Supporting Information

$P(NMe_2)_3$ mediated cyclopropanation of α-methylene-β-lactams for a rapid synthesis of spirocyclopropyl β-lactams

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General Information

Unless otherwise indicated, chemicals and solvents were purchased from commercial suppliers or purified by standard techniques.

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker (600 MHz) spectrometer. All chemical shifts (δ) were given in ppm. Data were reported as follows: chemical shift, integration, multiplicity (s = single, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet) and coupling constants (Hz). ^{19}F NMR spectra were recorded on a Bruker (600 MHz) spectrometer ($CFCl_3$ as outside standard and low field is positive).

Flash column chromatography was performed using H silica gel. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light.

Melting points were determined on a SGW X-4 melting point and were uncorrected.

Mass spectra analysis was performed on Agilent technologies 5973N and Waters Synapt G2 Si.

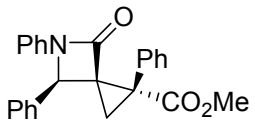
α-methylene-β-lactams were prepared according to the literature procedure[1,2,3] and stored at 4 ℃ prior to use. All α-keto esters were prepared following reported procedures[4] or purchased from commercial suppliers. All reactions were carried out employing oven dried glassware.

Procedure for the cyclopropanation reaction of α-methylene-β-lactams and α-keto ester

Conditions at RT: To a stirred solution of α-methylene-β-lactam **2** (0.2 mmol) and α-keto ester **1** (0.4 mmol) in THF (2 mL) was added $P(NMe_2)_3$ (72 μL, 0.4 mmol) by microsyringe. Then the resulting mixture was vigorously stirred at R.T. and monitored by TLC. After the reaction was completed, the mixture was directly purified by preparative TLC chromatography on silica gel (petroleum ether/ethyl acetate = 6/1 as the eluent) to furnish the corresponding product.
Conditions at 60 ℃: To a stirred solution of α-methylene-β-lactam **2** (0.2 mmol) and α-keto ester **1** (0.4 mmol) in THF (2 mL) was added $P(NMe_2)_3$ (72 μL, 0.4 mmol) by microsyringe. Then the resulting mixture was vigorously stirred and warmed to 60 ℃. After the reaction was complete, the mixture was allowed cool to RT and directly purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1 as the eluent) to furnish the corresponding product.

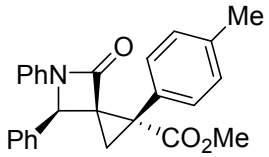
The two diastereoisomer mixtures generally were difficult to be purified sufficiently to obtain satisfying NMR spectra for minor diastereoisomers. For **3e**, two diastereoisomer was purified as well as possible. For **3a-3n** and **3ac**, the data of major diastereoisomers was provided. For **3ab** and **3ad**, they are inseparable diastereoisomer mixture.

***trans*-methyl 4-oxo-1,5,6-triphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3a)**



Major diastereoisomer, R_f = 0.60 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 165-167 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.37-7.35 (m, 3H), 7.34-7.32 (m, 3H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.23 (t, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 5.34 (s, 1H), 3.71 (s, 3H), 2.07 (d, *J* = 5.5 Hz, 1H), 1.63 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.9, 165.2, 137.6, 136.1, 133.9, 130.4, 129.0, 128.8, 128.6, 128.2, 128.1, 127.6, 123.6, 116.9, 61.9, 52.8, 52.1, 39.7, 20.7; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{21}NO_3)$ requires 383.1521, found 383.1525.

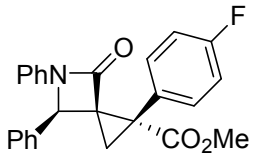
***trans*-methyl 4-oxo-5,6-diphenyl-1-(p-tolyl)-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3b)**



Major diastereoisomer, R_f = 0.55 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 159-162 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.23-7.21 (m, 4H), 7.17 (d, *J* = 7.4 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 5.33 (s, 1H), 3.70 (s, 3H), 2.36 (s, 3H), 2.04 (d, *J* = 6.1 Hz, 1H), 1.61 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.1, 165.3, 137.8, 137.6, 136.1, 130.9 130.2, 129.0, 128.9,

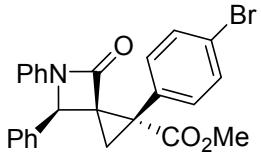
128.8, 128.6, 127.6, 123.6, 116.9, 61.9, 52.8, 52.2, 39.5, 21.3, 20.8; HRMS (ESI): calcd. For $[M]^+(C_{26}H_{23}NO_3)$ requires 397.1678, found 397.1673.

