Supporting Information

Calixarene-supported Pd-NHC complexes as efficient catalysts for scalable Suzuki-Miyaura cross-couplings

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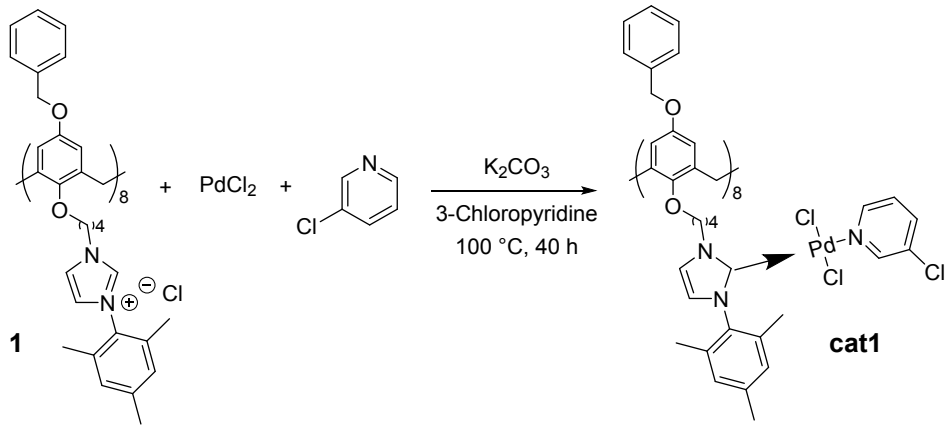
I. General remarks

All reactions were carried out under argon atmosphere and all glassware was flamed before use. Ethanol (EtOH) and ethyl acetate were purchased from ACROS Organics and Alfa Aesar. Potassium phosphate (K_3PO_4), palladium chloride, palladium bromide, pyridine, and 3-choloropyridine were purchased from Sigma Aldrich, Alfa Aesar, VWR, TCI and Strem. All commercially available reagents were used as received. Heterogeneous complexes **cat1** and **cat2** were prepared according to previously reported procedures.[1] The procedures for the preparation of these catalysts at a larger scale are described below. Homogeneous complex **cat3** was prepared from IMes•HCl (purchased from Sigma Aldrich) following a procedure previously reported.[2] The Suzuki-Miyaura reaction leading to 4-phenyltoluene can also be found in ref 1. The synthesis performed at the mole scale is detailed below. ^{1}H NMR and ^{13}C NMR spectra were recorded on either a Bruker DPX 250, Bruker 300 MHz, Bruker Avance 360 MHz, Bruker 400 (400 MHz) or Bruker DRX 400 (400 MHz) instrument and data are reported in ppm with the solvent signal as reference. The HR-MS analyses were performed with a Bruker MicroTOF-Q 2009 (direct injection QTOF) or with an atmospheric pressure photoionisation source (APCI-MS) in positive mode associated with a tandem Bruker MicroTOF-Q II analyser. Gas chromatography (GC) analyses were performed on a Varian 430-GC gas chromatograph (VF-1-MS Agilent, 15mx025mmx0.25µm) or a Shimadzu GC 2010 plus (ZB-5-MS Pehnomenex, 15mx025mmx0.25µm), with in all cases the following temperature program: 60 °C (1 min) to 250 °C (10 °C/min). GC-MS analyses were performed on a DSQ (Thermo Scientific). ICP-MS analyses were performed by IRAMIS (CEA-Saclay).

[1] I. Abdellah, P. Kasongo, A. Labattut, R. Guillot, E. Schulz, C. Martini and V. Huc, *Dalton Trans.*, 2018, **47**, 13843-13848.

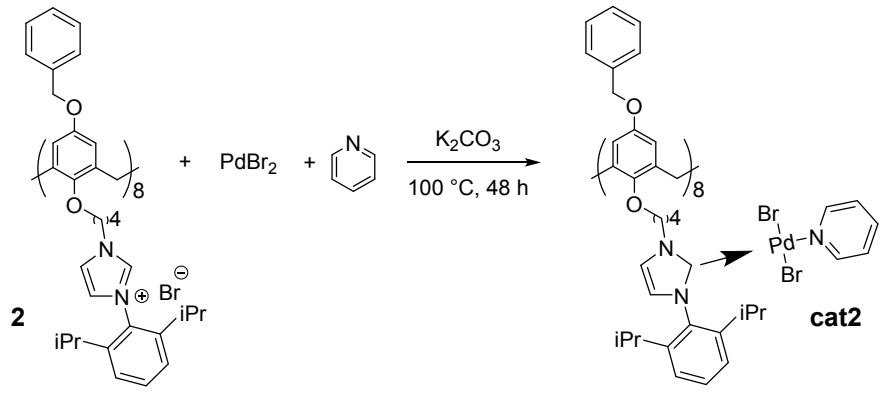
[2] C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson and M. G. Organ, *Chem. Eur. J.*, 2006, **12**, 4743-4748.

II. Procedure for large scale synthesis of cat1



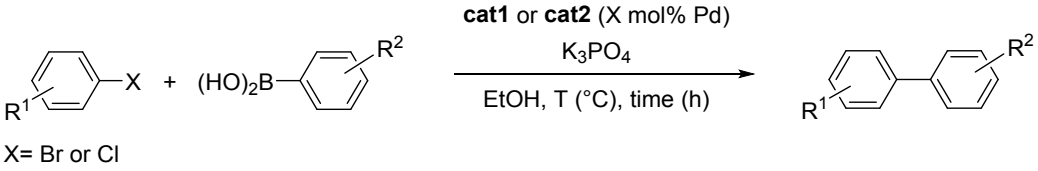
In an argon-flushed 250 mL 2-necked flask, equipped with a magnetic stirring bar, a reflux condenser and a septum, were introduced imidazolium **1** (9.0 g, 2.3 mmol, prepared following a procedure described in ref 1), potassium carbonate (dried under vacuum at 150 °C for 30 min, 9.0 g, 65.0 mmol) and palladium chloride (4.5 g, 25.4 mmol). The solids were dried under vacuum for 30 min. 3-Chloropyridine (75 mL) was then added under argon, and the mixture was degassed briefly before stirring at 100 °C. Evolution of the reaction was monitored by ^{1}H-NMR analysis of dried samples of the reaction mixture, and completion was reached after 40 hours. The reaction was then allowed to cool down, and DCM (180 mL) was added. The mixture was centrifuged and filtered on Dicalite^{TM} (washed with DCM). The solution was evaporated and the residue was solubilized in DCM (50 mL), and then poured slowly in 400 mL of Et_2O under vigorous stirring. The precipitate formed was filtered and washed with Et_2O (2x200 mL). The beige solid was dried under vacuum for 4 hours, before the addition of EtOH (300 mL). The mixture was stirred 16 hours under argon. The solid was filtered, washed with AcOEt (2x200 mL), Et_2O (4x200 mL) and dried under vacuum for 48 hours, affording a clear-beige solid (6.89 g, yield= 50%) which purity was confirmed by ^{1}H-NMR analysis in d^6-DMSO (see ref 1 for the precise characterization).

III. Procedure for large scale synthesis of cat2



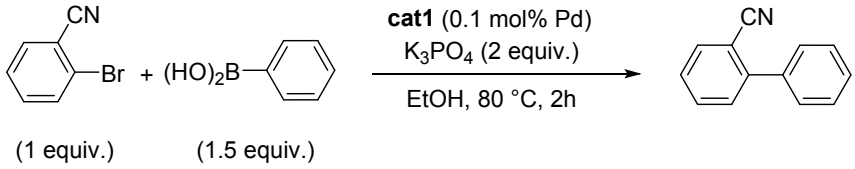
In an argon-flushed 250 mL 2-necked flask, equipped with a magnetic stirring bar, a reflux condenser and a septum were introduced imidazolium **2** (6.93 g, 1.505 mmol, prepared following a procedure described in ref 1), potassium carbonate (dried under vacuum at 150 °C for 30 min, 8.32 g, 60.2 mmol) and palladium bromide (3.45 g, 12.95 mmol). The solids were dried under vacuum for 30 min. Pyridine (70 mL) was then added under argon, and the mixture was degassed briefly before stirring at 100 °C. Evolution of the reaction was monitored by ^{1}H-NMR analysis of dried samples of the reaction mixture, and completion was reached after 48 hours. The reaction was then allowed to cool down, and DCM (180 mL) was added. The mixture was centrifuged and filtered on Dicalite™ (washed with DCM). The solution was evaporated and the residue was solubilized in DCM (50 mL), and then poured slowly in 400 mL of Et_2O under vigorous stirring. The precipitate formed was filtered and washed with Et_2O (2x200 mL). The beige solid was dried under vacuum for 4 hours, before the addition of EtOH (300 mL). The mixture was stirred 16 hours under argon. The solid was filtered, washed with Et_2O (4x200 mL) and dried under vacuum for 48 hours, affording a clear-beige solid (7.34 g, yield= 73%) which purity was confirmed by ^{1}H-NMR analysis in d^6-DMSO (see ref 1 for the precise characterization).

IV. General procedure for the catalytic Suzuki-Miyaura couplings



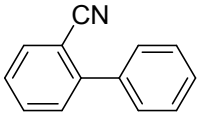
A 10 mL Schlenk-tube equipped with a magnetic stirring bar and a septum was charged with the aryl halide derivative (1 mmol, if solid), the boronic acid (1.5 mmol), K_3PO_4 (2 mmol) and the catalyst (x mol% Pd). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 2 mL) and the aryl halide derivative (1 mmol, if liquid) were then added under argon. The flask was flushed with three brief vacuum/argon cycles. The reaction mixture was subsequently stirred at 27 °C or 80 °C for two (or more) hours. The heterogeneous solution was then allowed to cool down to room temperature, filtered on a Whatman® grade 5 filter (rinsed with EtOH) and the filtrate was evaporated under reduced pressure. The residue was poured into water (20 mL) and extracted with DCM (3x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel, to afford the expected biaryl derivatives as pure products.

V. Procedure for the quarter-mole scale synthesis of [1,1'-biphenyl]-2-carbonitrile



An argon-flushed 2 L 3-necked flask equipped with a magnetic stirring bar, a reflux condenser and a septum was charged with 2-bromobenzonitrile (45.5 g, 0.25 mol), phenylboronic acid (45.7 g, 0.375 mol), K_3PO_4 (106.1 g, 0.5 mol) and **cat1** (186 mg, 0.1 mol% Pd). The mixture was dried under vacuum for 10 minutes, and EtOH (anhydrous, 500 mL) was then added under argon. The flask was flushed with three vacuum/argon cycles, and the reaction mixture was stirred at 80 °C for two hours, and then allowed to cool to room temperature. The heterogeneous mixture was filtered on a sintered glass filter (porosity 3) and washed with EtOH (2x60 mL). The filtrate was transferred to a 1 L graduated measuring cylinder, and volume was completed with EtOH to reach 700 mL precisely. This homogeneous solution was then divided into 7 fractions of 100 mL each ($C_{product}$ = 0.37 mol/L), and 6 of them were kept into dark glass bottles until further use for leaching tests (see **part VIII**, page **S10** of this Supporting Information for more details).

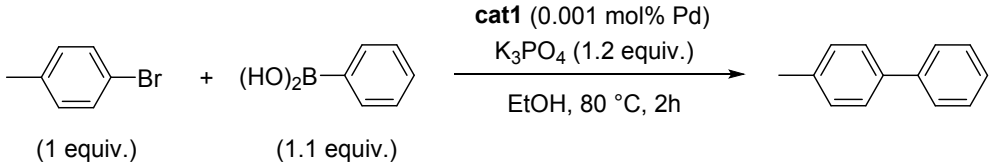
One of these fractions was used to determine conversion and yield. This 100 mL solution was concentrated under reduced pressure and dried under high vacuum, leading to 6.67 g of a crude white residue. A small sample of this residue was solubilised in AcOEt and analysed by GC, revealing a conversion of 95%, and a selectivity of nearly 100% (no traces of benzonitrile or bis-benzonitrile observed). A one-gram sample of this residue was then purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 97:3 > 95:5), to give 864 mg of the desired product as a white solid, which purity was confirmed by GC and ^{1}H-NMR. Thus, global weight of [1,1'-biphenyl]-2-carbonitrile formed during the reaction is calculated to be 40.3 g (yield = 90%).



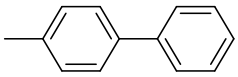
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (dd, J = 7.7 Hz and 1.4 Hz, 1H), 7.65 (ddd, J = 7.7 Hz, 7.7 Hz and 1.4 Hz, 1H), 7.60-7.41 (m, 7H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 145.4, 138.1, 133.7, 132.8, 130.0, 128.72 (2C), 128.69 (3C), 127.6, 118.7, 111.2.
HR-MS [ESI(+)]: m/z $[M+H]^+$ calculated for $[C_{13}H_{10}N]^+$: 180.0807, found: 180.0805.
The spectral data are in accordance with those reported in the literature.[3]

[3] Q. Yang, S. Ma, J. Li, F. Xiao and H. Xiong, *Chem. Commun.*, 2006, 2495-2497.

VI. Procedure for the mole scale synthesis of 4-phenyltoluene



An argon-flushed 2 L 3-necked flask equipped with a magnetic stirring bar, a reflux condenser and a septum was charged with 4-bromotoluene (171 g, 1 mol), phenylboronic acid (137 g, 1.1 mol), K_3PO_4 (263 g, 1.2 mol) and **cat1** (7.4 mg, 0.001 mol% Pd). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 500 mL) was then added under argon. The flask was flushed with three vacuum/argon cycles. The reaction mixture was stirred at 80 °C for two hours, and then allowed to cool to room temperature. The heterogeneous mixture was then filtered and washed with EtOH (2x500 mL) and the solution was evaporated under reduced pressure. The residue was washed with Et_2O (1 L), filtered and concentrated under reduced pressure, to give 169.2 g of a crude product. Analysis by ^{1}H-NMR, GC and GC-MS revealed that this crude material contains mainly the expected product, along with 5-10% of bromotoluene and traces of phenylboronic acid. Purification was performed on a 10 g sample of this crude material. First, 4-bromotoluene was quickly distilled off (oil bath at 100 °C/10 mmHg), leading to a bromotoluene-free crude sample. Flash column chromatography on silica gel (petroleum ether/EtOAc = 9:1) then afforded 7.65 g of 4-phenyltoluene as a white solid, which purity was confirmed by GC and ^{1}H-NMR. Thus, global weight of 4-phenyltoluene contained in the crude material is calculated to be 129.5 g (yield = 77%).



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74-7.67 (m, 2H), 7.62 (d, J = 8.2 Hz, 2H), 7.58-7.49 (m, 2H), 7.48-7.40 (m, 1H), 7.36 (d, J = 8.2 Hz, 2H), 2.51 (s, 3H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 141.2, 138.4, 137.0, 129.6 (2C), 128.8 (2C), 127.0 (5C), 21.1.
The spectral data are in accordance with those reported in the literature.[4]

VII. Procedure for the recycling of cat1

First test :

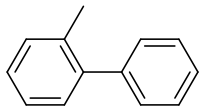
A 10 mL Schlenk-tube equipped with a magnetic stirring bar and a septum was charged with 4-bromotoluene (171 mg, 1 mmol), phenylboronic acid (187 mg, 1.5 mmol), K_3PO_4 (438 mg, 2 mmol) and **cat1** (0.5 mol% Pd). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 2 mL) was then added under argon. The flask was flushed with three brief vacuum/argon cycles. The reaction mixture was subsequently stirred at 27 °C for two hours. Under argon atmosphere, an aliquot was taken from the crude, diluted with AcOEt and full conversion was verified by gas chromatography. Same amount of reagents (4-bromotoluene (171 mg, 1 mmol), phenylboronic acid (187 mg, 1.5 mmol), K_3PO_4 (438 mg, 2 mmol)) were subsequently added to the crude containing Schlenk-tube under argon and the reaction mixture was again stirred at 27 °C for two hours. Complete conversion into 4-phenyl-toluene was proven again after taking a sample, diluting it and analyzing it under the same GC conditions.

Second test :

[4] R. Bandari, T. Höche, A. Prager, K. Dirnberger and M. R. Buchmeiser, *Chem. Eur. J.*, 2010, **16**, 4650-4658.

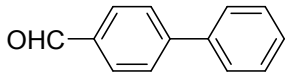
A 20 mL Schlenk-tube equipped with a magnetic stirring bar and a septum was charged with 4-bromotoluene (855 mg, 5 mmol), phenylboronic acid (915 mg, 7.5 mmol), K_3PO_4 (2.1 g, 10 mmol) and **cat1** (0.5 mol% Pd). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 10 mL) was then added under argon. The flask was flushed with three brief vacuum/argon cycles. The reaction mixture was subsequently stirred at 27 °C for two hours. Under argon atmosphere, an aliquot was taken from the crude, diluted with AcOEt and full conversion was verified by gas chromatography. The crude was then filtered through a Dicalite™ pad, which was washed with ethanol (3 x 40 mL). The catalyst was recovered as slightly brown powder from DCM solutions used to further wash the pad (3 x 40 mL) and their subsequent evaporation. After drying under vacuum, the Schlenk-tube containing the recovered **cat1** was again charged with 4-bromotoluene (855 mg, 5 mmol), phenylboronic acid (915 mg, 7.5 mmol), K_3PO_4 (2.1 g, 10 mmol). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 10 mL) was then added under argon. The flask was flushed with three brief vacuum/argon cycles. The reaction mixture was subsequently stirred at 27 °C for two hours. Complete conversion into 4-phenyl-toluene was proven again after taking a sample, diluting it with AcOEt and analyzing it under the same GC conditions.

VIII. Description of Suzuki-Miyaura coupling products



2-methyl-1,1'-biphenyl: colorless oil, 96 % (162 mg, 0.97 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/DCM = 96:4), obtained from 1-bromo-2-methylbenzene (1 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat1** (0.5 mol % Pd) in EtOH (0.5 M) at 80 °C.

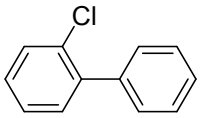
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.51 (m, 2H), 7.51-7.44 (m, 3H), 7.43-7.35 (m, 4H), 2.43 (s, 3H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 141.9, 141.9, 135.3, 130.3, 129.6, 129.2, 128.0, 127.2, 126.7, 125.7, 20.5.
The spectral data are in accordance with those reported in the literature.[5]



[1,1'-biphenyl]-4-carboxaldehyde: white solid, 88 % (161 mg, 0.88 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/EtOAc = 9:1), obtained from 4-bromobenzaldehyde (1 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat1** (0.05 mol % Pd) in EtOH (0.5 M) at 80 °C.

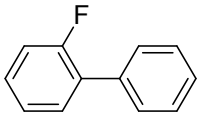
^{1}H NMR (300 MHz, $CDCl_3$): δ 10.07 (s, 1H), 7.96 (dt, J = 8.3 Hz and 1.7 Hz, 2H), 7.77 (dt, J = 8.3 Hz and 1.7 Hz, 2H), 7.68-7.61 (m, 2H), 7.53-7.37 (m, 3H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 191.8, 147.1, 139.6, 135.2, 130.2, 129.0, 128.5, 127.6, 127.3.
HR-MS [ESI(+)]: m/z $[M+H]^+$ calculated for $[C_{13}H_{11}O]^+$: 183.0804, found: 183.0800.
The spectral data are in accordance with those reported in the literature.[6]

[5] P. D. Stevens, J. Fan, H. M. R. Gardimalla, M. Yen and Y. Gao, *Org. Lett.*, 2005, **7**, 2085-2088.
[6] S. Santra, P. K. Hota, R. Bhattacharyya, P. Bera, P. Ghosh and S. K. Mandal, *ACS. Catal.,* 2013, **3**, 2776-2789.



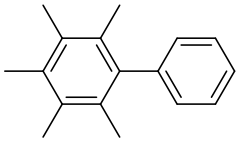
2-chloro-1,1'-biphenyl: colorless oil, 91 % (172 mg, 0.91 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/DCM = 98:2 > 95:5), obtained from 1-bromo-2-chlorobenzene (1 equiv.), phenylboronic acid (1.1 equiv.), K_3PO_4 (2 equiv.) and **cat2** (0.5 mol % Pd) in EtOH (0.5 M) at 80 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.43 (m, 5H), 7.43-7.32 (m, 3H), 7.32-7.26 (m, 1H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 140.6, 139.5, 132.6, 131.5, 130.0, 129.5 (2C), 128.6, 128.1 (2C), 127.7, 126.9.
HR-MS [APCI(+)]: *m/z* $[M]^+$ calculated for $[C_{12}H_9Cl]^+$: 188.0387, found: 188.0382.
The spectral data are in accordance with those reported in the literature.[7]



2-fluoro-1,1'-biphenyl: white solid, 62 % (213 mg, 1.23 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/EtOAc = 95:5), obtained from 1-bromo-2-fluorobenzene (1 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat2** (2 mol % Pd) in EtOH (0.5 M) at 80 °C.

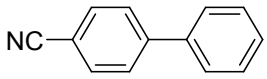
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.56 (m, 2H), 7.50-7.30 (m, 5H), 7.25-7.17 (m, 2H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 159.8 (d, J = 248.2 Hz), 135.9, 130.9 (d, J = 3.2 Hz), 129.2, 129.1 (2C), 129.0, 128.6 (2C), 127.8, 124.5 (d, J = 3.3 Hz), 116.2 (d, J = 22.4 Hz).
The spectral data are in accordance with those reported in the literature.[8]



2,3,4,5,6-pentamethyl-1,1'-biphenyl: white solid, 58 % (130 mg, 0.58 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/Et_2O = 99.5:0.5), obtained from 1-bromo-2,3,4,5,6-pentamethylbenzene (1 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat2** (2 mol % Pd) in EtOH (0.5 M) at 80 °C.

