Supporting Information

The facile synthesis of the 5Z,9Z-dienoic acids and their topoisomerase I inhibitory activity

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General information

All solvents were dried (hexane, THF, benzene over Na) and freshly distilled before use. All reactions were carried out under a dry argon atmosphere. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker AVANCE 400 spectrometer in $CDCl_3$ operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Elemental analyses were measured on a 1106 Carlo Erba apparatus. Mass spectra were obtained on MALDI TOF/TOF spectrometer in a 2,5-dihydroxybenzoic acid matrix and Shimadzu GCMS-QP2010 Plus spectrometer at 70 eV and working temperature 200 ^{o}C. Individuality and purity of the synthesized compounds were controlled using of TLC on Silufol UV-254 plates; anisic aldehyde in acetic acid was used as a developer. Column chromatography was carried out on Acrus silica gel (0.060–0.200 мм).

General Procedures

Starting Materials

Oxygen-containing allenes

Alkynol (2-propyn-1-ol, 3-butyn-1-ol, 4-pentyn-1-ol, 5-hexyn-1-ol, 7-octyn-1-ol) (20 mmol), dioxane (100 mL), paraformaldehyde (50 mmol), dicyclohexylamine (38 mmol) were placed in a 250 mL glass reactor equipped with a reflux condenser with stirring under dry argon at ~20 °C, followed by the addition of CuI (10 mmol). The reaction mixture was refluxed with stirring for 8 h, then cooled to 20-22 °C and filtered. The filtrate was concentrated *in vacuo*, the residue was washed with 5% solution of HCl in H_2O. The reaction products were extracted with diethyl ether, the extract was dried with MgSO4, the solvent was evaporated, the residue was subjected to chromatography on a column (SiO_2, eluent light petroleum-EtOAc (10 : 1)). The yields of O-containing allenes **1** were 70-75%.

Cross cyclomagnesiation of O-containing 1,2-dienes with terminal 1,2-dienes by EtMgBr in the presence of Mg metal and Cp_2TiCl_2 catalyst

Diethyl ether (10 mL), O-containing 1,2-diene (10 mmol), corresponding 1,2-diene (12 mmol), EtMgBr (40 mmol) (as 1.5 M solution in Et_2O), Mg powder (32 mmol), and Cp_2TiCl_2 (0.5 mmol) were charged into a glass reactor with stirring under argon (~0ºC). The reaction mixture was warmed-up to room temperature (20−22ºC) and stirred for 6−8 h. For identification of unsymmetrical substituted magnesacyclopentanes based on hydrolysis or deuterolysis products, the reaction mixture was treated with a 5% solution of HCl in H_2O. The products were extracted with diethyl ether, the extracts were dried with $MgSO_4$, the solvent was evaporated, and the residue was chromatographed on a column (SiO_2, elution with petroleum ether – EtOAc (50:1)).

DNA Topoisomerase I Assay

The inhibitory activity and the mechanism of inhibition of (5Z,9Z)-5,9-eicosadienoic acid were determined using the Topoisomerase I Drug Screening Kit TG-1018-2, (Topogen, USA) (the tested compound was added before topoisomerase I). The relaxation of supercoiled DNA under the action of topoisomerase I was carried out as follows: the reaction mixture (20 μL) containing 0.25 μg of the DNA plasmid pHOT (TopoGen, USA), 1 unit of recombinant

topoisomerase I (TopoGen, USA), and the tested compound: (5Z,9Z)-5,9-eicosadienoic acid was incubated in the buffer (35mM Tris-HCl, pH 8.0; 72 mM KCl, 5 mM MgCl, 5 mM dithiothreitol, 5 mM spermidine, and 0,01% bovine serum albumin) for 30 min at 370°C using a Biosan thermostat (Latvia). The tested compound was introduced in the reaction mixture prior to the addition of the enzyme topoisomerase I. The inhibiting action on topoisomerase I was monitored using the alkaloid camptothecin (TopoGEN, USA). The reaction was terminated by adding sodium dodecyl sulfate up to a concentration of 1%. After addition of a solution (5 mg/mL) of proteinase K (Sigma Chemical Co., USA) (1:10), the reaction mixture was incubated for 40 min at 370°C. A 0.1 % solution of bromophenol blue (1:10) was added and the samples were electrophoresed in the absence of ethidium bromide. The reaction products were separated in a 1% agarose gel (3 V/cm) for 4-6 h. After the electrophoresis, the gels were treated with a solution of ethidium bromide (0.5 μg/mL). The gels were visualized in the UV light in a Infinity VX2 1120/Blue X-Press gel documentation system (Vilber Lourmat, France). The possible action of the tested compounds on supercoiled DNA was checked by performing the reaction without topo I, the tested compounds being added in the same concentrations as in the reaction with the enzyme.

Characterization of Products

*2-(Tetradeca-3Z,7Z-dien-1-yloxy)tetrahydro-2H-pyrane (**4a**)*

Yield = 81% (2.38 g), as a colorless oil. n_d^{20} = 1.4695. R_f = 0.45 (hexan-EtOAc – 5:1). IR: 3007, 2927, 2856, 1730, 1455, 1380, 1364, 1260, 1200, 1137, 1033, 769, 669 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.89 (t, 3H, C(14)H_3, *J* = 7.2 Hz), 1.27-1.30 (m, 8H, C(10-13)H_2), 1.49-1.86 (m, 6H, C(16-18)H_2), 1.94-2.13 (m, 8H, C(2,5,6,9)H_2), 3.38-3.87 (m, 4H, C(1,19)H_2), 4.59 (t, 1H, C(15)H, *J* = 3.6 Hz), 5.35-5.46 (m, 4H, C(2)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C(14)), 19.5 (C(17)), 22.6 (C(13)), 25.5 (C(18)), 27.2 (C(5,6)(2C)), 27.5 (C(2)), 28.0 (C(9)), 29.0 (C(10)), 29.7 (C(11)), 30.7 (C(16)), 31.8 (C(12)), 62.2 (C(19)), 67.0 (C(1)), 98.6 (C(15)), 125.9 (C(3)), 128.9 (C(7)), 130.4 (C(4)), 131.2 (C(8)) ppm. MS m/z (EI, 70 eV) *m/z* (%): 294 $[M]^+$ (2), 85 (100), 55 (48), 105 (46), 43 (41), 57 (35), 41 (30), 207 (27), 101 (25), 131 (24), 69 (23), 77 (21), 167 (18), 73 (15), 129 (14), 70 (12). Anal. Calcd for $C_{19}H_{34}O_2$: C, 77.50; H, 11.64. Found: C, 77.36; H, 11.22.

*[(Tetradeca-3Z,7Z-dien-1-yloxy)methyl]benzene (**4b**)*

Yield = 88% (2.64 g), as a colorless oil. n_d^{20} = 1.5102. R_f = 0.46 (hexan-EtOAc – 5:1). IR: 3007, 2926, 2855, 1495, 1361, 1101, 1028, 735, 697 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.95 (t,

3H, C(14)H_3, *J* = 7.4 Hz), 1.21-1.50 (m, 8H, C(10-13)H_2), 2.11-2.47 (m, 8H, C(2,5,6,9)H_2), 3.56 (t, 2H, C(1)H_2, *J* = 8 Hz), 4.60 (s, 2H, C(15)H_2), 5.45-5.55 (m, 4H, C(3,4,7,8)H), 7.28-7.42 (m, 5H, C(17-21)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C(14)), 22.7 (C(13)), 27.3 (C(5,6)), 27.6 (C(9)), 28.1 (C(2)), 29.1 (C(10)), 29.8 (C(11)), 31.9 (C(12)), 70.1 (C(1)), 72.9 (C(15)), 125.9 (C(19)), 127.5 (C(3)), 127.7 (C(17,21)), 128.4 (C(18,20)), 129.0 (C(7)), 130.5 (C(4)), 131.3 (C(8)), 138.6 (C(16)) ppm. MS m/z (EI, 70 eV) *m/z* (%): 300 $[M]^+$ (2), 105 (100), 123 (83), 77 (44), 70 (21), 122 (20), 55 (13), 51 (11), 106 (10). Anal. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.72; H, 10.51.

*2-(Henicosa-4Z,8Z–dien-1-yloxy)tetrahydro-2H-pyrane (**4c**)*

Yield = 87% (3.41 g), as a colorless oil. n_d^{20} = 1.4801. R_f = 0.42 (hexan-EtOAc – 5:1). IR: 3005, 2924, 2853, 1441, 1401, 1380, 1260, 1200, 1182, 1159, 1137, 1121, 1078, 1034, 735, 671 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.89 (t, 3H, C(21)H_3, *J* = 6.8 Hz), 1.19-1.39 (m, 22H, C(2,11-20)H_2), 1.50-1.68 (m, 6H, C(23-25)H_2), 2.00-2.15 (m, 8H, C(3,6,7,10)H_2), 3.38-3.87 (m, 4H, C(1,26)H_2), 4.58 (t, 1H, C(22)H, *J* = 4 Hz), 5.36-5.41 (m, 4H, C(4,5,8,9)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C(21)), 19.6 (C(24)), 22.7 (C(20)), 23.9 (C(3)), 25.5 (C(25)), 27.3 (C(10)), 27.3 (C(6)), 27.4 (C(7)), 29.4 (C(2)), 29.5, 29.6, 29.7, 29.8 (C(11,12,13,14)), 29.6, 29.7 (C(15,16,17,18) (2C)), 30.8 (C(23)), 31.9 (C(19)), 62.2 (C(26)), 66.9 (C(1)), 98.8 (C(22)), 129.0 (C(9)), 129.4 (C(4)), 129.8 (C(9)), 130.4 (C(5)) ppm. MALDI TOF: 392.6. Anal. Calcd for $C_{26}H_{48}O_2$: C, 79.35; H, 12.82. Found: C, 79.18; H, 12.69.

*2-(Tetradeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**4d**)*

Yield = 84% (2.47 g), as a colorless oil. n_d^{20} = 1.4814. R_f = 0.39 (hexan-EtOAc – 5:1). IR: 2924, 2853, 1441, 1380, 1354, 1200, 1182, 1159, 1137, 1121, 1078, 1034, 739, 654 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.90 (t, 3H, C(14)H_3, *J* = 6.8 Hz), 1.27-1.33 (m, 14H, C(2,3,12,13,16-18)H_2), 2.03-2.07 (m, 8H, C(4,7,8,11)H_2), 3.40-3.89 (m, 4H, C(1,19)H_2), 4.58 (t, 1H, C(15)H, *J* = 3.6 Hz), 5.36-5.41 (m, 4H, C(5,6,9,10)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9 (C(14)), 19.7 (C(17)), 22.3 (C(13)), 25.5 (C(18)), 26.4 (C(3)), 27.0 (C(4)), 27.1 (C(2)), 27.37 (C(7)), 27.42 (C(8)), 29.5 (C(11)), 30.8 (C(12)), 31.9 (C(16)), 62.2 (C(19)), 67.4 (C(1)), 98.7 (C(15)), 129.1 (C(9)), 129.5 (C(6)), 129.9 (C(5)), 130.3 (C(10)) ppm. MALDI TOF: 294.5 $[M]^+$. Anal. Calcd for $C_{19}H_{34}O_2$: C, 77.50; H, 11.64. Found: C, 77.38; H, 11.48.

*2-[(11-Phenylundeca-5Z,9Z–dien-1-yl)oxy]tetrahydro-2H-pirane (**4e**)*

Yield = 86% (2.88 g), as a colorless oil. n_d^{20} = 1.5311. R_f = 0.45 (hexan-EtOAc – 5:1). IR: 3390, 2938, 2870, 1762, 1661, 1453, 1352, 1261, 1200, 1120, 1075, 1032, 747, 699 cm^{-1}. ^{1}H NMR

($CDCl_3$, 400 MHz): δ − 1.27-1.89 (m, 10H, C$\underline{H}_2$), 2.08-2.26 (m, 6H, C$\underline{H}_2$CH=), 3.48 (d, 2H, C$\underline{H}_2$-Ph, *J* = 6.8 Hz), 3.52-3.92 (m, 4H, C$\underline{H}_2$-O, *J* = 6.8 Hz), 4.58 (t, 1H, *J* = 3.6 Hz), 5.41-5.65 (m, 4H, C$\underline{H}$=C$\underline{H}$), 7.22-7.36 (m, 5H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.8 C(20), 25.5 C(21), 27.2 C(4), 27.3 C(2), 27.4 C(7), 27.5 C(8), 30.8 C(19), 33.6 C(11), 62.3 C(22), 67.5 C(1), 98.8 C(18), 125.9 C(15), 128.2 C(13,17), 128.4 C(14,16), 128.5 C(9), 129.2 C(6), 129.6 C(5), 130.3 C(10), 141.1 C(12) ppm. MALDI TOF: 328.4 $[M]^+$. Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.02; H, 9.73.

2-(Hexadeca-7Z,11Z–dien-1-yloxy)tetrahydro-2H-pyrane ***(4f)***

Yield = 94% (3.03 g), as a colorless oil. n_d^{20} = 1.4841. R_f = 0.38 (hexan-EtOAc – 5:1). IR: 3005, 2925, 2853, 1441, 1380, 1353, 1200, 1182, 1159, 1136, 1121, 1078, 1034, 729, 664 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.88 (t, 3H, C(16)H_3, *J* = 6.8 Hz), 1.26-1.33 (m, 12H, C(2-5,14,15)H_2), 1.50-1.65 (m, 6H, C(20-22)H_2), 2.02-2.16 (m, 8H, C(6,9,10,13)H_2), 3.38-3.88 (m, 4H, C(1,23)H_2), 4.57 (t, 1H, C(19)H, *J* = 4 Hz), 5.35-5.40 (m, 4H, C(7,8,11,12)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C(16)), 19.6 (C(19)), 22.6 (C(15)), 25.5 (C(20)), 26.2 (C(3)), 27.2 (C(13)), 27.4 (C(9),C(10)), 29.1 (C(14)), 29.6 (C(4)), 29.7 (C(2)), 30.8 (C(18)), 31.9 (C(5)), 62.2 (C(21)), 67.5 (C(1)), 98.8 (C(17)), 129.0 (C(11)), 129.1 (C(7)), 130.2 (C(12), 130.2 (C(8)) ppm. MALDI TOF:322.5 $[M]^+$. Anal. Calcd for $C_{21}H_{38}O_2$: C, 78.20; H, 11.88. Found: C, 78.08; H, 11.64.

2-(Hexadeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane ***(7a)***

Yield = 86%, as a colorless oil. n_d^{20} = 1.4831. R_f = 0.41 (hexan-EtOAc – 5:1). IR: 3005, 2924, 2853, 1650, 1441, 1380, 1353, 1200, 1182, 1159, 1137, 1121, 1078, 1034, 749, 635 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.87 (t, 3H, C(16)H_3, *J* = 7.2 Hz), 1.26-1.85 (m, 18H, C(2,3,12-15,18-20)H_2), 2.00-2.07 (m, 8H, C(4,7,8,11)H_2), 3.38-3.87 (m, 4H, C(1,21)H_2), 4.56 (t, 1H, C(17)H, *J* = 3.2 Hz), 5.34-5.38 (m, 4H, C(5,6,9,10)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0 (C(16)), 19.6 (C(19)), 22.6 (C(15)), 25.5 (C(20)), 26.4 (C(3)), 27.0 (C(4)), 27.2 (C(2)), 27.3 (C(7)), 27.4 (C(8)), 29.4 (C(11)), 29.7 (C(13)), 30.7 (C(18)), 31.8 (C(14)), 62.1 (C(21)), 67.4 (C(1)), 98.7 (C(17)), 129.0 (C(9)), 129.4 (C(6)), 129.9 (C(5)), 130.3 (C(10)) ppm. MALDI TOF: 322.5 $[M]^+$. Anal. Calcd for $C_{21}H_{38}O_2$: C, 84.51; H, 11.88. Found: C, 78.41; H, 11.69.