***trans*-methyl 1-(4-fluorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3c)**



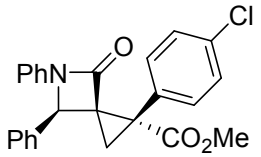
Major diastereoisomer, R_f = 0.51 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 182-185 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.28 (t, *J* = 7.9 Hz, 1H), 7.30-7-27 (m, 4H), 7.23 (t, *J* = 7.9 Hz, 2H), 7.05-7-02 (m, 3H), 5.31 (s, 1H), 3.70 (s, 3H), 2.01 (d, *J* = 5.4 Hz, 1H), 1.63 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.7, 165.1, 163.2 (d, $J_{C\text{-}F}$ = 247 Hz), 137.5, 135.9, 132.2 (d, $J_{C\text{-}F}$ = 7.8 Hz), 129.8, 129.1, 128.8, 128.7, 127.6, 123.8, 116.9, 115.3 (d, $J_{C\text{-}F}$ = 22.9 Hz), 61.9, 52.9, 52.1, 38.9, 20.9; ^{19}F NMR ($CDCl_3$, 564 MHz) δ -113.7; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{20}FNO_3)$ requires 401.1427, found 401.1428.

***trans*-methyl 1-(4-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3d)**



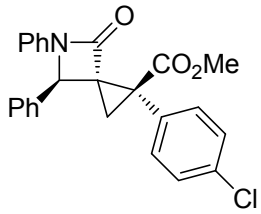
Major diastereoisomer, R_f = 0.47 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 162-165 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.1, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 5.32 (s, 1H), 3.71 (s, 3H), 2.01 (d, *J* = 5.5 Hz, 1H), 1.64 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.4, 164.9, 137.5, 135.8, 133.0, 132.1, 131.4, 129.1, 128.8, 128.7, 127.6, 123.8, 122.3, 116.9, 61.8, 52.9, 52.0, 39.0, 20.7; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{20}BrNO_2)$ requires 461.0627, found 461.0628.

***trans*-methyl 1-(4-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3e)**



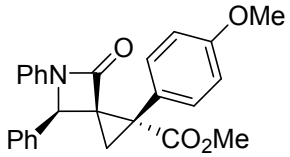
Major diastereoisomer, R_f = 0.49 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 182-185 °C; ^{1}H NMR (600 MHz, $CDCl_3$) 7.46 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.03 (t, *J* = 7.4 Hz, 1H), 5.31 (s, 1H), 3.70 (s, 3H), 2.01 (d, *J* = 6.2 Hz, 1H), 1.63 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.5, 164.9, 137.5, 135.8, 134.0, 132.5, 131.8, 129.1, 128.8, 128.7, 128.5, 127.6, 123.8, 116.9, 61.9, 52.9, 52.1, 38.9, 20.7; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{20}ClNO_3)$ requires 417.1132, found 417.1131.

***cis*-methyl 1-(4-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*cis*-3e)**



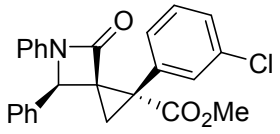
Minor diastereoisomer, R_f = 0.47 (petroleum ether/ethyl acetate, 80:20); Colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) 7.44-7.39 (m, 4H), 7.28-7.25 (m, 7H), 7.08-7.04 (m, 1H), 6.74-6.72 (m, 2H), 4.81 (s, 1H), 3.79 (s, 3H), 2.47 (d, *J* = 6.3 Hz, 1H), 1.29 (d, *J* = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.3, 165.5, 137.7, 135.0, 134.3, 133.3, 131.9, 129.1, 129.0, 128.9, 128.7, 126.4, 123.8, 116.8, 60.4, 52.9, 51.1, 38.5, 17.8; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{20}ClNO_3)$ requires 417.1132, found 417.1133.

