

Supporting Information For: Catalytic Dimerization of Crotonates

James C. A. Flanagan[†], Eun Joo Kang^{†§}, Nathaniel I. Strong[‡] and Robert M. Waymouth^{†*}

[†]Department of Chemistry, Stanford University, Stanford, CA 94305, United States. [‡]Department of Civil and Environmental Engineering, Stanford University, Stanford, CA 94305, United States. [§] Department of Applied Chemistry, Kyung Hee University, Yongin, 449-701, Korea.

*Email: waymouth@stanford.edu

Contents

1. General Considerations	S1
2. Materials	S2
3. 2-Alkenoate Dimerization Studies: Screening of Catalysts and Solvents	S3
4. Synthetic Procedures	S4
5. Reactions of Crotonates with other Organic Catalysts	S18
5a. Reactions of catalytic quantities of DBU and TBD with isopropyl crotonate	S18
5b. Reactions of stoichiometric quantity of TBD with isopropyl crotonate	S19
5c. Reaction of catalytic quantity of TPT with methyl crotonate	S22
5d. Reaction of stoichiometric quantity of TPT with methyl crotonate	S23
5e. Reaction of stoichiometric quantity of IMes with methyl crotonate	S24
5f. Reaction of $I^iPr_2Me_2$ with methyl methacrylate	S28
5g. Reaction of TPT with methyl methacrylate	S32
6. Mechanistic Studies by Mass Spectrometry	S33
6a. ESI Tandem MS-MS of 1 M isopropyl crotonate + 5 mol% $I^iPr_2Me_2$ in THF	S33
6b. ESI-MS: 1 M methyl crotonate + 5 mol% $I^iPr_2Me_2$ in THF (CH_3COOH quench)	S36
6c. ESI-MS: 1 M methyl crotonate + 5 mol% $I^iPr_2Me_2$ in THF (CH_3COOD quench)	S38
6d. ESI-MS: 1 M diisopropyl 2-ethylidene-3-methylpentanedioate + 1 M $I^iPr_2Me_2$ in THF, quenched with CH_3COOH	S40
6e. ESI-MS: 1 M diisopropyl 2-ethylidene-3-methylpentanedioate + 1 M $I^iPr_2Me_2$ in THF, quenched with CH_3COOD	S43
6f. ESI-MS: to assess potential contribution from H/D exchange on peak intensities in mass spec mechanistic experiments	S45
7. Attempted NHC-catalyzed Group Transfer Polymerization of isopropyl crotonate	S48
8. Polymerization Screening: Step-Growth By Transesterification	S49
9. NMR Spectra of Synthesized Compounds	S51
10. FTIR Spectra of Synthesized Compounds	S68
11. Mass Spectra for H/D Experiments Described in Section 6f	S75
12. References	S89

1. General Considerations

All reactions and polymerizations were performed in a nitrogen-filled glovebox or using standard Schlenk techniques under nitrogen unless otherwise specified. All glassware was oven-dried

and/or flame dried under vacuum prior to use. Nuclear magnetic resonance (NMR) spectra were recorded at room temperature on a 400 MHz, 500 MHz or 600 MHz spectrometer, with shifts reported in parts per million downfield from tetramethylsilane and referenced to the residual solvent peak. Gel permeation chromatography (GPC) was performed in tetrahydrofuran (THF) at a flow rate of 1.0 mL/min on a Waters chromatograph equipped with four 5 μ m Waters columns (300 mm x 7.7 mm) connected in series. Polymer solutions for GPC (ca. 5 mg/mL) were prepared by dissolving the polymer in THF. High-resolution mass spectra were obtained using a desorption electrospray ionization (DESI) nanoelectrospray ionization methods on a LTQ-Orbitrap XL Hybrid mass spectrometer in positive mode, using 10 microliters of a sample of concentration 0.01 M in methanol, with 10 microliters of an internal standard prepared from 1.63 mg caffeine and 1.85 mg gram of rhodamine-123 dissolved in 10 mL of methanol. High-resolution tandem mass spectrometry (MS-MS) spectra were also recorded on a hybrid LTQ-Orbitrap-XL in positive mode. (Infuse rate: 10 μ L/min, Spray (source) voltage: 3.4 kV, Nebulizing (sheath) gas: 120 psi N₂, Resolution: 30,000 at m/z 400). Nano-electrospray ionization (nano-ESI) mass spectra were recorded on a hybrid LTQ-Orbitrap-XL in positive mode. Electrospray ionization mass spectrometry (ESI-MS) was also performed at the Vincent Coates Foundation Mass Spectrometry Laboratory, Stanford University Mass Spectrometry using a Waters 2795 HPLC system with dual wavelength UV detector, and ZQ single quadrupole MS with electrospray ionization source. FTIR spectra were recorded on a Thermo Scientific Nicolet 6700 FTIR spectrometer using an attenuated total reflectance (ATR) method. CHN elemental analysis was performed by Robertson Microlit Laboratories, New Jersey, USA.

2. Materials

Methyl crotonate and methyl 2-nonenolate were purchased from Sigma-Aldrich and distilled from calcium hydride. Isopropyl crotonate and *tert*-butyl crotonate were purchased from TCI America and distilled from calcium hydride. Methyl methacrylate (Sigma-Aldrich) was twice washed with 5 wt% NaOH (aq), twice washed with deionized H₂O, and then dried with calcium hydride and vacuum distilled. Diisopropyl adipate (TCI America) and dimethyl adipate (Sigma-Aldrich) were dried with calcium hydride and vacuum distilled prior to use. Ethylene glycol (Sigma-Aldrich) was dried using 4A molecular sieves. 1,4-butanediol (Sigma-Aldrich) was dried with magnesium sulfate followed by filtration and distillation. 4-Nitrophenol (Sigma-Aldrich) was purified by recrystallization from toluene followed by sublimation. Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone and degassed three times via freeze-pump-thaw cycles. Anhydrous dimethylformamide (DMF) (Sigma-Aldrich), in a sure-seal bottle was used as received. 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (I^tPr₂Me₂) was prepared according to the literature procedure.¹ 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) (Sigma-Aldrich) was purified by sublimation. 1,3,4-triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene was prepared by heating the commercially available 5-methoxy-1,3,4-triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene at 80°C under high vacuum overnight.² 1,8-Diazabicyclo[5.4.0]undec-7-ene, (DBU), potassium *tert*-butoxide (KO^tBu), 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes), hydrochloric acid (ACS reagent grade, 37%), and CH₃COOD (98%D) were used as received from Sigma Aldrich. All other solvents were purchased from Fisher Scientific and used as received.

3. 2-Alkenoate Dimerization Studies: Screening of Catalysts and Solvents

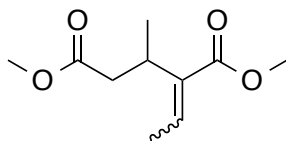
Table S1. Catalytic Dimerization of Crotonates and Alkenoates^a

Entry	R	R'	catalyst	cat. mol %	Time (h) ^b	Solvent	% Conversion ^c	Isolated Yield ^d %	E : Z : X ^e
1	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	5	2	d ⁸ -THF	99		80 : 20 : 0
2	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	1	24	THF		87	82 : 18 : 0
3	Me	Me	ⁱ Pr ₂ Me ₂	5	2 min	d ⁸ -THF	25		78 : 22 : 0
4	Me	Me	ⁱ Pr ₂ Me ₂	5	27 min	d ⁸ -THF	89		80 : 20 : 0
5	Me	Me	ⁱ Pr ₂ Me ₂	1	24	THF		90	83 : 17 : 0
6	^t Bu	Me	ⁱ Pr ₂ Me ₂	5	24	THF		72	68 : 32 : 0
7	ⁱ Pr	Me	DBU	10	24	THF	0		
8	ⁱ Pr	Me	TBD	10	24	THF	6 ^f		
9 ^g	Me	Me	TPT	10	18	d ⁸ -Toluene	10 ^f		
10	Me	Me	IMes	100	1	d ⁸ -THF	>99 ^f		
11	Me	Me	KO ^t Bu	5	15 s	THF		89	80 : 20 : 0
12	ⁱ Pr	Me	KO ^t Bu	5	15 s	THF	>99		78 : 22 : 0
13	^t Bu	Me	KO ^t Bu	5	15 s	THF	>99		83 : 27 : 0
14	Me	Hx	KO ^t Bu	5	30 min	THF	99		56 : 11 : 32 ^h
15	Me	Hx	KO ^t Bu	5	18	THF		94	69 : 13 : 18 ^h
16	Me	Hx	ⁱ Pr ₂ Me ₂	2	2	THF	98		31 : 23 : 46 ^h
17	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	10	24	Toluene	>99		73 : 27 : 0
18	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	10	24	DMF	>99		23 : 6 : 71 ⁱ
19	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	10	24	None	>99		51 : 20 : 29 ⁱ
20	ⁱ Pr	Me	ⁱ Pr ₂ Me ₂	1	24	None	>99		76 : 24 : 0
21	Me	Me	ⁱ Pr ₂ Me ₂	1	26	THF	99		80 : 20 : 0
22	^t Bu	Me	ⁱ Pr ₂ Me ₂	5	24	THF	>99		68 : 32 : 0

^aReactions were carried out at room temperature in a nitrogen atmosphere, with [alkenoate]₀ = 1 M. ^bTime in hours unless stated otherwise. ^cConversions of alkenoate monomer measured by ¹H-NMR integration. ^dIsolated yield of the E:Z:X mixture. X = double bond isomers (entries 14-15) or oligomeric products (entries 17-18) ^eRatios of E:Z:X isomers measured by ¹H-NMR integration. ^fStoichiometric products, see Section 5 of this Supporting Information. ^g80 °C. ^hX = Double-bond isomers: see synthesis of dimethyl (E)-2-heptylidene-3-hexylpentandioate from Section 4 of this Supporting Information. ⁱX = oligomeric products.

4. Synthetic Procedures

Dimethyl 2-ethylidene-3-methylpentanedioate



The reaction was performed in a 20 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (72.0 mg, 0.399 mmol) in THF (20 mL) was added methyl crotonate (4.00 g, 40.0 mmol) in one portion. The resulting solution was stirred at room temperature for 24 hours. The reaction was then quenched by adding approximately 100 mg of 4-nitrophenol. The reaction mixture was removed from the glovebox and the solvent evaporated *in vacuo*. Flash column chromatography (10% ethyl acetate: 90% hexanes by volume, R_f = 0.3 [E and Z appearing as one overlapping spot]) afforded 3.60 g (90% yield) of a colorless oil, dimethyl 2-ethylidene-3-methylpentanedioate in an 83:17 *E*:*Z* isomeric ratio).

$^1\text{H-NMR}$ (CDCl_3 , 500 MHz) of *E*-*Z* isomer mixture: *E* isomer: δ 6.74 (q, 1H, J = 7.2 Hz, =C-H), 3.63 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 3.19-3.24 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.65 (dd, 1H, J = 15.5, 8.0 Hz, diastereotopic CH_2), 2.51 (dd, 1H, J = 15.5, 7.1 Hz, diastereotopic CH_2), 1.77 (dd, 3H, J = 7.2, 0.8 Hz, =C- CH_3), 1.11 (d, 3H, J = 7.0, $\text{CH}(\text{CH}_3)$). *Z* isomer: δ 5.90 (qd, 1H, J = 7.2, 0.8 Hz, =C-H), 3.68 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3), 2.92-2.99 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.48 (dd, 1H, J = (obscured by adjacent peak), 6.5 Hz, diastereotopic CH_2), 2.26 (dd, 1H, J = 15.3, 8.2 Hz, diastereotopic CH_2), 1.83 (dd, 3H, J = 7.1, 0.6 Hz, =C CH_3), 1.03 (d, 3H, J = 6.9 Hz, $\text{CH}(\text{CH}_3)\text{CH}_2$).

$^{13}\text{C-NMR}$ (CDCl_3 , 125 MHz) of *E*-*Z* isomer mixture: *E* isomer: δ 173.3, 168.3, 138.2, 135.4, 51.3, 51.2, 39.2, 29.0, 18.9, 13.9. *Z* isomer: δ 172.8, 167.3, 136.5, 134.1, 51.4, 51.2, 40.7, 34.4, 19.7, 15.6.

IR (neat): $\tilde{\nu}$, cm^{-1} : 2953, 2359, 1735, 1709, 1639, 1435, 1374, 1355, 1329, 1289, 1247, 1192, 1169, 1144, 1076, 1019, 939, 892, 841, 807, 797, 760, 654, 597.

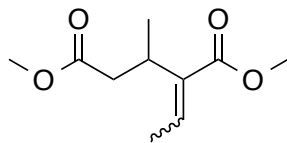
HRMS (DESI) calculated for $\text{C}_{10}\text{H}_{17}\text{O}_4^+$ $[\text{MH}]^+$ requires 201.1121; found 201.1121.

HRMS (DESI) calculated for $\text{C}_{10}\text{H}_{16}\text{O}_4\text{Na}^+$ $[\text{MNa}]^+$ requires 223.0941; found 223.0941.

$^1\text{H-NMR}$ spectrum is in good agreement with literature spectra.³⁻⁵

Dimethyl 2-ethylidene-3-methylpentanedioate

– alternative procedure using potassium *tert*-butoxide as catalyst



The reaction was performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of potassium *tert*-butoxide (14.0 mg, 0.1249 mmol) in THF (1 mL) was added methyl crotonate (250 mg, 2.497 mmol) in one portion. The resulting yellow solution was stirred at room temperature for 15 seconds. The reaction was then quenched by adding approximately 20 mg of hydrochloric acid (37%). The THF was removed *in vacuo*, before the crude product was placed in a separating funnel and 15 mL diethyl ether added. The mixture was then washed twice with water, and the ethereal layer dried with anhydrous MgSO₄, filtered and evaporated. Flash column chromatography (10% ethyl acetate: 90% hexanes by volume, R_f = 0.3 [E and Z appearing as one overlapping spot]) afforded 222 mg (89% yield) of a colorless oil, dimethyl 2-ethylidene-3-methylpentanedioate in an 80:20 *E*:*Z* isomeric ratio).

¹H-NMR spectrum (shown in Figure S1) matches that of the I^{*i*}Pr₂Me₂-catalyzed methyl crotonate dimerization and is also in good agreement with literature spectra.³⁻⁵

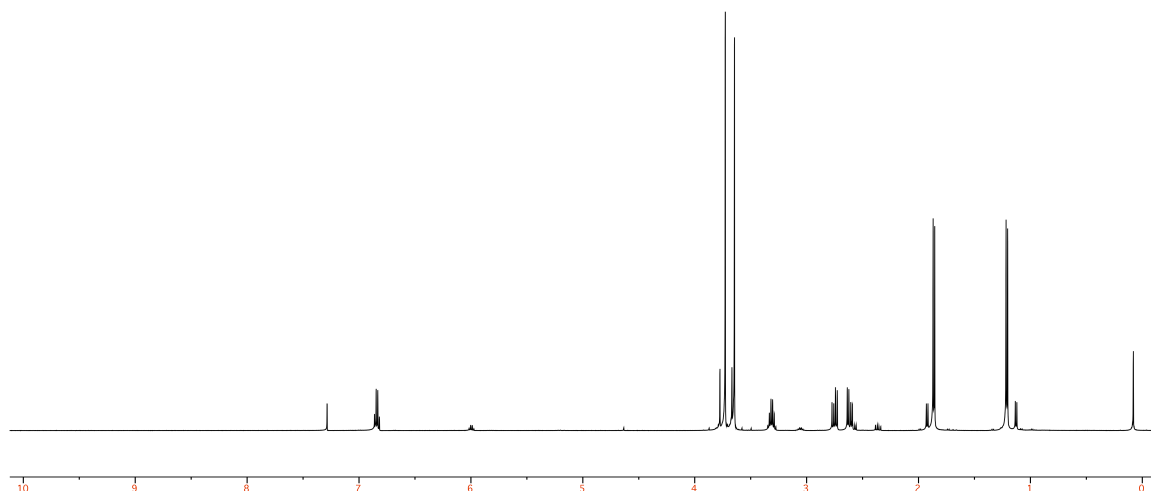
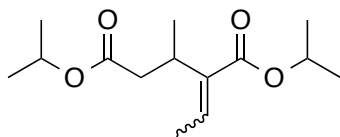


Figure S1. ¹H-NMR spectrum of dimethyl 2-ethylidene-3-methylpentanedioate prepared with KO^{*t*}Bu catalyst.

Diisopropyl 2-ethylidene-3-methylpentanedioate



The reaction was performed in a 20 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (28.1 mg, 0.156 mmol) in THF (13.4 mL) was added isopropyl crotonate (2.00 g, 15.6 mmol) in one portion. The resulting solution was stirred at room temperature for 24 hours. The reaction was then quenched by adding approximately 100 mg of 4-nitrophenol. The reaction mixture was removed from the glovebox and the solvent evaporated *in vacuo*. Flash column chromatography (5% ethyl acetate: 95% hexanes by volume) afforded a colorless oil, 1.75g (87% yield) of diisopropyl 2-ethylidene-3-methylpentanedioate in a 4:1 *E:Z* isomeric ratio). $R_f = 0.46$ in eluent of 10% ethyl acetate in hexanes [E and Z appearing as one overlapping spot]

$^1\text{H-NMR}$ (CDCl_3 , 500 MHz) of *E-Z* isomer mixture: *E* isomer: δ 6.74 (q, 1H, $J = 7.2$ Hz, $=\text{C-H}$), 4.86-5.10 (m, overlapping (*E*) (2H) and (*Z*) (2H) $\text{OCH}(\text{CH}_3)_2$), 3.19-3.28 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.65 (dd, 1H, $J = 14.9, 8.2$ Hz, diastereotopic CH_2), 2.48 (dd, 1H, $J = 14.8, 7.2$ Hz, diastereotopic CH_2), 1.78 (d, 3H, $J = 7.2$ Hz, $=\text{C-CH}_3$), 1.06-1.26 (m, overlapping (*E*) (12H) and (*Z*) (12H) $\text{OCH}(\text{CH}_3)_2$, and (*E*) (3H) and (*Z*) (3H) $\text{CH}(\text{CH}_3)\text{CH}_2$). *Z* isomer: δ 5.86 (qd, 1H, $J = 7.1, 0.9$ Hz, $=\text{C-H}$), 4.86-5.10 (m, overlapping (*E*) (2H) and (*Z*) (2H) $\text{OCH}(\text{CH}_3)_2$), 2.92-3.00 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.48 (dd, 1H, $J = 14.8, 6.8$ Hz, diastereotopic CH_2), 2.25 (dd, 1H, $J = 14.9, 8.2$ Hz, diastereotopic CH_2), 1.84 (dd, 3H, $J = 7.1, 0.6$ Hz, $=\text{C-CH}_3$), 1.06-1.26 (m, overlapping (*E*) (12H) and (*Z*) (12H) $\text{OCH}(\text{CH}_3)_2$, and (*E*) (3H) and (*Z*) (3H) $\text{CH}(\text{CH}_3)\text{CH}_2$).

$^{13}\text{C-NMR}$ (CDCl_3 , 125 MHz) of *E-Z* isomer mixture: *E* isomer: δ 172.8, 167.8, 137.6, 136.3, 67.6, 67.6, 40.1, 29.5, 22.1, 22.0, 19.4, 14.2. *Z* isomer: δ 172.2, 166.8, 137.3, 133.0, 67.9, 67.7, 41.4, 35.2, 22.2, 22.0, 19.9, 15.7.

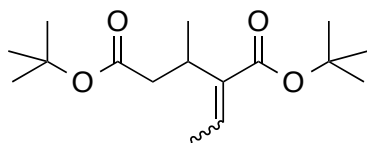
IR (neat): $\tilde{\nu}$, cm^{-1} : 2979, 2936, 2878, 1728, 1705, 1640, 1467, 1455, 1385, 1373, 1337, 1287, 1248, 1178, 1144, 1104, 1074, 994, 965, 930, 916, 899, 839, 820, 802, 760.

HRMS (DESI) calculated for $\text{C}_{14}\text{H}_{25}\text{O}_4^+ [\text{MH}]^+$ requires 257.1747; found 257.1747.

HRMS (DESI) calculated for $\text{C}_{14}\text{H}_{24}\text{O}_4\text{Na}^+ [\text{MNa}]^+$ requires 279.1567; found 279.1567.

CHN Analysis calculated for $\text{C}_{14}\text{H}_{24}\text{O}_4$ requires C 65.60%, H 9.44%, N 0.00%; found C 65.85%, H 9.48%, N < 0.02%.

Di-*tert*-butyl 2-ethylidene-3-methylpentanedioate



The reaction was performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (2.2 mg, 0.0122 mmol) in THF (0.2 mL) was added *tert*-butyl crotonate (34.7 mg, 0.2443 mmol) in one portion. The resulting solution was stirred at room temperature for 24 hours. The reaction was quenched by addition of “wet” CDCl_3 and a crude NMR was taken to determine conversion. The crude mixture was then passed through a plug of silica using a solvent mixture of 10% ethyl acetate: 90% hexanes by volume, before the solvent was removed *in vacuo* to give a colorless oil, di-*tert*-butyl 2-ethylidene-3-methylpentanedioate, isolated yield 25 mg (72%) (68:32 *E*:*Z* isomeric ratio).

^1H -NMR (CDCl_3 , 600 MHz) of *E*-*Z* isomer mixture: *E* isomer: δ 6.68 (q, 1H, $J = 7.2$ Hz, $=\text{C}-\text{H}$), 3.17-3.24 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.58 (dd, 1H, $J = 14.6, 8.2$ Hz, diastereotopic CH_2), 2.44 (dd, 1H $J = 14.6, 7.2$ Hz, diastereotopic CH_2), 1.79 (d, 3H, $J = 7.2$ Hz, $=\text{C}-\text{CH}_3$), 1.48 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.40 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.17 (d, 3H, $J = 7.0$ Hz, $\text{CH}(\text{CH}_3)\text{CH}_2$). *Z* isomer δ 6.80 (qd, 1H, $J = 7.1, 0.9$ Hz, $=\text{C}-\text{H}$), 2.87-2.94 (m, 1H, $-\text{CH}(\text{CH}_3)\text{CH}_2$), 2.45 (dd, 1H, $J = 14.7, 6.6$ Hz, diastereotopic CH_2), 2.21 (dd, 1H, $J = 14.7, 8.3$ Hz, diastereotopic CH_2), 1.85 (dd, 3H, $J = 7.1, 0.6$ Hz), 1.51 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.42 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.10 (d, 3H, $J = 6.9$ Hz, $\text{CH}(\text{CH}_3)\text{CH}_2$).

^{13}C -NMR (CDCl_3 , 150 MHz) of *E*-*Z* isomer mixture: *E* isomer: δ 172.7, 166.8, 137.3, 136.6, 80.3, 80.2, 41.2, 29.6, 28.5, 28.3, 19.3, 14.1. *Z* isomer: δ 172.1, 167.7, 138.5, 131.5, 80.9, 80.3, 42.4, 35.5, 28.5, 28.3, 19.7, 15.2.

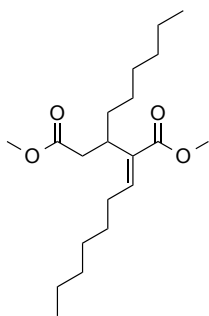
IR (neat): $\tilde{\nu}$, cm^{-1} : 2976, 2932, 2875, 1727, 1705, 1640, 1478, 1456, 1392, 1366, 1332, 1291, 1272, 1250, 1144, 1073, 1038, 988, 953, 920, 847, 825, 806, 760, 594.

HRMS (DESI) calculated for $\text{C}_{16}\text{H}_{29}\text{O}_4^+$ $[\text{MH}]^+$ requires 285.2060; found 285.2061.

HRMS (DESI) calculated for $\text{C}_{16}\text{H}_{28}\text{O}_4\text{Na}^+$ $[\text{MNa}]^+$ requires 307.1880; found 307.1880.

CHN Analysis calculated for $\text{C}_{16}\text{H}_{28}\text{O}_4$ requires C 67.57%, H 9.92%, N 0.00%; found C 67.50%, H 9.89%, N < 0.02%.

Dimethyl (*E*)-2-heptylidene-3-hexylpentandioate



The reaction was performed in a 20 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of potassium *tert*-butoxide (16.6 mg, 0.148 mmol) in THF (3 mL) was added methyl 2-nonenoate (501 mg, 2.942 mmol) in one portion. The resulting yellow solution was stirred at room temperature. Conversion to products was assessed by ¹H-NMR after 30 minutes (>99% conversion; ratio (*E*)-isomer : (*Z*)-isomer : side-product 56:11:32) and after 18 hours (>99% conversion; ratio (*E*)-isomer : (*Z*)-isomer : side-product 69:13:18).

After 18 hours the reaction was quenched by adding approximately 20 mg of hydrochloric acid (37%). The THF was removed *in vacuo*, and then the crude product was placed in a separating funnel and 15 mL diethyl ether added. The mixture was washed twice with water, and the ethereal layer dried with anhydrous MgSO₄, filtered and evaporated. The yield of crude product (containing (*E*)-isomer, (*Z*)-isomer and side-product) was 471 mg (94% yield).

Reverse-phase high performance liquid chromatography (HPLC), gradient 50 to 100% acetonitrile in water (containing 0.1% trifluoroacetic acid), was used demonstrate the isolation of the (*E*)-isomer product: 25 mg of the crude product mixture was dissolved in 1 mL of methanol and injected into the column. The HPLC trace is shown in Figure S2. Fractions 53-54 resulted in the (*E*)-isomer (colorless oil). Yield: 16 mg (64%).

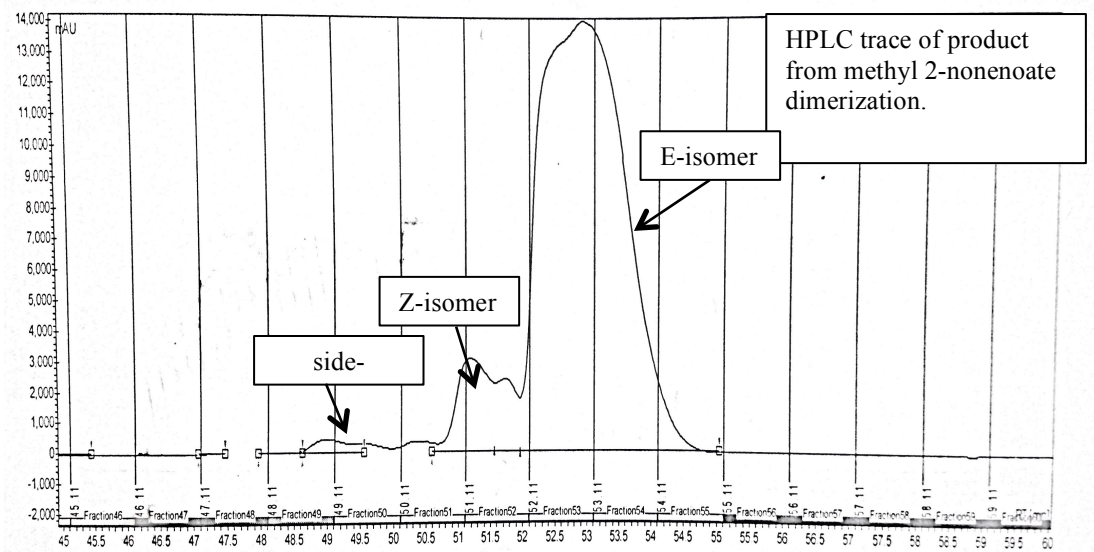


Figure S2. HPLC trace of product from methyl 2-nonenoate dimerization

(*E*-isomer): ^1H -NMR (CDCl_3 , 500 MHz): δ 6.80 (t, 1H, J = 7.5 Hz, =CH), 3.71 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3), 3.07-3.14 (m, 1H, $-\text{CH}(\text{CH}_2)_5\text{CH}_3$), 2.71 (dd, 1H, J = 15.2, 8.4 Hz, diastereotopic CH_2), 2.58 (dd, 1H, J = 15.2, 6.5 Hz, diastereotopic CH_2), 2.23 (dt, 2H, J = 7.4, 7.4 Hz, =CHCH $_{\text{CH}_2}$), 1.62-1.72 (m, 1H, CH_2), 1.45-1.52 (m, 1H, CH_2), 1.36-1.45 (m, 2H, CH_2), 1.10-1.35 (m, 14H, CH_2), 0.88 (t, 3H, J = 6.8 Hz, $-\text{CH}_2\text{CH}_3$), 0.85 (t, 3H, J = 6.7 Hz, $-\text{CH}_2\text{CH}_3$).

(*E*-isomer): ^{13}C -NMR (CDCl_3 , 125 MHz): δ 177.7, 167.7, 145.6, 132.7, 51.6, 51.5, 38.8, 35.1, 33.4, 31.9, 31.8, 29.4, 29.3, 29.0, 28.6, 28.0, 22.8, 22.7, 14.2, 14.2.

(*E*)-stereochemistry was confirmed by ^1H - ^1H NOESY NMR spectroscopy, which revealed an NOE between protons at δ 2.23 and δ 3.07-3.14 (Figure S3).

HRMS (nano-ESI): calculated for $\text{C}_{20}\text{H}_{36}\text{O}_4\text{Na}^+$ [MNa] $^+$ requires 363.2506; found 363.2497

HRMS (nano-ESI): calculated for $\text{C}_{20}\text{H}_{36}\text{O}_4\text{K}^+$ [MK] $^+$ requires 379.2245; found 379.2246

HRMS (nano-ESI): calculated for $\text{C}_{40}\text{H}_{72}\text{O}_8\text{Na}^+$ [$2\text{M}+\text{Na}$] $^+$ requires 703.5119; found 703.5119

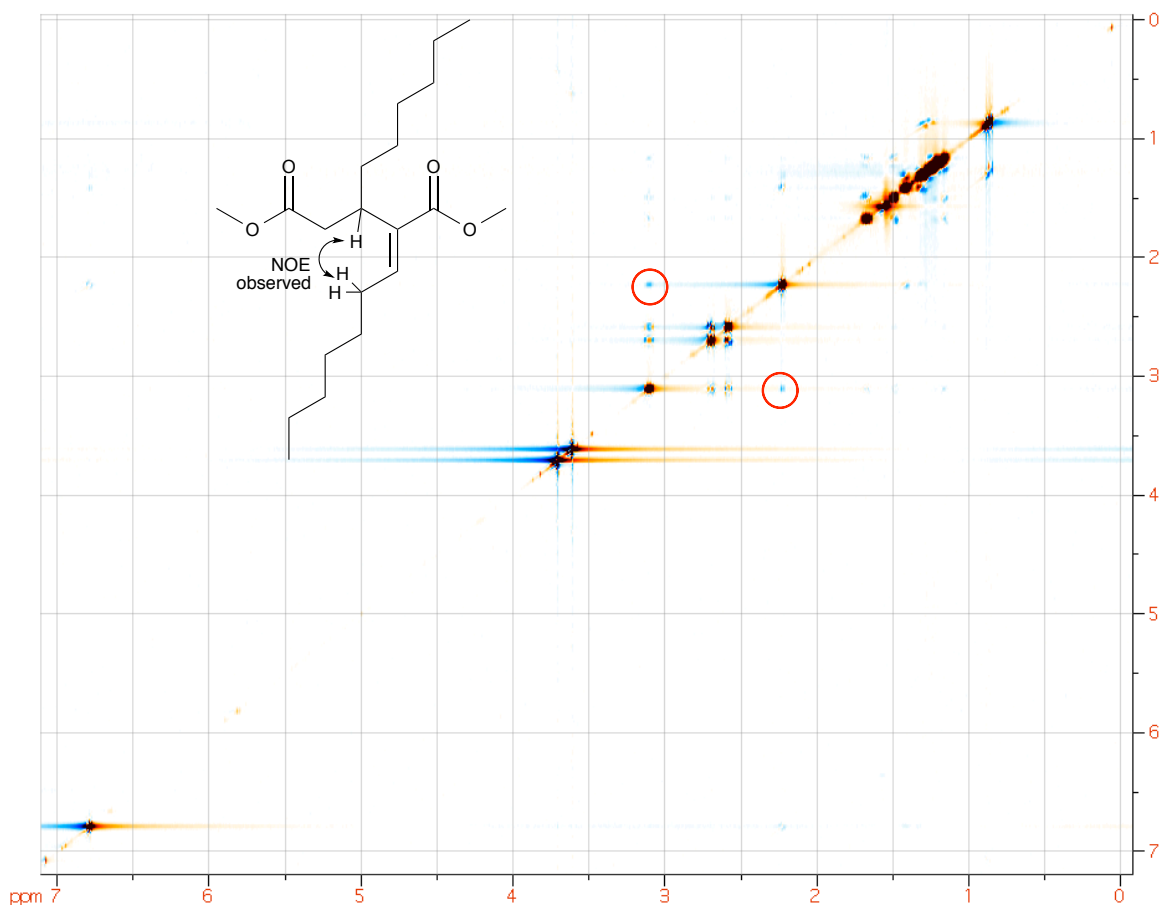


Figure S3. ^1H - ^1H NOESY spectrum of *E*-dimethyl 2-heptylidene-3-hexylpentandioate.

Fractions 51-52 (yield 3mg) contained 82% (*Z*)-isomer, 10% (*E*)-isomer and 8% side-product, calculated by integration of ^1H -NMR (Figure S4).

(*Z*)-isomer: ^1H -NMR (CDCl_3 , 600 MHz): δ 5.83 (t, 1H, $J = 7.5$ Hz, $=\text{CH}$), 3.74 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 2.79-2.86 (m, 1H, $-\text{CH}(\text{CH}_2)_5\text{CH}_3$), 2.55 (dd, 1H, $J = 15.2, 8.0$ Hz, diastereotopic CH_2), 2.45 (dd, 1H, $J = 15.2, 6.9$ Hz, diastereotopic CH_2), 2.27-2.35 (m, 2H, $=\text{CHCH}_2-$), 1.62-1.72 (m, 1H, CH_2), 1.44-1.53 (m, 1H, CH_2), 1.33-1.44 (m, 2H, CH_2), 1.15-1.33 (m, 14H, CH_2), 0.87 (t, 3H, $J = 6.8$ Hz, $-\text{CH}_2\text{CH}_3$), 0.86 (t, 3H, $J = 6.8$ Hz, $-\text{CH}_2\text{CH}_3$).

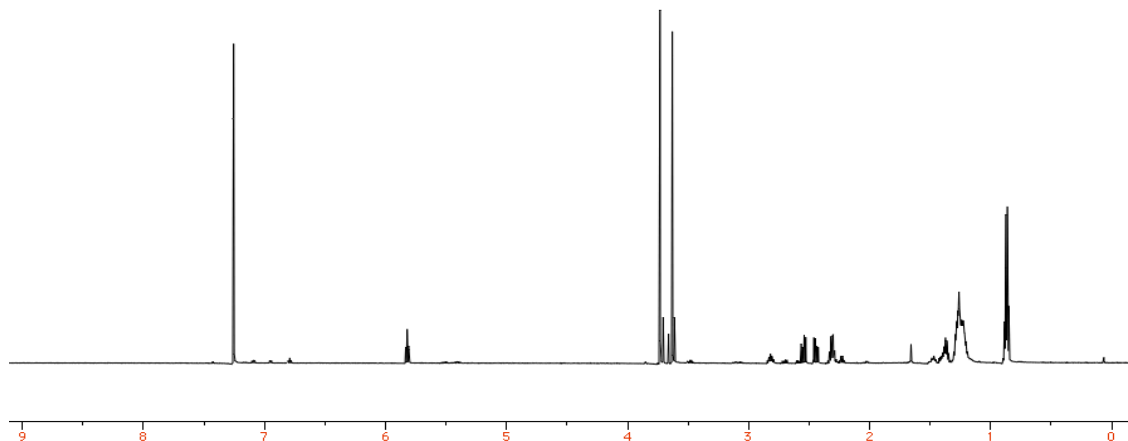


Figure S4. ^1H -NMR of fractions 51-52 (containing mainly (*Z*)-isomer).

Fraction 50 (yield 1 mg) contained the side-product (Figure S5). The side-product was assigned as dimethyl 2-(hept-1-en-1-yl)-3-hexylpentanedioate based on ^1H - ^1H COSY (Figure S6), and defined as isomer *X* in Scheme 2 of the main paper.

Dimethyl (*E*)-2-(hept-1-en-1-yl)-3-hexylpentanedioate ^1H -NMR (CDCl_3 , 600 MHz): δ 5.50-5.58 (m, 1H, $=\text{CH}$), 5.33-5.41 (m, 1H, $=\text{CH}$), 3.67 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.00 (dd, 1H, $J = 9.4, 8.0$ Hz, $-\text{CH}(\text{CH})_2(\text{CH}_2)_4\text{CH}_3$), 2.41 (dd, 1H, $J = 15.7, 5.3$ Hz, diastereotopic CH_2), 2.27-2.35 (m, 1H, $-\text{CH}(\text{CH}_2)_5\text{CH}_3$), 2.18 (dd, 1H, $J = 15.6, 7.5$ Hz, diastereotopic CH_2), 2.00 (dt, 2H, $J = 7.4, 7.4$ Hz, $=\text{CHCH}_2-$), 1.31-1.38 (m, 2H, CH_2), 1.18-1.31 (m, 14H, CH_2), 0.87 (t, 3H, $J = 7.1$ Hz, $-\text{CH}_2\text{CH}_3$), 0.87 (t, 3H, $J = 7.0$ Hz, $-\text{CH}_2\text{CH}_3$).

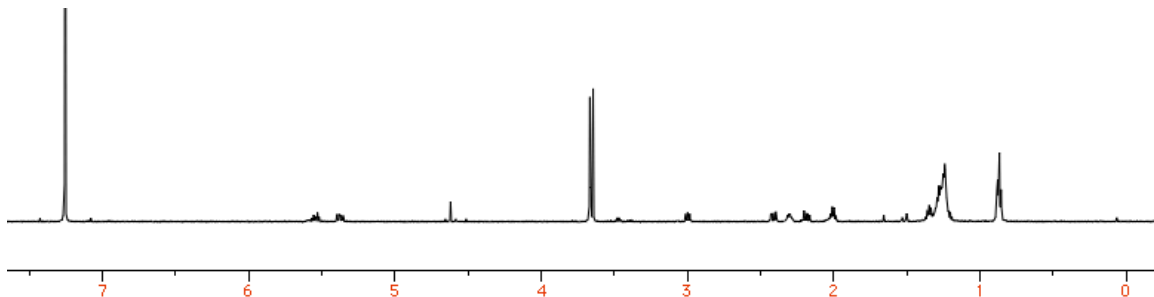


Figure S5. Crude ^1H -NMR of fraction 50 (containing the side-product).

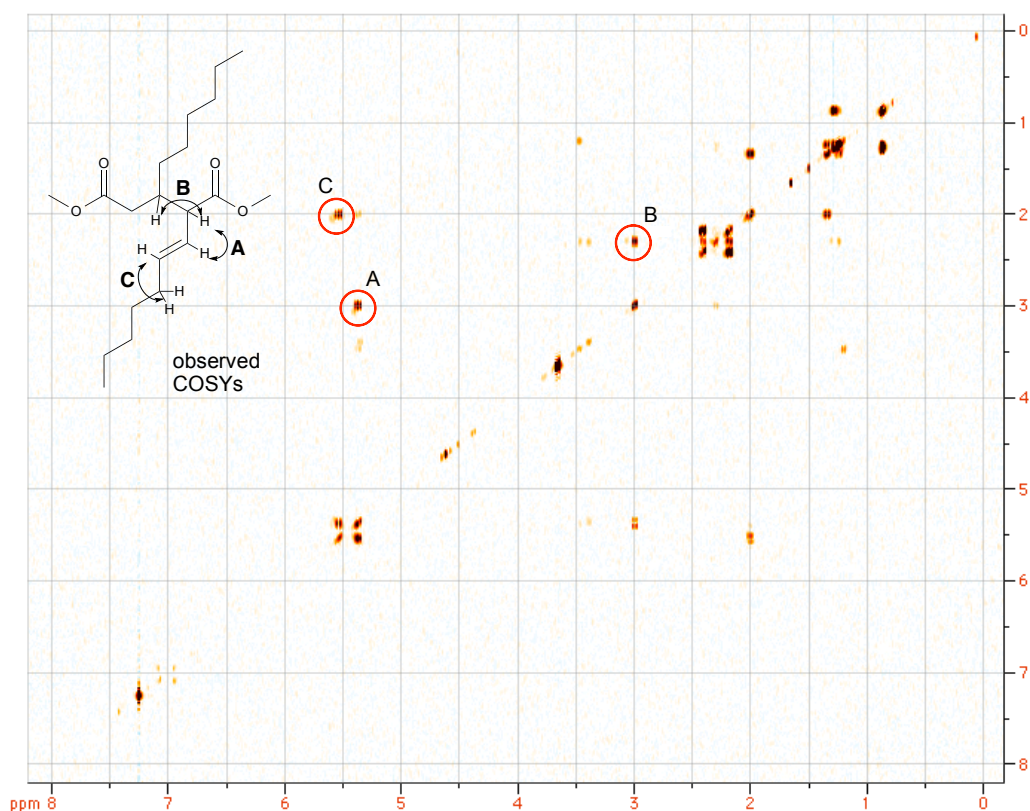
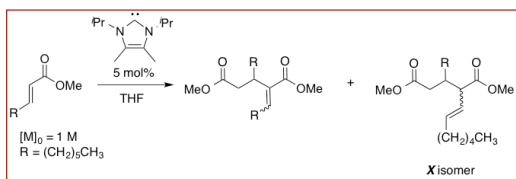
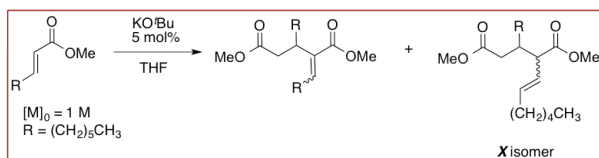
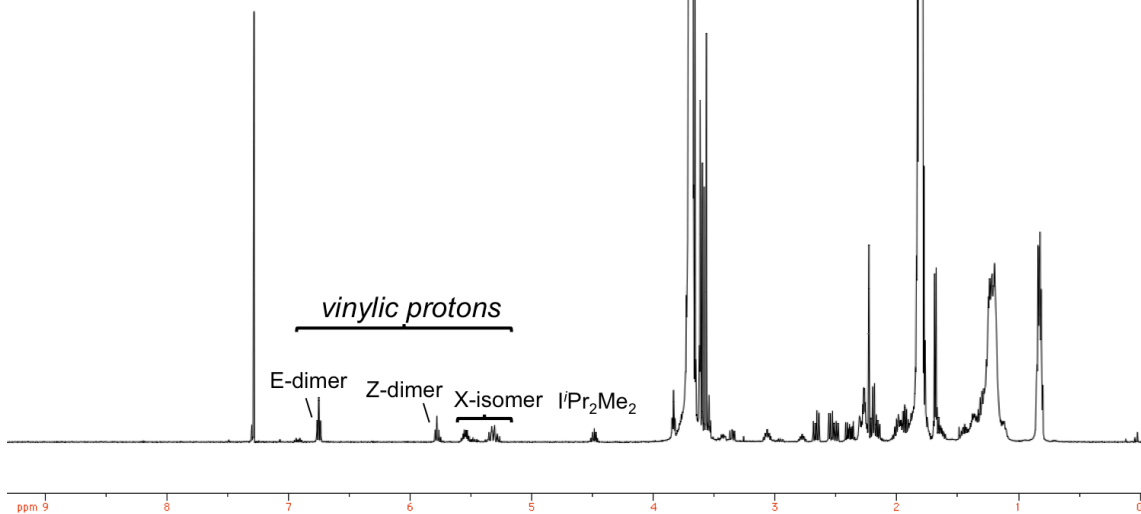


Figure S6. ^1H - ^1H COSY of fraction 50 showing COSY correlations consistent with dimethyl 2-(hept-1-en-1-yl)-3-hexylpentanedioate.

