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Synthesis of functionalised *N*-heterocyclic carbene ligands bearing a long spacer and their use in olefin metathesis

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GENERAL

The catalyst preparation was carried out under argon in pre-dried glassware using Schlenk techniques. The anhydrous solvents were dried by distillation over the following drying agents and were transferred under argon: THF (K/benzophenone), toluene (Na), *n*-pentane, *n*-hexane, CH_2Cl_2 (CaH_2). Flash column chromatography was performed using ALDRICH silica gel 60 (230-400 mesh). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F_{254} precoated plates (0.25 mm thickness) with a fluorescent indicator. NMR spectra were recorded on Varian; Unity Plus 200 MHz, INOVA 500 MHz, Mercury 400 MHz, VNMRS 600 MHz in $CDCl_3$, CH_2Cl_2; chemical shifts (δ) are given in ppm relative to TMS, coupling constants are (*J*) in Hz. IR spectra were recorded on PE SPECTRUM 2000 and JASCO FT/IR-6200: wavenumbers are in cm^{-1}. MS (ESI) spectra were recorded by Quattro LC (triple quadrupole mass spectrometer). GC measurements were done on PE Clarus 580 with InertCap 5MS-Sil column and GC/MS on PE Clarus 680/600S with InertCap 5 column. Ru contents were measured using ICP-MS spectrometer type Elan 9000 Perkin Elmer. Model substrates (**20a**, **20b**, **23**, **25**, **27**, **30**) and products (**21a**, **21b**, **24**, **26**, **28**, **31**) were previously obtained and characterized.[1,2,3,4,5] All other commercially available chemicals were used as received.

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2.Synthesis procedures and analytical data

Synthesis of compound 5

To solution of **4** (1.48 mmol) in dry THF (23 mL), 9-BBN (4.44 mmol, 8.9 mL of 0.5M solution) was added. The reaction mixture was stirred at room temperature for eight hours. 10% NaOH and 30% H_2O_2 were added to reaction mixture and was stirred overnight at room temperature. The solvents were evaporated and residue was dissolved in CH_2Cl_2 and washed with water and brine, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography (SiO_2, 50% EtOAc : *c*-hex) to afford **5** (440 mg, 84%) as a light yellow oil. IR (film): 3363, 2940, 2917, 2859, 1484, 1448, 1230, 1055, 1031, 1012, 854, 738 cm^{-1};^{1}H NMR (200 MHz, $CDCl_3$) δ 6.94-6.72 (m, 4H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.56-3.41 (m, 1H), 3.16 (dd, *J* = 11.9, 5.2 Hz, 1H), 2.97 (br s, 3H), 2.81 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.40-2.11 (m, 18H), 1.85-1.45 (m, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.3, 141.3, 131.2, 130.8, 129.7, 129.4, 129.4, 128.7, 62.7 (CH_2), 57.1, 52.8 (CH_2), 30.8 (CH_2), 29.8 (CH_2), 20.4, 20.4, 19.2, 18.2 ppm; DEPT (50 MHz, $CDCl_3$) δ 130.0, 129.7, 63.0, 57.5, 53.1, 31.1, 30.1, 20.8, 20.8, 19.5, 18.6 ppm; HRMS (ESI) cald for $C_{23}H_{25}N_2O$ $[M+H]^+$: 355.2752, found: 355.2749.

Synthesis of compound 6

Compound **5** (1.13 mmol) and ammonium tetrafluoroborate (1.13 mmol) were dissolved in triethylorthoformate (5 mL) and the reaction mixture was stirred at 110 °C overnight. The reaction mixture was cooled and the volatile compounds were removed under vacuum. The residue was dissolved in CH_2Cl_2, washed with water to remove unreacted ammonium tetrafluoroborate and dried over sodium sulfate. The product **6** was dried under vacuum; yield: 0.70 g, 61%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.94-6.72 (m, 4H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.56-3.41 (m, 1H), 3.16 (dd, *J* = 11.9, 5.2 Hz, 1H), 2.97 (br s, 3H), 2.81 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.40-2.11 (m, 18H), 1.85-1.45 (m, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.2, 140.3, 140.2, 135.4, 135.1, 130.2, 129.9, 129.8, 128.7, 64.3, 61.1, 56.6, 29.6, 27.8, 20.9, 18.3, 17.8, 17.3 ppm; DEPT (50 MHz, $CDCl_3$) δ 158.2, 130.2, 129.9, 129.8, 64.3, 61.1 (CH_2), 56.6 (CH_2), 29.6 (CH_2), 27.8 (CH_2), 20.9, 18.3, 17.8, 17.3 ppm; HRMS (ESI) cald for $C_{24}H_{33}N_2O$ $[M]^+$: 365.2596, found: 365.2593.

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Synthesis of compound 11

Compound **10** (5.6 mmol) and 2,4,6-trimethylaniline (10.5 mL, 72.8 mmol) were heated together at 125 °C overnight. Reaction mixture was then cooled down to room temperature and alkalized with sodium hydroxide aq (15 %). Product was extracted with dichloromethane. Organic layer was washed with water and dried over sodium sulfate. Drying agent was filtered off and solvent was evaporated. Then excess of 2,4,6-trimethylaniline was removed under reduced pressure (3 mbar). Crude product was purified by column chromatography (SiO_2, 50% EtOAc : *c*-hex). Removal of solvents afforded **11** (1.70 g, 72 %) as a light-brown oil. IR (film): 3361, 2927, 2854, 1483, 1465, 1454, 1230, 1057, 1031, 853, 568 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.83 (br s, 4H), 3.63 (t, *J* = 6.5 Hz, 1H), 3.55-3.35 (m, 1H), 3.22 (dd, *J* = 11.8, 4.5 Hz, 1H), 2.77 (dd, *J* = 11.8, 7.1 Hz, 1H), 2.85-2.50 (m, 2H), 2.29 (s, 6H), 2.25 (s, 12H), 1.68-1.41 (m, 5H), 1.42-1.12 (m, 10H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.7, 141.8, 131.0, 130.4, 129.6, 129.4, 128.7, 62.9, 57.1, 52.9, 34.0, 32.7, 29.7, 29.4, 29.3, 26.3, 25.6, 20.5, 20.4, 19.2, 18.3 ppm; DEPT (50 MHz, $CDCl_3$) δ 129.7, 129.5, 63.0, 57.1, 53.0, 34.0, 32.7, 29.7, 29.5, 29.3, 26.4, 25.7, 20.5, 19.3, 18.4 ppm; MS (ESI): 425.4 $[M+H]^+$, 447.4 $[M+Na]^+$.

