

Supporting Information

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„Regioselective Carbene Insertion on Polysubstituted Dihydroaromatic Compounds”

General procedure for the cobalt-catalysed Diels-Alder reaction

To a solution of the alkyne in dry CH₂Cl₂ were subsequently added CoBr₂(dppe) (5-10 mol%), anhydrous ZnI₂ (50 mol%), Zn dust (50 mol%) or NBu₄BH₄ (1.1 equiv.) and the 1,3-diene (1.2 equiv.) The resulting mixture was stirred 4 hours at room temperature, then filtered with the appropriate eluent (pentane or diethyl ether) over a short pad of silica gel. The filtrate was concentrated under reduced pressure and purified by Kugelrohr distillation under vacuum or column chromatography on silica gel.

General procedure for the rhodium-catalysed C-H activation reaction

A solution of the diazoester (2 equiv.) in 2 mL of dry CH₂Cl₂ was added over one hour *via* syringe pump to a 0°C solution of freshly made dihydroaromatic compound and Rh₂(OAc)₄ (0.5 mol%) in 3.0 mL of dry CH₂Cl₂. After the addition was completed the reaction mixture was stirred one additional hour at room temperature and then filtered over a short pad of silica gel using pentane:diethyl ether = 2:1 as eluent. The filtrate was concentrated under reduced pressure to give a residue that was dissolved in benzene (5.0 mL) and oxidized by DDQ (1.2 equiv.) at room temperature. After 2 hours the reaction mixture was filtered over a short pad of silica gel using pentane:diethyl ether = 2:1 as eluent, concentrated under reduced pressure and purified by column chromatography on silica gel.

Analytical data for the new compounds

2-(4,5-Dimethyl-biphenyl-3-yl)-propionic acid ethyl ester (**5b**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (600 MHz, CDCl₃): δ = 7.67-7.61 (m, 2H), 7.47 (t, 2H, *J* = 7.7 Hz), 7.43 (br s, 1H), 7.40-7.35 (m, 2H), 4.28-4.16 (m, 2H), 4.12 (q, 1H, *J* = 7.2 Hz), 2.43 (s, 3H), 2.36 (s, 3H), 1.59 (d, 3H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.2 Hz).

¹³C-NMR (150.9 MHz, CDCl₃): δ = 174.9, 141.0, 139.6, 138.6, 137.4, 133.3, 128.7, 127.4, 126.9, 123.1, 60.6, 41.9, 21.1, 18.1, 14.9, 14.1.

IR (film): 2979, 1732, 1474, 1191, 1097, 762, 698 cm⁻¹.

MS (EI): *m/z* 282 (M⁺), 209, 179, 152, 115.

HRMS (EI): *m/z* calcd. for C₁₉H₂₂O₂: 282.1620, found 218.1623.

(4,5-Dimethyl-biphenyl-3-yl)-phenyl-acetic acid methyl ester (**5c**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (600 MHz, CDCl₃): δ = 7.60 (d, 2H, *J* = 7.9 Hz), 7.49-7.30 (m, 10H), 5.41 (s, 1H), 3.82 (s, 3H), 2.42 (s, 3H), 2.28 (m, 3H).

¹³C-NMR (150.9 MHz, CDCl₃): δ = 173.3, 140.9, 138.4, 137.9, 137.6, 137.2, 134.0, 128.9, 128.6, 128.5, 127.9, 127.2, 127.0, 126.9, 124.7, 54.2, 52.3, 21.0, 15.1.

IR (film): 3029, 2949, 1740, 1599, 1473, 1196, 1009, 762, 699 cm⁻¹.

MS (EI): *m/z* 330 (M⁺), 271, 241, 181, 91.

HRMS (EI): *m/z* calcd. for C₂₃H₂₂O₂: 330.1620, found 330.1609.

2-(4,5-Dimethyl-biphenyl-3-yl)-4-phenyl-but-3-enoic acid ethyl ester (9a)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 15:1)

¹H-NMR (300 MHz, CDCl₃): δ = 7.51-7.44 (m, 2H), 7.38-7.05 (m, 10H), 6.54 (dd, 1H, J = 16.0, 7.6 Hz), 6.32 (d, 1H, J = 16.0 Hz), 4.68 (dd, 1H, J = 7.6, 1.0 Hz), 4.17-4.04 (m, 2H), 2.26 (s, 3H), 2.21 (s, 3H), 1.15 (t, 3H, J = 7.1 Hz).

¹³C-NMR (75 MHz, CDCl₃): δ = 172.8, 140.9, 138.6, 137.6, 137.2, 133.7, 132.2, 128.6, 128.4, 127.8, 127.5, 127.2, 126.9, 126.8, 126.4, 124.6, 61.1, 51.8, 21.1, 15.2, 14.1.

IR (film): 3435, 2980, 1730, 1473, 1235, 1178, 1027, 759, 698 cm⁻¹.

MS (EI): *m/z* 370 (M⁺), 297, 219, 165, 115, 91, 47.

HRMS (EI): *m/z* calcd. for C₂₆H₂₆O₂: 370.1933, found 370.1924.

(2,3-Dimethyl-5-trimethylsilyl-phenyl)-phenyl-acetic acid methyl ester (9b)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (600 MHz, CDCl₃): δ = 7.40-7.35 (m, 2H), 7.34-7.27 (m, 5H), 5.36-5.34 (m, 1H), 3.80 (s, 3H), 2.36 (s, 3H), 2.22 (s, 3H), 0.29 (s, 9H).

¹³C-NMR (150.9 MHz, CDCl₃): δ = 173.5, 138.0, 137.1, 136.5, 136.0, 135.8, 134.1, 130.9, 128.9, 128.4, 127.1, 54.3, 52.2, 20.8, 15.3, -1.2.

IR (film): 2952, 1732, 1150, 906, 834 cm⁻¹.

MS (EI): *m/z* 326 (M⁺), 311, 267, 251, 193, 178, 89, 73.

HRMS (EI): *m/z* calcd. for C₂₀H₂₆O₂Si: 326.1702, found 326.1707.

(2,3-Diethyl-5,6-dimethyl-phenyl)-phenyl-acetic acid methyl ester (9c)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (300 MHz, CDCl₃): δ = 7.27-7.00 (m, 5H), 6.94 (s, 1H), 5.38 (s, 1H), 3.62 (s, 3H), 2.68-2.51 (m, 3H), 2.50-2.33 (m, 1H), 2.16 (s, 3H), 1.88 (s, 3H), 1.15 (t, 3H, J = 7.5 Hz), 0.98 (t, 3H, J = 7.6 Hz).

¹³C-NMR (75 MHz, CDCl₃): δ = 174.1, 139.5, 138.6, 137.3, 135.1, 134.6, 134.0, 129.9, 128.9, 127.9, 126.5, 52.2, 50.9, 26.0, 22.6, 20.6, 17.1, 15.6, 15.0.

IR (film): 2965, 1738, 1448, 1196, 1174, 1014, 757 cm⁻¹.

MS (EI): *m/z* 310 (M⁺), 251, 223, 161, 117, 91, 77.

HRMS (EI): *m/z* calcd. for C₂₁H₂₆O₂: 310.1933, found 310.1924.

(2,3-Diethyl-5methyl-phenyl)-phenyl-acetic acid methyl ester (9d)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (500 MHz, CDCl₃): δ = 7.41-7.36 (m, 2H), 7.35-7.29 (m, 3H), 7.09 (s, 1H), 7.06 (s, 1H), 5.42 (s, 1H), 3.81 (s, 3H), 2.80-2.65 (m, 4H), 2.37 (s, 3H), 1.32 (t, 3H, J = 7.5 Hz), 1.21 (t, 3H, J = 7.6 Hz).

¹³C-NMR (75 MHz, CDCl₃): δ = 173.7, 142.3, 138.9, 136.9, 135.9, 135.2, 128.8, 128.7, 128.3, 127.0, 126.9, 52.9, 52.1, 25.8, 21.3, 21.1, 15.5, 15.1.

IR (film): 2965, 1742, 1609, 1452, 1160, 698 cm⁻¹.

MS (EI): *m/z* 296 (M⁺), 237, 209, 192, 117, 91.

HRMS (EI): *m/z* calcd. for C₂₀H₂₄O₂: 296.1776, found 296.1772.

(2,3-Bis-methoxymethyl-5-methyl-phenyl)-phenyl-acetic acid methyl ester (**9e**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 2:1)

¹H-NMR (500 MHz, CDCl₃): δ = 7.38-7.25 (m, 5H), 7.16 (s, 1H), 7.13 (1H), 5.58 (s, 1H), 4.58 (dd, 2H, J = 11.5, 4.3 Hz), 4.52 (dd, 2H, J = 11.5, 7.2 Hz), 3.77 (s, 3H), 3.44 (s, 3H), 3.40 (s, 3H), 2.33 (s, 3H).

¹³C-NMR (125.5 MHz, CDCl₃): δ = 173.2, 138.7, 138.6, 137.8, 137.2, 131.5, 129.7, 129.2, 128.6, 128.3, 126.9, 72.9, 67.2, 58.0, 57.9, 52.5, 52.0, 21.1.

IR (film): 2924, 1737, 1611, 1452, 1194, 1158, 1090 cm⁻¹.

MS (ESI): m/z 351 (M+Na⁺).

HRMS (ESI): m/z calcd. for C₂₀H₂₄O₄Na: 351.1573 (M+Na⁺), found 351.1567 (M+Na⁺).

(2,3-Bis-methoxymethyl-5,6-dimethyl-phenyl)-phenyl-acetic acid methyl ester (**9f**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 2:1)

¹H-NMR (300 MHz, CDCl₃): δ = 7.23-7.09 (m, 4H), 7.07-6.99 (m, 2H), 5.59 (s, 1H), 4.44-4.39 (m, 2H), 4.35 (d, 1H, J = 11.4 Hz), 4.22 (d, 1H, J = 11.4 Hz), 3.61 (s, 3H), 3.32 (s, 3H), 3.16 (s, 3H), 2.19 (s, 3H), 1.94 (s, 3H).

¹³C-NMR (75 MHz, CDCl₃): δ = 173.7, 137.6, 137.3, 137.0, 136.5, 135.1, 133.3, 130.5, 128.6, 127.9, 126.4, 72.9, 68.2, 58.1, 57.9, 52.1, 50.8, 20.8, 16.9.

