yield of **3** is 51%). Because **3** and **3'** were impossible to separate by column chromatography, the mixture of **3** and **3'** was utilized directly in the synthesis of **4**. $^1$H NMR (300 MHz, $CDCl_3$) δ 6.29(s, 1H, C=C*H*H), 6.22 (s, 1H, C=C*H*H), 5.69, (s, 1H, C=CH*H*), 5.66 (s, 1H, C=CH*H*), 4.25-4.14 (m, 8H, -OC$H_2$C$H_3$), 3.34 (dt, $^2J_{PH}$ = 22.8 Hz, $^3J_{HH}$ = 7.50 Hz, 1H,

C*H*P(O)(OEt)$_2$), 2.90 (t, $J$ = 8.30 Hz, 2H, $H_2C$=CC$H_2$), 1.38-1.24 (m, 12H, -OCH$_2$C$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 168. 6, 166.2, 137.1 (d, $^3J_{PC}$ = 15.9 Hz, 1C), 127.5, 63.0 (d, $^2J_{PC}$ = 6.00 Hz, 1C), 62.8 (d, $^2J_{PC}$ = 5.70 Hz, 1C), 61.5, 61.0, 44.5 (d, $^1J_{PC}$ = 129.5 Hz, 1C), 29.9, 16.5, 16.4, 14.3 (2C); $^{31}$P NMR (121 MHz, $CDCl_3$), δ 22.71; HRMS calcd. for $C_{14}H_{26}O_7P^+$ 337.1416, Found 337.1411.

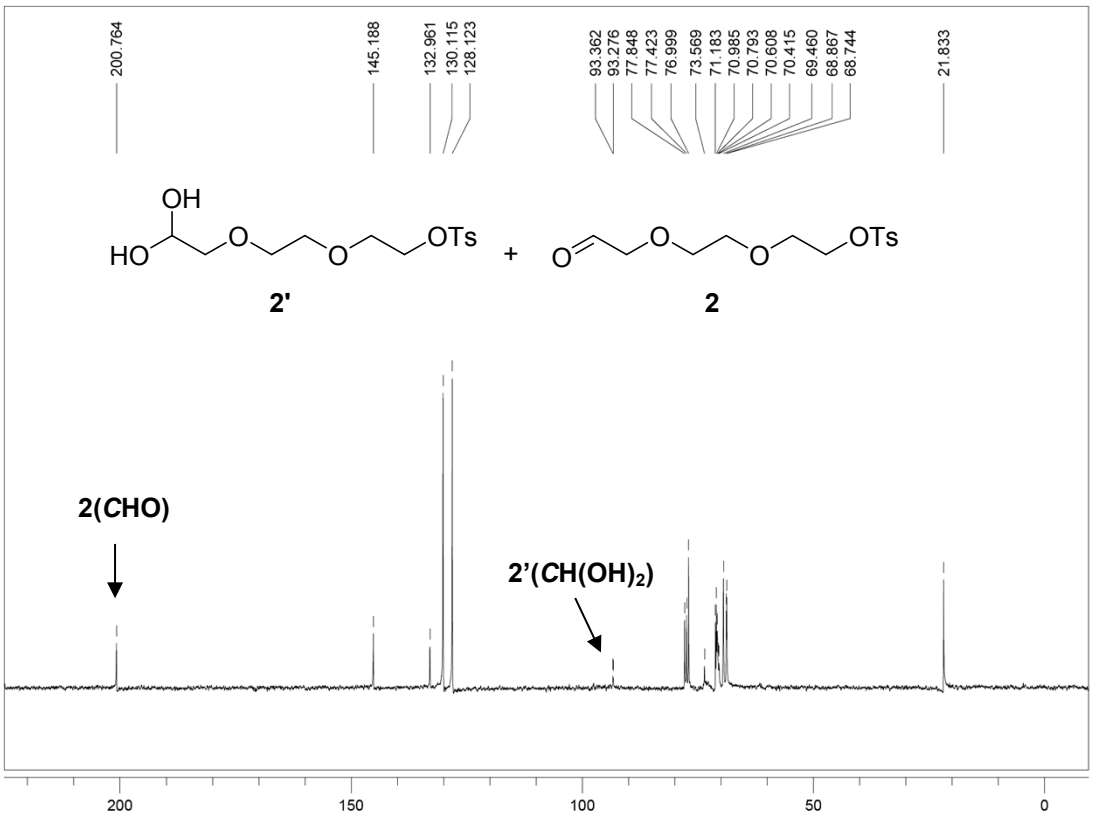
**6:** To a mixture of Merrifield resin (200 mg, 0.620 mmol) in 10.0 mL DMF were added propargylamine (176 mg, 3.10 mmol) and $K_2CO_3$ (956 mg, 6.92 mmol). The reaction mixture was stirred at 60 $^o$C under microwave irradiation for 2 h, then allowed to cool down to room temperature and filtered to get the crude resin. The obtained resin was washed successively with DMF, water, MeOH, $CH_2Cl_2$ and diethyl ether (30.0 mL for each) then dried in vacuum, yielding 200 mg resin **6** as a yellow powder. IR (cm$^{-1}$) υ 3289 (≡C-H); $^{13}$C CPMAS NMR δ 81.5 (-*C*≡C-), 72.4 (-C≡*C*-).