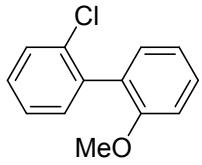
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.44 (m, 2H), 7.43-7.36 (m, 1H), 7.22-7.17 (m, 2H), 2.39 (s, 3H), 2.34 (s, 6H), 2.02 (s, 6H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 143.2, 140.0, 134.1, 132.5 (2C), 131.8 (2C), 129.7 (2C), 128.4 (2C), 126.4, 18.5 (2C), 17.0, 16.8 (2C).
HR-MS [APCI(+)]: *m/z* $[M+H]^+$ calculated for $[C_{17}H_{21}]^+$: 225.1638, found: 225.1622.
The spectral data are in accordance with those reported in the literature.[9]

[7] G. Dilauro, S. Mata García, D. Tagarelli, P. Vitale, F. M. Perna and V. Capriati, *ChemSusChem*, 2018, **11**, 3495-3501.
[8] W. Liu, H. Cao, J. Xin, L. Jin and A. Lei, *Chem. Eur, J.*, 2011, **17**, 3588-3592.
[9] T. E. Storr and M. F. Greaney, *Org. Lett.*, 2013, **15**, 1410-1413.



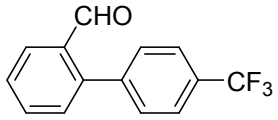
[1,1'-biphenyl]-4-carbonitrile: white solid, 56 % (100 mg, 0.56 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/Et_2O = 90:10), obtained from 4-chlorobenzonitrile (1 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat2** (2 mol % Pd) in EtOH (0.5 M) at 80 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.63 (m, 4H), 7.63-7.54 (m, 2H), 7.54-7.38 (m, 3H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 145.6, 139.1, 132.6, 129.1, 128.7, 127.7, 127.2, 119.0, 110.9.
HR-MS [APCI(+)]: *m/z* $[M+H]^+$ calculated for $[C_{13}H_{10}N]^+$: 180.0808, found: 180.0799.
The spectral data are in accordance with those reported in the literature.[10]



2-chloro-2'-methoxy-1,1'-biphenyl: white solid, 38 % (83 mg, 0.38 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/DCM = 98:2 > 95:5), obtained from 1,2-dichlorobenzene (1 equiv.), (2-methoxyphenyl)boronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat2** (2 mol % Pd) in EtOH (0.5 M) at 80 °C.

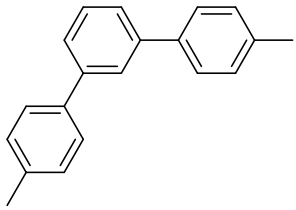
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.46 (m, 1H), 7.41 (ddd, J = 8.2 Hz, 7.4 Hz and 1.8 Hz, 1H), 7.36-7.28 (m, 3H), 7.23 (dd, J = 7.4 Hz and 1.8 Hz, 1H), 7.06 (ddd, J = 7.4 Hz, 7.4 Hz and 1.0 Hz, 1H), 7.04-6.99 (m, 1H), 3.81 (s, 3H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 156.9, 137.9, 134.0, 131.8, 131.1, 129.5, 129.4, 128.7, 128.6, 126.5, 120.5, 111.1, 55.7.
HR-MS [APCI(+)]: *m/z* $[M+H]^+$ calculated for $[C_{13}H_{12}ClO]^+$: 219.0571, found: 219.0561.
The spectral data are in accordance with those reported in the literature.[11]



4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxaldehyde: light yellow oil, 70 % (175 mg, 0.70 mmol) isolated yield, after purification by silica gel column chromatography (*n*-pentane/EtOAc = 9:1), obtained from 2-bromobenzaldehyde (1 equiv.), 4-(trifluoromethyl)phenyl boronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat1** (2 mol % Pd) in EtOH (0.5 M) at 80 °C.

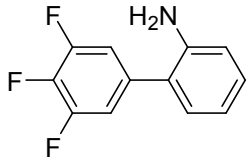
^{1}H NMR (250 MHz, $CDCl_3$): δ 9.96 (d, J = 0.8 Hz, 1H), 8.06 (dd, J = 7.5 Hz and 1.2 Hz, 1H), 7.79-7.70 (m, 2H), 7.67 (dd, J = 7.5 Hz and 1.2 Hz, 1H), 7.61-7.48 (m, 3H), 7.43 (dd, J = 8.0 Hz and 1.2 Hz, 1H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 191.7, 144.3, 141.7, 133.9, 133.8, 131.0, 130.8, 130.7, 130.5, 130.3, 129.9, 128.7, 128.5, 125.5, 125.5.
HRMS [ESI(+)]: *m/z* $[M+Na]^+$ calculated for $[C_{14}H_9F_3NaO]^+$: 273.0503, found 273.0489.
The spectral data are in accordance with those reported in the literature.[12]

[10] O. Grossman and D. Gelman, *Org. Lett.*, 2006, **8**, 1189-1191.
[11] E. K. Reeves, J. N. Humke and S. R. Neufeldt, *J. Org. Chem.*, 2019, **84**, 11799-11812.



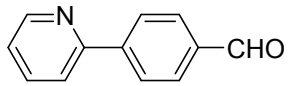
4,4''-dimethyl-1,1':3',1''-terphenyl: white solid, 98 % (253 mg, 0.98 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/EtOAc = 97:3), obtained from 1-bromo-4-methylbenzene (2.5 equiv.), 1,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene (1 equiv.), K_3PO_4 (3 equiv.) and **cat1** (0.5 mol % Pd) in EtOH (0.5 M) at 80 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80-7.75 (br.s, 1H), 7.58-7.45 (m, 3H), 7.55 (d, J = 8.2 Hz, 4H), 7.27 (d, J = 8.2 Hz, 4H), 2.41 (s, 6H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 141.7 (2C), 138.4 (2C), 137.1 (2C), 129.6 (4C), 129.2, 127.1 (4C), 125.8 (3C), 21.2 (2C).
HR-MS [ESI(+)]: m/z $[M+Na]^+$ calculated for $[C_{20}H_{18}Na]^+$: 281.1301, found: 281.1291.
The spectral data are in accordance with those reported in the literature.[13]



3',4',5'-trifluoro-[1,1'-biphenyl]-2-amine: white solid, 94 % (209 mg, 0.94 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/EtOAc/NEt_3 = 80:17:3), obtained from 1-bromo-3,4,5-trifluorobenzene (1 equiv.), 2-aminophenylboronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat1** (1 mol % Pd) in EtOH (0.5 M) at 80 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (ddd, J = 7.6 Hz, 7.6 Hz and 1.6 Hz, 1H), 7.15-7.03 (m, 3H), 6.83 (dd, J = 7.6 Hz and 7.6 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 3.87 (br.d, 2H).
^{13}C NMR (90 MHz, $CDCl_3$): δ 151.4 (ddd, J = 250.0 Hz, 9.8 Hz and 4.3 Hz, 2C), 143.4, 139.0 (dt, J = 250 Hz and 15.3 Hz), 135.7 (m), 130.2, 129.5, 124.5, 119.0, 116.1, 113.3 (m, 2C).
HR-MS [ESI(+)]: m/z $[M+H]^+$ calculated for $[C_{12}H_9NF_3]^+$: 224.0682, found: 224.0674.
The spectral data are in accordance with those reported in the literature.[14]



4-(pyridin-2-yl)benzaldehyde: slightly yellow solid, 51 % (93 mg, 0.51 mmol) isolated yield, after purification by silica gel column chromatography (petroleum ether/EtOAc = 80:20), obtained from 2-bromopyridine (1 equiv.), (4-formylphenyl)boronic acid (1.5 equiv.), K_3PO_4 (2 equiv.) and **cat1** (2 mol % Pd) in *n*BuOH (0.25 M) at 100 °C.

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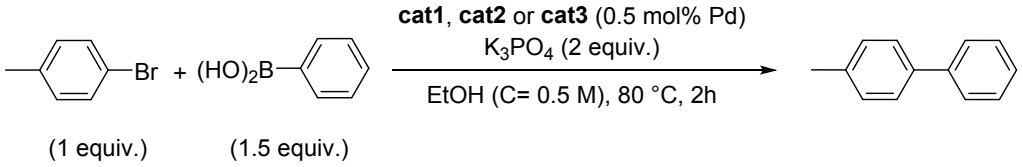
[12] J. A. Varela, D. Pena, B. Goldfuss, D. Denisenko, J. Kulhanek, K. Polborn and P. Knochel, *Chem. Eur. J.*, 2004, **10**, 4252-4264.
[13] Z. Xi, B. Liu and W. Chen, *J. Org. Chem.*, 2008, **73**, 3954-3957.
[14] Z. Li, X. Zhang, J. Qin, Z. Tan, M. Han and G. Jin, *Org. Process Res. Dev.*, 2019, **23**, 1881-1886.

^{1}H NMR (360 MHz, $CDCl_3$): δ 10.02 (s, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H), 7.76-7.70 (m, 2H), 7.26-7.22 (m, 1H).
^{13}C NMR (360 MHz, $CDCl_3$): δ 192.0, 155.8, 149.9, 144.8, 137.2, 136.4, 130.2 (2C), 127.5 (2C), 123.2, 121.3.
The spectral data are in accordance with those reported in the literature. [15]

IX. Preparation of samples for ICP-MS analyses (leaching tests)

Caution: all the glassware used for the reaction, for the storage of solutions and for the filtration operations were thoroughly washed with aqua regia, rinsed with distilled water and oven-dried before their use in the residual palladium content determination tests.

For the leaching tests described **Figure 2**, the procedure was performed as described below:



A 10 mL Schlenk-tube equipped with a magnetic stirring bar and a septum was charged with bromotoluene (171 mg, 1 mmol), phenylboronic acid (183 mg, 1.5 mmol), K_3PO_4 (424.5 mg, 2 mmol) and the corresponding catalyst (**cat1**, **cat2** or **cat3**, 0.5 mol% Pd). The mixture was dried under vacuum for 10 minutes and EtOH (anhydrous, 2 mL) was added under argon. The flask was flushed with three brief vacuum/argon cycles. The reaction mixture was subsequently stirred at 80 C for two hours. The heterogeneous solution was allowed to cool down to room temperature and filtered on a Whatman® grade 5 filter (rinsed with EtOH). The solvent was then evaporated under reduced pressure. At this stage, a liquid/liquid extraction was performed in order to eliminate the remaining boronic acid derivatives, since we noticed that these side-products interferes with the leaching analysis. Thus, the residue was poured into water (10 mL) and extracted with Et_2O (3x10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The crude residue was heated under high vacuum (10^{-1} mmHg) at 205 °C for 1 h, and the remaining solid was mineralized in nitric acid (69%, TraceMetal grade) at 140 °C for 3 h until obtaining a homogeneous light-yellow solution, which was used to perform the ICP-MS analyses.

The leaching tests described **Figure 3** were performed following a slightly modified procedure, more adapted to the larger scale employed for this experiment (250 mmol *vs* 1 mmol for **Figure 2**):
Following the synthesis described **part V**, page **S5** of this Supporting Information, 6 solutions of crude product in EtOH (100 mL) were obtained, each of them containing an equal amount of material, and therefore the same concentration of coupling product ($C_{product}$ = 0.37 mol/L). These solutions were then filtered on different equipment:
> Sintered glass filter (porosity 5)
> Whatman® paper (Grade 5, 2.5 µm)
> Polypropylene filter (3M™, 0.5 µm)
> Dicalite™
> Carbon filter (3M™, R52).

[15] L. Vandromme, H. –U. Reißig, S. Gröper and J. P. Rabe, *Eur. J. Org. Chem.,* 2008, **2008**, 2049-2055.

In each case, at the end of the filtration the equipment was rinsed with a minimum volume of EtOH and completed to 100 mL, in order to keep a known concentration ($C_{product}$ = 0.37 mol/L). For each solution, a 2.7 mL sample (1 mmol) was collected and evaporated under reduced pressure, before adding Et_2O (10 mL) to the residue. A white precipitate formed quickly, which was filtered over a Whatman® grade 5 filter (rinsed with Et_2O), and the filtrate was evaporated under reduced pressure. The removal of this white precipitate (mainly phenylboronic acid and its derivatives) is crucial, since we noticed that these boron side-products interfere with the ICP-MS measurements. Finally, the crude residue was heated under high vacuum (10^{-1} mmHg) at 205 °C for 1 h, and the remaining solid was mineralized in nitric acid (69%, TraceMetal grade) at 140 °C for 3 h until obtaining a homogeneous light-yellow solution, which was used to perform the ICP-MS analyses.

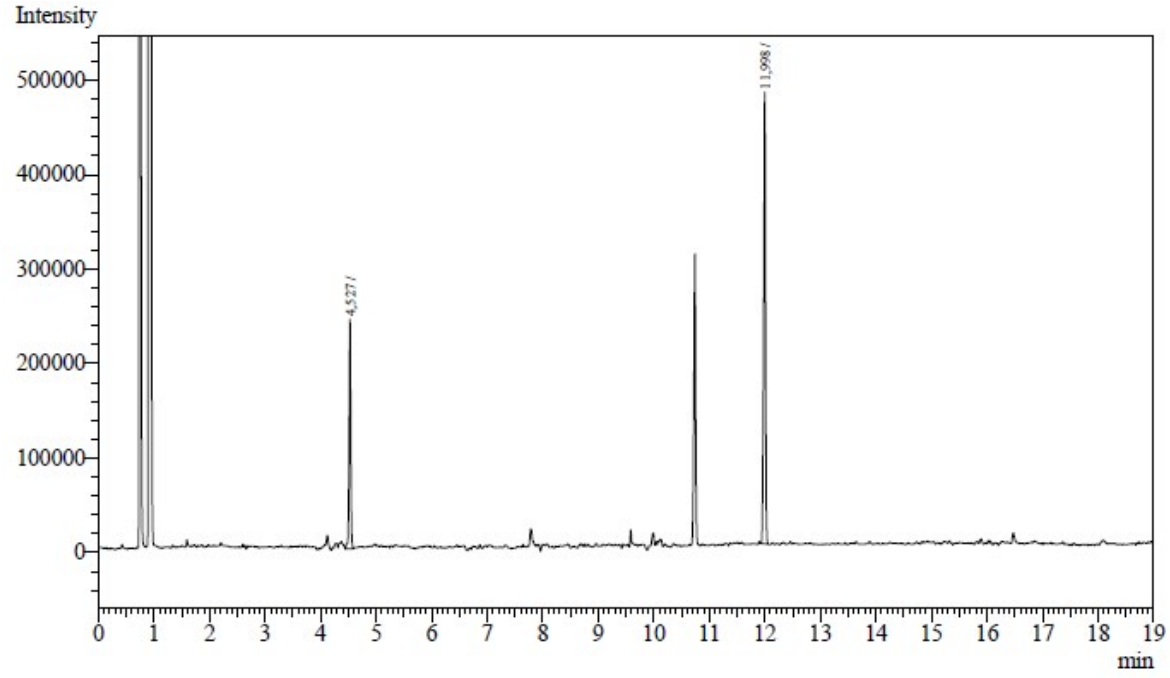
X. Copy of GC chromatograms for the catalyses

Scheme 1. GC chromatograms for the kinetics

(Shimadzu) Internal standard (Hexadecane): retention time: 12.0, Product (4-phenyltoluene): retention time: 10.7, Substrate (4-bromotoluene): retention time: 4.5, Response factor = 2.58.

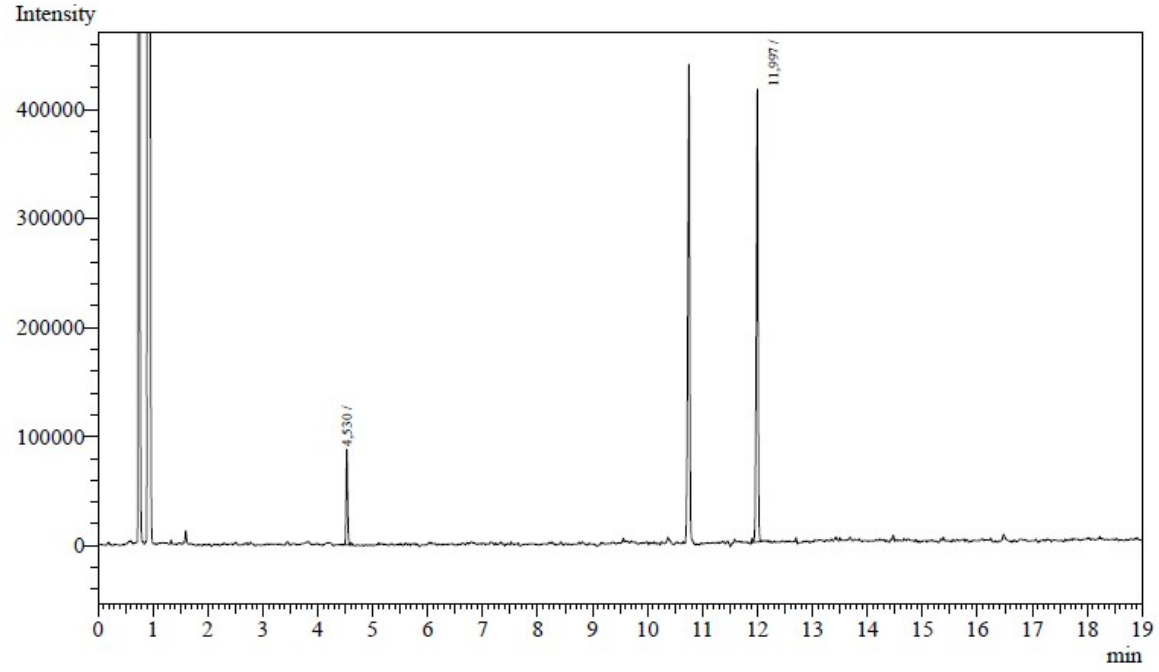
Catalysis performed with cat1

GC spectrum at t = 2 minutes (41 % conv)



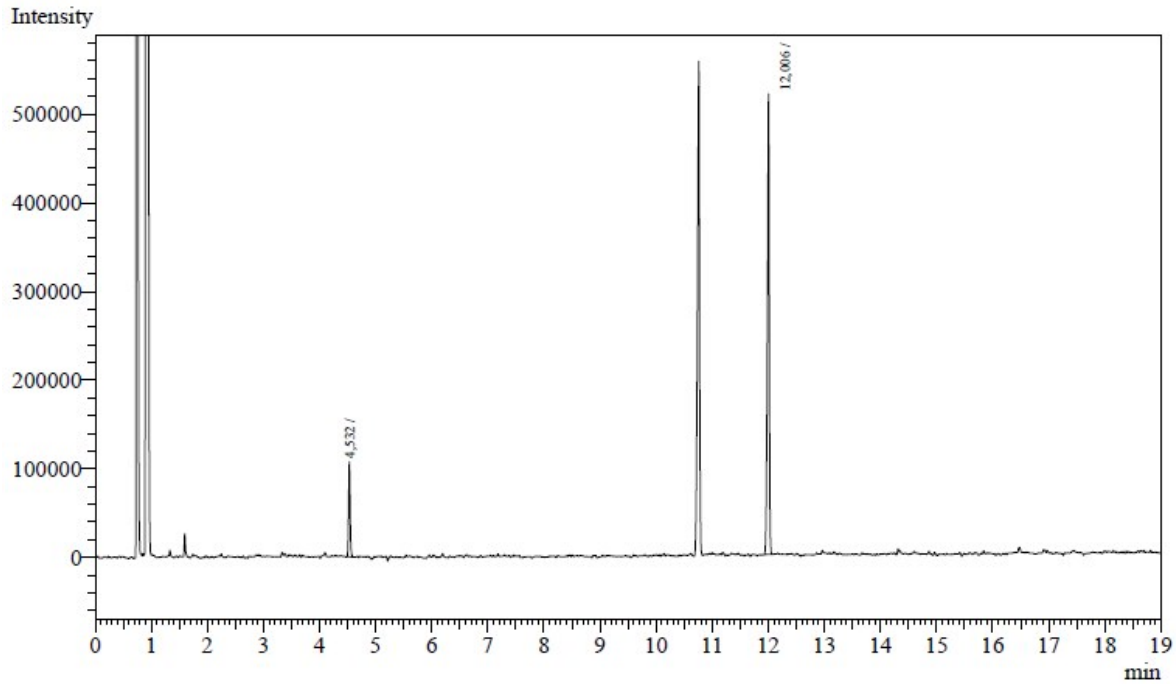
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,527	482572	239062	31,433				
2	11,998	1052666	469423	68,567				
Total		1535238	708485					

GC spectrum at t = 4 minutes (76 % conv)



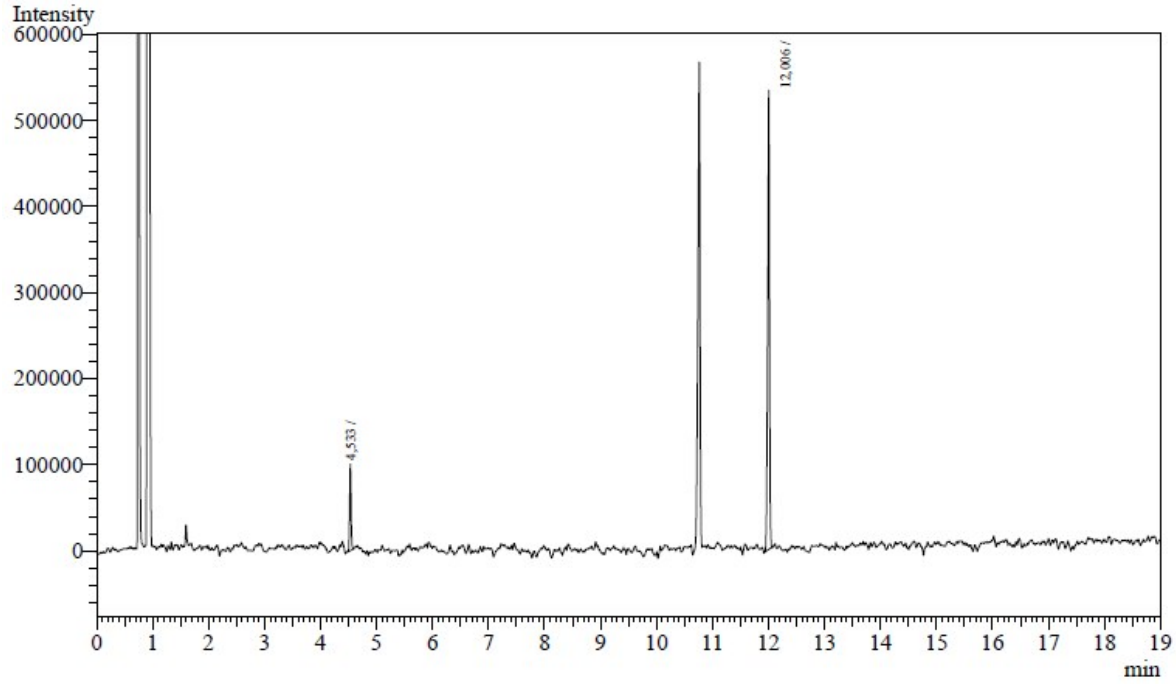
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,530	168567	87121	15,641				
2	11,997	909171	409975	84,359				
Total		1077738	497096					