The reaction was repeated with 5 mol% $\text{I}^i\text{Pr}_2\text{Me}_2$ instead of KO^tBu (Table 1, Entry 16 in the main paper). Comparing crude NMR spectra (Figure S7) of the reaction mixture of both these reactions, it is clear that the dimethyl 2-heptylidene-3-hexylpentanedioate and dimethyl 2-(hept-1-en-1-yl)-3-hexylpentanedioate (defined as Isomer **X** in Scheme 2 of the main paper) are formed in both $\text{I}^i\text{Pr}_2\text{Me}_2$ and KO^tBu -catalyzed dimerization.



$^1\text{H-NMR}$ (CDCl_3) of aliquot of reaction mixture after 2h



$^1\text{H-NMR}$ (CDCl_3) of aliquot of reaction mixture after 2h

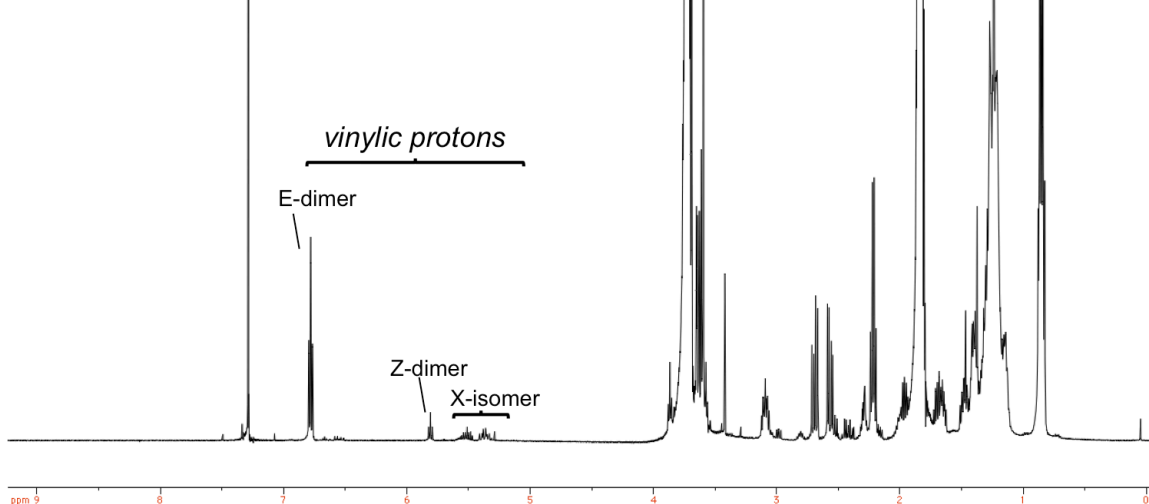
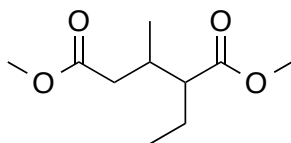


Figure S7. $^1\text{H-NMR}$ (CDCl_3) of $i\text{Pr}_2\text{Me}_2$ (top) and KO^tBu (bottom) catalyzed methyl 2-nonenoate dimerization

Dimethyl 2-ethyl-3-methylpentanedioate



A 100 mL round bottom flask was charged with 20 mL anhydrous methanol and dimethyl 2-ethylidene-3-methylpentanedioate (1.00 g, 4.99 mmol) and sealed with a rubber septum. Nitrogen gas was bubbled through the mixture for 15 minutes to remove any oxygen gas present. 10% Pd on C (132.2 mg, 0.125 mmol) was then added in one portion to the mixture, the rubber septum replaced, and N₂ bubbled through the mixture for another 15 minutes. The nitrogen was then replaced for a balloon filled with hydrogen gas. The reaction was then stirred under this hydrogen gas for 24 hours, after which time the atmosphere in the flask was replaced with N₂, and the flask then was opened to the air. The reaction mixture was then filtered through celite wetted with ethyl acetate (taking care not to let the celite dry out). The filtrate was then concentrated on a rotary evaporator to remove volatiles. Flash column chromatography (40% ethyl acetate: 60% hexanes by volume) afforded 0.906 g (90% yield) of a colorless liquid, R_f = 0.8.

¹H-NMR: (CDCl₃, 500 MHz), (mixture of diastereomers) δ 3.58 (overlapping s, 6H), 2.28-2.41 (m, 1H), 2.11-2.22 (m, 2H), 2.01-2.09 (m, 1H), 1.49-1.62 (m, 1H), 1.36-1.48 (m, 1H), 0.82-0.88 (m, 3H), 0.76-0.82 (m, 3H).

¹³C-NMR: (CDCl₃, 500 MHz), (mixture of diastereomers) δ 175.5, 175.3, 173.3, 173.2, 52.4, 52.0, 51.6, 51.4, 51.4, 51.4, 39.1, 38.9, 32.3, 32.3, 22.8, 22.3, 17.6, 17.2, 12.3, 12.2.

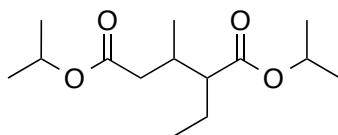
IR (neat): $\tilde{\nu}$, cm⁻¹: 2966, 2879, 1731, 1459, 1435, 1384, 1368, 1327, 1306, 1270, 1235, 1193, 1170, 1086, 1056, 1028, 998, 884, 836, 797, 760.

HRMS (DESI) calculated for C₁₀H₁₉O₄⁺ [MH]⁺ requires 203.1278; found 203.1277.

HRMS (DESI) calculated for C₁₀H₁₈O₄Na⁺ [MNa]⁺ requires 225.1097; found 225.1097.

CHN Analysis calculated for C₁₀H₁₈O₄ requires C 59.39% H 8.97%, N 0.00%; found C 59.68% H 8.84%, N < 0.02%.

Diisopropyl 2-ethyl-3-methylpentanedioate



A 10 mL round bottom flask was charged with 2 mL anhydrous methanol and diisopropyl 2-ethylidene-3-methylpentanedioate (100 mg, 0.387 mmol) and sealed with a rubber septum. Nitrogen gas was bubbled through the mixture for 15 minutes to remove any oxygen gas present. 10% Pd on C (10 mg, 0.00940 mmol) was then added in one portion to the mixture, the rubber septum replaced, and N₂ bubbled through the mixture for another 15 minutes. The nitrogen was then replaced for a balloon filled with hydrogen gas. The reaction was then stirred under this hydrogen gas for 16 hours, after which time the atmosphere in the flask was replaced with N₂, and the flask then was opened to the air. The reaction mixture was then filtered through celite wetted with ethyl acetate (taking care not to let the celite dry out). The filtrate was then concentrated on a rotary evaporator to remove volatiles. Flash column chromatography (20% ethyl acetate: 80% hexanes by volume) afforded 91 mg (90% yield) of a colorless liquid, R_f = 0.3.

¹H-NMR: (CDCl₃, 500 MHz), (mixture of diastereomers): δ 4.94-5.06 (m, 2H), 2.33-2.43 (m, 1H), 2.11-2.28 (m, 2H), 2.04-2.10 (m, 1H), 1.55-1.68 (m, 1H), 1.43-1.54 (m, 1H), 1.19-1.23 (m, 12H), 0.93 (t, 3H, J = 7.0 Hz), 0.87 (t, 3H, J = 7.4 Hz).

¹³C-NMR: (CDCl₃, 125 MHz), (mixture of diastereomers): δ 174.7, 174.5, 172.6, 172.5, 67.8, 67.7, 67.6, 67.6, 52.7, 52.4, 39.9, 39.6, 32.6, 32.6, 22.2, 22.1, 22.1, 22.1, 22.0, 22.0, 17.5, 17.1, 12.3, 12.3.

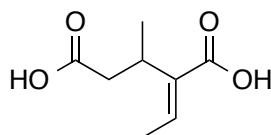
IR (neat): $\tilde{\nu}$, cm⁻¹: 2977, 2936, 2878, 1725, 1459, 1373, 1342, 1322, 1303, 1268, 1238, 1179, 1144, 1105, 1028, 973, 961, 901, 820.

HRMS (DESI) calculated for C₁₄H₂₇O₄⁺ [MH]⁺ requires 259.1904; found 259.1903.

HRMS (DESI) calculated for C₁₄H₂₆O₄Na⁺ [MNa]⁺ requires 281.1723; found 281.1723.

CHN Analysis calculated for C₁₄H₂₆O₄ requires C 65.09%, H 10.14%, N 0.00%; found C 65.38%, H 10.20%, N < 0.02%.

(E)-2-ethylidene-3-methylpentanedioic acid



In a 25 mL round bottom flask with stirbar was added dimethyl 2-ethylidene-3-methylpentanedioate (300 mg, 83:17 *E*:*Z* isomer ratio, 1.245 mmol *E* : 0.255 mmol *Z*) and 1 mL methanol. The flask was placed in an oil bath at 45 °C. Potassium hydroxide pellets were crushed up using a mortar and pestle and the powder (342 mg, 6.00 mmol) added in one portion. The flask was stoppered with a rubber septum and stirred for 3 hours. Over time solid began to precipitate and the reaction mixture turned slightly yellow. Water (5 mL) was added to quench the reaction, and the reaction mixture then transferred to a separating funnel. Diethyl ether (2 x 5 mL) was added to remove any unreacted ester, and the organic layers discarded. 1N HCl was added to the aqueous layer until pH 2 was reached. Diethyl ether was added (3 x 10 mL), the ethereal layers combined, dried with sodium sulfate and concentrated on a rotary evaporator, and placed on a high vacuum line to dry. Flash column chromatography (67% hexanes : 33% ethyl acetate to 50% hexanes : 50% ethyl acetate) enabled the separation of the *E* isomer from the remainder of the reaction mixture as a white solid, isolated yield (150 mg, 0.871 mmol, 58% isolated yield, 70% of the theoretical maximum yield of *E* isomer).

¹H-NMR: (CDCl₃, 500 MHz): δ 10.00-12.50 (br, 2H, COOH), 7.03 (q, 1H, *J* = 7.2 Hz, =CH), 3.26-3.35 (m, 1H, -CH(CH₃)CH₂), 2.85 (dd, 1H, *J* = 16.0, 8.4 Hz, diastereotopic CH₂), 2.64 (dd, 1H, *J* = 16.0, 6.8 Hz, diastereotopic CH₂), 1.89 (d, 3H, *J* = 7.2 Hz, =CCH₃), 1.23 (d, 3H, *J* = 7.1 Hz, CH(CH₃)CH₂).

¹³C-NMR: (CDCl₃, 150 MHz): 179.1, 172.5, 141.8, 134.7, 39.2, 28.8, 19.2, 14.5.

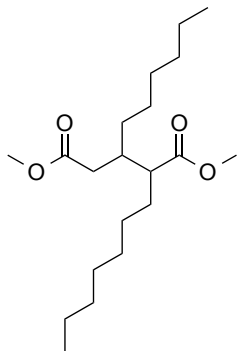
IR (neat): $\tilde{\nu}$, cm⁻¹: 3300-2200 (br), 2968, 2936, 2907, 2874, 2636, 2542, 1707, 1693, 1668, 1630, 1462, 1417, 1402, 1370, 1331, 1296, 1274, 1235, 1211, 1166, 1134, 1080, 1066, 1019, 984, 932, 865, 799, 759, 689, 644, 603, 574, 536.

HRMS (DESI): calculated for C₈H₁₂O₄Na⁺ [MNa]⁺ requires 195.0628; found 195.0628.

CHN Analysis calculated for C₁₄H₂₆O₄ requires C 55.81%, H 7.03%, N 0.00%; found C 55.73%, H 7.02%, N < 0.02%.

Dimethyl 2-heptyl-3-hexylpentanedioate

The crude product mixture from the dimerization of methyl 2-nonenoate (*vida supra*) was hydrogenated, transforming to a single product, namely dimethyl 2-heptyl-3-hexylpentanedioate.



A 10 mL round bottom flask was charged with 3 mL anhydrous methanol and 150 mg crude dimethyl 2-heptylidene-3-hexylpentandioate and sealed with a rubber septum. Nitrogen gas was bubbled through the mixture for 15 minutes to remove any oxygen gas present. 10% Pd on C (10 mg, 0.0094 mmol) was then added in one portion to the mixture, the rubber septum replaced, and N₂ bubbled through the mixture for another 15 minutes. The nitrogen was then replaced for a balloon filled with hydrogen gas. The reaction was then stirred under this hydrogen gas for 24 hours, after which time the atmosphere in the flask was replaced with N₂, and the flask then was opened to the air. The reaction mixture was then filtered through celite wetted with ethyl acetate (taking care not to let the celite dry out). The filtrate was then concentrated on a rotary evaporator to remove volatiles. The crude product ¹H-NMR spectrum indicated that only one main product was formed (Figure S8). A final purification was performed using flash column chromatography (5% ethyl acetate: 95% hexanes by volume), which afforded 120 mg (80% yield) of a colorless liquid.

¹H-NMR (CDCl₃, 600 MHz), (mixture of diastereomers): δ 3.66 (overlapping s, 6H), 2.39-2.49 (m, 2H), 2.18-2.27 (m, 1H), 2.12-2.17 (m, 1H), 1.58-1.67 (m, 1H), 1.31-1.42 (m, 1H), 1.17-1.32 (m, 20H), 0.87 (t, 6H, J = 6.9 Hz).

¹³C-NMR (CDCl₃, 150 MHz), (mixture of diastereomers): δ 175.9, 175.7, 173.9, 173.6, 51.7, 51.5, 48.3, 48.0, 37.5, 37.4, 36.2, 36.2, 32.2, 31.9, 31.9, 31.9, 31.8, 31.8, 29.7, 29.6, 29.6, 29.5, 29.5, 29.3, 28.5, 28.1, 28.0, 27.2, 26.7, 22.8, 22.7, 14.2, 14.2. (Several C peaks are likely overlapping).

HRMS (nano-ESI): calculated for C₂₀H₃₈O₄⁺ [MH]⁺ requires 343.2843; found 343.2845

HRMS (nano-ESI): calculated for C₂₀H₃₈O₄Na⁺ [MNa]⁺ requires 365.2662; found 365.2662

HRMS (nano-ESI): calculated for C₂₀H₃₈O₄K⁺ [MK]⁺ requires 381.2402; found 381.2401

HRMS (nano-ESI): calculated for C₄₀H₇₆O₈Na⁺ [2M+Na]⁺ requires 707.5432; found 707.5432

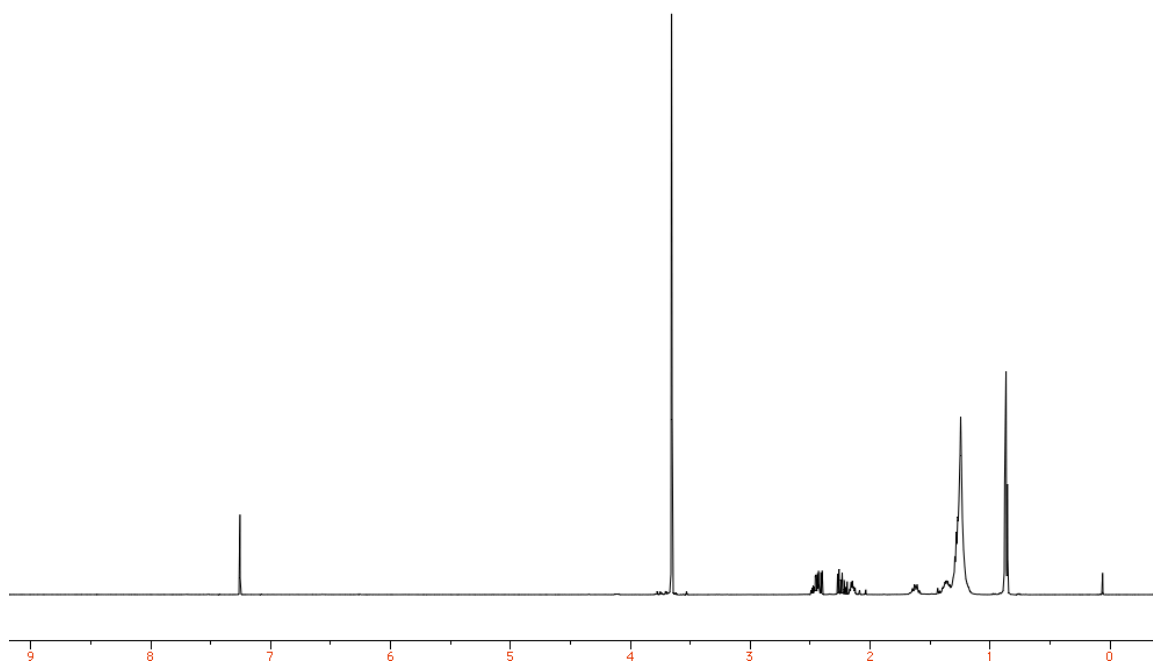
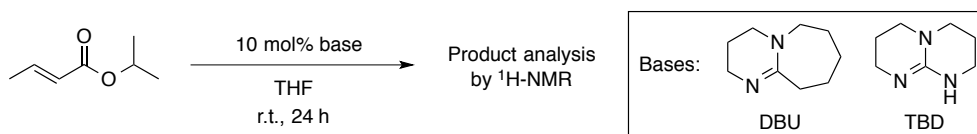


Figure S8. The crude ^1H -NMR spectrum for the Pd/C-catalyzed hydrogenation of the product mixture from methyl 2-nonenoate dimerization

5. Reactions of Crotonates with other Organic Catalysts

5a. Reactions of catalytic quantities of DBU and TBD with isopropyl crotonate

Experimental



The reactions were performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of base – either TBD or DBU – (0.0780 mmol) in THF (0.6 mL) was added isopropyl crotonate (100 mg, 0.780 mmol) in one portion. The resulting solution was stirred at room temperature for 24 hours. After this time, a small aliquot was withdrawn, CDCl_3 added, and a crude NMR was taken to determine monomer conversion.

Results

The reaction of 10 mol% DBU with isopropyl crotonate in THF resulted in no visible monomer conversion by $^1\text{H-NMR}$ (Figure S9).

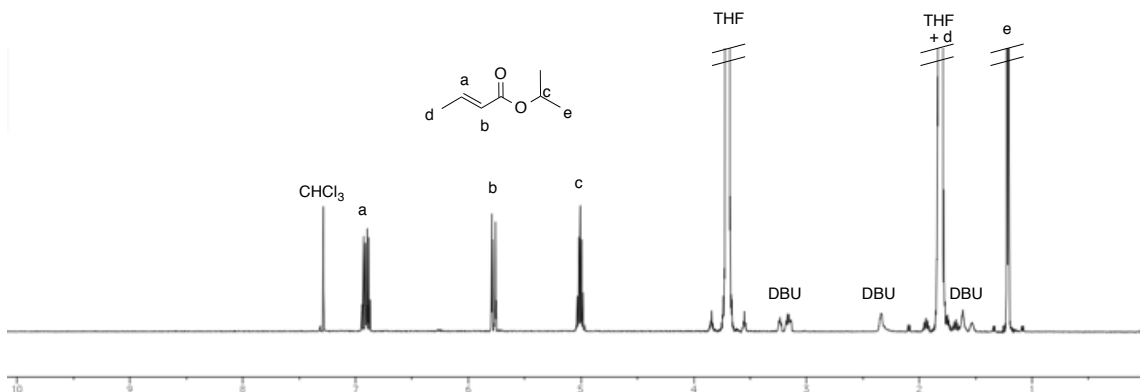


Figure S9. Crude $^1\text{H-NMR}$ spectrum of reaction mixture of 10 mol% DBU and isopropyl crotonate in THF (24 h)

The reaction of 10 mol% TBD with isopropyl crotonate in THF resulted in approximately 6% conversion of the isopropyl crotonate to a “3-TBD butanoate” addition product (Figure S10).

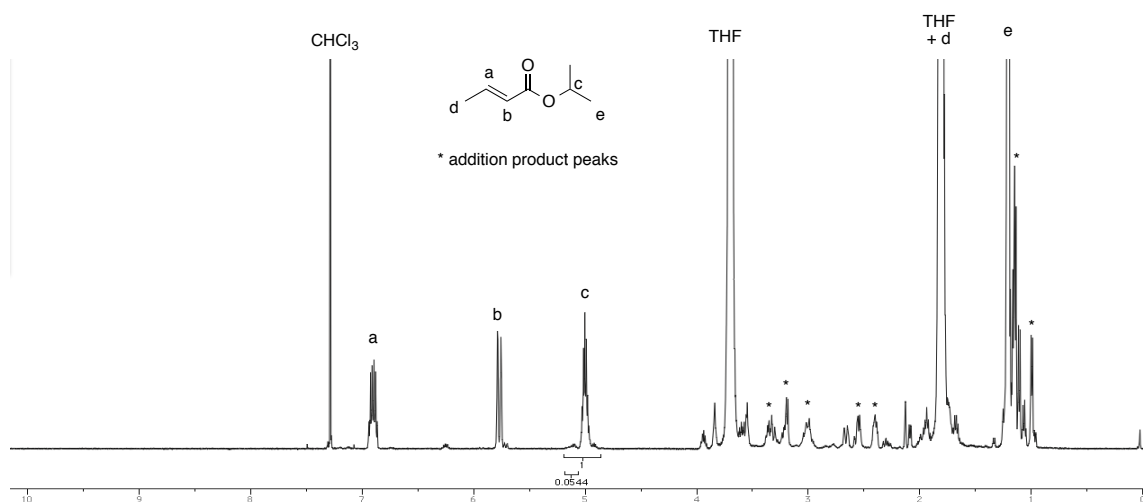
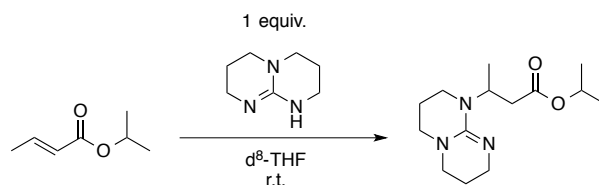


Figure S10. Crude ^1H -NMR of reaction mixture of 10 mol% TBD and isopropyl crotonate in THF (24 h)

5b. Reactions of stoichiometric quantity of TBD with isopropyl crotonate

To confirm the presence of the “3-TBD butanoate addition” product described in Section 5a, the reaction of a stoichiometric amount of TBD with isopropyl crotonate was carried out.

Experimental



In a nitrogen-filled glovebox to a J-Young tube was added a solution of TBD (69.6 mg, 0.500 mmol) in $\text{d}^8\text{-THF}$ (0.5 mL) and then isopropyl crotonate (64.1 mg, 0.500 mmol) in one portion. A small amount of the TBD failed to dissolve. The tube was sealed and taken out of the glovebox. A ^1H -NMR spectrum was taken after 15 minutes, 145 minutes and 1010 minutes.

Results

After 15 minutes (Figure S11), the conversion of monomer to the “isopropyl 3-TBD butanoate” addition product is approximately 30%.

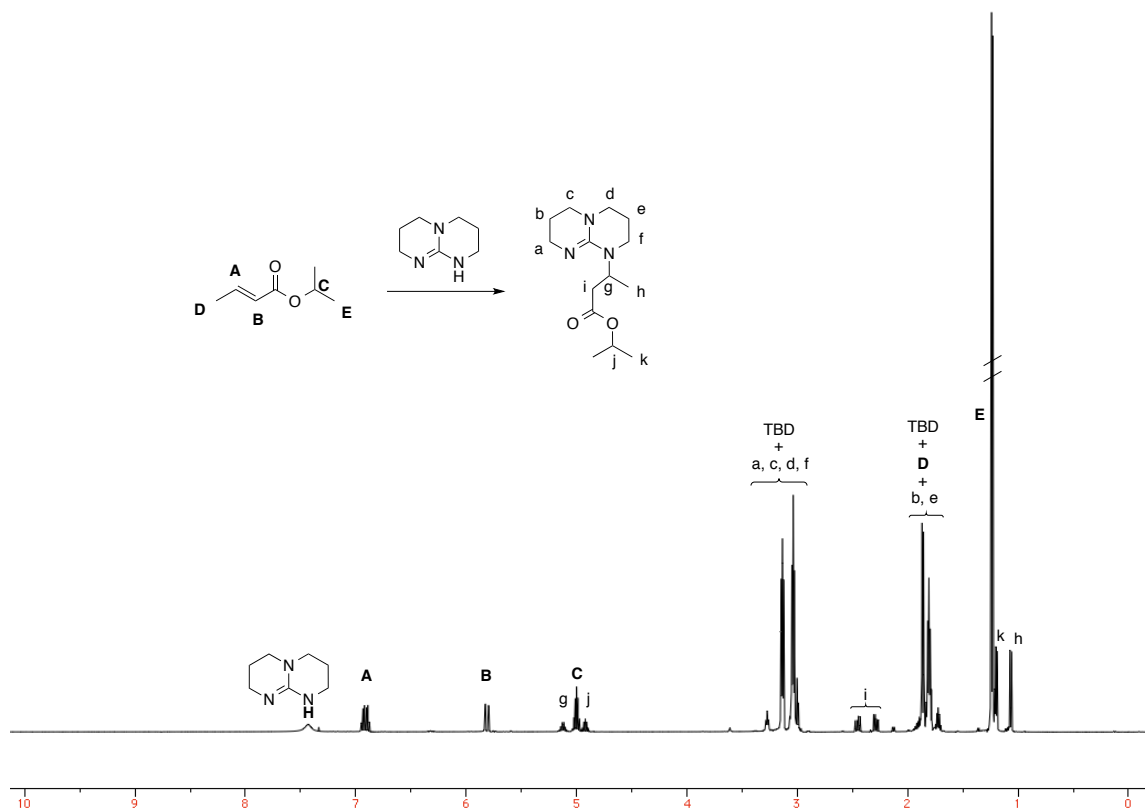


Figure S11. ^1H -NMR of reaction mixture of 1 equiv. TBD and 1 equiv. isopropyl crotonate in d^8 -THF (15 min)

After 145 minutes (Figure S12), the conversion of monomer to the “isopropyl 3-TBD butanoate” addition product is approximately 70%. Isopropyl alcohol also begins to appear in the spectrum and by 1010 minutes (Figure S13) has significantly increased in concentration. After 1010 minutes the ^1H -NMR spectrum also contains significant (unassigned) side-products.

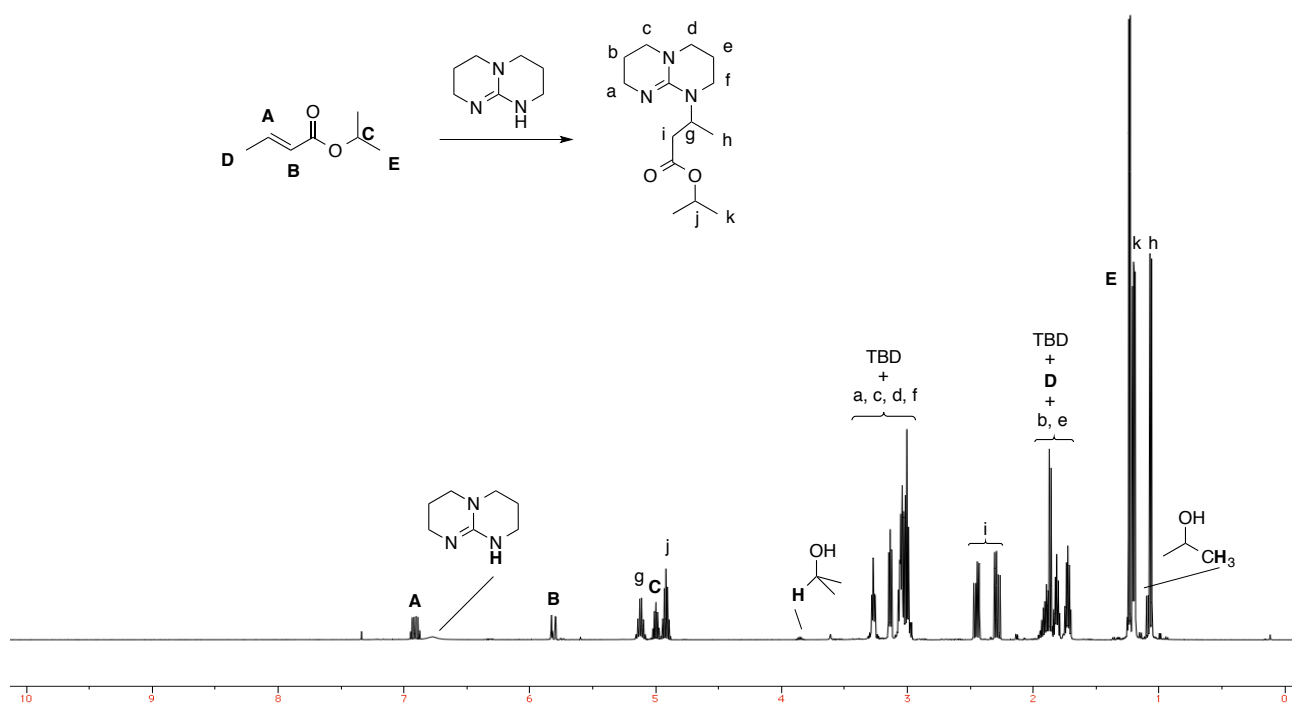


Figure S12. ^1H -NMR of reaction mixture of 1 equiv. TBD and 1 equiv. isopropyl crotonate in d^8 -THF (145 min)

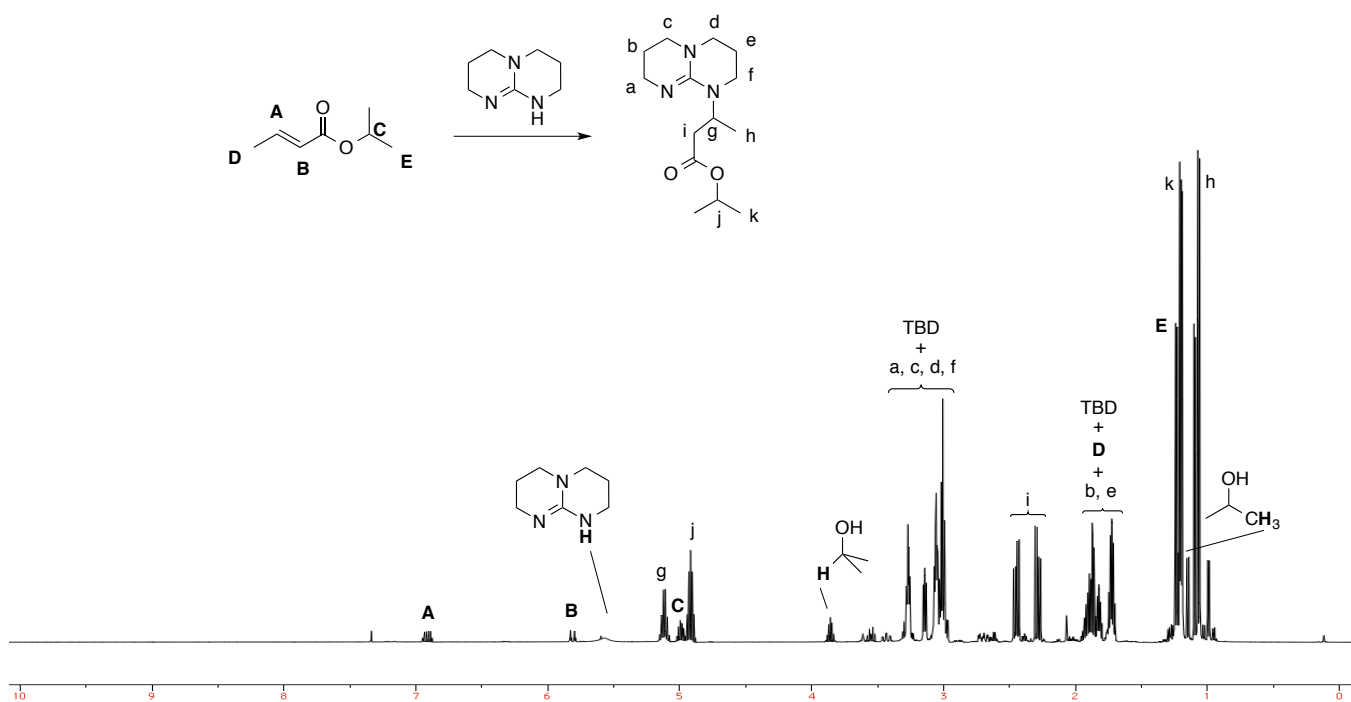
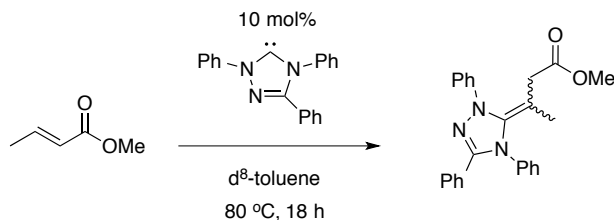


Figure S13. ^1H -NMR of reaction mixture of 1 equiv. TBD and 1 equiv. isopropyl crotonate in d^8 -THF (1010 min)

5c. Reaction of catalytic quantity of TPT with methyl crotonate

Experimental



In a nitrogen-filled glovebox, TPT (6.7 mg, 0.023 mmol, 0.1 equiv.) was added to a 4 mL vial with Teflon screw top, followed by methyl crotonate (22.7 mg, 0.227 mmol, 1 equiv.), and 1 mL d^8 -toluene, and a magnetic stirbar. The vial was sealed, removed from the glove box, and stirred in an oil bath at 80°C for 18 hours. After this time, the vial was brought back into a glove-box and added to a J-Young tube. ^1H -NMR was then taken to assess conversion.

Results

The reaction of 10 mol% TPT with methyl crotonate in d^8 -toluene resulted in conversion of 10% of the methyl crotonate and all present TPT to the single-addition product (Figure S14). The isomeric ratio of products is 2:1, however we were unable to ascertain whether the *E* or *Z* isomer was the major product.

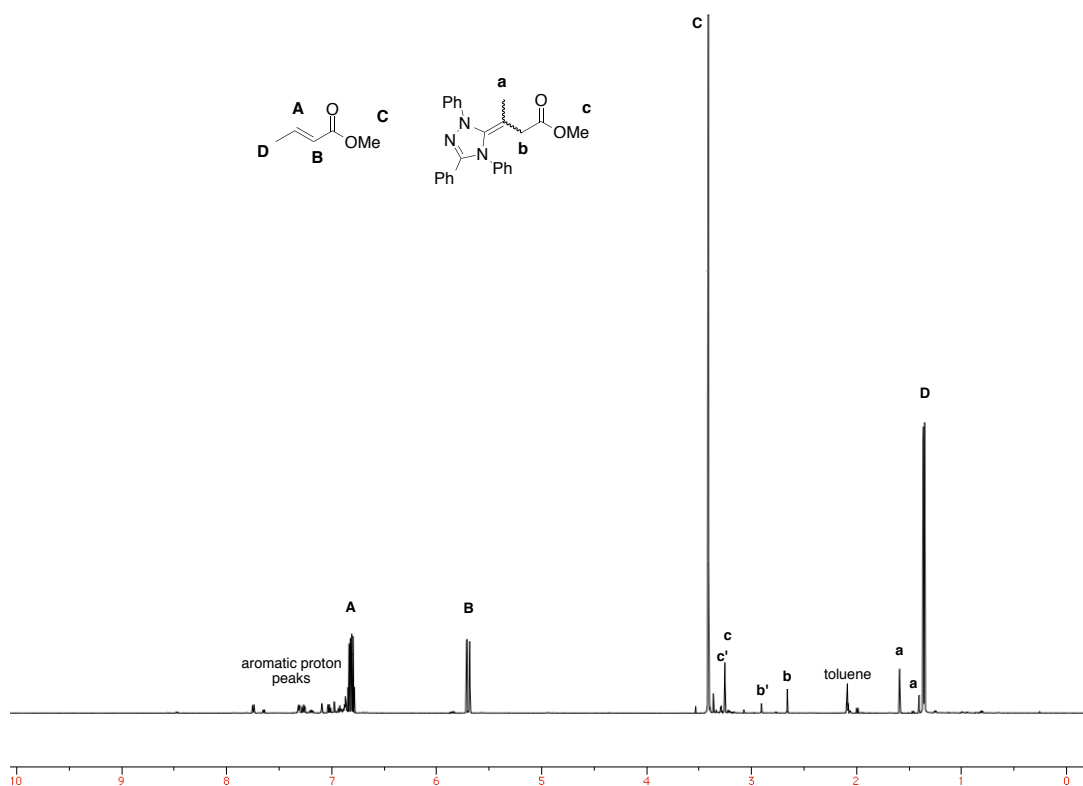
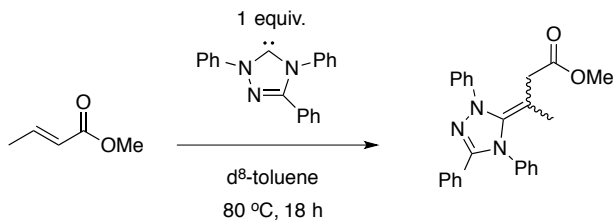


Figure S14. ^1H -NMR (d^8 -toluene) of reaction between methyl crotonate and 10 mol% TPT. (a', b' and c' refer to the analogous peaks on the geometric isomer)

5d. Reaction of stoichiometric quantity of TPT with methyl crotonate

Experimental



The reaction was then repeated using the same conditions but with 1 equiv. TPT (67.4 mg, 0.227 mmol) and 1 equiv. methyl crotonate (22.7 mg, 0.227 mmol). Again, ¹H-NMR was taken to assess conversion, and high-res mass spectrometry was used to confirm the mass of the product.

Results

The reaction of 1 equiv. TPT with methyl crotonate in d^8 -toluene resulted in 91% conversion of the methyl crotonate to the single-addition product (Figure S15). The isomeric ratio of products is 2.7:1, however we were unable to ascertain whether the *E* or *Z* isomer was the major product. The mass of the product was confirmed by high-resolution mass spectrometry (Figure S16).

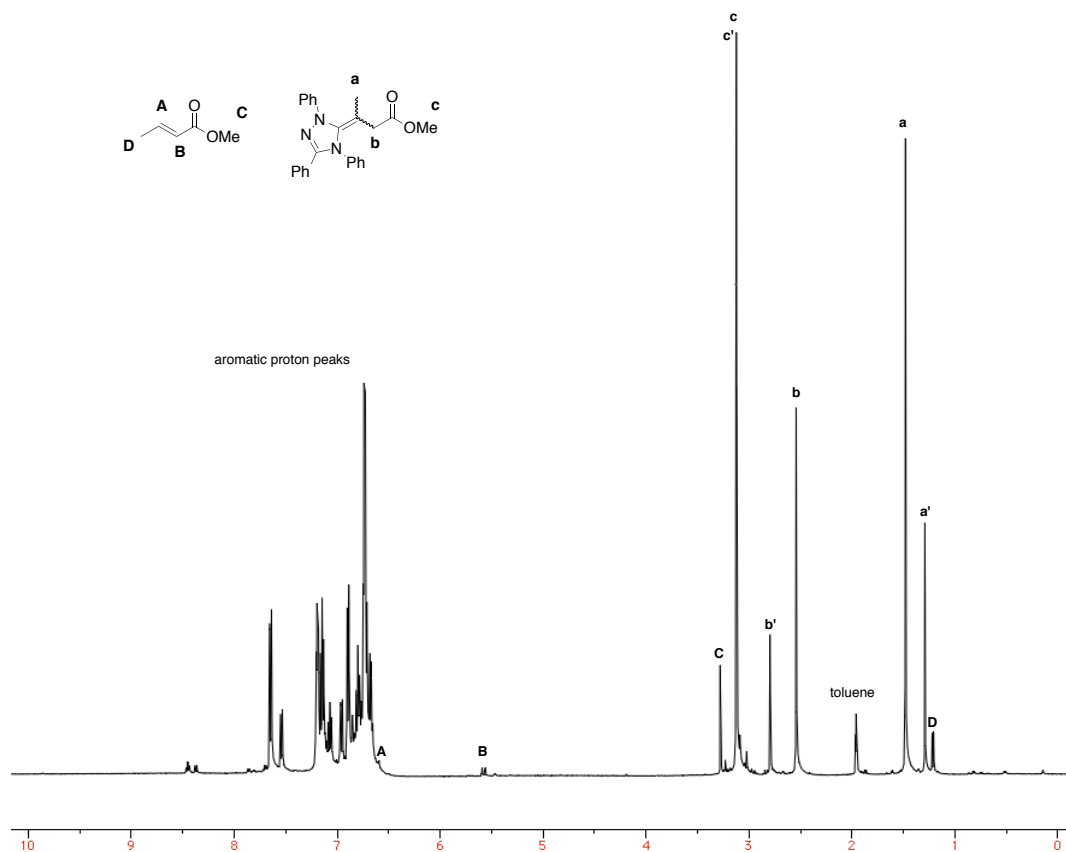


Figure S15. ^1H -NMR (d^8 -toluene) of reaction between methyl crotonate and 1 equiv. TPT. (a', b' and c' refer to the analogous peaks on the geometric isomer)

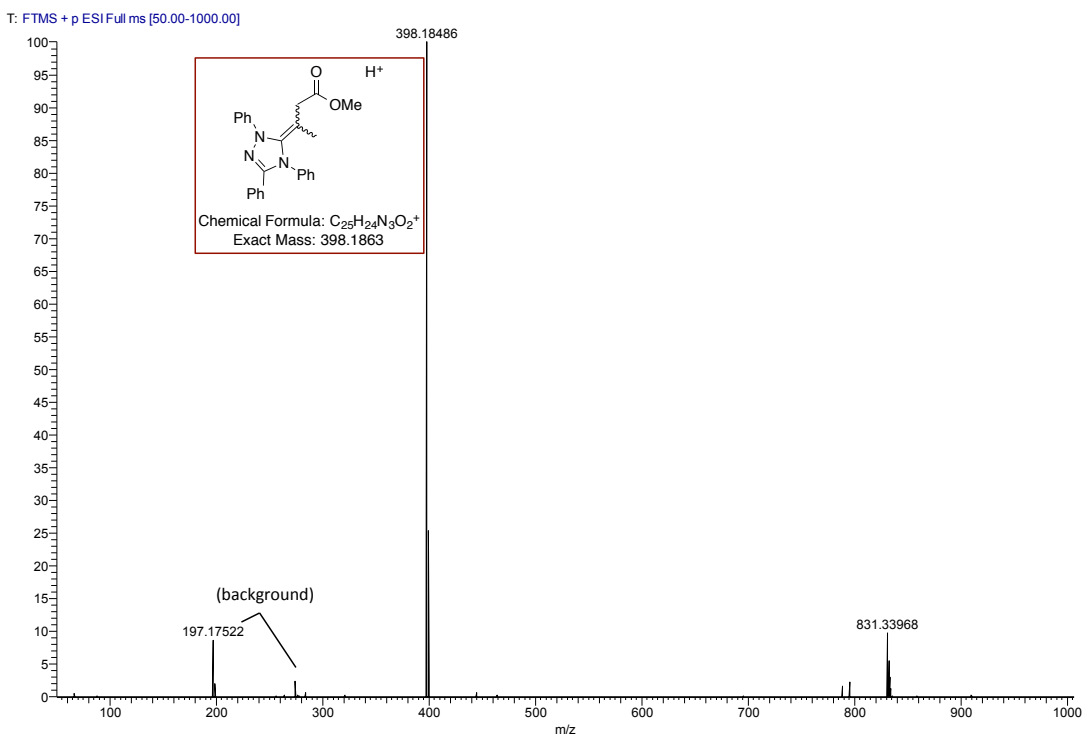
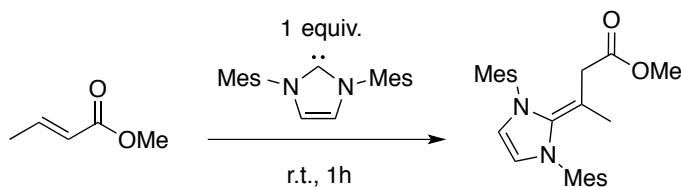


Figure S16. High-resolution DESI mass spectrum of reaction between methyl crotonate and 1 equiv. TPT in toluene

5e. Reaction of stoichiometric quantity of IMes with methyl crotonate



Experimental

In a nitrogen-filled glovebox, IMes (21.9 mg, 0.0719 mmol, 1 equiv.) was added to a 4 mL vial, followed by d^8 -THF (0.5 mL) and methyl crotonate (7.2 mg, 0.0719 mmol, 1 equiv.). The resulting reaction mixture was immediately transferred to a J-Young tube, and the tube sealed and removed from the box. 1 hour later, the reaction mixture was analyzed by 1H -, ^{13}C -, 1H - ^{13}C HMBC and 1H - ^{13}C HSQC NMR spectroscopy (Figures S17 – S20), and nano-ESI mass spectrometry (Figure S21).