***trans*-methyl 1-(4-methoxyphenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3f)**



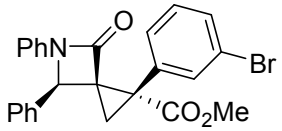
Major diastereoisomer, R_f = 0.41 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 133-135 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) 7.47 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 8.3 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 5.32 (s, 1H), 3.81 (s, 3H), 3.71 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 1H), 1.62 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.2, 165.3, 159.2, 137.6, 136.1, 131.5, 129.0, 128.8, 128.6, 127.6, 126.0, 123.6, 116.9, 113.6, 61.9, 55.1, 52.8, 52.2, 39.1, 20.9; HRMS (EI): calcd. For $[M]^+(C_{26}H_{23}NO_4)$ requires 413.1627, found 413.1625.

***trans*-methyl 1-(3-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3g)**



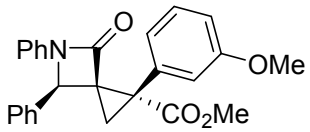
Major diastereoisomer, R_f = 0.51 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 128-130 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) 7.46 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.32-7.30 (m, 3H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 5.32 (s, 1H), 3.71 (s, 3H), 2.04 (d, *J* = 6.3 Hz, 1H), 1.63 (d, *J* = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.3, 164.7, 137.5, 135.9, 135.8, 133.9, 130.5, 129.4, 129.1, 128.8, 128.7, 128.4, 127.6, 123.8, 116.9, 61.8, 52.9, 52.1, 39.1, 20.6; HRMS (EI): calcd. For $[M]^+(C_{25}H_{20}ClNO_3)$ requires 417.1132, found 417.1131.

***trans*-methyl 1-(3-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3h)**



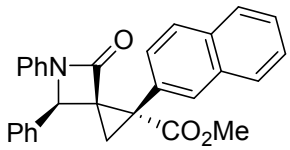
Major diastereoisomer, R_f = 0.44 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 132-135 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (t, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.1 Hz, 1H), 7.28-7.26 (m, 3H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 5.31 (s, 1H), 3.71 (s, 3H), 2.03 (d, *J* = 5.5 Hz, 1H), 1.62 (d, *J* = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.3, 164.7, 137.5, 136.2, 135.8, 133.3, 131.3, 129.6, 129.3, 129.1, 128.8, 128.7, 127.6, 123.8, 122.1, 116.9, 61.8, 52.9, 52.1, 39.1, 20.6; HRMS (EI): calcd. For $[M]^+$($C_{25}H_{20}BrNO_3$) requires 461.0627, found 461.0623.

***trans*-methyl 1-(3-methoxyphenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3i)**



Major diastereoisomer, R_f = 0.40 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 123-125 °C; ^{1}H NMR (600 MHz, $CDCl_3$) 7.47 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.1 Hz, 1H), 7.29-7.26 (m, 3H), 7.22 (t, *J* = 7.4 Hz, 2H), 7.01 (t, *J* = 7.0 Hz, 1H), 6.93 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.86 (s, 1H), 5.33 (s, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 2.05 (d, *J* = 5.0 Hz, 1H), 1.60 (d, *J* = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.8, 165.1, 159.2, 137.6, 136.1, 135.3, 129.1, 129.0, 128.8, 128.6, 127.6, 123.6, 122.9, 116.9, 116.5, 113.2, 61.9, 55.2, 52.8, 52.2, 39.7, 20.7; HRMS (ESI): calcd. For $[M]^+$($C_{26}H_{23}NO_4$) requires 413.1627, found 413.1625.

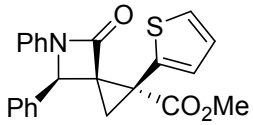
***trans*-methyl 1-(naphthalen-2-yl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3j)**



Major diastereoisomer, R_f = 0.43 (petroleum ether/ethyl acetate, 80:20); Light yellow solid. m.p. = 150-152 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.82 (d, *J* = 6.4 Hz, 1H), 7.78 (s, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.48-7.45 (m, 2H), 7.43 (d, *J* = 9.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.03 (t, *J* = 7.0 Hz, 1H), 5.39 (s, 1H), 3.70 (s, 3H), 2.20 (d, *J* = 5.4 Hz, 1H), 1.71 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.9, 165.1, 137.6, 136.1, 133.1, 133.0, 131.5, 129.2, 129.0, 128.8, 128.4, 128.1, 127.8, 127.7, 126.2, 126.1, 123.7, 116.9, 61.9, 52.9, 52.2, 39.9, 20.9; HRMS (ESI): calcd. For $[M]^+$($C_{29}H_{23}NO_3$) requires 433.1678, found 433.1675.