## $^{1}$H, $^{13}$C and $^{31}$P NMR spectra

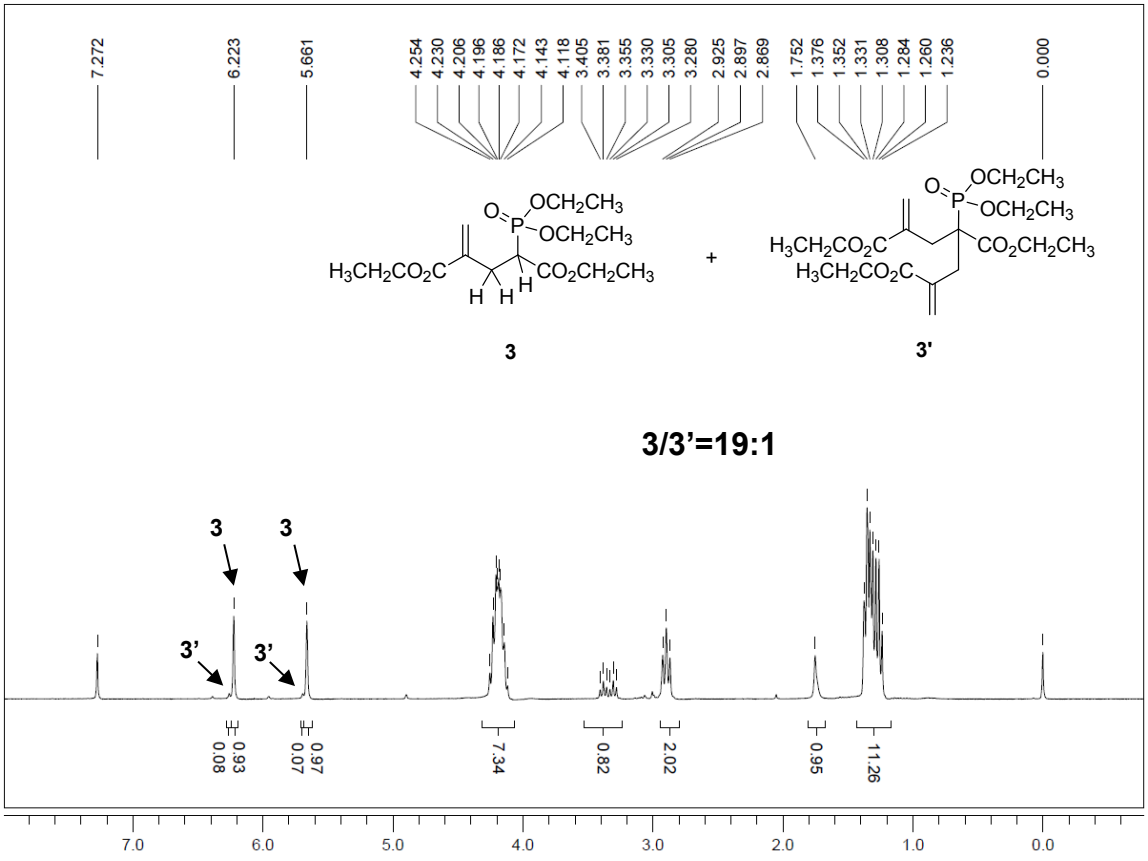
$^{1}$H NMR spectrum of **2**



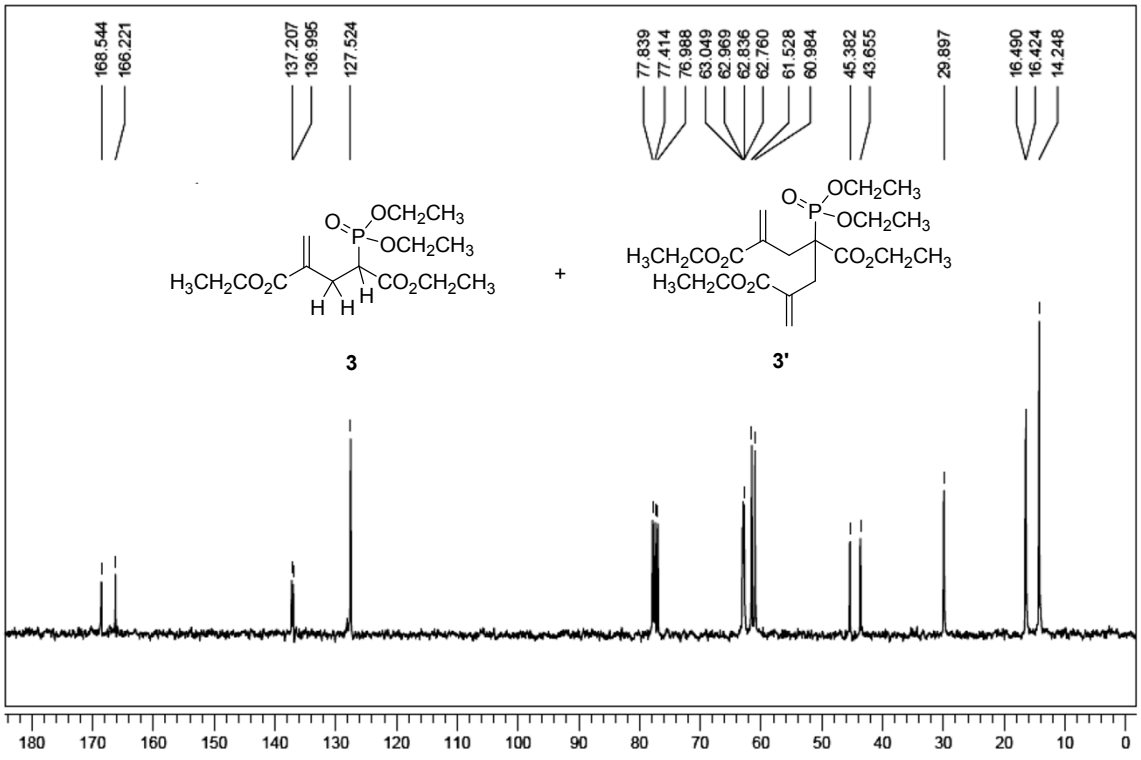