Results

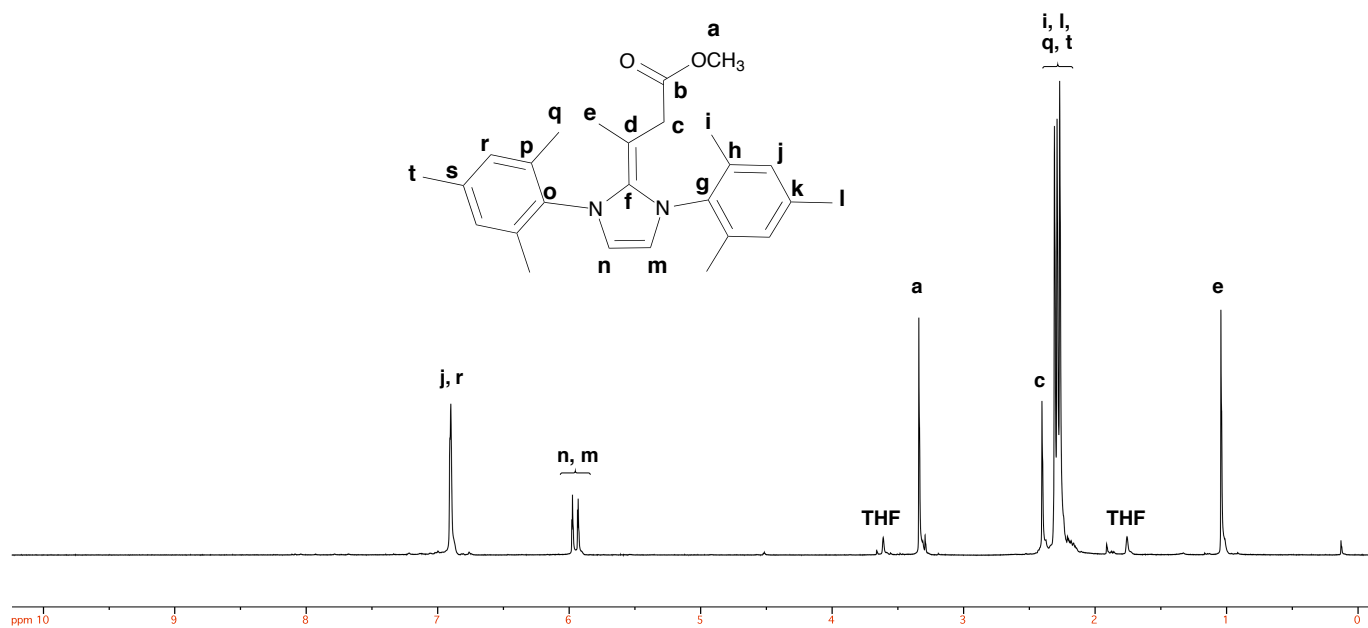


Figure S17. ^1H -NMR (d^8 -THF) of reaction between methyl crotonate and 1 equiv. IMes.

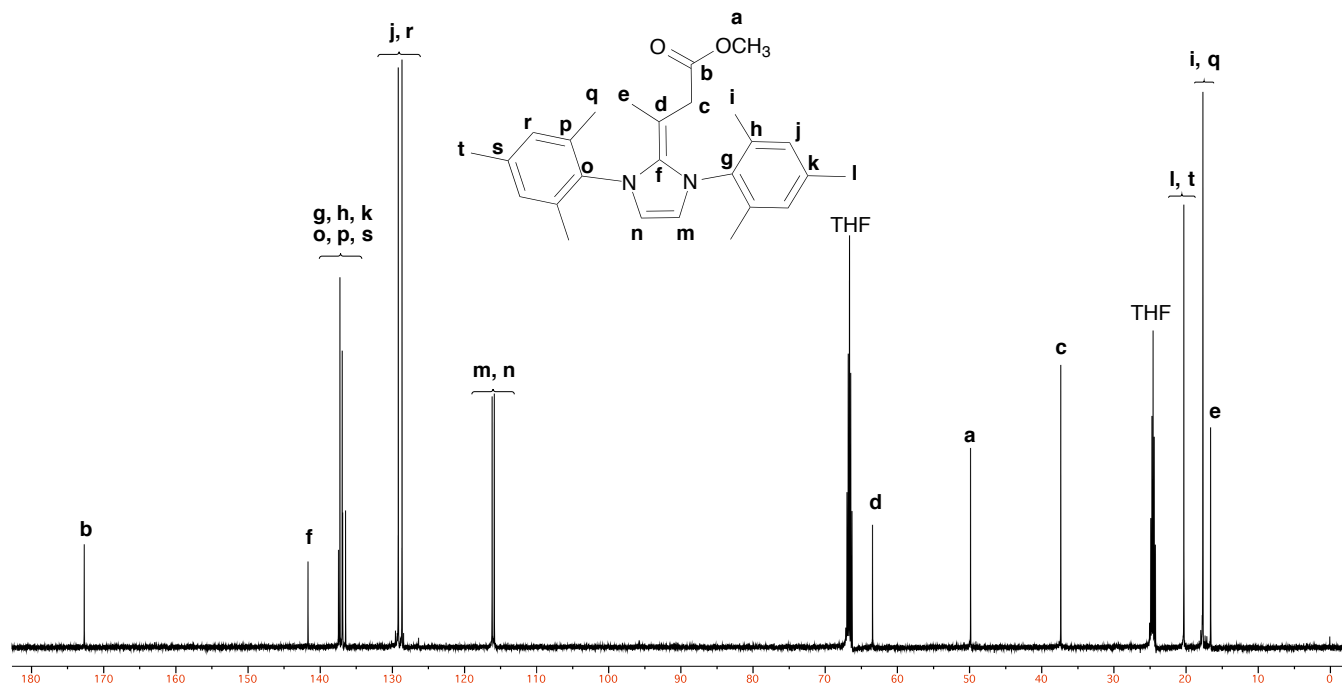


Figure S18. ^{13}C -NMR (d^8 -THF) of reaction between methyl crotonate and 1 equiv. IMes.

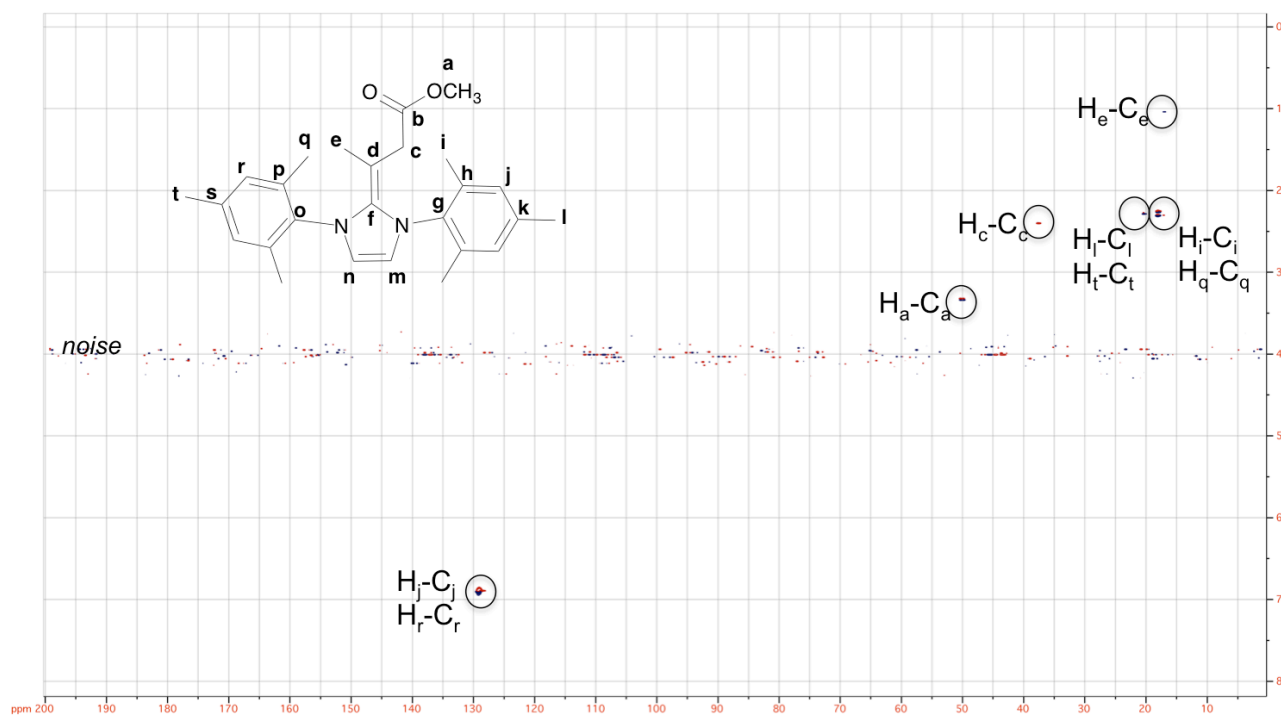


Figure S19. ^1H - ^{13}C HSQC NMR (d 8 -THF): methyl crotonate and 1 equiv. IMes.

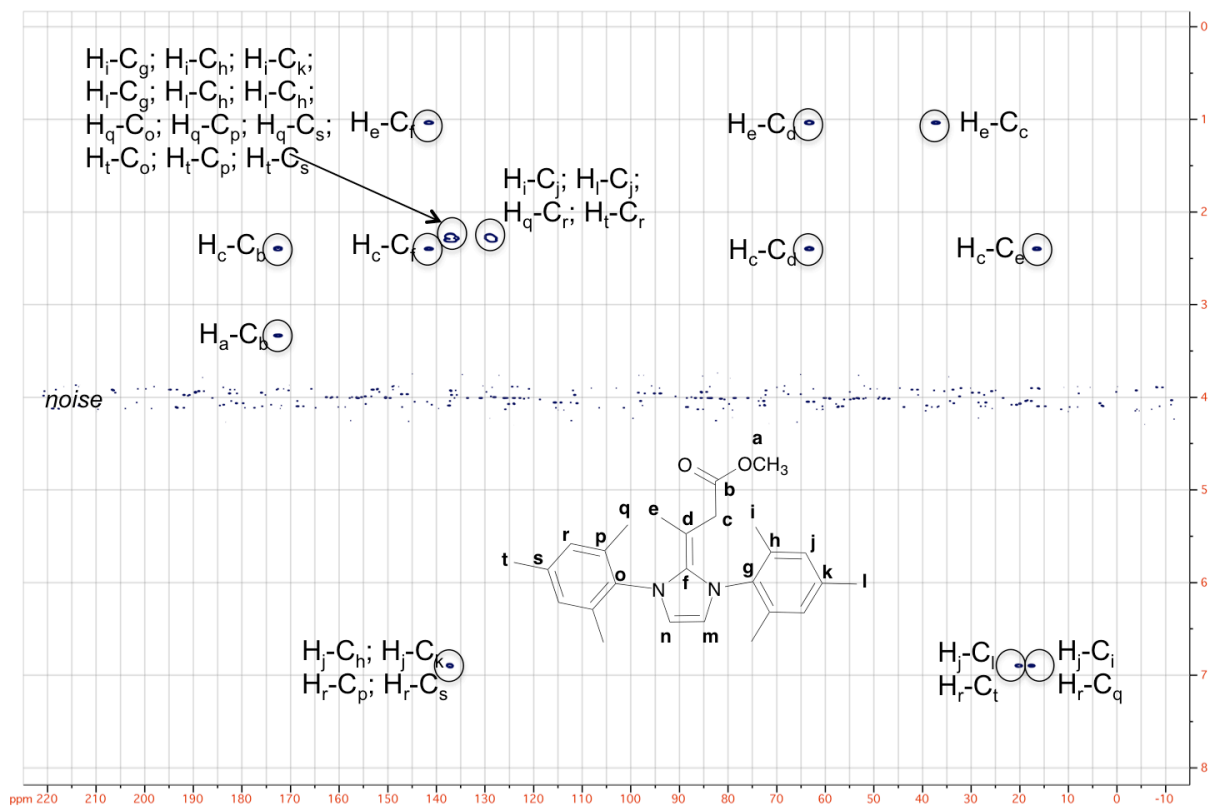


Figure S20. ^1H - ^{13}C HMBC NMR (d 8 -THF): methyl crotonate and 1 equiv. IMes.

JF-6-95_150609170945 #3-50 RT: 0.02-0.49 AV: 48 NL: 3.08E7

T: FTMS + p ESI Full ms [100.00-1000.00]

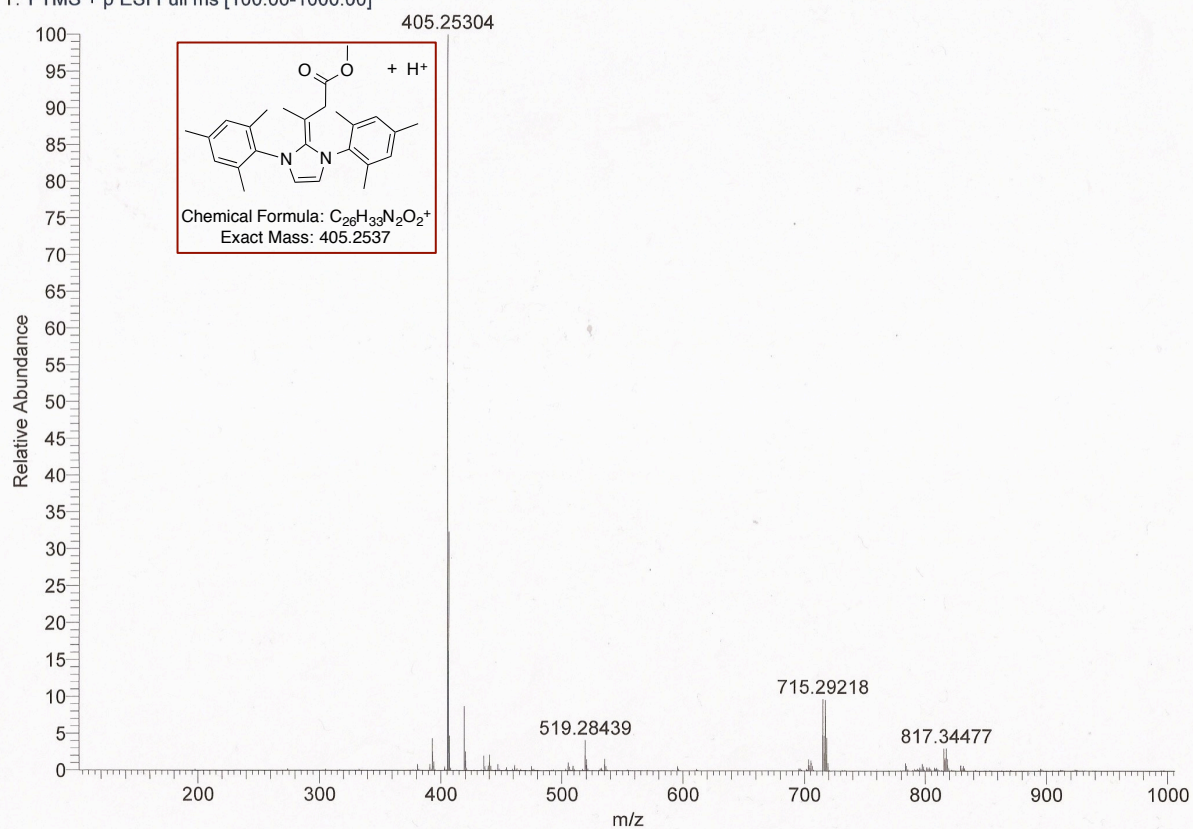
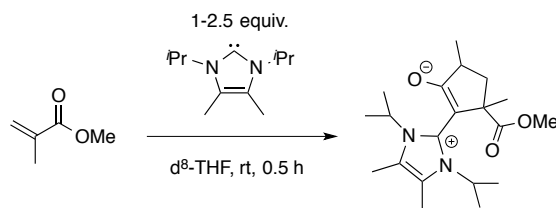


Figure S21. nano-ESI mass spectrum (0.002 M in THF) of crude reaction mixture of methyl crotonate and 1 equiv. IMes.

5f. Reaction of methyl methacrylate with $I^tPr_2Me_2$

Experimental



In a nitrogen-filled glovebox, a J-Young tube was charged with methyl methacrylate (10.1 mg), d^8 -THF (0.45 mL), and $I^tPr_2Me_2$ (18.2 mg). The tube was sealed, removed from the box, and a 1H -NMR was taken to assess conversion after 30 minutes (Figure S22 (iii)). The J-Young tube was returned to the glovebox, where another 15 mg of methyl methacrylate was added to the tube to give a total of 2.5 equiv. of methyl methacrylate to 1.0 equiv of $I^tPr_2Me_2$. The tube was sealed, removed from the box, and a 1H -NMR was taken after a further 30 minutes (Figure S22 (iv)). HSQC and HMBC (Figures S24 and S25) aided product assignments. High-resolution mass spectrometry (Figure S26) was used to confirm product mass.

Results

The 1H -NMR spectra (Figure S22) shows that there is 2:1 stoichiometry of methacrylate: $I^tPr_2Me_2$ in the product. The 1H -NMR spectra of the starting materials methyl methacrylate and $I^tPr_2Me_2$ are also shown in Figures S22(i) and (ii) respectively for comparison. There is quantitative conversion of the carbene. A ^{13}C -NMR spectrum is also included (Figure S23). HSQC (Figure S24) and HMBC (Figure S25) show that the product is likely to be of the type reported recently by Taton and coworkers.⁶ 1H - and ^{13}C -NMR assignments are shown on the right. High-resolution mass spectrometry (Figure S26) confirmed product mass. There was a 2.5:1.0 isomeric ratio, however we were unable to ascertain which isomer was the major product.

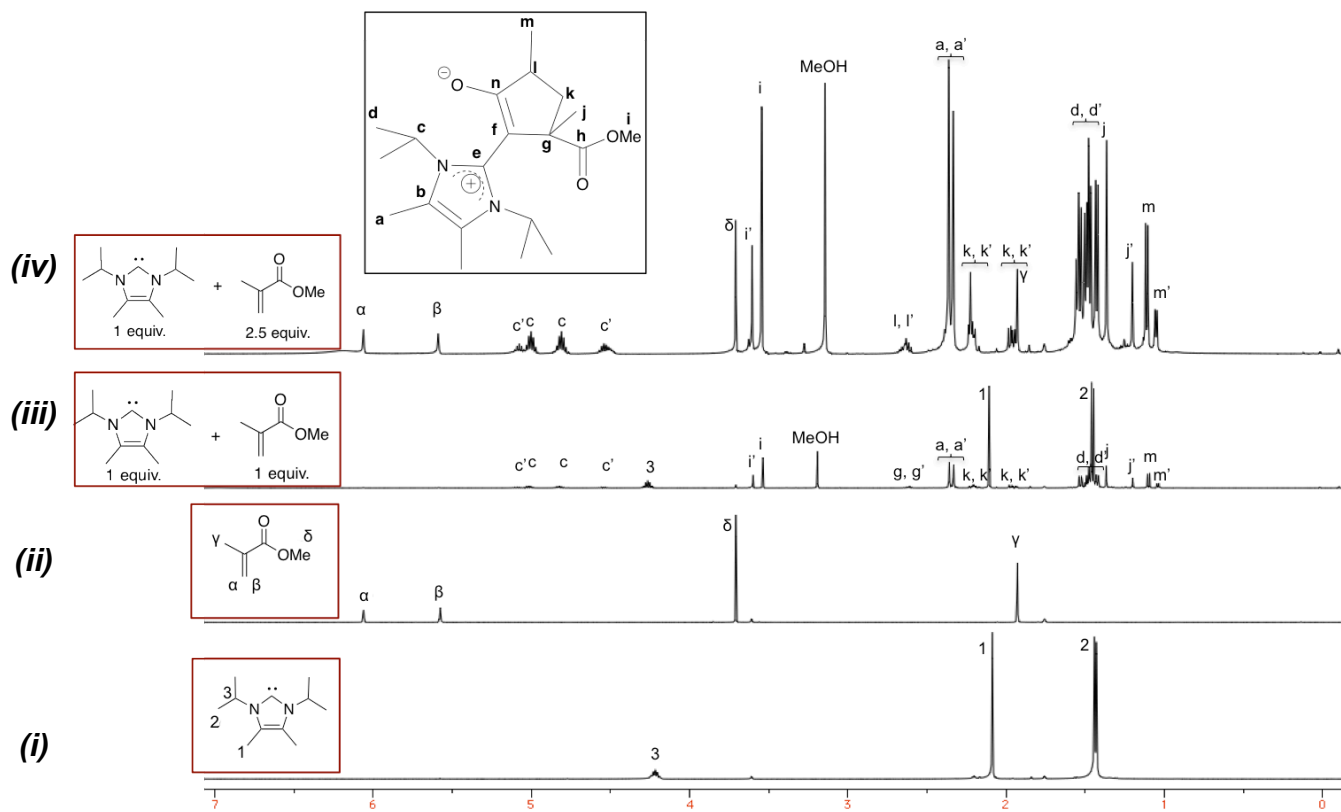


Figure S22. ^1H -NMR spectra (d 8 -THF) of (i) $\text{I}'\text{Pr}_2\text{Me}_2$, (ii) methyl methacrylate (MMA), (iii) a 1:1 mixture of $\text{I}'\text{Pr}_2\text{Me}_2$: MMA, and (iv) a 1:2.5 mixture of $\text{I}'\text{Pr}_2\text{Me}_2$: MMA

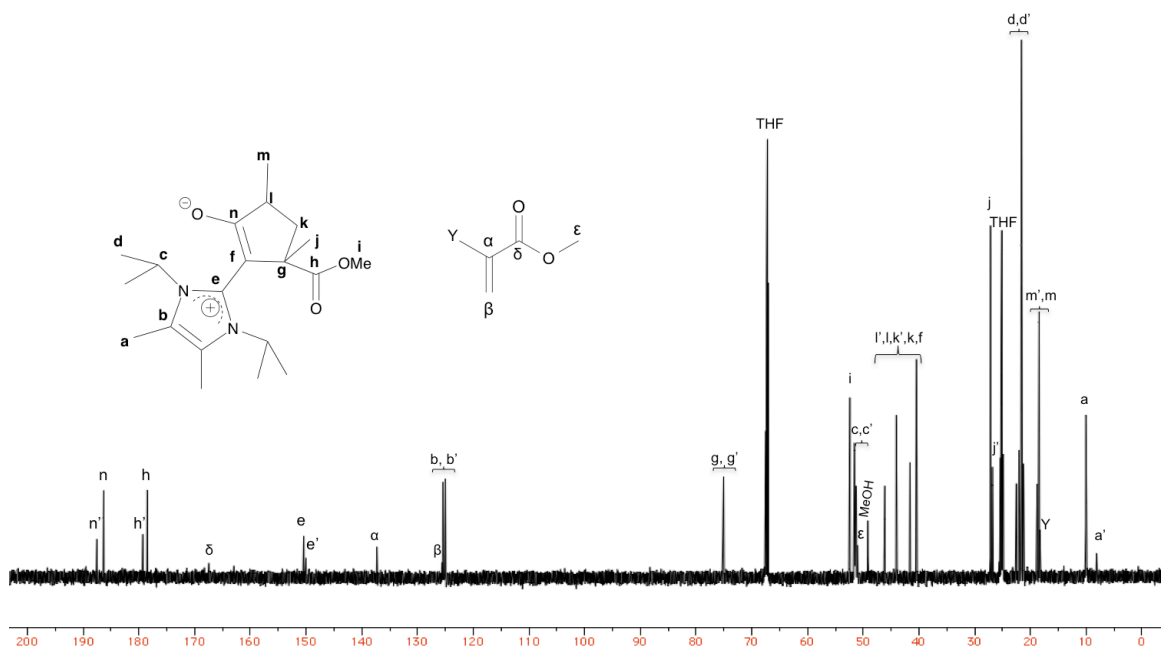
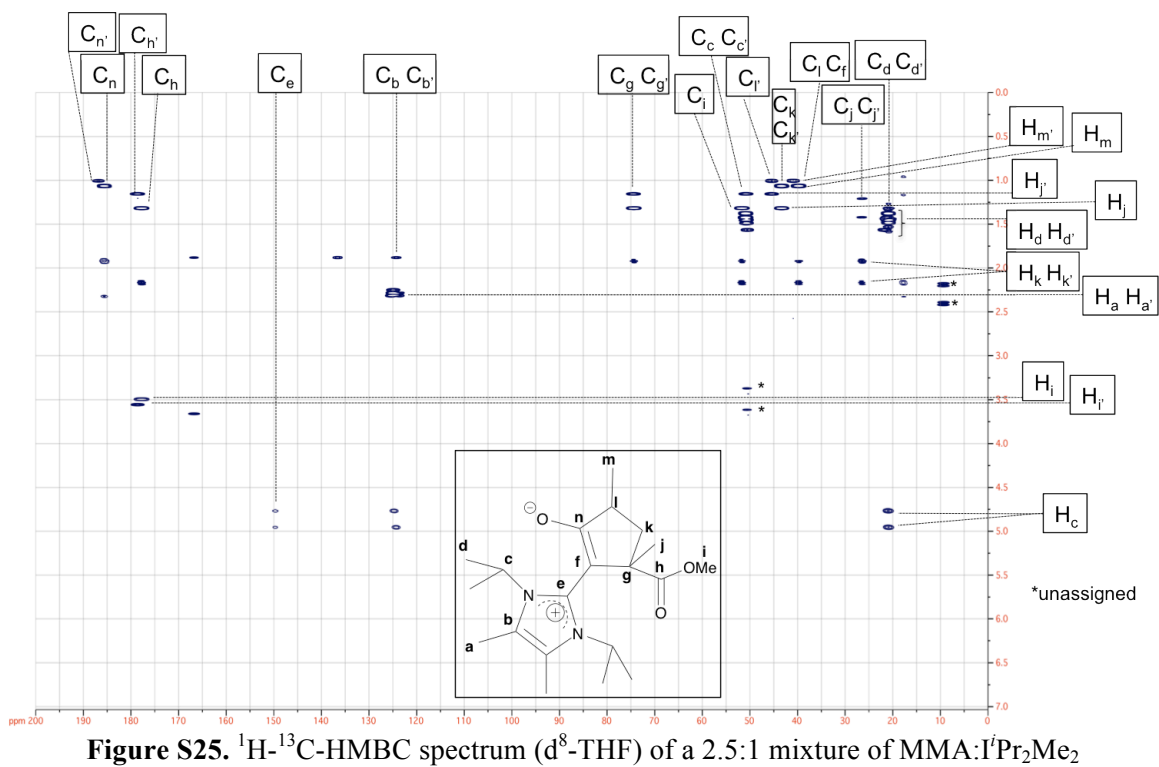
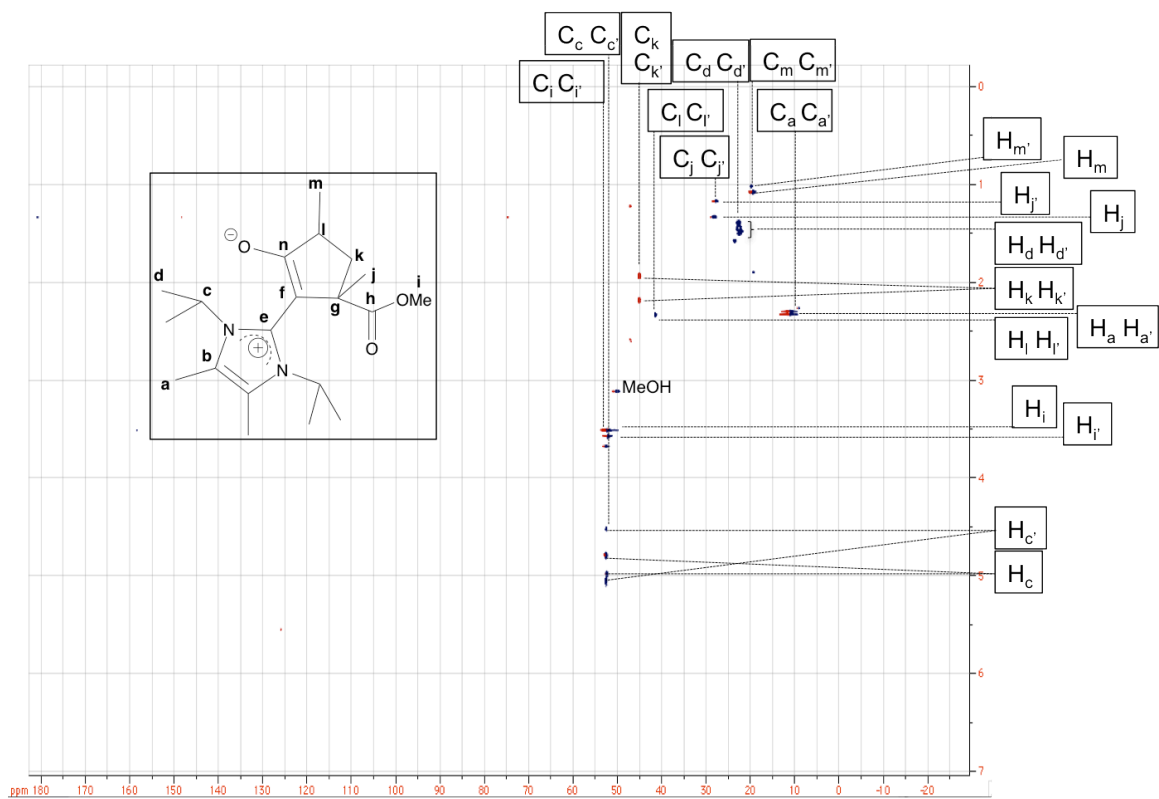


Figure S23. ^{13}C -NMR spectrum (d 8 -THF) of a 2.5:1 mixture of methyl methacrylate: $\text{I}'\text{Pr}_2\text{Me}_2$



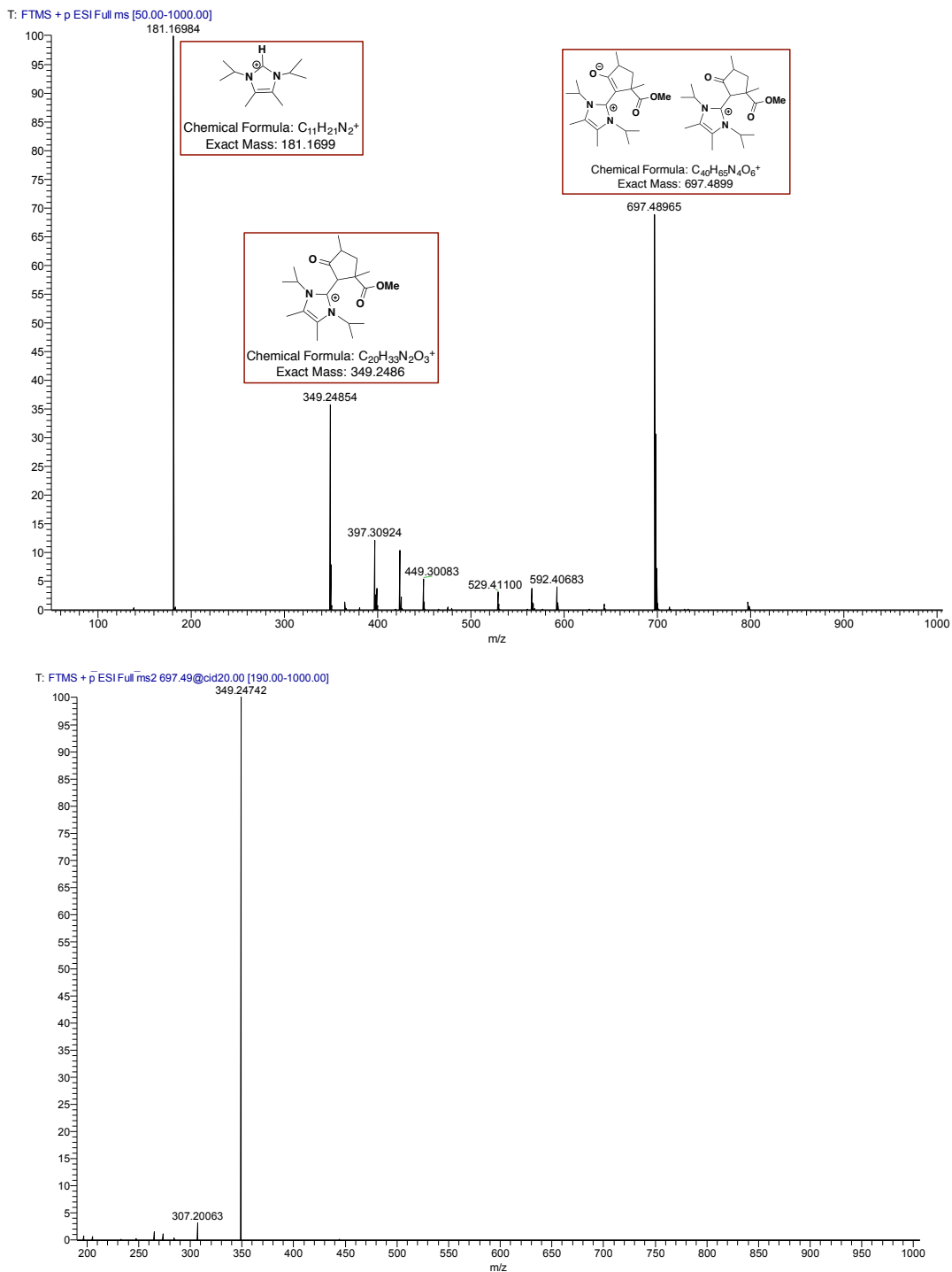
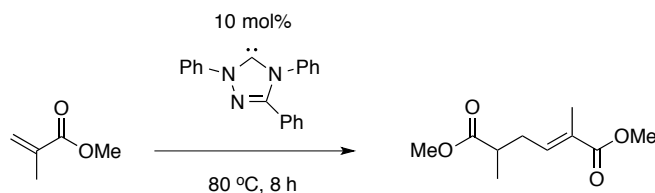


Figure S26. High-resolution DESI mass spectrum of a mixture of spectrum of a 2.5:1 mixture of methyl methacrylate: $I^tPr_2Me_2$ in THF. Top: full spectrum. Bottom: Tandem MS-MS of peak at 697, suggesting that species is an ion pair of two cyclic dimers

5g. Reaction of methyl methacrylate with TPT

Experimental

This was a repeat of literature experiments⁷⁻⁹ to ensure the TPT was of sufficient quality to carry out subsequent reactions with crotonates.



The reagents were added in a nitrogen-filled glovebox, and the reaction vessel used was a 1 dram vial with a screw cap septum. To 50.1 mg of methyl methacrylate (0.500 mmol) was added 14.9 mg of TPT (0.050 mol). The vial was removed from the glovebox, and stirred under nitrogen in an oil bath for 8 hours at 80 °C. An aliquot was then removed, CDCl₃ added and a ¹H-NMR spectrum taken to assess conversion (Figure S27).

Results

Conversion to the tail-to-tail dimer (measured by NMR) was 60%. A crude spectrum is shown in Figure S27.

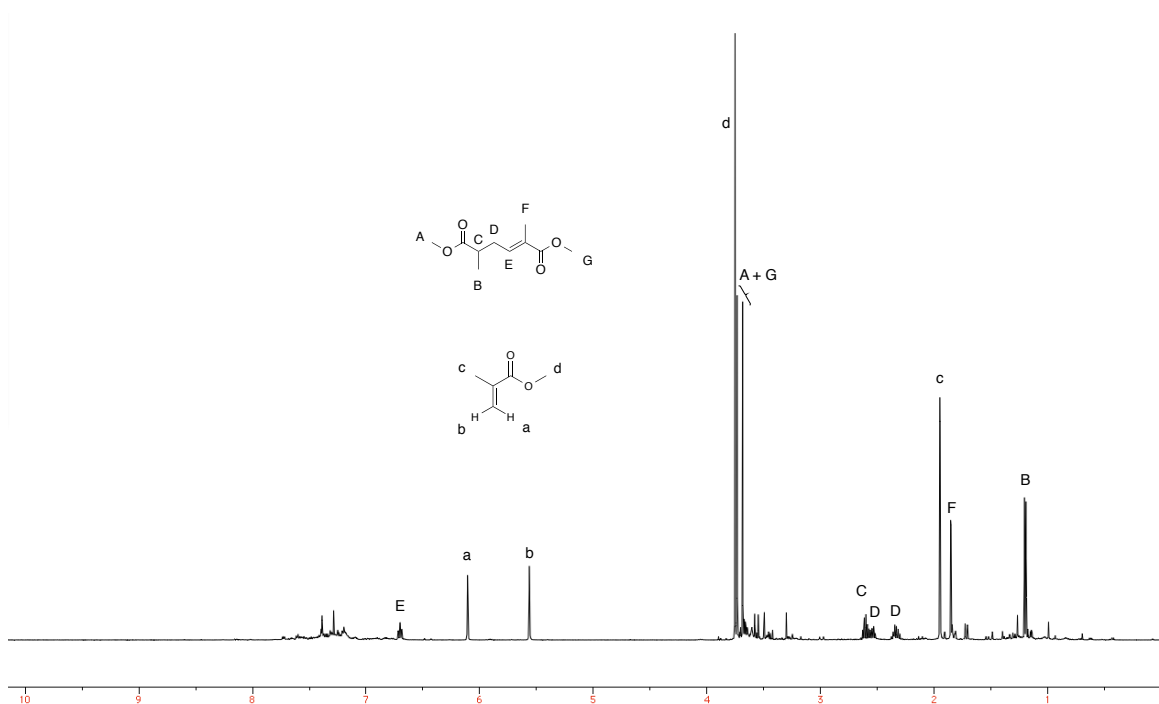
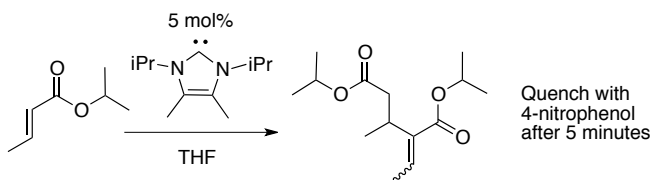


Figure S27. Crude ¹H-NMR spectrum (CDCl₃): methyl methacrylate + 10 mol% TPT (8 h, bulk, 80 °C)

6. Mechanistic Studies by Mass Spectrometry

6a. ESI Tandem MS-MS of 1 M isopropyl crotonate + 5 mol% $I^iPr_2Me_2$ in THF (Scheme 4A, Main Paper)

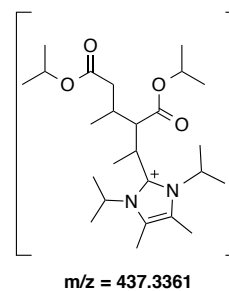
Experimental

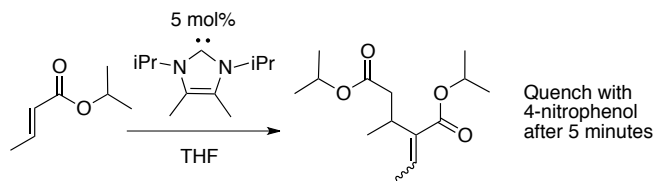


The reaction was performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (10.0 mg, 0.0555 mmol) in THF (1 mL) was added isopropyl crotonate (142.2 mg, 1.10932 mmol) in one portion. The resulting solution was stirred for 5 minutes and then quenched with excess 4-nitrophenol. The solution was diluted to 0.0001 M in THF and injected into a hybrid LTQ-Orbitrap-XL to perform tandem MS-MS. A full spectrum is shown in Figure S28. The peak at m/z 437 (corresponding to the dimer-carbene) adduct was then fragmented by collision induced dissociation (CID). Figure S29 shows the *successive* fragmentation of the peaks at m/z 437.34 (Spectrum A), then 395.29 (Spectrum B), then 353.24 (Spectrum C) and then 311.20 (Spectrum D) respectively.

Results

From Figure S28, a large peak at m/z 437.3361 corresponds to the mass of the isopropyl crotonate dimer plus $I^iPr_2Me_2$. Tandem MS-MS was then performed which allowed for fragmentation of the peak at m/z 437.3361 (Figure S29). The fragmentation pattern shows peaks corresponding to the loss of one (peak a), two (peak b) and three (peak c) isopropyl (C_3H_7) groups from the cation. Further fragmentation of peak b at m/z 353.2419 reveals the loss of the final isopropyl group. At no point in the tandem MS-MS experiment is the loss of $I^iPr_2Me_2$ from the m/z 437.3361 species detected, and we can therefore be confident that the peak at m/z 437.3361 is indeed an addition product between $I^iPr_2Me_2$ and the dimer and not simply an ion pair between $I^iPr_2Me_2$ and dimer. Interestingly, a peak corresponding to an addition product of monomeric isopropyl crotonate and $I^iPr_2Me_2$ was not detected in the ESI-MS experiment, suggesting that either addition of crotonate to $I^iPr_2Me_2$ is followed by rapid enolate addition into a second monomer, or that the peak at m/z 437.3361 is formed by addition of the $I^iPr_2Me_2$ directly into the dimer and that such an addition species may not necessarily be part of the catalytic cycle (Scheme 3, Main Paper).