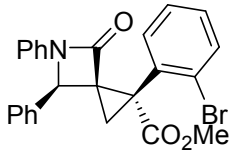
***trans*-methyl 4-oxo-5,6-diphenyl-1-(thiophen-2-yl)-5-azaspiro[2.3]hexane-1-carboxylate**

(*trans*-3k)



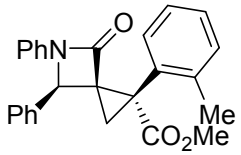
Major diastereoisomer, R_f = 0.40 (petroleum ether/ethyl acetate, 80:20); Light yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 4.8 Hz, 1H), 7.27-7.25 (m, 4H), 7.23-7.20 (m, 3H), 7.04-7.01 (m, 2H), 6.93 (d, *J* = 3.3 Hz, 1H), 6.86 (d, *J* = 4.7 Hz, 2H), 4.84 (s, 1H), 3.82 (s, 3H), 2.56 (d, *J* = 6.5 Hz, 1H), 1.48 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.8, 165.1, 137.6, 137.4, 135.3, 129.1, 128.9, 128.7, 127.8, 126.7, 126.5, 123.8, 116.8, 60.6, 52.9, 52.5, 34.6, 19.1; HRMS (ESI): calcd. For $[M]^+(C_{23}H_{19}NO_3S)$ requires 389.1086, found 389.1083.

***trans*-methyl 1-(2-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3l)**



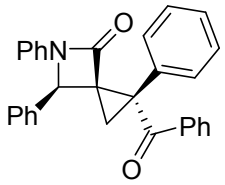
Major diastereoisomer, R_f = 0.63 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 172-175 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.31 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.23 (t, *J* = 8.1 Hz, 1H), 7.22 (t, *J* = 8.2 Hz, 2H), 7.01 (t, *J* = 7.3 Hz, 1H), 5.53 (s, 1H), 3.69 (s, 3H), 2.10 (d, *J* = 5.3 Hz, 1H), 1.59 (s,1H) (overlap with water peak); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.2, 165.1, 137.8, 136.2, 132.5, 131.0, 129.9, 129.6, 129.0, 128.8, 128.5, 127.8, 127.5, 123.6, 116.9, 61.7, 52.9, 52.8, 39.9, 22.6; HRMS (ESI): calcd. For $[M]^+(C_{25}H_{20}BrNO_3)$ requires 461.0627, found 461.0621.

***trans*-methyl 4-oxo-5,6-diphenyl-1-(o-tolyl)-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3m)**



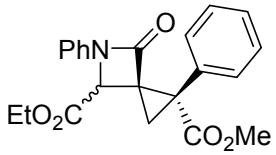
Major diastereoisomer, R_f = 0.43 (petroleum ether/ethyl acetate, 80:20); White solid. m.p. = 173-176 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.42 (t, *J* = 8.2 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.28-7.26 (m, 3H), 7.22-7.21 (m, 3H), 7.20 (t, *J* = 7.0 Hz, 2H), 7.02 (t, *J* = 7.0 Hz, 1H), 5.41 (s, 1H), 3.69 (s, 3H), 2.25 (s, 3H), 2.07 (d, *J* = 4.9 Hz, 1H), 1.60 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.1, 165.4, 138.5, 137.6, 136.1, 132.8, 130.1, 129.9, 129.0, 128.8, 128.6, 128.3, 127.7, 125.9, 123.6, 116.9, 61.8, 52.8, 52.7, 38.5, 21.5, 19.3; HRMS (ESI): calcd. For $[M]^+(C_{26}H_{23}NO_3)$ requires 397.1678, found 397.1672.