$^{13}$C NMR spectrum of **2**



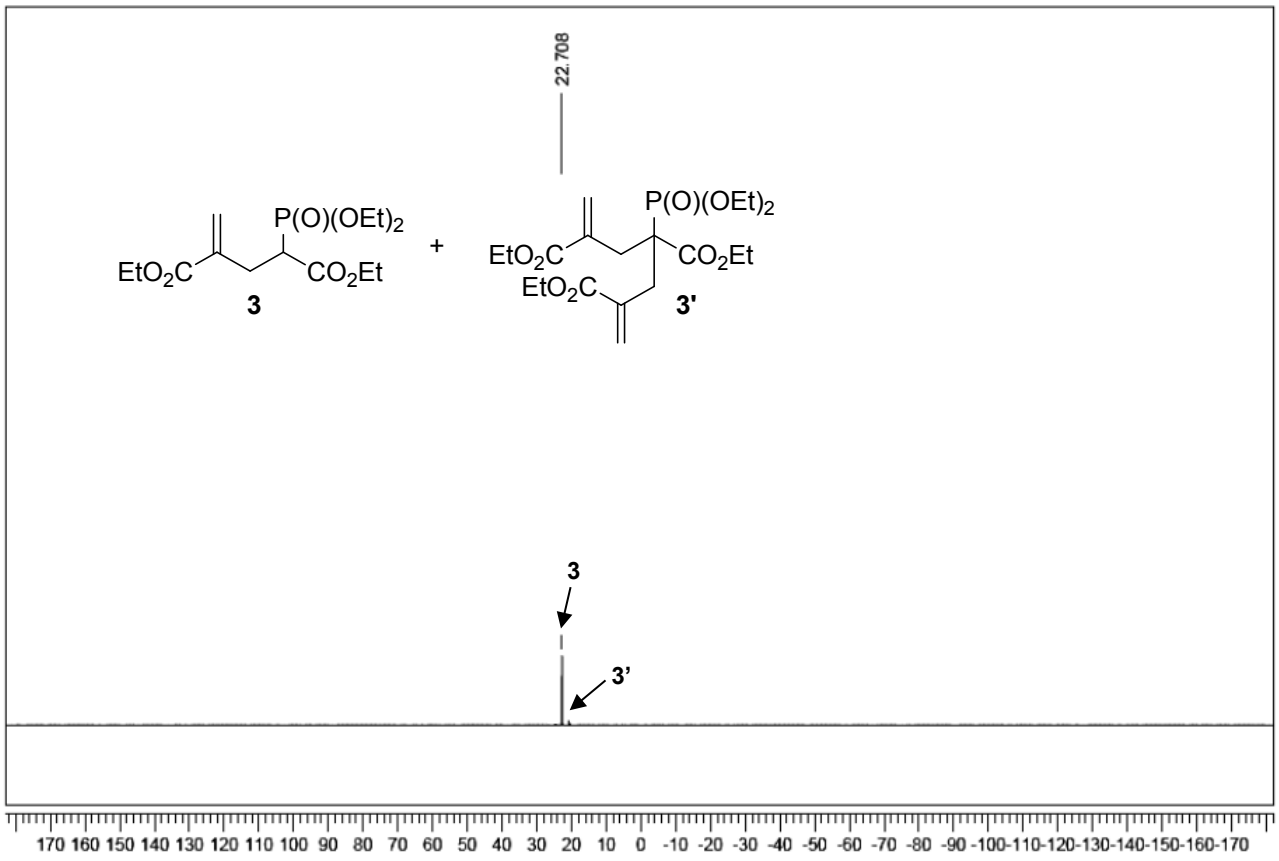
$^{1}$H NMR spectrum of **3**



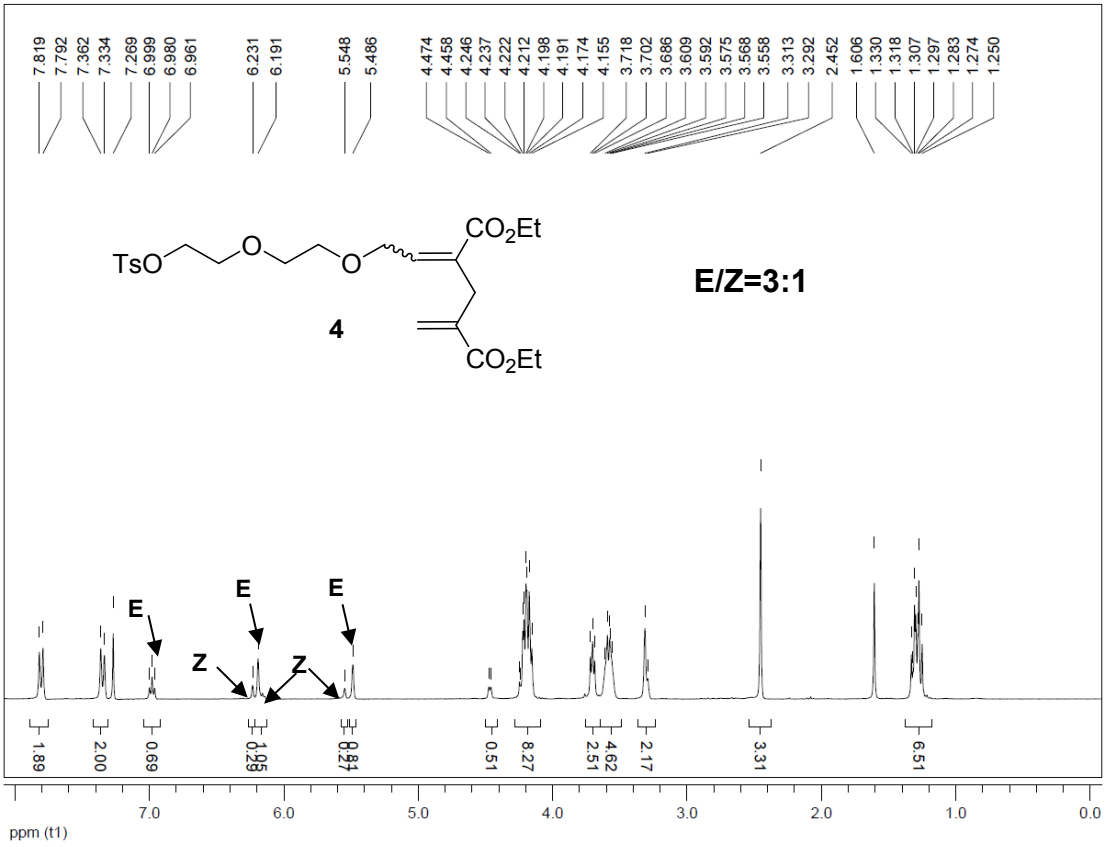

$^{13}$C NMR spectrum of **3**