5Z,9Z-Hexadecadienoic acid ***(8a)***

Yield = 74%, as a colorless oil. Rf = 0.45 (hexan-EtOAc – 5:1). IR: 3006, 2928, 2856, 1743, 1655, 1464, 1385, 1365, 1238, 1038, 969, 727 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.90 (t, 3H, C(16)H_3, *J* = 7.2 Hz); 1.30-1.32 (m, 8H, C(4,5,14,15)H_2); 1.70 (q, 2H, C(3)H_2, *J* = 7.6 Hz);

2.01-2.14 (m, 8H, C(4,7,8,11)H_2); 2.37 (t, 2H, C(2)H_2, *J* = 7.2 Hz); 5.33-5.46 (м, 4H, C(5,6,9,10)H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C(16)); 22.6 (C(15)); 24.6 (C(3)); 26.5 (C(11)); 27.3 (C(7,8)); 27.40 (C(4)); 28.99 (C(12)); 29.69 (C(13)); 31.78 (C(14)); 33.3 (C(2)); 128.6 (C(10)); 128.9 (C(9)); 130.5 (C(5)); 130.6 (C(6)); 179.57 (C(1)) ppm. MALDI TOF: 252.4. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.01; H, 11.05.

*2-(Nonadeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**7b**)*

Yield = 89%, as a colorless oil. R_f = 0.44 (hexan-EtOAc – 5:1). IR: 2926, 2853, 1662, 1441, 1382, 1354, 1200, 1180, 1159, 1125, 1078, 1034, 729, 676 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.86 (t, 3H, C$\underline{H}_3$, *J* = 7.0 Hz), 1.25-1.82 (m, 24H, C$\underline{H}_2$), 2.00-2.05 (m, 8H, C$\underline{H}_2$CH=), 3.32-3.86 (m, 4H, C$\underline{H}_2$-O), 4.55 (t, 1H, O-C$\underline{H}$-O, *J* = 3.6 Hz), 5.33-5.35 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.03 C(19), 19.54 C(22), 22.65 C(18), 25.52 C(23), 26.37 C(3), 27.01 C(4), 27.16 C(2), 27.35 C(11), 27.39 C(7), C(8), 29.29 C(13), 29.32 C(14), 29.59 C(15,16), 29.68 C(17), 30.71 C(21), 31.89 C(12), 62.00 C(24), 67.33 C(1), 98.62 C(20), 129.00 C(9), 129.39 C(6), 129.84 C(5), 130.26 C(10) ppm. MALDI TOF: 364.5 [M]$^+$. Anal. Calcd for $C_{19}H_{34}O_2$: C, 79.06; H, 12.16. Found: C, 78.88; H, 12.10.

*5Z,9Z-Nonadecadienoic acid (**8b**)*

Yield = 73%, as a colorless oil. R_f = 0.51 (hexan-EtOAc – 5:1). IR: 3012, 2927, 2856, 1741, 1664, 1468, 1385, 1368, 1238, 1030, 968, 728 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.90 (t, 3H, C$\underline{H}_3$, *J* = 6.8 Hz), 1.29-1.35 (m, 14H, C$\underline{H}_2$), 1.72 (k, 2H, C$\underline{H}_2$, *J* = 7.2 Hz), 2.01-2.15 (m, 8H, C$\underline{H}_2$CH=), 2.38 (t, 2H, C$\underline{H}_2$-COOH, *J* = 7.2 Hz), 5.35-5.45 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.10 C(19), 22.69 C(18), 24.58 C(3), 26.49 C(11), 27.27 C(7,8), 27.40 C(4), 29.33 C(13), 29.36 C(14), 29.58 C(15), 29.62 C(16), 29.74 C(17), 31.93 C(12), 33.48 C(2), 128.59 C(10), 128.90 C(9), 130.53 C(6), 130.61 C(5), 180.33 C(1) ppm. MALDI TOF: 294.5. Anal. Calcd for $C_{19}H_{34}O_2$: C, 77.50; H, 11.64. Found: C, 77.21; H, 11.45.

*2-(Eicosa-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**7c**)*

Yield = 88%, as a colorless oil. R_f = 0.46 (hexan-EtOAc – 5:1). IR: 2926, 2853, 1660, 1441, 1382, 1354, 1200, 1180, 1159, 1125, 1078, 1034, 769, 676 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ − 0.89 (t, 3H, C$\underline{H}_3$, *J* = 7.2 Hz), 1.25-1.80 (m, 26H, C$\underline{H}_2$), 2.01-2.06 (m, 8H, C$\underline{H}_2$CH=), 3.41-3.89 (m, 4H, C$\underline{H}_2$-O), 4.61 (m, 1H, O-C$\underline{H}$-O), 5.37-5.48 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 C(20), 19.5 C(23), 22.7 C(19), 25.5 C(24), 27.2 C(3), 27.5 C(4), 27.9 C(2), 29.3 C(11), 29.4 C(7),C(8), 29.5 C(17), 29.6 C(16), 29.4 C(13), 29.5 C(12), 29.6 C(15), 29.7 C(14), 30.7 C(22), 31.9 C(18), 62.1 C(25), 67.0 C(1), 98.6 C(21), 125.9 C(9), 128.9 C(6),

130.4 C(5), 131.2 C(10). ppm. MALDI TOF: 378.5 $[M]^+$. Anal. Calcd for $C_{25}H_{46}O_2$: C, 79.30; H, 12.50. Found: C, 78.98; H, 12.42.

*5Z,9Z-Eicosadienoic acid (**8c**)*

Yield = 75%, as a colorless oil. R_f = 0.52 (hexan-EtOAc – 5:1). IR: 3012, 2927, 2856, 1741, 1661, 1468, 1385, 1368, 1238, 1030, 728 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.90 (t, 3H, C$\underline{H}_3$, *J* =7.0 Hz), 1.27-1.37 (m, 16H, C$\underline{H}_2$), 1.73 (k, 2H, C$\underline{H}_2$, *J* = 7.2 Hz), 2.03-2.11 (m, 8H, C$\underline{H}_2$CH=), 2.38 (t, 2H, C$\underline{H}_2$-COOH, *J* = 7.2 Hz), 5.38-5.44 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 C(20), 22.7 C(19), 24.6 C(3), 26.5 C(11), 27.3 C(7,8), 27.4 C(4), 29.3 C(17), 29.4 C(16), 29.6 C(13), 29.7 C(12,15), 29.7 C(14), 31.9 C(18), 33.3 C(2), 128.60 C(10), 128.91 C(9), 130.57 C(6), 130.6 C(5), 179.6 C(1) ppm. MALDI TOF: 308.5. Anal. Calcd for $C_{20}H_{36}O_2$: C, 77.87; H, 11.76. Found: C, 77.32; H, 11.51.

*2-(Docosa-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane **(7d)***

Yield = 90%, as a colorless oil. R_f = 0.44 (hexan-EtOAc – 5:1). IR: 2925, 2851, 1654, 1445, 1380, 1352, 1200, 1180, 1159, 1135, 1121, 1078, 1034, 767, 662 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.89 (t, 3H, C$\underline{H}_3$, *J* = 6.8 Hz), 1.26-1.82 (m, 30H, C$\underline{H}_2$), 2.01-2.17 (m, 8H, C$\underline{H}_2$CH=), 3.39-3.90 (m, 4H, C$\underline{H}_2$-O), 4.59 (t, 1H, O-C$\underline{H}$-O, *J* = 4 Hz), 5.36-5.48 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0 C(22), 19.6 C(25), 22.6 C(21), 25.5 C(26), 25.8 C(3), 26.2 C(4), 26.4 C(2), 27.0 C(11), 27.2 C(7), 27.4 C(8), 29.3 C(19), 29.4 C(18), 29.5 C(16), 29.6 C(17,19), 29.7 C(12,13,14,15), 30.7 C(24), 31.9 C(20), 62.1 C(27), 67.5 C(1), 98.7 C(23), 129.0 C(9), 129.4 C(6), 129.9 C(5), 130.3 C(10) ppm. MALDI TOF: 406.6 $[M]^+$. Anal. Calcd for $C_{27}H_{50}O_2$: C, 79.74; H, 12.39. Found: C, 79.48; H, 12.18.

*5Z,9Z-Docosadienoic acid (**8d**)*

Yield = 74%, as a colorless oil. R_f = 0.51 (hexan-EtOAc – 5:1). IR: 3010, 2925, 2856, 1741, 1655, 1466, 1385, 1365, 1238, 1035, 724 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.91 (t, 3H, C$\underline{H}_3$, *J* = 6.8 Hz), 1.28-1.33 (m, 20H, C$\underline{H}_2$), 1.72 (k, 2H, C$\underline{H}_2$, *J* = 7.2 Hz), 2.03-2.15 (m, 8H, C$\underline{H}_2$CH=), 2.38 (t, 2H, C$\underline{H}_2$-COOH, *J* = 7.2 Hz), 5.38-5.44 (m, 4H, C$\underline{H}$=C$\underline{H}$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 C(22), 22.7 C(21), 24.6 C(3), 26.5 C(11), 27.3 C(7,8), 27.4 C(4), 29.34 C(19), 29.37, 29.57, 29.66(2C), 29.7(2C) 29.74 C(13-18), 31.9 C(20), 33.4 C(2), 128.6 C(10), 128.9 C(9), 130.56 C(6), 130.6 C(5), 180.1 C(1) ppm. MALDI TOF: 336.5. Anal. Calcd for $C_{22}H_{40}O_2$: C, 78.51; H, 11.98. Found: C, 78.21; H, 11.92.

*2-(Tetracosa-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane **(7e)***

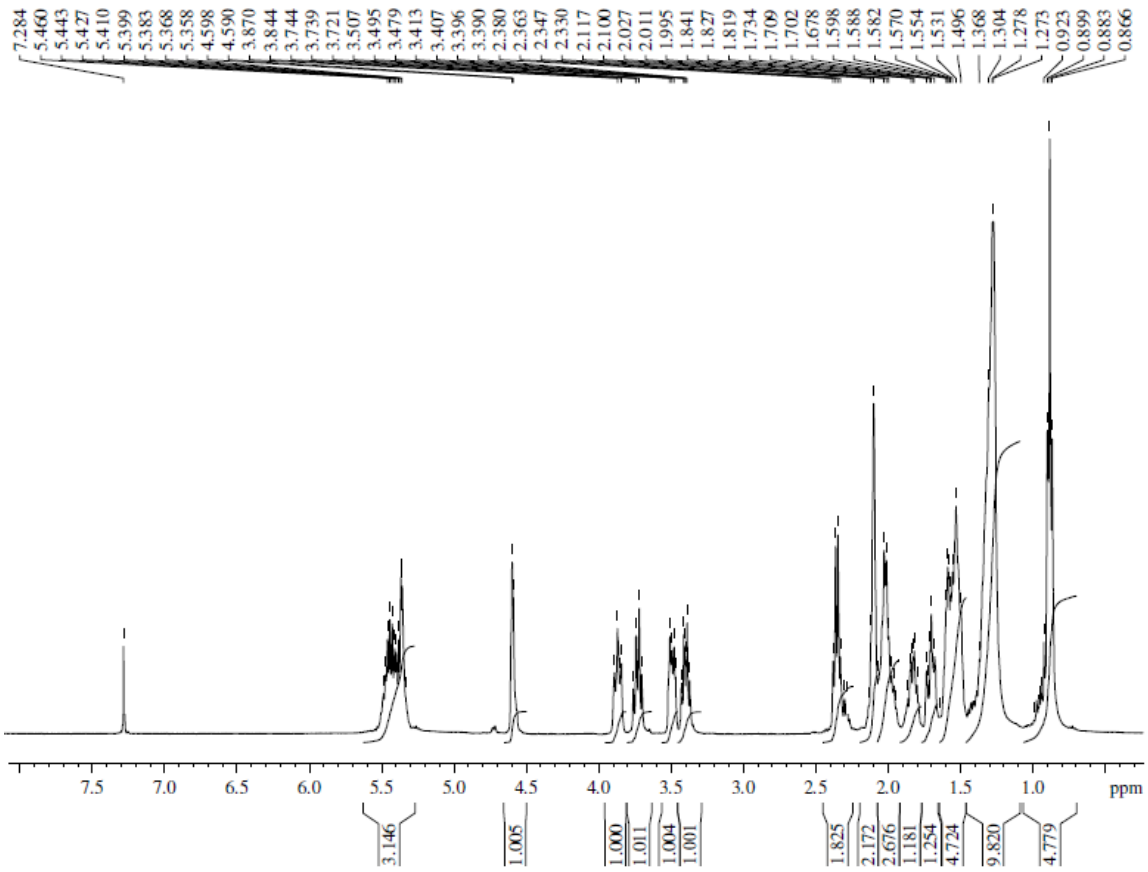
Yield = 92%, as a colorless oil. R_f = 0.43 (hexan-EtOAc – 5:1). IR: 2925, 2851, 1660, 1445, 1380, 1352, 1200, 1180, 1159, 1135, 1121, 1078, 1034, 767, 665 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.87 (t, 3H, C<u>H</u>$_3$, *J* = 6.8 Hz), 1.26-1.84 (m, 34H, C<u>H</u>$_2$), 2.00-2.07 (m, 8H, C<u>H</u>$_2$CH=), 3.37-3.88 (m, 4H, C<u>H</u>$_2$-O), 4.57 (t, 1H, O-<u>CH</u>-O, *J* = 4 Hz), 5.36-5.40 (m, 4H, C<u>H</u>=C<u>H</u>) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.07 C(24), 19.58 C(27), 22.67 C(23), 25.51 C(28), 25.80 C(3), 26.19 C(4), 26.38 C(2), 27.03 C(11), 27.24 C(7), 27.36 C(8), 29.32 C(21), 29.36 C(20), 29.46 C(16), 29.56 C(17,19), 29.66 C(12,13,19), 29.69 C(14,15,18), 30.73 C(26), 31.92 C(22), 62.12 C(29), 67.40 C(1), 98.71 C(25), 129.03 C(9), 129.44 C(6), 129.89 C(5), 130.33 C(10) ppm. MALDI TOF: 434.7 $[M]^+$. Anal. Calcd for $C_{29}H_{54}O_2$: C, 80.12; H, 12.52. Found: C, 79.88; H, 12.48.