***trans*-1-benzoyl-1,5,6-triphenyl-5-azaspiro[2.3]hexan-4-one (*trans*-3n)**



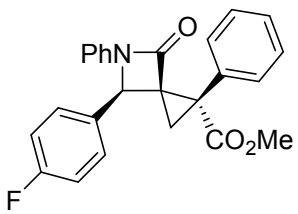
Major diastereoisomer, R_f = 0.37 (petroleum ether/ethyl acetate, 80:20); Light yellow solid. m.p. = 147-149 ^oC; ^1H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.3 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.33-7.30 (m, 5H), 7.27 (d, *J* = 6.9 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 1H), 5.92 (s, 1H), 2.38 (d, *J* = 5.5 Hz, 1H), 1.43 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 196.9, 165.9, 137.8, 136.0, 135.9, 134.8, 132.8, 129.4, 128.9, 128.8, 128.7, 128.5, 128.3, 127.8, 127.3, 123.5, 116.9, 60.5, 51.3, 43.7, 19.4; HRMS (ESI): calcd. For $[M]^+(C_{30}H_{23}NO_2)$ requires 429.1729, found 429.1726.

4-ethyl 1-methyl 6-oxo-1,5-diphenyl-5-azaspiro[2.3]hexane-1,4-dicarboxylate (3ab)



Inseparable diastereoisomer mixture with a ratio of 1.4/1, R_f = 0.53 (petroleum ether/ethyl acetate, 80:20); Colorless oil; ^1H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.3 Hz, 1H; both isomers, ArH), 7.42 (d, *J* = 6.3 Hz, 1H; major, ArH), 7.39 (d, *J* = 7.7 Hz, 1H; minor, ArH), 7.37-7.33 (m, 3H; both isomers, ArH), 7.33-7.31 (m, 2H; both isomers, ArH), 7.31-7.30 (m, 2H; minor, ArH), 7.29 (t, *J* = 7.3 Hz, 2H; major, ArH), 7.11 (t, *J* = 7.0 Hz, 1H; major, ArH), 7.10 (t, *J* = 7.3 Hz, 1H; minor, ArH), 4.81 (s, 1H; major, C**H**CO_2Et), 4.31 (s, 1H; minor, C**H**CO_2Et), 4.35-4.30 (m, 2H; major, $CO_2C\mathbf{H_2}CH_3$), 4.14-4.03 (m, 2H; minor, $CO_2C\mathbf{H_2}CH_3$), 3.76 (s, 3H; minor, $CO_2C\mathbf{H_3}$), 3.73 (s, 3H; major, $CO_2C\mathbf{H_3}$), 2.58 (d, *J* = 6.5 Hz, 1H; minor, CC$\mathbf{H_2}$C), 2.20 (d, *J* = 5.9 Hz, 1H; major, CC$\mathbf{H_2}$C), 2.12 (d, *J* = 5.9 Hz, 1H; major, CC$\mathbf{H_2}$C), 1.85 (d, *J* = 6.5 Hz, 1H; minor, CC$\mathbf{H_2}$C), 1.30 (t, *J* = 7.3 Hz, 3H; major, $CO_2CH_2C\mathbf{H_3}$), 1.10 (t, *J* = 6.9 Hz, 3H; minor, $CO_2CH_2C\mathbf{H_3}$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.3, 168.7, 168.4, 168.0, 164.3, 163.9, 137.6, 137.5, 134.1, 133.2, 130.3, 130.0, 129.7, 129.3, 129.2, 129.1, 128.7, 128.5, 128.3, 128.2, 124.2, 124.1, 116.3, 116.1, 116.0, 61.9, 61.7, 58.7, 56.6, 53.0, 48.3, 47.5, 39.0, 38.8, 20.8, 17.3, 14.3, 14.0 (additional peaks and line broadenings are observed due to diastereoisomers); HRMS (ESI): calcd. For $[M]^+(C_{22}H_{21}NO_5)$ requires 379.1420, found 379.1425.