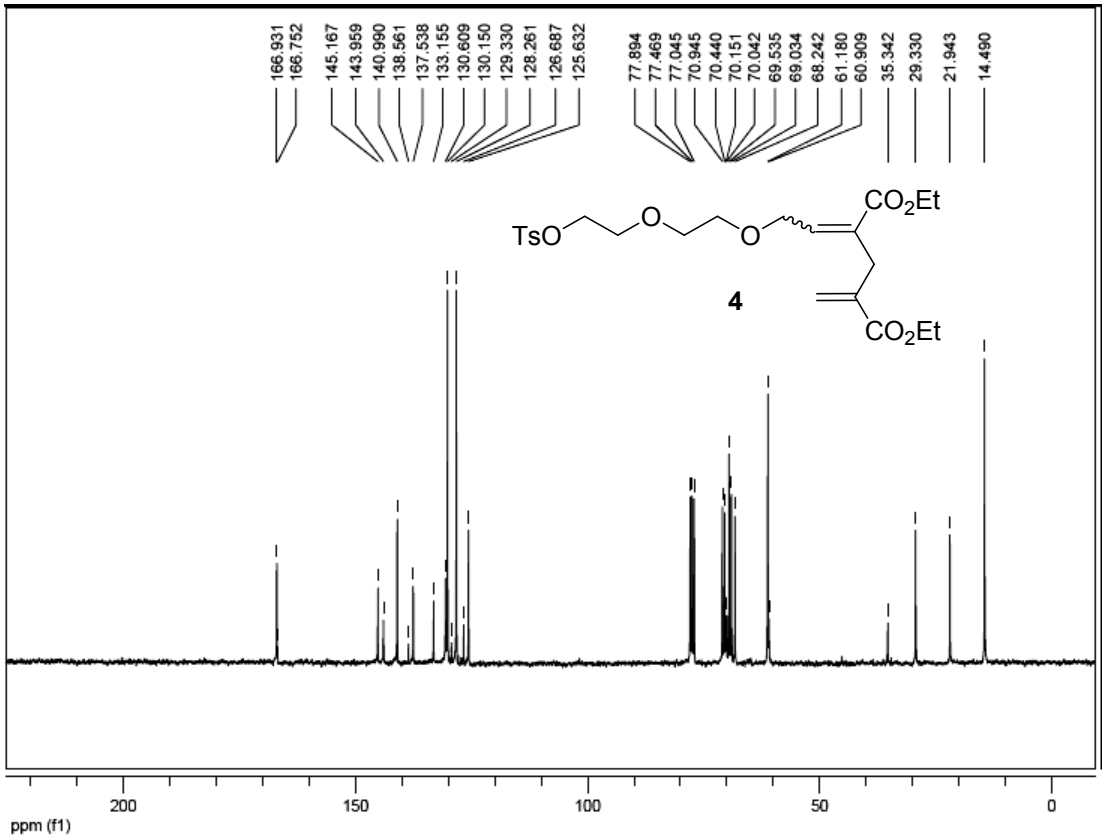
$^{31}$P NMR spectrum of **3**



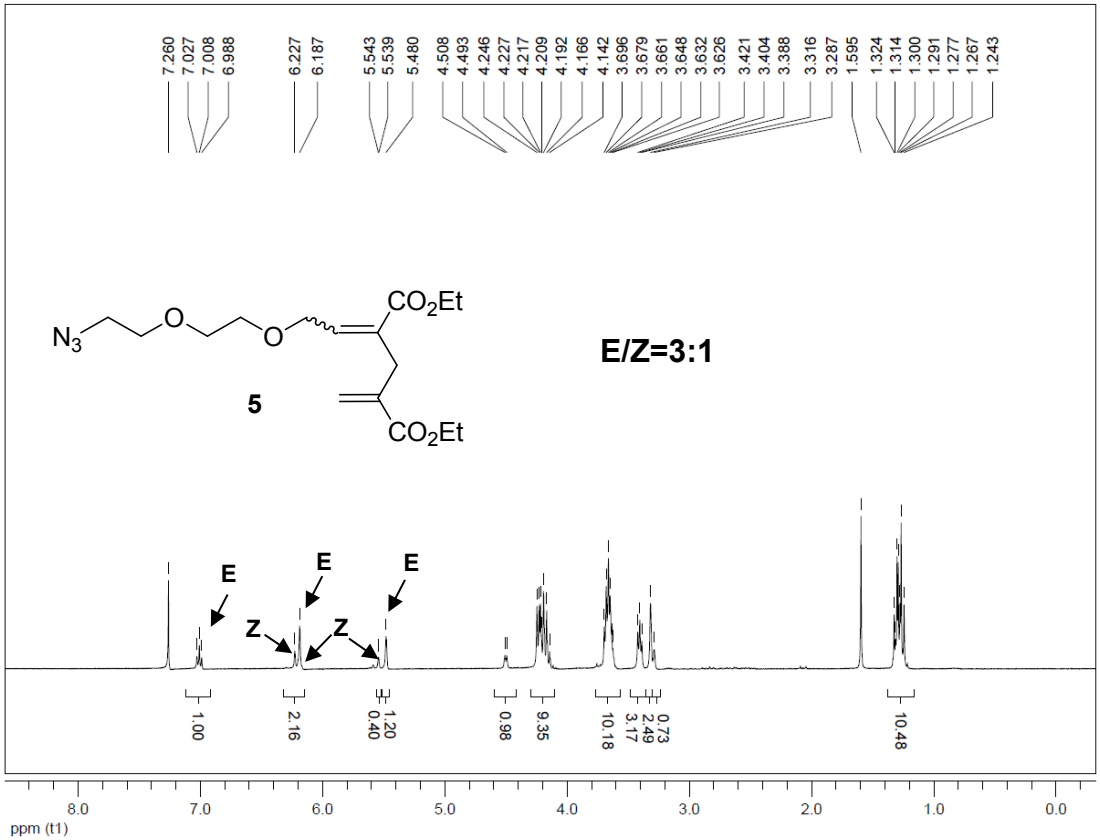
$^{1}$H NMR spectrum of **4** as a mixture of E/Z isomers