T: FTMS + p ESI Full ms [50.00-1000.00]

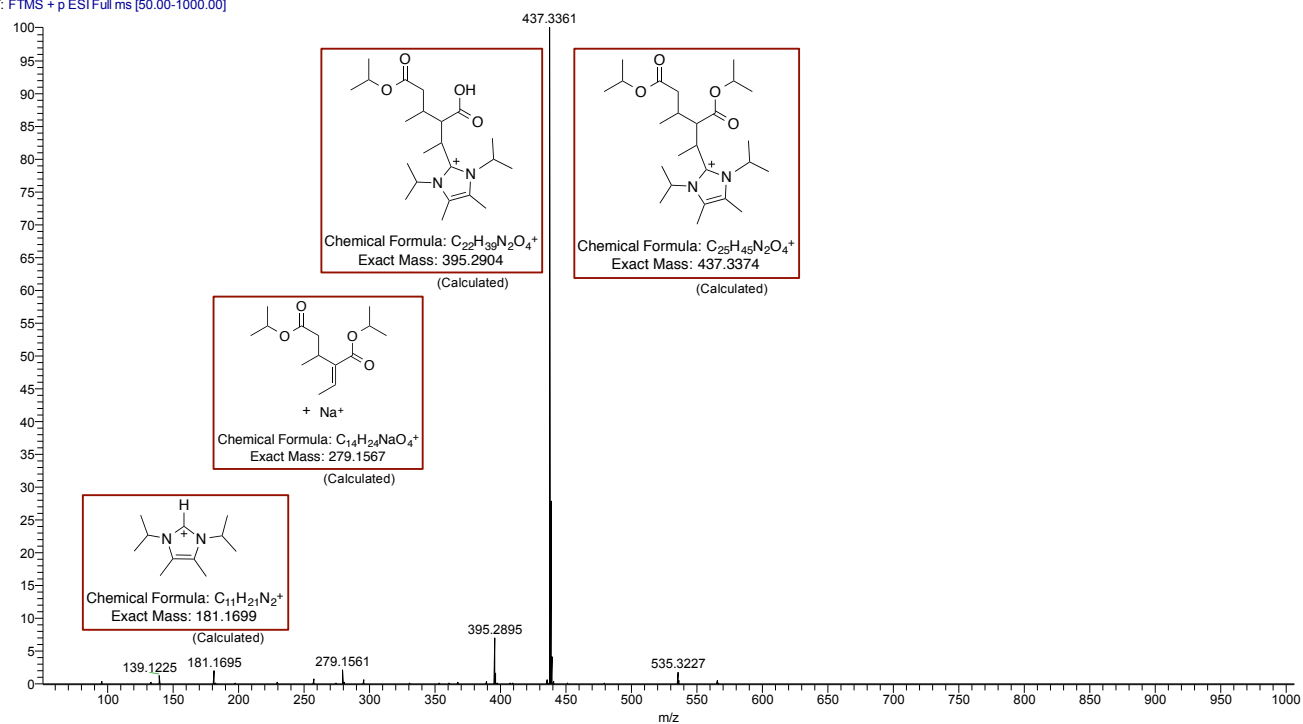
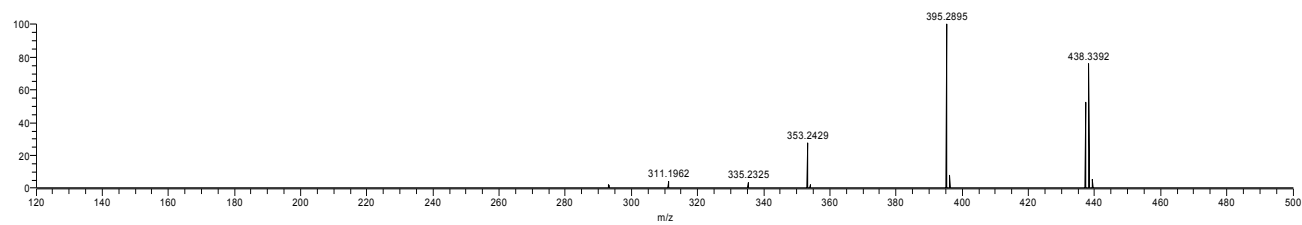
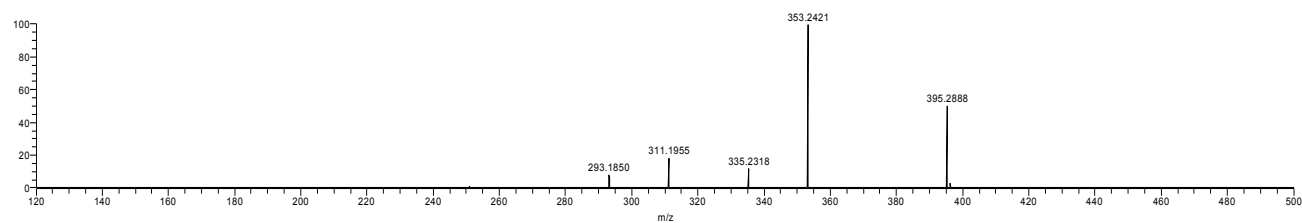


Figure S28. Full high-resolution ESI mass spectrum of 1 M isopropyl crotonate + 5 mol% iPr_2Me_2 in THF, quenched with 4-nitrophenol after 5 minutes

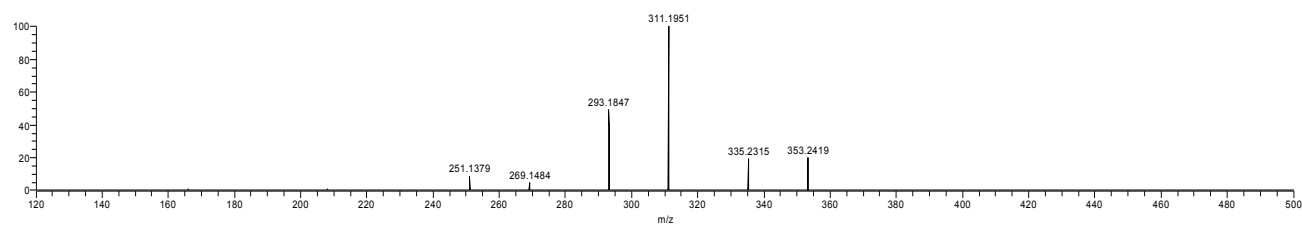
Spectrum A



Spectrum B



Spectrum C



Spectrum D

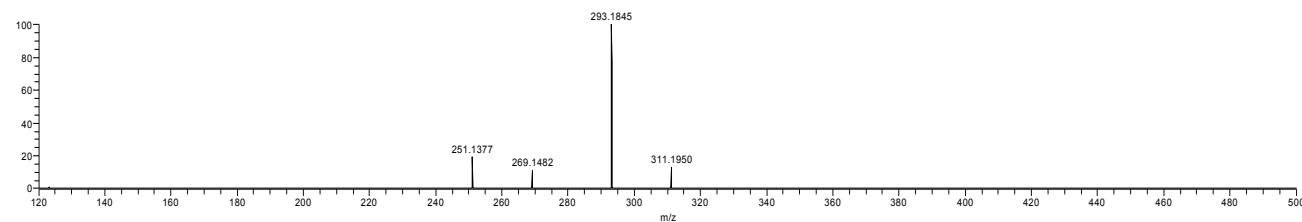
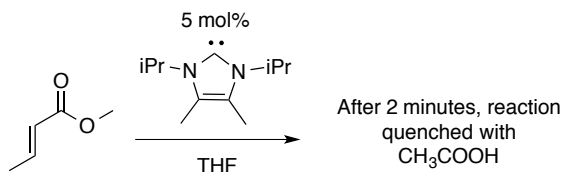


Figure S29. Tandem MS-MS studies successive fragmentation of the peaks at 437.34 (Spectrum A), 395.29 (Spectrum B), 353.24 (Spectrum C) and 311.20 (Spectrum D) respectively

6b. High-resolution ESI-MS study of $i\text{Pr}_2\text{Me}_2$ -catalyzed dimerization of methyl crotonate, quenched with CH_3COOH

Experimental



The reaction was performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (4.5 mg, 0.02496 mmol) in THF (0.5 mL) was added methyl crotonate (50.0 mg, 0.4992 mmol) in one portion. The resulting solution was stirred at room temperature for 120 seconds (corresponding to a monomer conversion of ~25%). The reaction was then quenched by addition of approximately 60 mg of CH_3COOH . The reaction mixture was diluted 100-fold in THF, and immediately taken to a mass spectrometer, where high-resolution ESI-MS was performed.

Results

The resulting spectrum is shown in Figure S30, with zoom-ins of the regions m/z 180-185 and 380-385 shown in Figures S31 and S32 respectively.

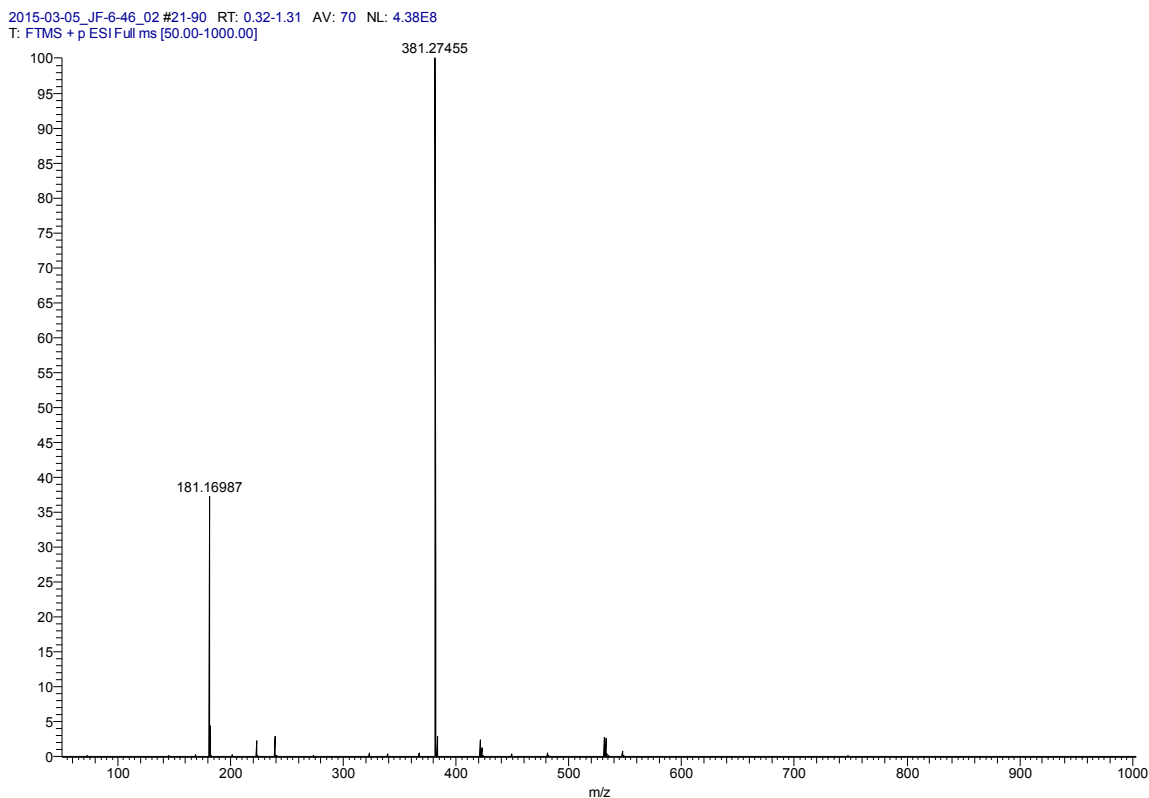


Figure S30. High-resolution ESI-MS of methyl crotonate + 5 mol% $i\text{Pr}_2\text{Me}_2$ in THF, quenched after 2 minutes with CH_3COOH

2015-03-05_JF-6-46_02 #21-90 RT: 0.32-1.31 AV: 70 NL: 1.63E8
T: FTMS + p ESI Full ms [50.00-1000.00]

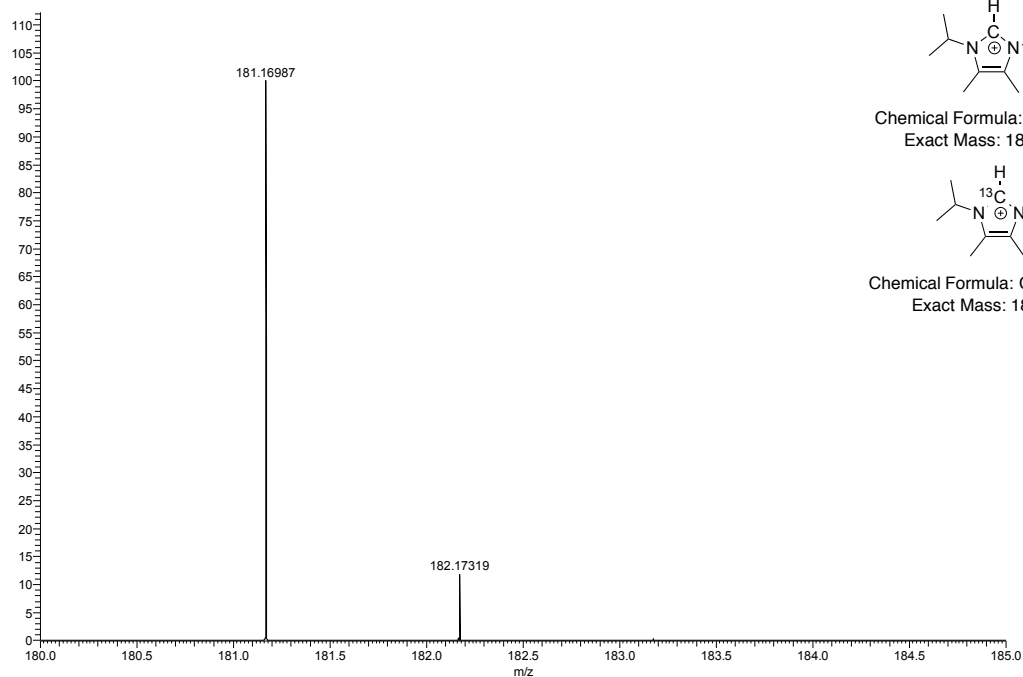


Figure S31. High-resolution ESI-MS of methyl crotonate + 5 mol% iPr_2Me_2 in THF, quenched after 2 minutes with CH_3COOH . (Zoom-in of m/z 180-185)

2015-03-05_JF-6-46_02 #21-90 RT: 0.32-1.31 AV: 70 NL: 4.38E8
T: FTMS + p ESI Full ms [50.00-1000.00]

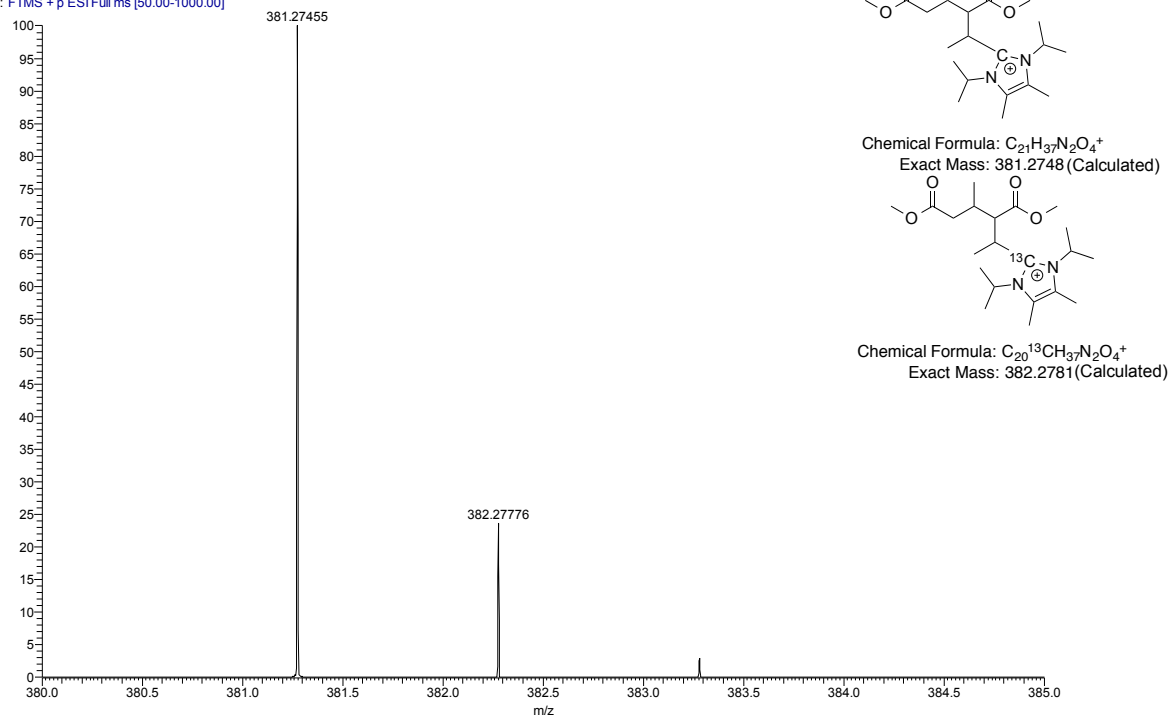
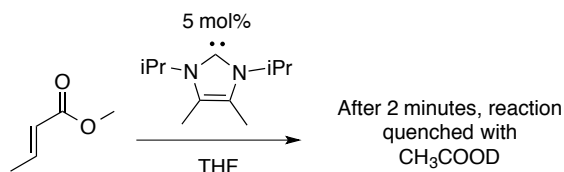


Figure S32. High-resolution ESI-MS of methyl crotonate + 5 mol% iPr_2Me_2 in THF, quenched after 2 minutes with CH_3COOH . (Zoom-in of m/z 380-385)

6c. High-resolution ESI-MS study of $i\text{Pr}_2\text{Me}_2$ -catalyzed dimerization of methyl crotonate, quenched with CH_3COOD

Experimental



The reaction was performed in a 4 mL vial in a nitrogen-filled glovebox at room temperature. To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (4.5 mg, 0.02496 mmol) in THF (0.5 mL) was added methyl crotonate (50.0 mg, 0.4992 mmol) in one portion. The resulting solution was stirred at room temperature for 120 seconds (corresponding to a monomer conversion of ~25%). The reaction was then quenched by addition of approximately 60 mg of CH_3COOD . The reaction mixture was diluted 100-fold in THF, and immediately taken to a mass spectrometer, where high-resolution ESI-MS was performed.

Results

The resulting spectrum is shown in Figure S33, with zoom-ins of the regions m/z 180-185 and 380-385 shown in Figures S34 and S35 respectively.

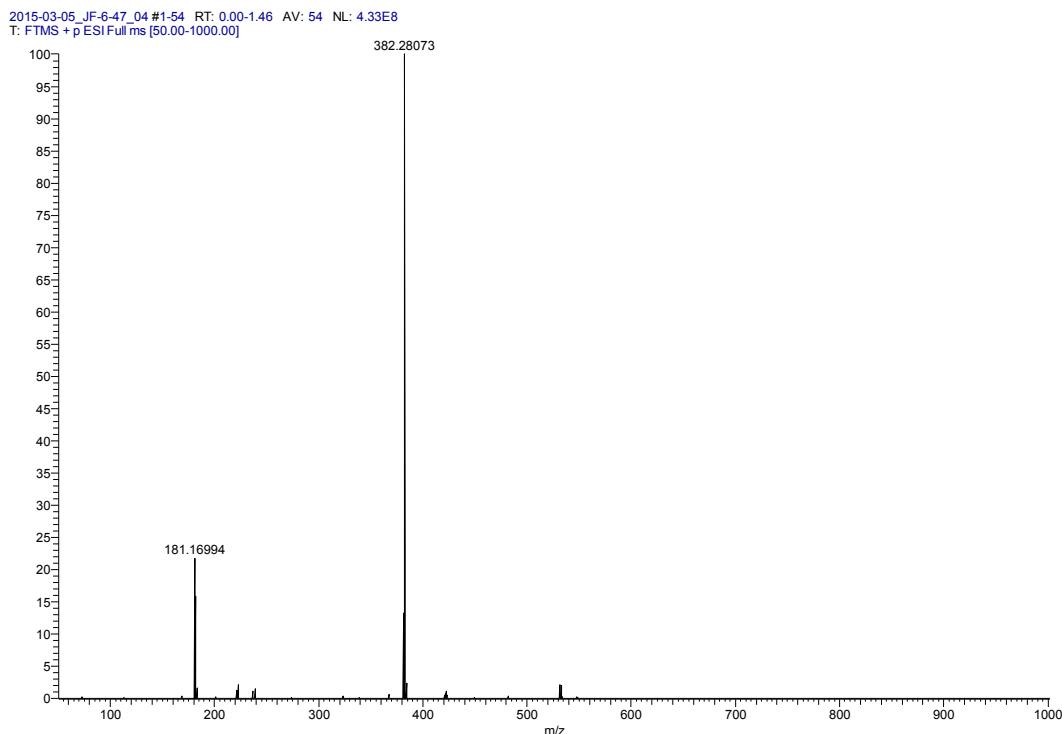
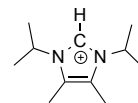
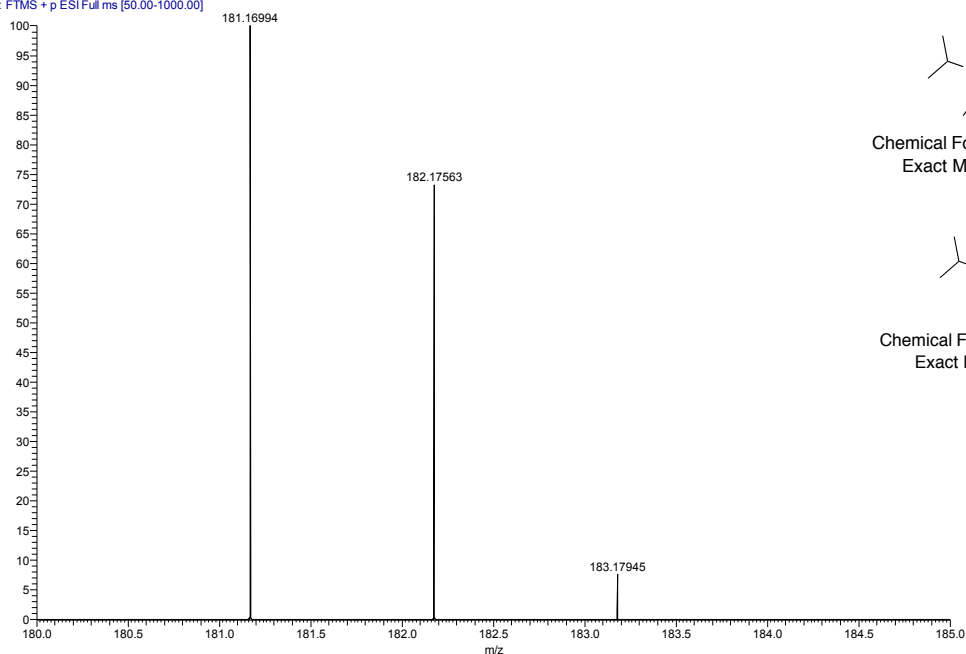
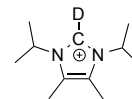


Figure S33. High-resolution ESI-MS of methyl crotonate + 5 mol% $i\text{Pr}_2\text{Me}_2$ in THF, quenched after 2 minutes with CH_3COOD

2015-03-05_JF-6-47_04 #1-54 RT: 0.00-1.46 AV: 54 NL: 9.41E7
T: FTMS + p ESI Full ms [50.00-1000.00]



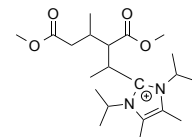
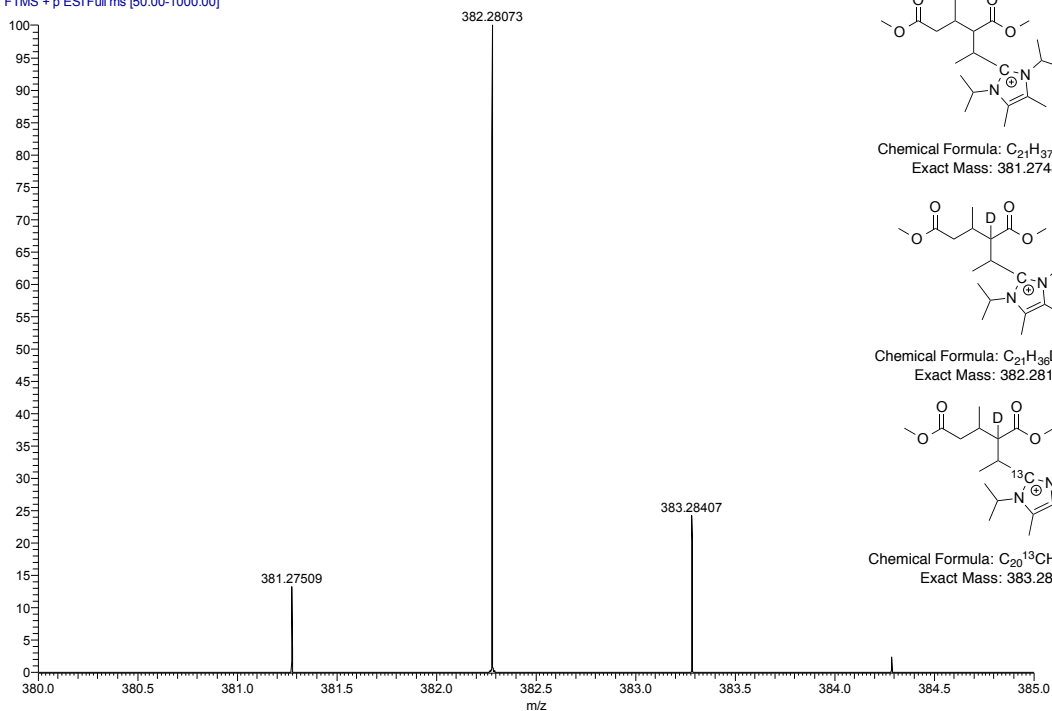
Chemical Formula: $C_{11}H_{21}N_2^+$
Exact Mass: 181.1699 (Calculated)



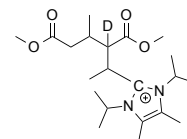
Chemical Formula: $C_{11}H_{20}DN_2^+$
Exact Mass: 182.1762 (Calculated)

Figure S34. High-resolution ESI-MS of methyl crotonate + 5 mol% I'Pr₂Me₂ in THF, quenched after 2 minutes with CH₃COOD. (Zoom-in of *m/z* 180-185)

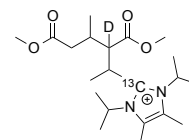
2015-03-05_JF-6-47_04 #1-54 RT: 0.00-1.46 AV: 54 NL: 4.33E8
T: FTMS + p ESI Full ms [50.00-1000.00]



Chemical Formula: $C_{21}H_{37}N_2O_4^+$
Exact Mass: 381.2748 (Calculated)



Chemical Formula: $C_{21}H_{36}DN_2O_4^+$
Exact Mass: 382.2811 (Calculated)



Chemical Formula: $C_{20}^{13}CH_3DN_2O_4^+$
Exact Mass: 383.2844 (Calculated)

Figure S35. High-resolution ESI-MS of methyl crotonate + 5 mol% I'Pr₂Me₂ in THF, quenched after 2 minutes with CH₃COOD. (Zoom-in of *m/z* 380-385)

6d. ESI-MS: 1 M diisopropyl 2-ethylidene-3-methylpentanedioate and 1 M $i^i\text{Pr}_2\text{Me}_2$ in THF, quenched with CH_3COOH

Experimental

To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (7.0 mg, 0.0390 mmol) in THF (0.080 mL) was added diisopropyl 2-ethylidene-3-methylpentanedioate (10.0 mg, 0.0390 mmol) (prepared via KO^tBu -catalyzed dimerization) in one portion. The resulting solution was stirred for 5 minutes and then quenched with 35 mg CH_3COOH . The solution was diluted to 0.0001 M in THF and injected into a hybrid LTQ-Orbitrap-XL to perform ESI mass spectrometry.

Results

Figure S36 shows the spectrum obtained with zoomed-in areas displayed on the subsequent pages.

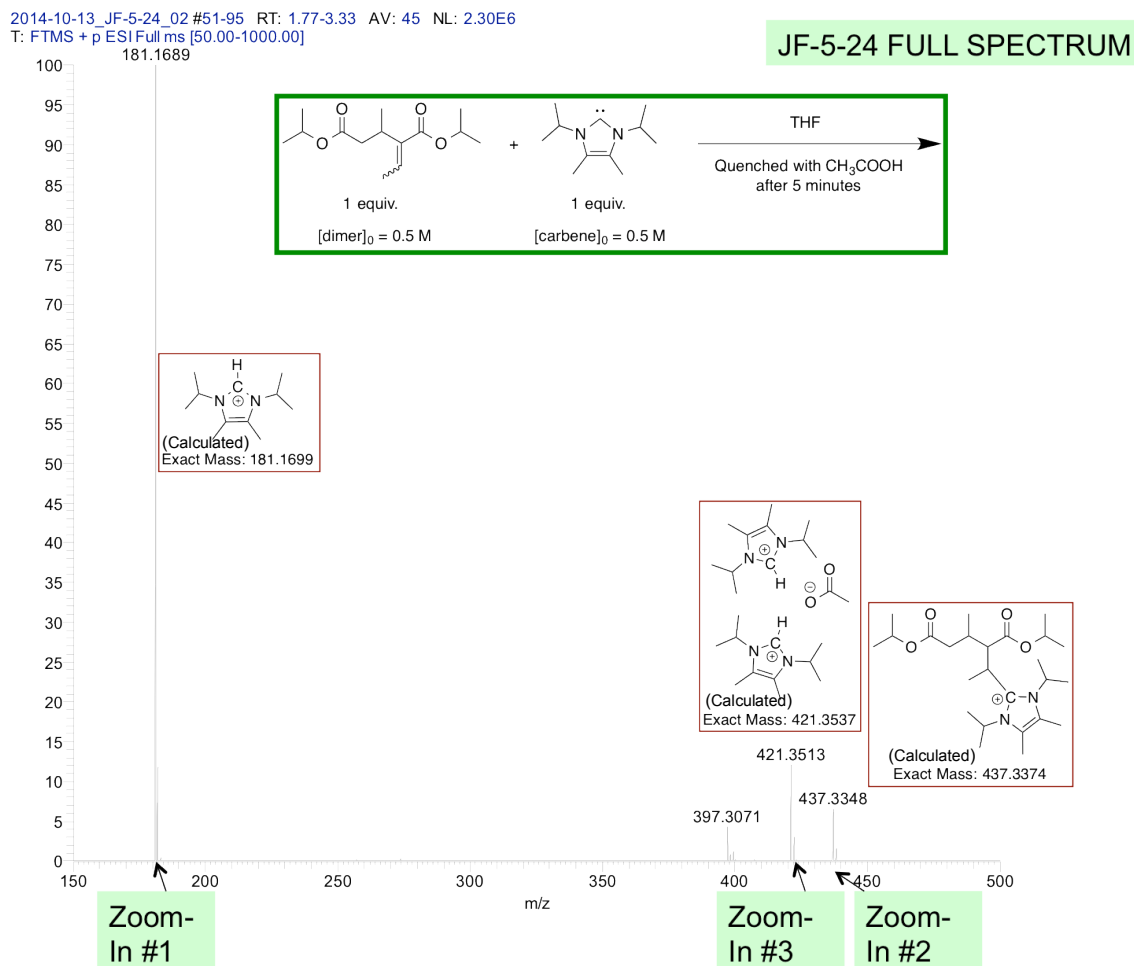


Figure S36. ESI-MS studies of 1 equiv. diisopropyl 2-ethylidene-3-methylpentanedioate + 1 equiv. $i^i\text{Pr}_2\text{Me}_2$, quenched with CH_3COOH after 5 minutes: full spectrum shown, along with the zoomed-in areas displayed on the next two pages

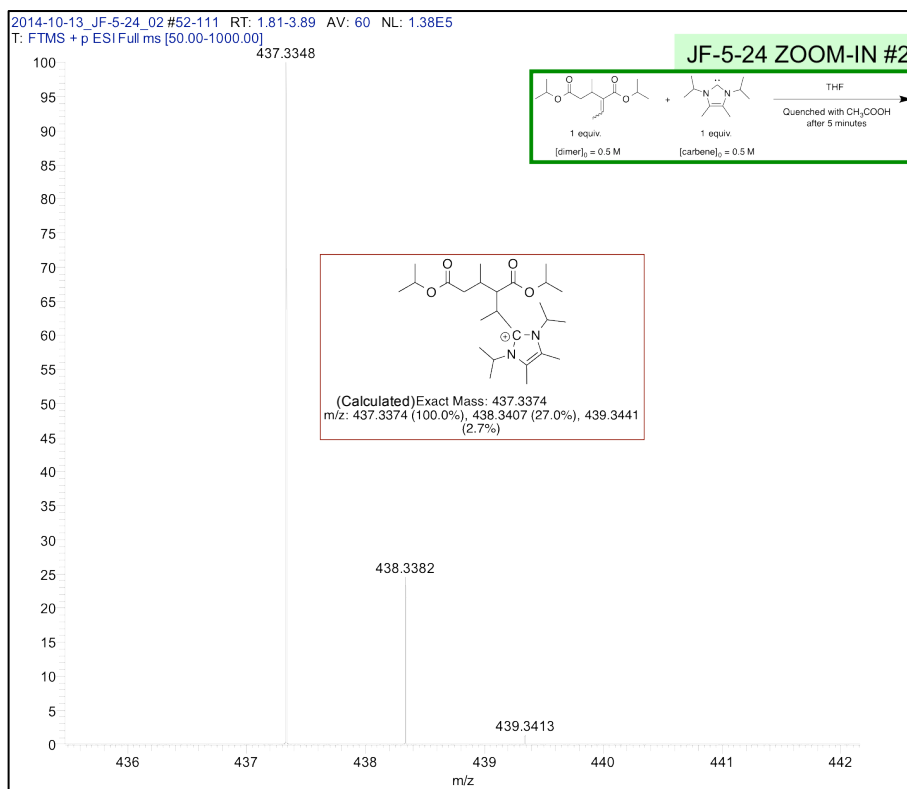
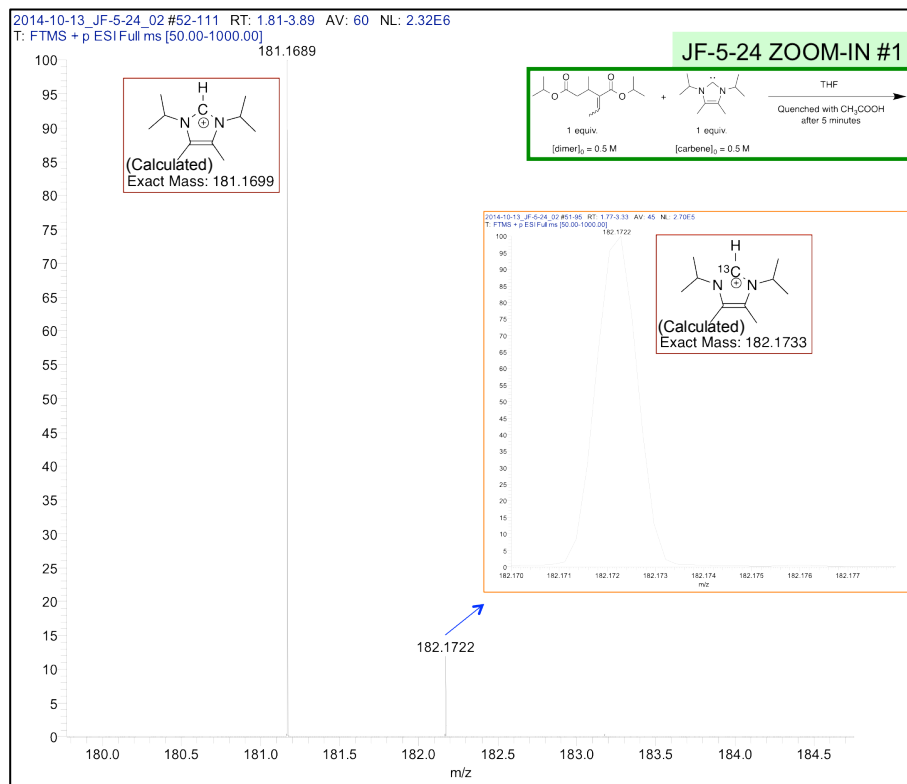


Figure S36 (continued)

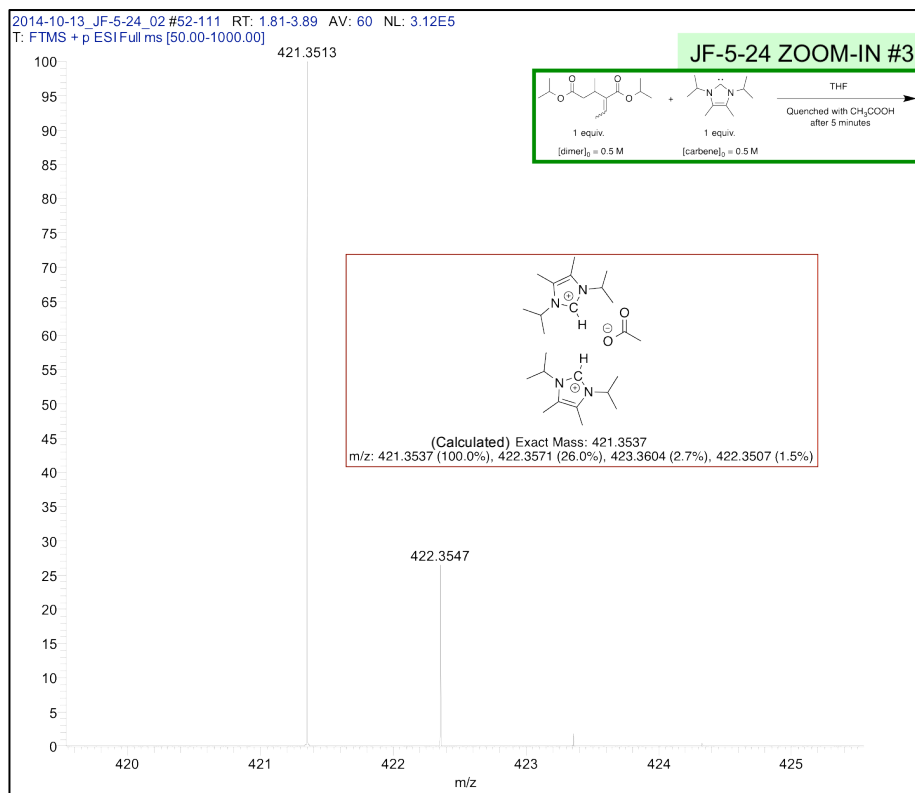


Figure S36 (continued)

6e. ESI-MS: 1 M diisopropyl 2-ethylidene-3-methylpentanedioate and 1 M $i\text{Pr}_2\text{Me}_2$ in THF, quenched with CH_3COOD

Experimental

To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (7.0 mg, 0.0390 mmol) in THF (0.080 mL) was added diisopropyl 2-ethylidene-3-methylpentanedioate (10.0 mg, 0.0390 mmol) (prepared via KO^tBu -catalyzed dimerization) in one portion. The resulting solution was stirred for 5 minutes and then quenched with 35 mg CH_3COOD . The solution was diluted to 0.0001 M in THF and injected into a hybrid LTQ-Orbitrap-XL to perform ESI mass spectrometry.

Results

Figure S37 shows the spectrum obtained with zoomed-in areas.