GC spectrum at t = 6 minutes (78 % conv)



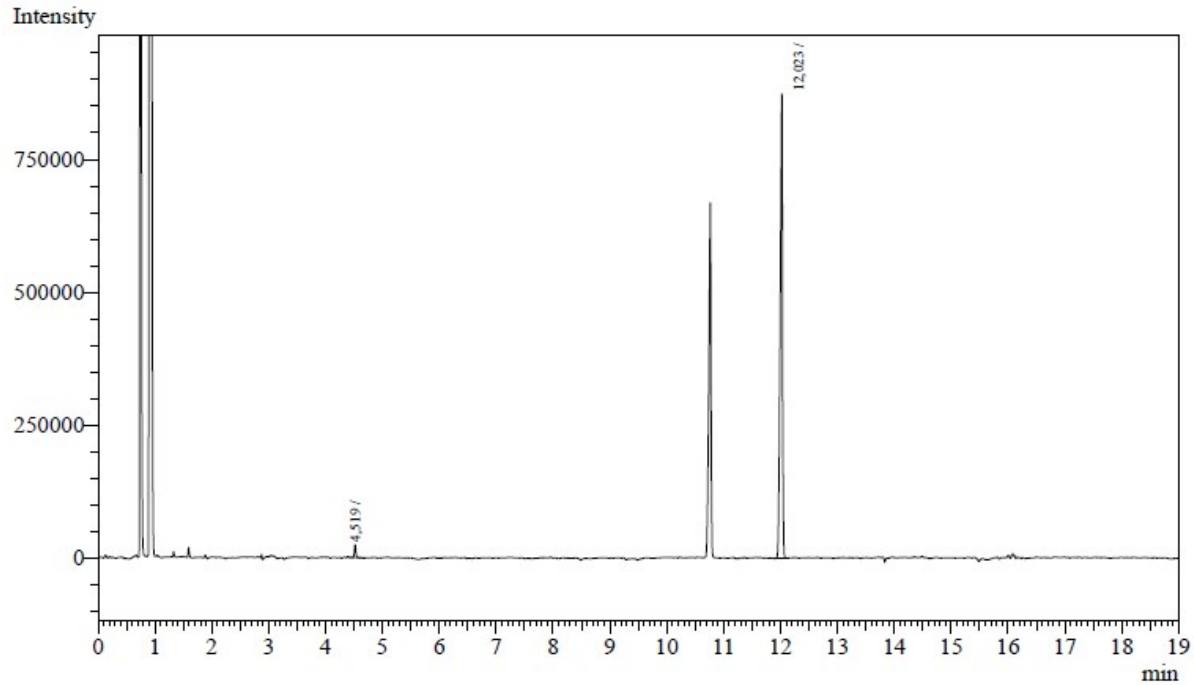
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,532	199904	103942	14,470				
2	12,006	1181587	513901	85,530				
Total		1381491	617843					

GC spectrum at t = 15 minutes (80 % conv)



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,533	179341	99114	13,164				
2	12,006	1182967	527769	86,836				
Total		1362308	626883					

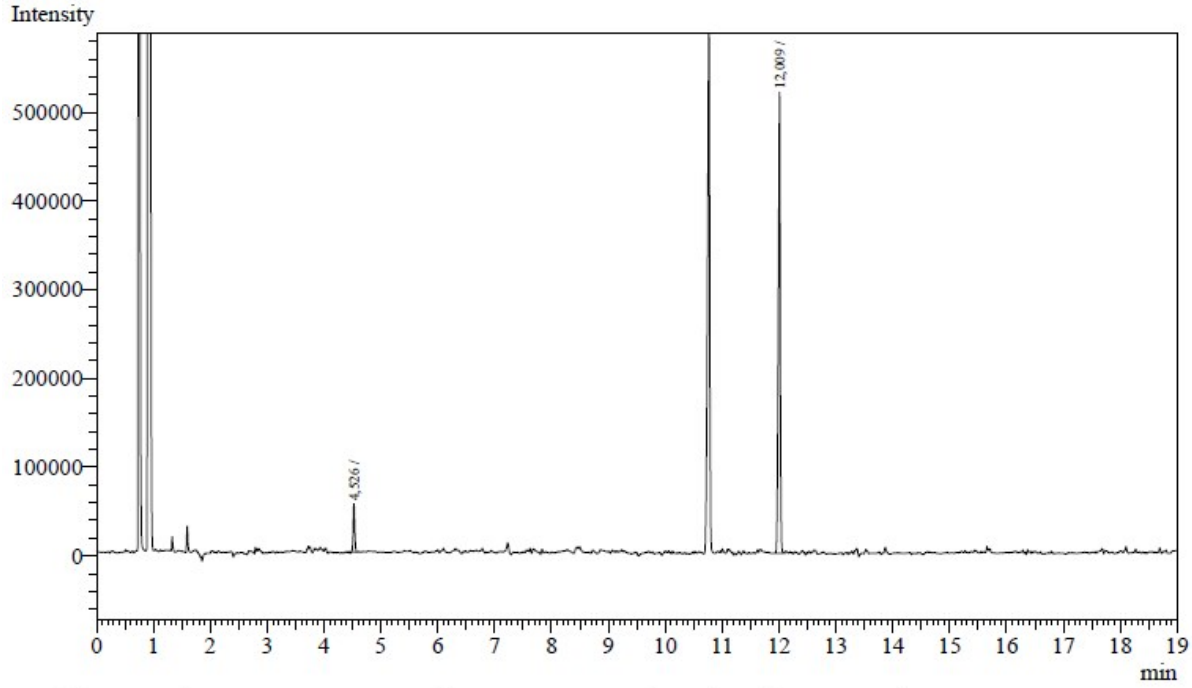
GC spectrum at t = 60 minutes (95 % conv)



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,519	42551	23671	1,715				
2	12,023	2439193	864827	98,285				
Total		2481744	888498					

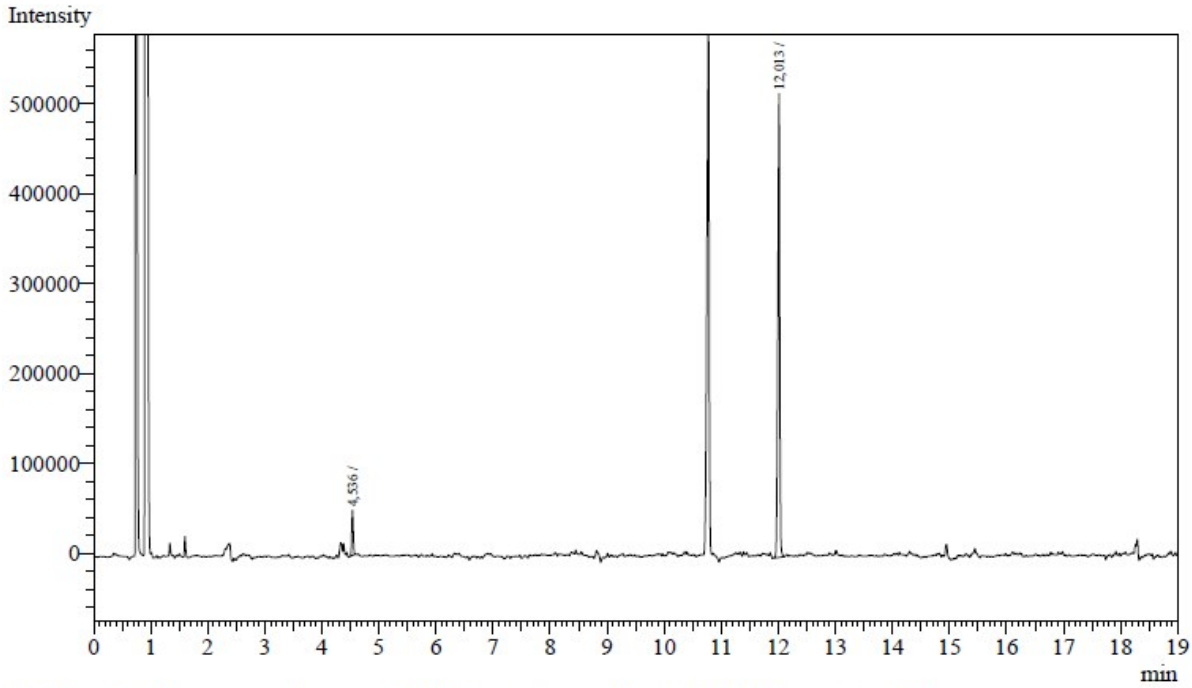
Catalysis performed with cat3

GC spectrum at t = 2 minutes (89 % conv)



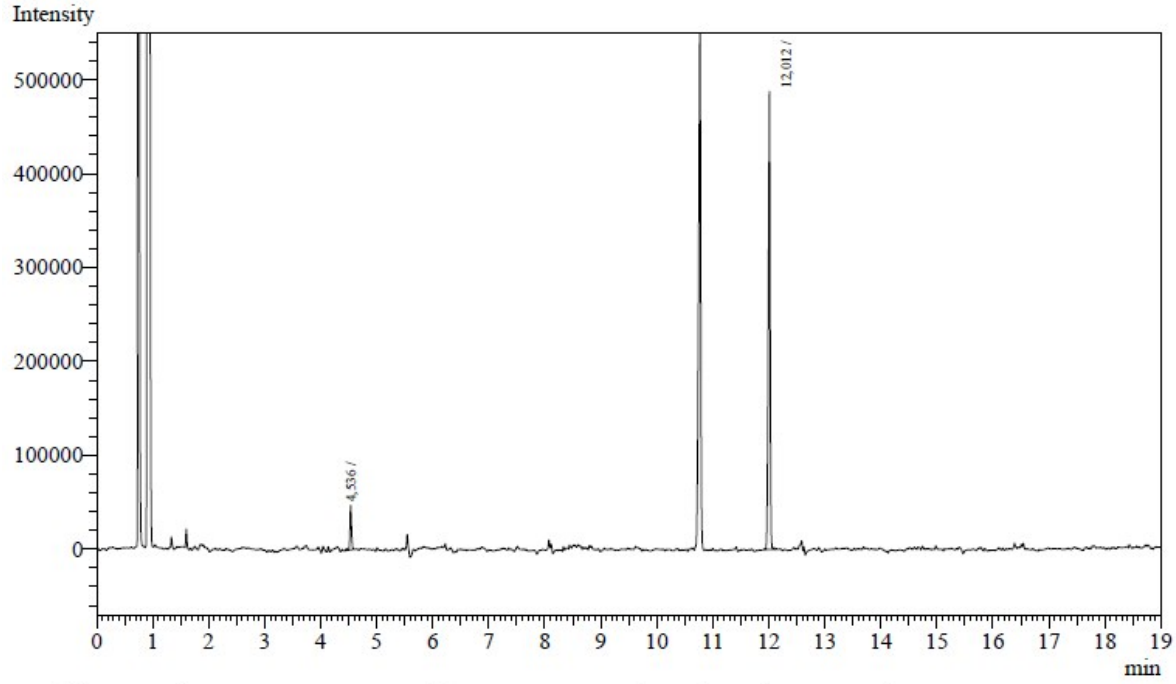
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,526	96971	53297	7,616				
2	12,009	1176252	513997	92,384				
Total		1273223	567294					

GC spectrum at t = 4 minutes (89 % conv)



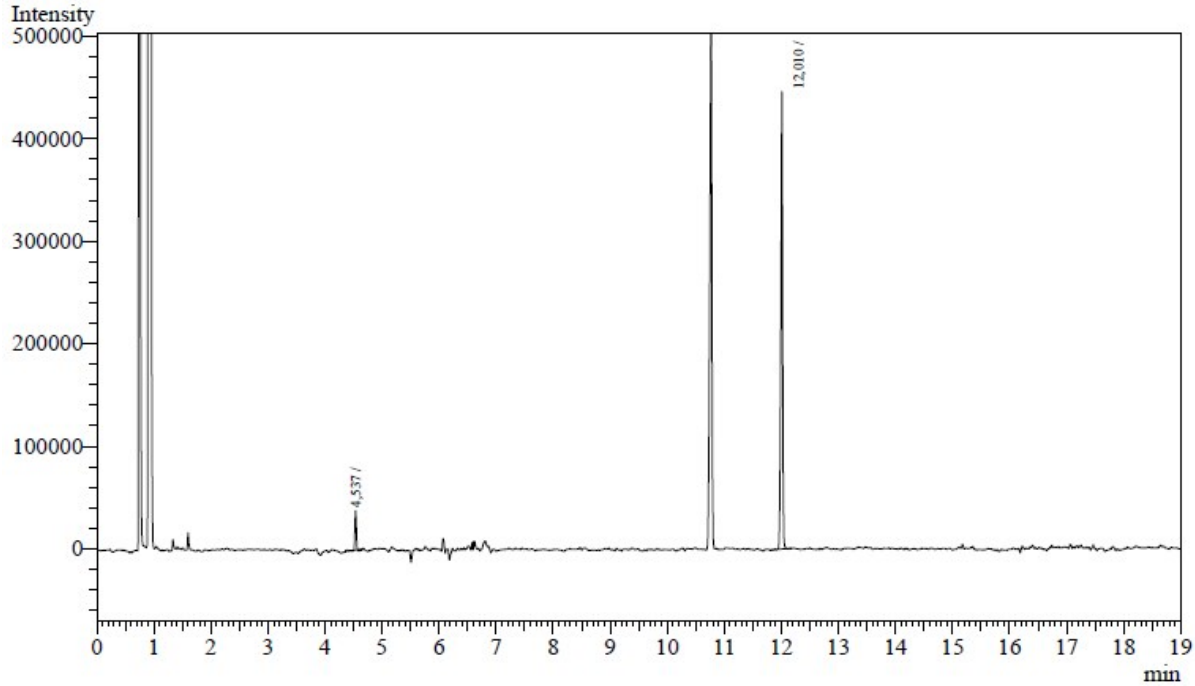
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,536	92607	49169	7,289				
2	12,013	1177829	507121	92,711				
Total		1270436	556290					

GC spectrum at t = 6 minutes (89 % conv)



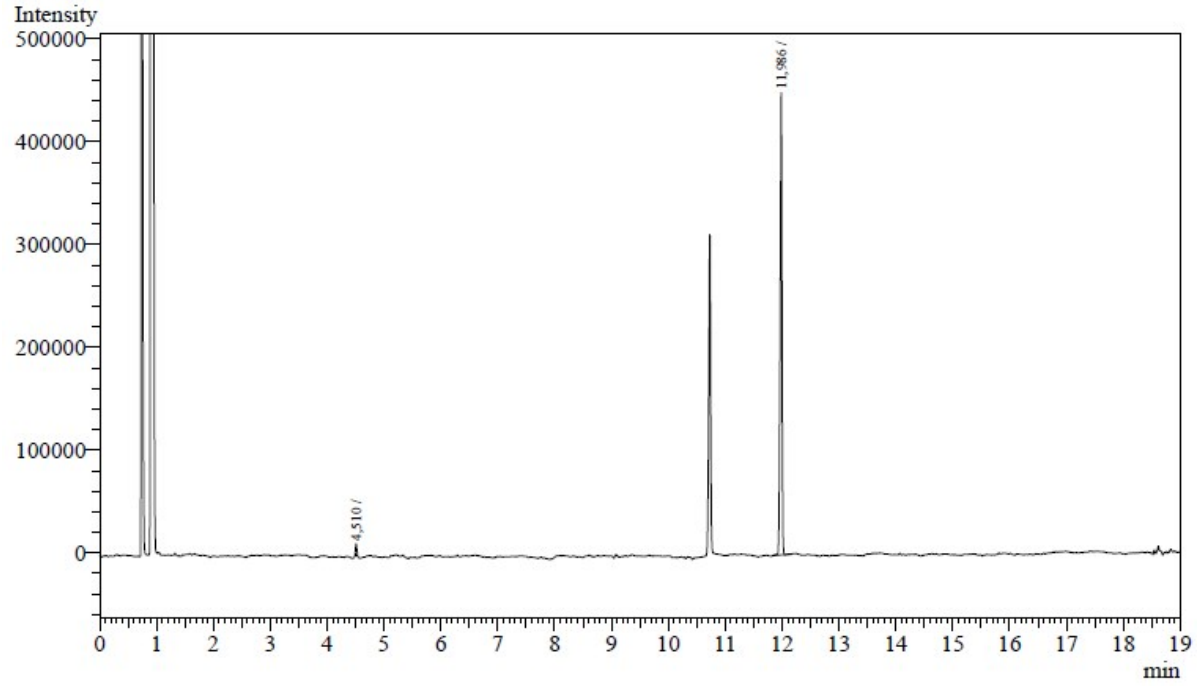
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,536	90374	46176	7,663				
2	12,012	1088984	479164	92,337				
Total		1179358	525340					

GC spectrum at t = 15 minutes (91 % conv)



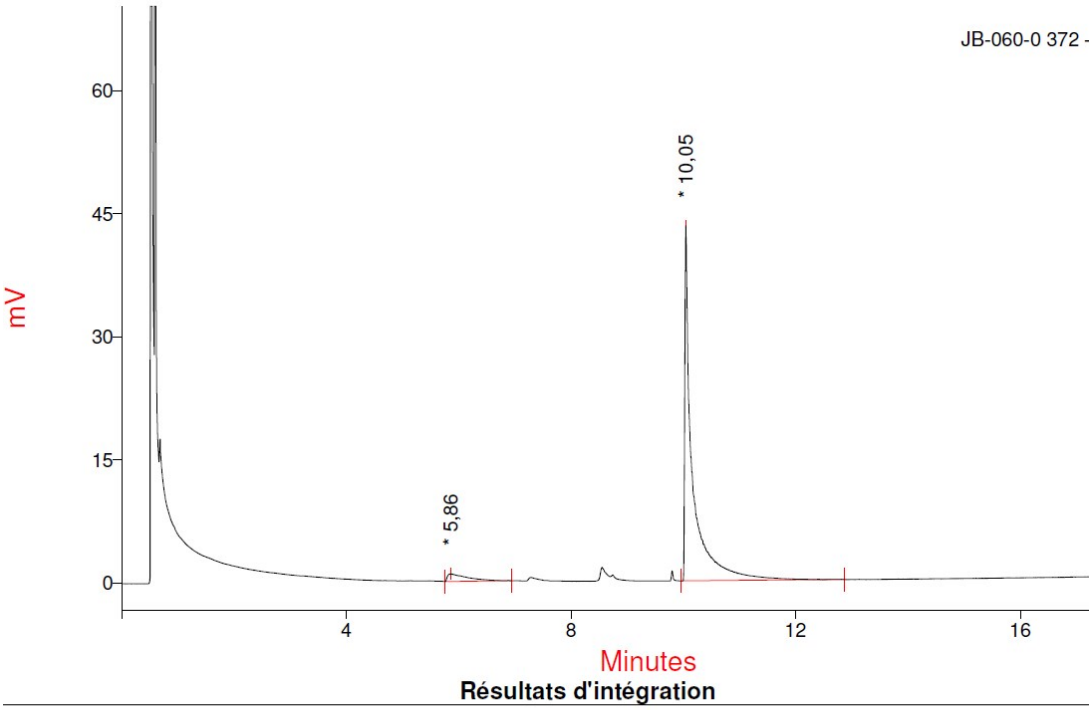
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,537	62573	37560	6,187				
2	12,010	948744	442421	93,813				
Total		1011317	479981					

GC spectrum at t = 60 minutes (95 % conv)



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	4,510	16990	10946	1,692				
2	11,986	987425	445165	98,308				
Total		1004415	456111					

GC chromatogram for Figure 3 (Varian)

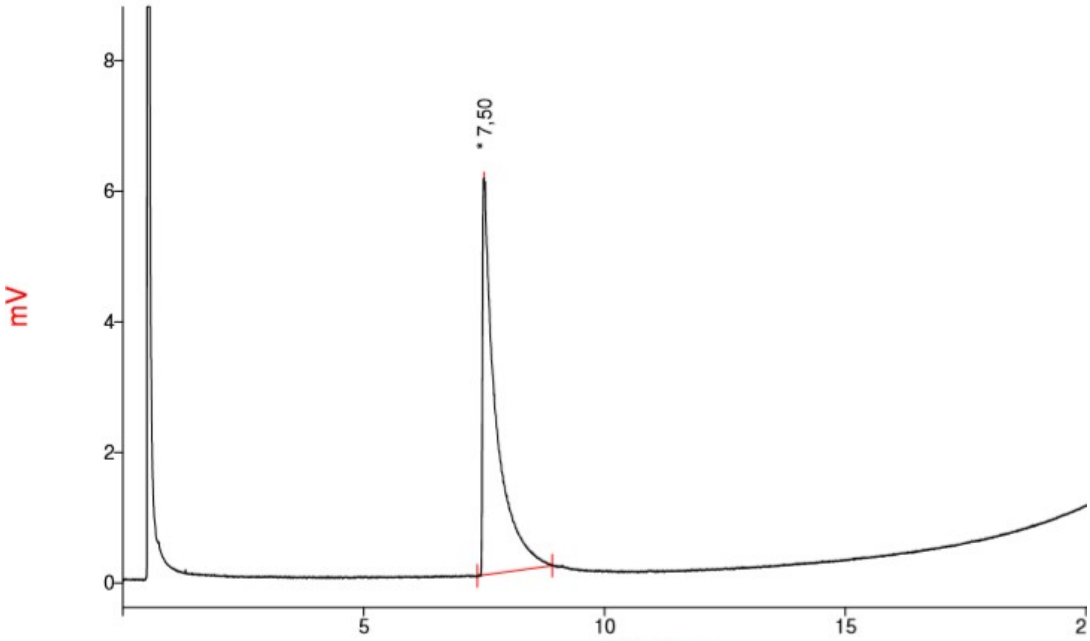


Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		5,86	22,80	**5,38**	0,91	0,37	1382,89
2		10,05	401,22	**94,62**	43,28	0,07	101144,63
SOMME			**424,02**	**100,00**	**44,19**		