IR (film): 2925, 1736, 1448, 1384, 1197, 1094 cm⁻¹.

MS (ESI): m/z 365 (M+Na⁺).

HRMS (ESI): m/z calcd. for C₂₁H₂₆O₂Na: 365.1729 (M+Na⁺), found 365.1723 (M+Na⁺).

2-(2,3-Dimethyl-5-trimethylsilanyl-phenyl)-propionic acid ethyl ester (**9g**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 30:1)

¹H-NMR (600 MHz, CDCl₃): δ = 7.29 (s, 1H), 7.27 (s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 4.06 (q, 1H, J = 7.1 Hz), 2.37 (s, 3H), 2.32 (s, 3H), 1.53 (d, 3H, J = 7.2 Hz), 1.27 (t, 3H, J = 7.1 Hz), 0.31 (s, 9H).

¹³C-NMR (150.9 MHz, CDCl₃): δ = 175.0, 138.6, 137.3, 136.2, 135.0, 133.6, 129.4, 60.6, 42.0, 20.9, 18.1, 15.1, 14.1, -1.1.

IR (film): 2956, 1734, 1248, 1184, 906, 834, 755 cm⁻¹.

MS (EI): m/z 278 (M⁺), 263, 205, 191, 73, 43.

HRMS (EI): m/z calcd. for C₁₆H₂₆O₂Si: 278.1702, found 278.1707.

2-(2,3-Diethyl-5,6-dimethyl-phenyl)-propionic acid ethylester (**9h**)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 20:1)

¹H-NMR (500 MHz, CDCl₃): δ = 6.94 (s, 1H), 4.28-4.18 (m, 1H), 4.16-4.07 (m, 2H), 2.80-2.53 (m, 4H), 2.22 (s, 3H), 2.07 (s, 3H), 1.50 (d, 3H, J = 7.2 Hz), 1.29-1.14 (m, 9H).

¹³C-NMR (125.5 MHz, CDCl₃): δ = 175.9, 139.2, 138.1, 137.3, 135.0, 132.3, 129.2, 60.6, 40.6, 26.2, 22.4, 20.6, 16.8, 16.2, 15.7, 15.4, 14.2.

IR (film): 2966, 1726, 1445, 1377, 1216, 1097, 1066 cm⁻¹.

MS (EI): m/z 262 (M⁺), 189, 161, 129, 91.

HRMS (EI): m/z calcd. for C₁₇H₂₆O₂: 262.1933, found 262.1929.

[6-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-4-methyl-biphenyl-2-yl]-phenyl-acetic acid methyl ester (11d)

Column chromatography on silica gel (eluent: pentane:diethyl ether = 2:1)

The main component of the inseparable mixture of regioisomers (ratio 85:11:4) was determined by means of two dimensional NMR techniques.

¹H-NMR (500 MHz, CDCl₃) signals for the major regioisomer (**11d**): δ = 7.77-7.68 (m, 2H), 7.65-7.56 (m, 2H), 7.51-7.45 (m, 1H), 7.40-7.31 (m, 3H), 7.25-7.18 (m, 3H), 7.16 (s, 1H), 7.05-6.99 (m, 3H), 6.92 (s, 1H), 4.86 (s, 1H), 4.51 (s, 2H), 3.63 (s, 3H), 2.28 (s, 3H).

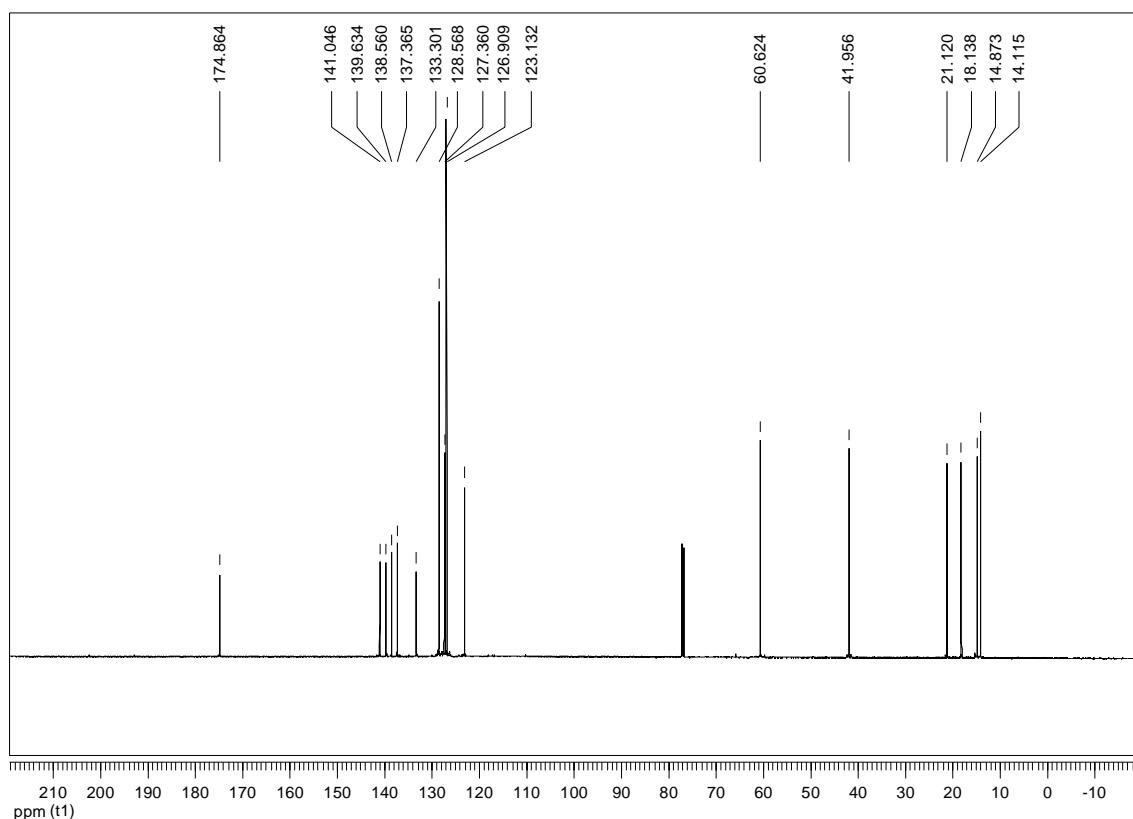
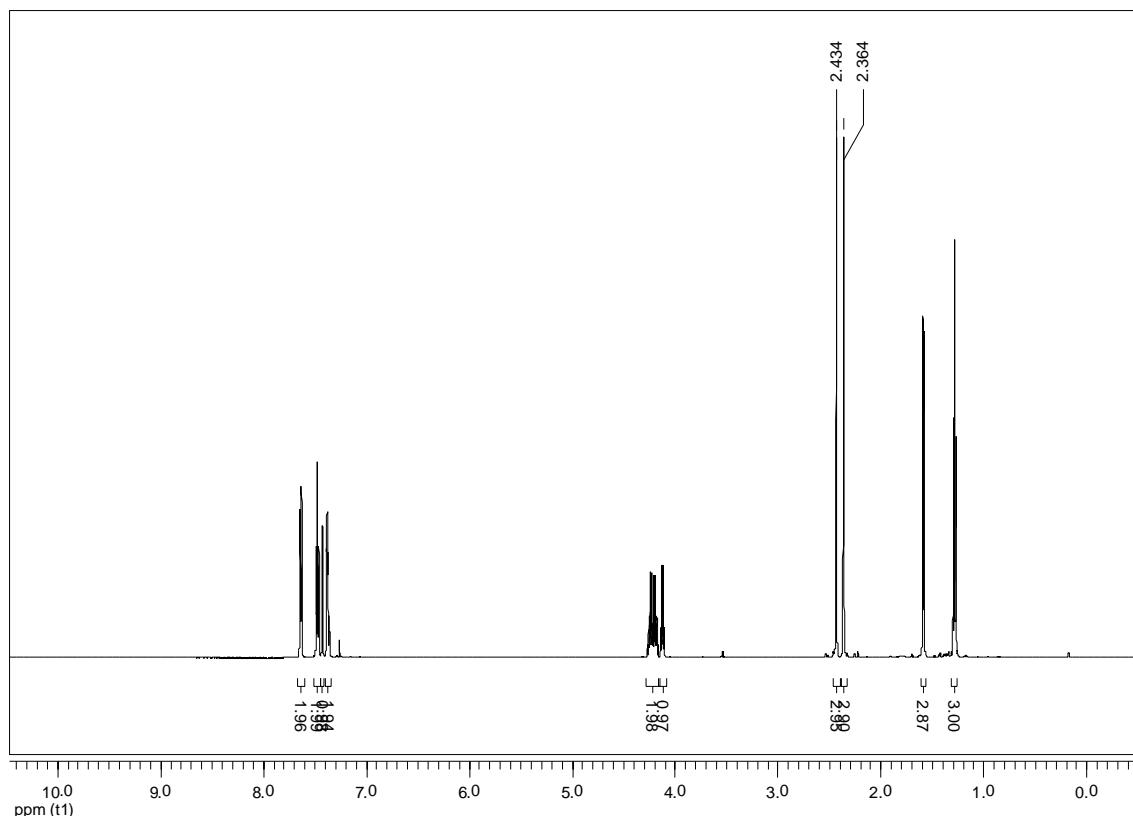
¹³C-NMR (125.7 MHz, CDCl₃) resolved signals for the major regioisomer (**11d**): δ = 173.2, 167.9, 138.0, 137.5, 134.3, 133.9, 132.0, 128.1, 126.1, 123.2, 53.4, 52.0, 39.9, 21.4. The remaining signals are unresolved.

IR (KBr): 3029, 1718, 1389, 1161, 953, 715 cm⁻¹.