*5Z,9Z-Tetracosadienoic acid (**8e**)*

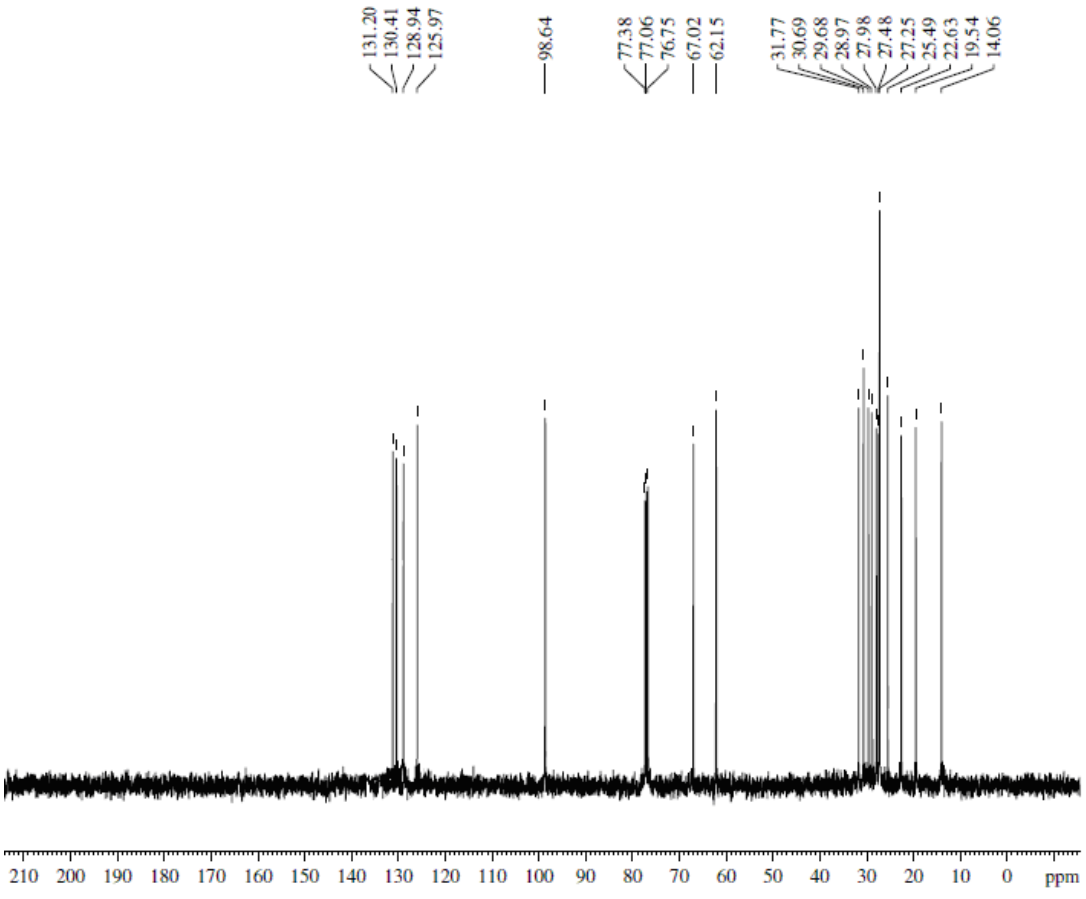
Yield = 75%, as a colorless oil. R_f = 0.51 (hexan-EtOAc – 5:1). IR: 3010, 2925, 2856, 1741, 1657, 1466, 1385, 1365, 1238, 1035, 734 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ − 0.90 (t, 3H, C<u>H</u>$_3$, *J* = 6.8 Hz), 1.28-1.35 (m, 24H, C<u>H</u>$_2$), 1.72 (k, 2H, C<u>H</u>$_2$, *J* = 7.2 Hz), 2.02-2.13 (m, 8H, C<u>H</u>$_2$CH=), 2.37 (t, 2H, C<u>H</u>$_2$-COOH, *J* = 7.2 Hz), 5.37-5.43 (m, 4H, C<u>H</u>=C<u>H</u>) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.11 C(24), 22.69 C(23), 24.59 C(3), 26.49 C(11), 27.27 C(7,8), 27.40 C(4), 29.33 C(21), 29.36 C(20), 29.41 C(16), 29.58 C(17,19), 29.67 C(12,13,19), 29.70 C(14,15,18), 31.93 C(22), 33.40 C(2), 128.61 C(10), 128.91 C(9), 130.55 C(6), 130.61 C(5), 179.68 C(1) ppm. MALDI TOF: 364.6. Anal. Calcd for $C_{24}H_{44}O_2$: C, 79.06; H, 12.16. Found: C, 78.71; H, 12.05.

1H NMR and 13C NMR Spectra of the Products

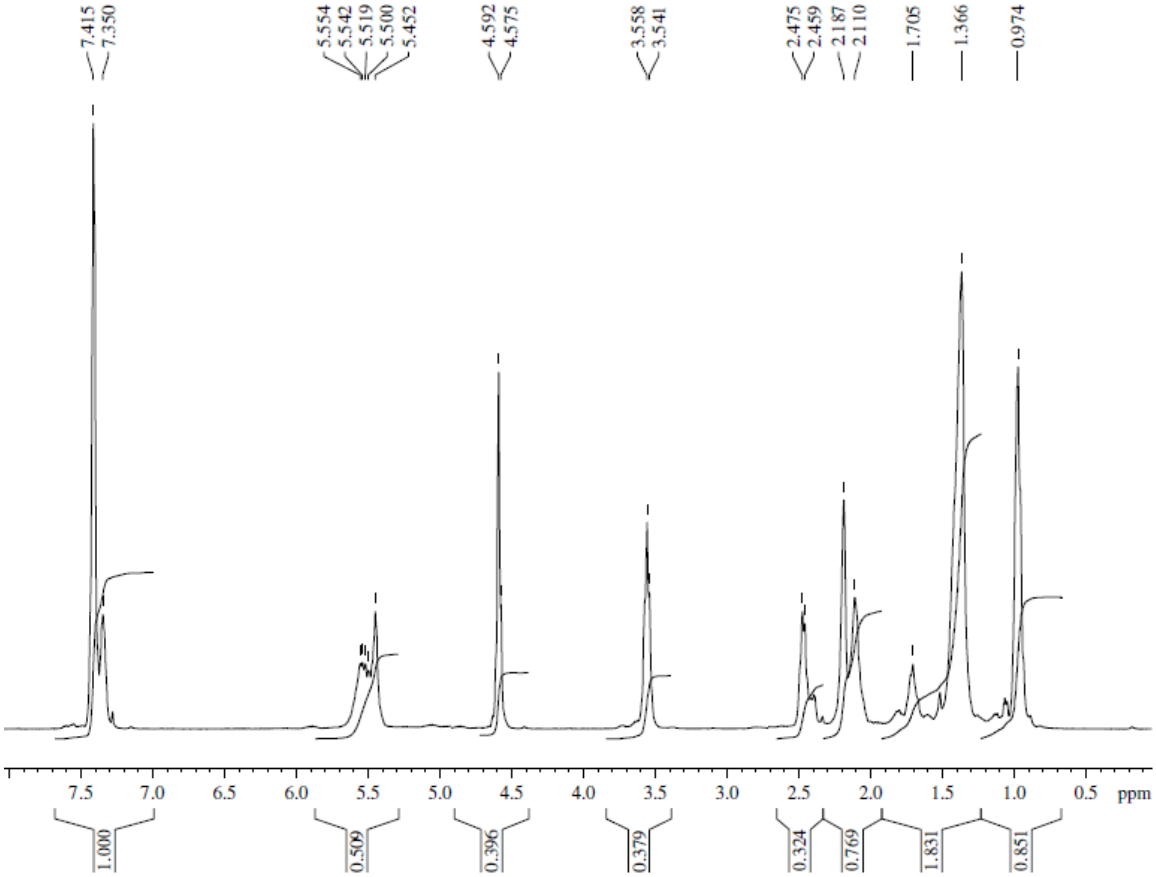
*2-(Tetradeca-3Z,7Z-dien-1-yloxy)tetrahydro-2H-pyrane (**4a**)*, 1H



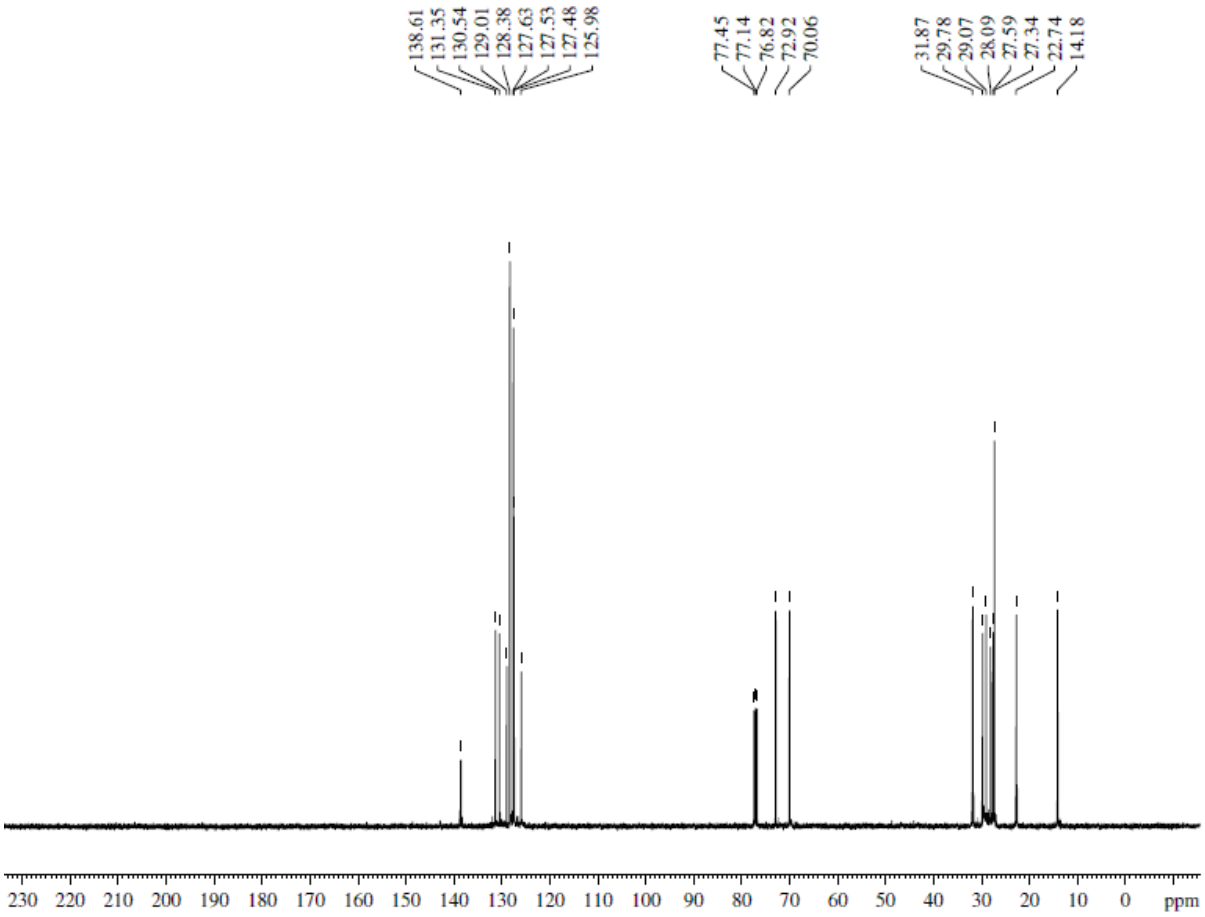
13C



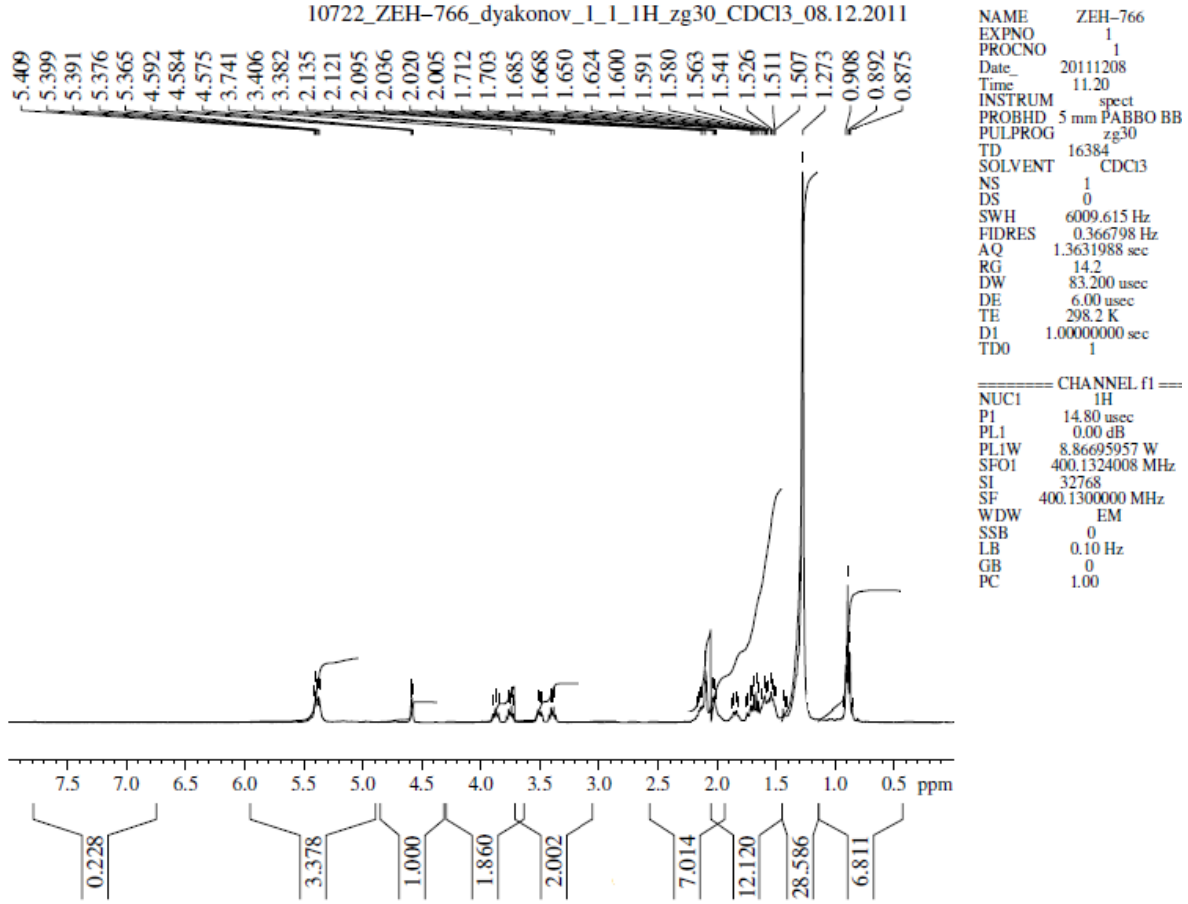
*[(Tetradeca-3Z,7Z-dien-1-yloxy)methyl]benzene (**4b**)*, 1H



13C



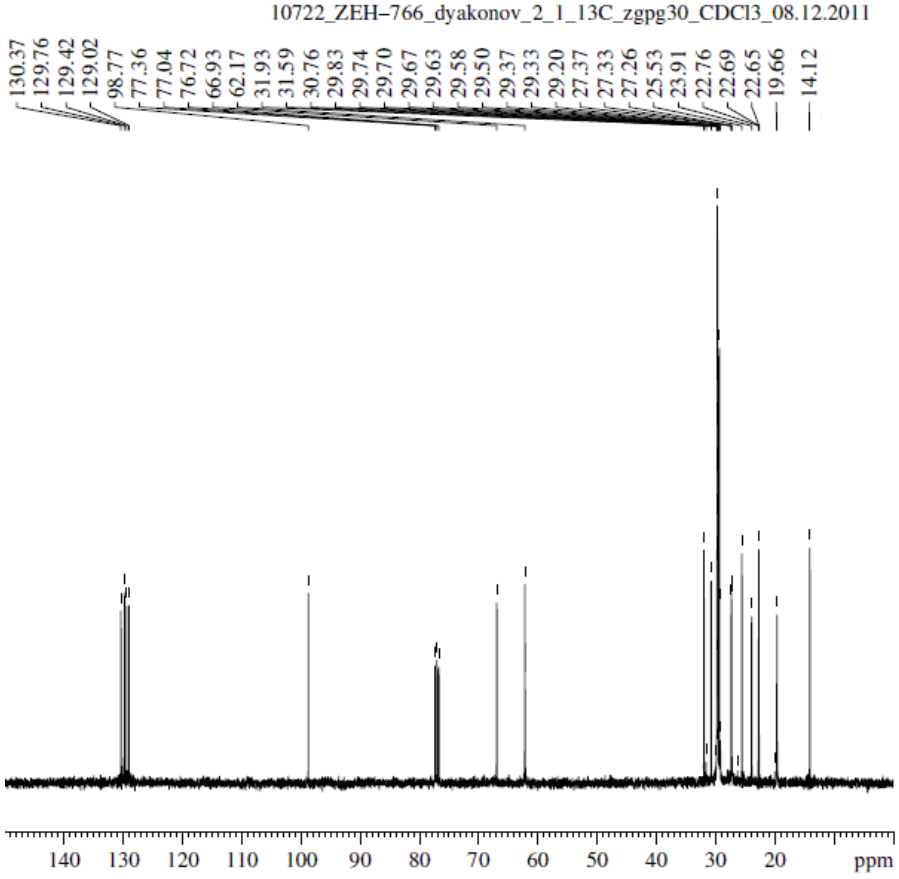
*2-(Henicosa-4Z,8Z–dien-1-yloxy)tetrahydro-2H-pyrane (**4c**)*, 1H