GC chromatograms for Table 1

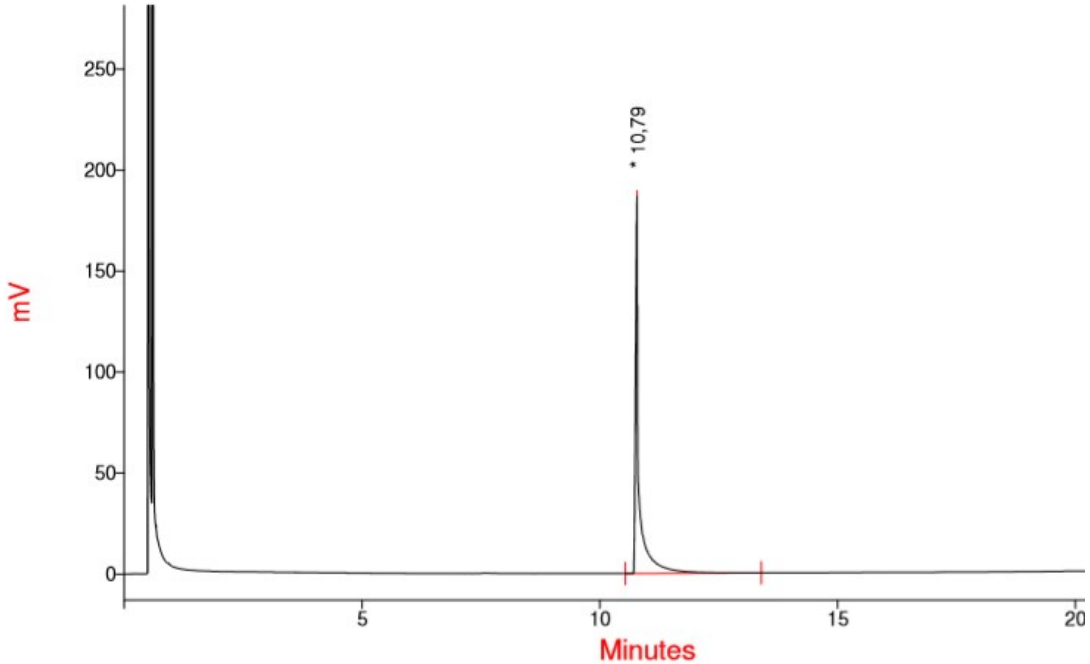
entry 1 (Varian)



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		7,50	115,26	**100,00**	6,08	0,22	6313,49
SOMME			**115,26**	**100,00**	**6,08**		

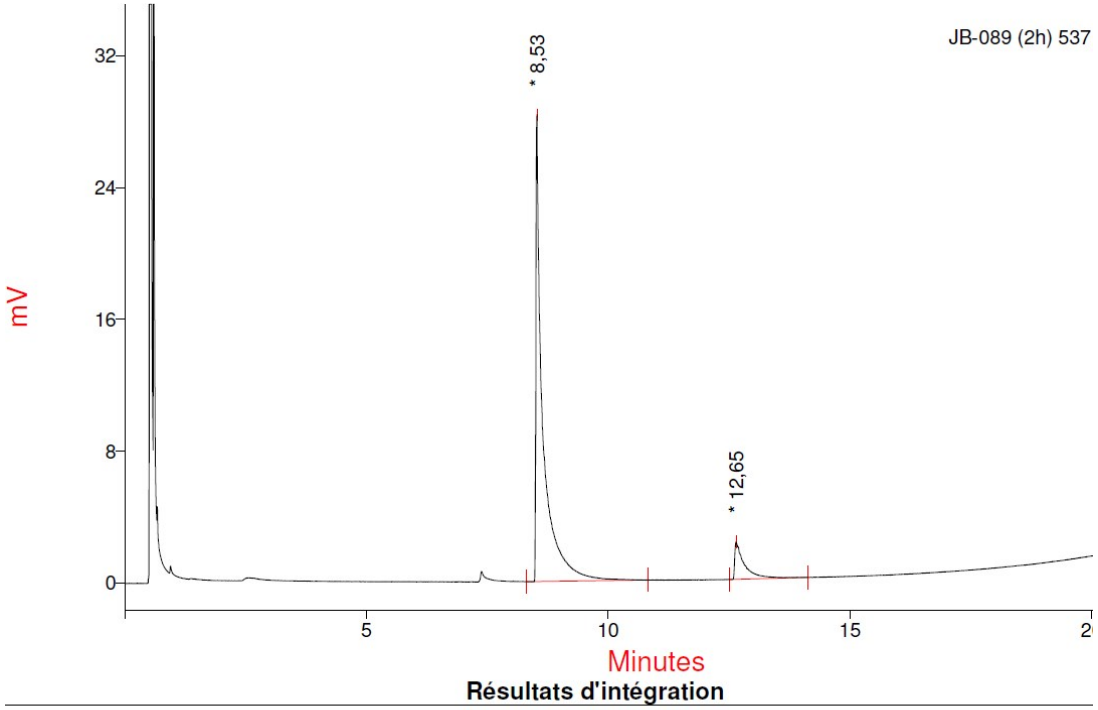
entry 2 (Varian)



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		10,79	942,47	**100,00**	186,90	0,04	356580,54
SOMME			**942,47**	**100,00**	**186,90**		

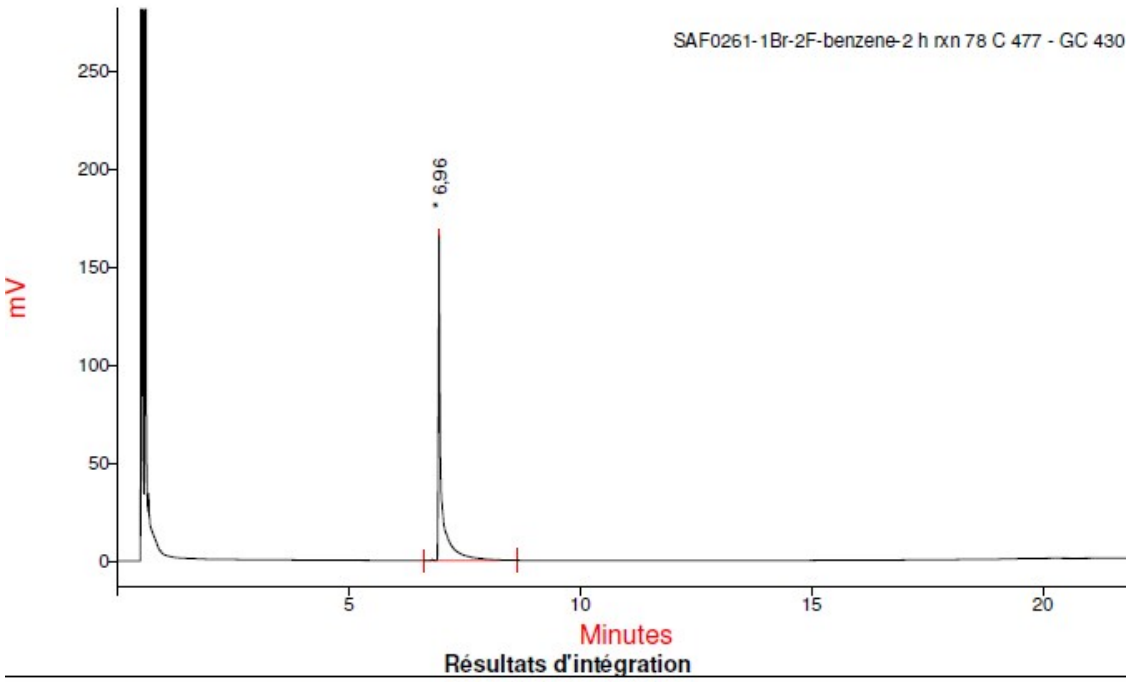
entry 3 (Varian)



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		8,53	280,73	**90,01**	28,35	0,09	48656,71
2		12,65	31,15	**9,99**	2,27	0,16	34575,76
SOMME			**311,88**	**100,00**	**30,62**		

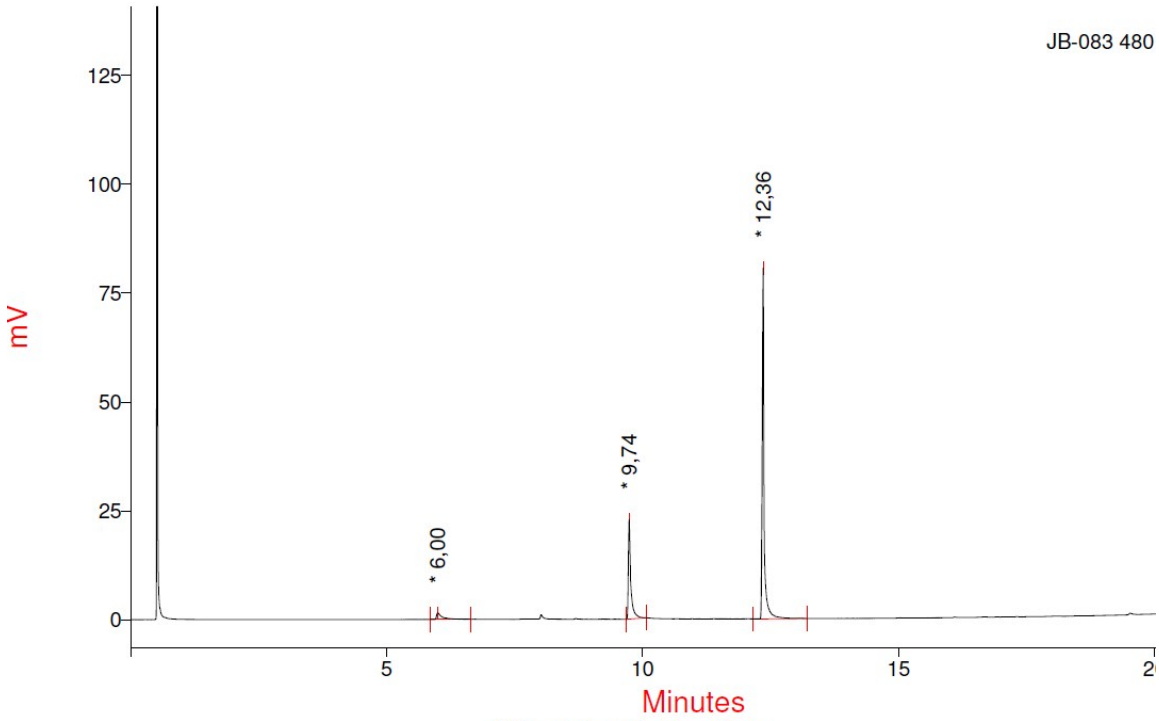
entry 4 (Varian)



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		6,96	720,77	**100,00**	166,08	0,03	259850,93
SOMME			**720,77**	**100,00**	**166,08**		

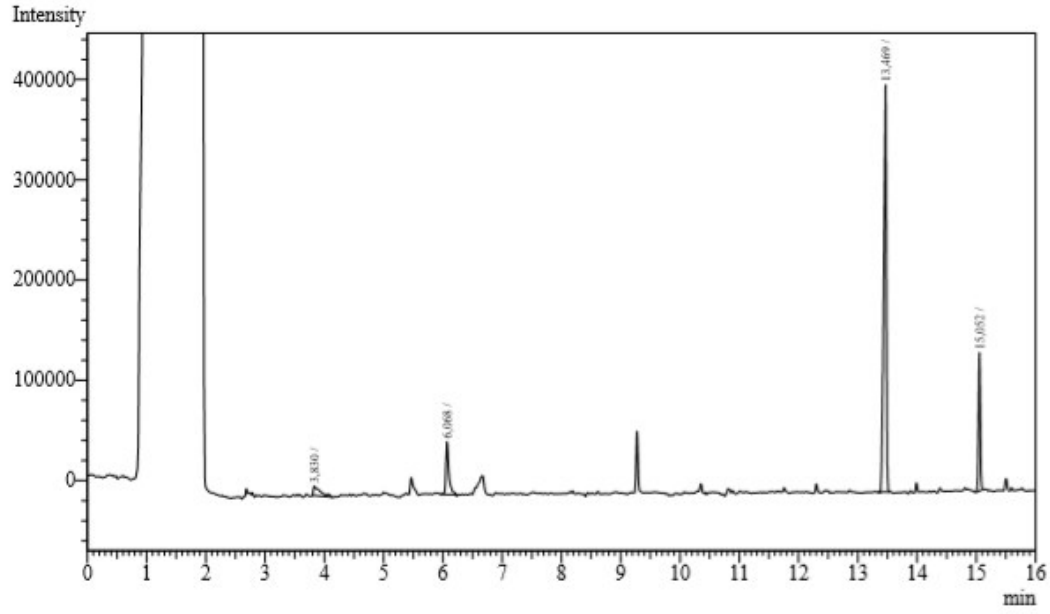
entry 5 (Varian)



Résultats d'intégration

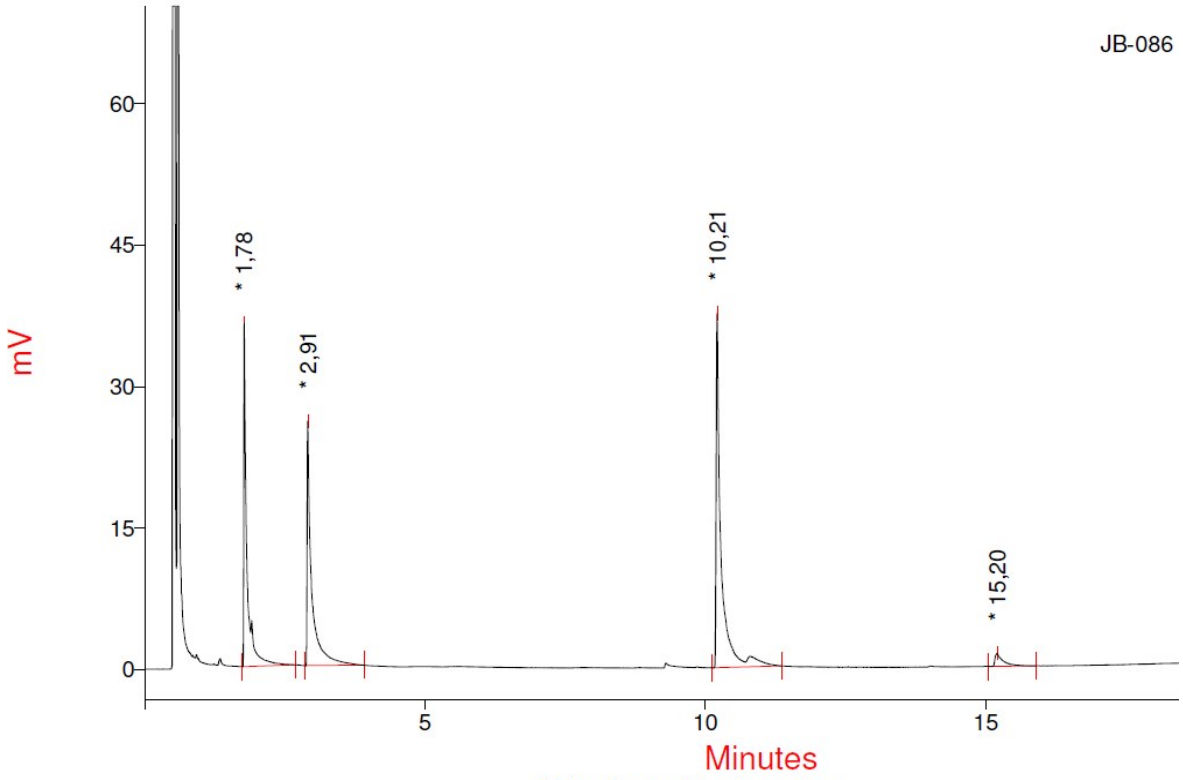
#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		6,00	10,96	**3,69**	1,49	0,09	26882,10
2		9,74	75,81	**25,54**	22,90	0,04	321424,40
3		12,36	210,03	**70,76**	80,56	0,03	809706,07
SOMME			**296,80**	**100,00**	**104,95**		

entry 6 (Varian)



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	3,830	78770	9300	4,419				
2	6,068	181855	52341	10,203				
3	13,469	1244017	400484	69,793				
4	15,052	277785	135950	15,585				
Total		1782427	598075					

entry 7 (Varian)

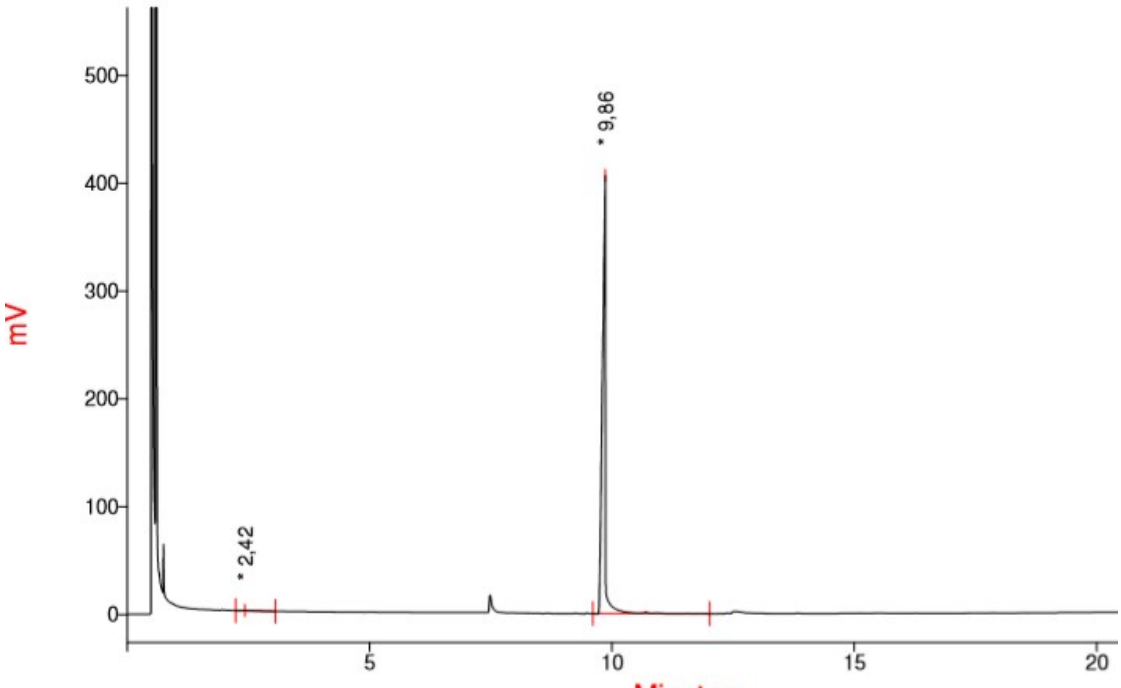


Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		1,78	135,90	**26,10**	36,42	0,04	13568,29
2		2,91	143,32	**27,52**	25,92	0,05	18800,03
3		10,21	227,98	**43,78**	37,59	0,06	186706,58
4		15,20	13,59	**2,61**	1,39	0,13	81427,73
SOMME			**520,79**	**100,00**	**101,33**		

GC chromatograms for Scheme 2

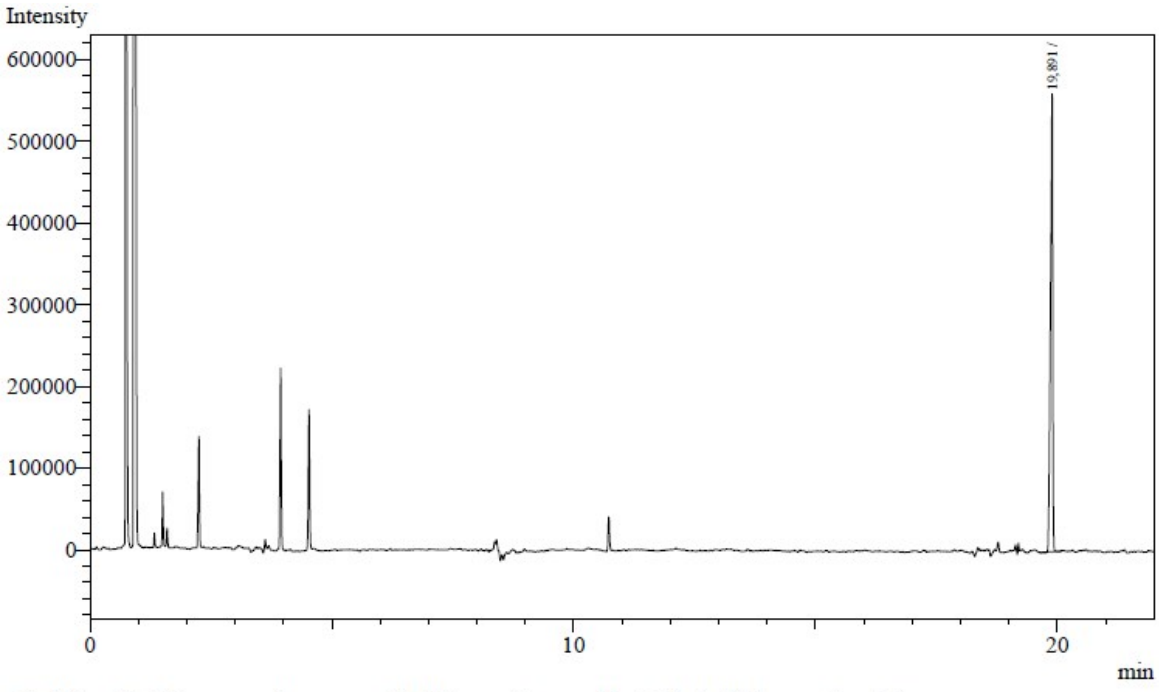
(eq. 1) (Varian)