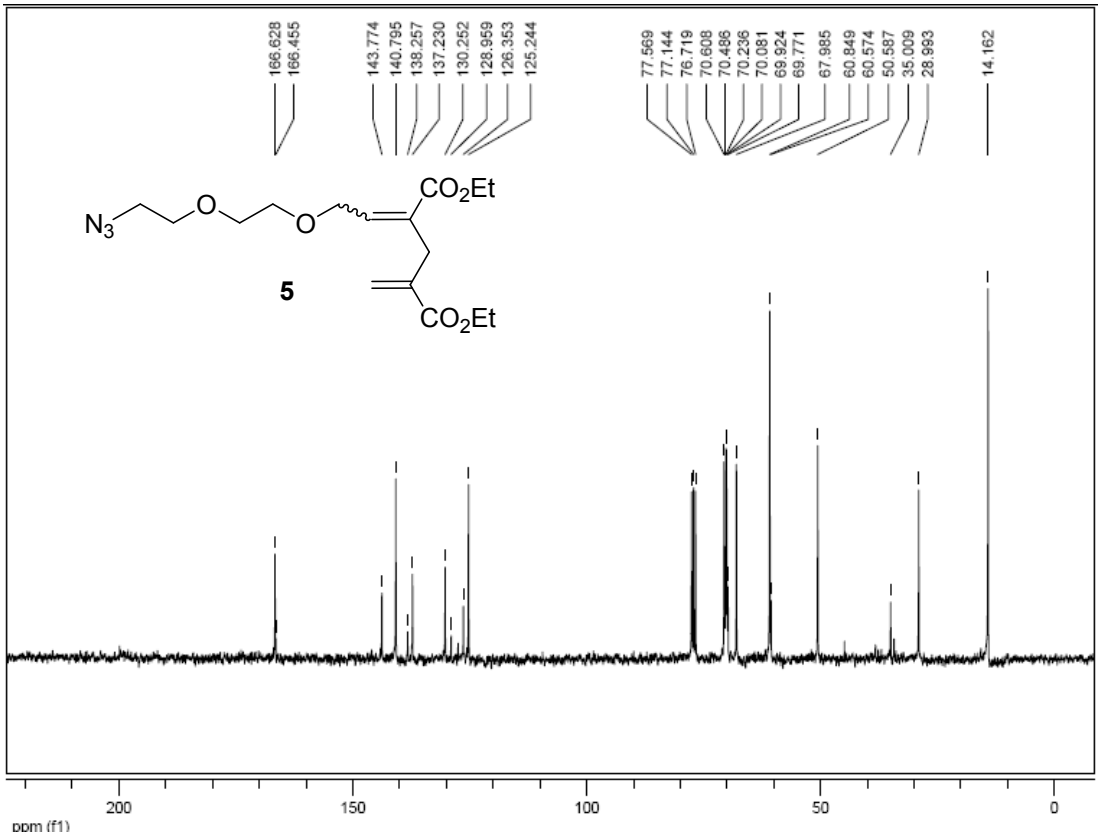

$^{13}$C NMR spectrum of **4** as a mixture of E/Z isomers



$^{1}$H NMR spectrum of **5** as a mixture of E/Z isomers

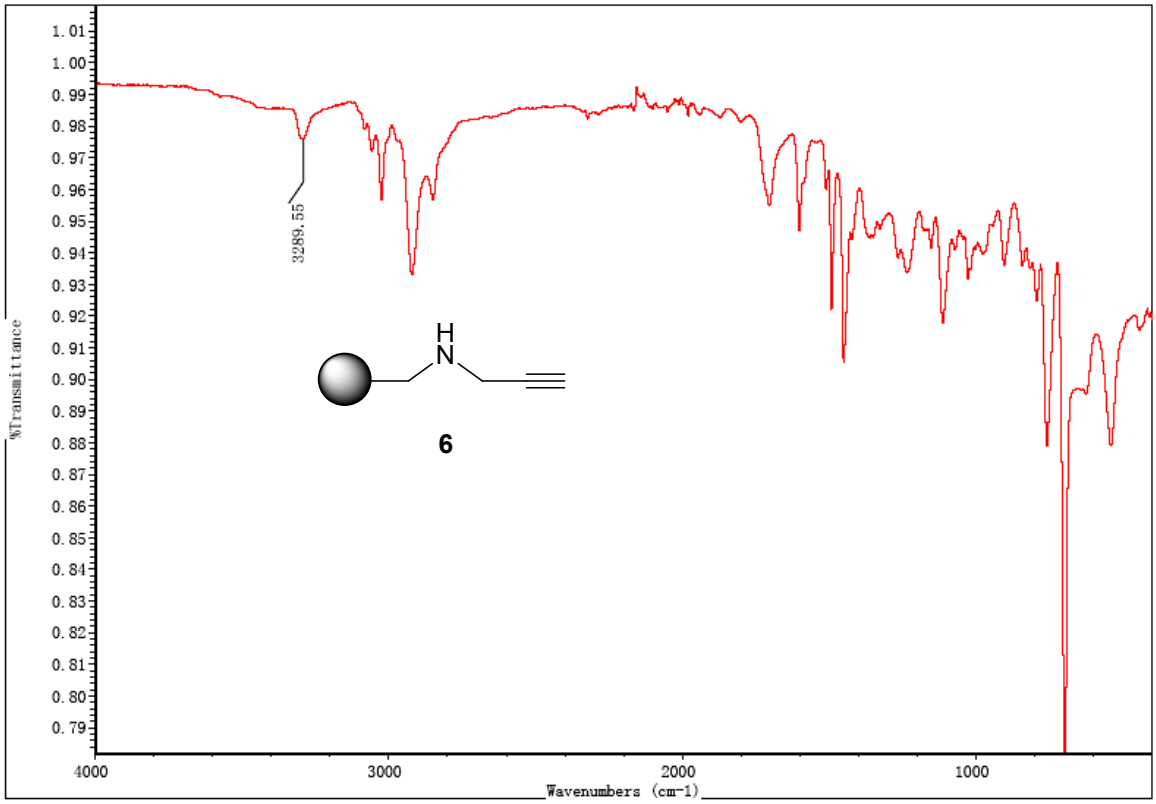