NAME ZEH–766
EXPNO 1
PROCNO 1
Date_ 20111208
Time 11.20
INSTRUM spect
PROBHD 5 mm PABBO BB
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 1
DS 0
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 14.2
DW 83.200 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ===
NUC1 1H
P1 14.80 usec
PL1 0.00 dB
PL1W 8.86695957 W
SFO1 400.1324008 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

13C



NAME ZEH–766
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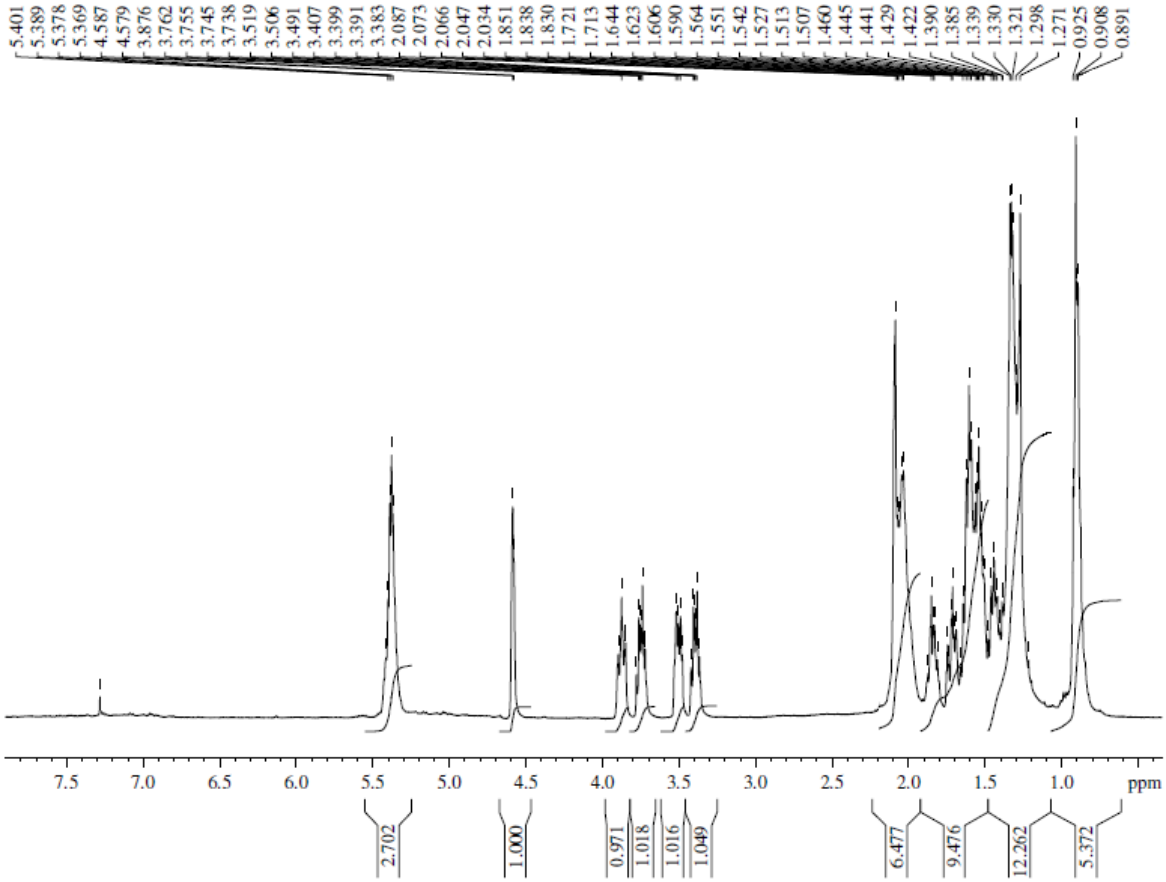
PROCNO 1
Date_ 20111208
Time 11.35
INSTRUM spect
PROBHD 5 mm PABBO BB–
PULPROG zgpg30
TD 16384
SOLVENT CDCl3
NS 51
DS 2
SWH 25252.525 Hz
FIDRES 1.541292 Hz
AQ 0.3244532 sec
RG 2050
DW 19.800 usec
DE 6.00 usec
TE 298.6 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 8

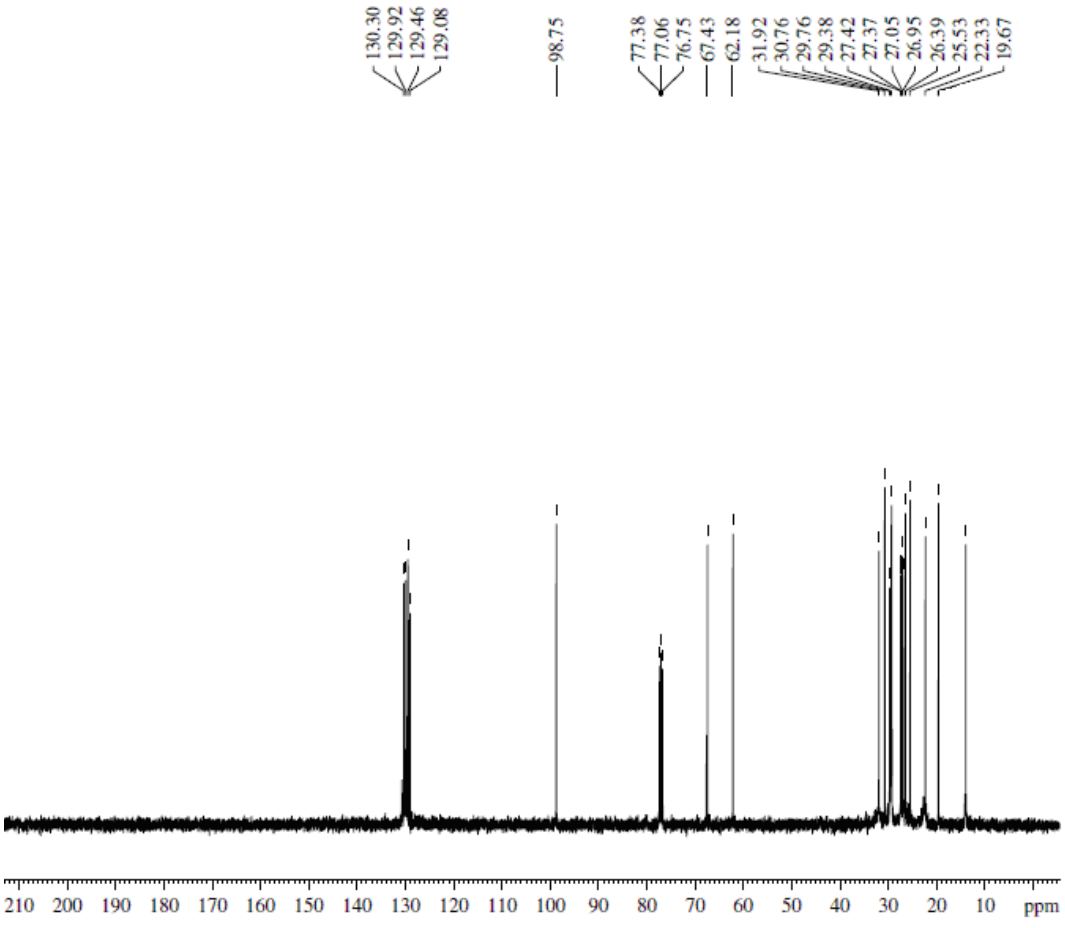
======== CHANNEL f1 =====
NUC1 13C
P1 10.00 usec
PL1 0.00 dB
PL1W 33.91046524 W
SFO1 100.6248425 MHz

======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 15.68 dB
PL13 18.70 dB
PL2W 8.86695957 W
PL12W 0.23975886 W
PL13W 0.11961196 W
SFO2 400.1316005 MHz
SI 65536
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

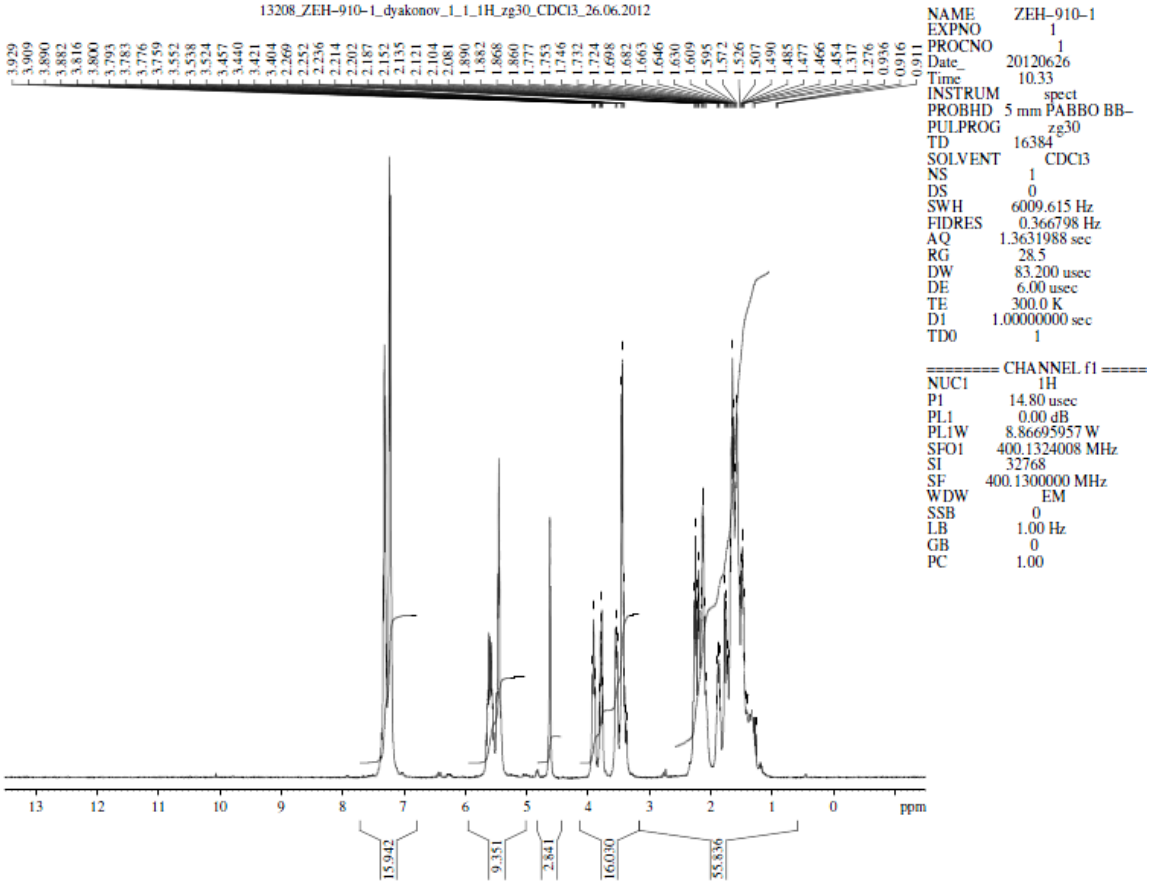
*2-(Tetradeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**4d**)*, 1H