Résultats d'intégration

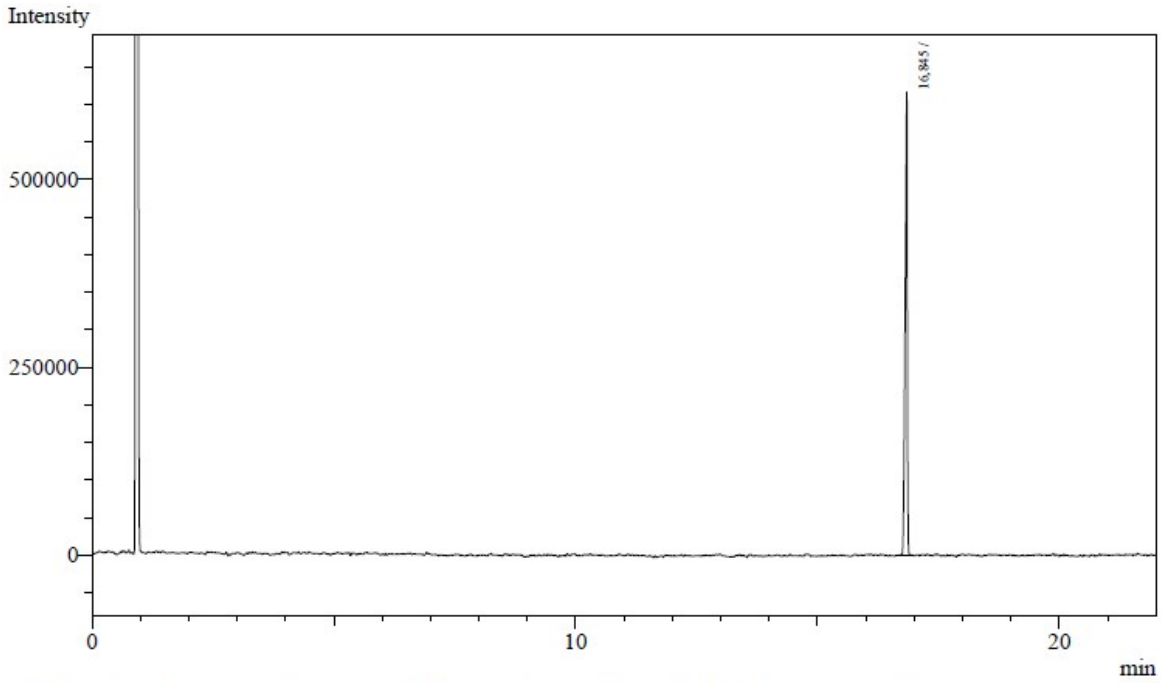
#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		2,42	5,23	**0,28**	0,33	0,19	938,83
2		9,86	1837,51	**99,72**	406,60	0,07	111573,24
SOMME			**1842,74**	**100,00**	**406,93**		

(eq. 2) (Shimadzu)



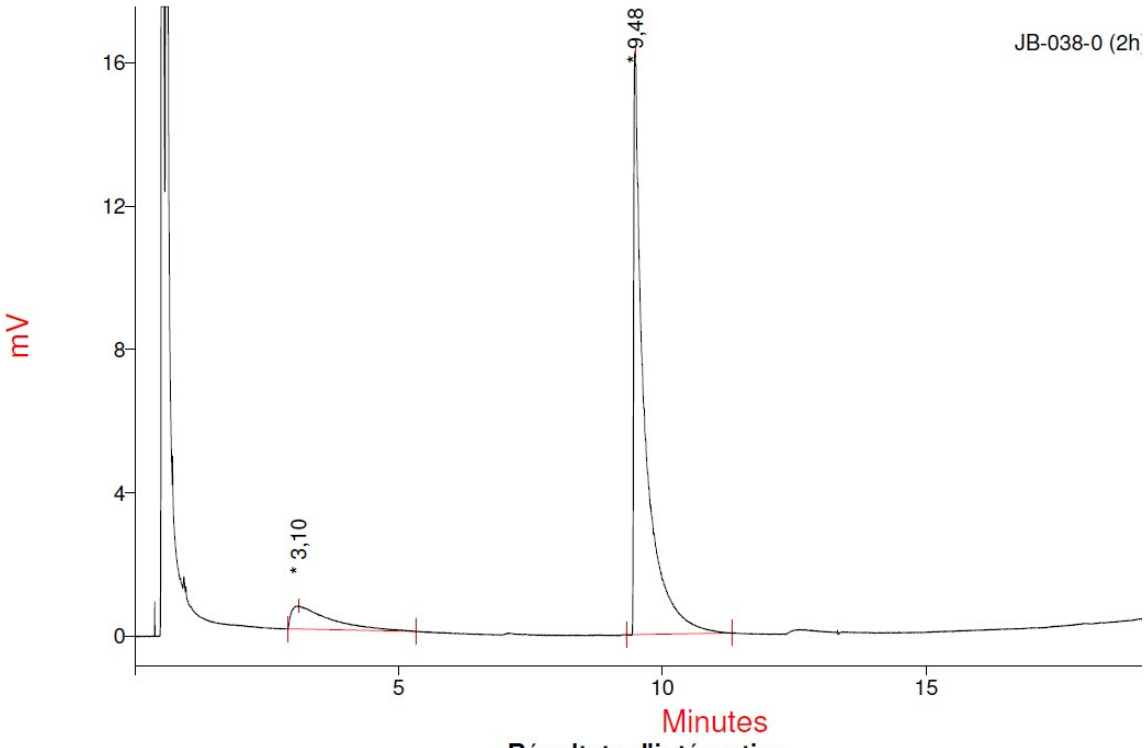
Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	19,891	1766376	556885	100,000				
Total		1766376	556885					

Below, the GC spectrum of the starting boron derivative partner



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	16,845	1888474	613486	100,000				
Total		1888474	613486					

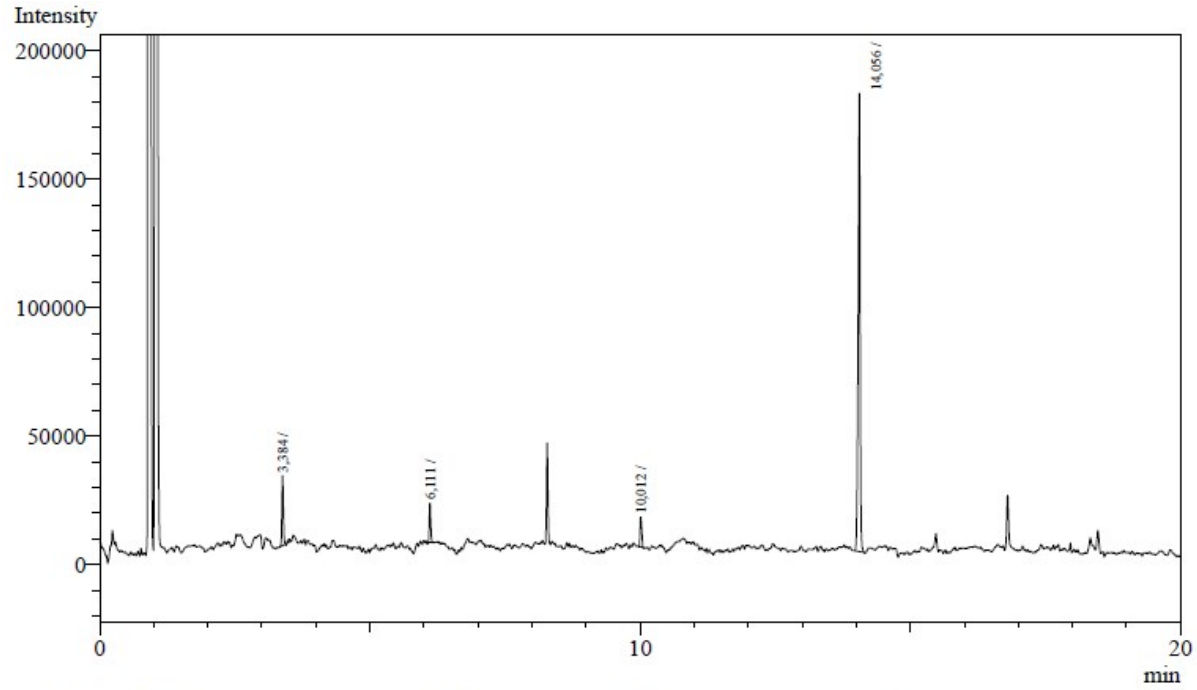
(eq. 3) (Varian)



Résultats d'intégration

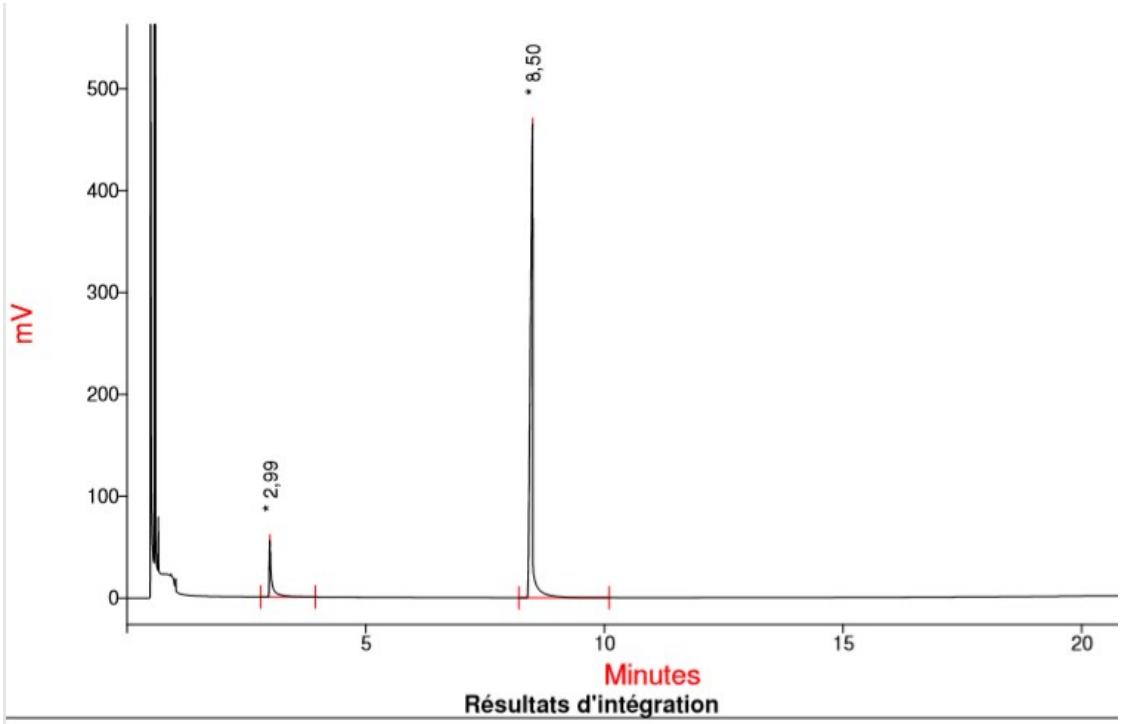
#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		3,10	32,07	**12,20**	0,65	0,65	126,82
2		9,48	230,81	**87,80**	16,28	0,15	23143,50
SOMME			**262,88**	**100,00**	**16,93**		

(eq. 4) (Shimadzu)



Peak#	Ret.Time	Area	Height	Conc.	Unit	Mark	ID#	Cmpd Name
1	3,384	53871	26636	9,777				
2	6,111	27101	15182	4,918				
3	10,012	24461	11485	4,439				
4	14,056	445596	176545	80,866				
Total		551029	229848					

Scheme 3. GC chromatograms for the mole scale synthesis of 4-phenyltoluene (Varian)

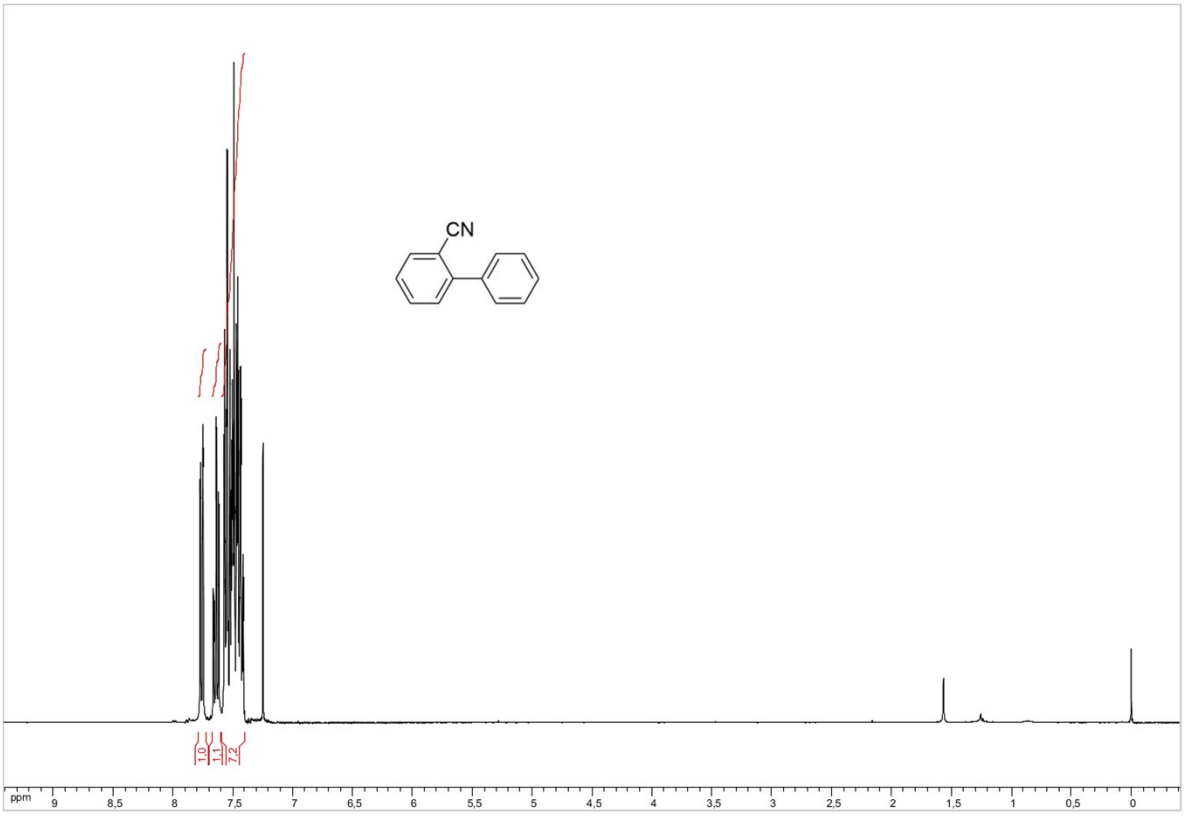


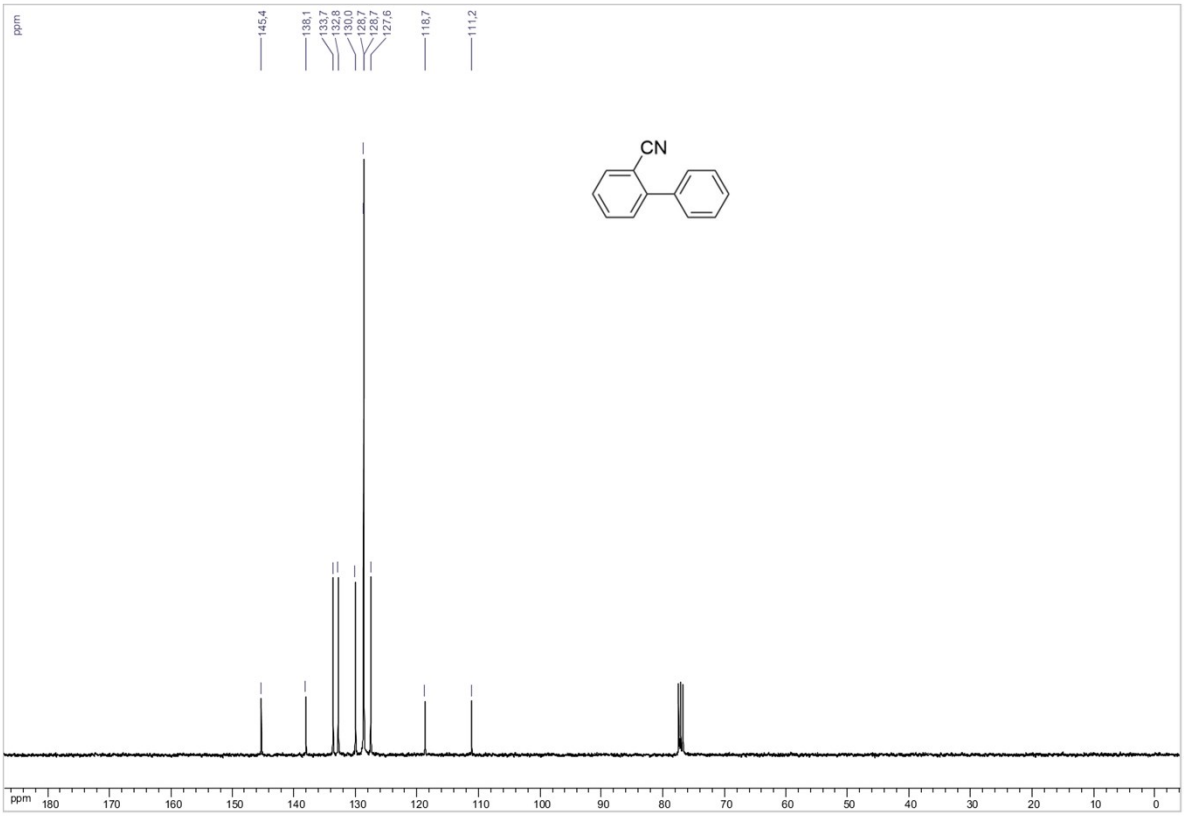
Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Hauteur	Largeur (50%)	Plateaux (EP)
1		2,99	196,36	**10,19**	55,67	0,03	49064,39
2		8,50	1730,73	**89,81**	465,48	0,05	136705,57
SOMME			**1927,09**	**100,00**	**521,15**		