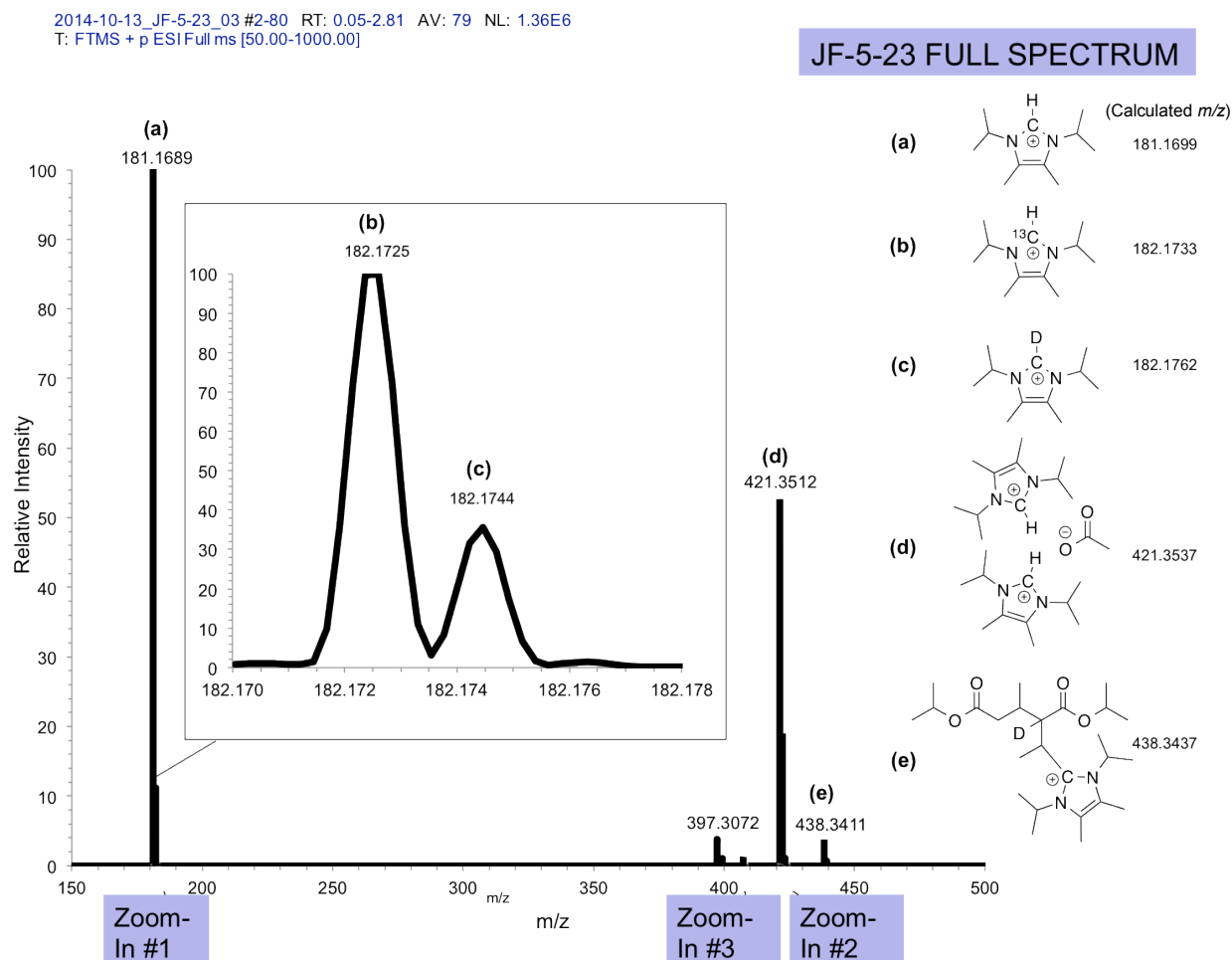


Figure S37. ESI MS studies of 1 equiv. diisopropyl 2-ethylidene-3-methylpentanedioate + 1 equiv. $i\text{Pr}_2\text{Me}_2$, quenched with CH_3COOD after 5 minutes: full spectrum shown, with zoomed in areas displayed on the next two pages (Lines have been thickened to aid inspection)

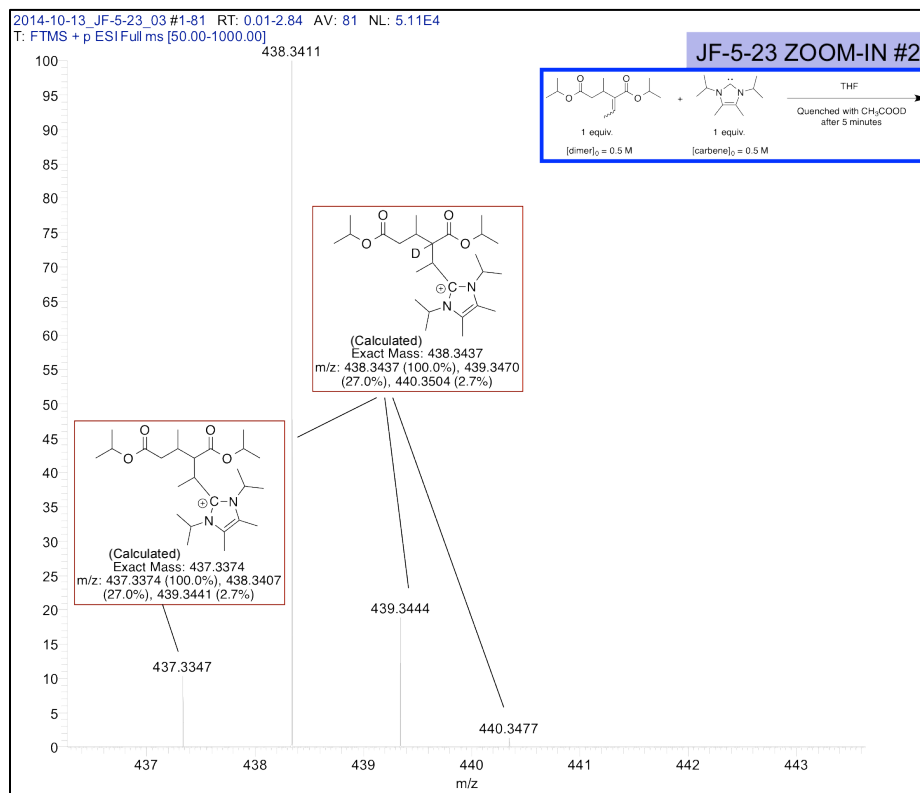
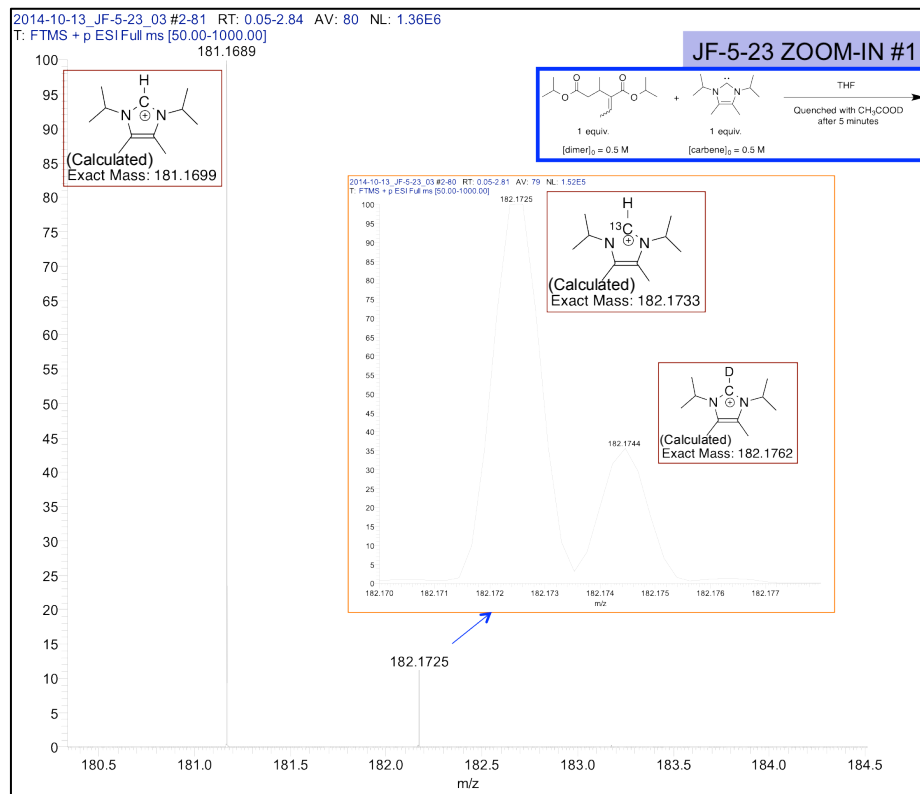


Figure S37 (continued)

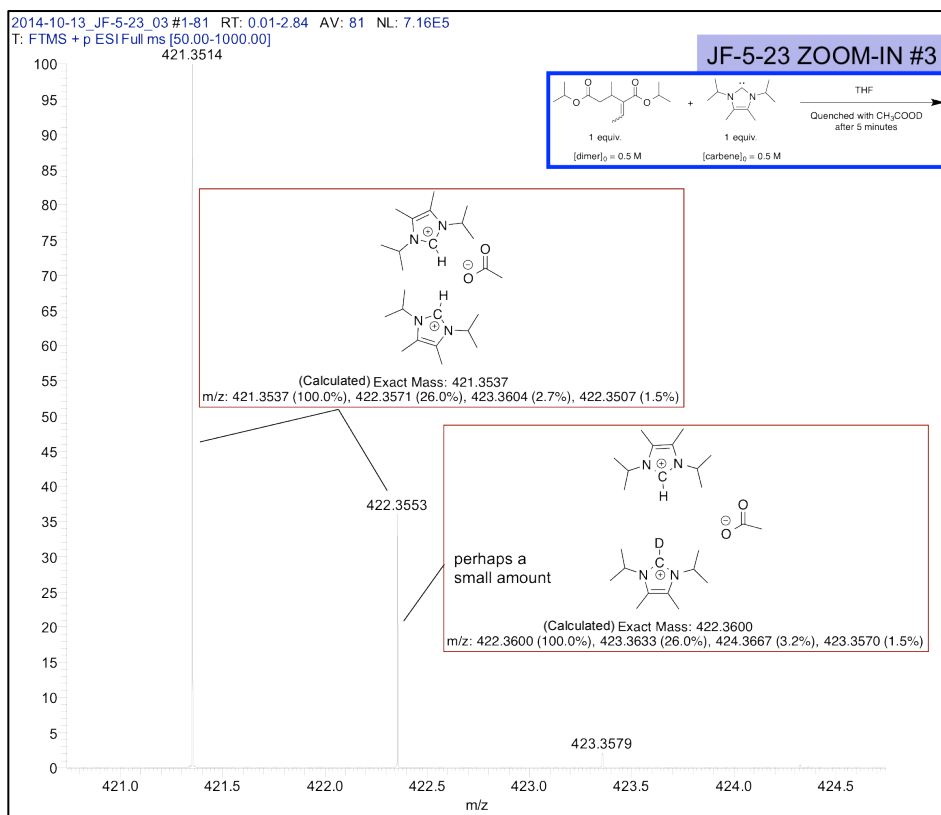
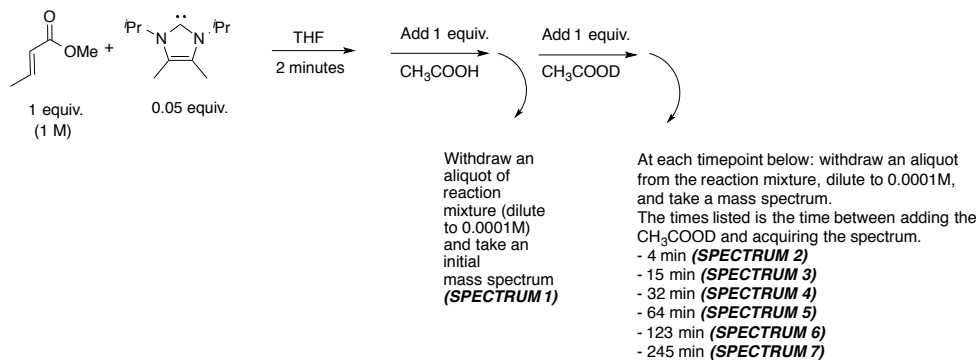


Figure S37 (continued)

6f. ESI-MS: to assess potential contribution from H/D exchange on peak intensities in mass spec mechanistic experiments

Experimental



To a stirred solution of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (9.0 mg) in THF (0.5 mL) was added a solution of diisopropyl 2-ethylidene-3-methylpentanedioate (100.1 mg) in THF (0.5 mL) in one portion. The resulting solution was stirred for 5 minutes and then quenched with 60 mg CH_3COOH . 0.1mL of the reaction mixture was removed, diluted to 0.0001M in THF, and injected into a hybrid LTQ-Orbitrap-XL to perform ESI mass spectrometry. To the remaining reaction mixture (0.9 mL) was added CH_3COOD . At various time-points, 0.1mL aliquots were removed, diluted to 0.0001M in THF, and injected into a hybrid LTQ-Orbitrap-XL to perform ESI mass spectrometry, and the observed relative peak intensities noted in Tables S2 and S3.

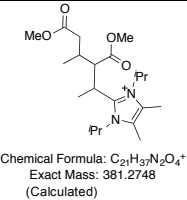
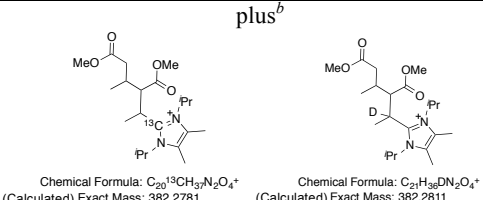
Results

Table S2. Imidazolium peaks at (m/z) 181-182 at each time-point

Spectrum ^a	Time (minutes) after addition of CH_3COOD to the already CH_3COOH -quenched reaction mixture	Relative Peak Intensities		
		 Chemical Formula: $\text{C}_{11}\text{H}_{21}\text{N}_2^+$ Exact Mass: 181.1699 (Calculated)	 Chemical Formula: $\text{C}_{10}^{13}\text{CH}_{21}\text{N}_2^+$ Exact Mass: 182.1733 (Calculated)	 Chemical Formula: $\text{C}_{11}\text{H}_{20}\text{DN}_2^+$ Exact Mass: 182.1762 (Calculated)
Spectrum 1	no CH_3COOD	100	12	< 0.1
Spectrum 2	4	100	12	0.2
Spectrum 3	15	100	12	0.1
Spectrum 4	32	100	12	0.2
Spectrum 5	64	100	12	0.3
Spectrum 6	123	100	12	0.1
Spectrum 7	245	100	12	0.1

^aSee Section 11 of this Supporting Information for these spectra.

Table S3. NHC-dimer adduct peaks at (*m/z*) 381-382 at each time-point

Spectrum ^a	Time (minutes) after addition of CH ₃ COOD to the already CH ₃ COOH- quenched reaction mixture	Relative Peak Intensities	
			plus ^b 
Spectrum 1	no CH ₃ COOD	100	23
Spectrum 2	4	100	23
Spectrum 3	15	100	23
Spectrum 4	32	100	24
Spectrum 5	64	100	23
Spectrum 6	123	100	24
Spectrum 7	245	100	24

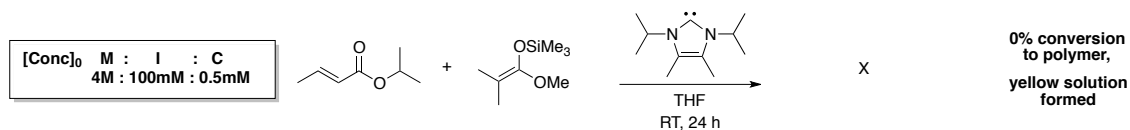
^aSee Section 11 of this Supporting Information for these spectra.

^bIn this case the deuterated peak and the ¹³C peak may have merged.

From these results we can see that the addition of an equimolar amount of CH₃COOD to an already CH₃COOH-quenched reaction mixture has a negligible impact on species detected by mass spec, even after 4 hours. All the mass spectra in this paper were acquired within 1 hour of quenching the reaction mixture. Therefore, we can be confident that species in the mass spectra in this manuscript are not ascribable to H/D exchange arising from quenching the reaction mixture.

The mass spectra for this experiment are given in Section 11 of this Supporting Information.

7. Attempted NHC-catalyzed Group Transfer Polymerization of isopropyl crotonate



(where M = isopropyl crotonate; I = initiator = MTS silyl ketene acetal; C = catalyst = $\text{I}^t\text{Pr}_2\text{Me}_2$)

The reaction was performed inside a nitrogen-filled glovebox. A stock solution of $\text{I}^t\text{Pr}_2\text{Me}_2$ was prepared by dissolving 3.0 mg (0.0166 mmol) of $\text{I}^t\text{Pr}_2\text{Me}_2$ in 2 mL of THF. From this solution, 0.100 mL was withdrawn and added to a vial (equipped with a magnetic stir bar) containing 0.570 mL of THF. To this vial was added 0.035 mL (0.174 mmol) of MTS silyl ketene acetal. With stirring, 1.000 mL of isopropyl crotonate (6.94 mmol) was then added over 3 minutes at room temperature. Immediately after addition of the isopropyl crotonate the solution turned yellow. After 24h, methanol was added to quench the reaction and the solution turned clear. The solution was then analyzed by ^1H -NMR (Figure S38), which showed negligible transformation of any of the starting crotonate.

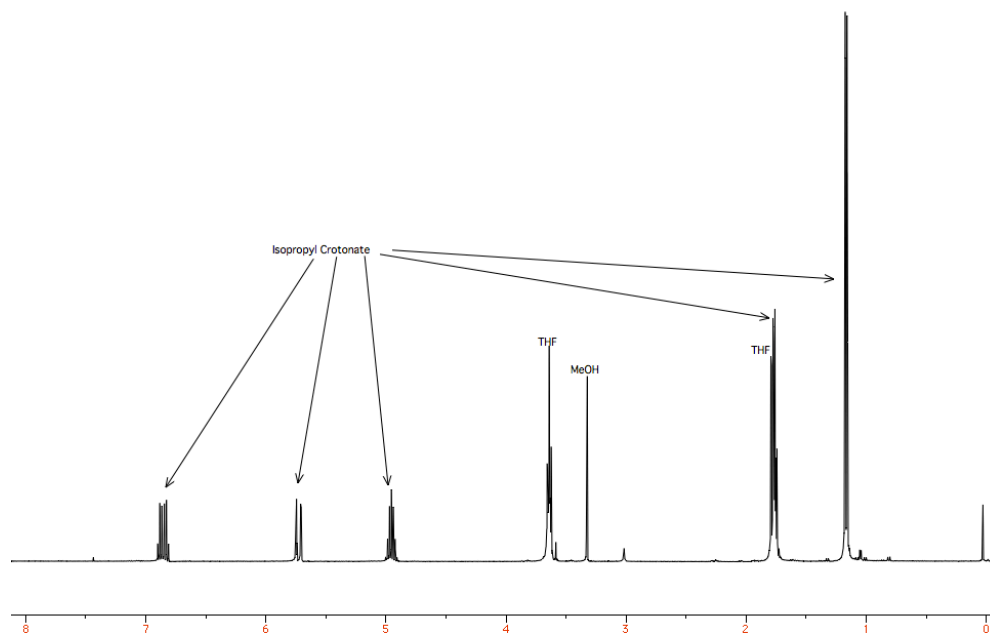
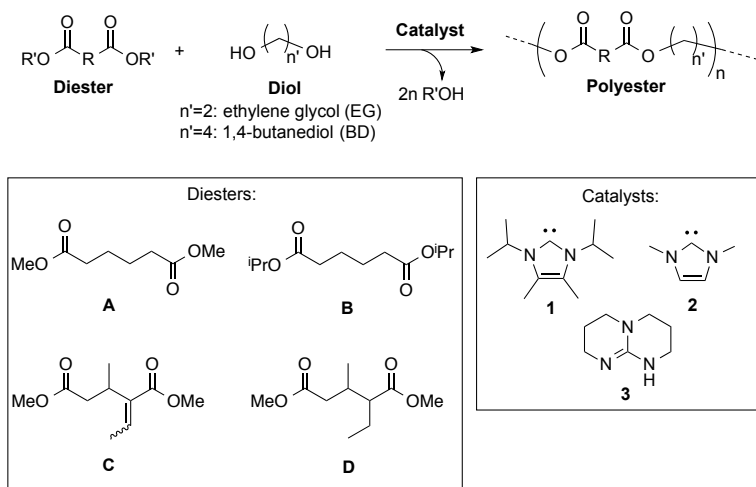


Figure S38. ^1H -NMR (CDCl_3) of attempted $\text{I}^t\text{Pr}_2\text{Me}_2$ -catalyzed GTP of isopropyl crotonate (24 hours)

8. Polymerization Screening: Step-growth by transesterification

Reactions were carried out in a Schlenk flask or in glass vials fitted with a septum screw cap. In a nitrogen-filled glovebox, the diester, diol and catalyst were added to the reaction flask, the flask sealed and brought into a fume hood. The reaction mixture was then subjected to the conditions listed in Table S4.

Table S4. Polymerization Screening



Entry	Diester	Diol	Stoichiometry diester:diol	Catalyst	Conditions	% Yield ^a	M _n ^a	M _w /M _n ^a
1	A	EG	1:1	2	^b	73	3569	1.38
2	A	EG	1:1.2	3	^c	24	2688	1.26
3	A	EG	1:1	1	^d	43	4933	1.33
4	A	EG	1:2	1	^d	^e	634	1.08
5	A	EG	1:5	1	^d	^e	654	1.05
6	A	EG	1:1.3	1	^f	45	6126	1.35
7	A	BD	1:1	1	^d	43	9210	1.46
8	A	BD	1:1	1	^f	39	9309	1.50
9	A	BD	1:1.1	1	^f	40	9965	1.47
10	A	BD	1:1.3	1	^f	48	16325	1.33
11	A	BD	1:1.5	1	^f	47	7013	1.30
12	A	BD	1:1	none	^g	6	2543	1.62
13	B	EG	1:1	1	^h	13, 82 ⁱ	1625, 1173 ⁱ	1.27, 1.01 ⁱ
14	B	EG	1:1.5	3	^j	24	757	1.25
15	C	BD	1:1.3	1	^f	17, 78 ⁱ	9522, 3254 ⁱ	3.30, 3.33 ⁱ
16	C	BD	1:1.3	1	^k	87	4213	3.81
17	D	BD	1:1.3	1	^k	86	4036	1.78
18	D	BD	1:1.3	3	^k	85	875	1.72

Conditions for Table S4:

^aIn most cases the yield, M_n and M_w/M_n are taken for the crude sample, with any residual solvent simply evaporated at the end of the reaction, and the weight, M_n (by PS-calibrated GPC) and M_w/M_n (by PS-calibrated GPC) of the crude sample recorded.

^bCatalyst **2** was generated in situ by the reaction of 0.1 equiv. 1,3-dimethylimidazolium methyl sulphate with 0.08 equiv. potassium *tert*-butoxide in 2 mL THF, and stirred for 1 h before being filtered into a Schlenk flask, to which diester A (0.531 g, 1 equiv.) and EG (1 equiv.) were added. The Schlenk flask was then evacuated on a vacuum line and stirred for 24 hours at 65 °C.

^cCatalyst **3** (0.002 equiv.) was added to A (0.531 g, 1 equiv.) and EG (1.2 equiv.) in a round bottom flask in a nitrogen-filled glovebox and sealed with a rubber septum. The flask was then removed from the glovebox and placed in a hood, and the septum quickly exchanged for a short-path vacuum distillation apparatus. The flask was then heated at 105 °C under N₂ for 2 hours, and then cooled to 80 °C before being slowly opened to vacuum. When full vacuum was achieved the flask was heated in steps to (temperature °C, time hrs): (85,0.5 ; 90,0.5 ; 100,1.25 ; 115,1 ; 130,0.5 ; 150,0.5 ; 170,0.5).

^dIn a nitrogen-filled glovebox, catalyst **1** (0.05 equiv) was added to a solution of diester A (50 mg) and diol in 2 mL THF in a 4 mL vial with a septum screw cap. The vial was removed from the glovebox, placed on a vacuum line and stirred under vacuum for 24 hours at 65 °C.

^eCrude reaction mixture at end of reaction consisted primarily of monomer.

^fIn a nitrogen-filled glovebox, catalyst **1** (0.05 equiv) was added to a solution of diester A (50 mg) and diol in 2 mL THF in a 4 mL vial with a septum screw cap. The vial was removed from the glovebox, placed on a vacuum line and stirred under vacuum for 24 hours at 65 °C, 23 hours at 100 °C and 1 hour at 120 °C.

^gIn a nitrogen-filled glovebox, diester A (50 mg) was added to the diol in 2 mL THF in a 4 mL vial with a septum screw cap. The vial was removed from the glovebox, placed on a vacuum line and stirred under vacuum for 24 hours at 65 °C, 23 hours at 100 °C and 1 hour at 120 °C.

^hIn a nitrogen-filled glovebox, in a round bottomed flask fitted with a vacuum adapter, catalyst **1** (0.001 equiv.) was added to diester B (0.531 g, 1 equiv.) and EG (1 equiv.). The flask was removed from the glovebox and the reaction mixture stirred under vacuum for 24h at 85 °C.

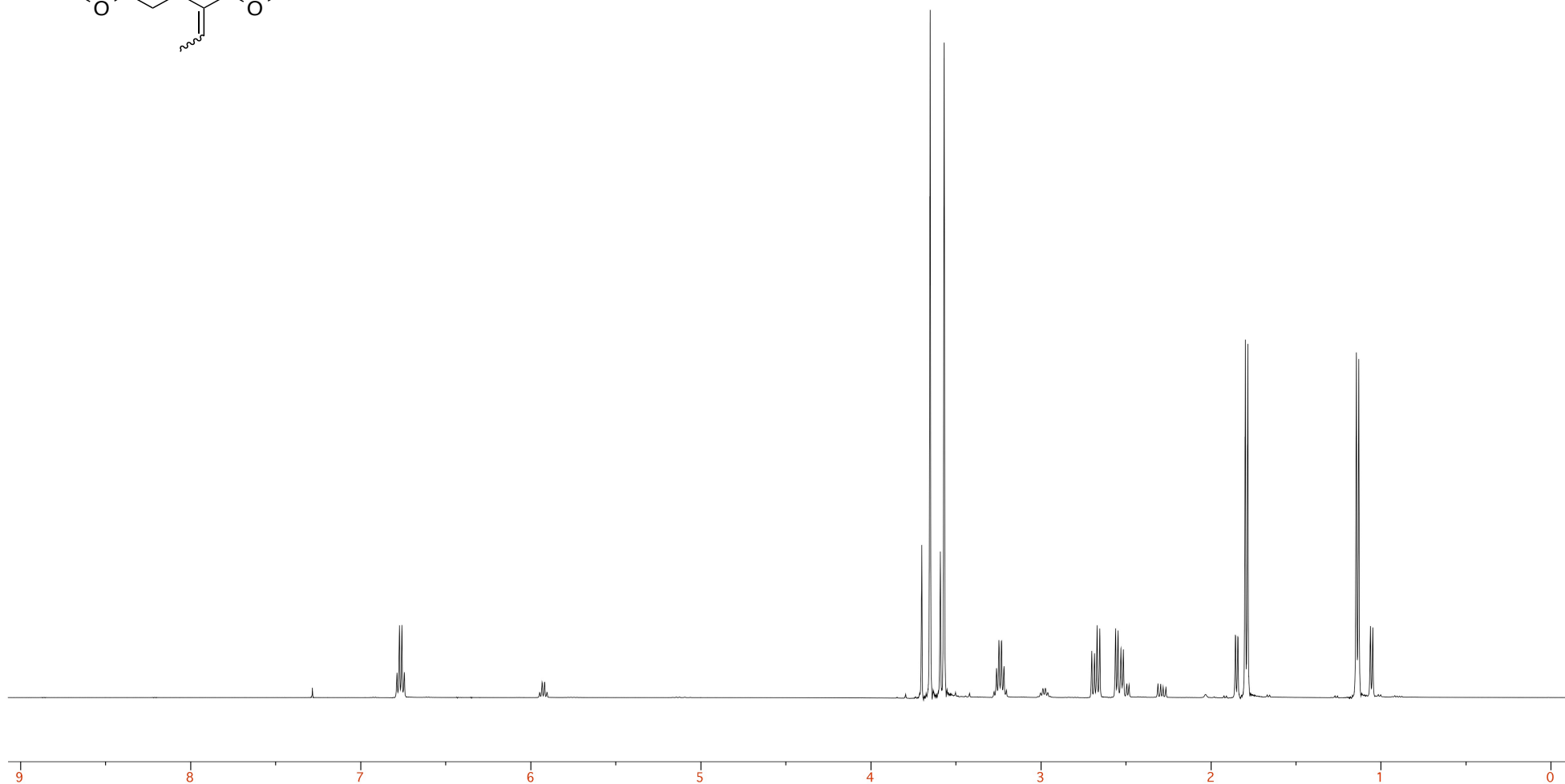
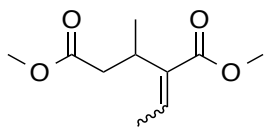
ⁱIn these cases, the crude polymer produced was precipitated in methanol. The first number details the methanol-insoluble fraction, the second number details the methanol-soluble fraction.

^jCatalyst **3** (0.002 equiv.) added to diester B (1.277 g, 1 equiv.) and EG (1.5 equiv.) in a round bottom flask in a nitrogen-filled glovebox and sealed with a rubber septum. The flask was then removed from the glovebox and placed in a hood, and the septum quickly exchanged for a short-path vacuum distillation apparatus. The flask was then placed on a vacuum distillation apparatus and heated under nitrogen in steps to (temperature °C, time hrs): (100,0.5 ; 125,0.25 ; 140,0.25 ; 150,0.5 ; 130,0.5 ; 150,0.5 ; 180,1 ; 200,1.5). After this time (and at 200 °C) the flask was opened to vacuum and the reaction stirred for a further 3.5 hours.

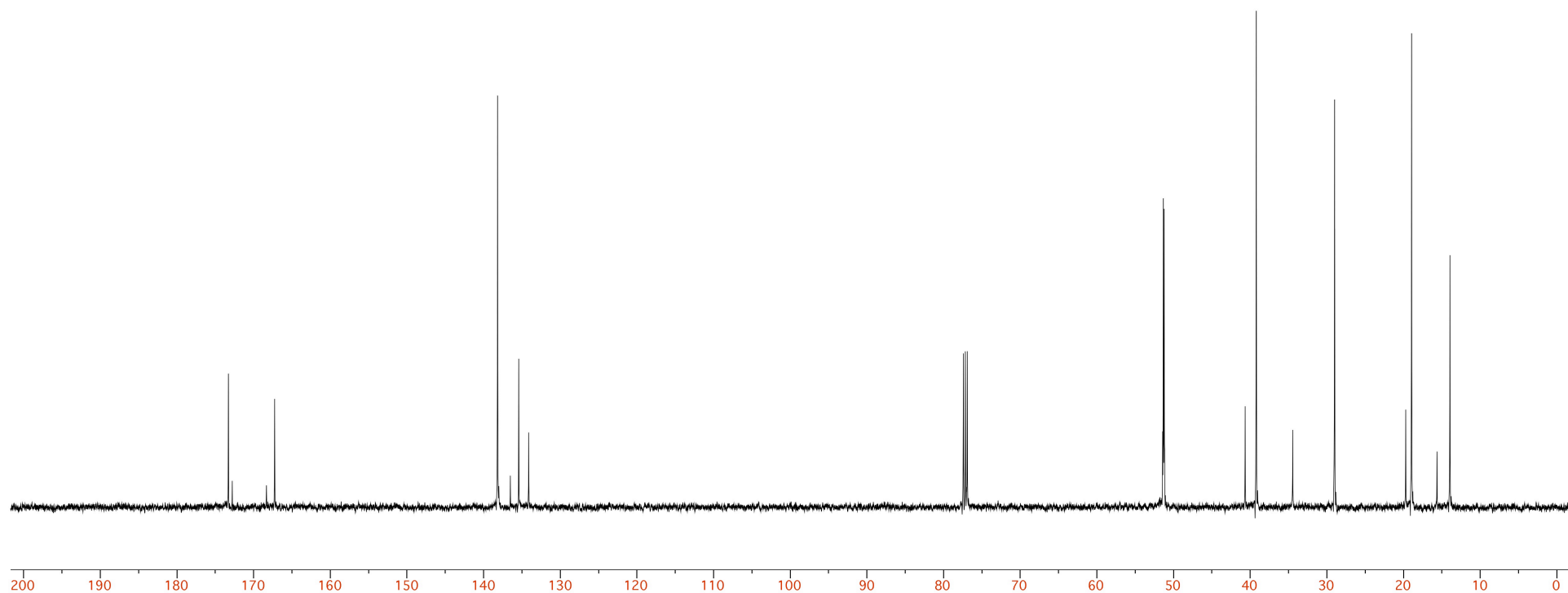
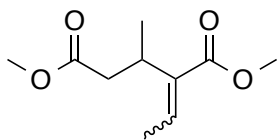
^kIn a nitrogen-filled glovebox, catalyst **1** (0.05 equiv) was added to the diester (~50 mg) and diol in 2 mL THF in a 4 mL vial with a septum screw cap. The vial was removed from the glovebox, placed on a vacuum line and stirred under vacuum for 18 hours at 65 °C, 18 hours at 100 °C and 5 hours at 120 °C.

9. NMR Spectra of Synthesized Compounds

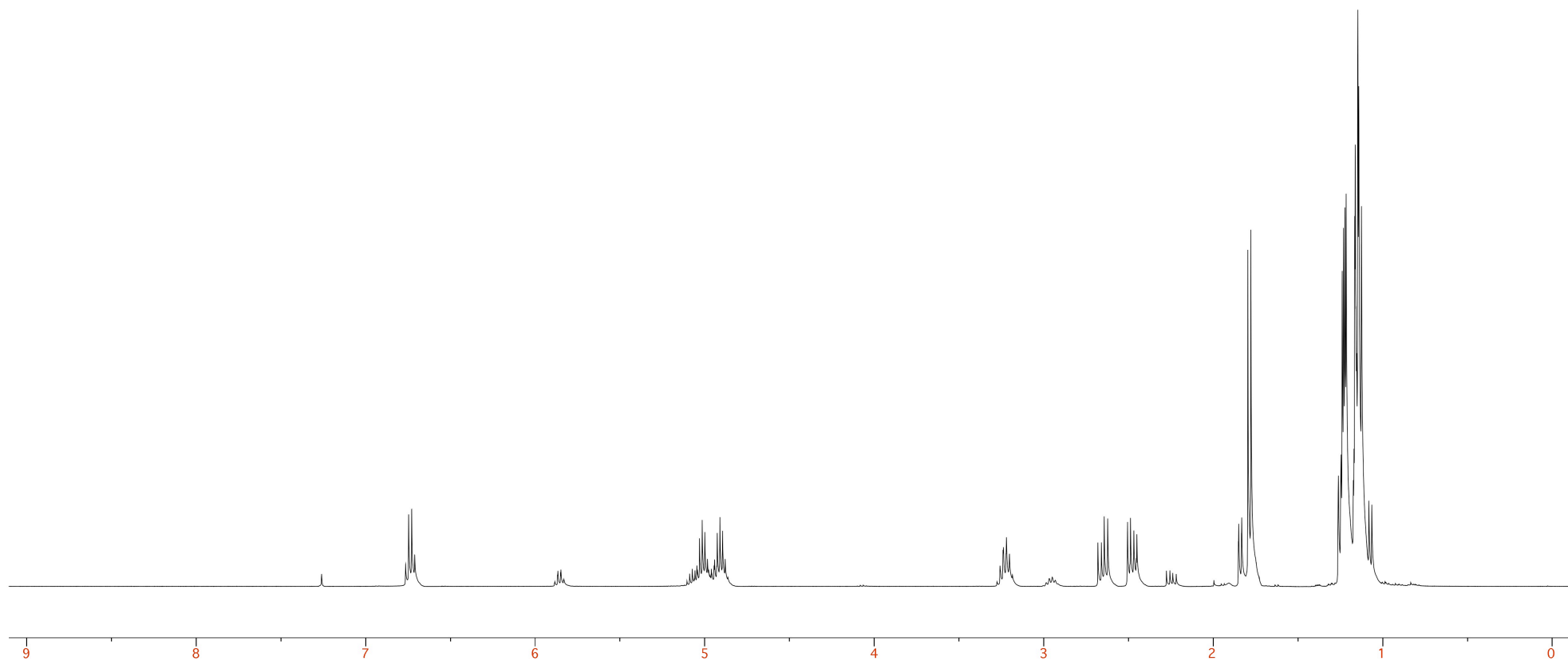
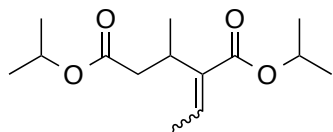
dimethyl 2-ethylidene-3-methylpentanedioate (^1H -NMR, 500 MHz, CDCl_3)



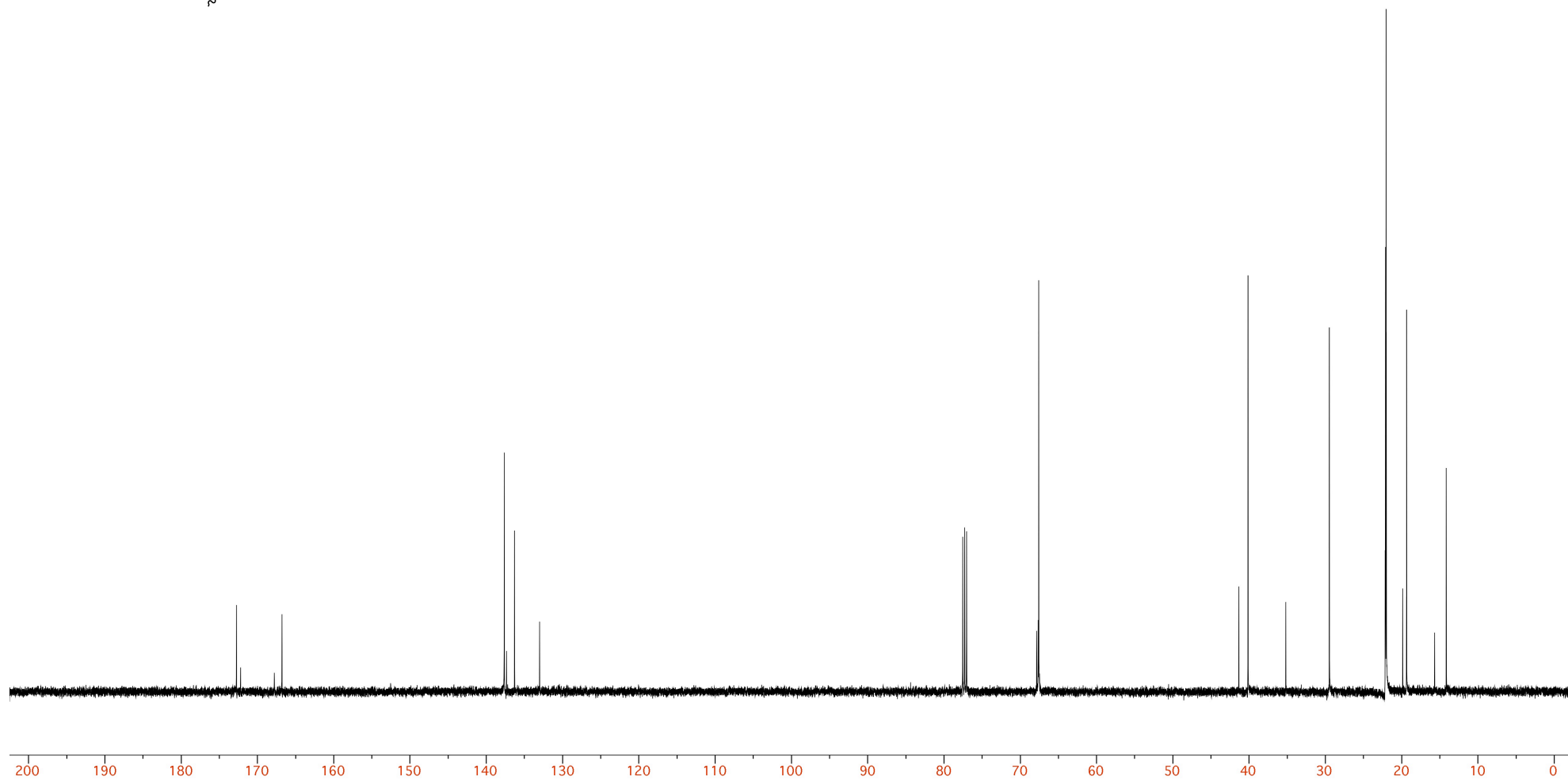
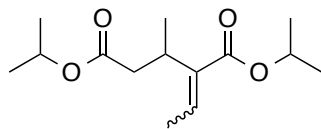
dimethyl 2-ethylidene-3-methylpentanedioate (^{13}C -NMR, 125 MHz, CDCl_3)



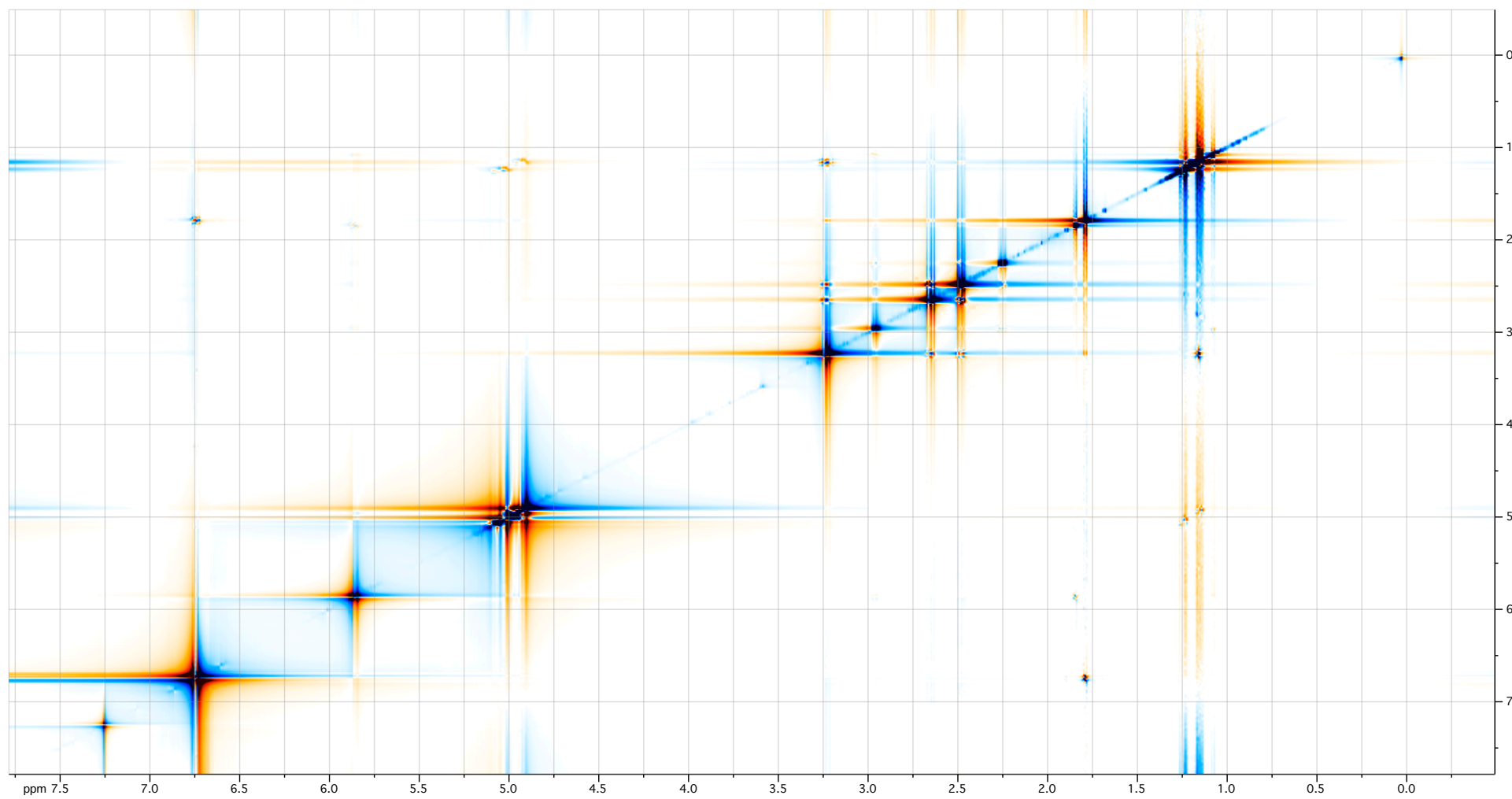
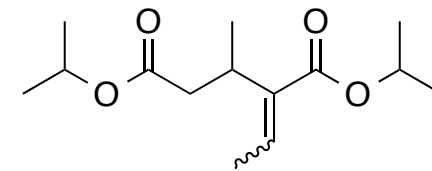
diisopropyl 2-ethylidene-3-methylpentanedioate (¹H-NMR, 500 MHz, CDCl₃)