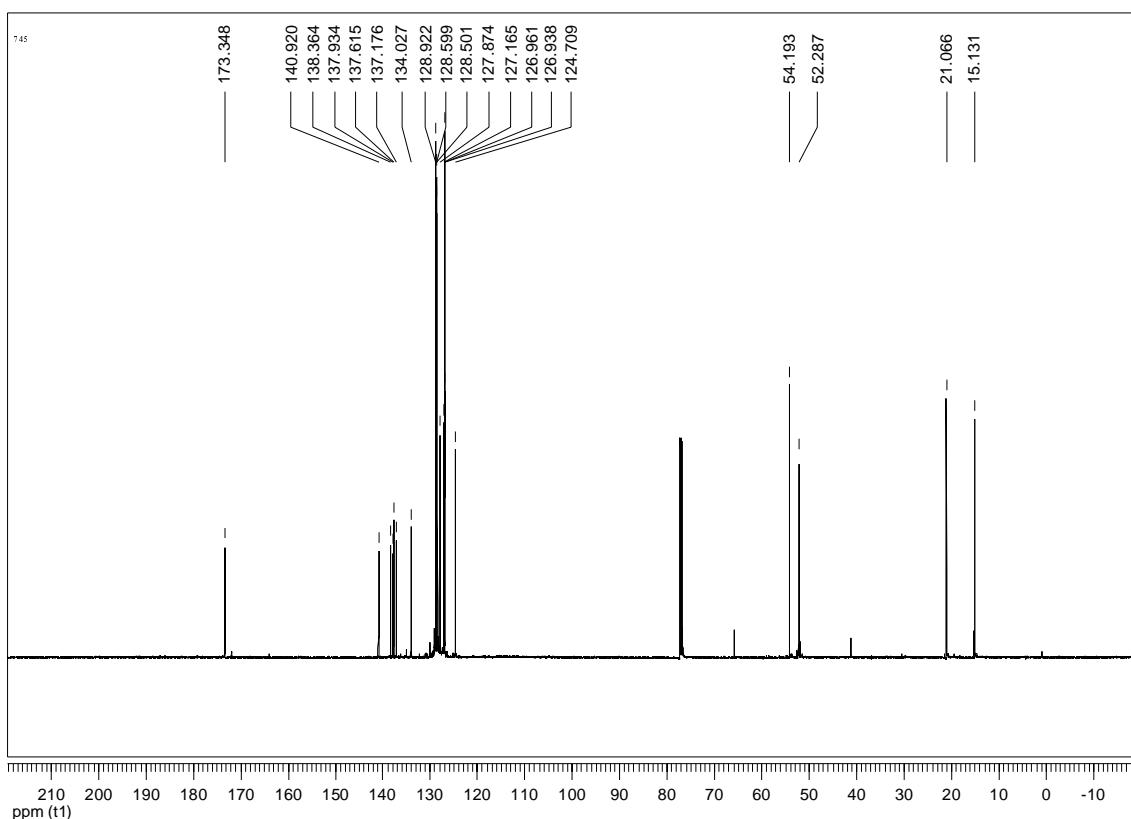
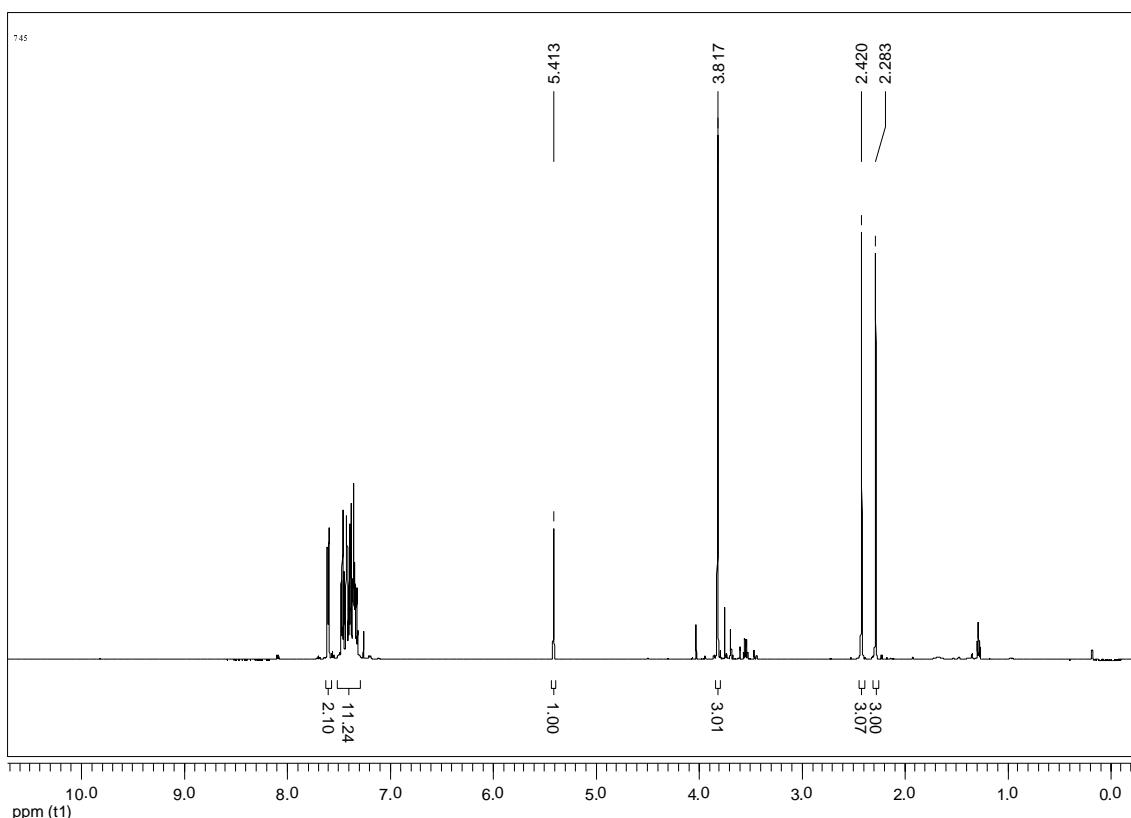
MS (ESI): *m/z* 498 (M+Na⁺).

HRMS (ESI): *m/z* calcd. for C₃₁H₂₅NO₄Na: 498.1682 (M+Na⁺), found 498.1661 (M+Na⁺).

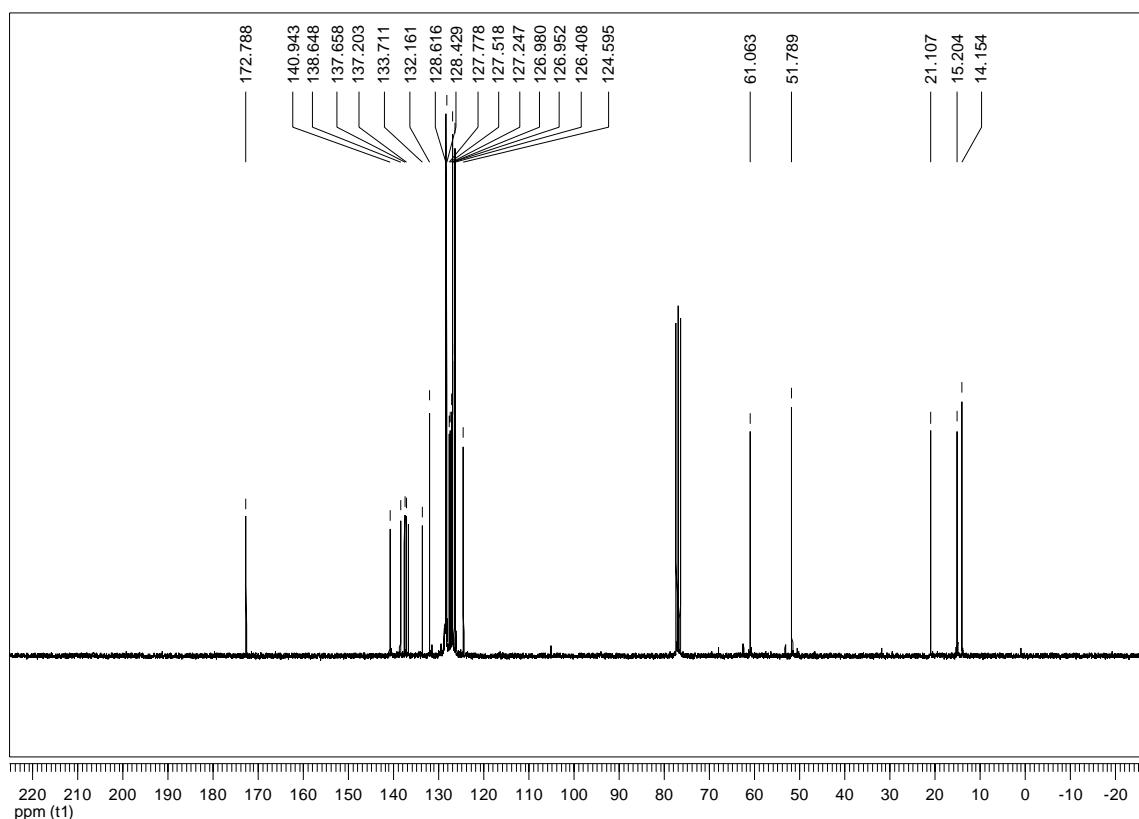
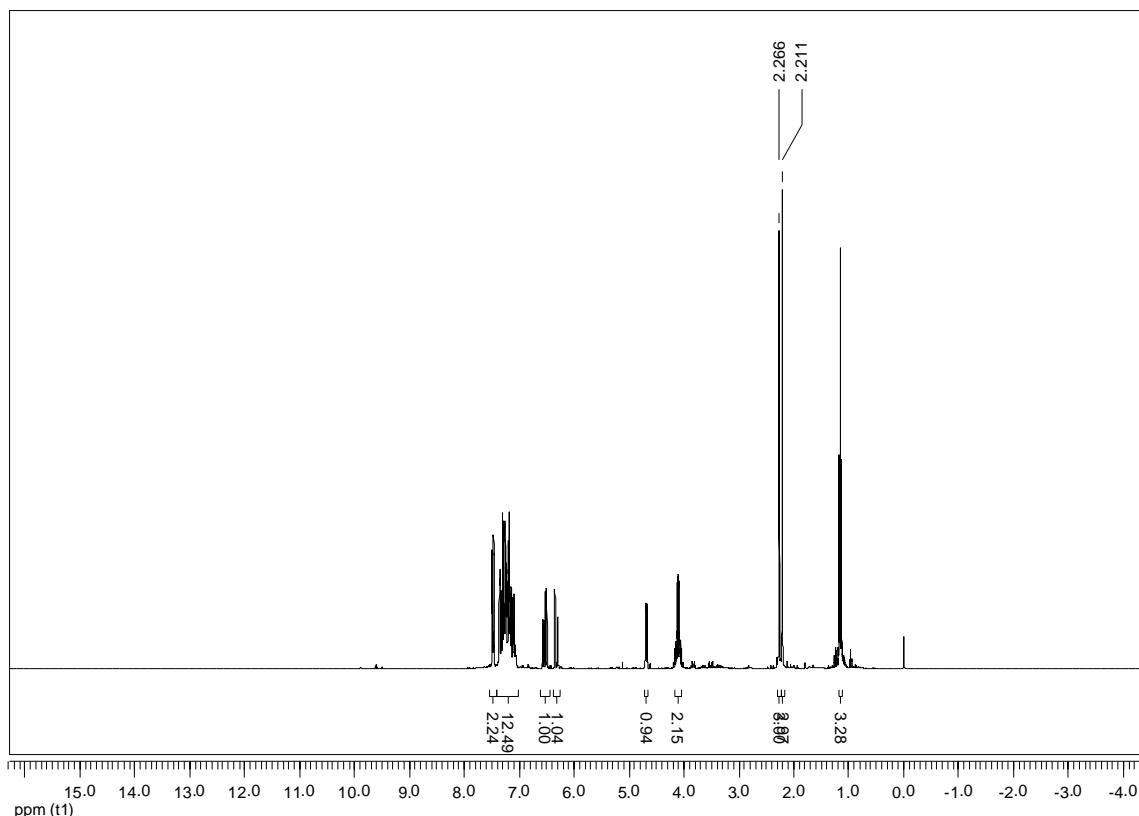
¹H- and ¹³C NMR of compound 5b