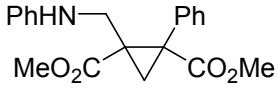
***trans*-methyl 4-(4-fluorophenyl)-6-oxo-1,5-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3ac)**



Major diastereoisomer, R_f = 0.42 (petroleum ether/ethyl acetate, 85:15); White solid. m.p. = 155-

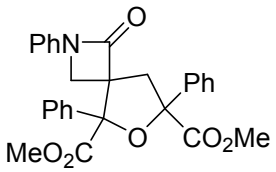
158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.1, 5.0 Hz, 2H), 7.37-7.33 (m, 3H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 8.5 Hz, 2H), 7.03 (td, *J* = 7.3, 1.2 Hz, 1H), 5.33 (s, 1H), 3.70 (s, 3H), 2.05 (d, *J* = 5.6 Hz, 1H), 1.60 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.0, 165.0, 163.6 (d, J_{C-F} = 247 Hz), 137.4, 133.8 (d, J_{C-F} = 2.6 Hz), 131.9 (d, J_{C-F} = 2.9 Hz), 130.4, 129.4 (d, J_{C-F} = 8.8 Hz), 129.1, 128.2, 128.1, 123.8, 116.9, 115.9 (d, J_{C-F} = 22.3 Hz), 61.2, 52.9, 52.2, 39.7, 20.8; ^{19}F NMR ($CDCl_3$, 564 MHz) δ -113.1; HRMS (EI): calcd. For $[M+H]^+(C_{25}H_{20}FNO_3)$ requires 401.1427, found 401.1429.

Dimethyl 1-phenyl-2-((phenylamino)methyl)cyclopropane-1,2-dicarboxylate (3ad)



Inseperable diastereomeric mixture with a ratio of 4.1/1, the *cis*-isomer (minor) underwent a lactamization reaction spontaneously (methyl 4-oxo-3,5-diphenyl-3-azabicyclo[3.1.0]hexane-1-carboxylate), R_f = 0.40 (petroleum ether/ethyl acetate, 85:15); Colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 2H; minor, ArH), 7.47 (d, *J* = 6.2 Hz, 2H; major, ArH), 7.39 (t, *J* = 7.5 Hz, 2H; minor, ArH), 7.36-7.34 (m, 3H; major, ArH), 7.33-7.30 (m, 5H; minor, ArH), 7.17 (t, *J* = 7.2 Hz, 1H; minor, ArH), 7.10 (t, *J* = 7.4 Hz, 2H; major, ArH), 6.68 (t, *J* = 7.0 Hz, 1H; major, ArH), 6.40 (d, *J* = 7.7 Hz, 2H; major, ArH), 4.78 (d, *J* = 10.1 Hz, 1H; minor, N**C**$\mathbf{H_2}$C), 3.88 (d, *J* = 9.7 Hz, 1H; minor, N**C**$\mathbf{H_2}$C), 3.74 (s, 3H; major, $CO_2\mathbf{CH_3}$), 3.64 (s, 3H; major, $CO_2\mathbf{CH_3}$), 3.53 (d, *J* = 13.0 Hz, 1H; major, N**C**$\mathbf{H_2}$C), 3.48 (s, 3H; minor, $CO_2\mathbf{CH_3}$), 2.61 (d, *J* = 6.8 Hz, 1H; minor, C**C**$\mathbf{H_2}$C), 2.61 (d, *J* = 14.0 Hz, 1H; major, N**C**$\mathbf{H_2}$C), 2.32 (d, *J* = 5.6 Hz, 1H; major, C**C**$\mathbf{H_2}$C), 1.69 (d, *J* = 5.1 Hz, 1H; major, C**C**$\mathbf{H_2}$C), 1.61 (d, *J* = 5.5 Hz, 1H; minor, C**C**$\mathbf{H_2}$C); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.7, 170.7, 168.8, 139.0, 134.1, 132.1, 130.2, 130.1, 129.1, 129.0, 128.6, 128.4, 128.3, 128.2, 124.8, 119.7, 118.2, 113.3, 52.7, 52.6, 52.1, 49.4, 46.0, 45.8, 42.2, 36.2, 31.8, 22.8, 22.1 (additional peaks and line broadenings are observed due to isomers); HRMS (EI): calcd. For $[M]^+(C_{20}H_{21}NO_4)$ requires 339.1471, found 339.1470,.