13C



*2-[(11-Phenylundeca-5Z,9Z–dien-1-yl)oxy]tetrahydro-2H-pirane (**4e**)*, 1H



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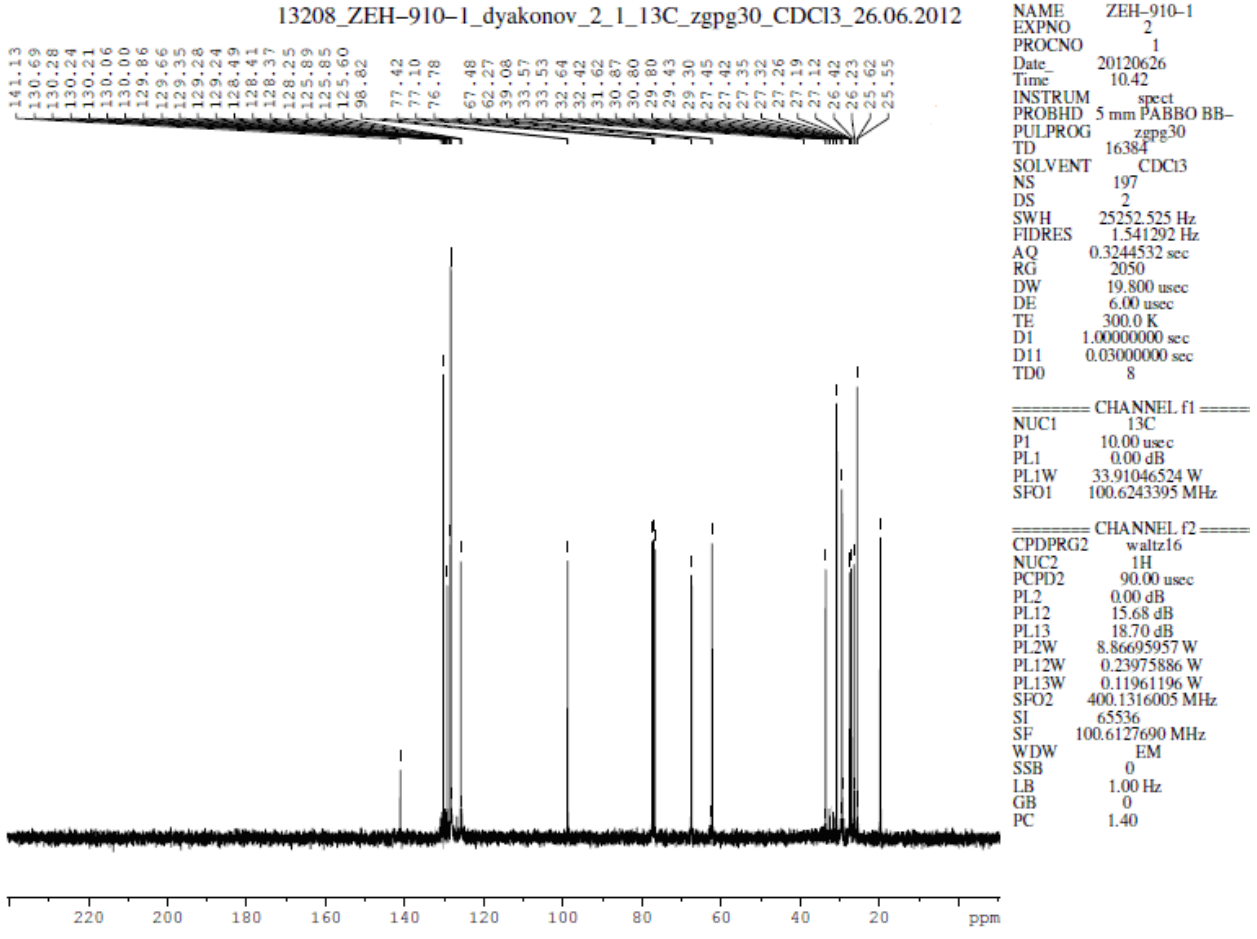
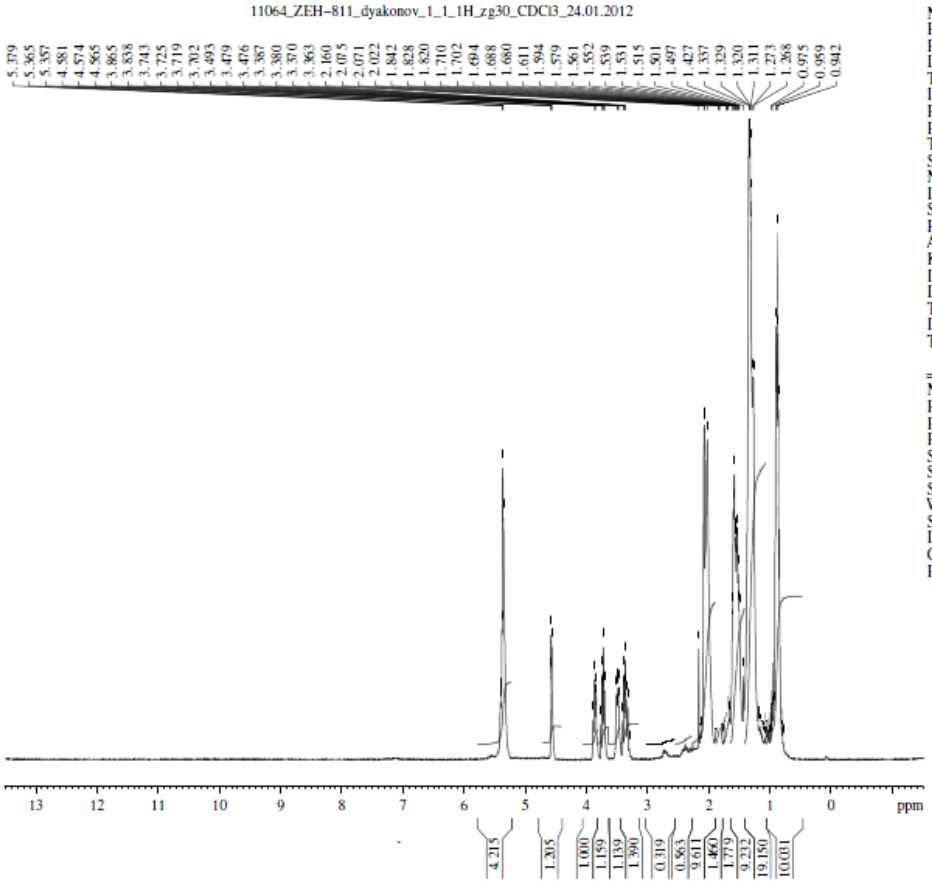


*2-(Hexadeca-7Z,11Z–dien-1-yloxy)tetrahydro-2H-pyrane (**4f**)*, 1H



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EXPNO 1
PROCNO 1
Date_ 20120124
Time 11.54
INSTRUM spect
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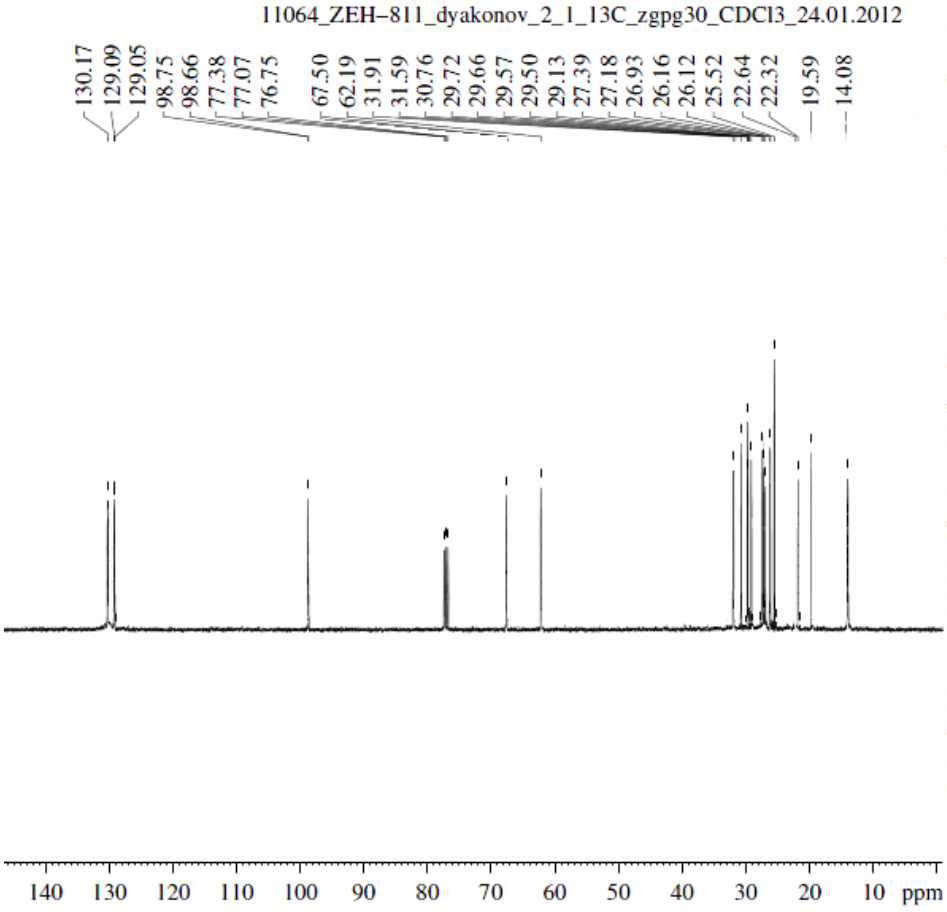
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 1
DS 0
SWH 6009.615 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 16
DW 83.200 usec
DE 6.00 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 =====
NUC1 1H
P1 14.80 usec
PL1 0.00 dB
PL1W 8.86695957 W
SFO1 400.1324008 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

13C



NAME ZEH–811
EXPNO 2
PROCNO 1
Date_ 20120124
Time 12.01
INSTRUM spect
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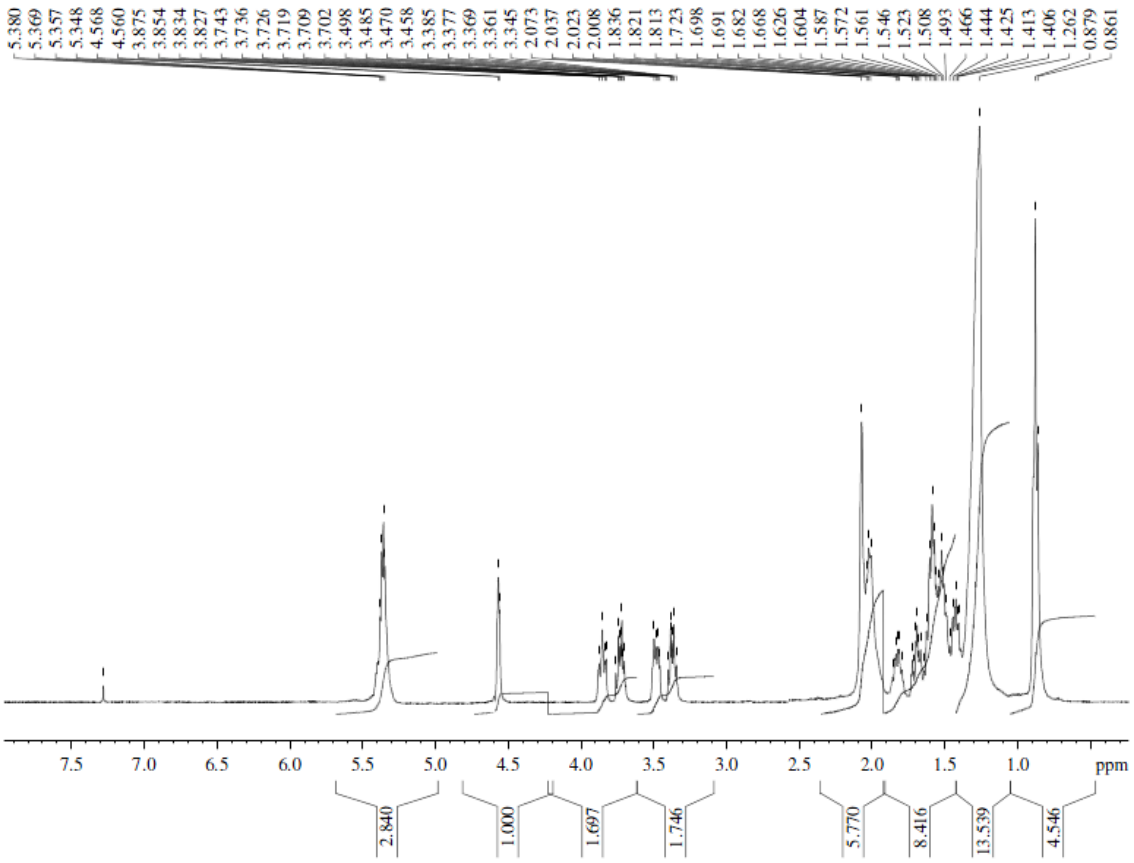
PULPROG zgpg30
TD 16384
SOLVENT CDCl3
NS 248
DS 2
SWH 25252.525 Hz
FIDRES 1.541292 Hz
AQ 0.3244532 sec
RG 2050
DW 19.800 usec
DE 6.00 usec
TE 296.4 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 8

======== CHANNEL f1 ====
NUC1 13C
P1 10.00 usec
PL1 0.00 dB
PL1W 33.91046524 W
SFO1 100.6248425 MHz

======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 15.68 dB
PL13 18.70 dB
PL2W 8.86695957 W
PL12W 0.23975886 W
PL13W 0.11961196 W
SFO2 400.1316005 MHz
SI 65536
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

2-(Hexadeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane ***(7a)***, 1H



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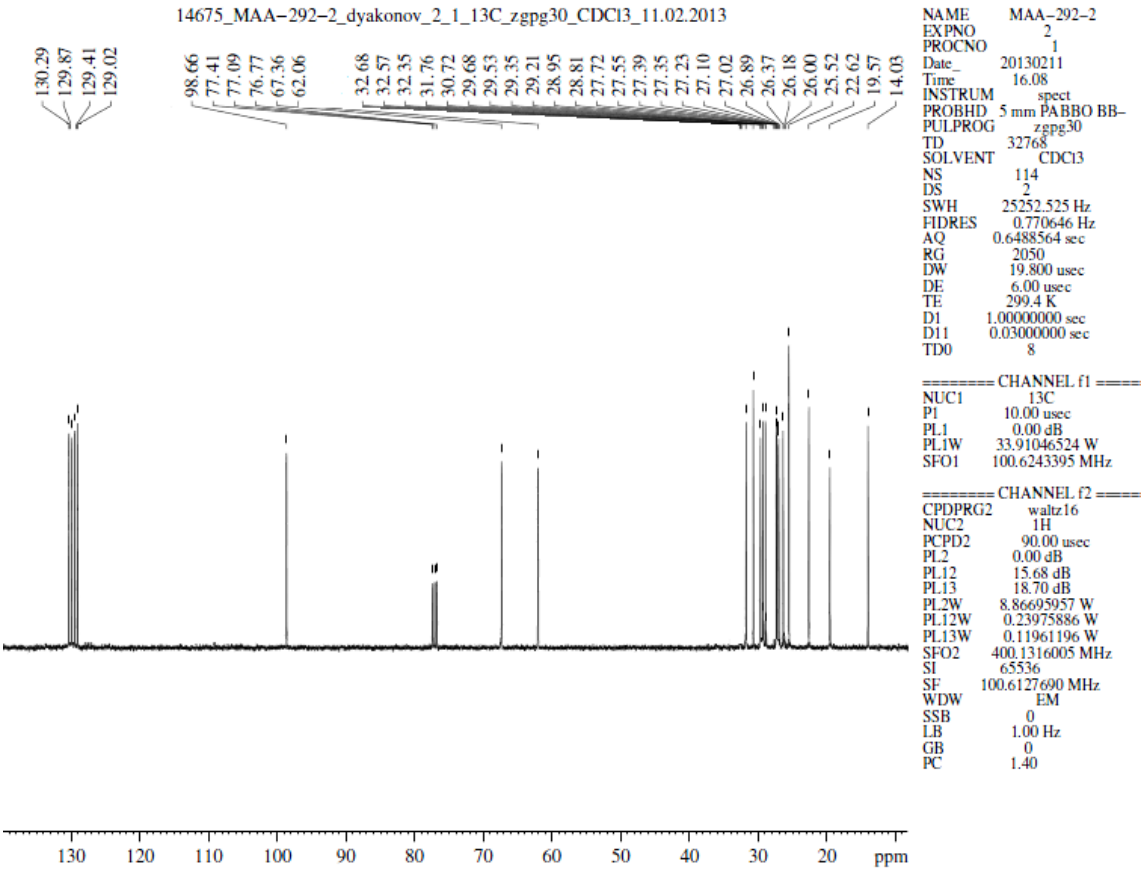
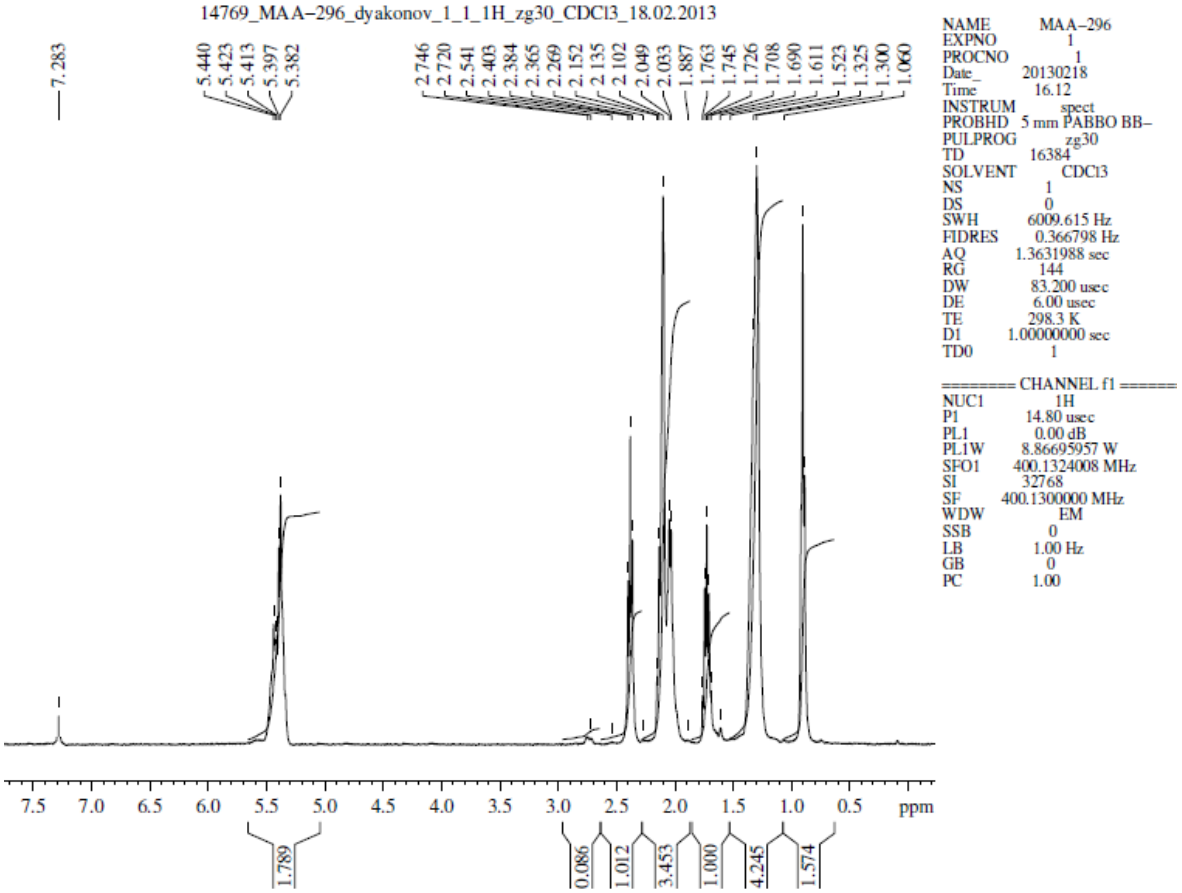