Synthesis of compound 12

To cooled solution of **11** in benzene PBr_3 was added drop-wise. Reaction mixture was stirred at 0 °C to the disappearance of substrate (monitored by TLC). Then mixture was warmed to room temperature and solvent evaporated under vacuum. The residue was extracted with dichloromethane, washed with water, dried over magnesium sulfate. Crude product was purified by column chromatography (SiO_2, 20% EtOAc : *c*-hex) to afford bromide **11a** (115 mg, 15%) as a oil. ^1H NMR (200 MHz, $CDCl_3$) δ 6.87 (br s, 4H), 3.44 (br t, *J* = 6.8 Hz, 2H), 3.26 (dd, *J* = 11.8, 4.3 Hz, 2H), 2.81 (dd, *J* = 11.7, 7.1 Hz, 1H), 2.33 (s, 6H), 2.28 (s, 12H), 2.03-1.75 (m, 2H), 1.72-0.80 (m, 14H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.6, 141.8, 130.9, 130.4, 129.6, 129.3, 128.7, 57.1, 52.9, 33.9, 33.9, 32.7, 29.6, 29.2, 28.6, 28.0, 26.3, 20.5, 19.2, 18.3 ppm; DEPT (50 MHz, $CDCl_3$) δ 129.7, 129.4, 57.1, 52.9 (CH_2), 34.0 (CH_2), 33.9 (CH_2), 32.8 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 26.3 (CH_2), 20.5, 19.3, 18.4 ppm; MS (ESI): 487.2 and 489.2 $[M+H]^+$. Bromide (0.24 mmol) and pyridine (2.6 mL) were heated together at 100 °C overnight. Reaction mixture was then cooled down to room temperature and the excess of pyridine was removed under reduced pressure (3 mbar). Crude product **11b** (86 mg, 65%) was used to next step without purification. ^1H NMR (200 MHz, $CDCl_3$) δ 9.50

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(d, *J* = 5.7 Hz, 2H), 8.45 (t, *J* = 7.6 Hz, 1H), 8.08 (t, *J* = 6.8 Hz, 2H), 6.75 (s, 4H), 4.92 (t, *J* = 7.1 Hz, 2H), 3.47-2.93 (m, 4H), 2.68 (dd, *J* = 11.8, 7.0 Hz, 1H), 2.20 (s, 6H), 2.15 (s, 12H), 2.08-1.78 (m, 2H), 1.54-0.71 (m, 12H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.9, 143.4, 141.6, 130.8, 130.2, 129.5, 129.2, 128.5, 128.2, 61.7, 56.9, 52.7, 33.8, 31.8, 29.5, 29.1, 28.8, 26.2, 25.8, 20.3, 19.1, 18.2, ppm; DEPT (50 MHz, $CDCl_3$) δ 144.9, 129.5, 129.2, 128.3, 61.7 (CH_2), 56.9, 52.7 (CH_2), 33.8 (CH_2), 31.8 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 28.8 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 20.3, 19.1, 18.2 ppm. Diamine derivative (0.18 mmol) and ammonium chloride (0.18 mmol) were dissolved in triethylorthoformate (5 mL) and the reaction mixture was stirred at 120 °C overnight. The reaction mixture was cooled and the volatile compounds were removed under vacuum. The residue was dissolved in CH_2Cl_2, washed with water to remove unreacted ammonium chloride and dried over sodium sulfate. The product **12** was dried under vacuum (57 mg, 53%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.69 (br s, 2H), 9.20 (s, 1H), 8.32 (br s, 1H), 8.09-7.70 (m, 2H), 6.82 (s, 1H), 6.80 (s, 1H), 4.81 (br s, 2H), 2.31-2.09 (m, 18H), 2.08-2.00 (m, 2H), 1.98-1.74 (m, 1H), 1.72-1.50 (m, 1H), 1.35-0.65 (m, 10H) ppm; MS (ESI): 248.7 $[M]^{2+}$, 532.4 $[M+Cl]^+$, 576.4 and 578.4 $[M+Br]^+$.

Synthesis of compound 13

Triphenylphosphine (11.3 mmol) and imidazole (15.1 mmol) were dissolved in mixture of solvents Et_2O/CH_3CN (3/1, 60 mL) at room temperature. To resulting mixture was added iodine (11.3 mmol) at 0 °C. After the addition was completed, the mixture was stirred at 0 °C for additional 20 min. To mixture was added portion-wise of compound **11** (7.53 mmol) over 15 min. The reaction mixture was warmed to room temperature and stirred for two hours. Then the solvent was evaporated and residue was dissolved in dichloromethane. White precipitate was filtered off and the filtrate was passed through thin pad of silica gel (Florisil). The solvent was evaporated and crude product **13** was used to next step.