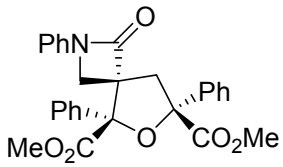
Dimethyl 1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4a)



The tetrahydrofuran product **4** include four diastereoisomers with a ratio of 1.7/1.3/1.2/1 (**4a**/**4b**/**4'**/**4c**), the NMR data of **4a**, **4b** and **4c** was provided as follow. Isomer **4'**, mixed with direct cyclopropanation product (methyl 4-oxo-1,5-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate), can not be purified properly. R_f = 0.53 (petroleum ether/ethyl acetate, 75:25); Colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.4 Hz, 2H), 7.62 (d, *J* = 6.7 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.02 (t, *J* = 7.0 Hz, 1H), 4.21 (d, *J* = 7.6 Hz, 1H), 3.89 (d, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 3.69 (d, *J* = 14.2 Hz, 1H), 3.08 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.0, 171.6, 163.9, 140.3, 137.5, 134.6, 129.0, 128.9, 128.4, 128.3, 128.1, 125.4, 125.3,116.3, 89.7, 86.8, 65.3, 53.1, 52.9, 46.3, 42.9; HRMS (EI): calcd. For

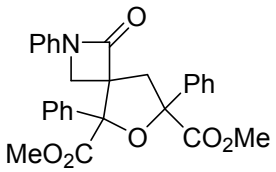
$[M]^+(C_{28}H_{25}NO_6)$ requires 471.1862, found 471.1855.

Dimethyl (4*S,5*R**,7*R**)-1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4b)**



R_f = 0.57 (petroleum ether/ethyl acetate, 75:25); White solid. m.p. = 145-147 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.6 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.36-7.31 (m, 4H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.08 (t, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 3.82 (s, 3H), 3.80 (d, *J* = 13.5 Hz, 1H), 3.24 (d, *J* = 6.1 Hz, 1H), 2.85 (d, *J* = 5.9 Hz, 1H), 2.84 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.3, 170.5, 163.6, 140.9, 137.6, 136.7, 129.1, 128.6, 128.5, 128.2, 126.0, 124.9, 124.3, 116.5, 89.6, 87.2, 64.6, 53.1, 53.0, 49.0, 43.8; HRMS (EI): calcd. For $[M]^+(C_{28}H_{25}NO_6)$ requires 471.1862, found 471.1860.

Dimethyl 1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4c)



R_f = 0.60 (petroleum ether/ethyl acetate, 75:25); Colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.4 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37-7.33 (m, 4H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 3.51 (d, *J* = 13.1 Hz, 1H), 3.41 (d, *J* = 6.1 Hz, 1H), 3.26 (d, *J* = 12.2 Hz, 1H), 3.24 (d, *J* = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.0, 170.2, 163.0, 139.8, 137.6, 136.8, 129.2, 128.3, 128.2, 128.1, 126.1, 125.3, 124.4, 116.6, 89.9, 88.1, 65.7, 52.9, 52.8, 50.0, 43.5; HRMS (EI): calcd. For $[M]^+(C_{28}H_{25}NO_6)$ requires 471.1862, found 471.1856.

References

(1) V. Dočekal, M. Šimek, M. Dračínský and J. Veselý, *Chem. Eur. J.*, 2018, **24**, 13441;