*5Z,9Z-Hexadecadienoic acid (**8a**)*, 1H



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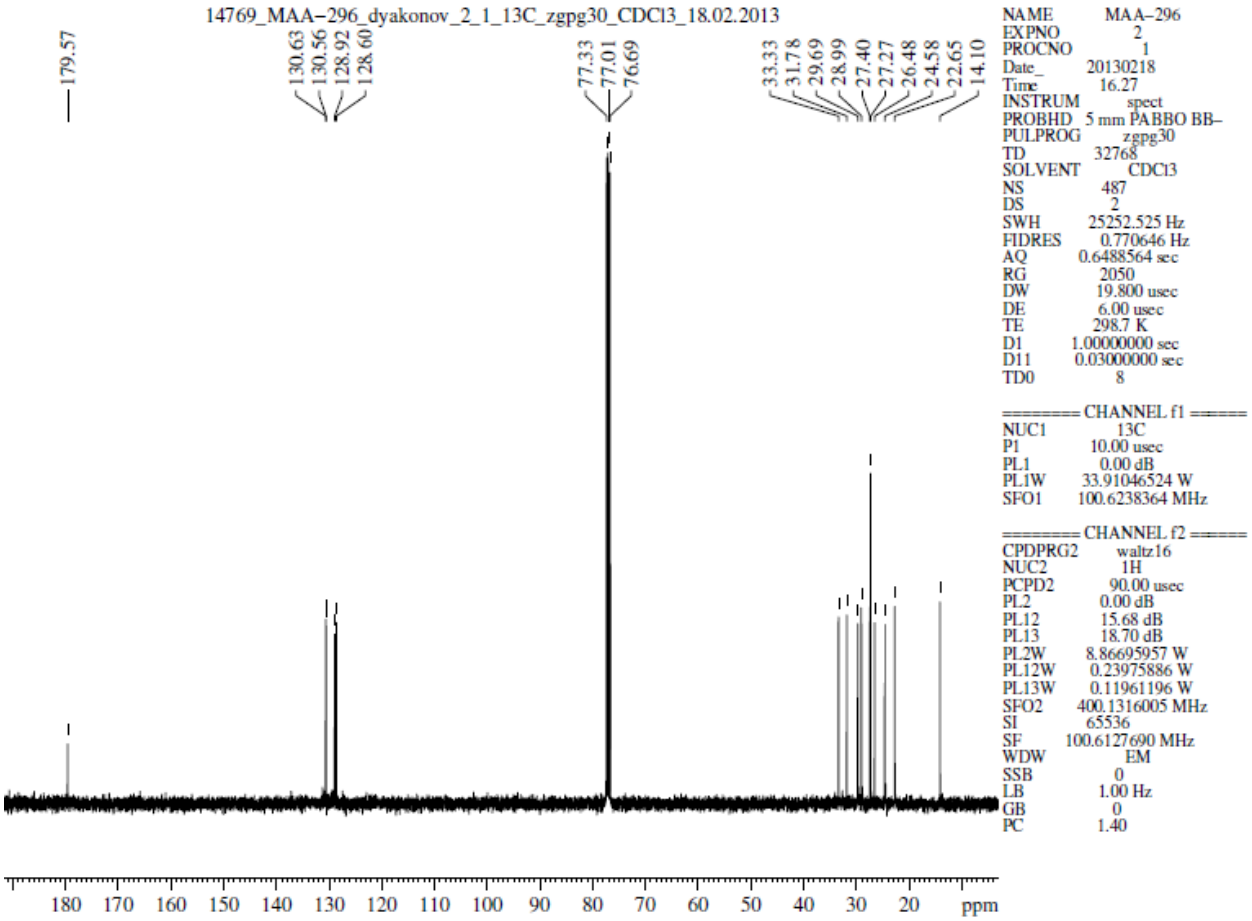
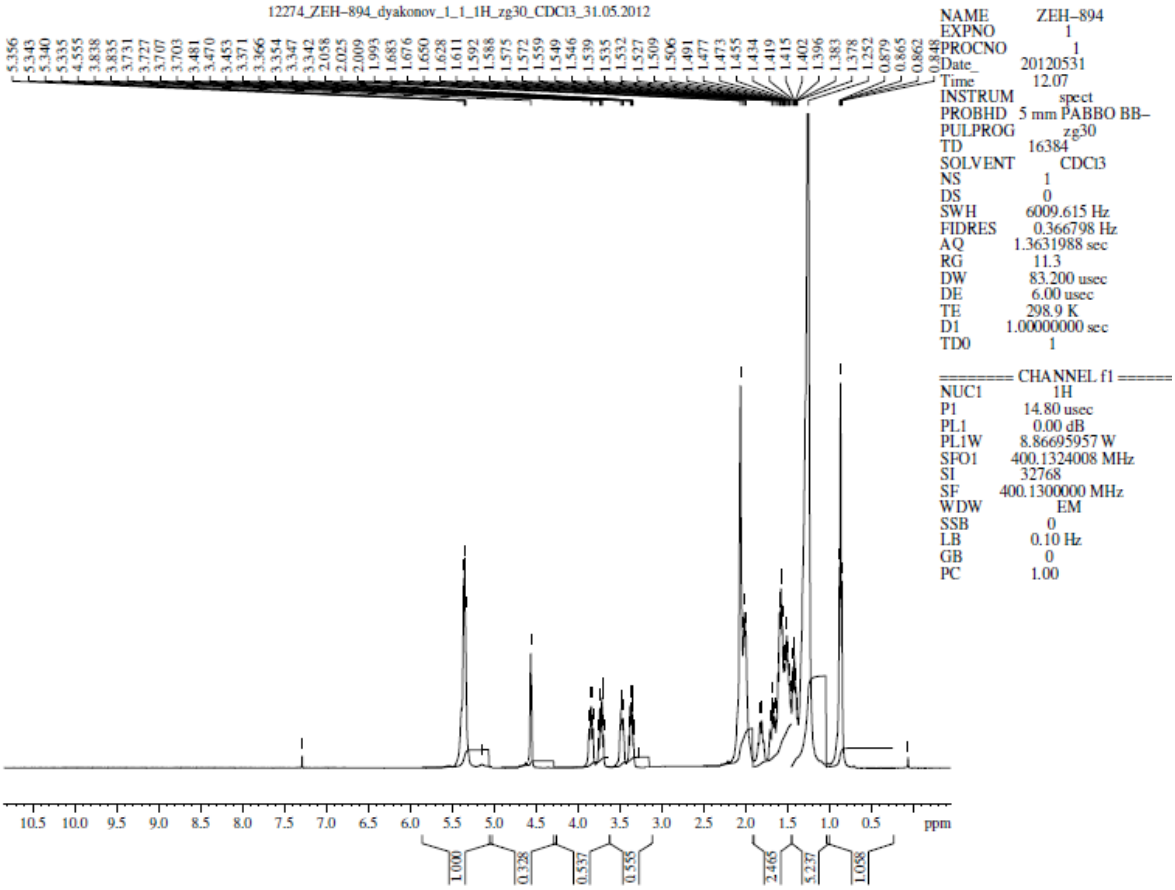


*2-(Nonadeca-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**7b**)*, 1H



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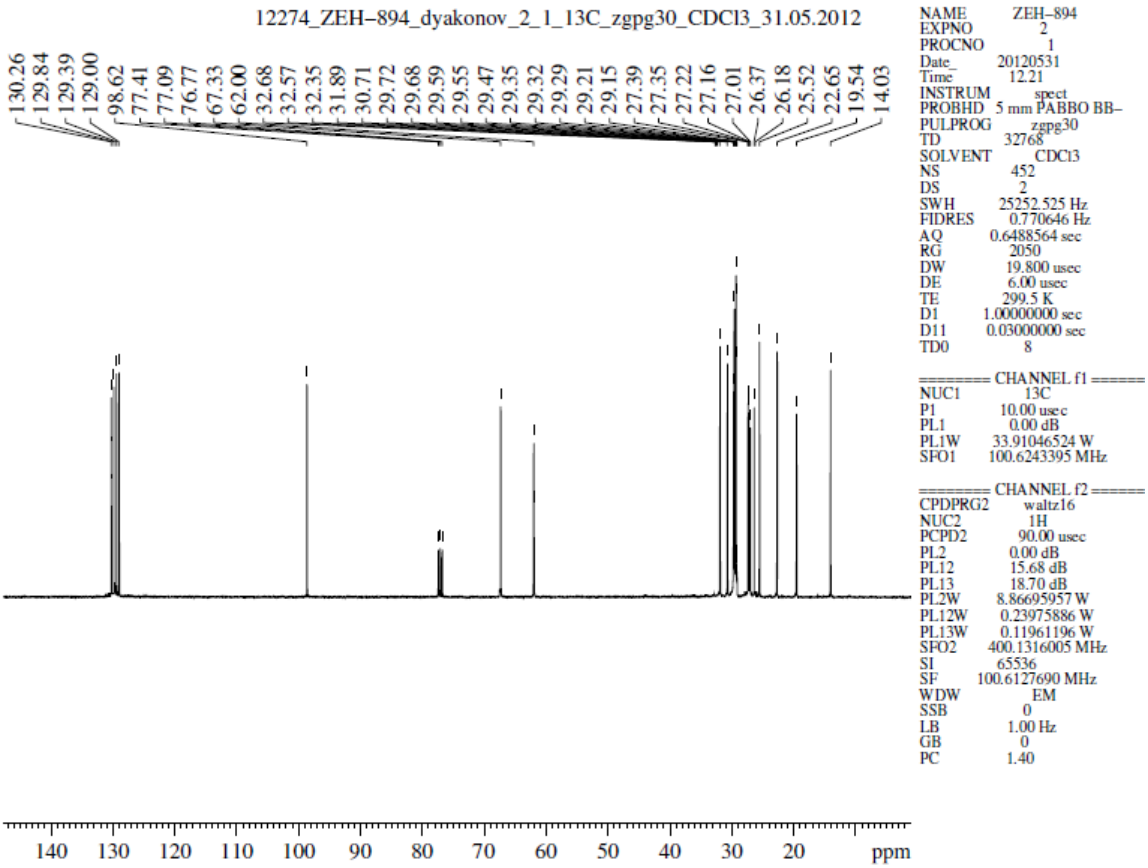
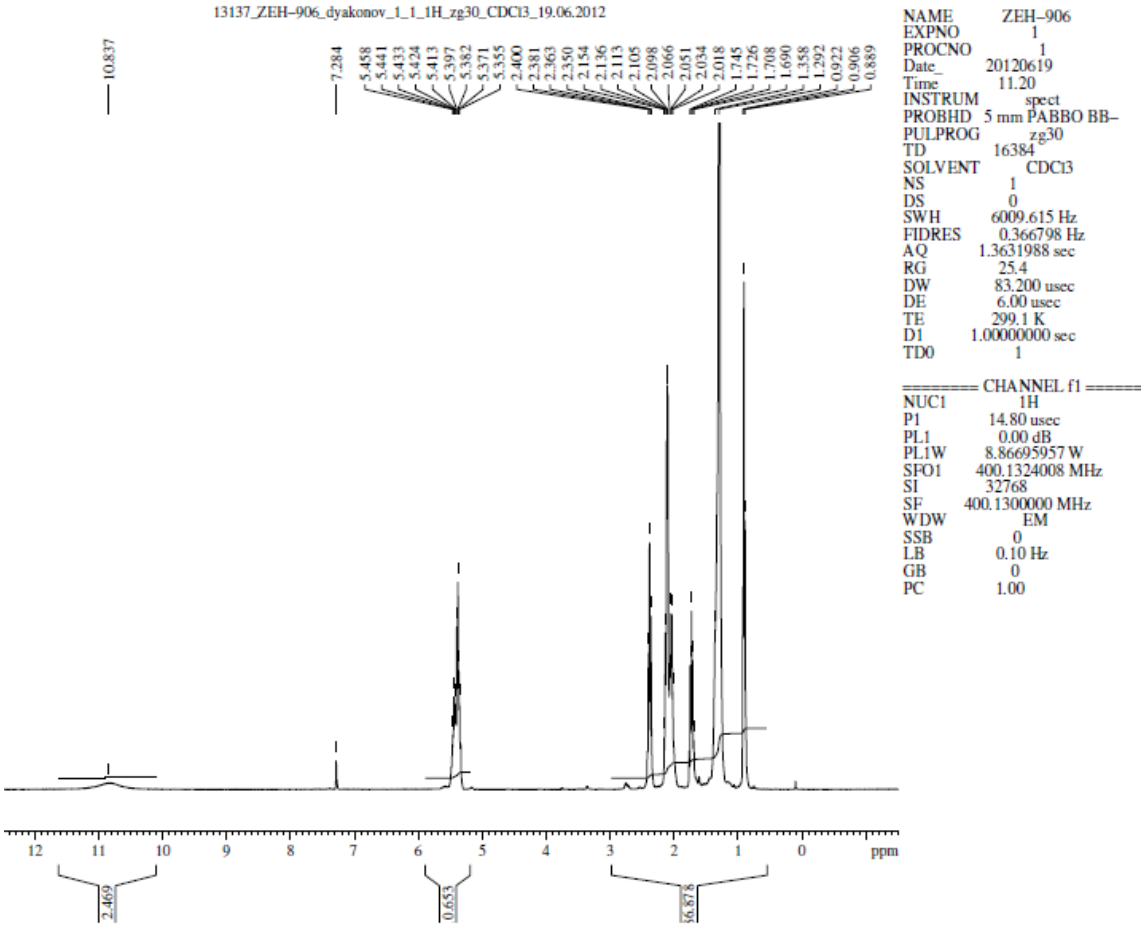