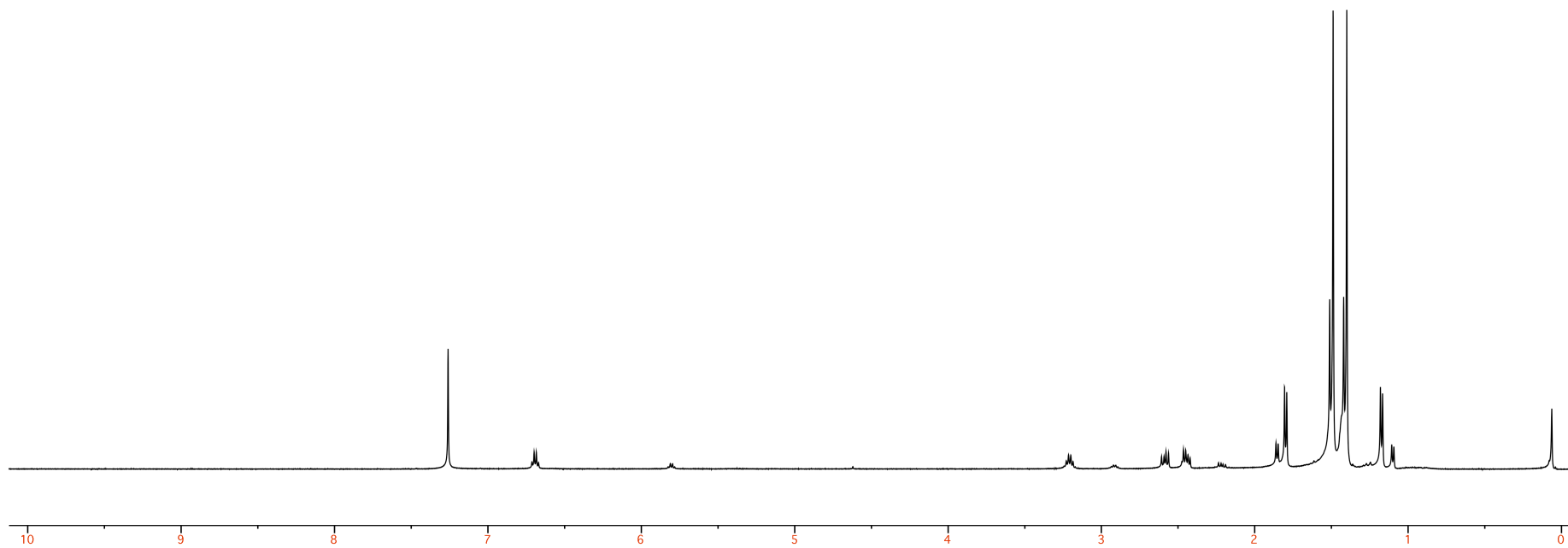
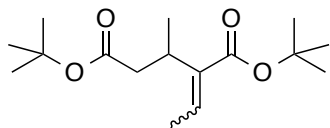
diisopropyl 2-ethylidene-3-methylpentanedioate (^{13}C -NMR, 125 MHz, CDCl_3)



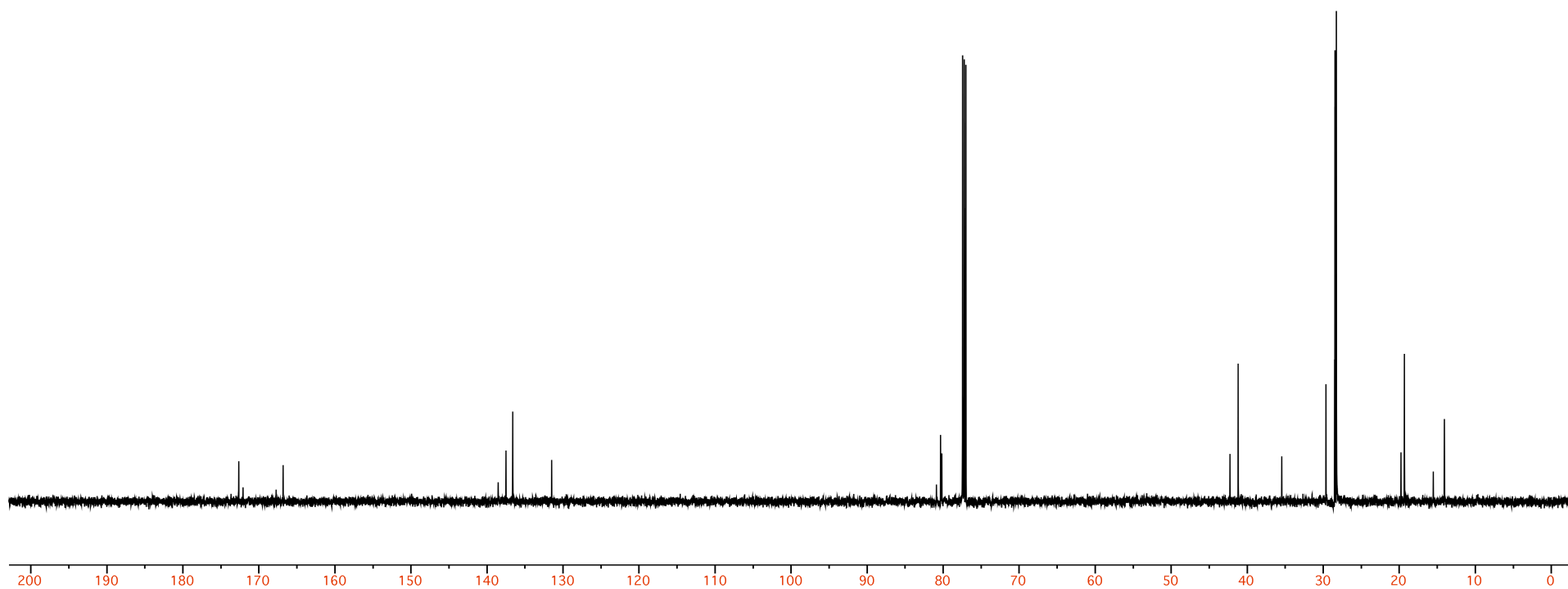
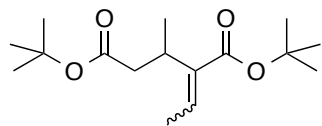
diisopropyl 2-ethylidene-3-methylpentanedioate (^1H - ^1H NOESY 600 MHz, CDCl_3)



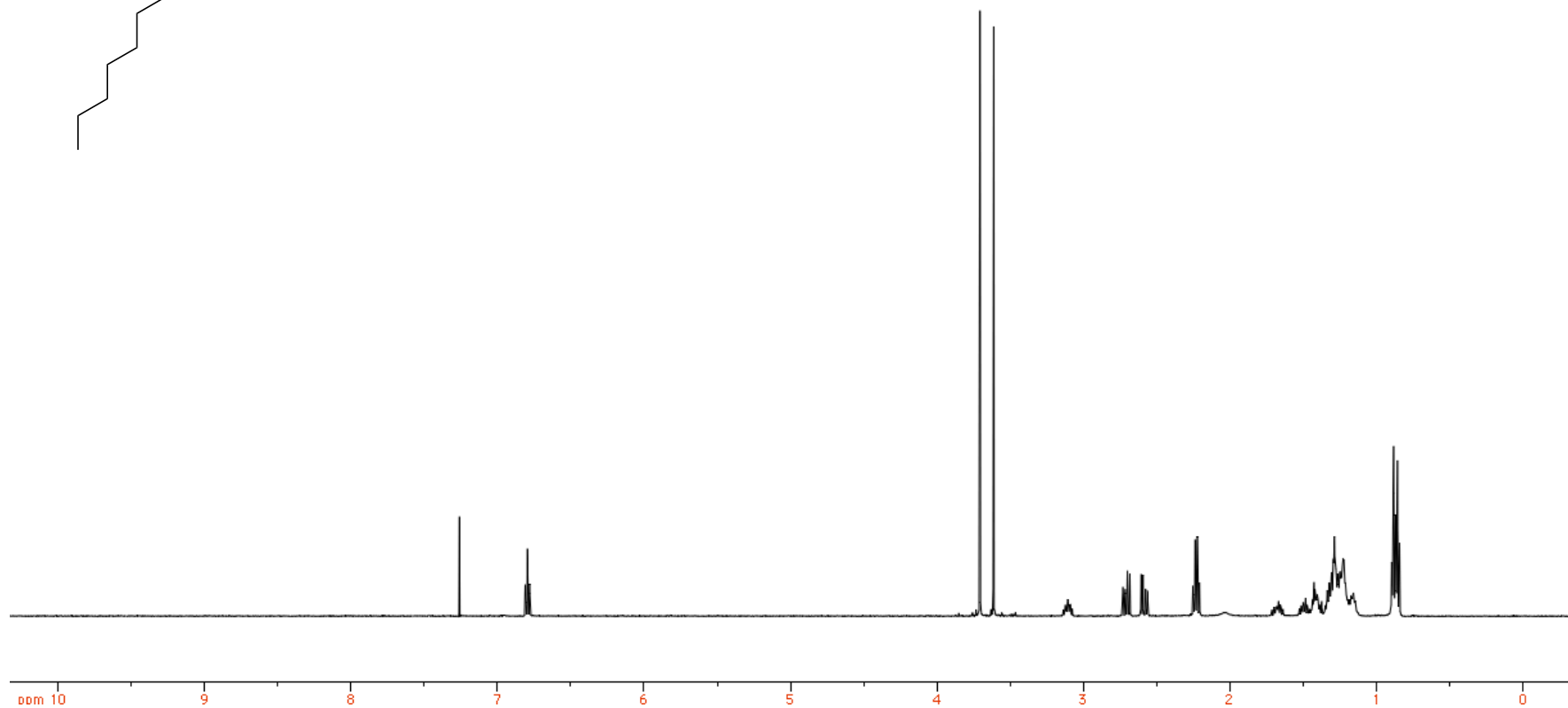
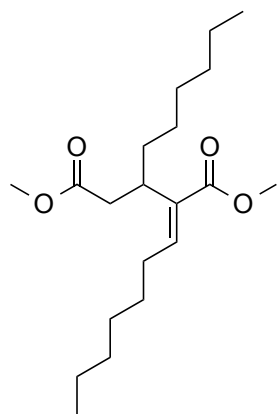
di-*tert*-butyl 2-ethylidene-3-methylpentanedioate (¹H-NMR, 500 MHz, CDCl₃)



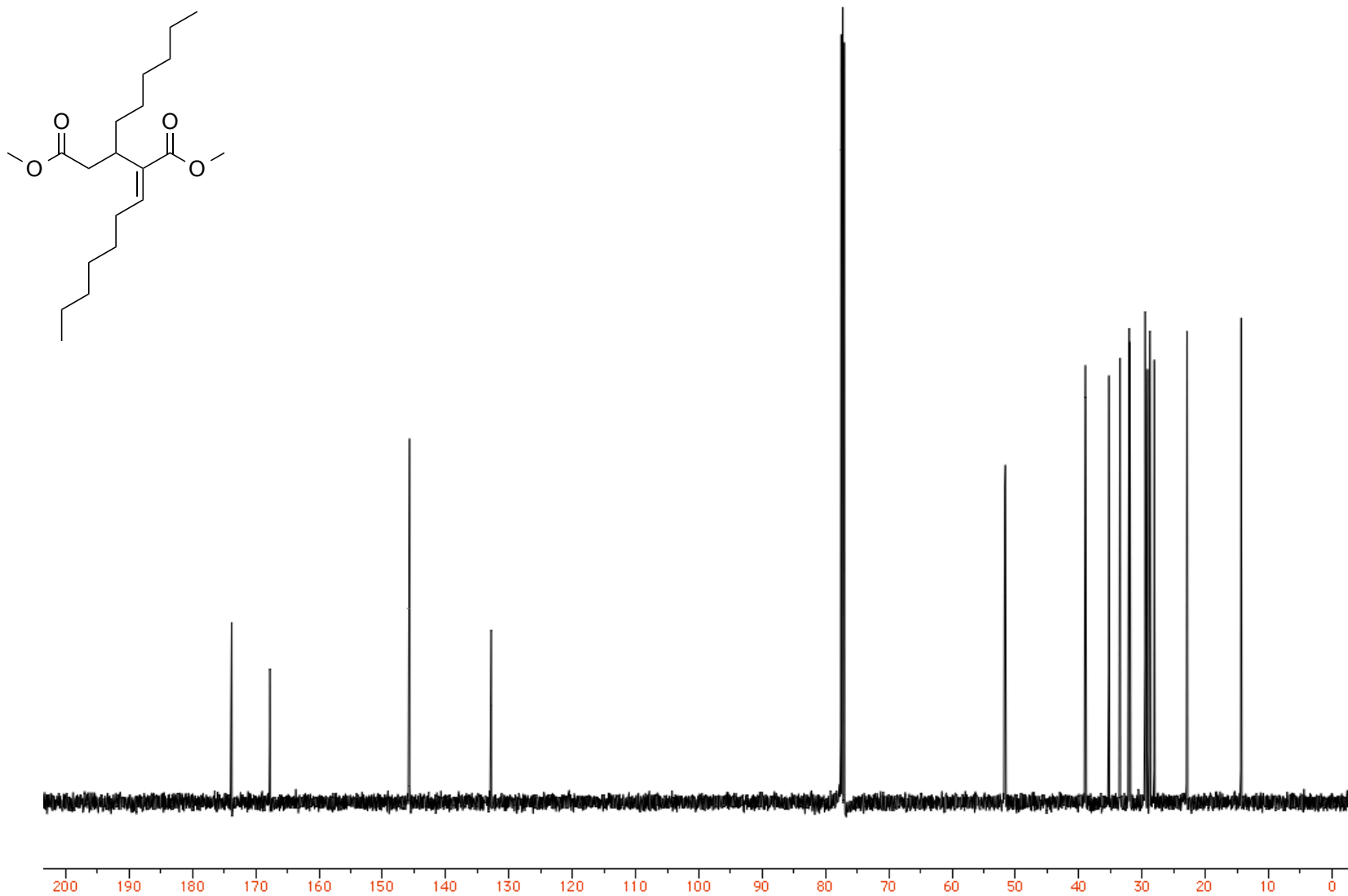
di-*tert*-butyl 2-ethylidene-3-methylpentanedioate (^{13}C -NMR, 150 MHz, CDCl_3)



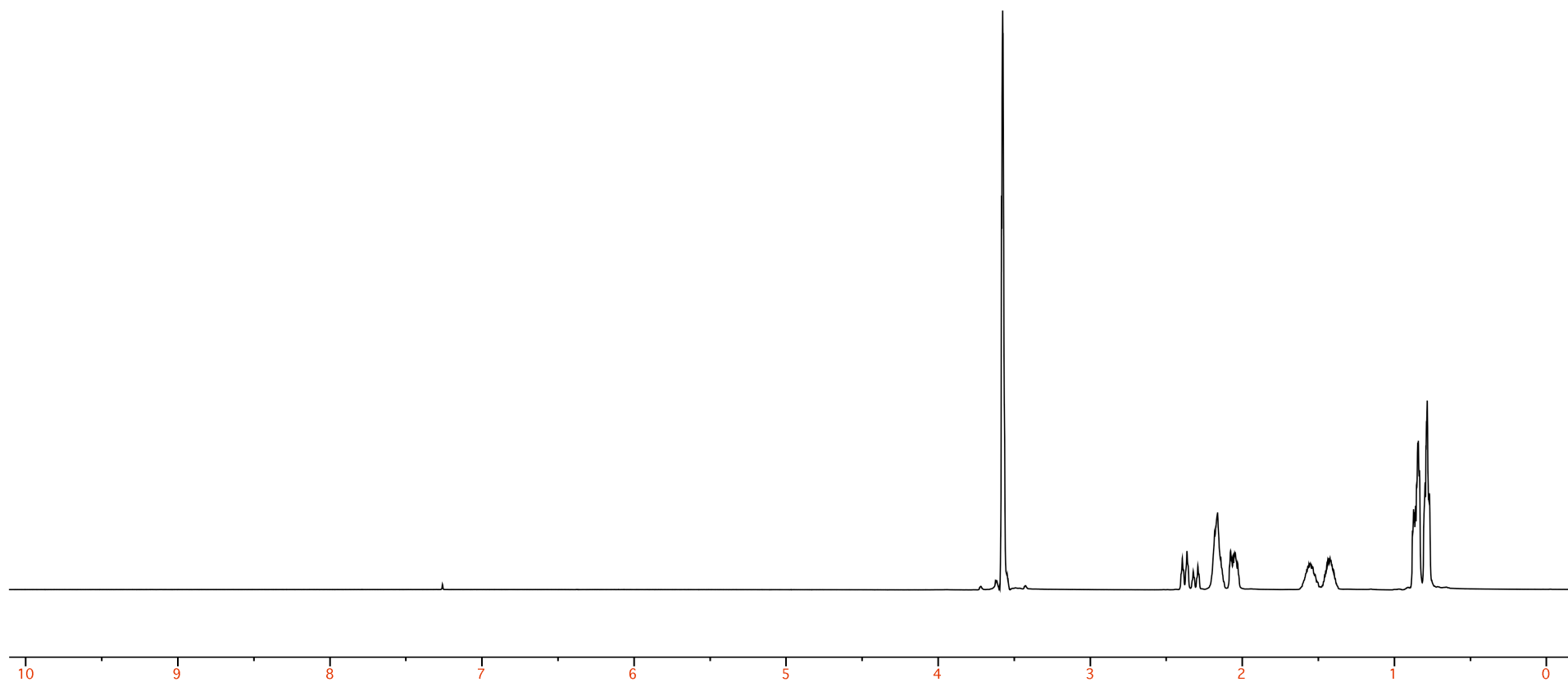
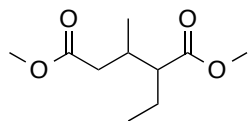
dimethyl (*E*)-2-heptylidene-3-hexylpentanedioate (^1H -NMR, 600 MHz, CDCl_3)



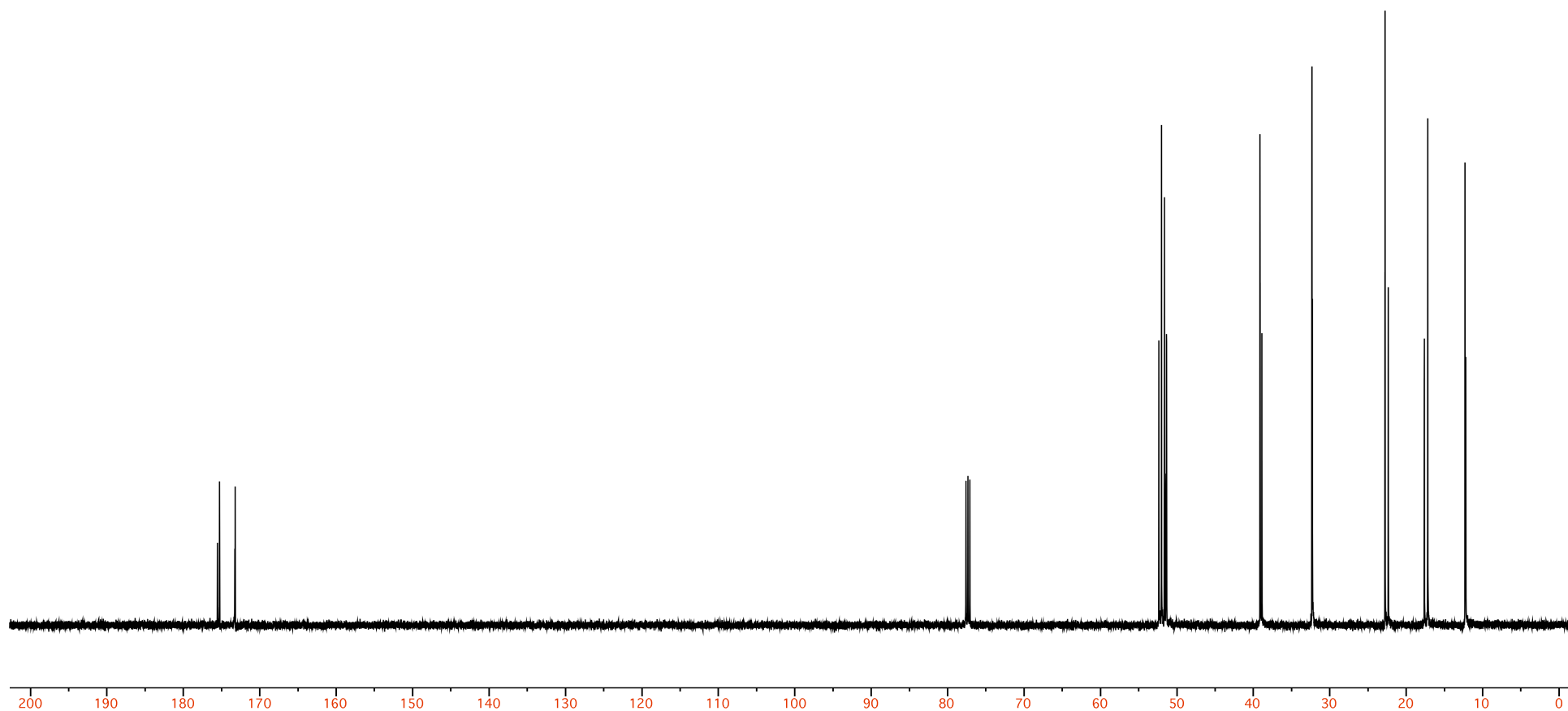
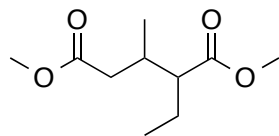
dimethyl (*E*)-2-heptylidene-3-hexylpentanedioate (^{13}C -NMR, 150 MHz, CDCl_3)



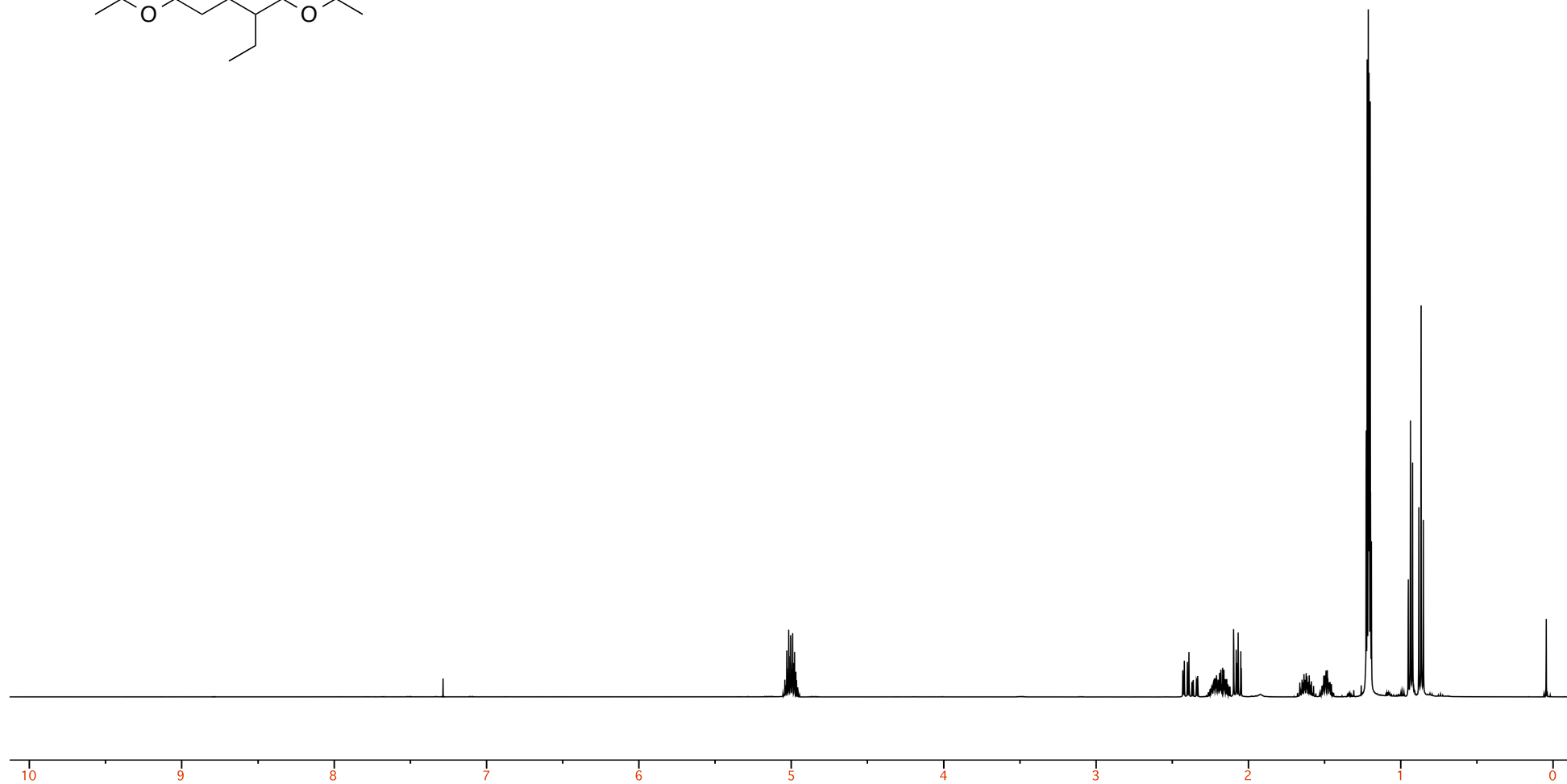
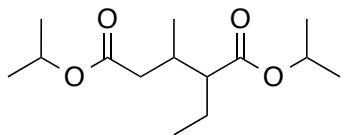
dimethyl 2-ethyl-3-methylpentanedioate (^1H -NMR, 500 MHz, CDCl_3) – mixture of diastereomers



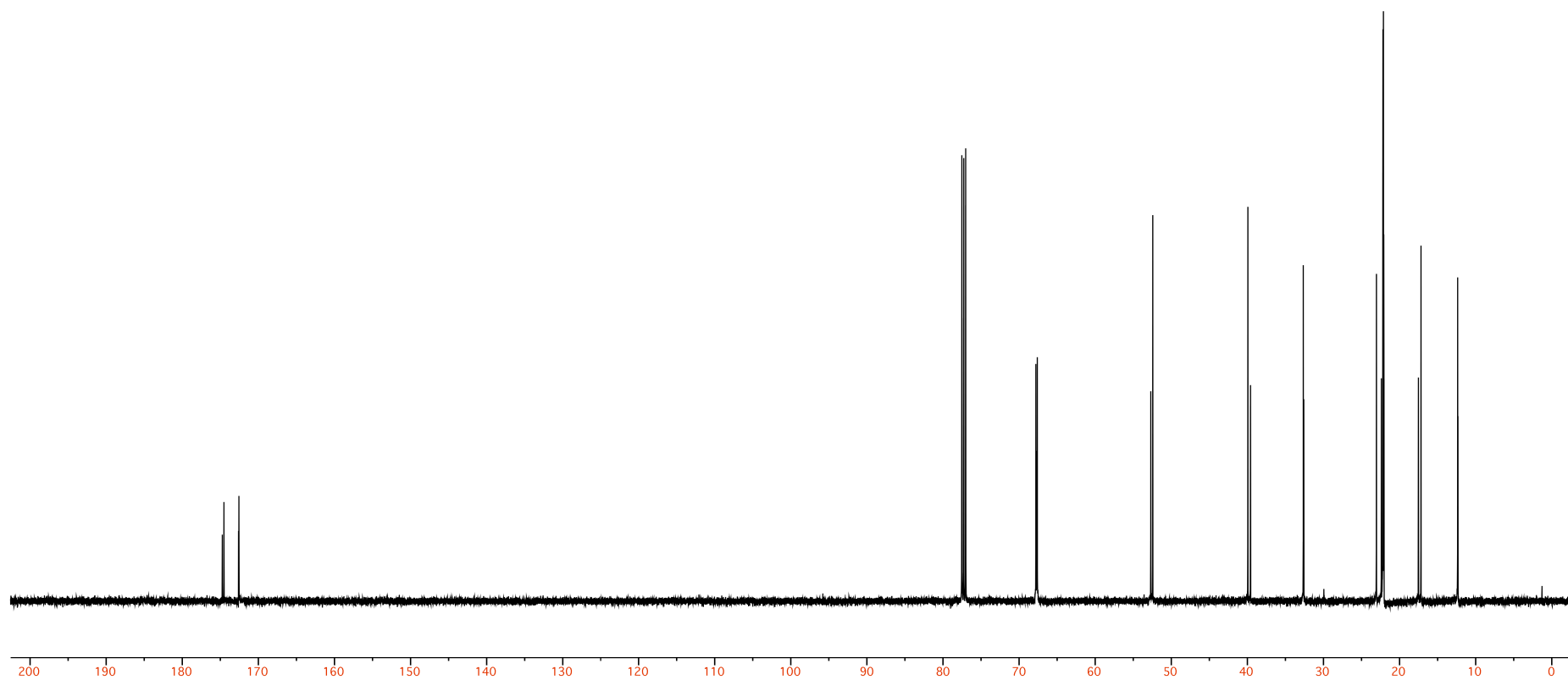
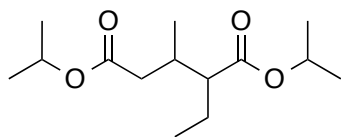
dimethyl 2-ethyl-3-methylpentanedioate (^{13}C -NMR, 125 MHz, CDCl_3) – mixture of diastereomers



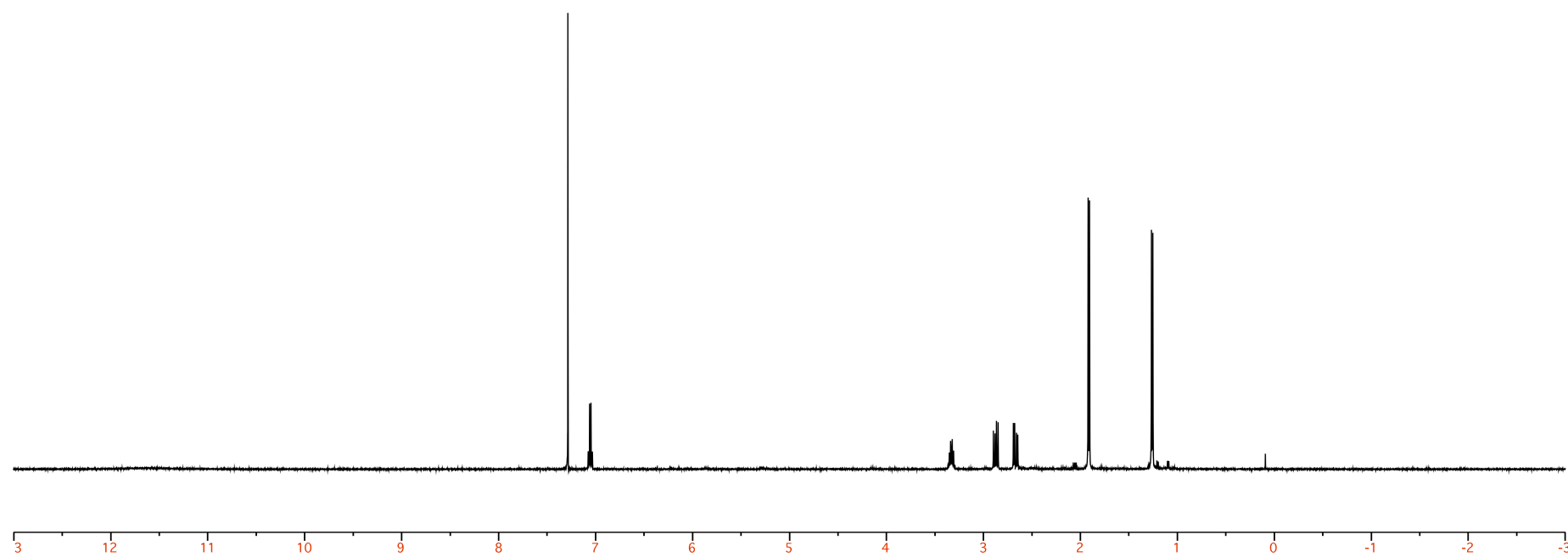
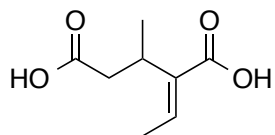
diisopropyl 2-ethyl-3-methylpentanedioate (^1H -NMR, 500 MHz, CDCl_3) – mixture of diastereomers



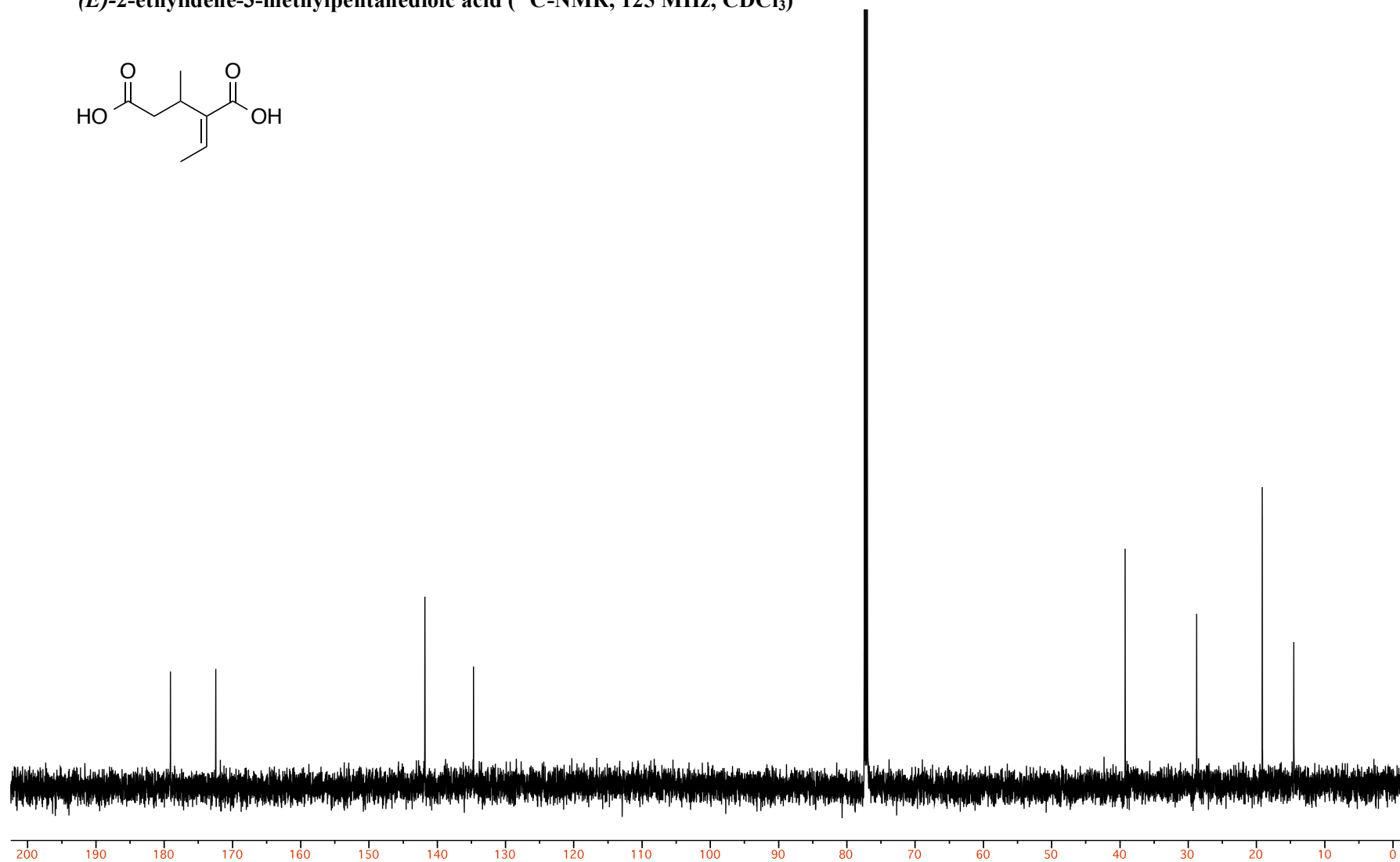
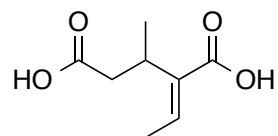
diisopropyl 2-ethyl-3-methylpentanedioate (^{13}C -NMR, 125 MHz, CDCl_3) – mixture of diastereomers



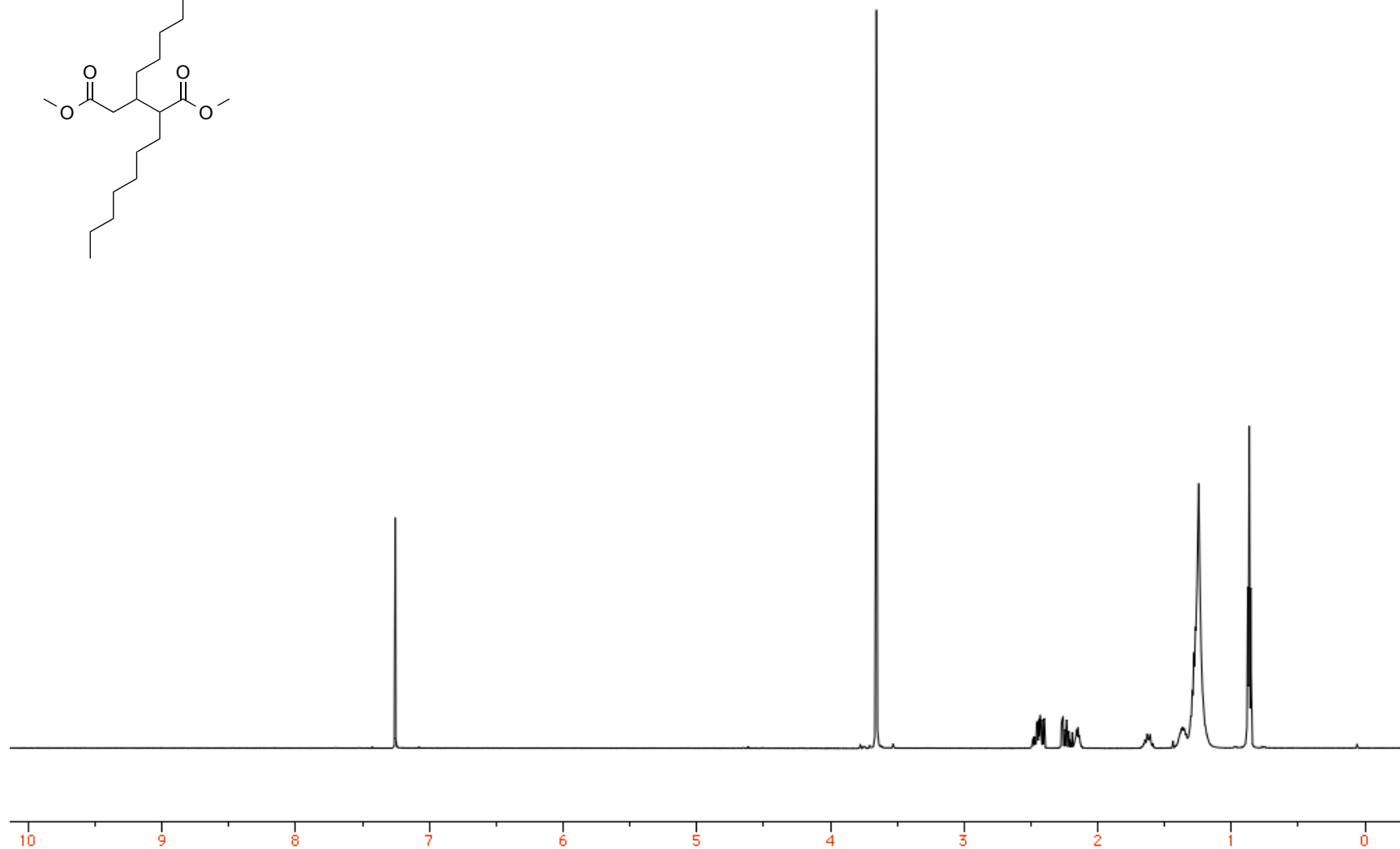
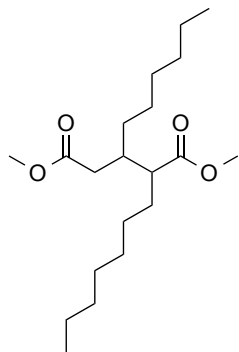
(*E*)-2-ethylidene-3-methylpentanedioic acid (^1H -NMR, 500 MHz, CDCl_3)



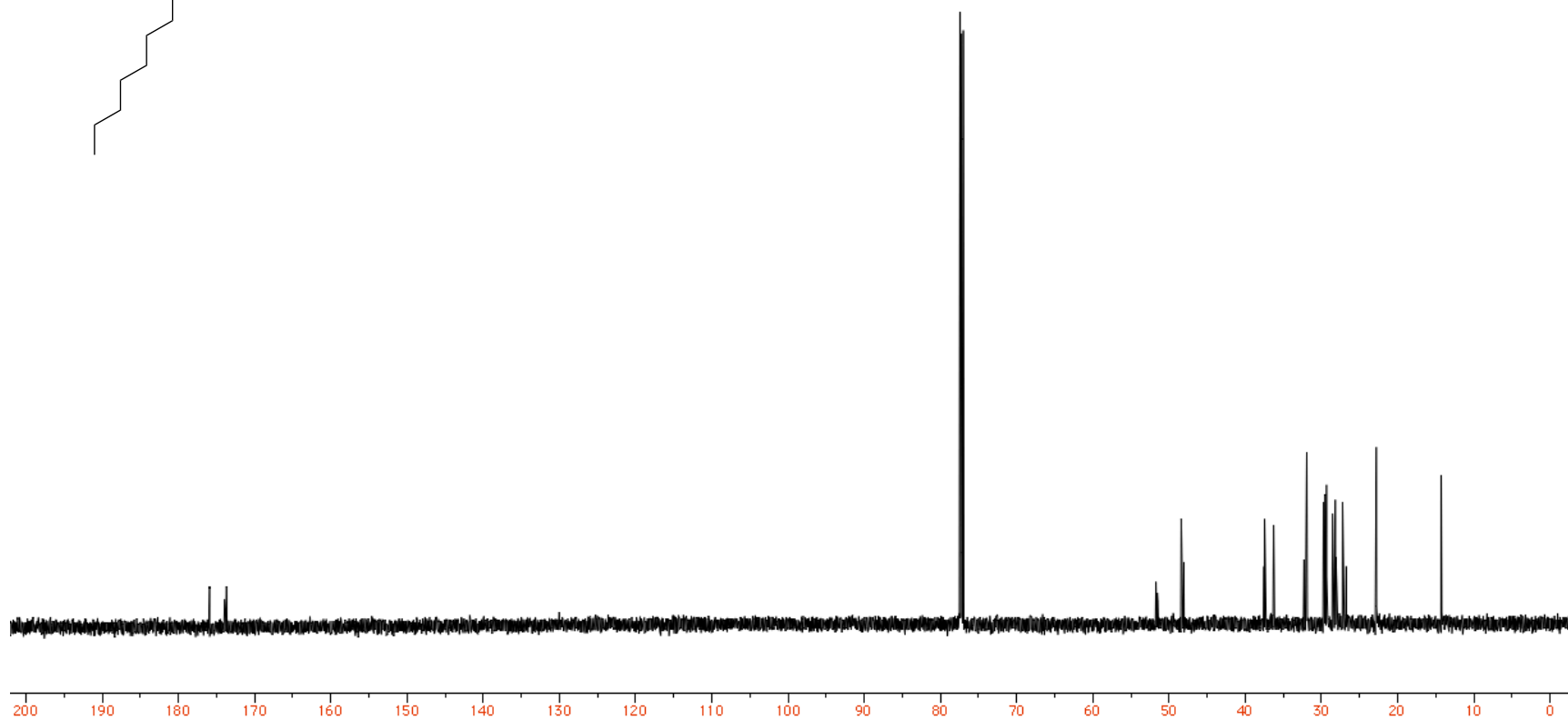
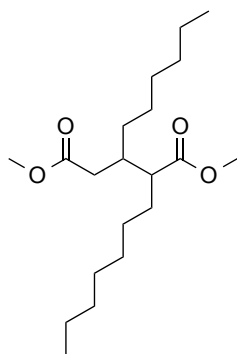
(*E*)-2-ethylidene-3-methylpentanedioic acid (^{13}C -NMR, 125 MHz, CDCl_3)



dimethyl 2-heptyl-3-hexylpentanedioate (^1H -NMR, 600 MHz, CDCl_3)