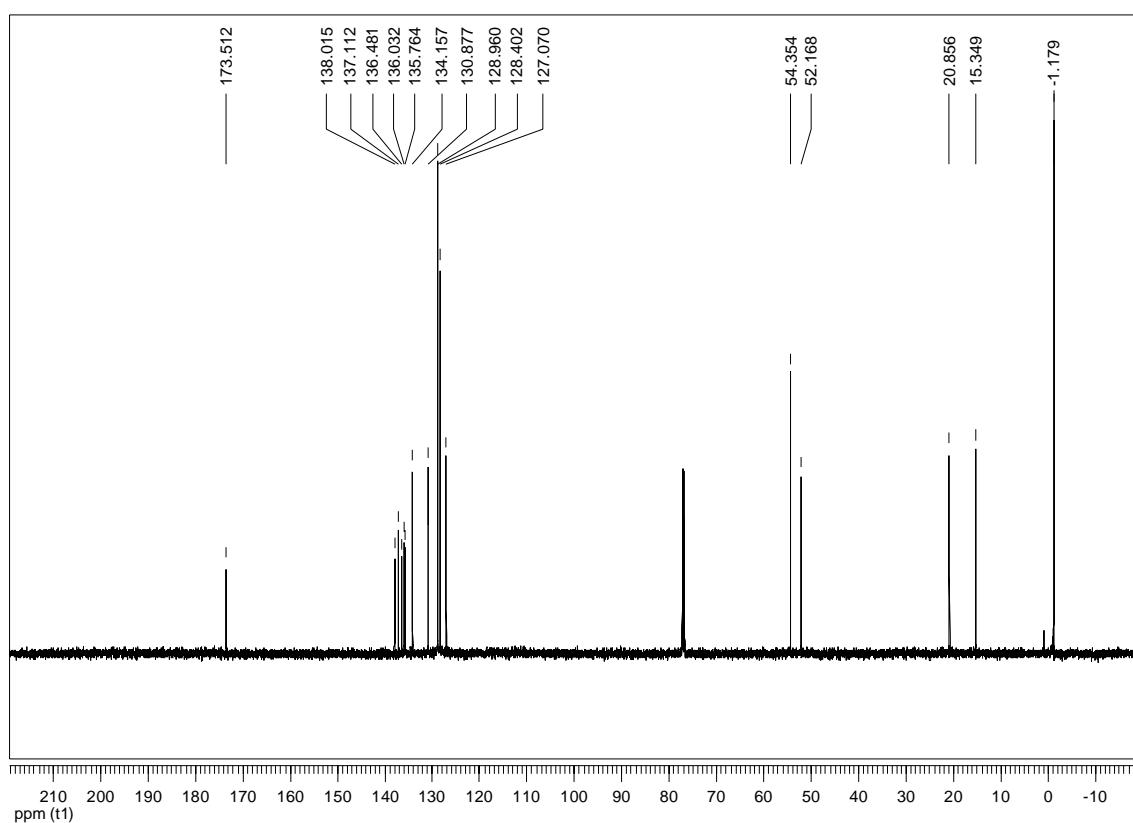
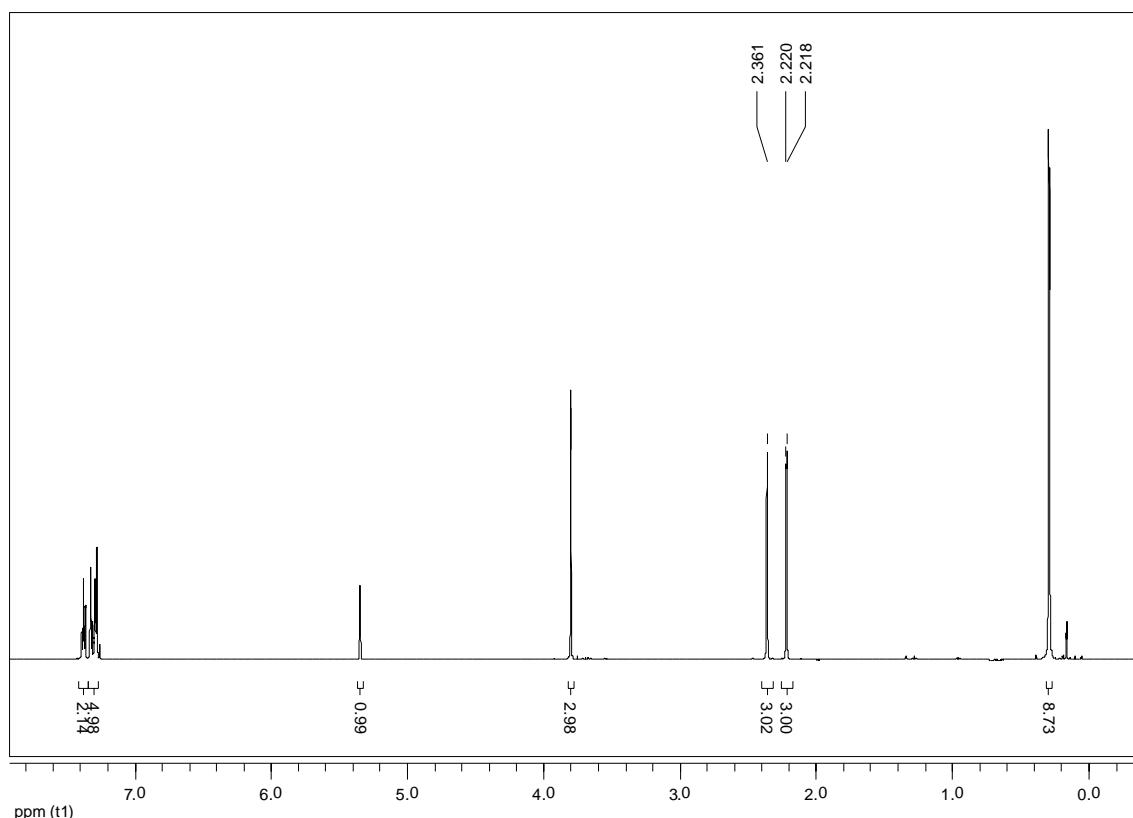
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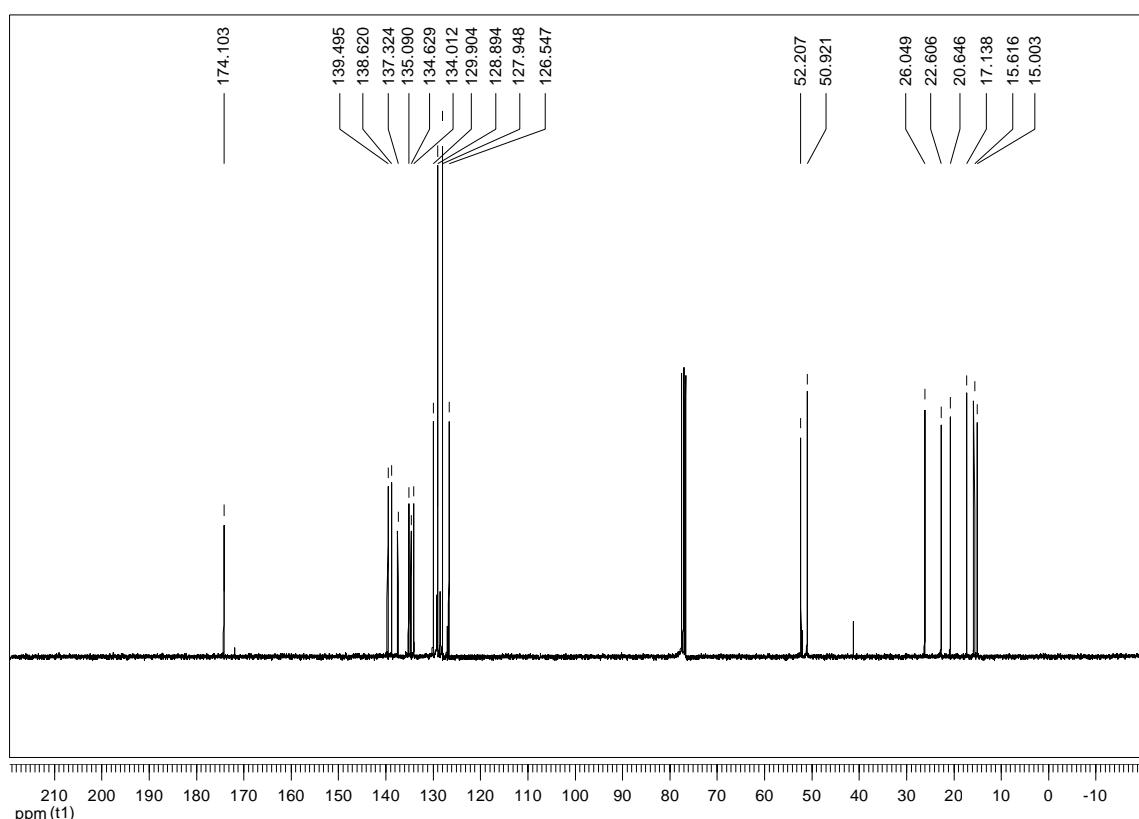
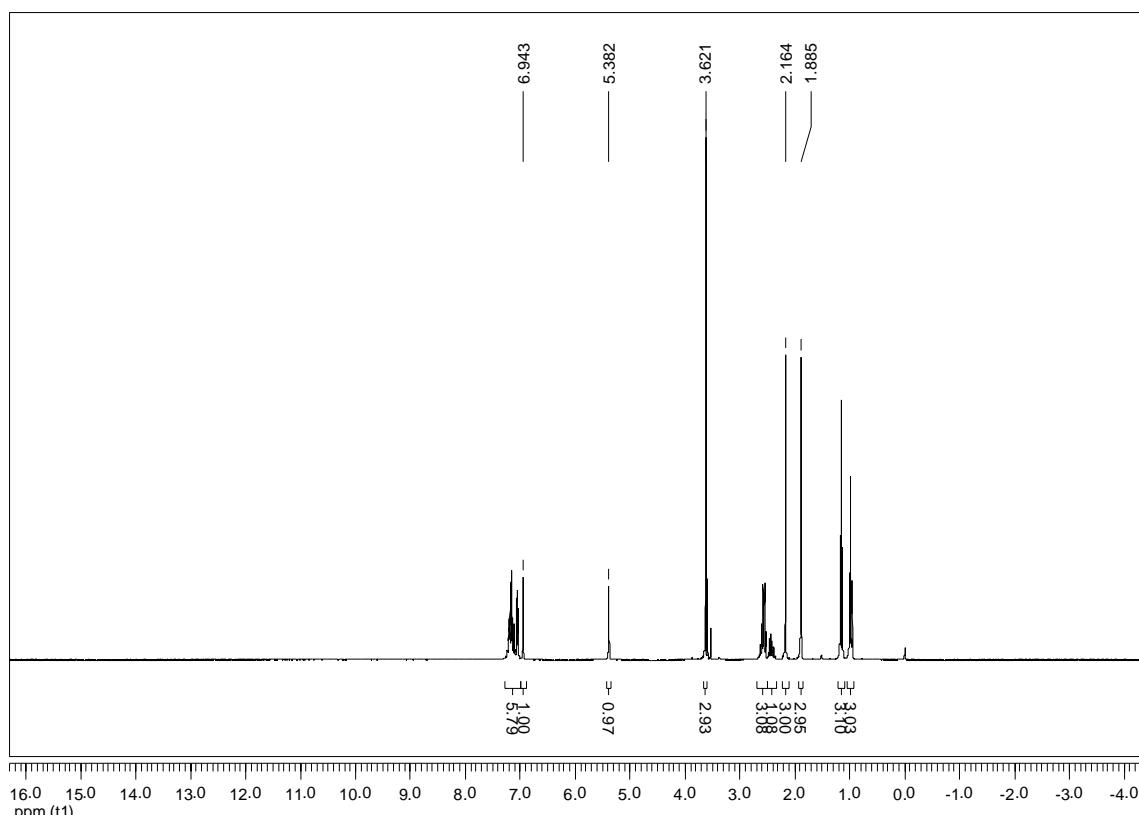
¹H- and ¹³C NMR of compound 9a