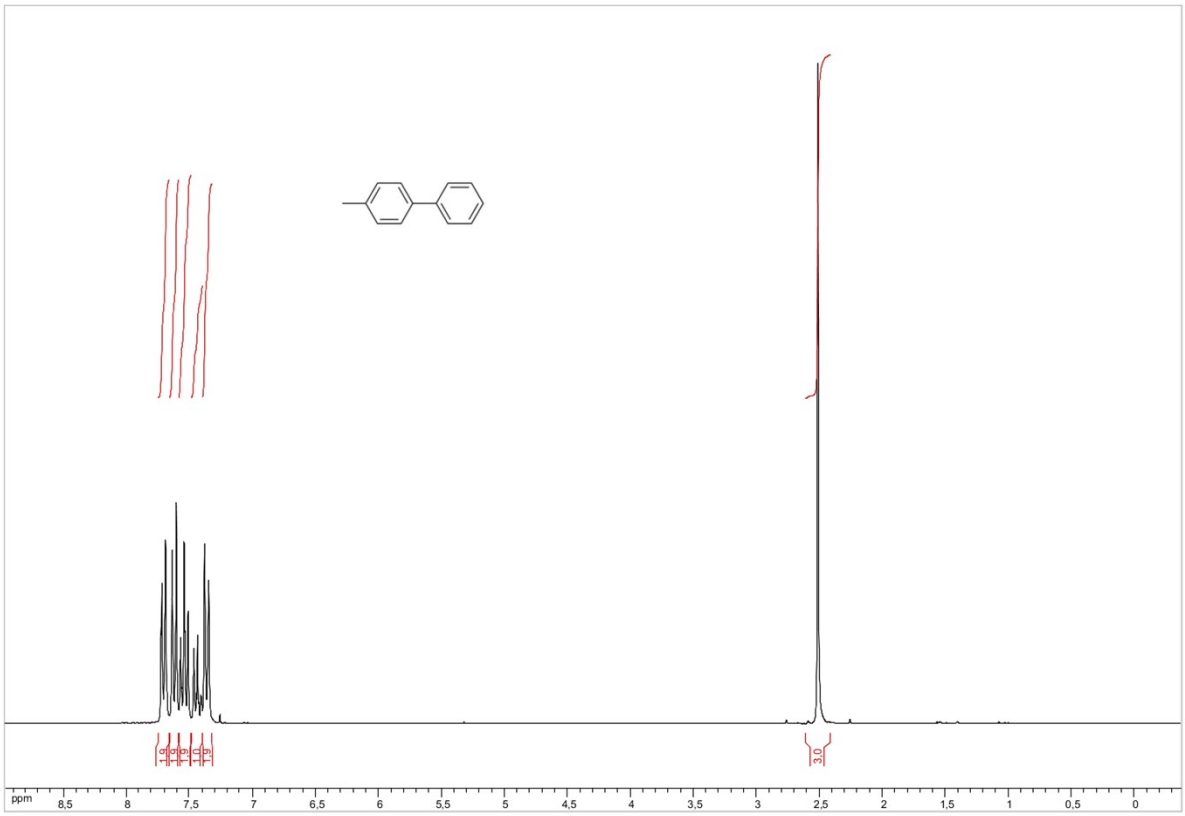
XI. Copy of NMR spectra

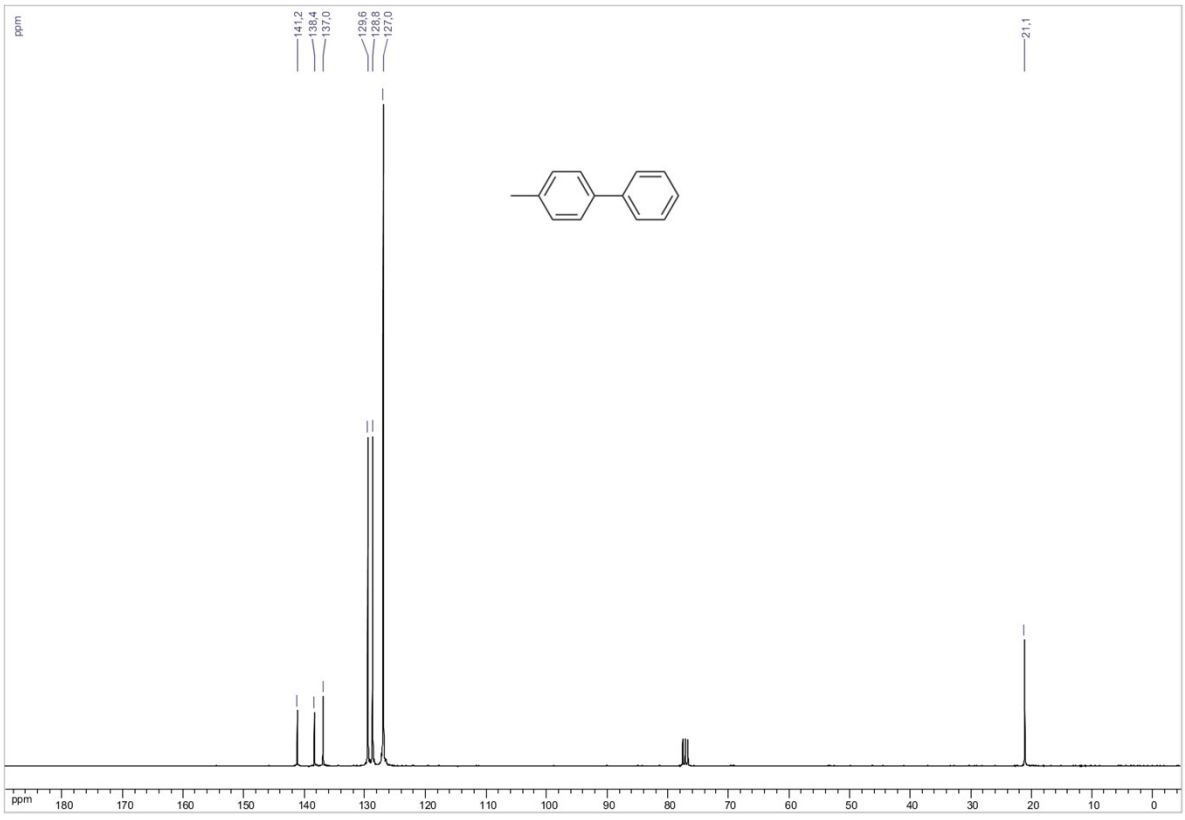
[1,1'-biphenyl]-2-carbonitrile



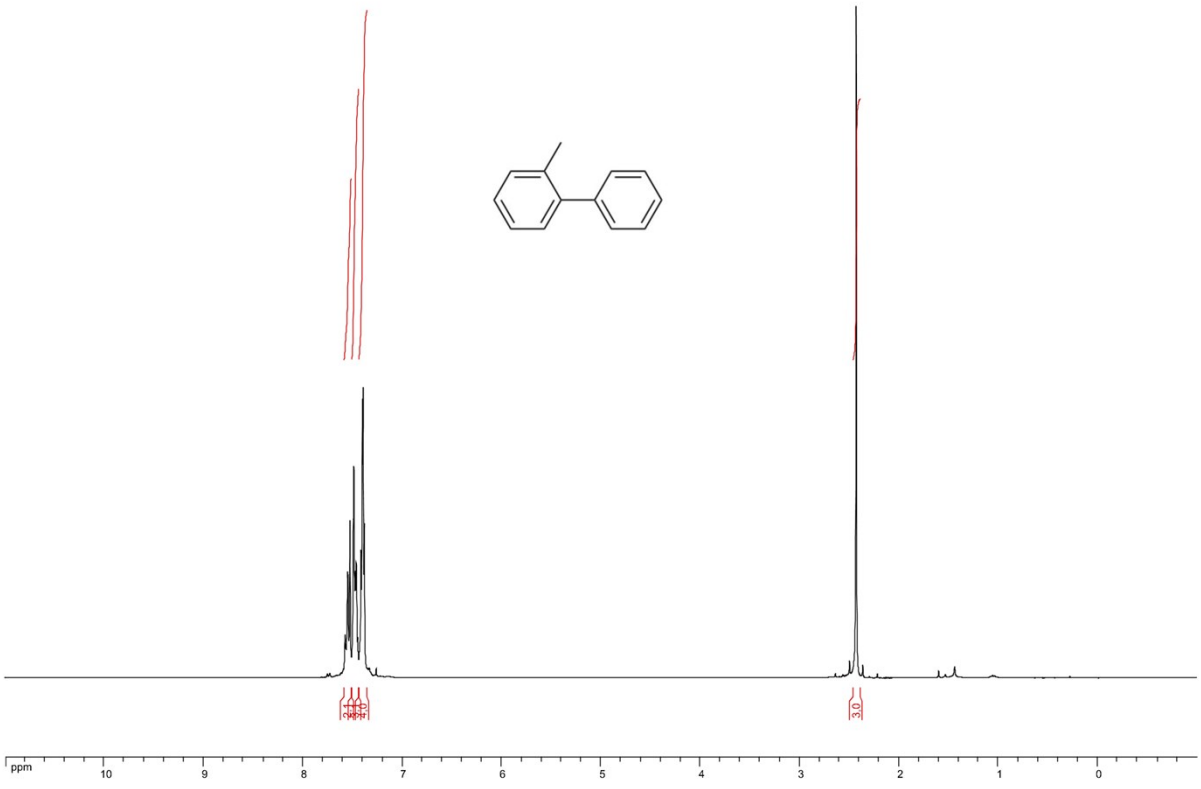


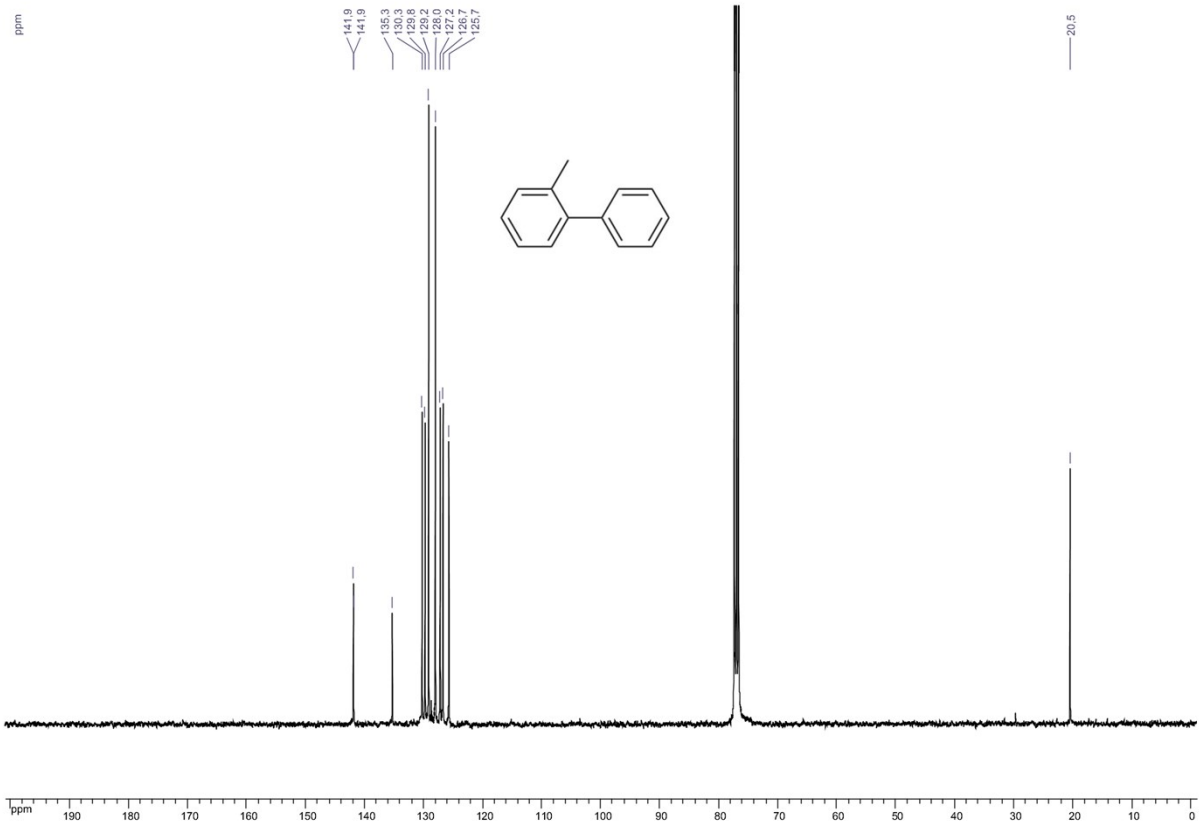
4-phenyltoluene



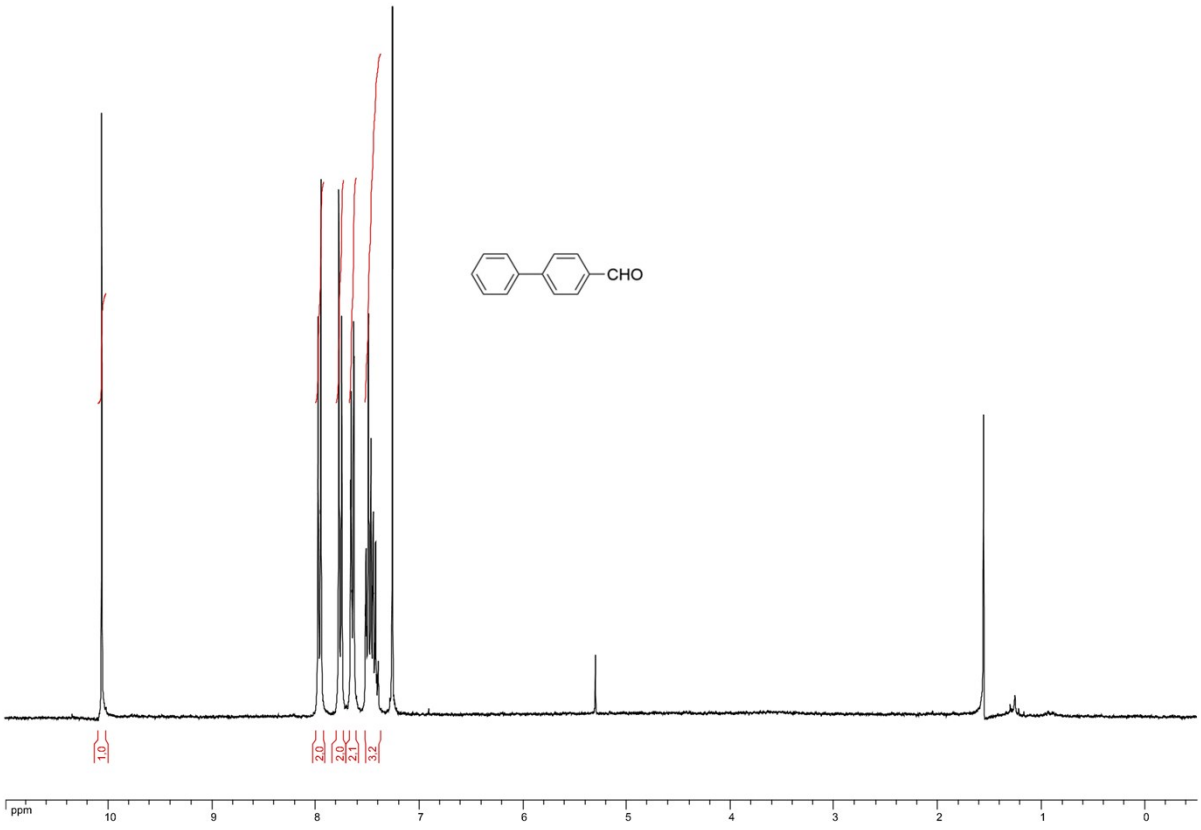


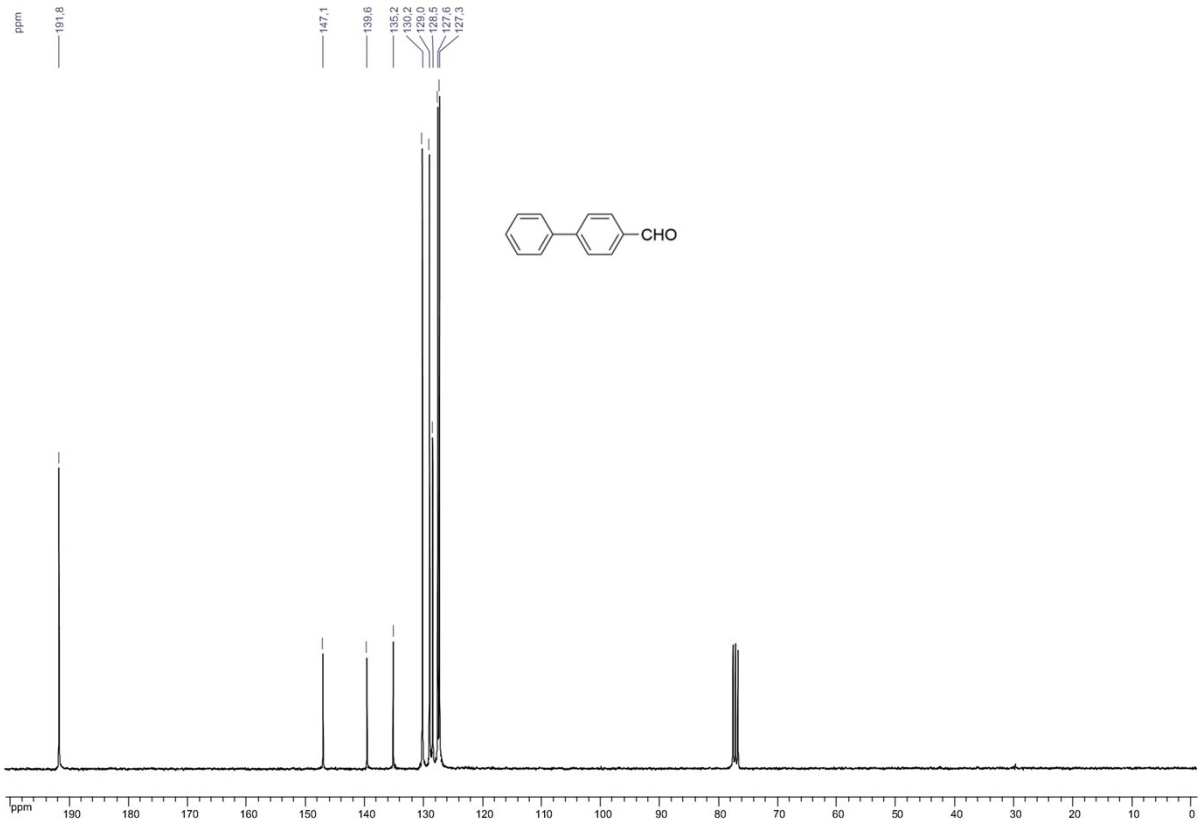
2-methyl-1,1’-biphenyl



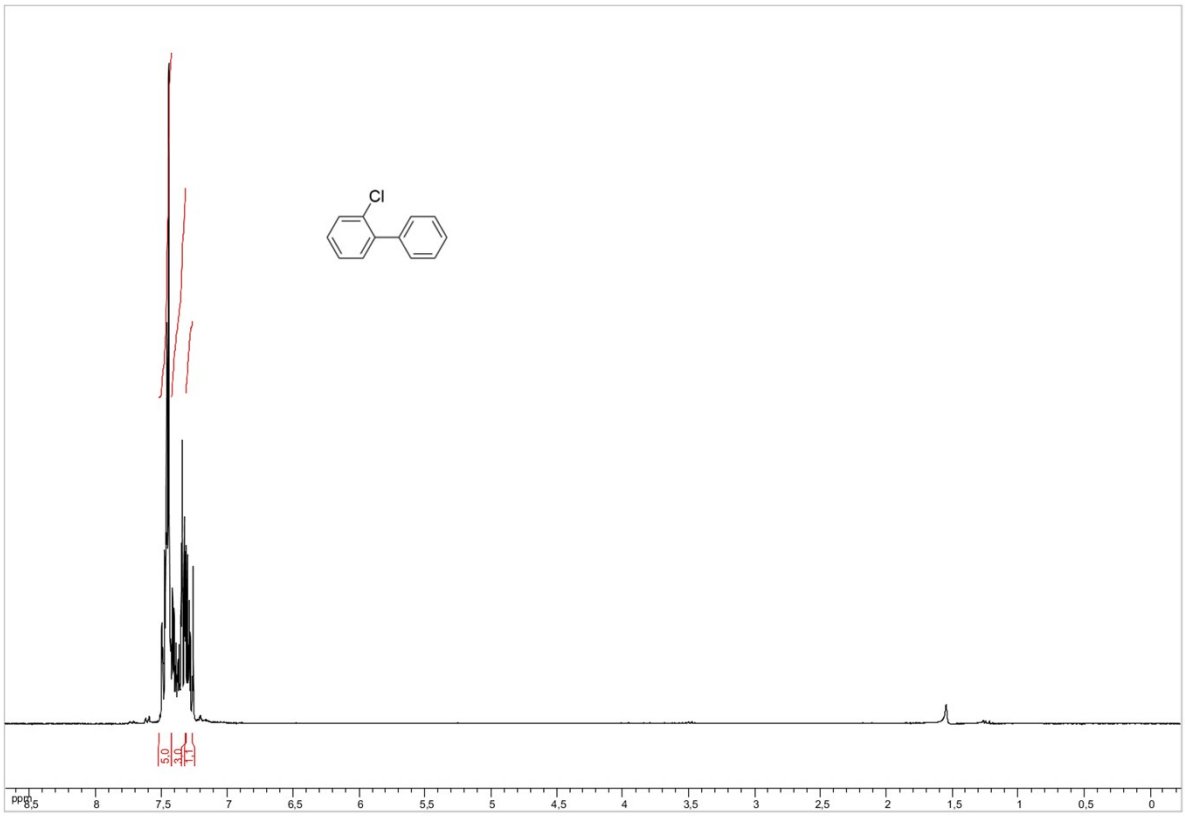


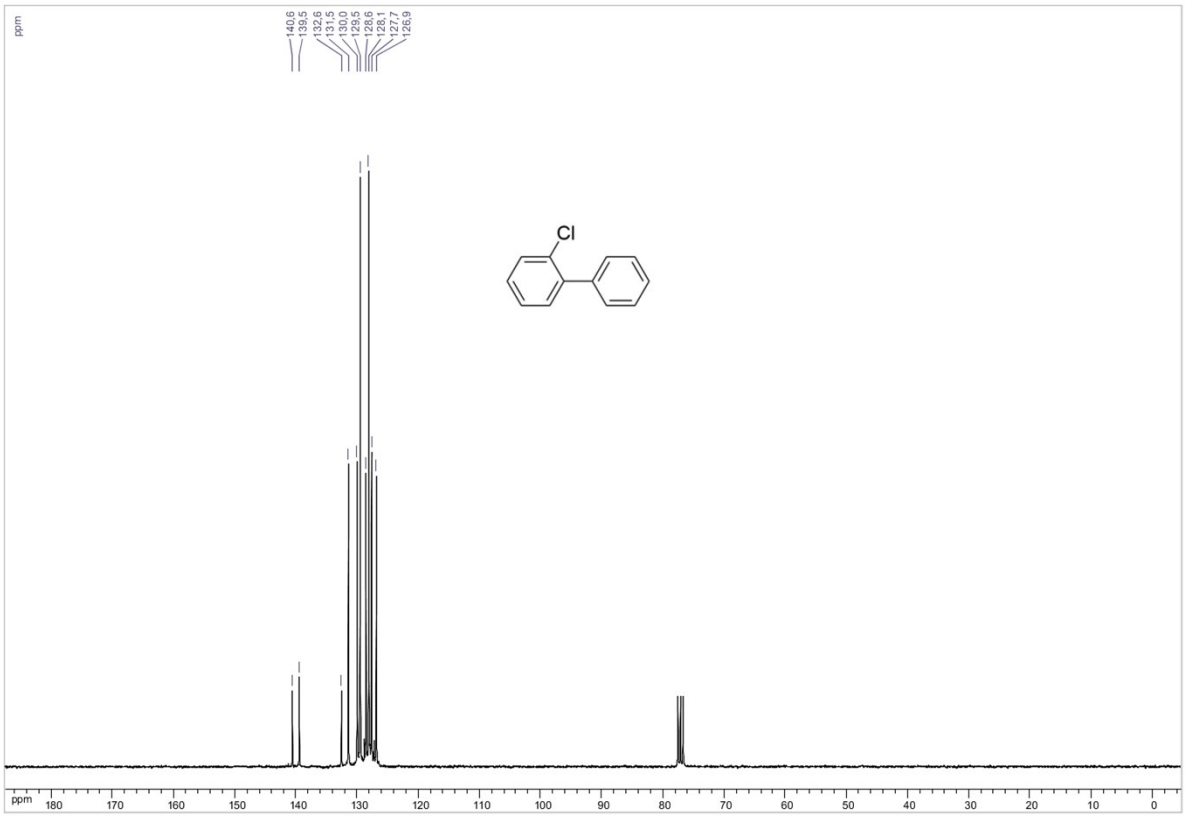
[1,1'-biphenyl]-4-carboxaldehyde