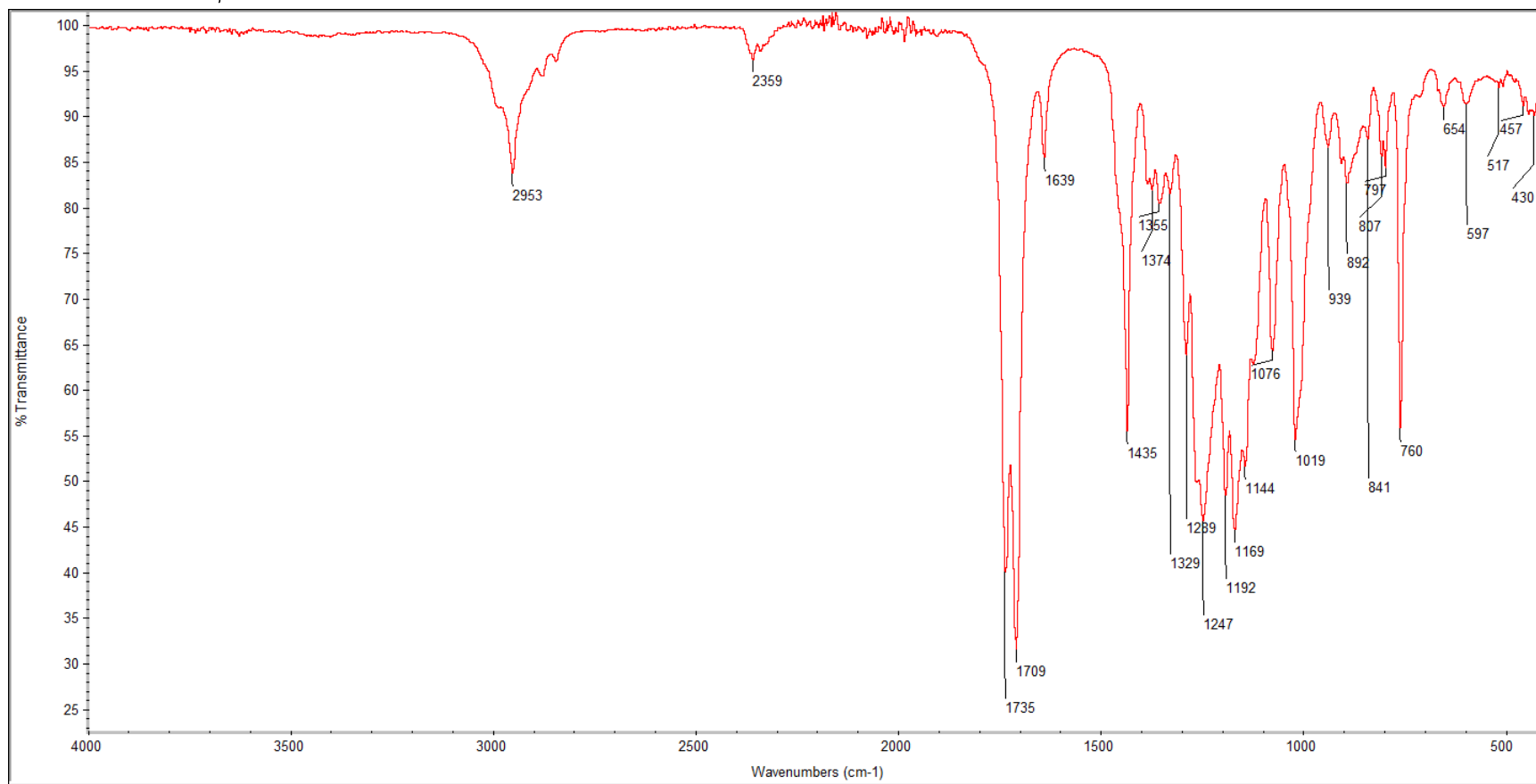
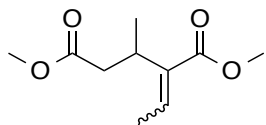


dimethyl 2-heptyl-3-hexylpentanedioate (^{13}C -NMR, 150 MHz, CDCl_3)

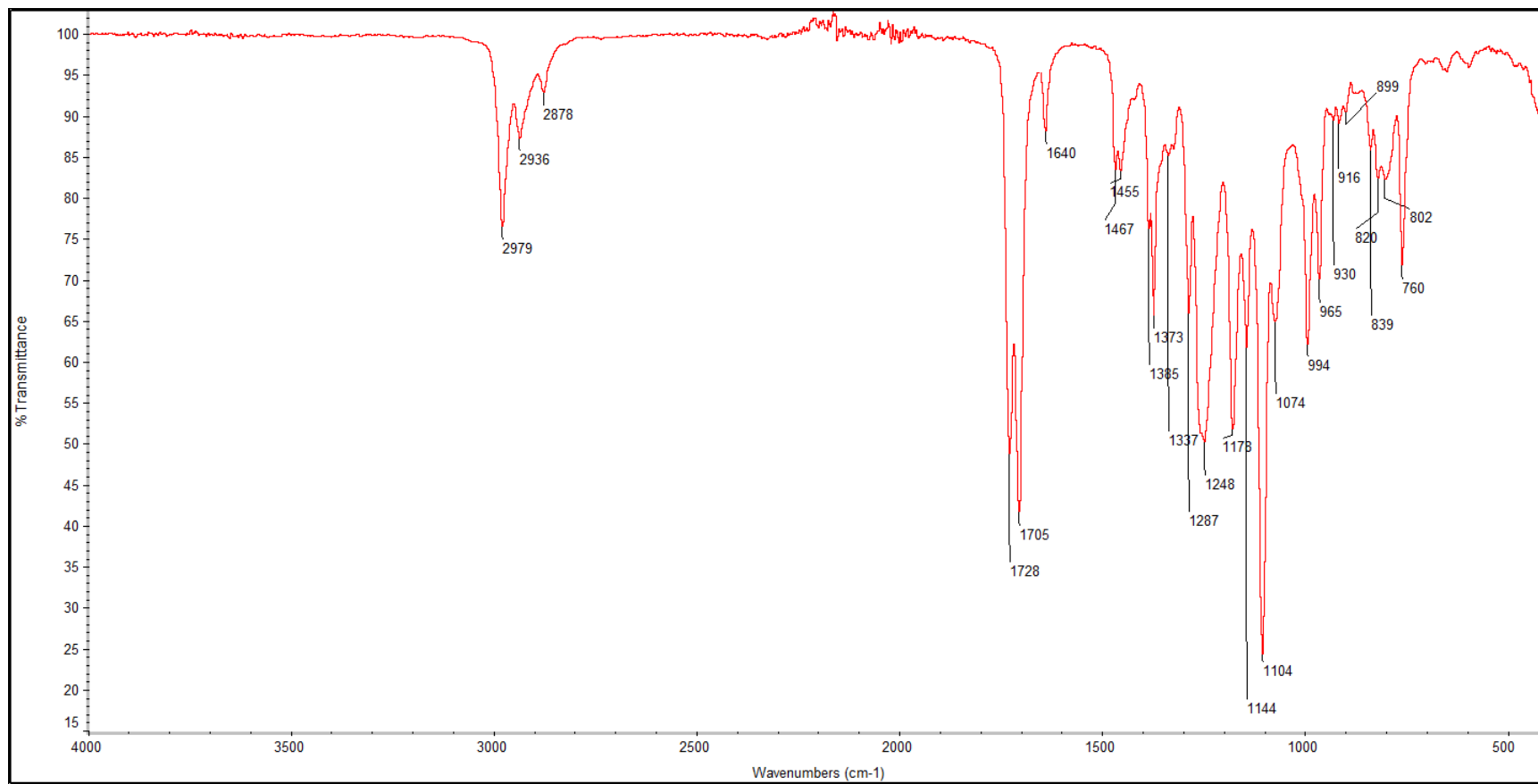
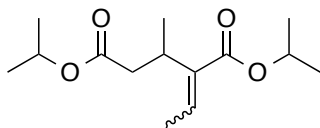


10. FTIR Spectra of Synthesized Compounds

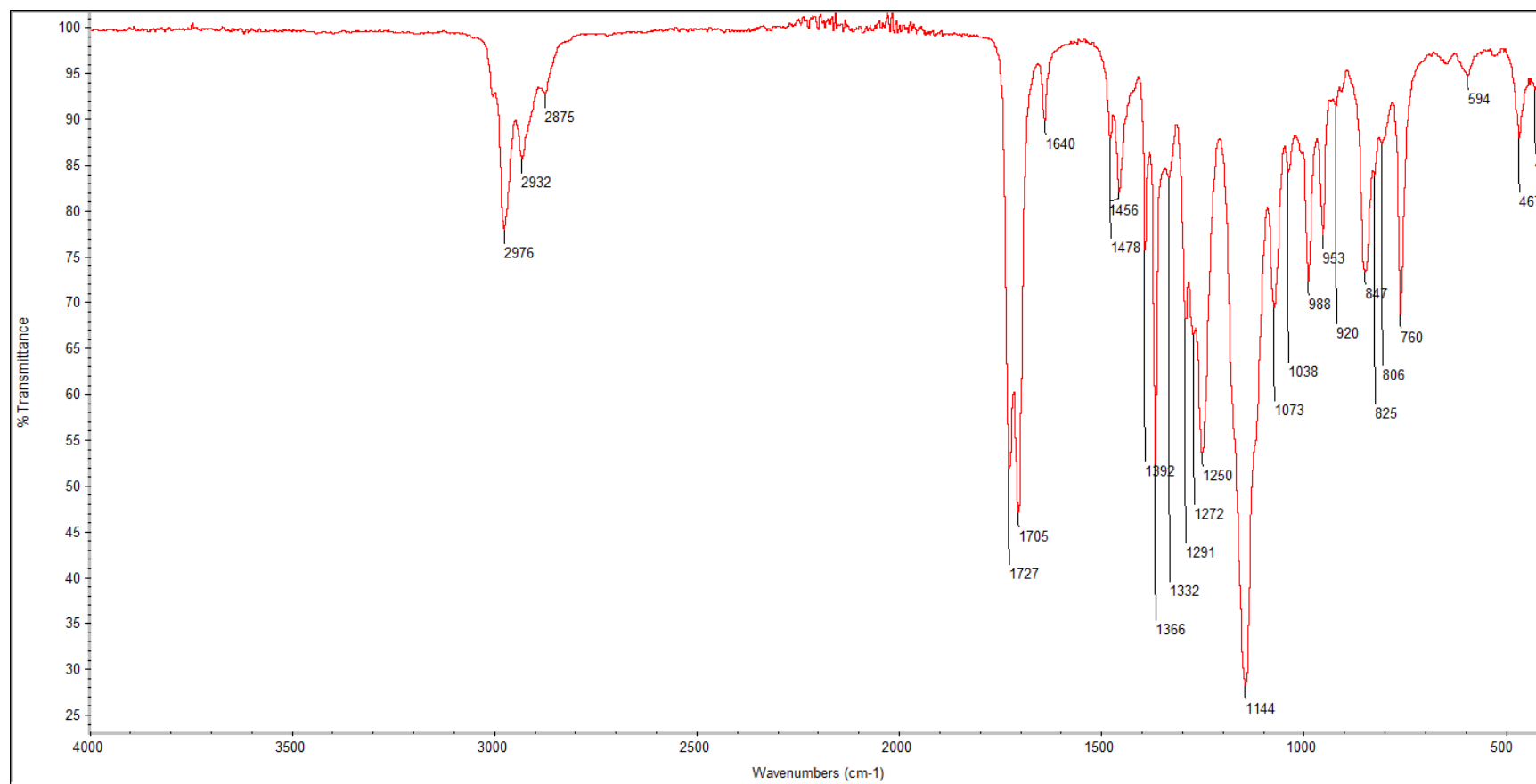
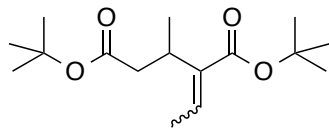
dimethyl 2-ethylidene-3-methylpentanedioate



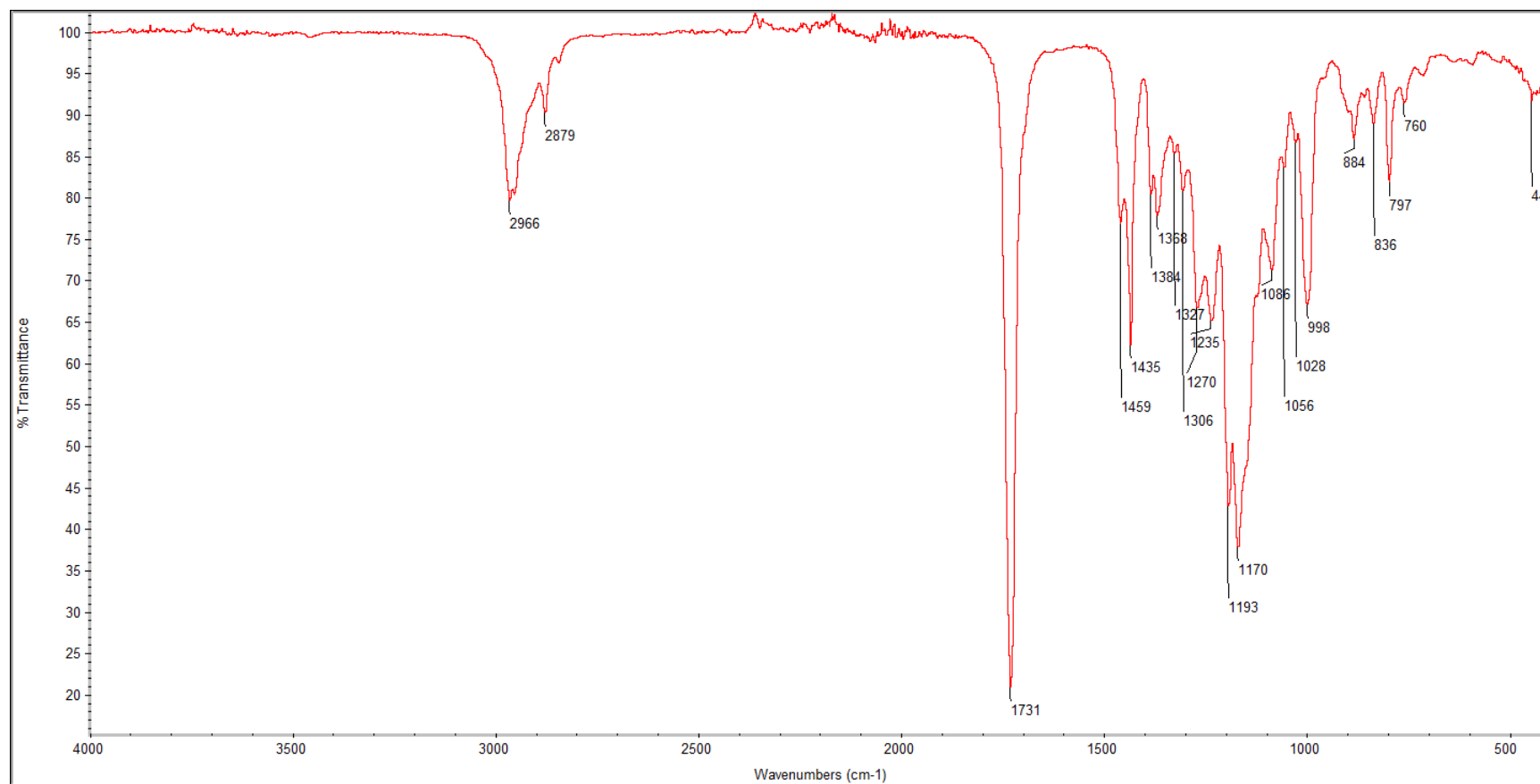
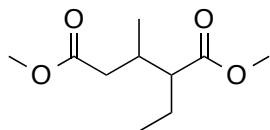
diisopropyl 2-ethylidene-3-methylpentanedioate



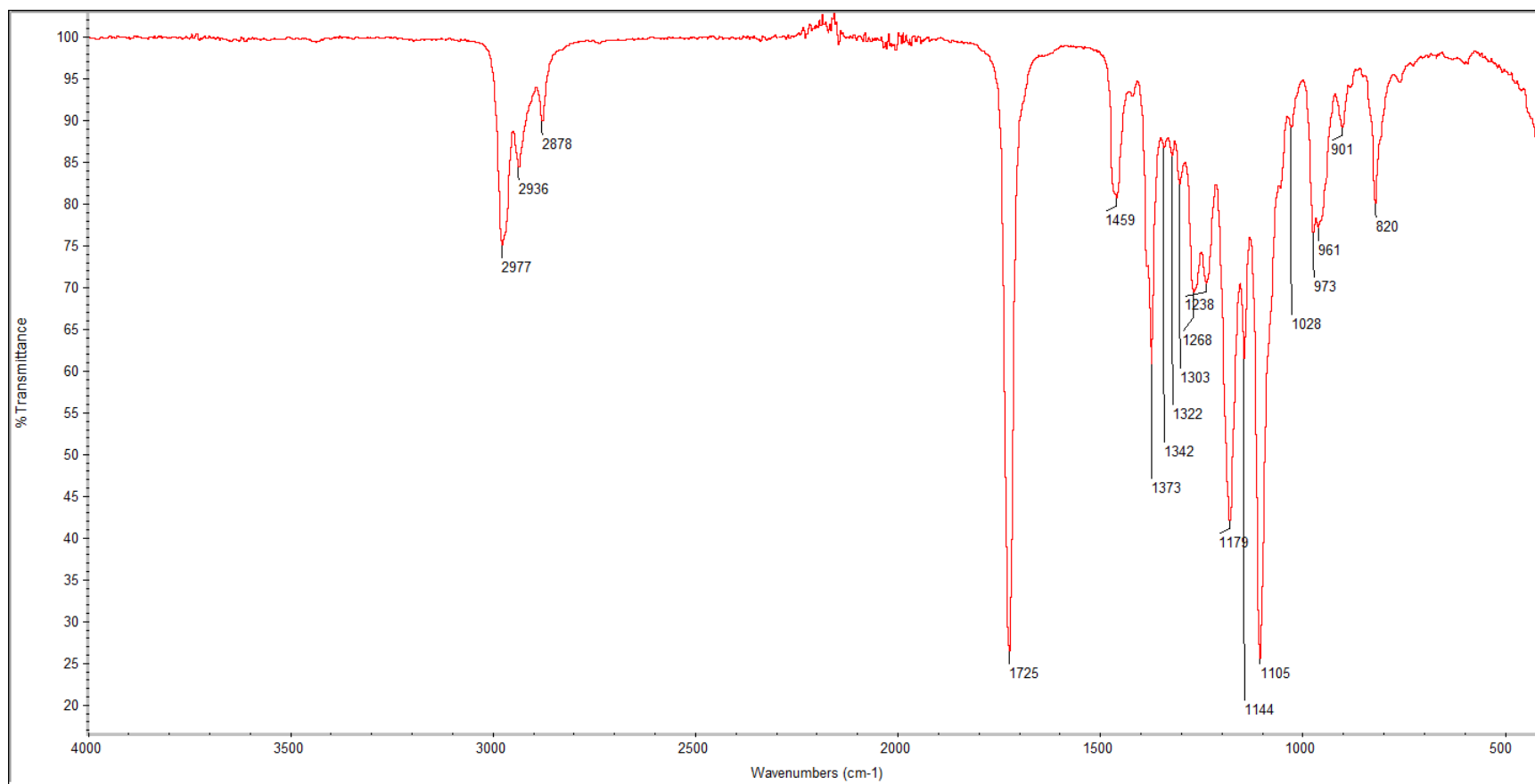
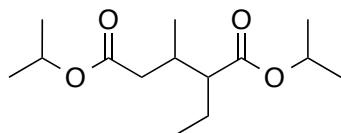
di-*tert*-butyl 2-ethylidene-3-methylpentanedioate



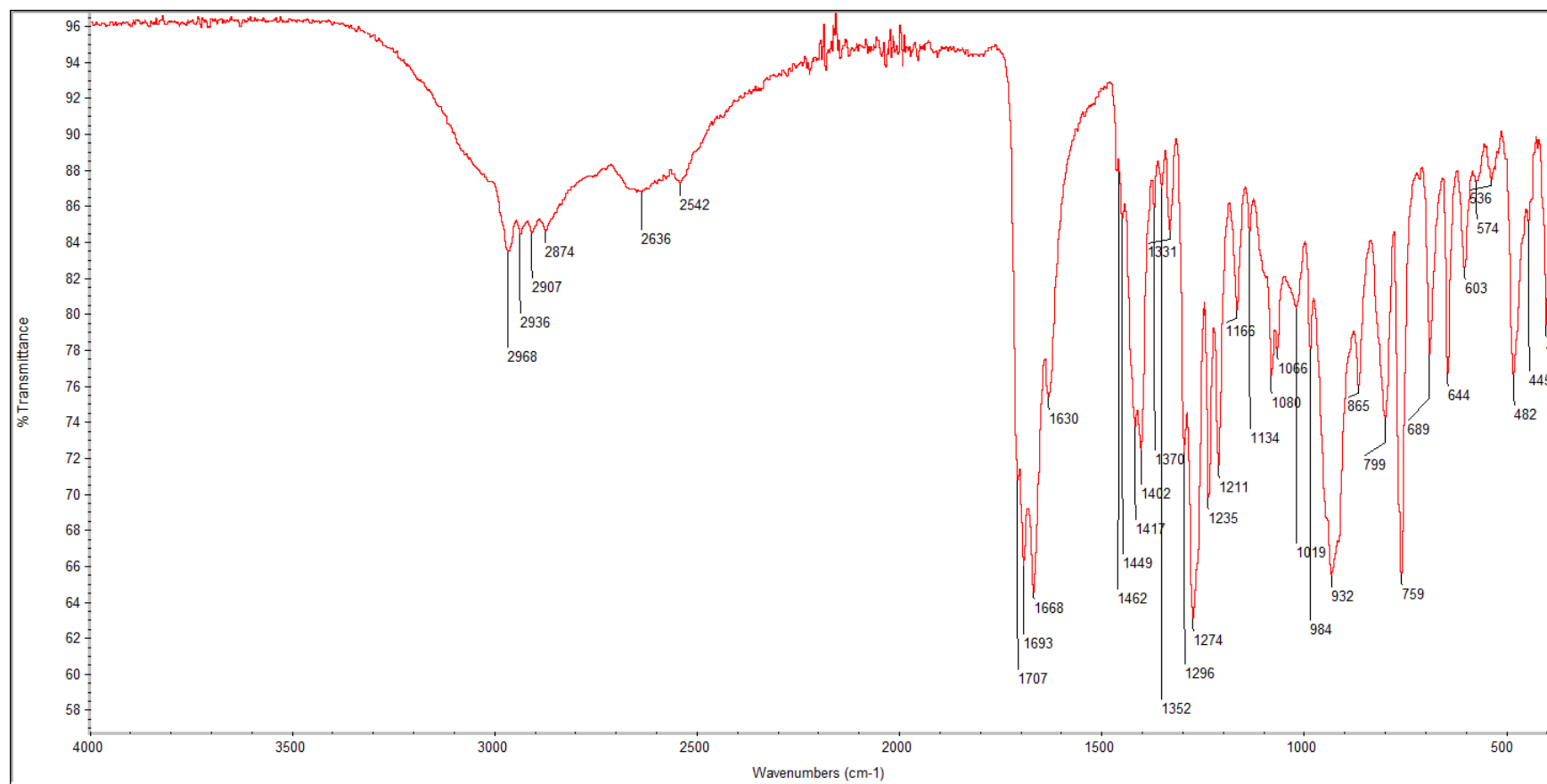
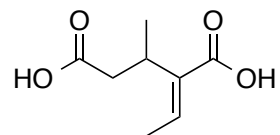
dimethyl 2-ethyl-3-methylpentanedioate



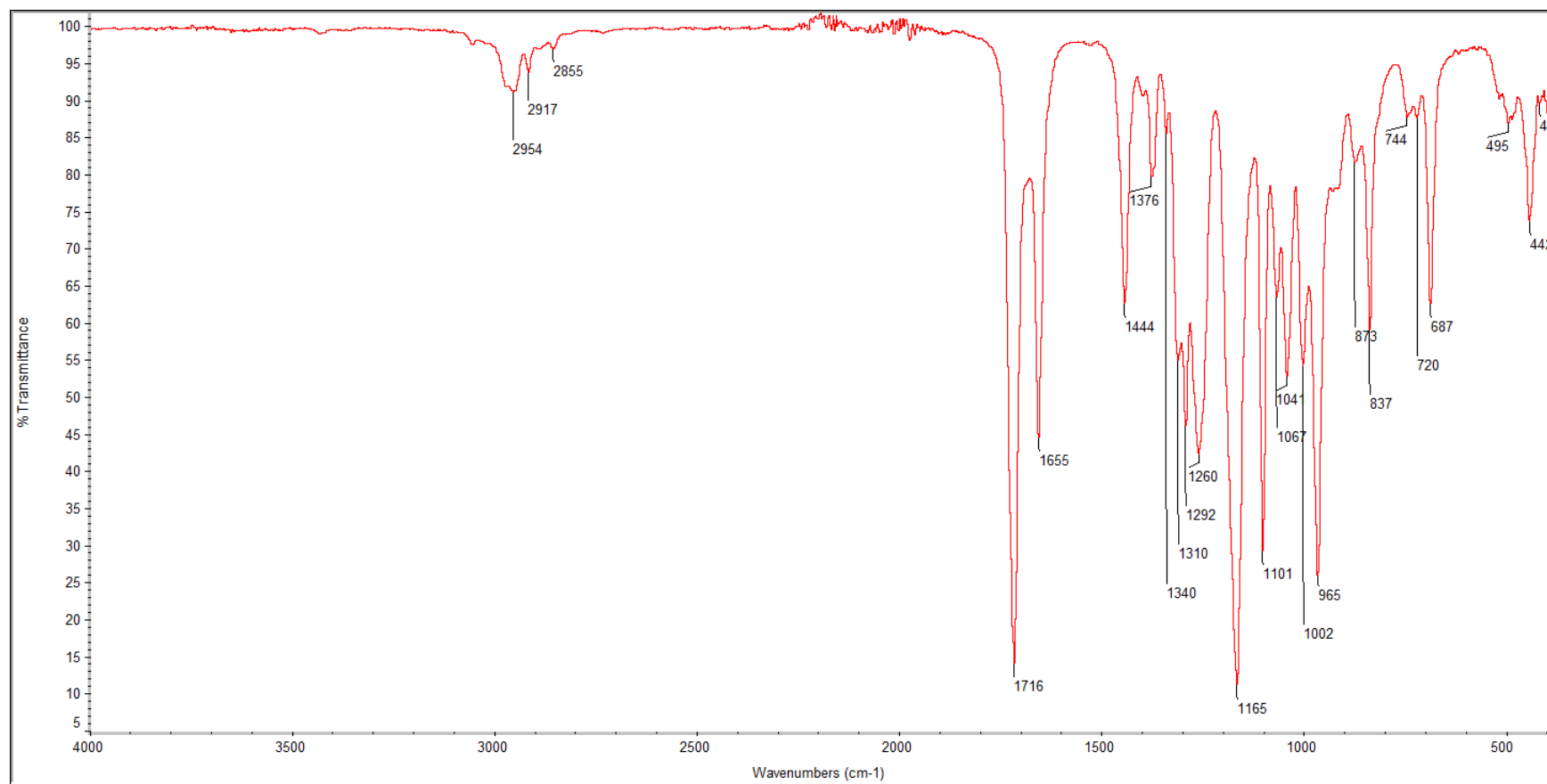
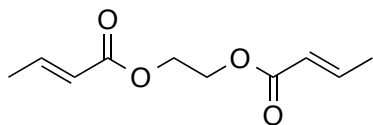
diisopropyl 2-ethyl-3-methylpentanedioate



(E)-2-ethylidene-3-methylpentanedioic acid



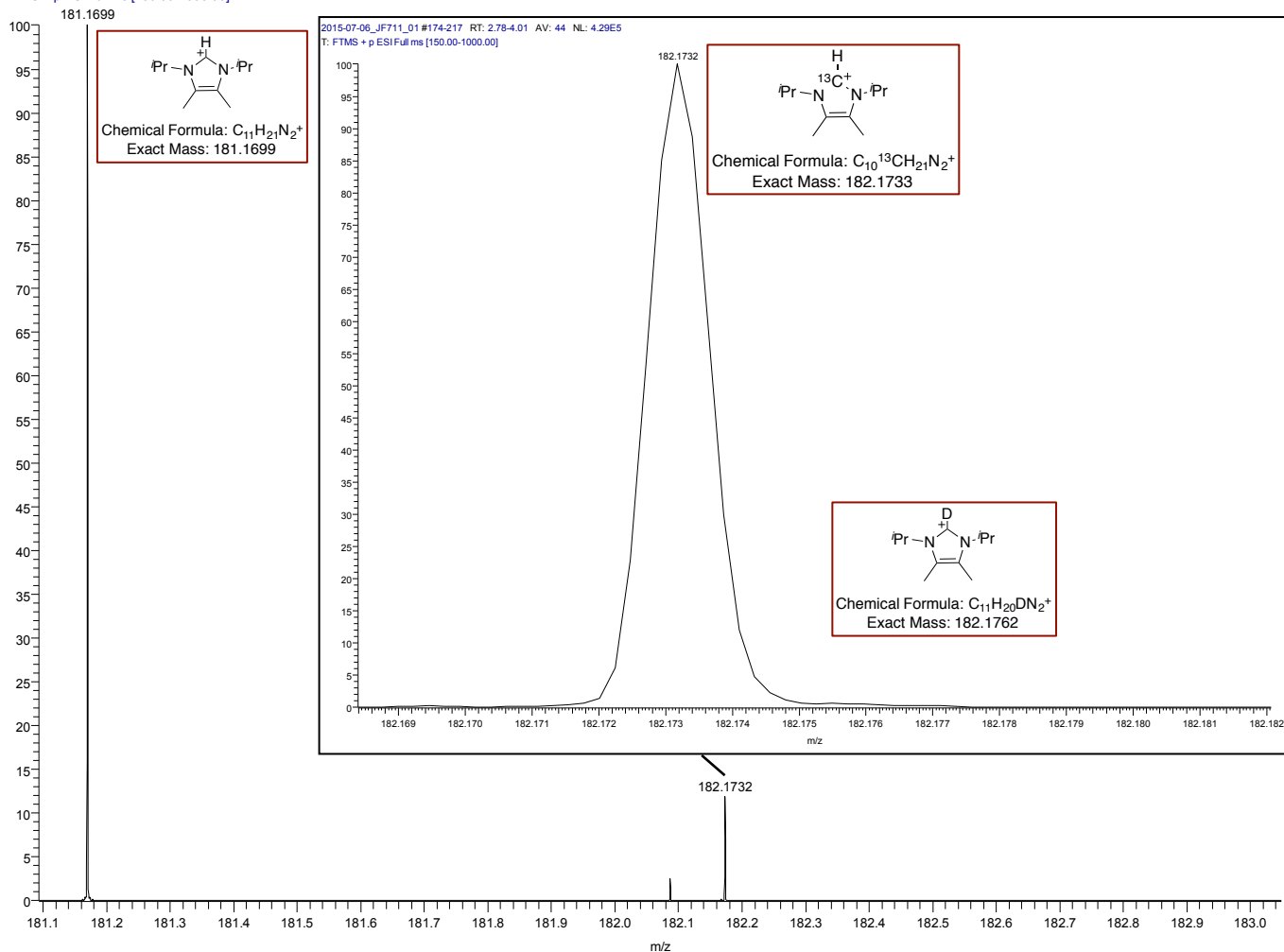
Ethane-1,2-diyl (2*E*,2'*E*)-bis(but-2-enoate)



11. Mass Spectra for H/D Experiments Described in Section 6f
(Spectra for Table S2: p. S75 – S81; Spectra for Table S3: p. S82-S88)

SPECTRUM 1 (after CH₃COOH addition but before CH₃COOD addition)

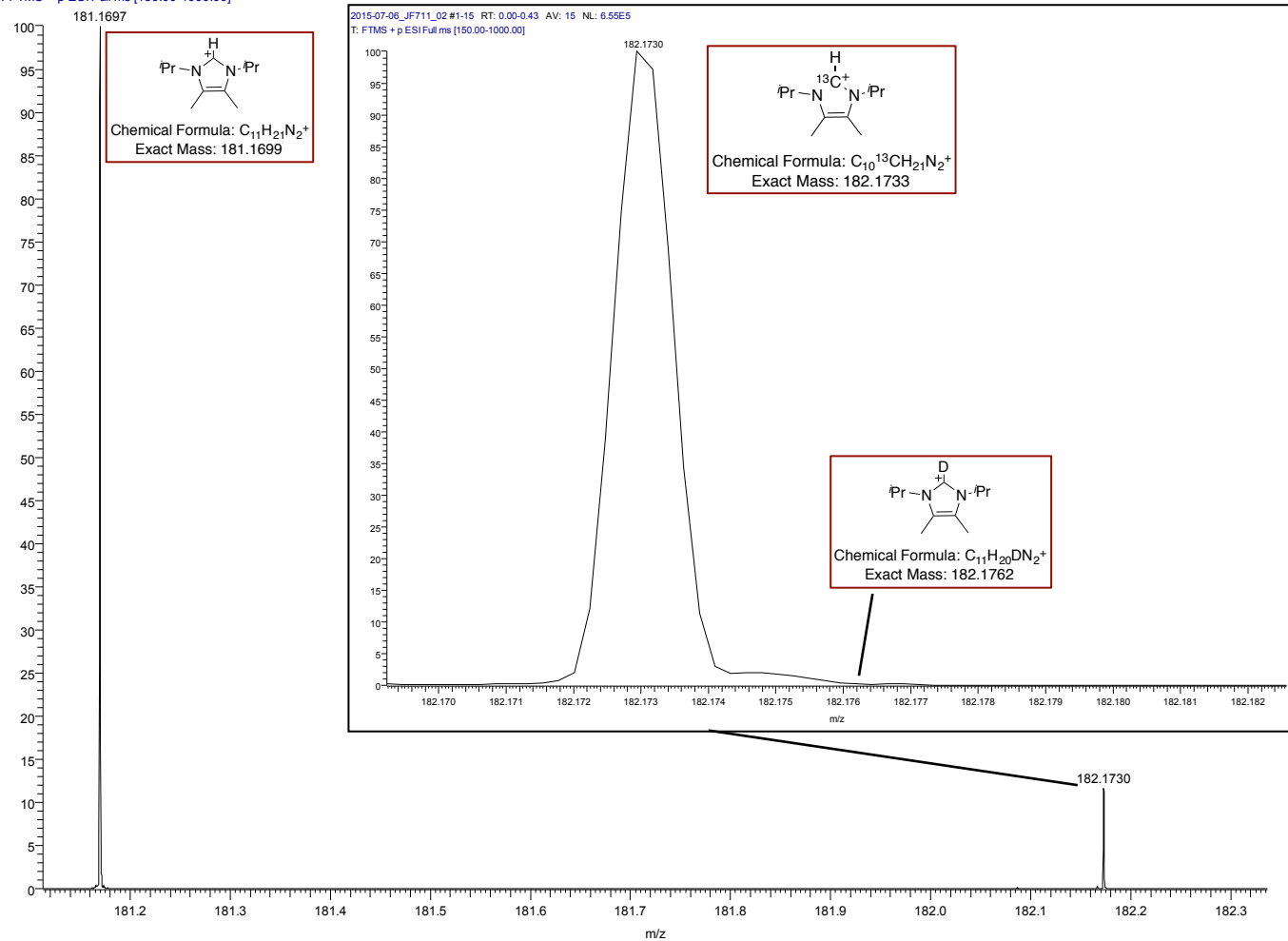
2015-07-06_JF711_01 #174-217 RT: 2.78-4.01 AV: 44 NL: 3.61E6
T: FTMS + p ESI Full ms [150.00-1000.00]



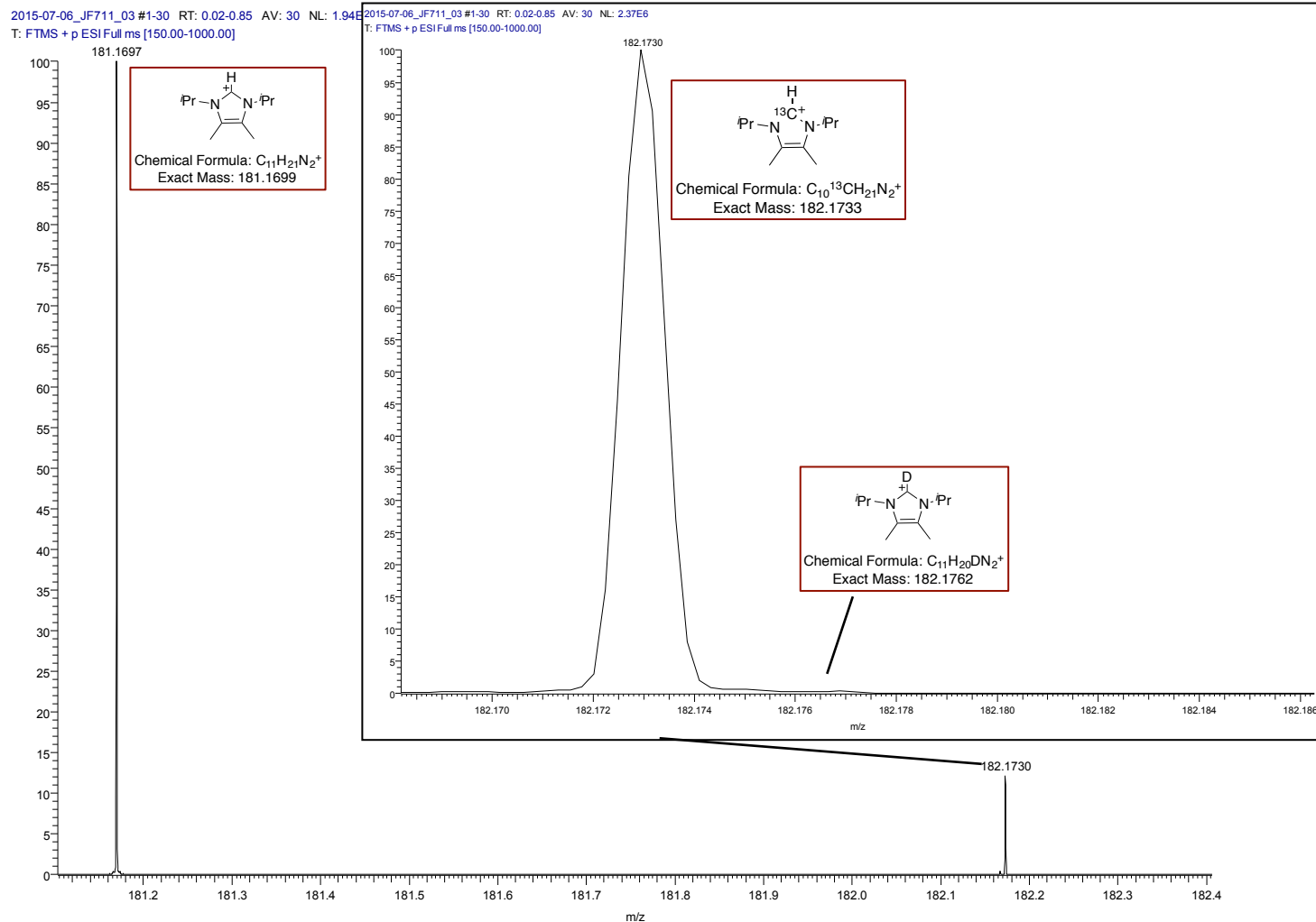
SPECTRUM 2 (4 minutes after CH₃COOD addition)

2015-07-06_JF711_02 #1-15 RT: 0.00-0.43 AV: 15 NL: 5.62E6

T: FTMS + p ESI Full ms [150.00-1000.00]



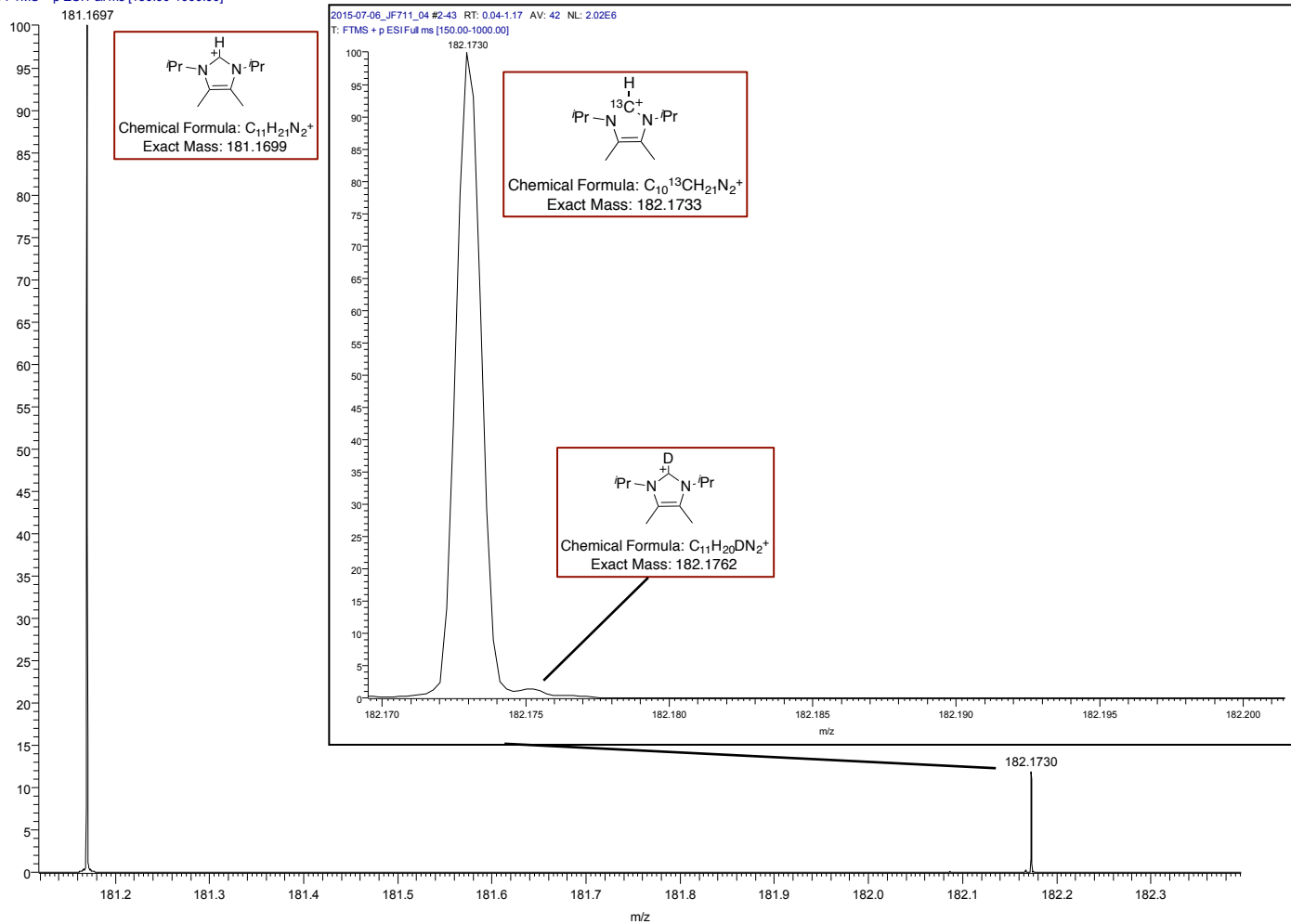
SPECTRUM 3 (15 minutes after CH₃COOD addition)