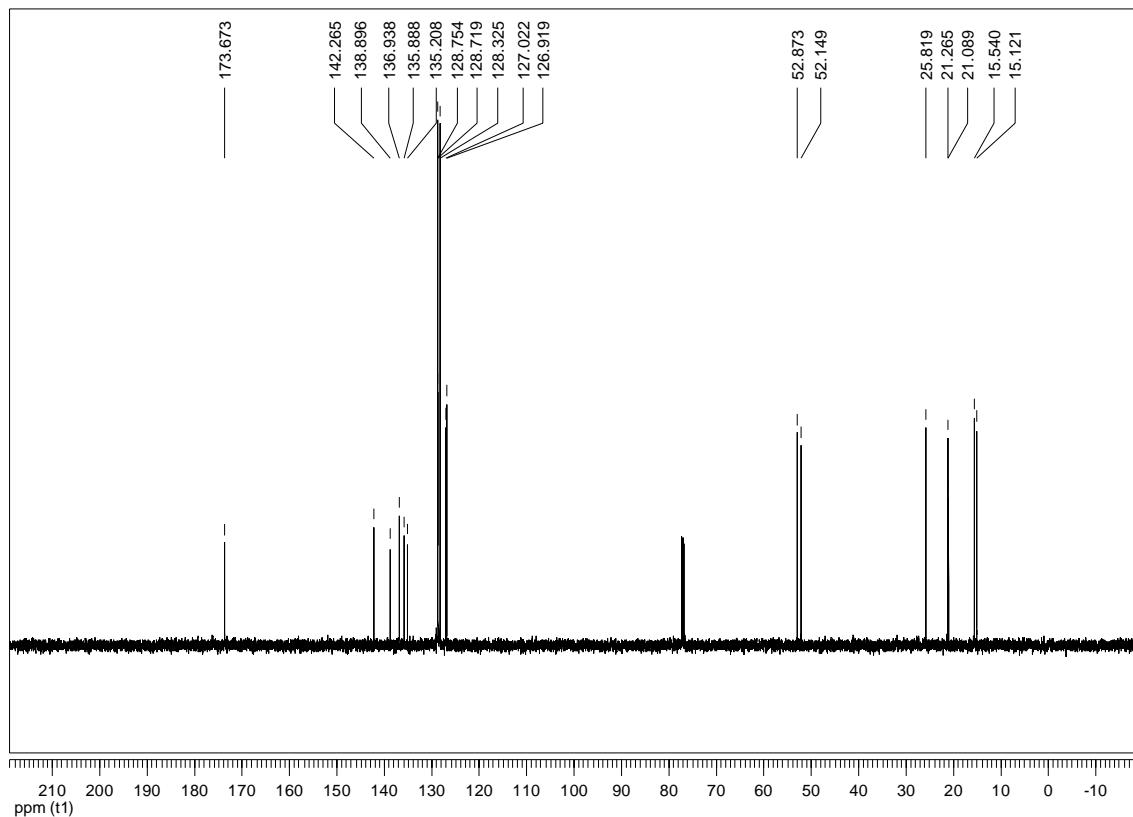
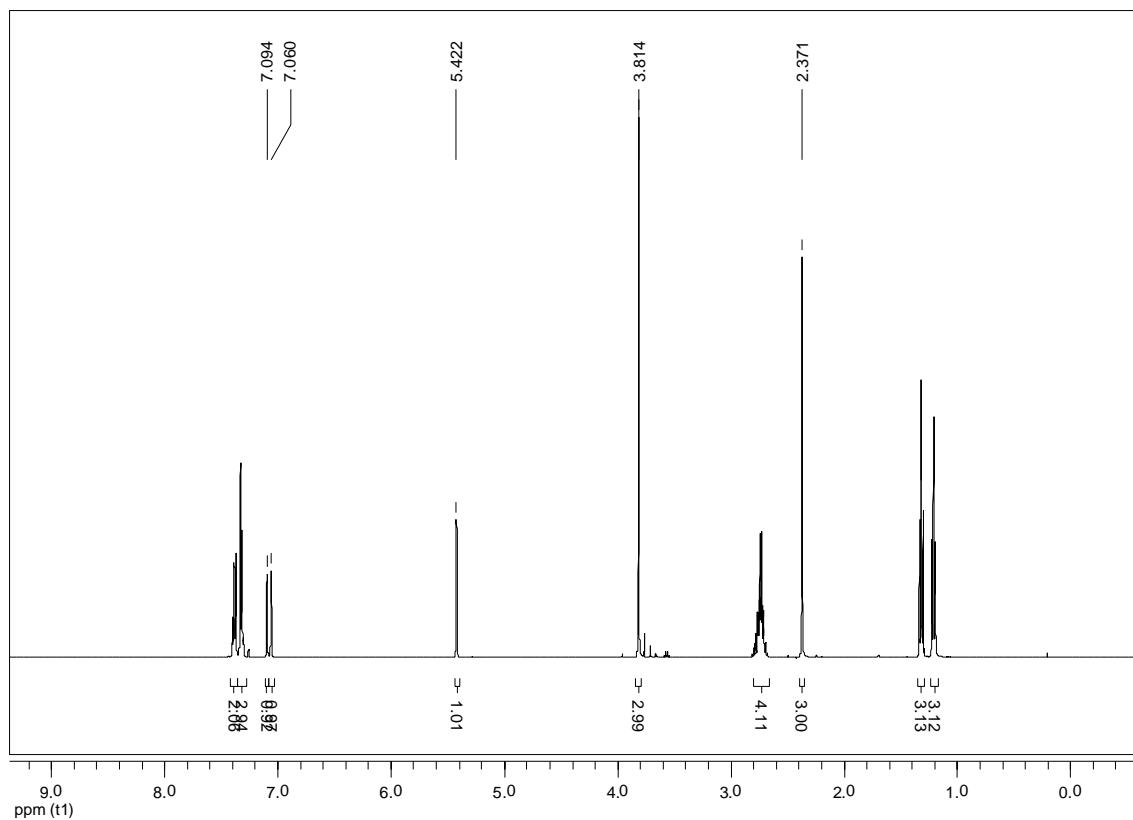
^1H - and ^{13}C NMR of compound 9b