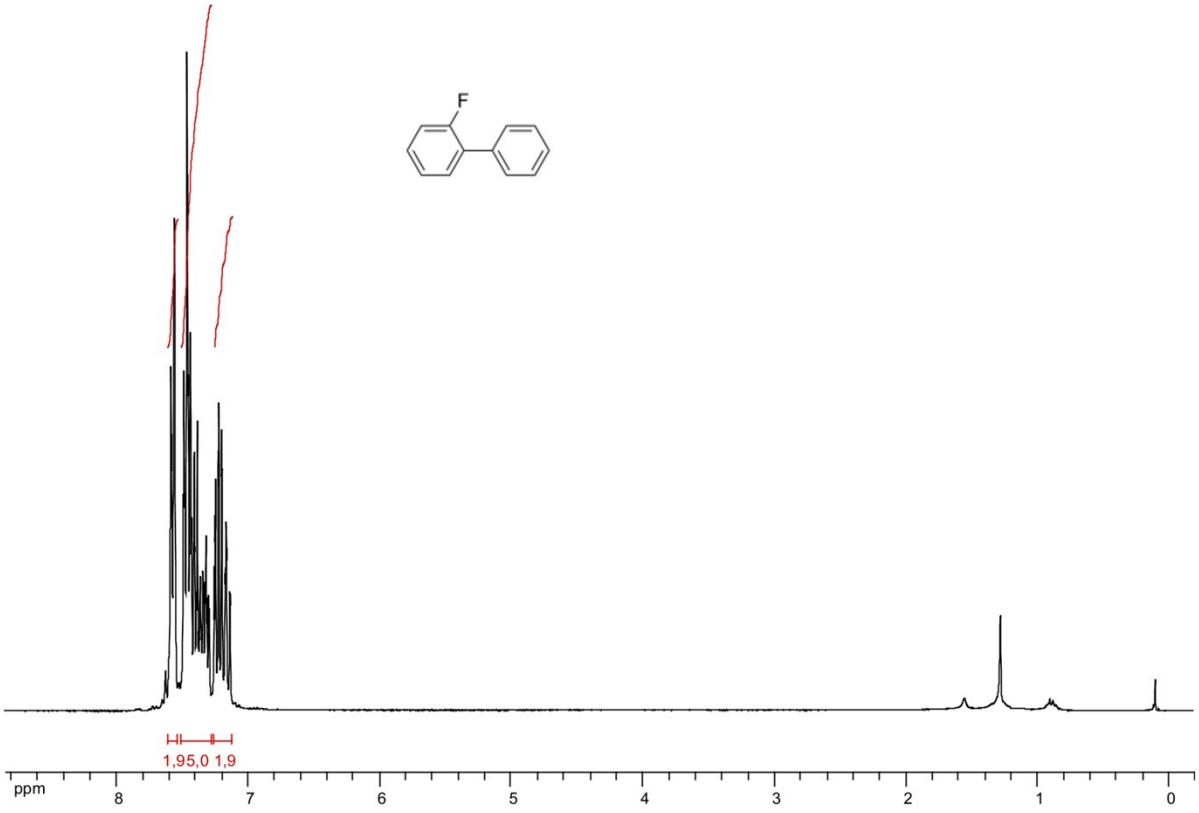


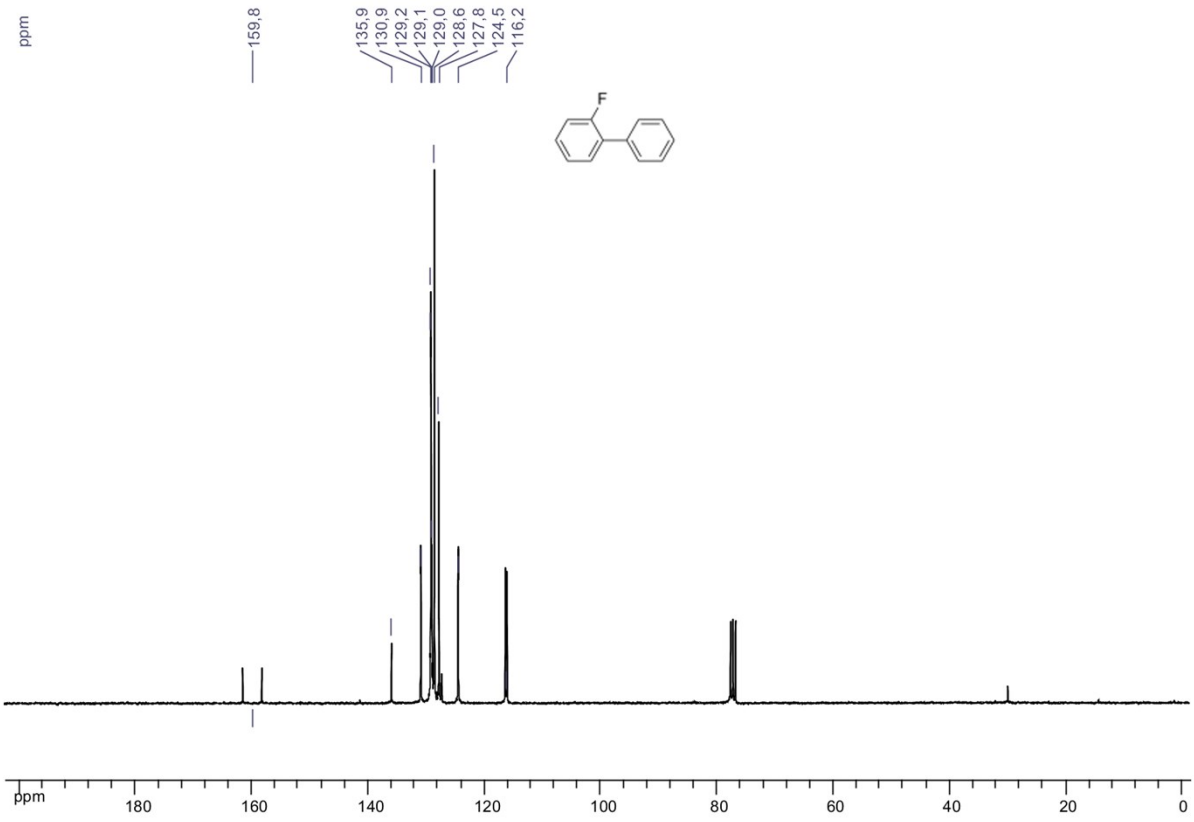
2-chloro-1,1’-biphenyl



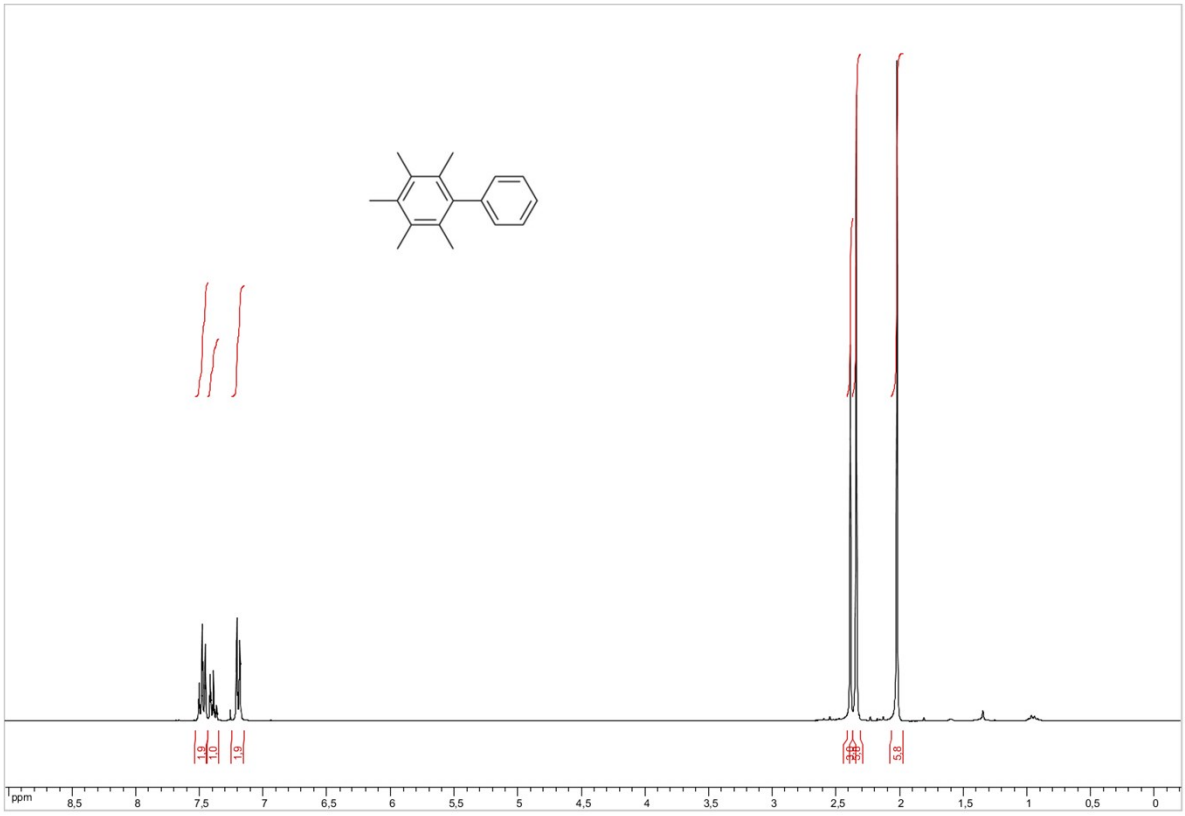


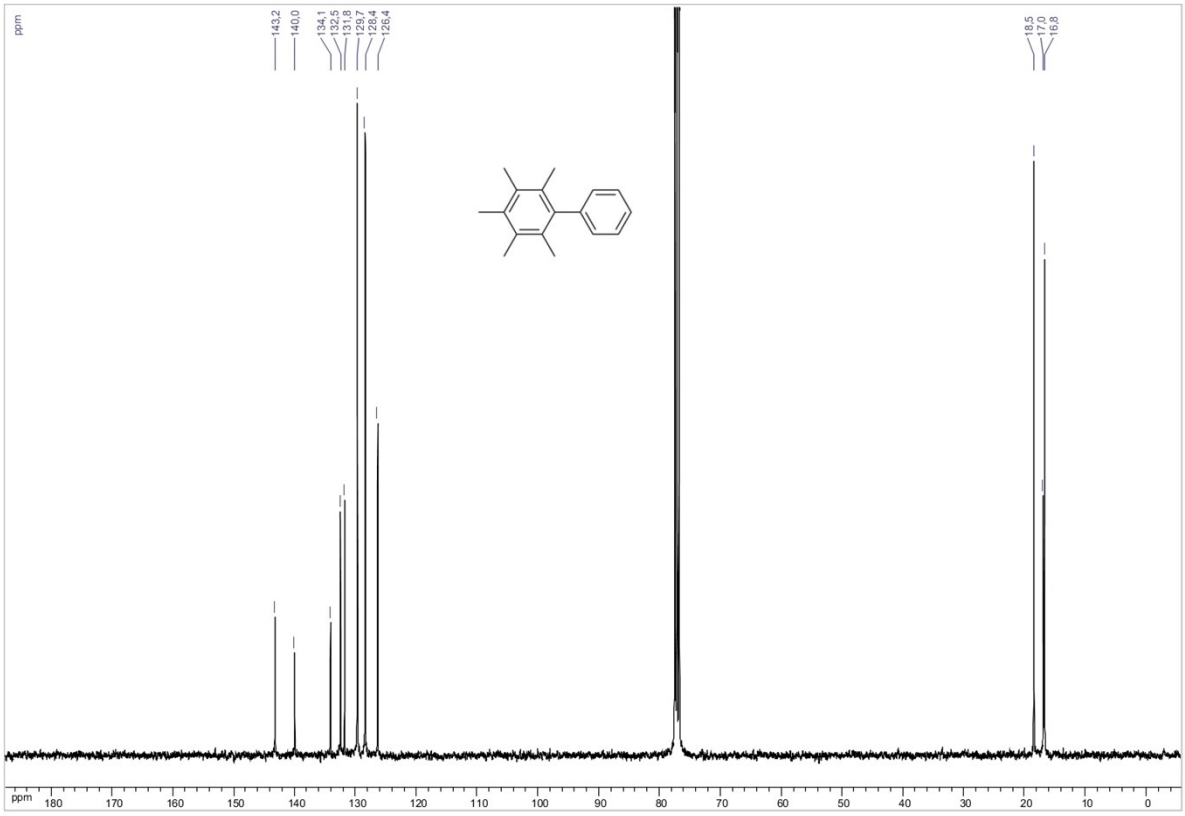
2-fluoro-1,1’-biphenyl



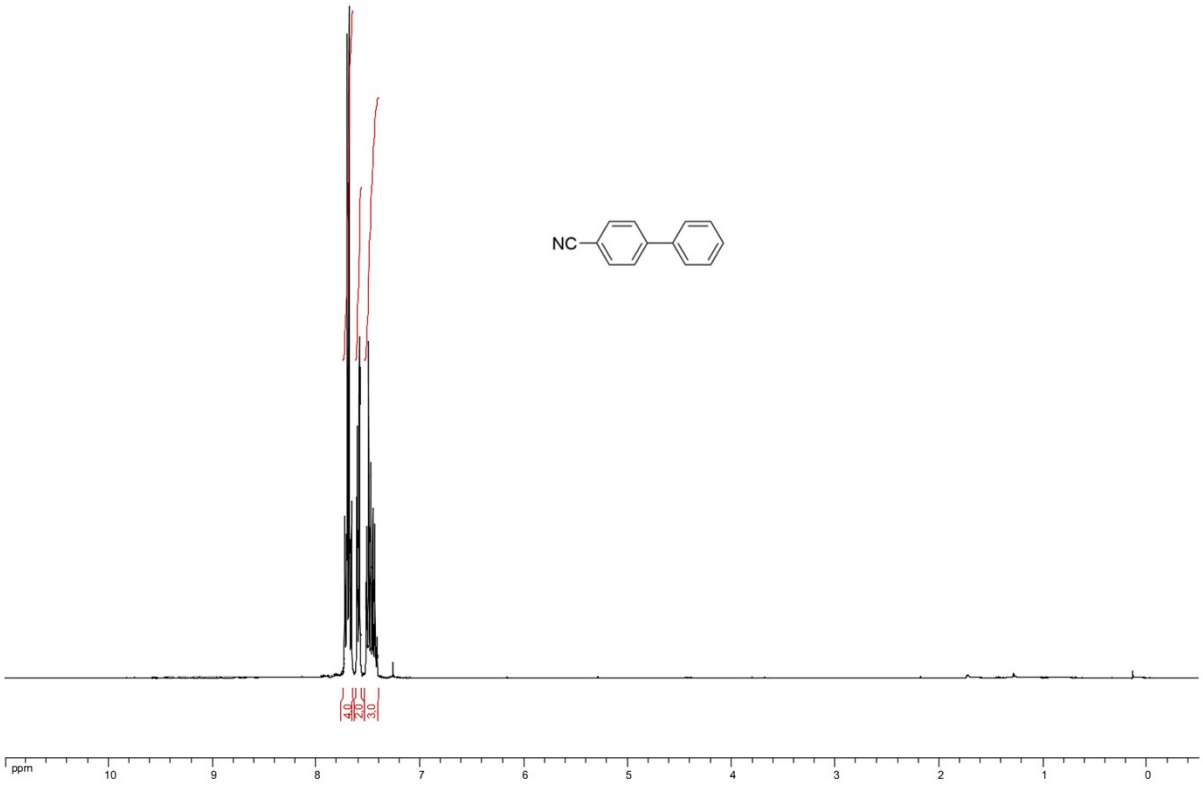


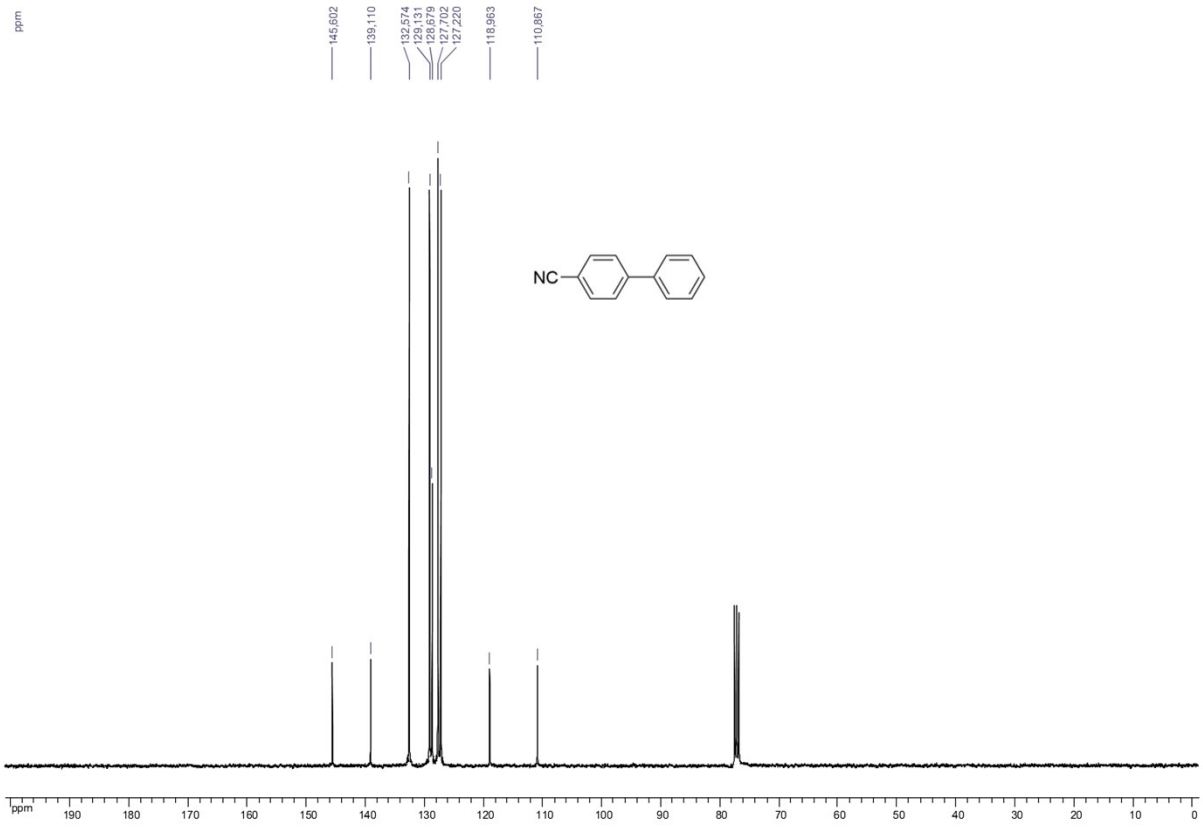
2,3,4,5,6-pentamethyl-1,1’-biphenyl



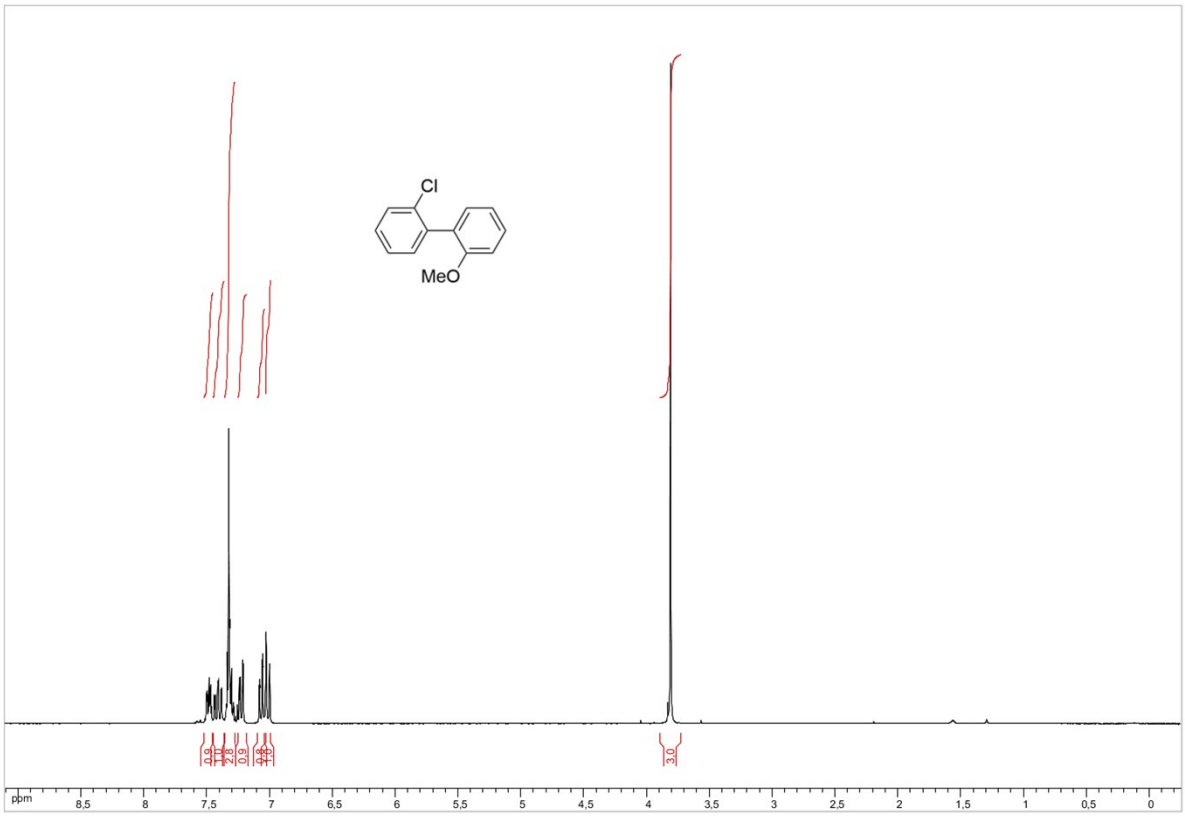


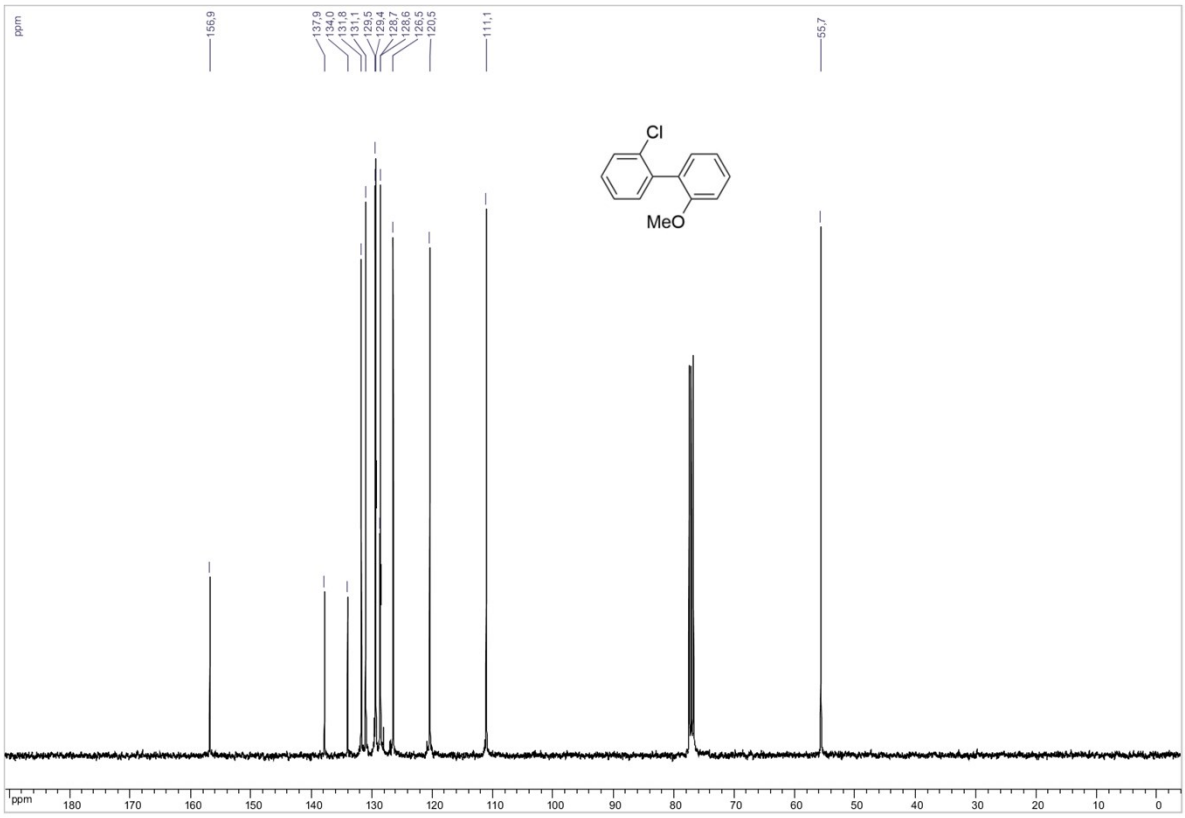
[1,1’-biphenyl]-4-carbonitrile