Synthesis of compound 14

Compound **13** (7.5 mmol) was placed under argon in pressure flask and 45 mL of 33% solution of dimethylamine in absolute ethanol was added. The reaction mixture was stirred at 120 °C for 30 min. After that time mixture was cooled to room temperature (be careful when opening the pressure flask) and the excess of dimethylamine end solvent were evaporated under reduced pressure. The residue was purified by column chromatography (Al_2O_3 neutral, 50% EtOAc : *c*-hex) to afford **14** (2.58 g, 76%) as a light-brown oil. IR (film): 3368, 2928,

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2854, 2813, 2762, 1484, 1466, 1231, 852 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92-6.76 (m, 4H), 3.55-3.35 (m, 1H), 3.21 (dd, *J* = 11.8, 4.4 Hz, 1H), 3.28-2.88 (m,2H), 2.76 (dd, *J* = 11.8, 7.1 Hz, 1H), 2.29-2.27 (m,6H), 2.27-2.24 (m, 7H), 2.24-2.23 (m, 6H), 2.23-2.20 (m, 5H), 1.55-1.40 (m, 5H), 1.40-1.20 (m, 11H) ppm; ^{13}C NMR (101MHz, $CDCl_3$): 143.7, 141.9, 131.0, 130.4, 129.7, 129.4, 129.4, 128.7, 59.9, 57.1, 52.9, 45.5, 34.0, 29.7, 29.5, 27.7, 27.4, 26.4, 20.5, 20.5, 19.2, 18.4 ppm; DEPT (101 MHz, $CDCl_3$) δ 129.7, 129.4, 59.9 (CH_2), 57.1, 52.9 (CH_2), 45.5, 34.0 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 26.9 (CH_2), 26.3 (CH_2), 20.5, 20.5, 19.2, 18.4 ppm; MS (ESI): 452.5 $[M+H]^+$ 474.4 $[M+Na]^+$.

Synthesis of compound 15b

Compound **14** (1.4 mmol), ammonium tetrafluoroborate (1.4 mmol) and triethylorthoformate (5 mL) were placed in microwave tube and irradiated (120 °C, 30min).The excess of triethylorthoformate was removed under vacuum. The residue was dissolved in CH_2Cl_2, washed with water to remove unreacted ammonium tetrafluoroborate and dried over magnesium sulfate. Crude product was purified by column chromatography (Al_2O_3 neutral, 5% MeOH : DCM) to afford **15b** (550 mg, 73%) as a light-yellow solid (foam). IR (film): 2930, 2856, 2816, 2775, 1630, 1482, 1465, 1260, 1060, 853, 572 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 6.97 (s, 2H), 6.95 (s, 2H), 4.93-4.75 (m, 1H), 4.64 (t, *J* = 11.7 Hz, 1H), 3.89 (dd, *J* = 11.9, 9.2 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 6H), 2.31 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H), 2.21 (s, 6H), 1.80-1.64 (m, 2H), 1.47-1.35 (m, 2H), 1.33-1.13 (m, 12H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 140.6, 140.4, 135.3, 135.3, 130.5, 130.1, 123.0, 128.8, 64.4, 59.6, 56.8, 45.2, 33.1, 29.2, 29.1, 29.1, 27.4, 27.2, 25.3, 21.0, 21.0, 18.5, 18.0, 17.5 ppm; DEPT (101 MHz, $CDCl_3$) δ 158.7, 130.5, 130.0, 64.4, 59.6 (CH_2), 56.8 (CH_2), 45.2, 33.1(CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 25.3 (CH_2), 21.0, 21.0, 18.5, 18.0, 17.5 ppm; MS (ESI): 462.3 $[M]^+$.

Synthesis of compound 18

Potassium *tert*-pentoxide (1.7 M in toluene, 70.6 µl, 0.12 mmol) was added at room temperature to a suspension of **15b** (66 mg, 0.12 mmol) in dry toluene (6 mL) under argon. Reaction mixture was stirred at room temperature for 30 min., then I generation of Grubbs (82 mg, 0.1 mmol) was added and stirring was continued at 80 °C for 1 h. After cooling down, reaction mixture was filtered through a short pad of silica gel (10% Et_3N : EtOAc) under argon. Solvents were evaporated, crude catalyst was dried under vacuum to afford complex **17** (74 mg,

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74%) as a dark brown solid (foam). Compound **17** was used to next reaction without full characterization. IR (film): 3057, 2926, 2853, 2814, 2763, 1897, 1678, 1482, 1445, 1418, 1260, 849, 739 cm^{-1}; The diagnostic benzylidene proton shifts ^{1}H NMR (400 MHz, CD_2Cl_2) δ 19.12 ppm; MS (ESI): m/z 968.5 $[M-Cl]^+$; HRMS: calcd for $C_{56}H_{86}N_3PClRu$ 968.5291, found 968.5251. 1-Isopropoxy-2-vinylbenzene (19.5 mg, 0.11 mmol) and CuCl (11 mg, 0.11 mmol) were placed in a Schlenk flask. The flask was filled with argon and then dry toluene (5 mL) was added. Afterwards complex **17** (0.76 g, 0.77 mmol) was added and the resulting solution was stirred at 80 °C for 5min. The reaction mixture was cooled down to room temperature and filtered through a short pad of silica gel (10% Et_3N : EtOAc) under argon. Removal of solvents afforded complex **18** (55 mg, 70%) as dark green solid (foam). IR (film): 3381, 2928, 2855, 2814, 2763, 1607, 1589, 1575, 1477, 1453, 1418, 1383, 1260, 1113, 746, 578 cm^{-1}; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 16.47 (br s, 1H), 7.62-7.49 (m, 1H), 7.15-7.01 (m, 4H), 6.99-6.80 (m, 3H), 4.87 (sep, *J* = 6.1 Hz, 1H), 4.45 (ddd, *J* = 20.8, 10.4, 3.4 Hz, 1H), 4.23-4.14 (m, 1H), 3.86-3.79 (m, 1H), 2.52-2.30 (m, 18H), 2.32-2.25 (m, 3H), 2.22 (s, 6H), 1.78-1.60 (m, 2H), 1.52-1.33 (m, 3H), 1.32-1.10 (m, 14H) ppm; ^{13}C NMR (151 MHz, CD_2Cl_2) δ 296.0, 211.7, 151.9, 145.2, 138.8, 138.6, 129.3, 122.23, 122.1, 112.9, 75.0, 59.3, 44.7, 33.9, 29.4, 29.3, 27.2, 27.0, 26.1, 20.8, 20.8 ppm; MS (ESI): m/z 746.3 $[M-Cl]^+$, 782.3 $[M+H]^+$; HRMS: calcd for $C_{41}H_{60}N_3OCl_2Ru$ 782.3157, found 782.3130.