*5Z,9Z-Nonadecadienoic acid (**8b**)*, 1H



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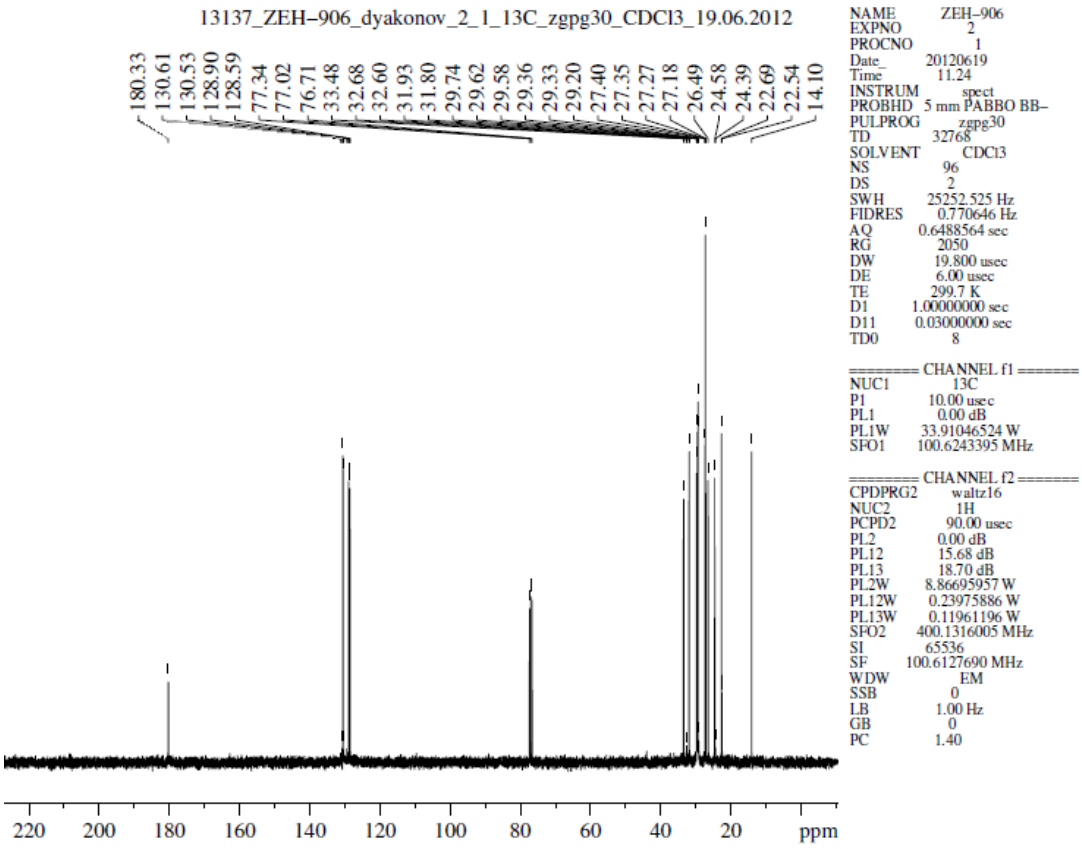
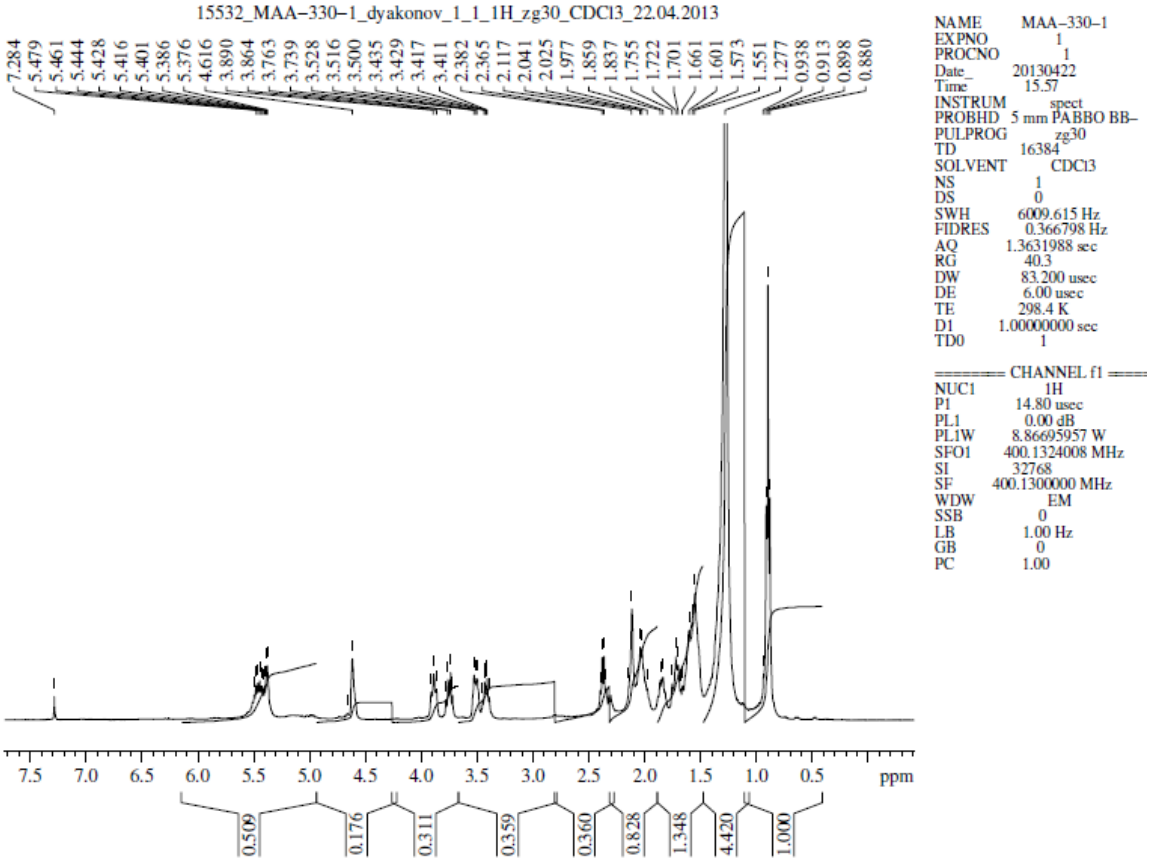


*2-(Eicosa-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane (**7c**), 1H*



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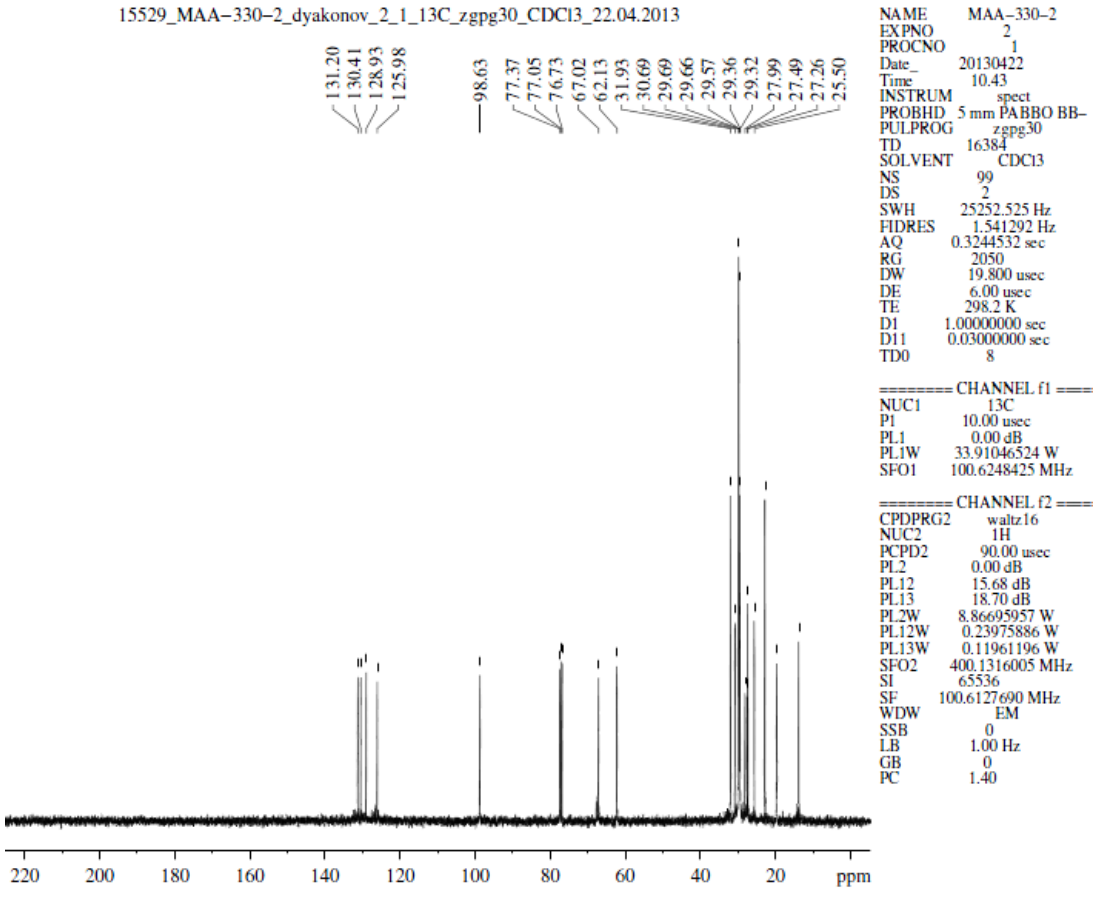
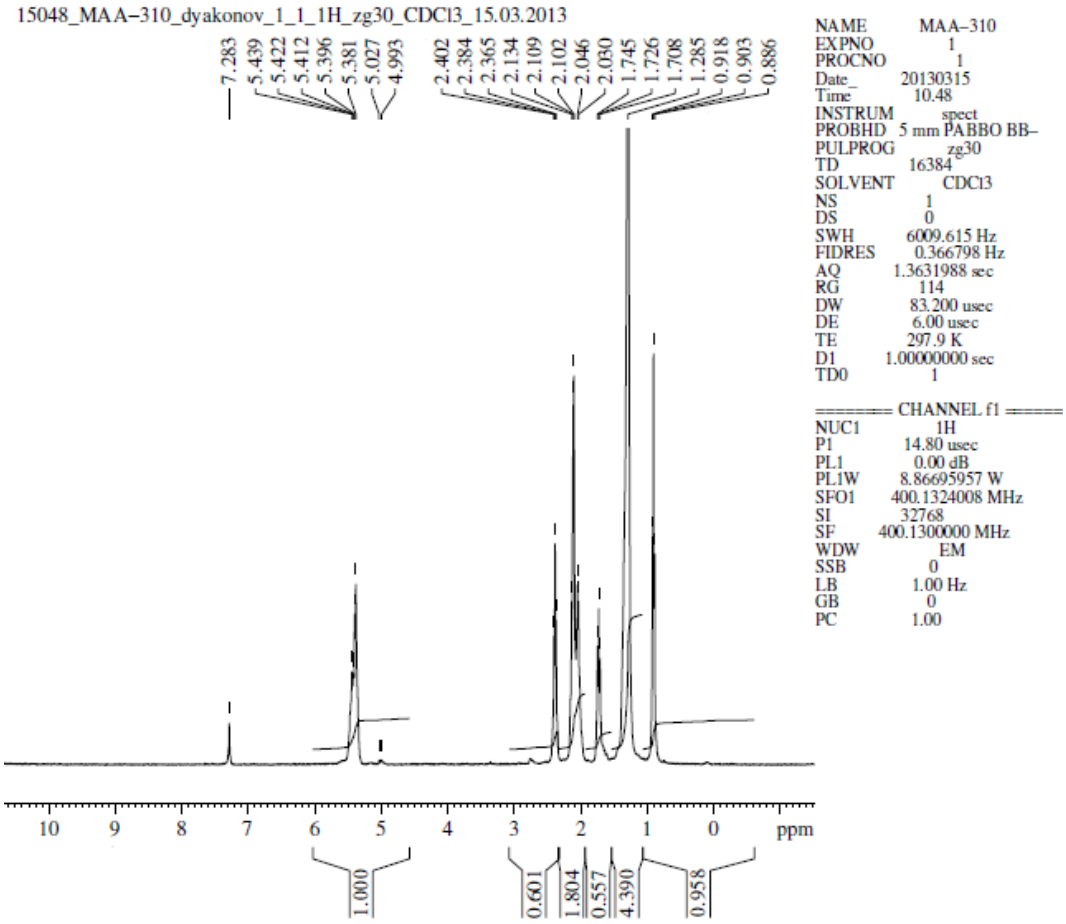