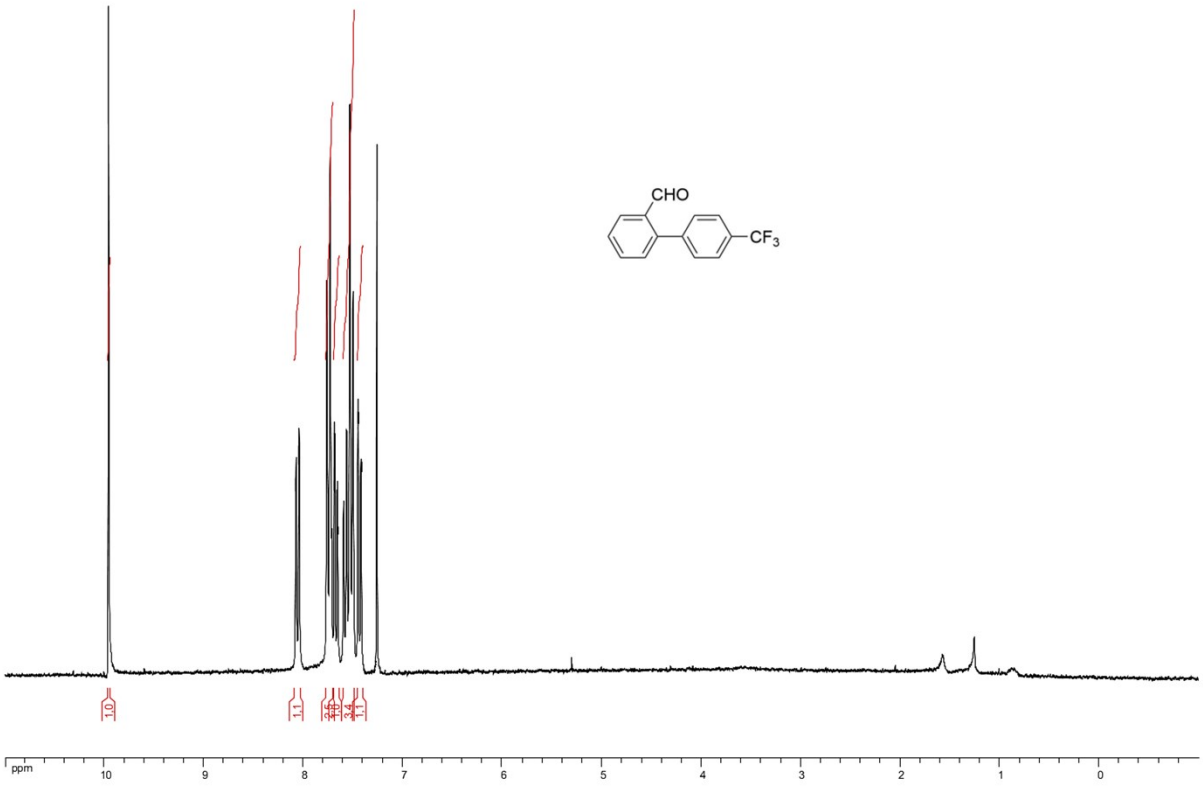


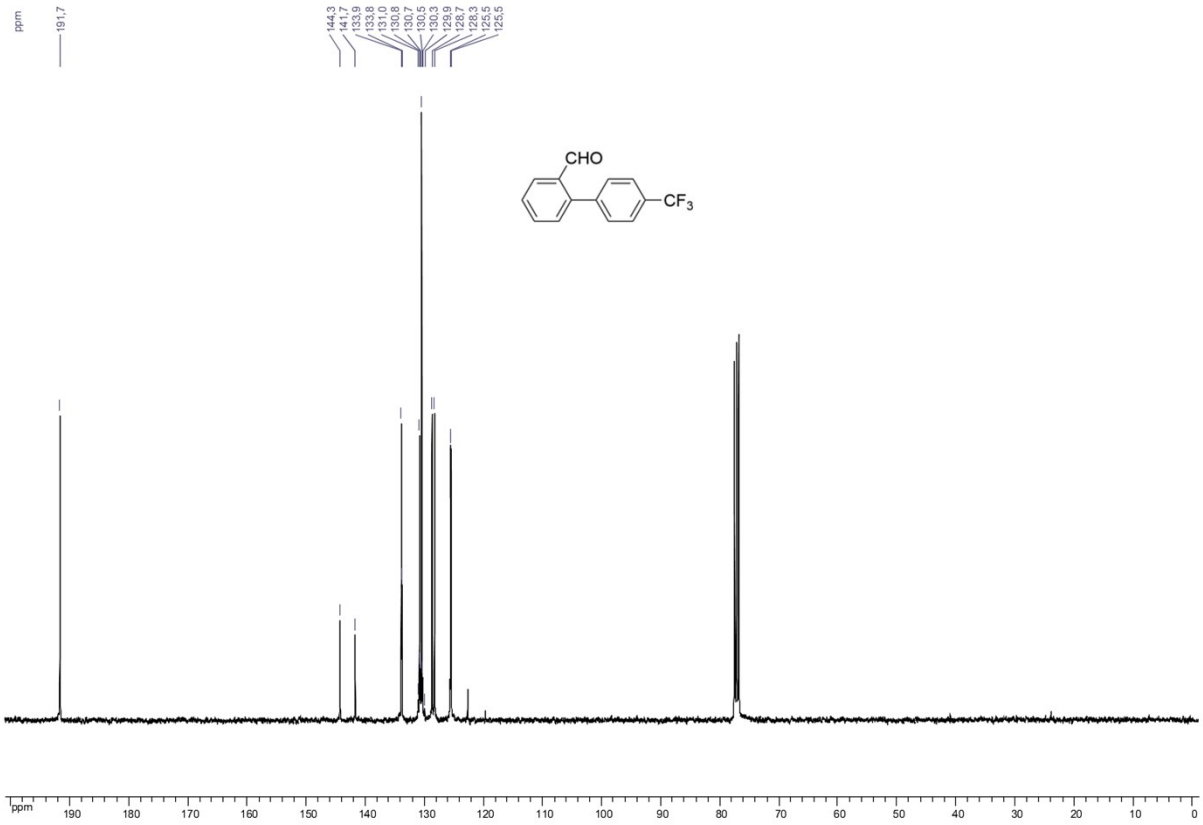
2-chloro-2'-methoxy-1,1'-biphenyl



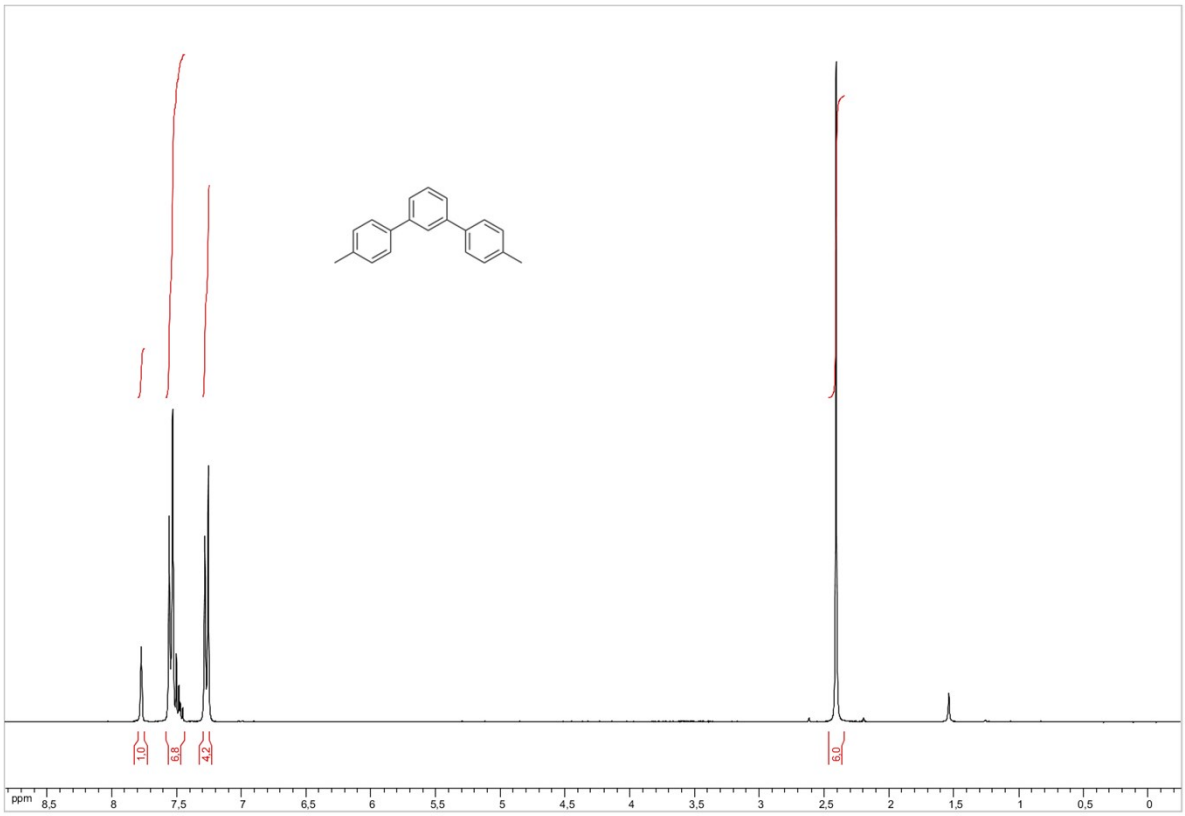


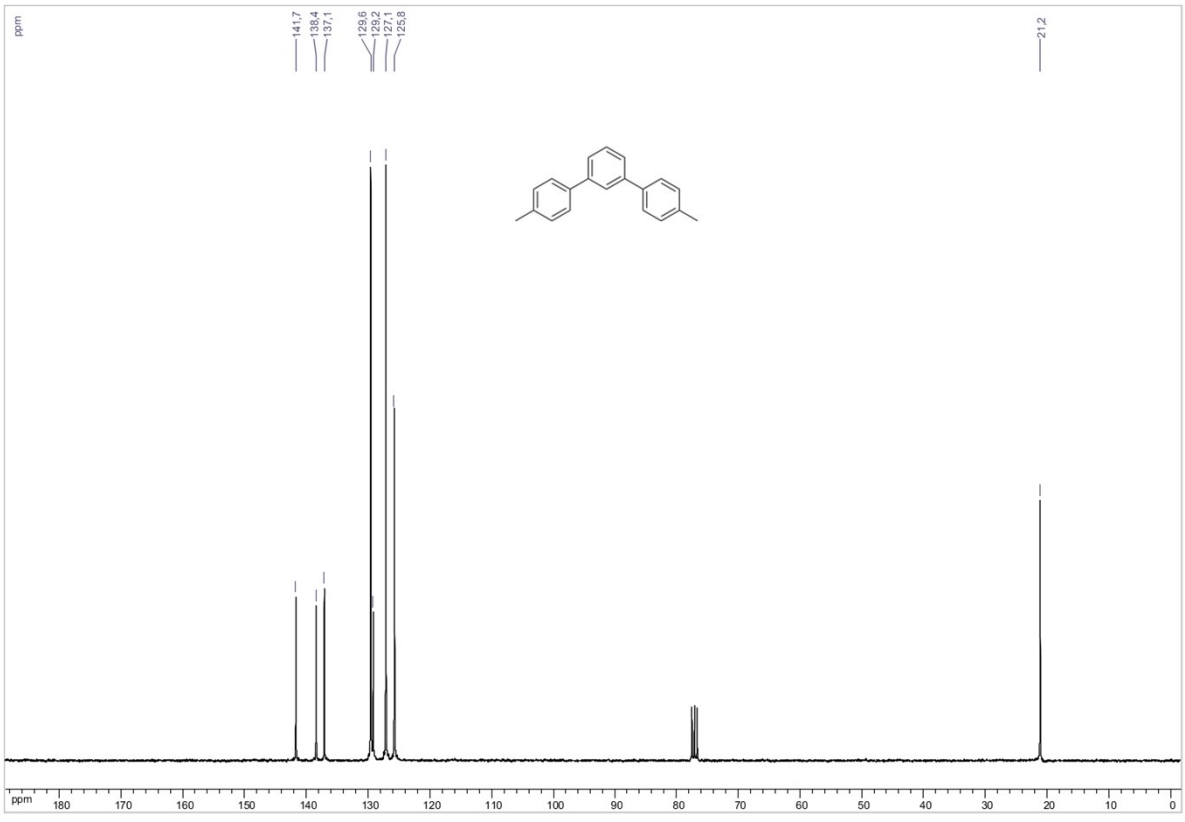
4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxaldehyde



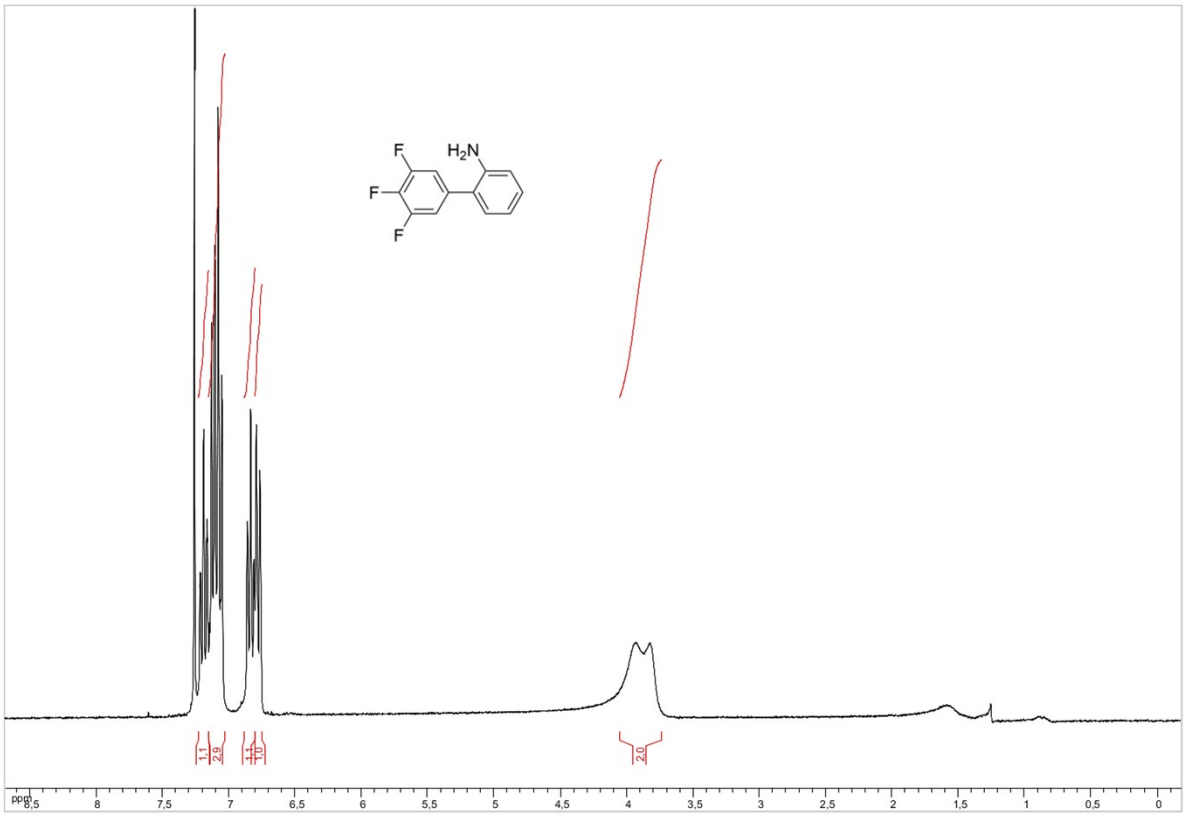


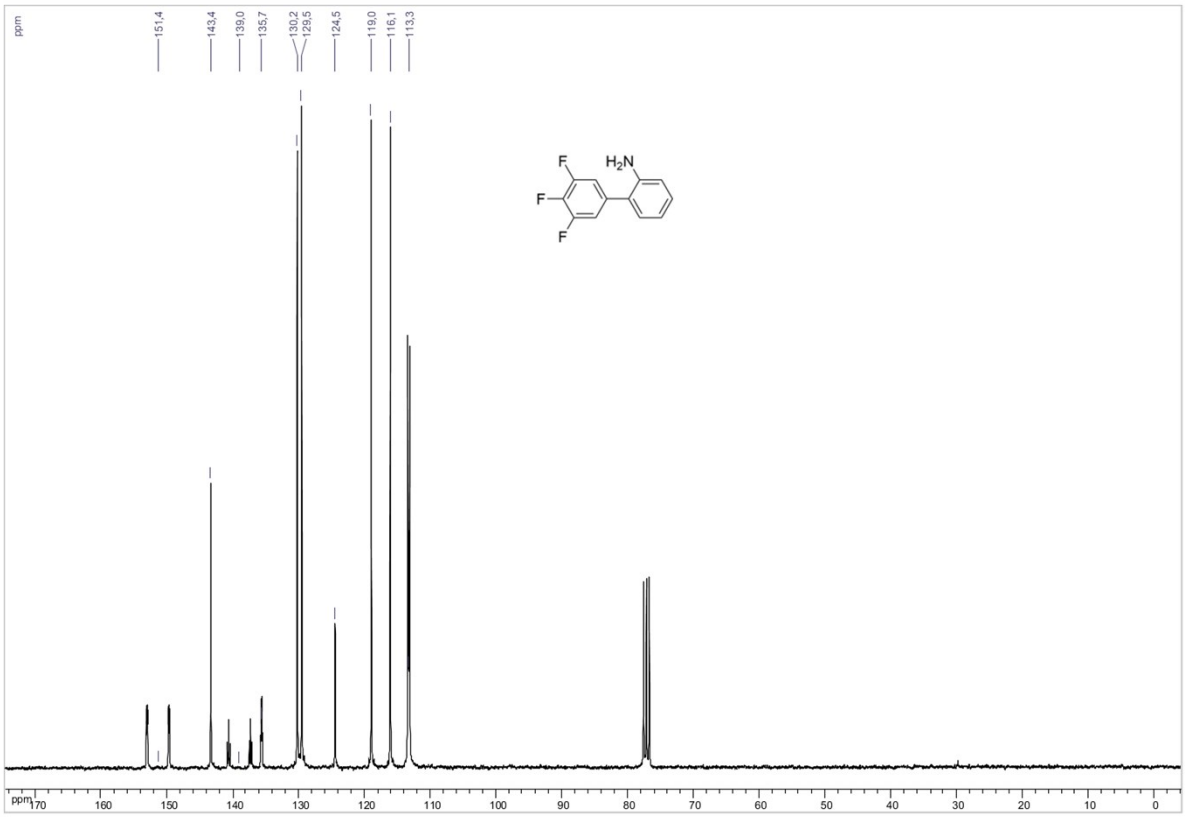
4,4''-dimethyl-1,1':3',1''-terphenyl





3',4',5'-trifluoro-[1,1'-biphenyl]-2-amine





4-(pyridin-2-yl)benzaldehyde