Synthesis of compound 19

Complex **18** (446 mg, 0.57 mmol) was placed under argon in pressure flask and dry methanol (6 mL) was added. The solution was cooled down to -78 °C and cold liquid (cooled to -78 °C) of chloromethane (ca 6 mL) was added. The reaction mixture was slowly warmed up to room temperature, then placed in oil bath and heated to 50 °C and stirred for 72 hours. After that time flask was opened carefully to remove the excess of chloromethane and the mixture was concentrated under reduced pressure. Residue was purified by filtration through a short pad of Al_2O_3 neutral (5% MeOH : DCM). The solvents were evaporated and dried under vacuum to afford complex **19** (380 mg, 80%) as a green solid (foam). IR (film): 3389, 3014, 2926, 2855, 1671, 1480, 1453, 1264, 1114, 937, 852, 748, 580 cm^{-1}; ^{1}H NMR (501 MHz, CD_2Cl_2) δ 16.46 (br s, 1H), 7.60-7.48 (m, 1H), 7.13-7.00 (m, 4H), 6.99-6.78 (m, 3H), 4.93-4.79 (m, 1H), 4.44 (qd, *J* = 10.3, 3.4 Hz, 1H), 4.25-4.12 (m, 1H), 3.84 (t, *J* = 9.5 Hz, 1H), 3.53-3.40 (m, 2H), 3.38-3.27 (m, 9H), 2.58-2.31 (m, 18H), 2.31-2.23 (m, 2H), 1.91-1.54 (m, 6H), 1.43-1.08 (m, 12H) ppm; ^{13}C NMR (126 MHz, CD_2Cl_2) δ 296.6, 212.3, 164.7, 152.4, 145.7, 139.4, 139.2,

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130.0, 129.9, 129.9, 128.5, 122.8, 122.6, 113.5, 75.6, 29.9, 29.7, 29.5, 26.6, 21.4, 21.3 ppm; MS (ESI): m/z 796.3 $[M\text{-}Cl]^+$; HRMS: calcd for $C_{42}H_{62}N_3OCl_2Ru$ 796.3313, found 796.3315.

Metathesis in DCM – removal of ruthenium-containing impurities by filtration of reaction mixture through silica gel.

Complex **19** (1 mol%) was added under argon to a solution of **20a** (99 mg, 0.406 mmol) in dichloromethane (4.06 mL). Reaction mixture was stirred at 40 °C for 5 h then cooled down to room temperature and filtered through a pad of silica gel (990 mg). Additional portion of DCM (4.1 mL) was used to remove product from silica gel. DCM was removed on vacuum to gave **21a** (85 mg, 97 %) as a colorless oil. Purity of product was determined using GC method, residual ruthenium was measured using ICP MS method (the samples were prepared for measurement as described in the publication: M. Mauduit et al. *Chem. Eur. J.* 2012, **18**, 16369-16382 and were measured by ICP-MS spectrometer type Elan 9000 Perkin Elmer).

General procedure for metathesis reactions

Comparative RCM experiments with substrates **20a**, **20b**, **23**, **25**, **27**, **29** (CH_2Cl_2, c = 0.1 M, 40 °C, refer to Table 1 and Fig. 2, 3) were performed as follows. To a stirred solution of substrate **23** (200 mg, 0.845 mmol) and durene (used as an internal standard, 0.845 mmol) in CH_2Cl_2 (8.45 mL) placed under argon in a Schlenk tube catalyst **19** (1 mol%) in CH_2Cl_2 was added in a single portion at 40 °C and the reaction mixture was stirred for 5 h at the same temperature. Aliquots (0.25 mL), taken in regular intervals, were quenched immediately with ice-cold solution of ethyl-vinyl ether (0.1 mL) and analyzed by GC, using EP Clarus 580 chromatograph with InertCap MS5/Sil column.

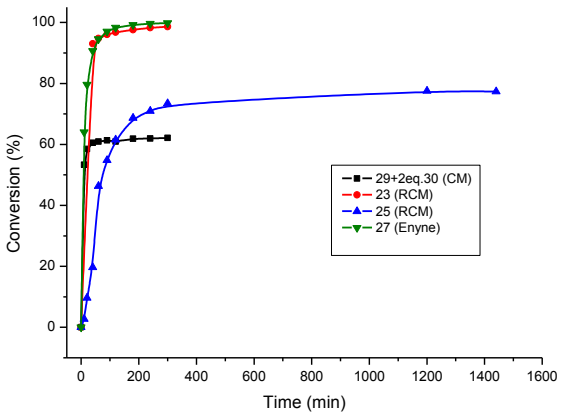

Fig. 4 Reaction profile of metathesis reaction of **23** (RCM), **25** (RCM), **27** (Enyne), **29**+**30** (CM), 1 mol% of catalyst **19**, CH_2Cl_2 (0.1M), 40 °C

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RCM of diene 20a with catalyst 18

In the case of RCM of diene **20a** catalysed by **18** we observed that the reaction is not fully selective, as a side product of cycloisomerisation **22** (28% GC) was formed during the reaction. GC analysis confirmed that the two products (**21a** and **22**) were formed from the beginning of the reaction. To confirmed our results, the reaction mixture was analyzed by GC/MS, using PE Clarus 680/600S chromatograph with InertCap 5 column. The formation of side product was observed only in this case.