$^{13}$C NMR spectrum of **5** as a mixture of E/Z isomers

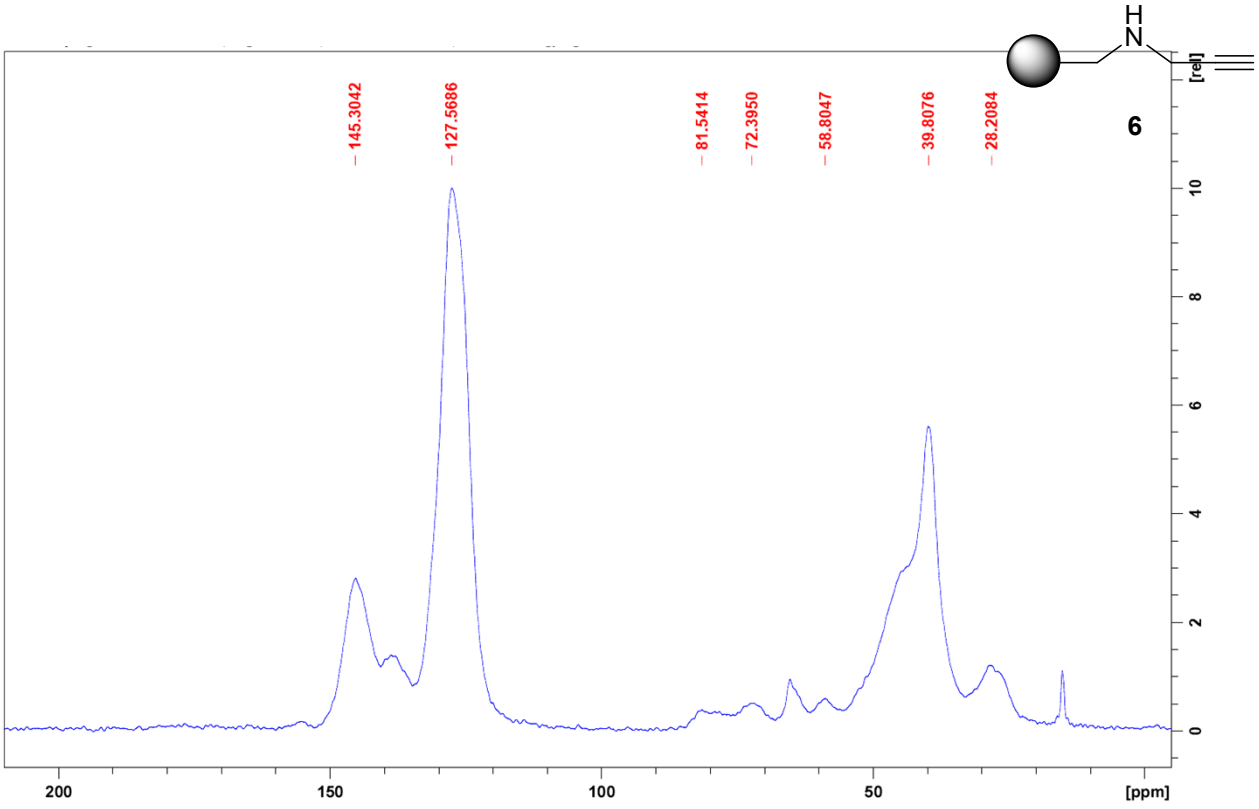


## IR and $^{13}$C CPMAS NMR spectra

IR spectrum of **6**