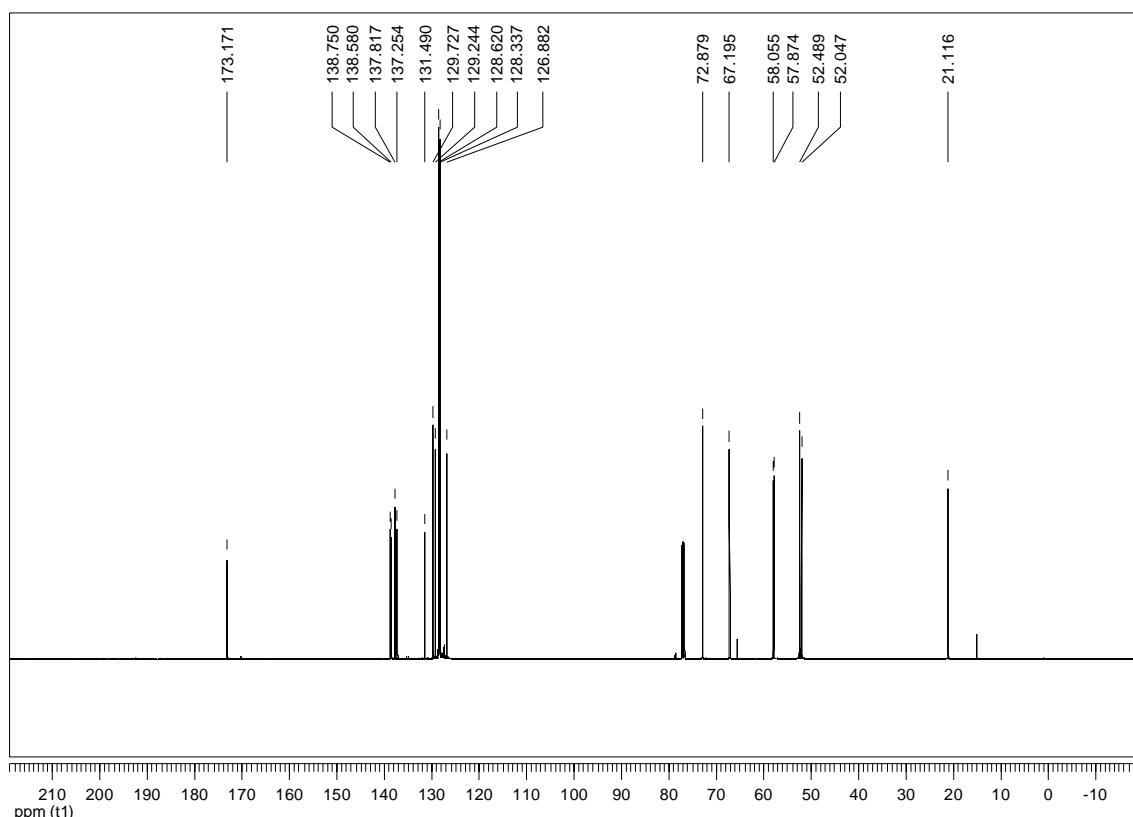
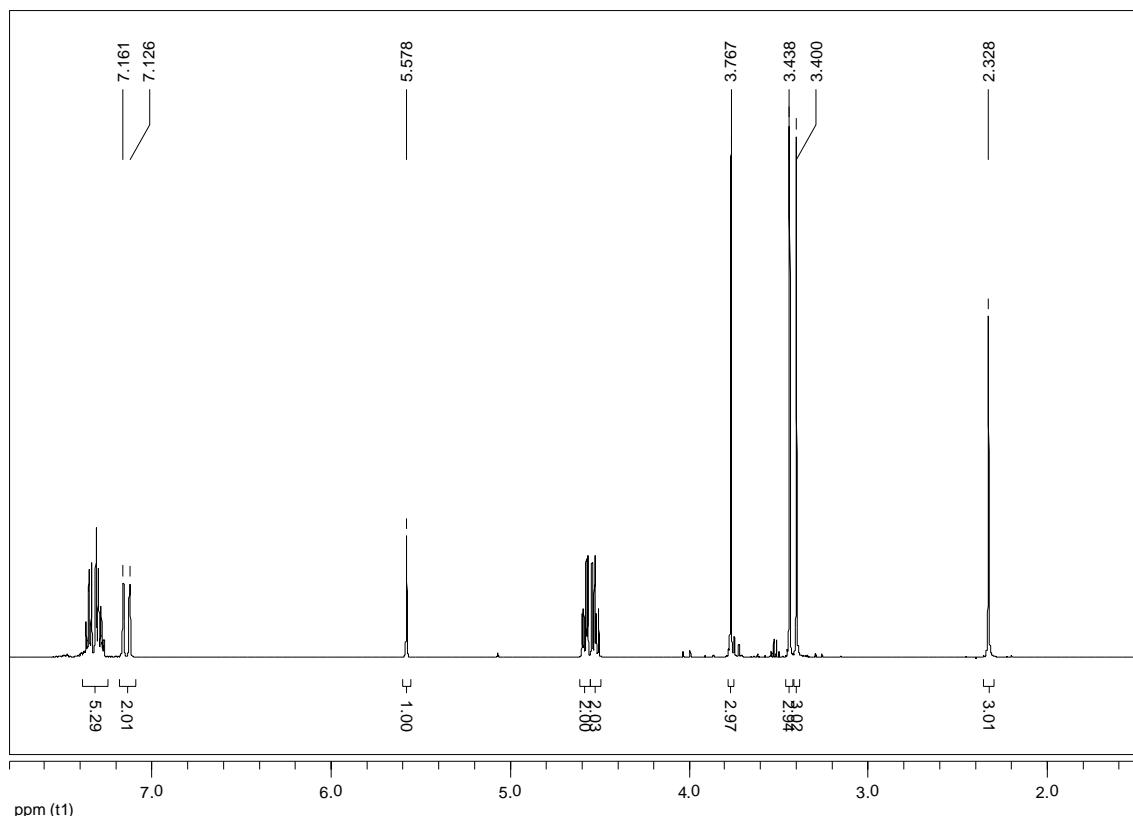
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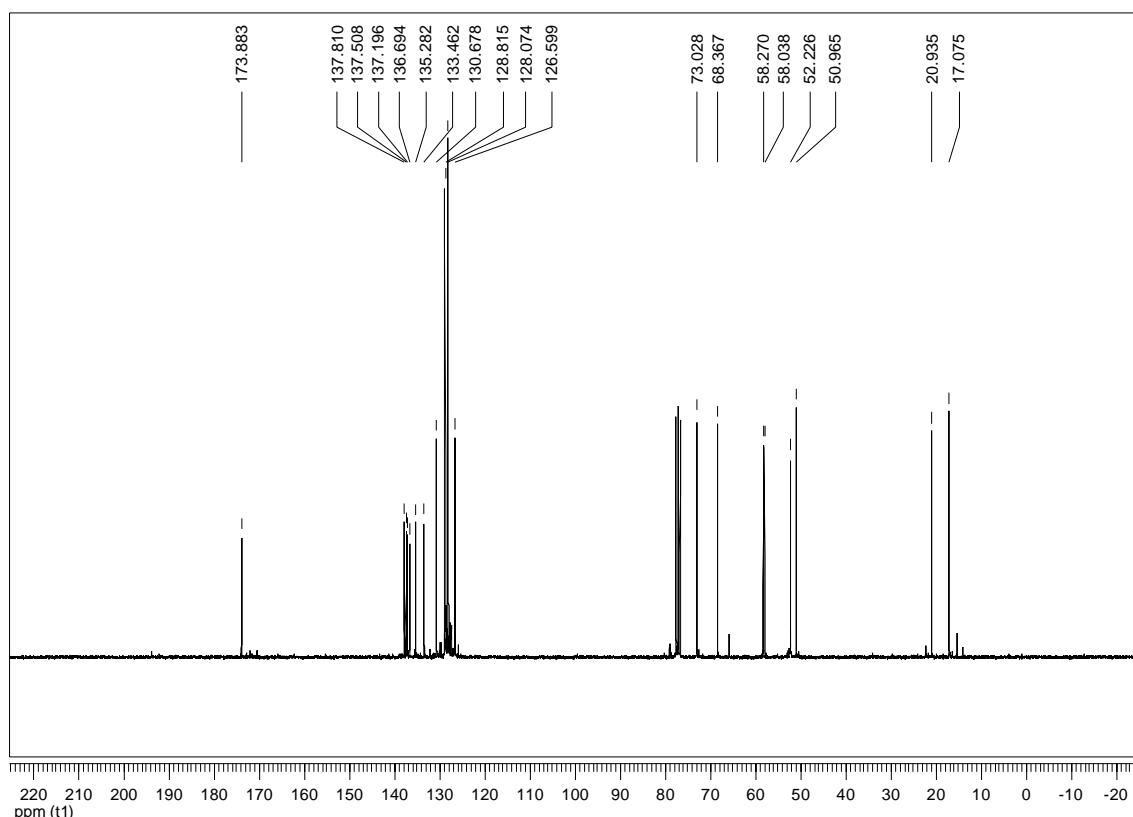
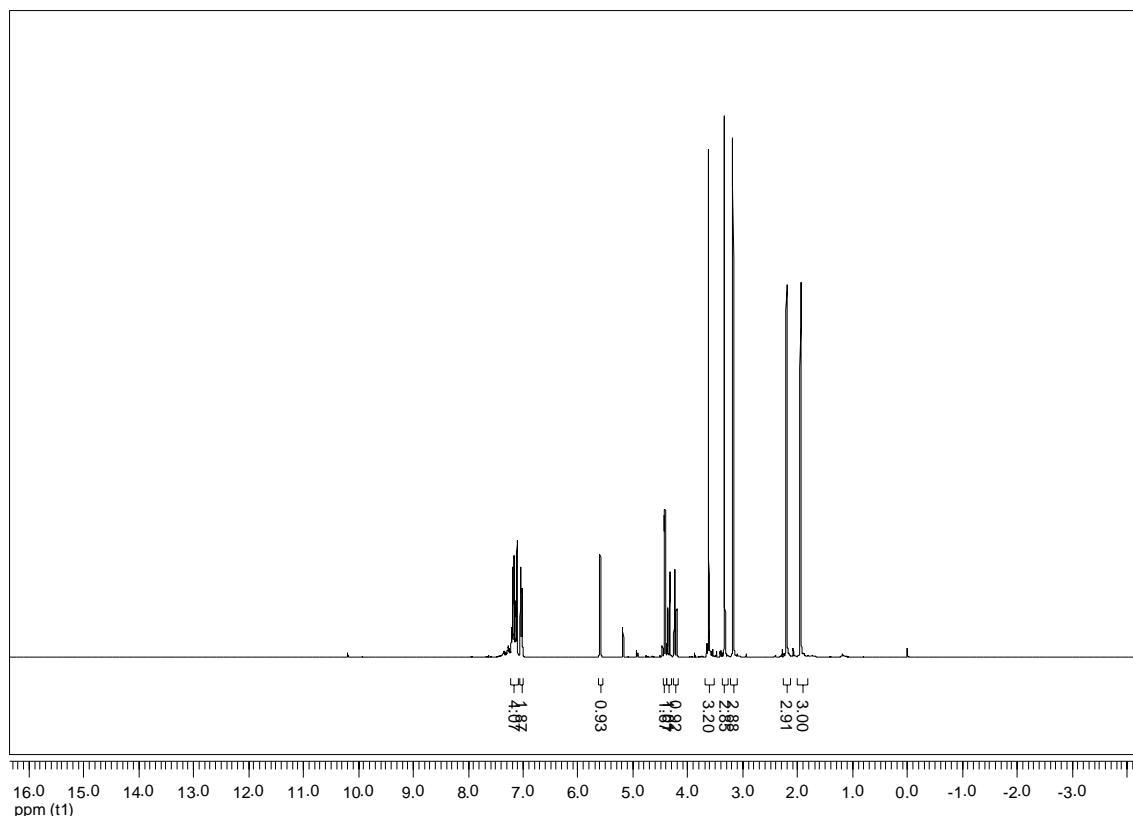
¹H- and ¹³C NMR of compound 9d