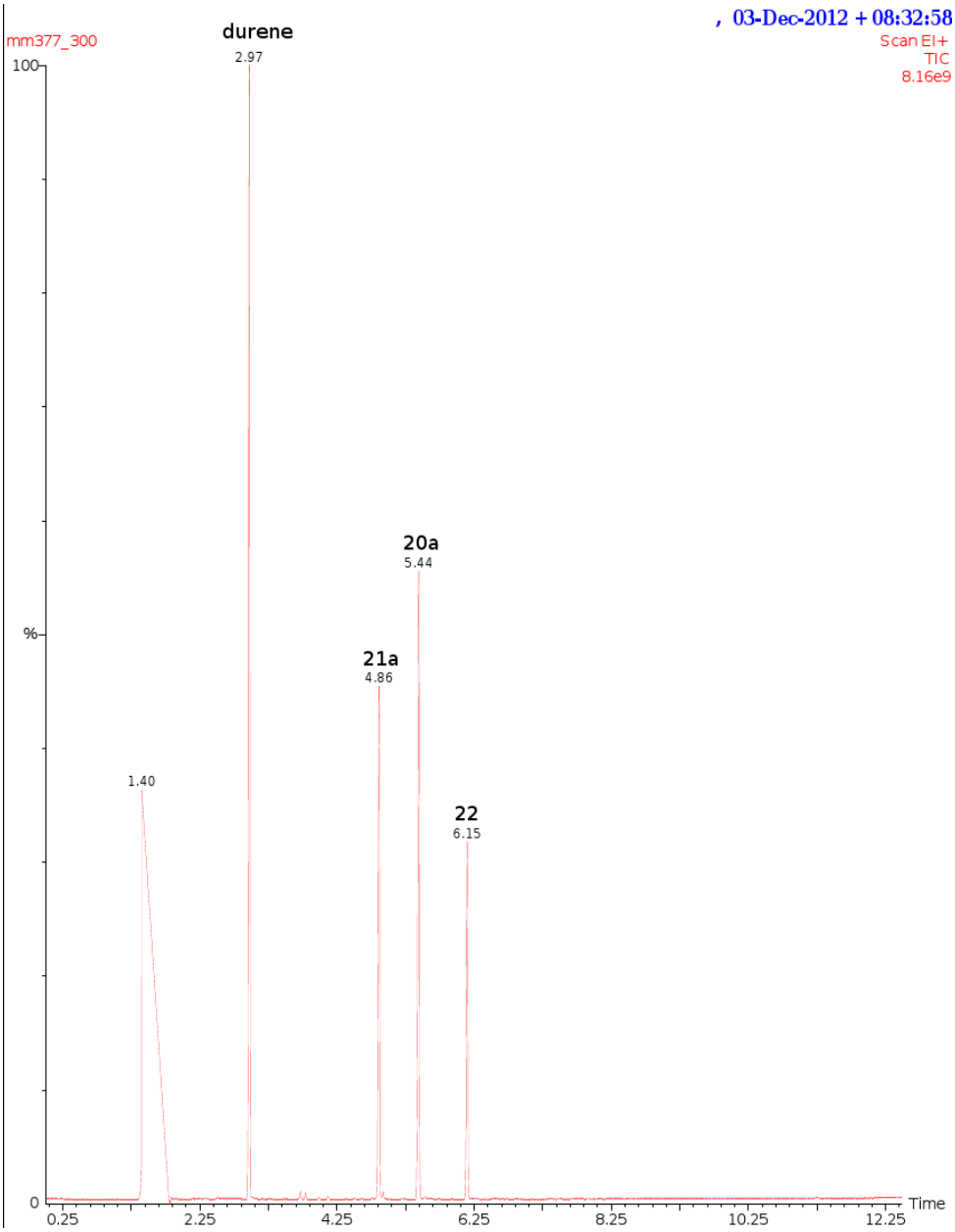

Fig. 5 GC/MS chromatogram of RCM of diene **20a** with catalyst **18**

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