$^{13}$C CPMAS NMR spectrum of **6**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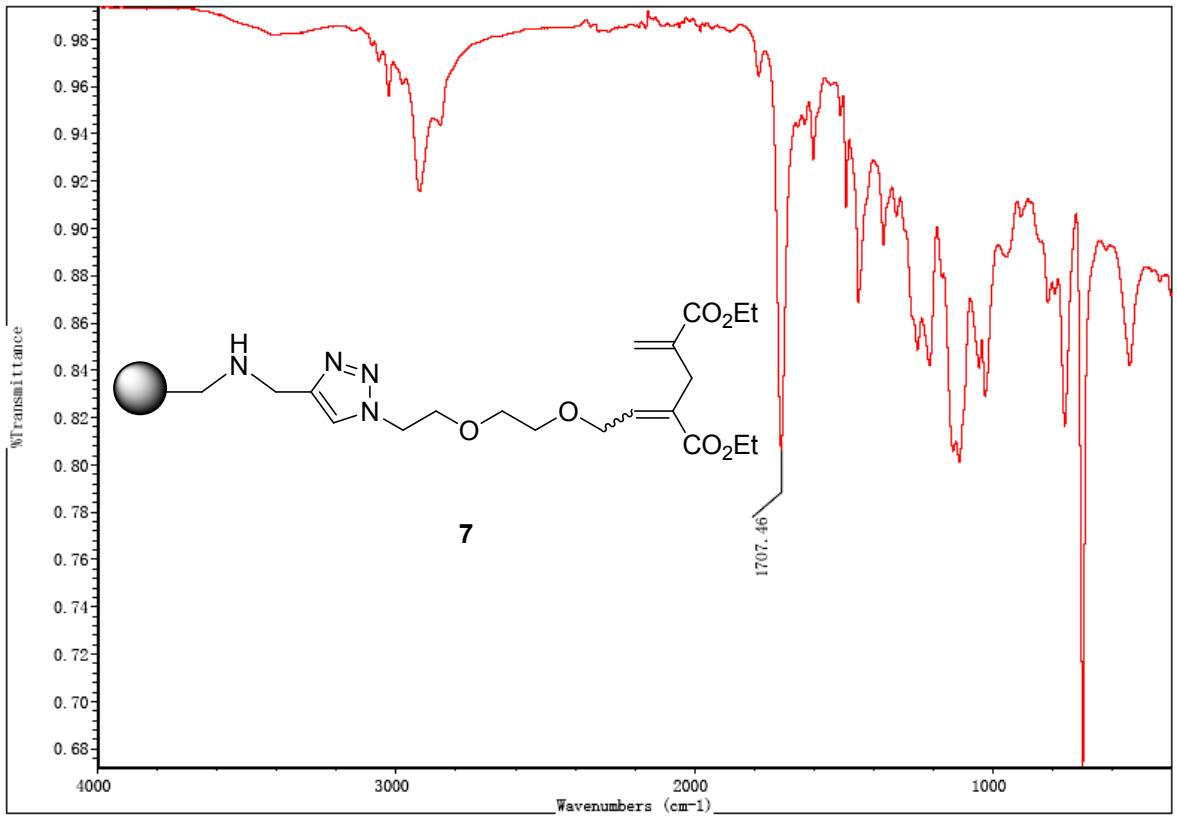
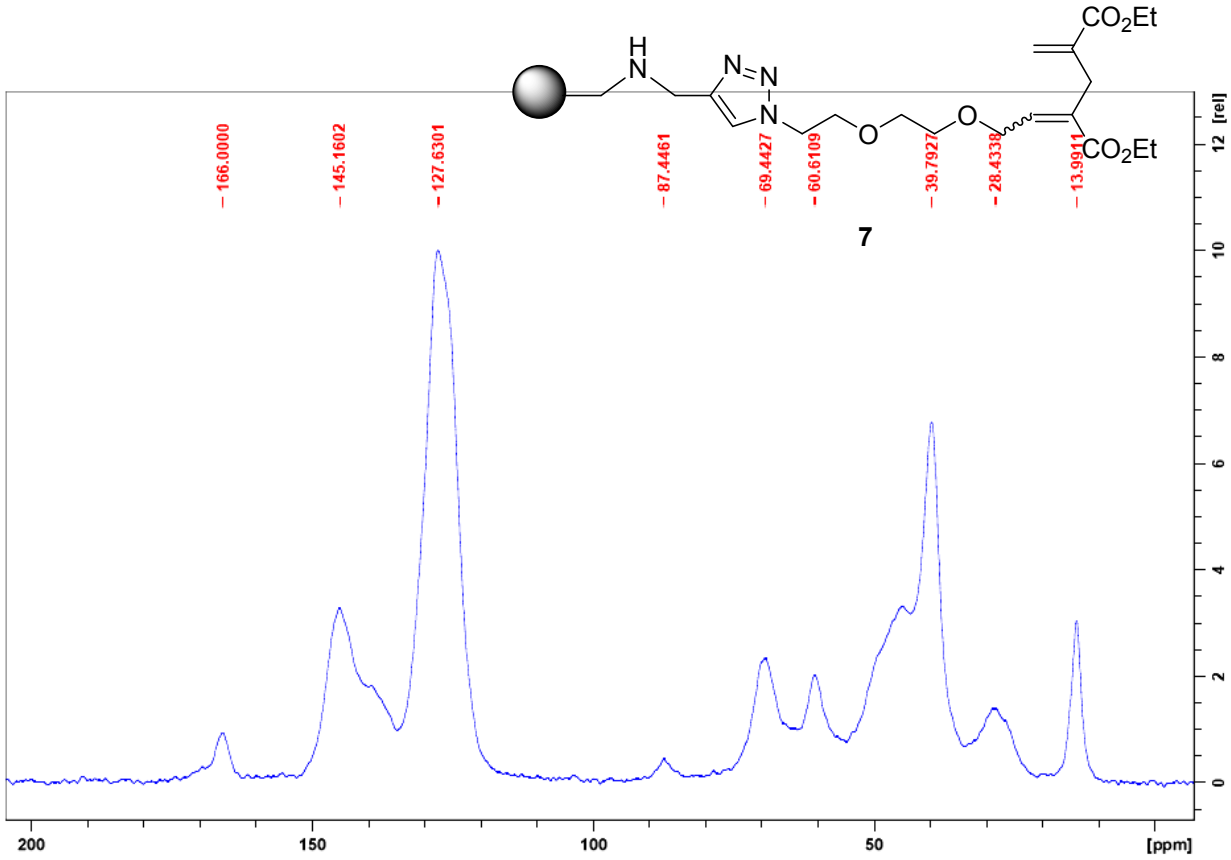
IR spectrum of **7**