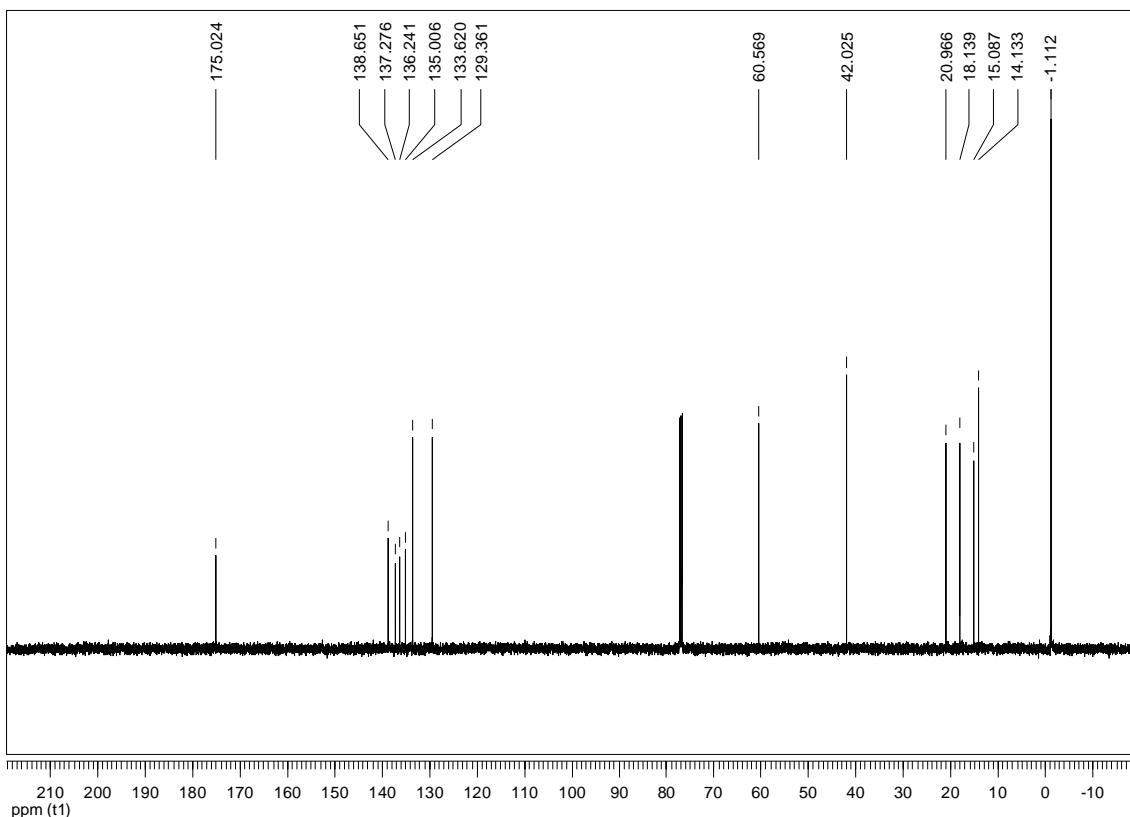
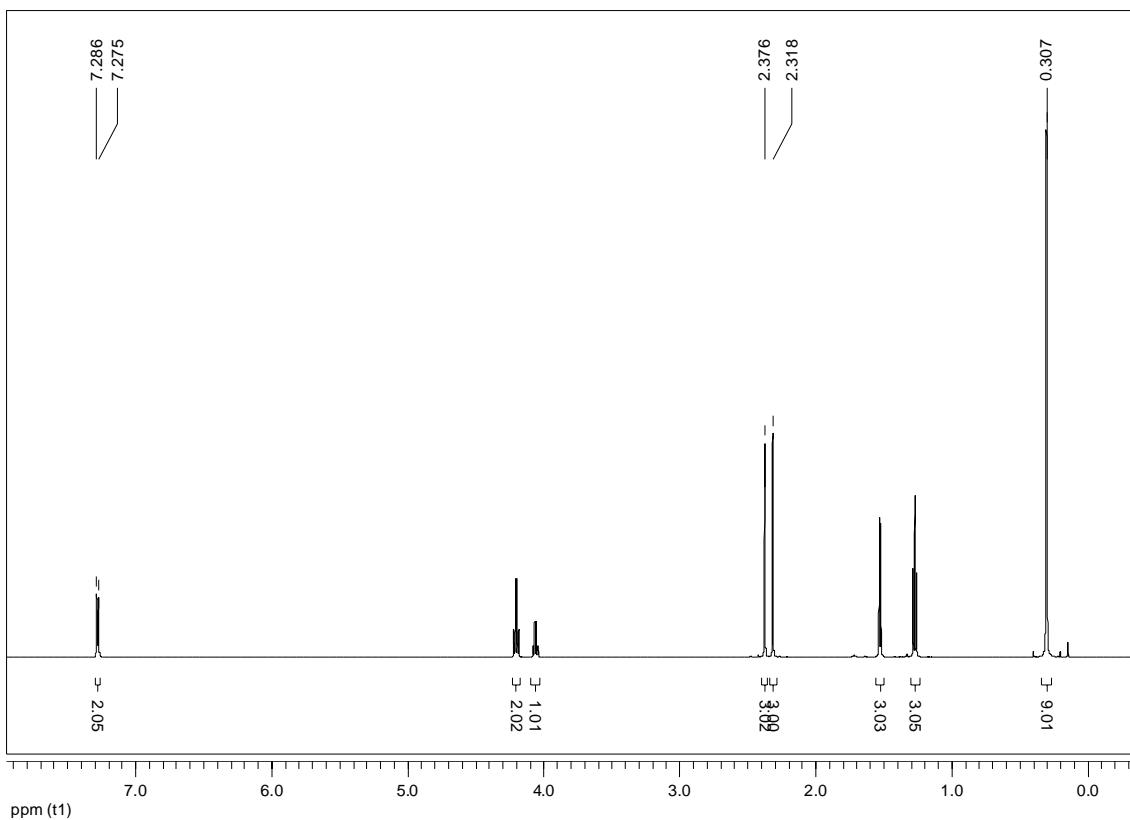
¹H- and ¹³C NMR of compound 9e