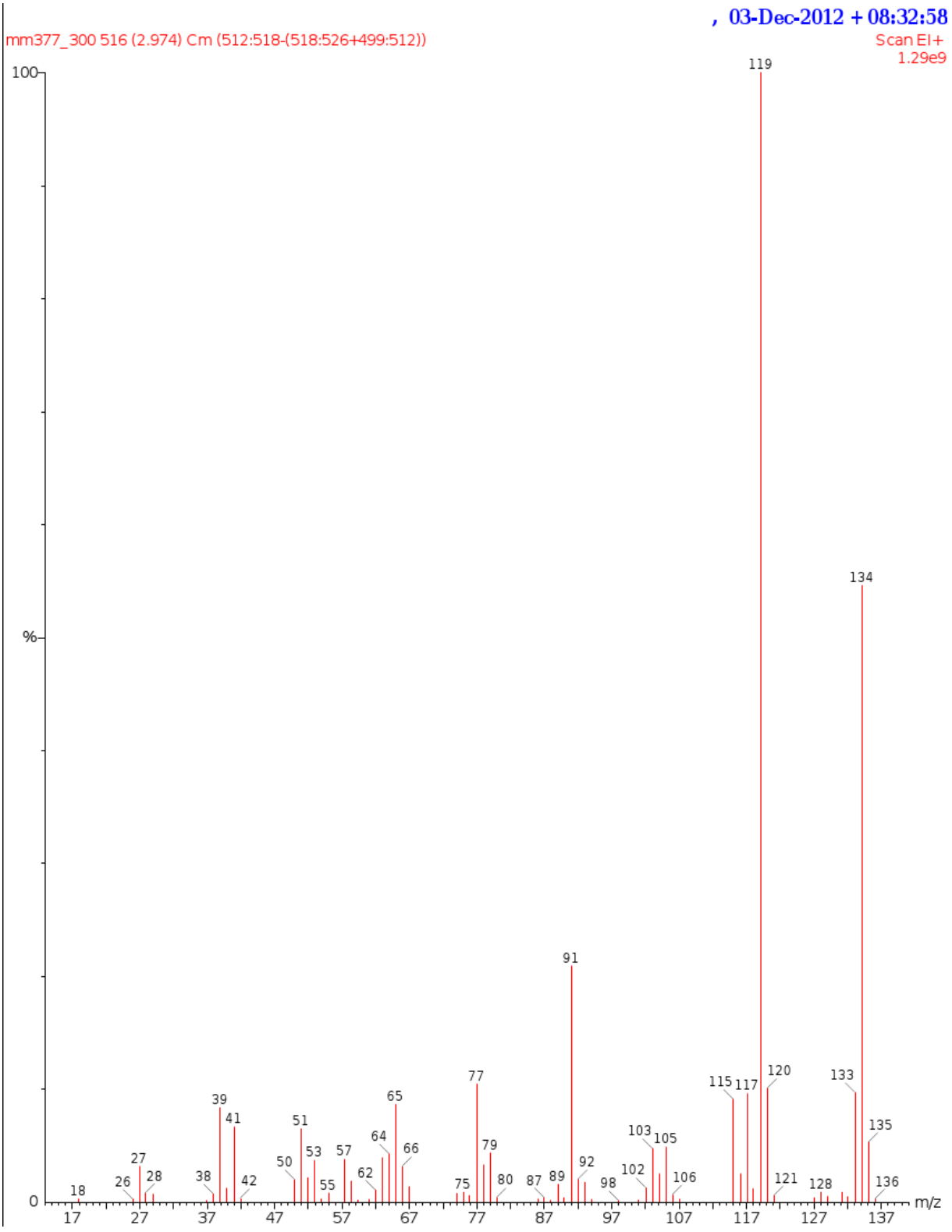

Fig. 5a GC/MS spectrum of durene (R_t = 2.97 min.)

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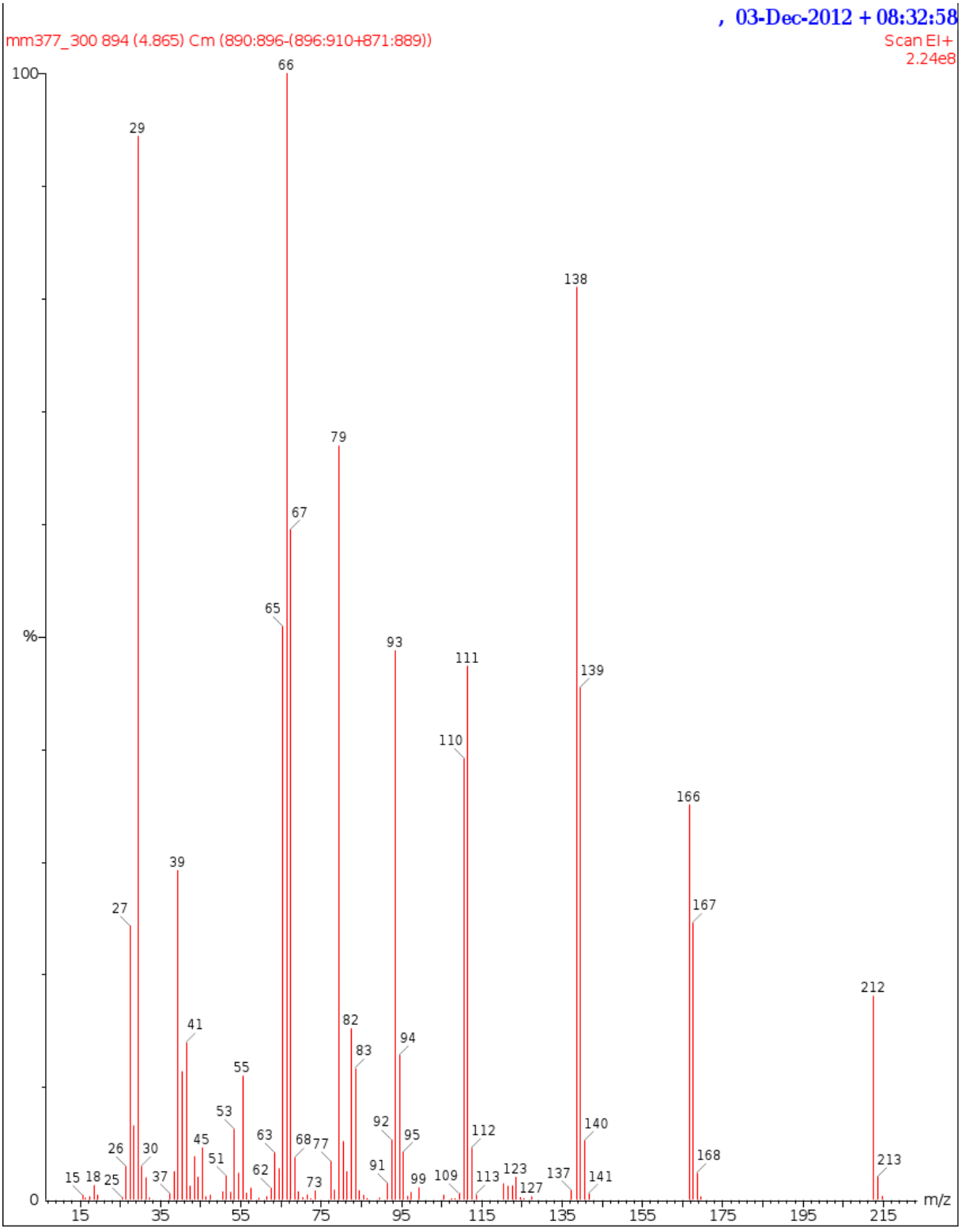