SPECTRUM 4 (32 minutes after CH₃COOD addition)

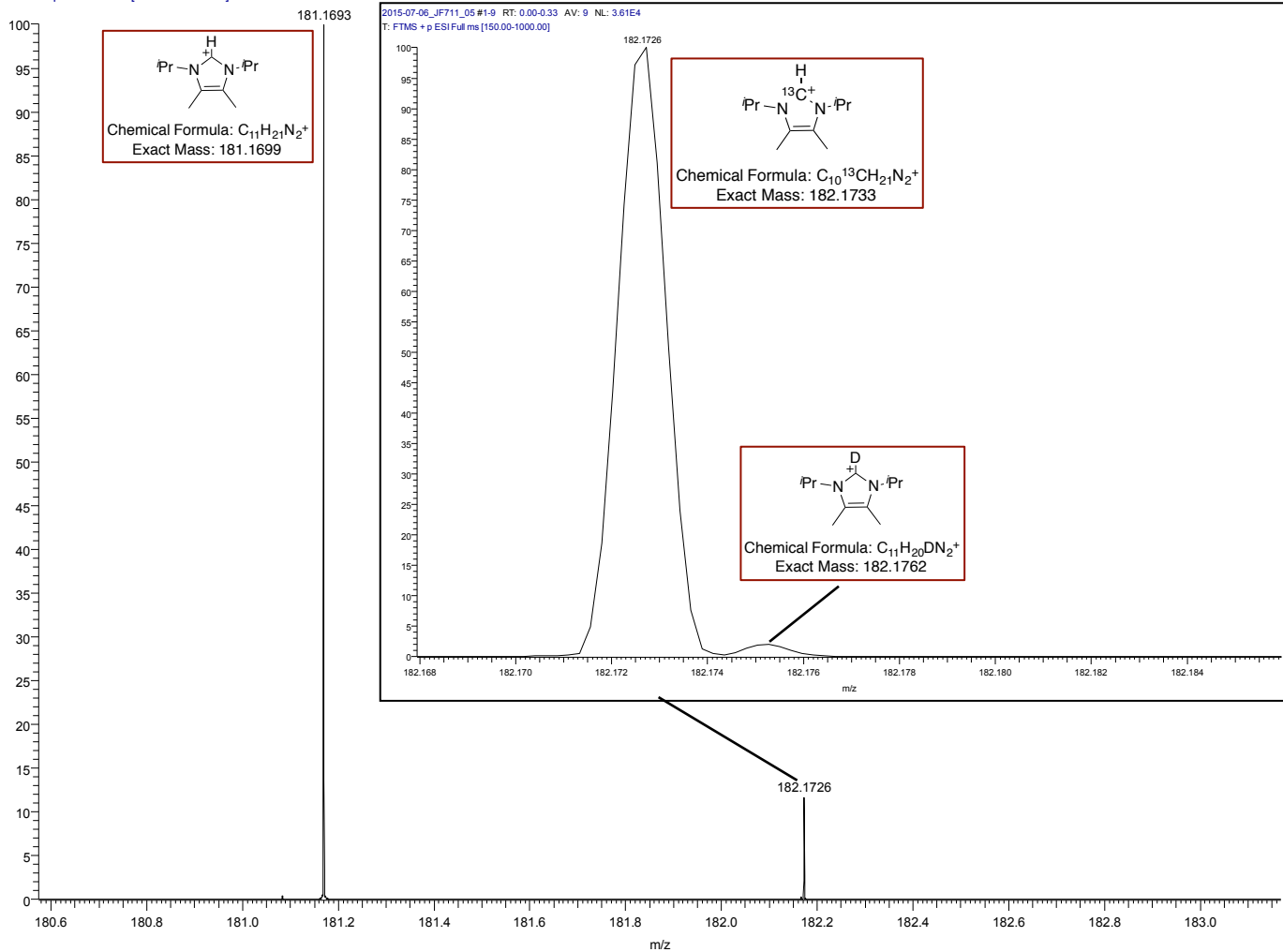
2015-07-06_JF711_04 #2-43 RT: 0.04-1.17 AV: 42 NL: 1.70E7

T: FTMS + p ESI Full ms [150.00-1000.00]



SPECTRUM 5 (64 minutes after CH₃COOD addition)

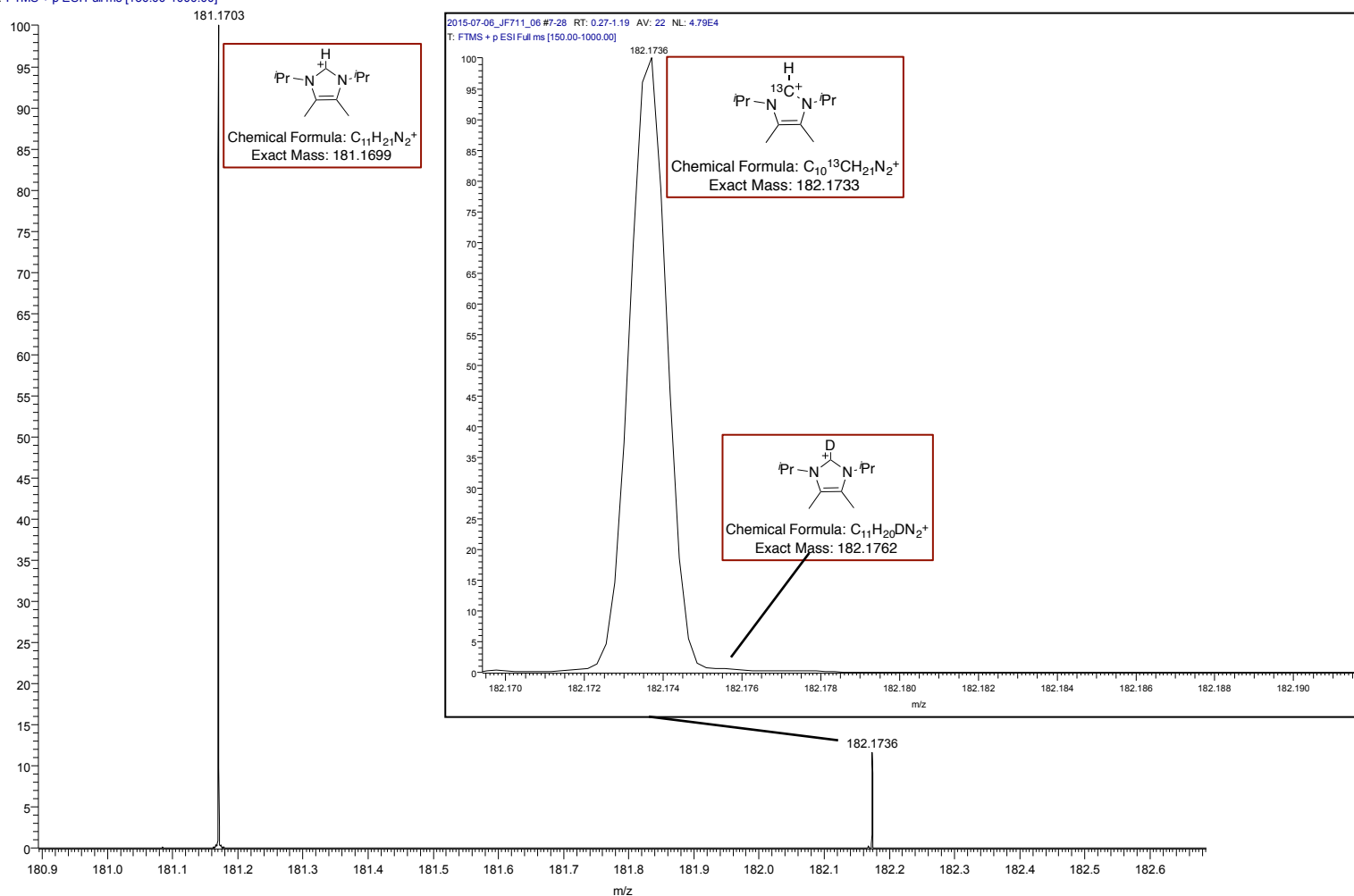
2015-07-06_JF711_05 #1-9 RT: 0.00-0.33 AV: 9 NL: 3.10E5
T: FTMS + p ESI Full ms [150.00-1000.00]



SPECTRUM 6 (123 minutes after CH₃COOD addition)

2015-07-06_JF711_06 #7-28 RT: 0.27-1.19 AV: 22 NL: 4.11E5

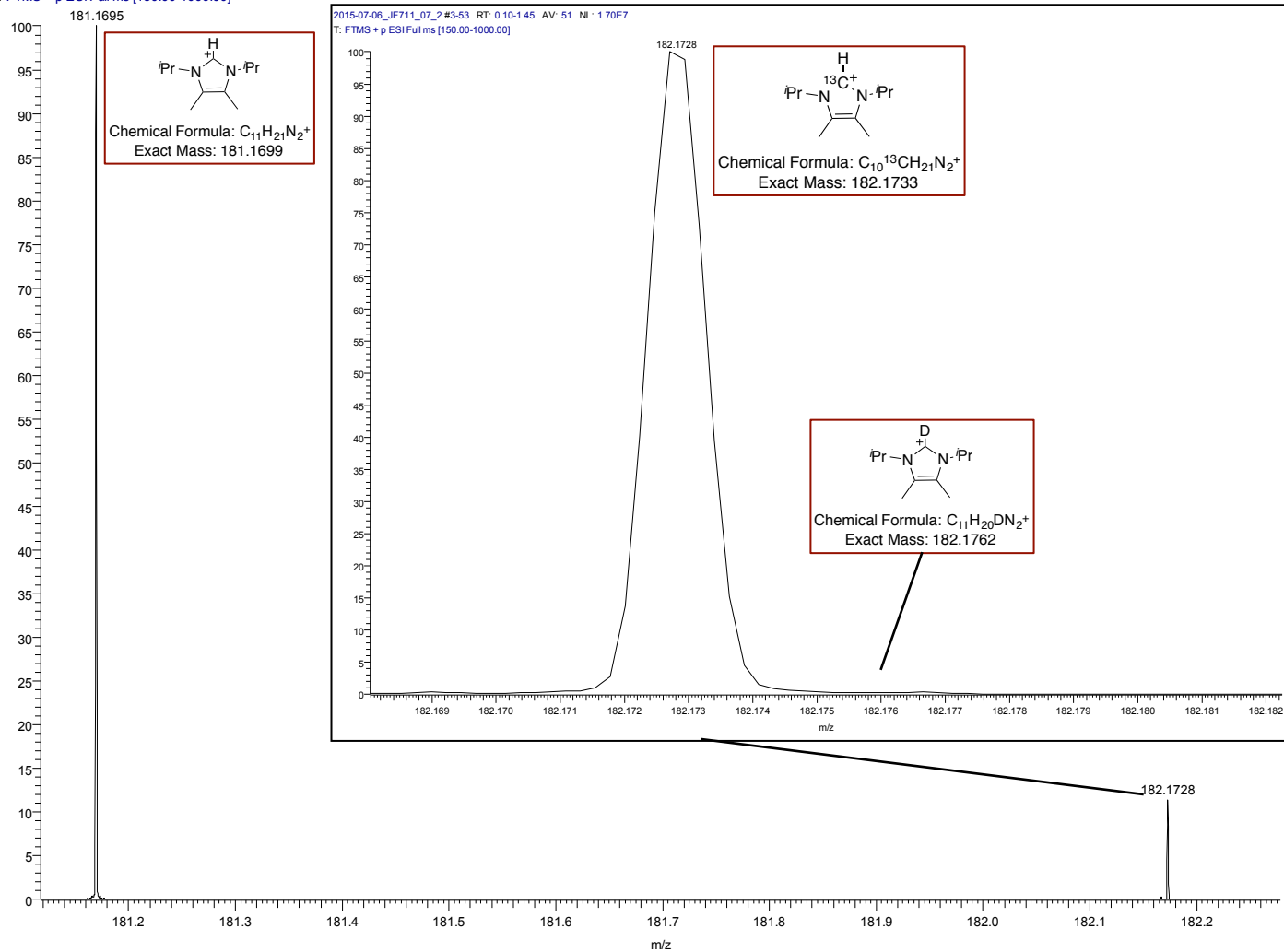
T: FTMS + p ESI Full ms [150.00-1000.00]



SPECTRUM 7 (245 minutes after CH₃COOD addition)

2015-07-06_JF711_07_2 #3-53 RT: 0.10-1.45 AV: 51 NL: 1.48E8

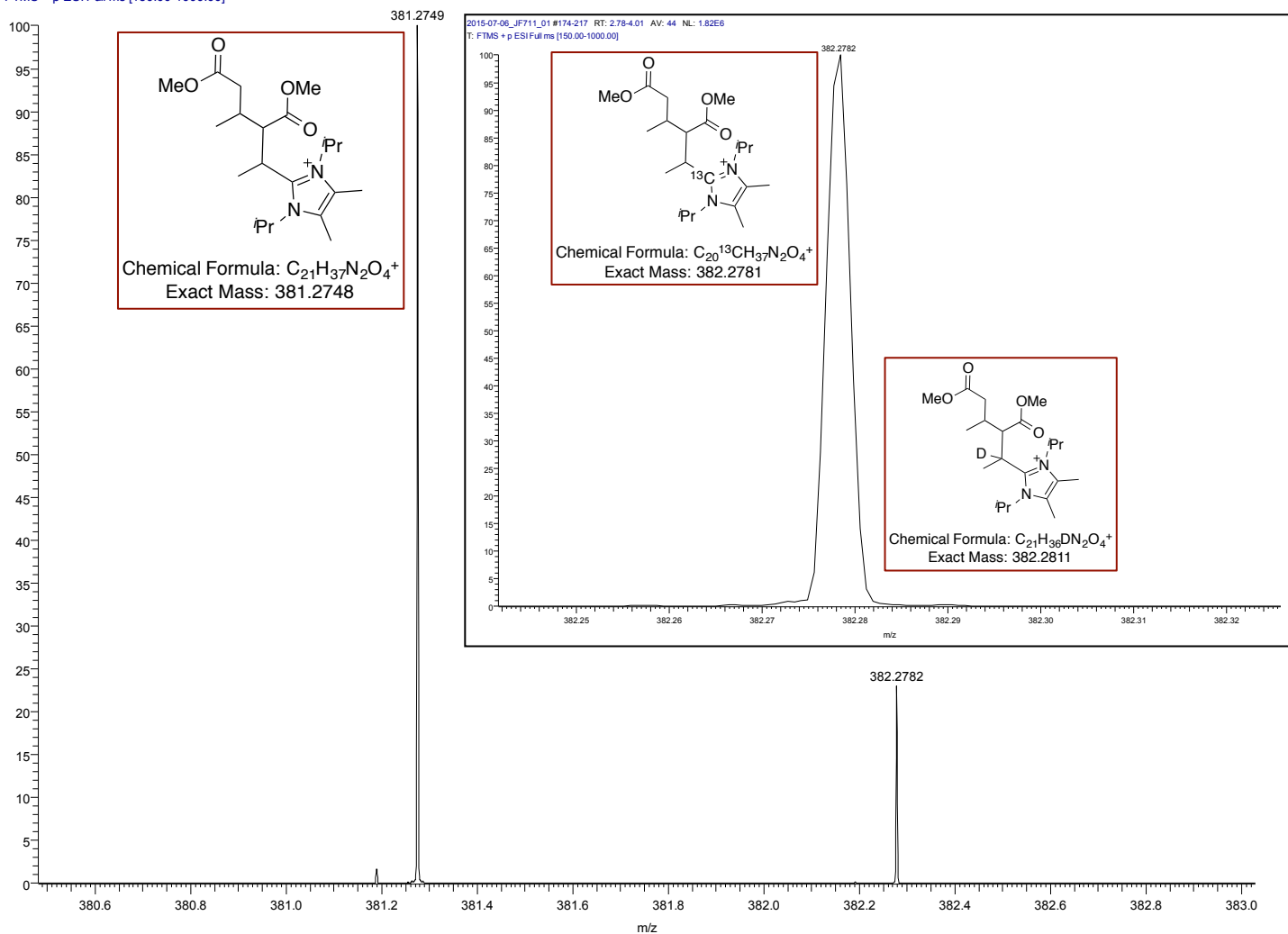
T: FTMS + p ESIFull ms [150.00-1000.00]



SPECTRUM 1 (after CH₃COOH addition but before CH₃COOD addition)

2015-07-06_JF711_01 #174-217 RT: 2.78-4.01 AV: 44 NL: 7.92E6

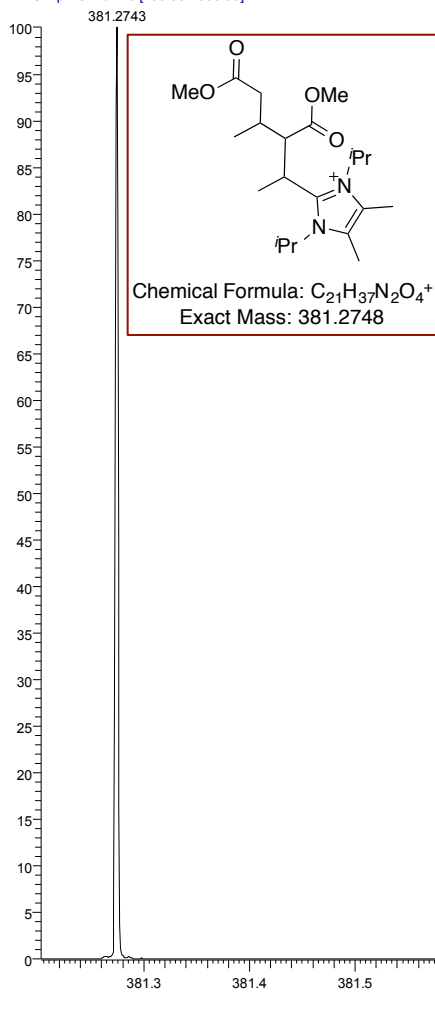
T: FTMS + p ESI Full ms [150.00-1000.00]



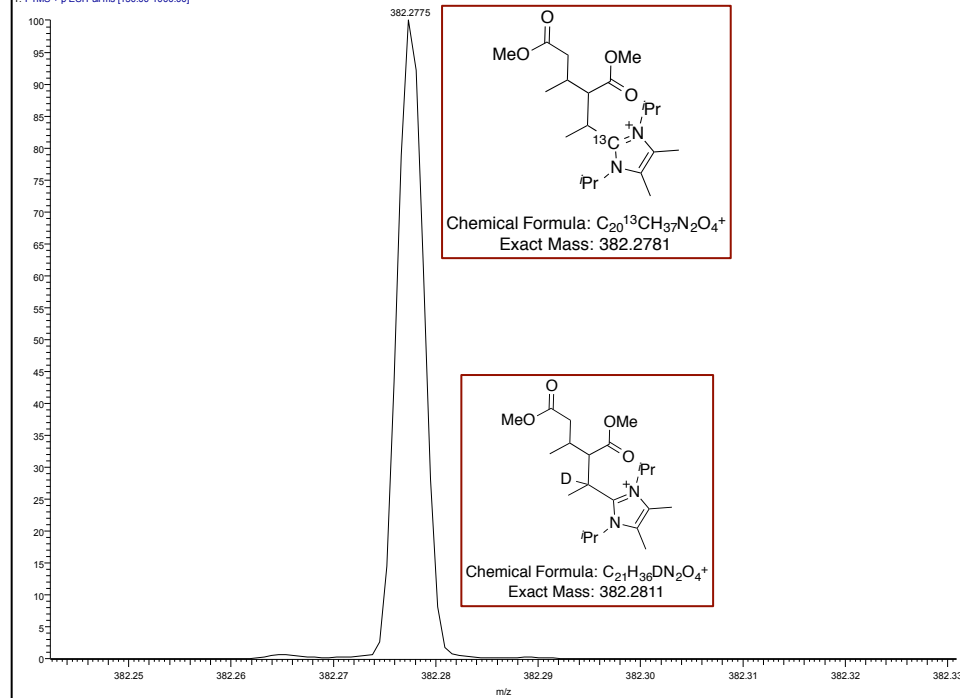
SPECTRUM 2 (4 minutes after CH₃COOD addition)

2015-07-06_JF711_02 #1-15 RT: 0.00-0.43 AV: 15 NL: 1.39E7

T: FTMS + p ESI Full ms [150.00-1000.00]



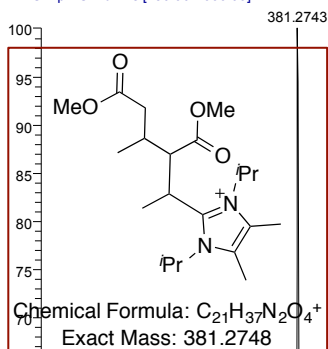
2015-07-06_JF711_02 #1-15 RT: 0.00-0.43 AV: 15 NL: 3.22E6
T: FTMS + p ESI Full ms [150.00-1000.00]



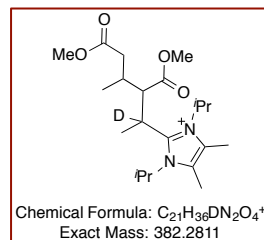
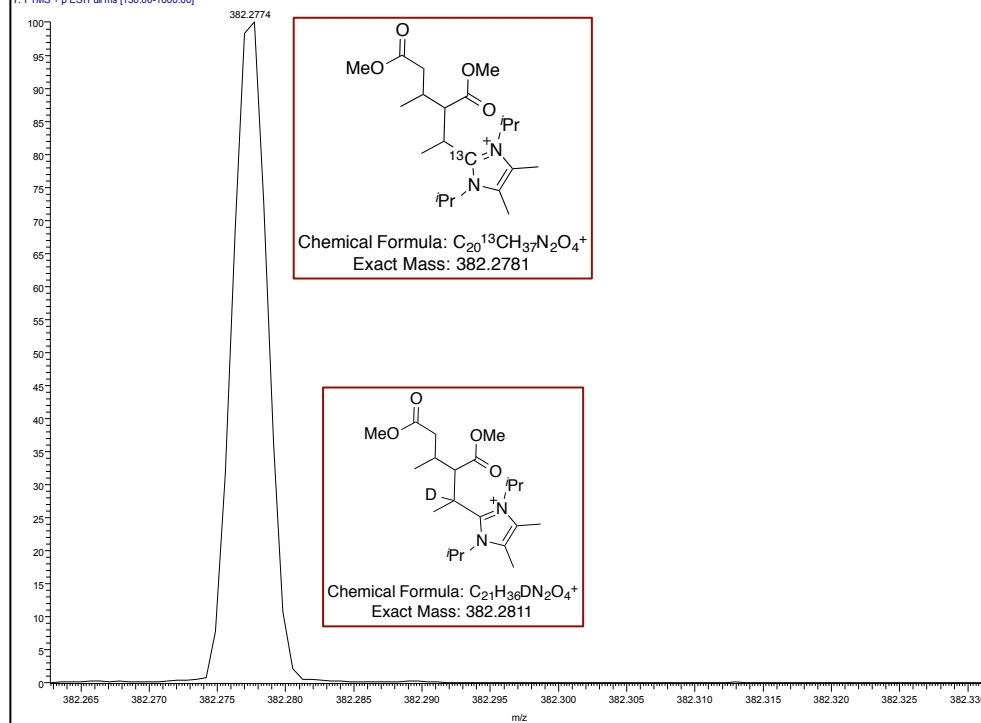
382.2775

SPECTRUM 3 (15 minutes after CH₃COOD addition)

2015-07-06_JF711_03 #1-30 RT: 0.02-0.85 AV: 30 NL: 3.62E7
T: FTMS + p ESI Full ms [150.00-1000.00]



2015-07-06_JF711_03 #1-30 RT: 0.02-0.85 AV: 30 NL: 8.38E6
T: FTMS + p ESI Full ms [150.00-1000.00]



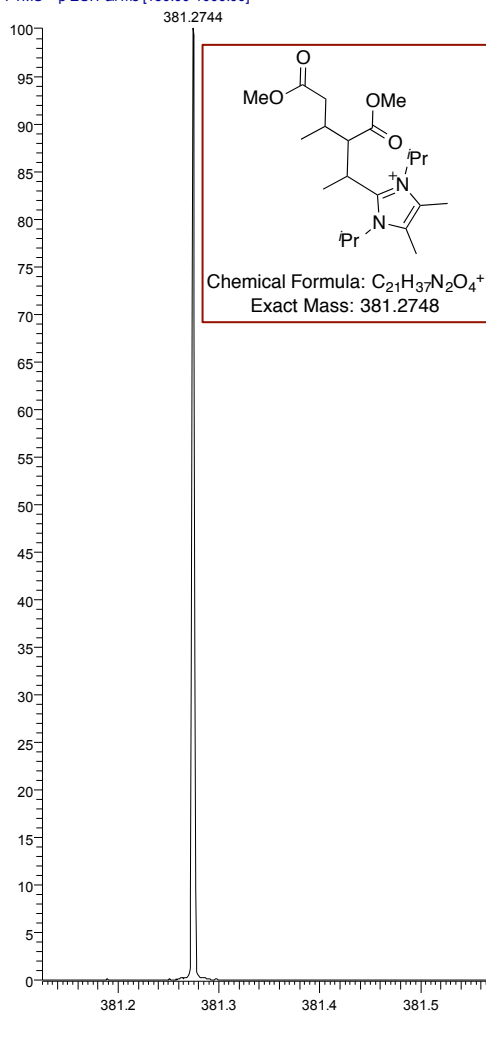
382.2774

m/z

SPECTRUM 4 (32 minutes after CH₃COOD addition)

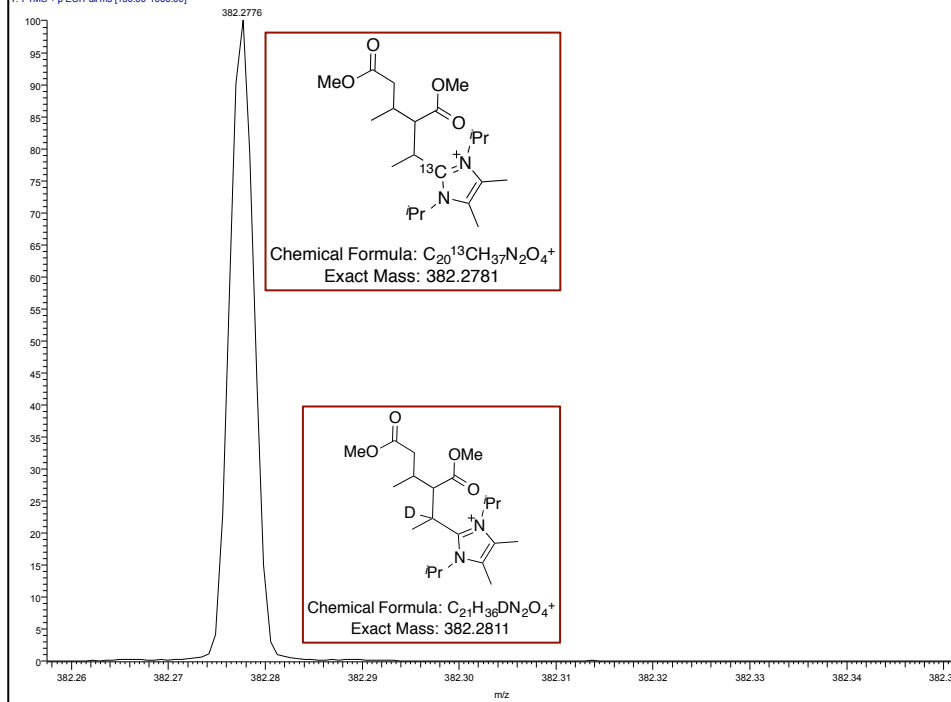
2015-07-06_JF711_04 #2-43 RT: 0.04-1.17 AV: 42 NL: 4.35E7

T: FTMS + p ESI Full ms [150.00-1000.00]



2015-07-06_JF711_04 #2-43 RT: 0.04-1.17 AV: 42 NL: 1.05E7

T: FTMS + p ESI Full ms [150.00-1000.00]

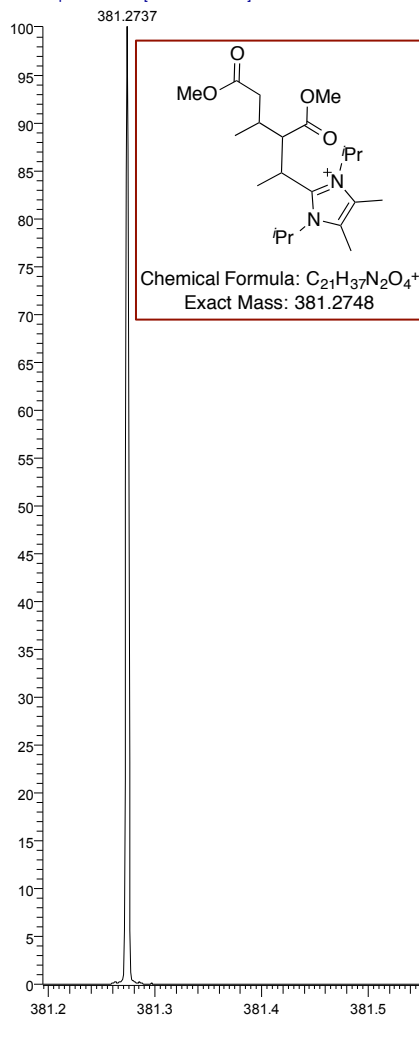


382.2776

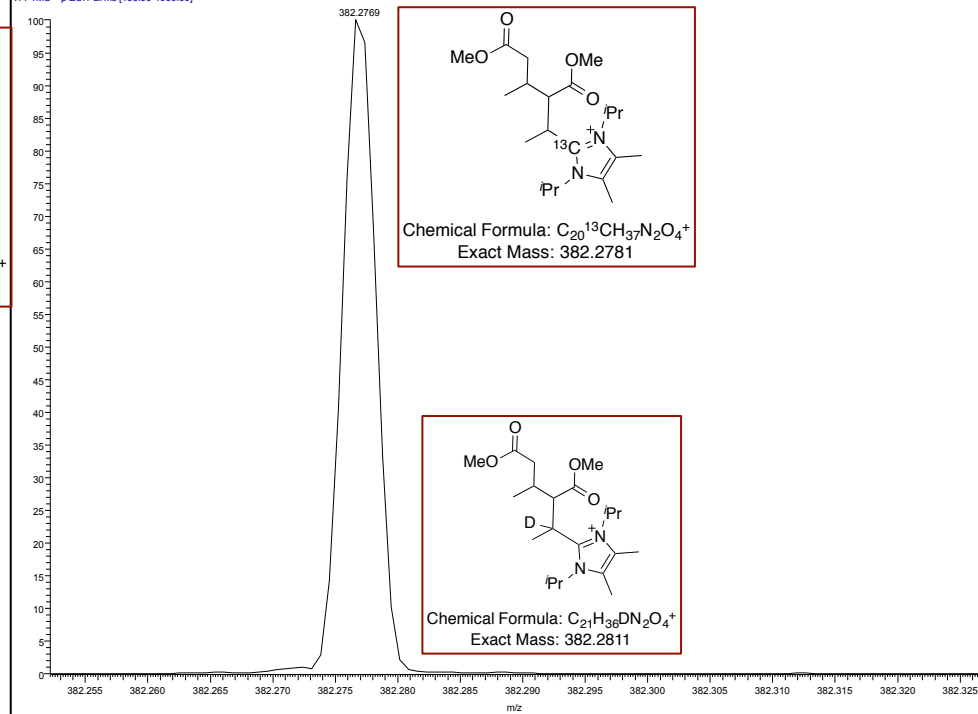
SPECTRUM 5 (64 minutes after CH₃COOD addition)

2015-07-06_JF711_05 #1-9 RT: 0.00-0.33 AV: 9 NL: 1.43E6

T: FTMS + p ESI Full ms [150.00-1000.00]



2015-07-06_JF711_05 #1-9 RT: 0.00-0.33 AV: 9 NL: 3.28E5
T: FTMS + p ESI Full ms [150.00-1000.00]

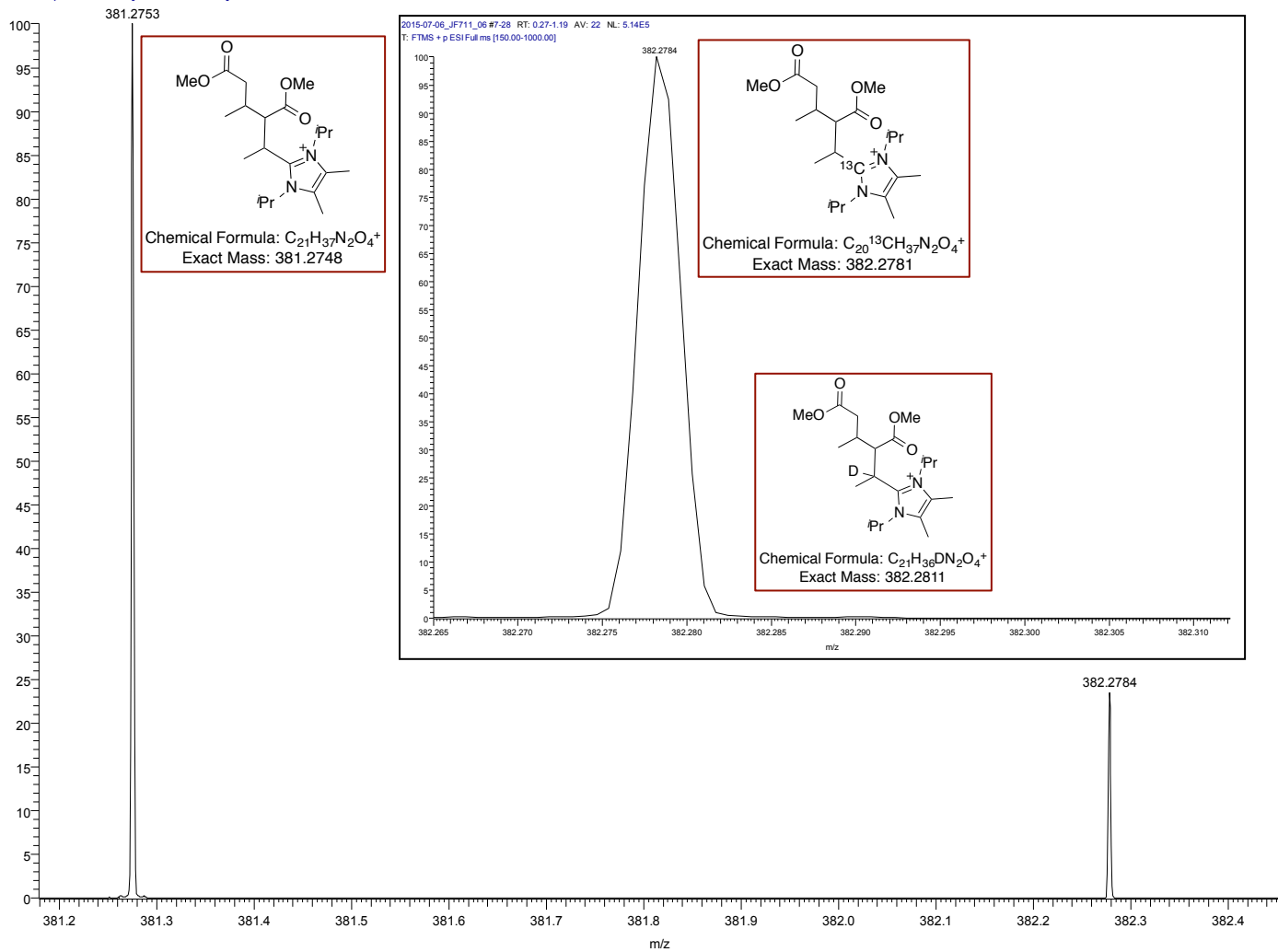


382.2769

m/z

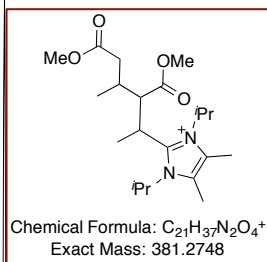
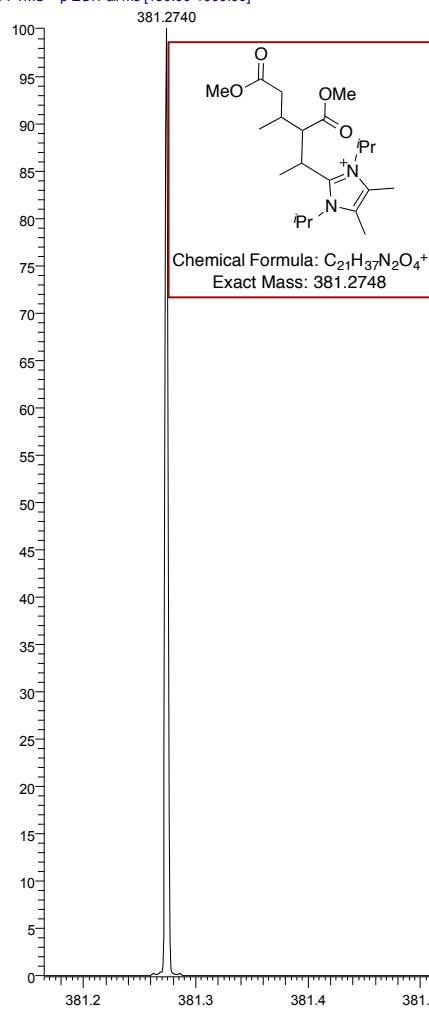
SPECTRUM 6 (123 minutes after CH₃COOD addition)

2015-07-06_JF711_06 #7-28 RT: 0.27-1.19 AV: 22 NL: 2.18E6
T: FTMS + p ESI Full ms [150.00-1000.00]

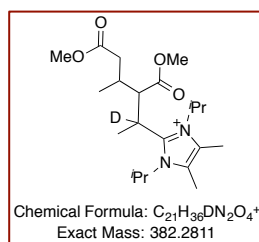
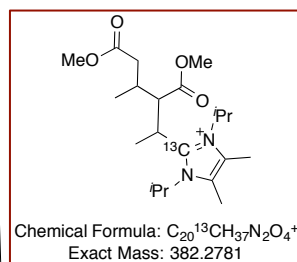
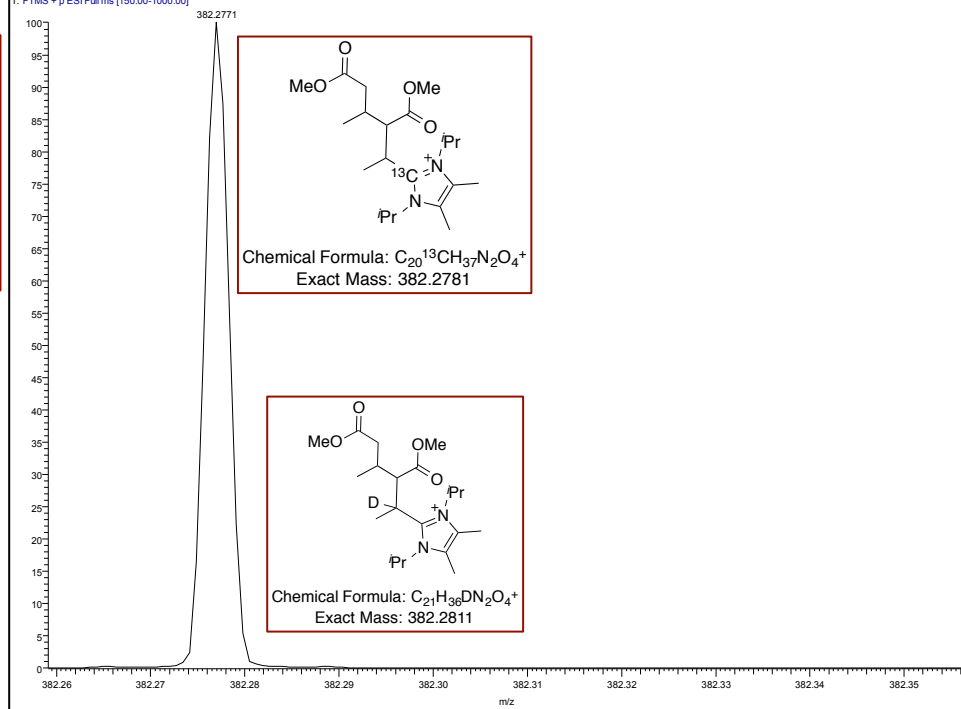


SPECTRUM 7 (245 minutes after CH₃COOD addition)

2015-07-06_JF711_07_2 #3-53 RT: 0.10-1.45 AV: 51 NL: 3.20E8
T: FTMS + p ESI Full ms [150.00-1000.00]



2015-07-06_JF711_07_2 #3-53 RT: 0.10-1.45 AV: 51 NL: 7.59E7
T: FTMS + p ESI Full ms [150.00-1000.00]



382.2771

12. References

- (1) Kuhn, N.; Kratz, T. *Synthesis* **1993**, 561-562.
- (2) Enders, D.; Breuer, K.; Kallfass, U.; Balensiefer, T. *Synthesis* **2003**, 1292-1295.
- (3) Jenner, G. *Tetrahedron Lett.* **2000**, 41, 3091-3094.
- (4) Alcock, S. G.; Baldwin, J. E.; Bohlmann, R.; Harwood, L. M.; Seeman, J. I. *J. Org. Chem.* **1985**, 50, 3526-3535.
- (5) Saal, W. V. D.; Reinhardt, R.; Seidenspinner, H.-M.; Stawitz, J.; Quast, H. *Liebigs Ann. Chem.* **1989**, 703-712.
- (6) Nzahou Ottou, W.; Bourichon, D.; Vignolle, J.; Wirotius, A.-L.; Robert, F.; Landais, Y.; Sotiropoulos, J.-M.; Miqueu, K.; Taton, D. *Chem. Eur. J.* **2014**, 20, 3989-3997.
- (7) Biju, A. T.; Padmanaban, M.; Wurz, N. E.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, 50, 8412-8415.
- (8) Matsuoka, S.; Ota, Y.; Washio, A.; Katada, A.; Ichioka, K.; Takagi, K.; Suzuki, M. *Org. Lett.* **2011**, 13, 3722-3725.
- (9) Zhang, Y.; Chen, E. Y.-X. *Angew. Chem., Int. Ed.* **2012**, 51, 2465-2469.