*5Z,9Z-Eicosadienoic acid (**8c**), 1H*



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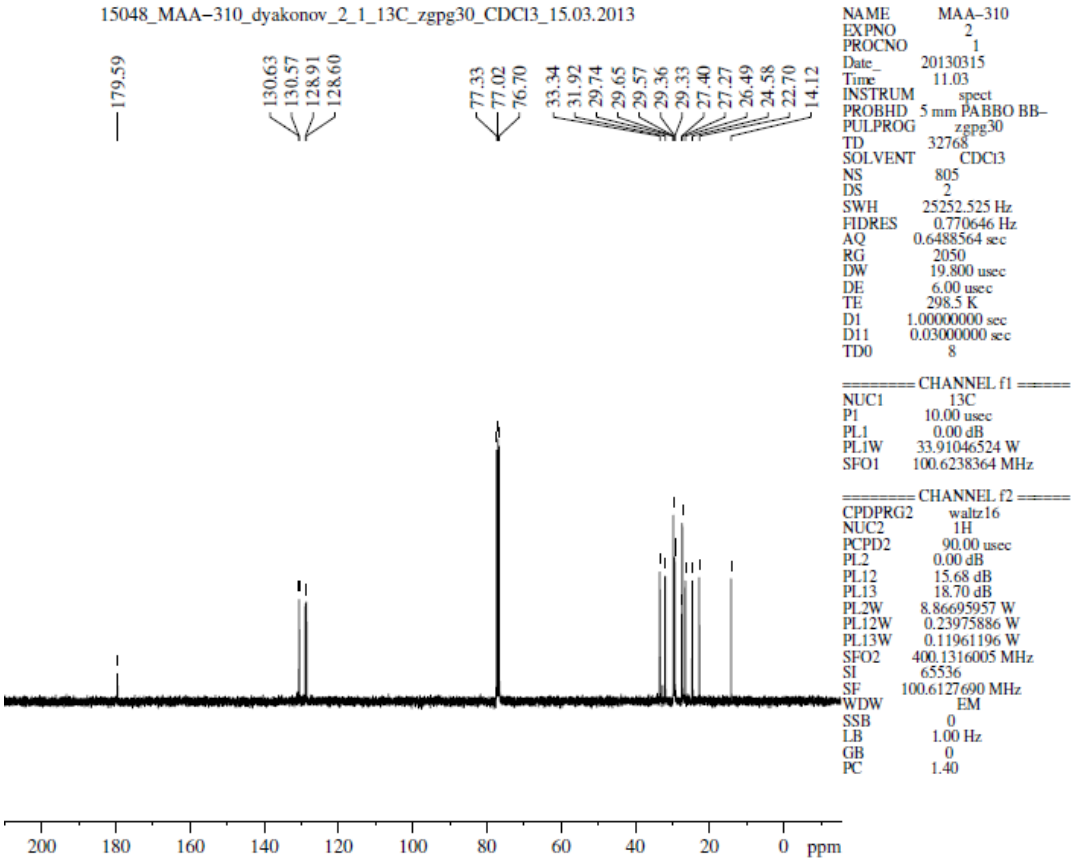
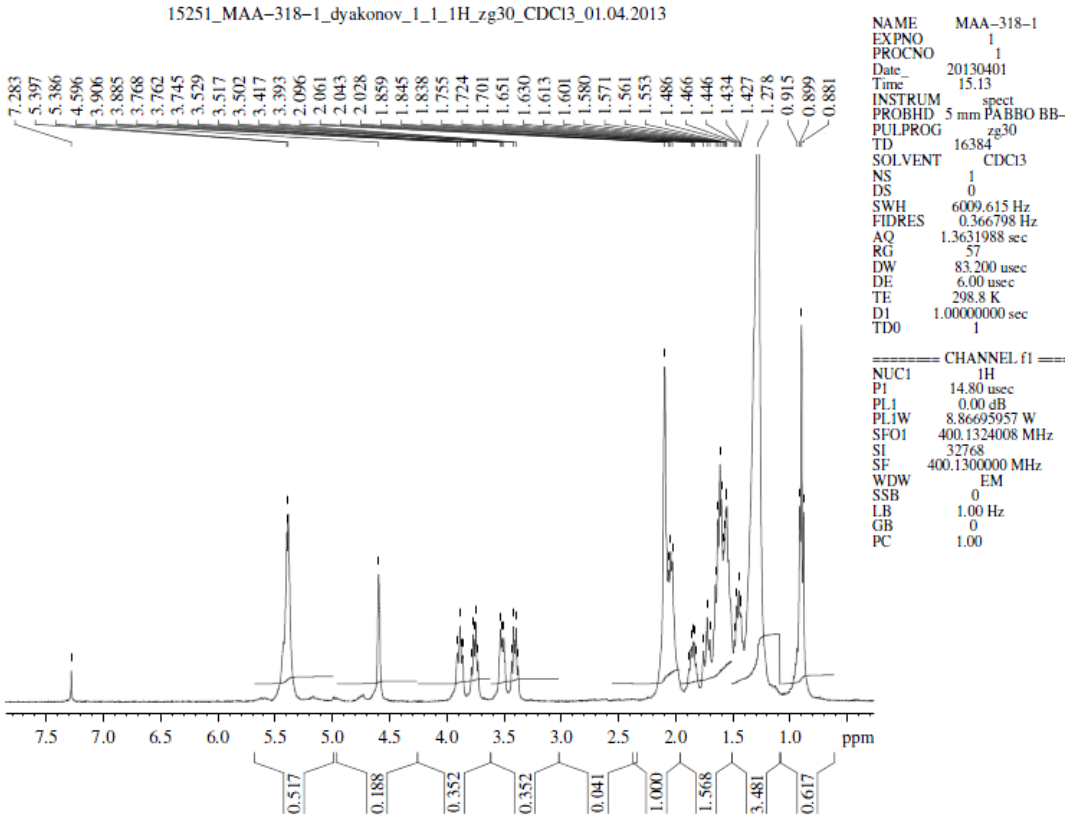
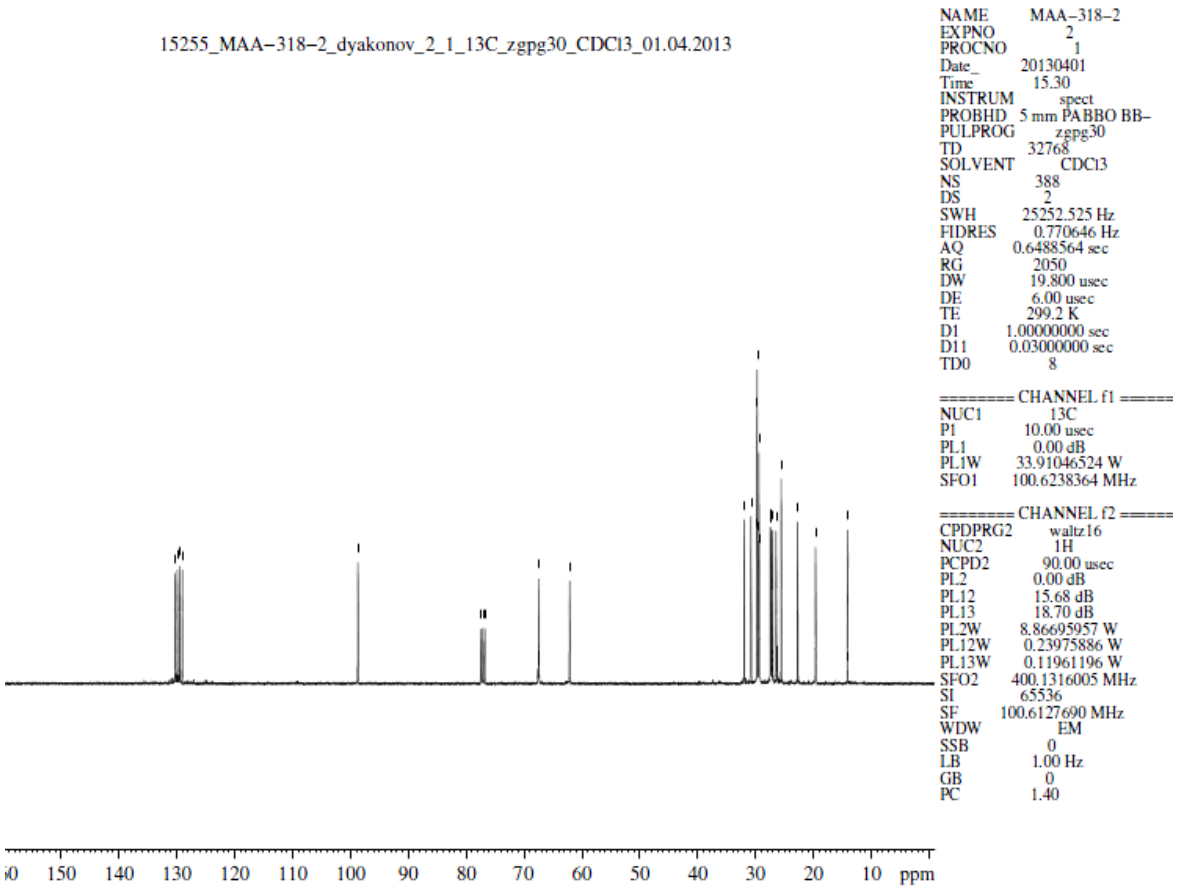


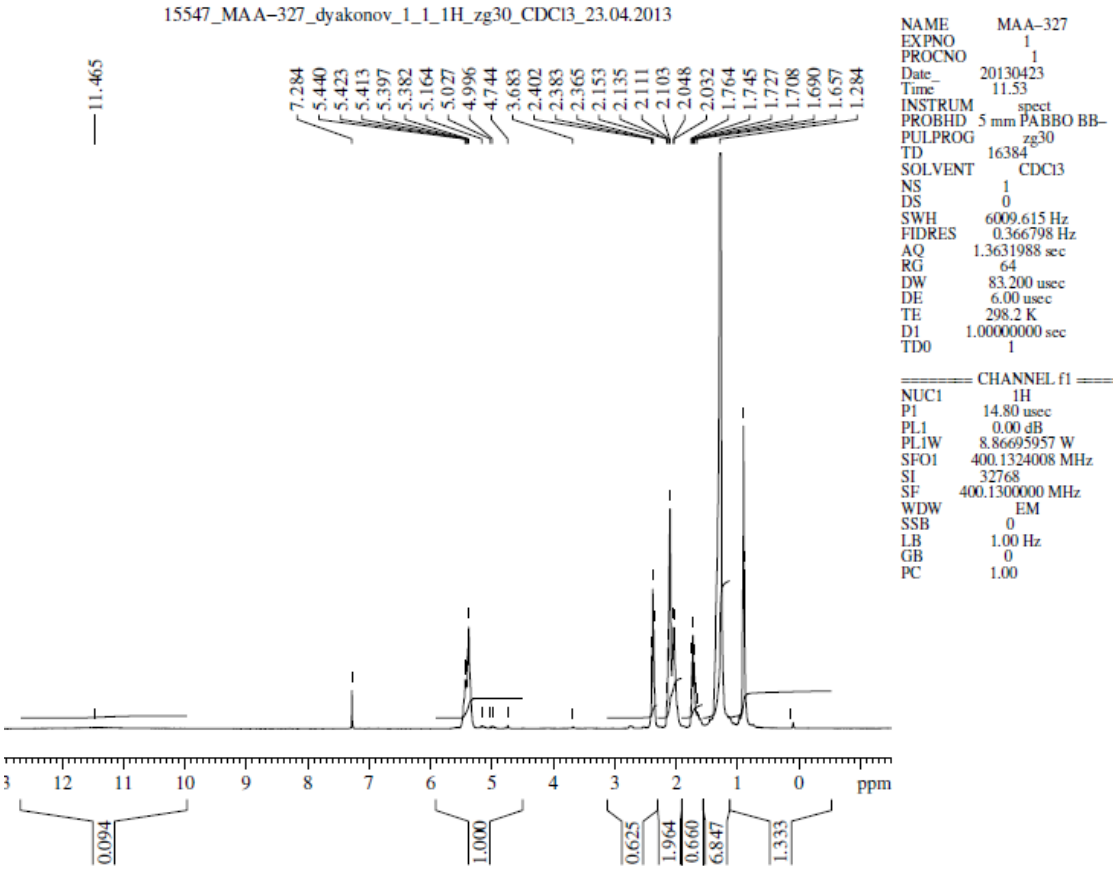
2-(Docosa-5Z,9Z–dien-1-yloxy)tetrahydro-2H-pyrane ***(7d)****, 1H*



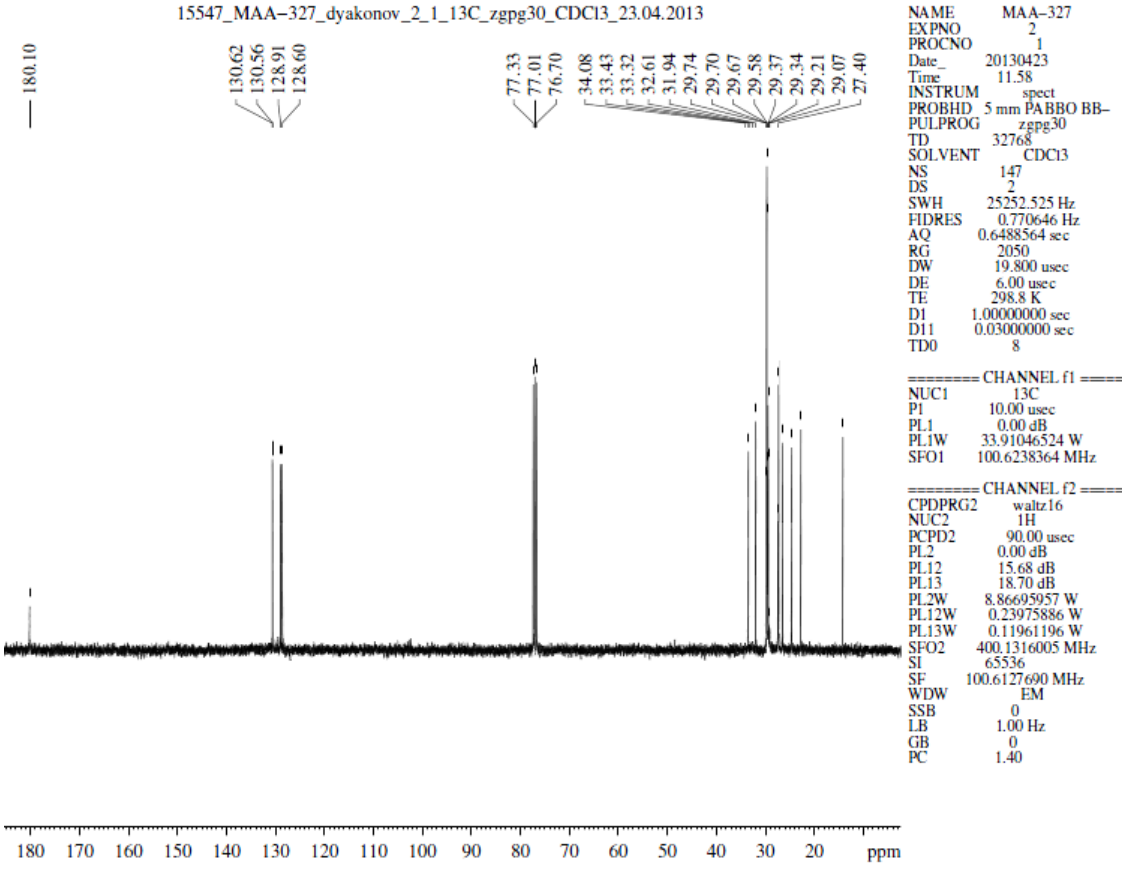
13C



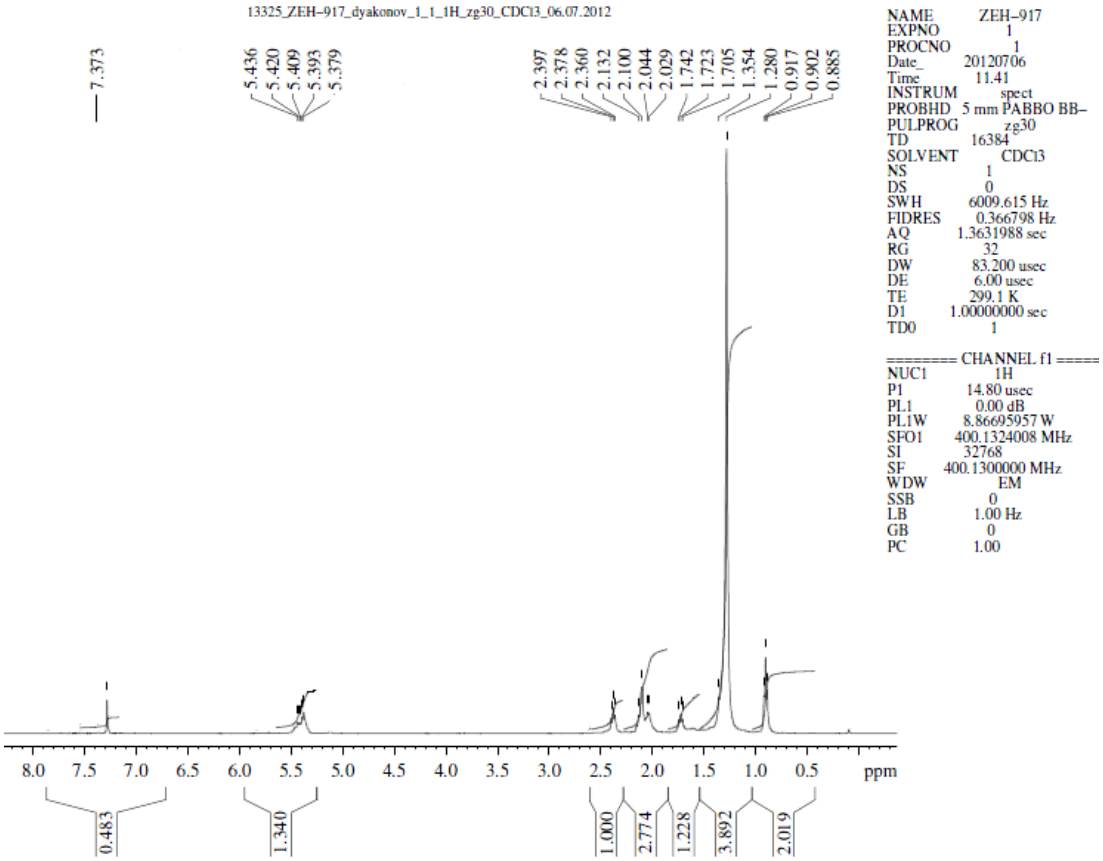
*5Z,9Z-Docosadienoic acid (**8d**), 1H*



13C



*5Z,9Z-Tetracosadienoic acid (**8e**),* 1H



13C