Fig. 5b GC/MS spectrum of product **21a** (R_t = 4.86 min.)

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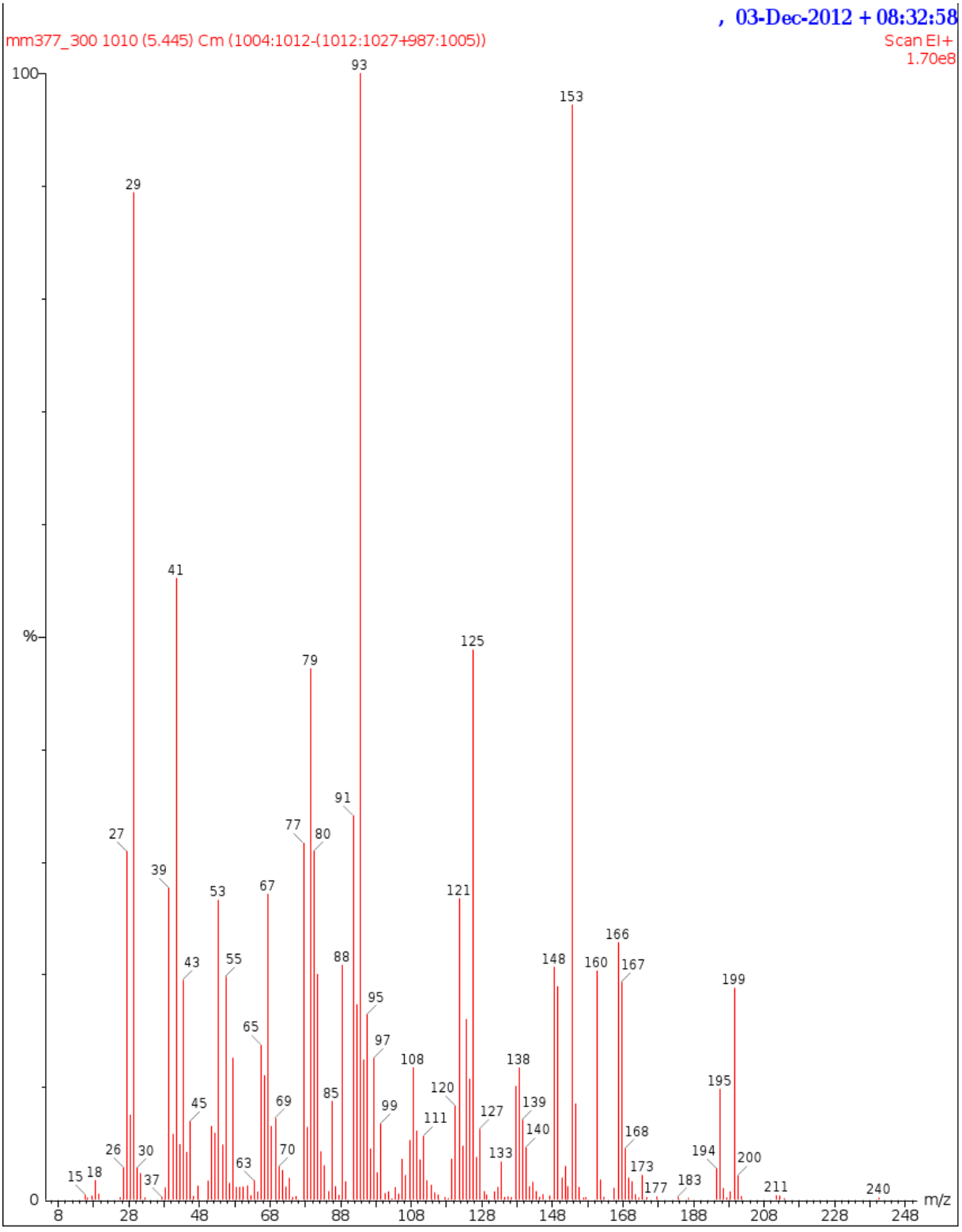

Fig. 5c GC/MS spectrum of substrate **20a** (R_t = 5.44 min.)