$^{13}$C CPMAS NMR spectrum of **7**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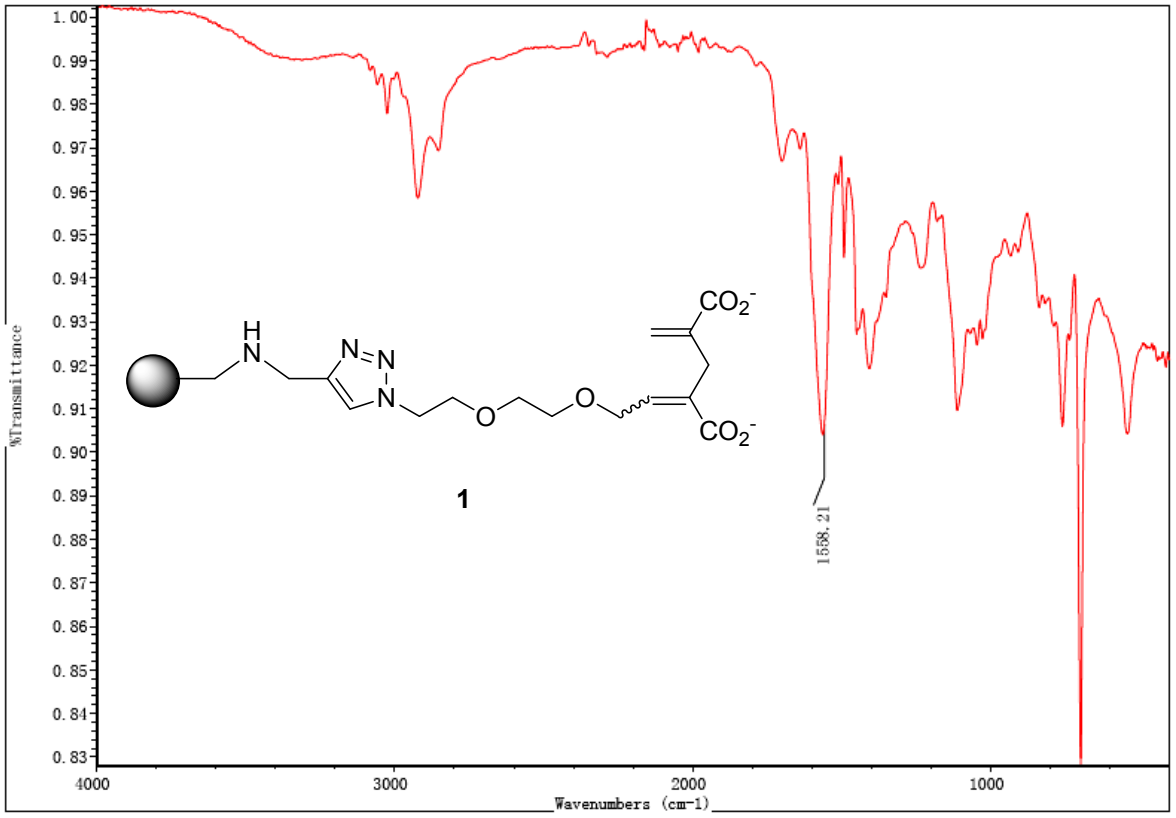
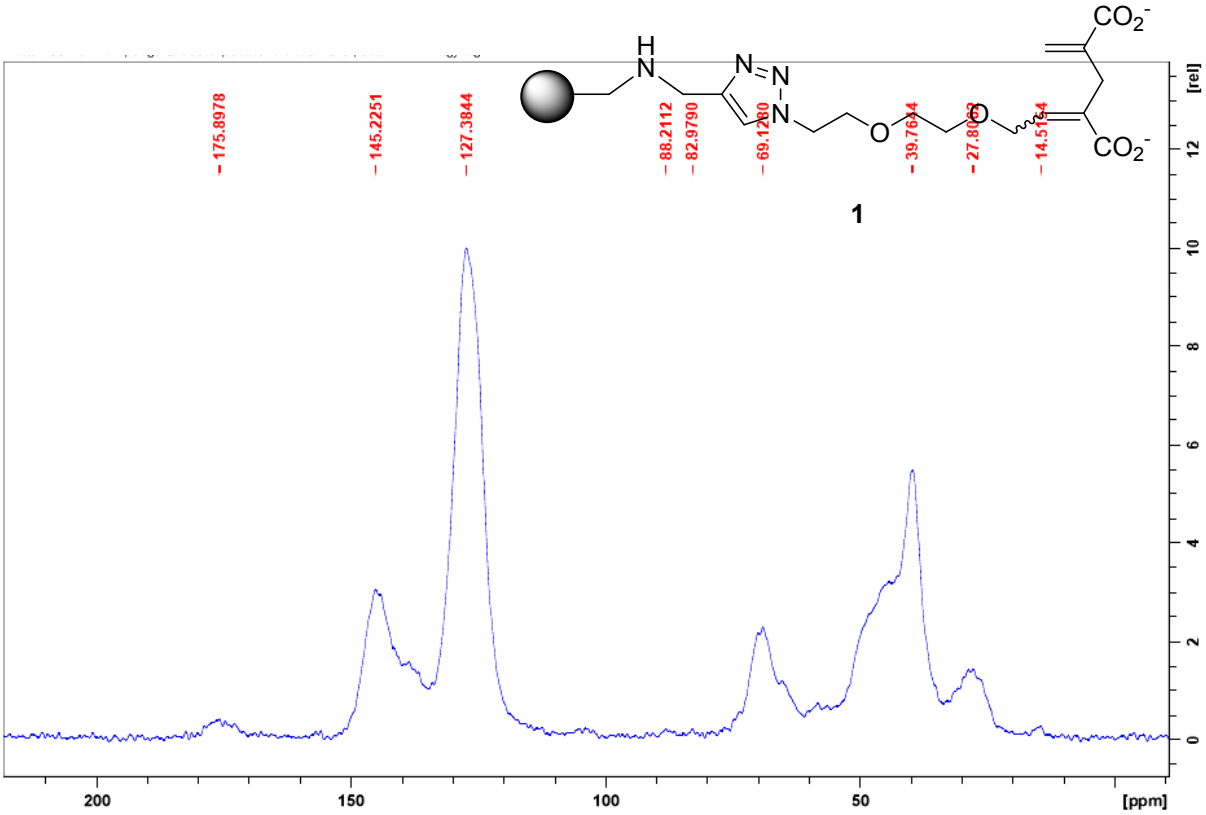
IR spectrum of **1**




$^{13}$C CPMAS NMR spectrum of **1**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