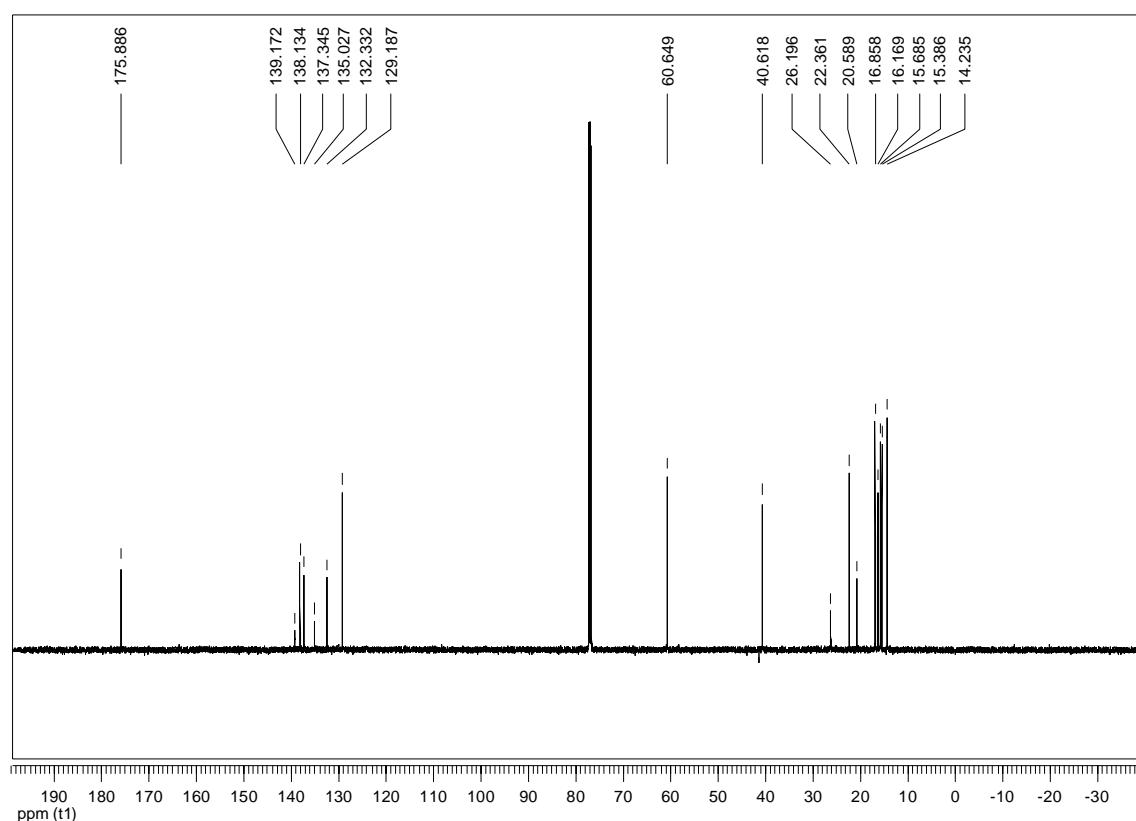
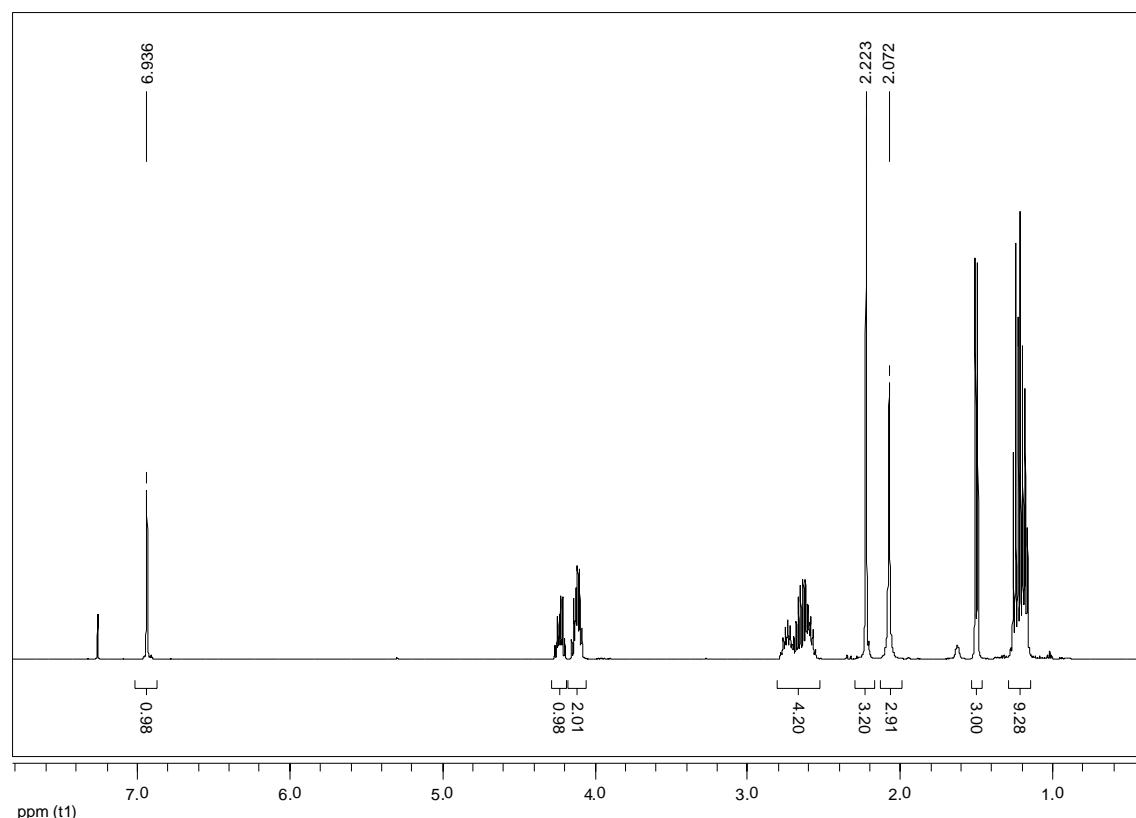
¹H- and ¹³C NMR of compound 9f



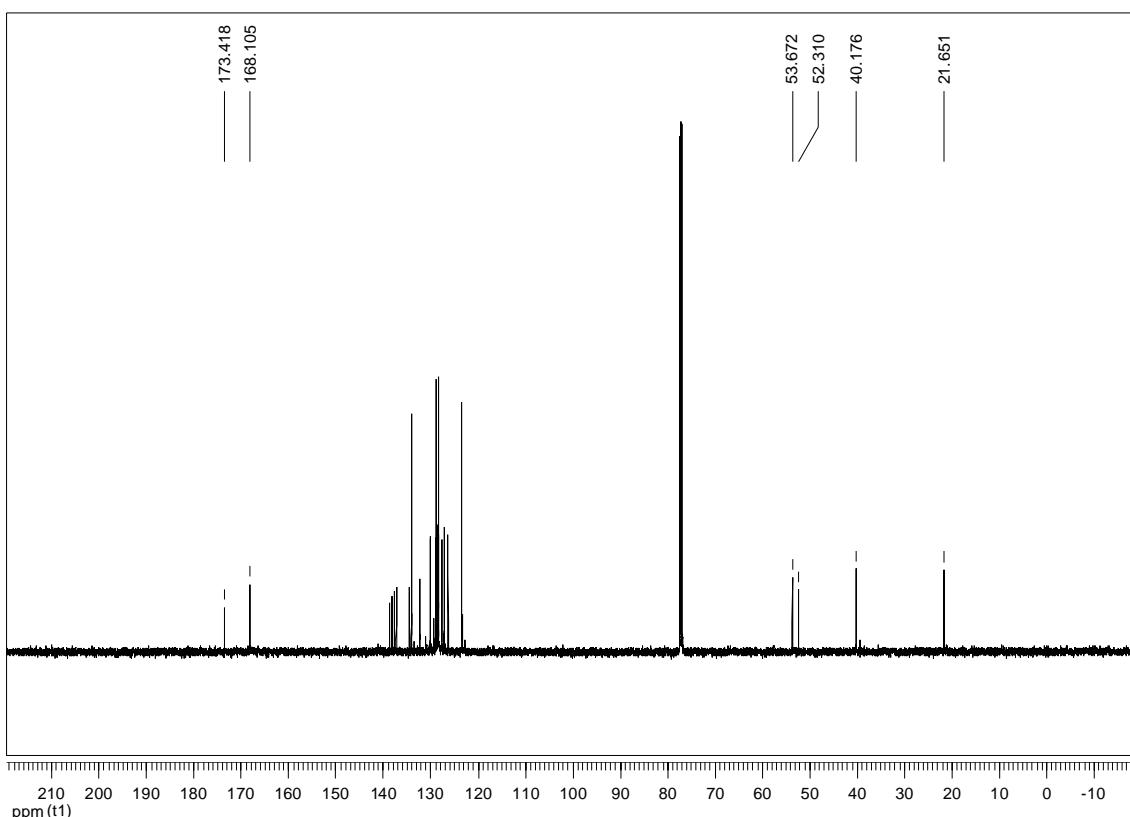
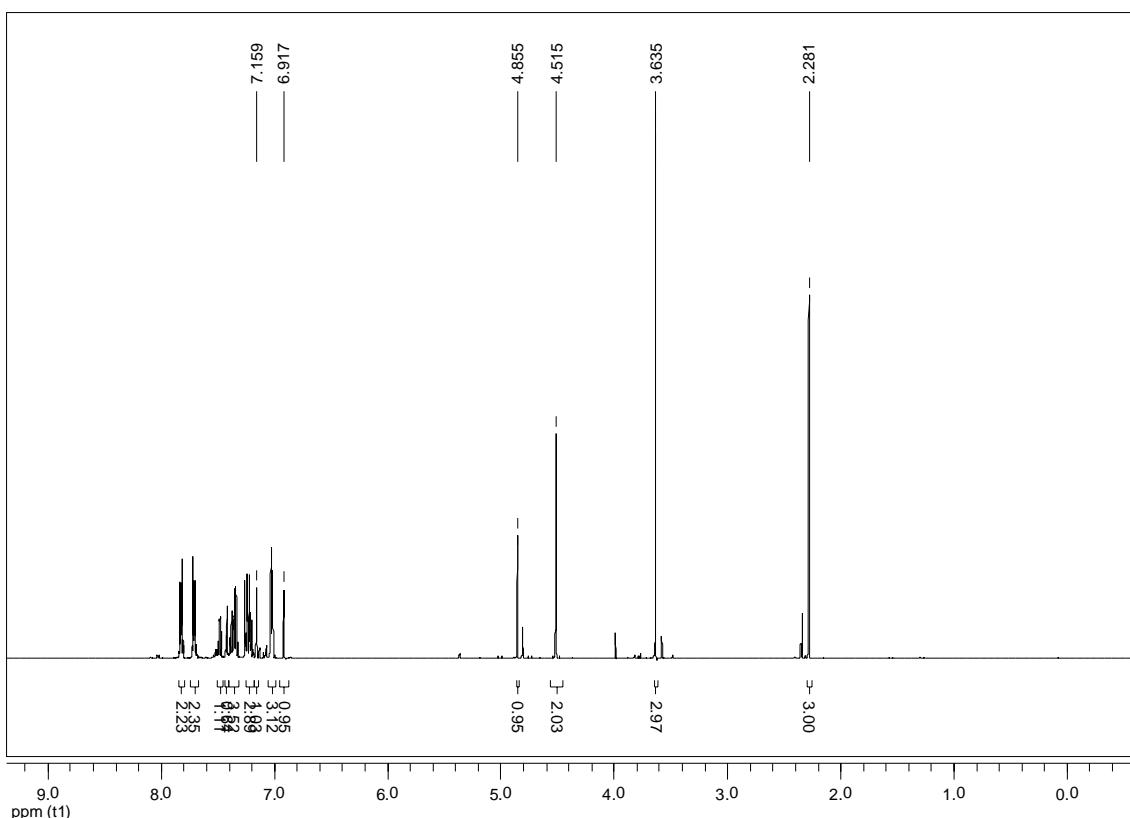
¹H- and ¹³C NMR of compound 9g



^1H - and ^{13}C NMR of compound 9h



¹H- and ¹³C NMR of compound 11a-d



HMBC of the mixture 11a-d