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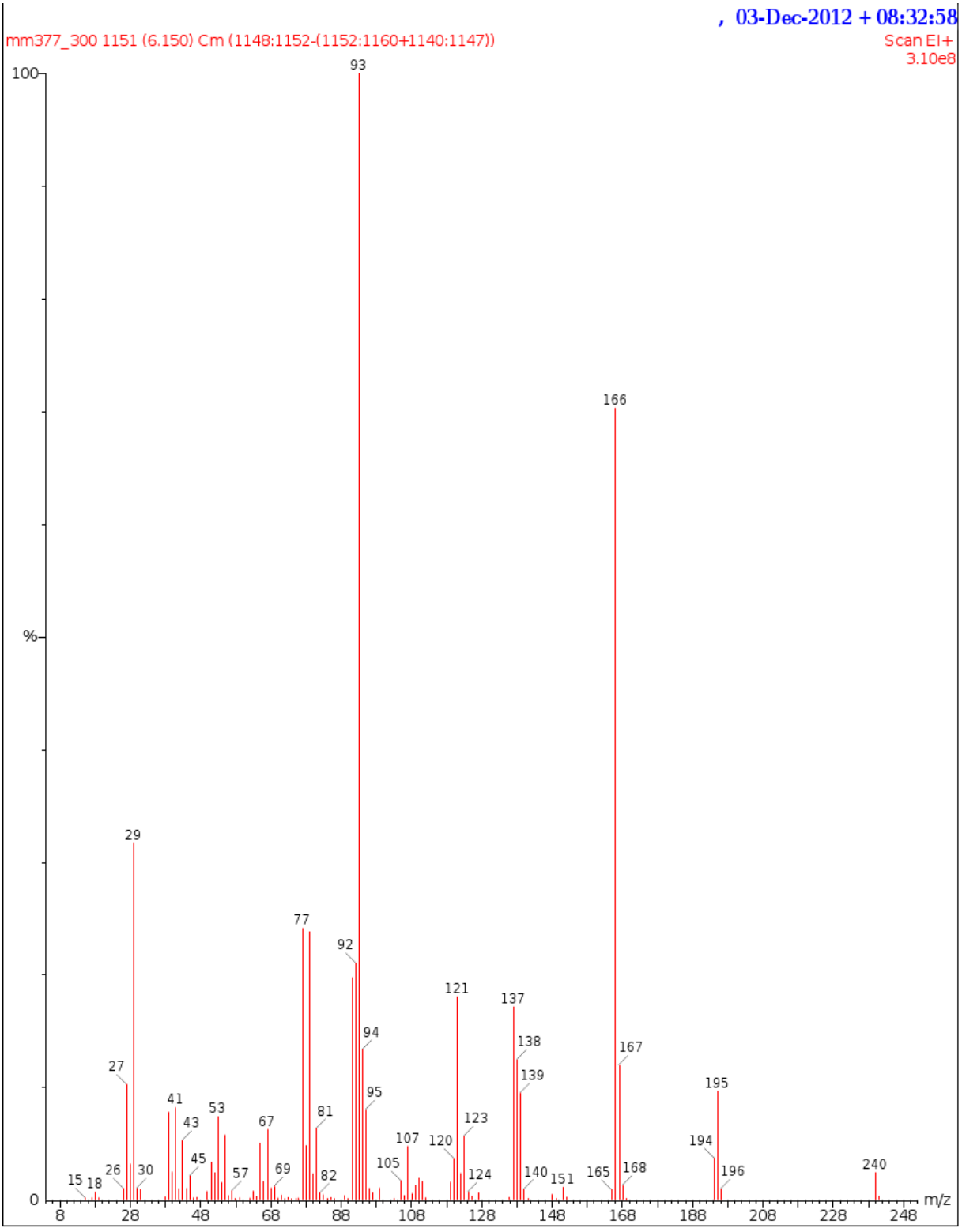
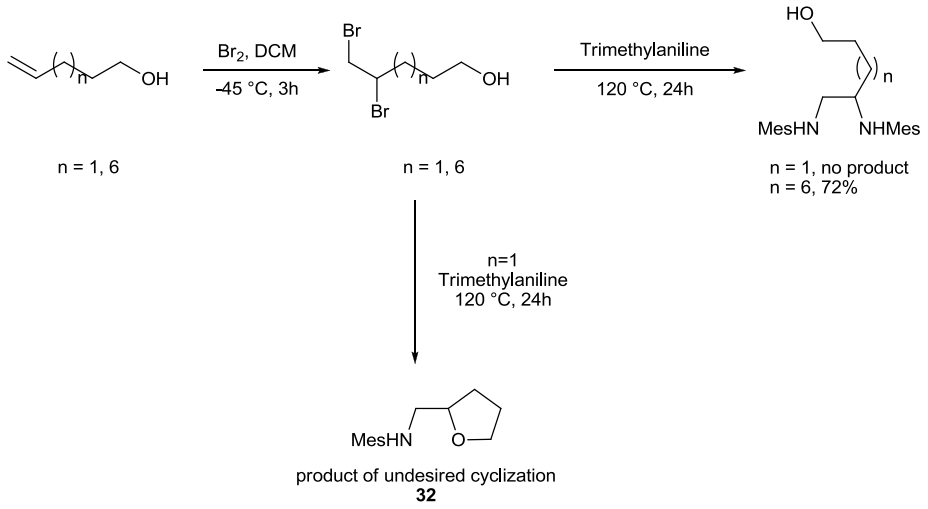


Fig. 5d GC/MS spectrum of side product (R_t = 6.15 min.)

DOI: 10.1039/c3dt33010a



Scheme 8 Synthesis of diamine derivatives.

Synthesis of compound 32

This reaction was performed according to the procedure for synthesis compound **11**.

^{1}H NMR (200 MHz, $CDCl_3$) δ 6.87 (br s, 1H), 6.83 (br s, 1H), 4.09 (qd, *J* = 7.0, 3.5 Hz, 1H), 4.02-3.78 (m, 2H), 3.49 (br s, 1H), 3.10 (dd, *J* = 12.4, 3.6 Hz, 1H), 2.95 (dd, *J* = 12.4, 7.7 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 2.21 (s, 3H), 2.09-1.85 (m, 3H), 1.79-1.53 (m, 1H) ppm; MS (ESI): 242.2 $[M+Na]^+$.

In order to obtain the diamine derivatives with shorter spacers, starting from C-5 or C-6 unsaturated alcohols as substrates, it is necessary to protect the free OH group first, to avoid the undesired cyclization of the corresponding dibromo derivatives via theintramolecular SN2 reaction.