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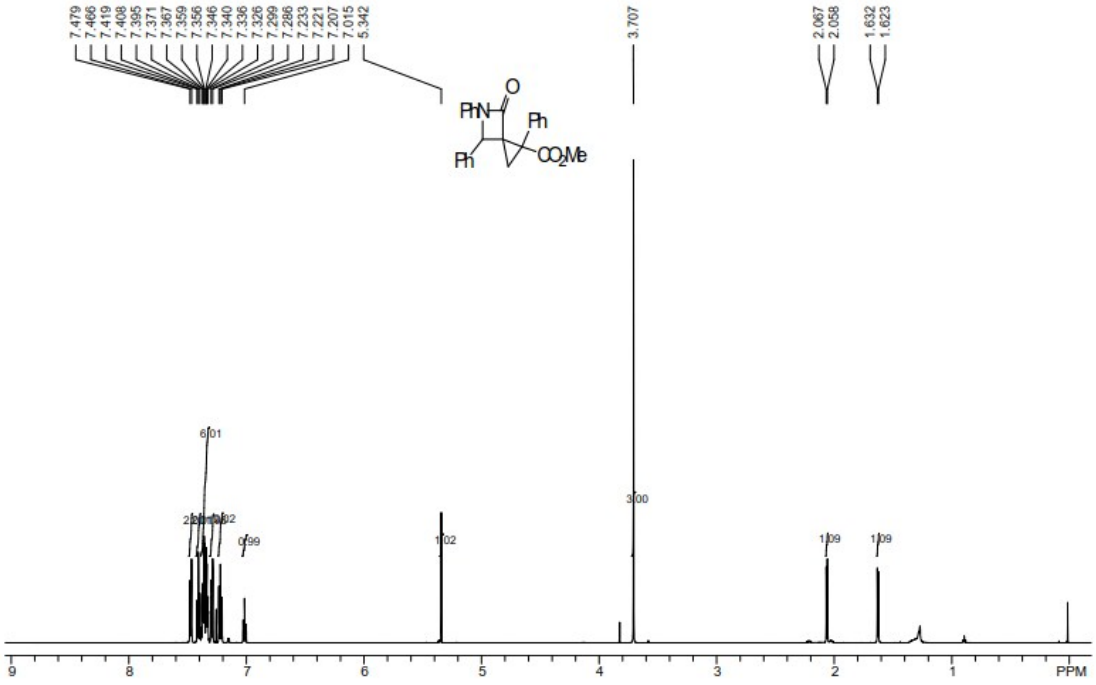
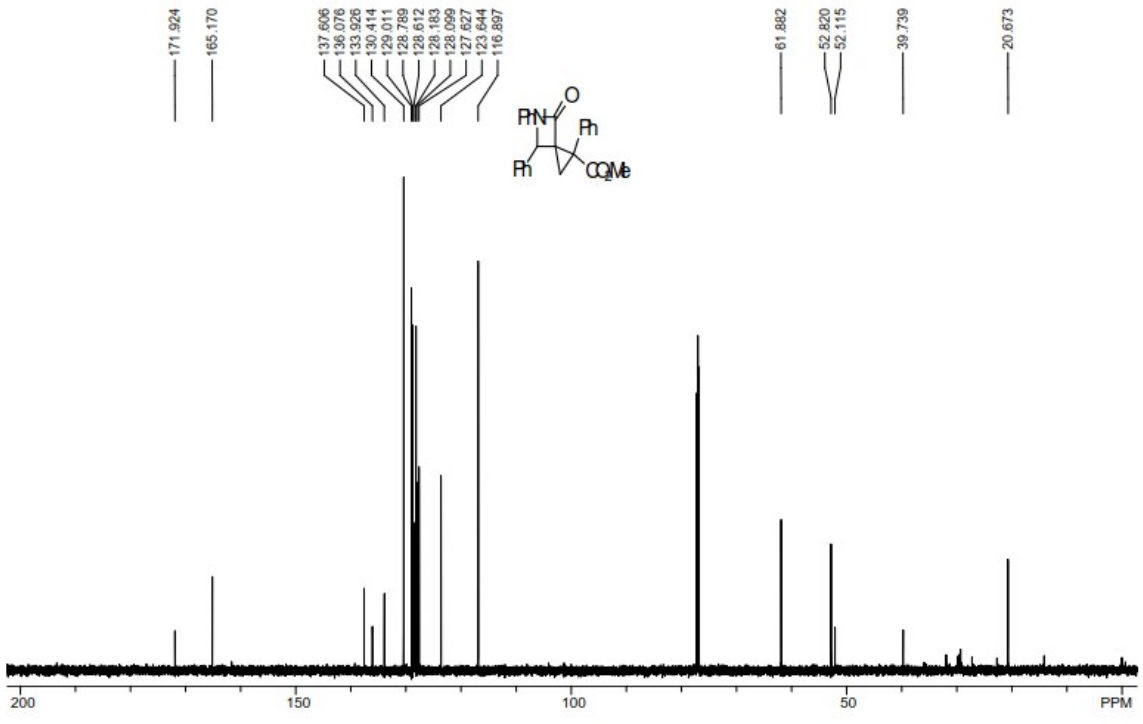
(3) S. R. Fletcher and I. T. Kay, *Journal of the Chemical Society, Chemical Communications*, 1978, **20**, 903;

(4) J. S. Nimitz and H. S. Mosher, *J. Org. Chem.*, 1981, **46**, 211.

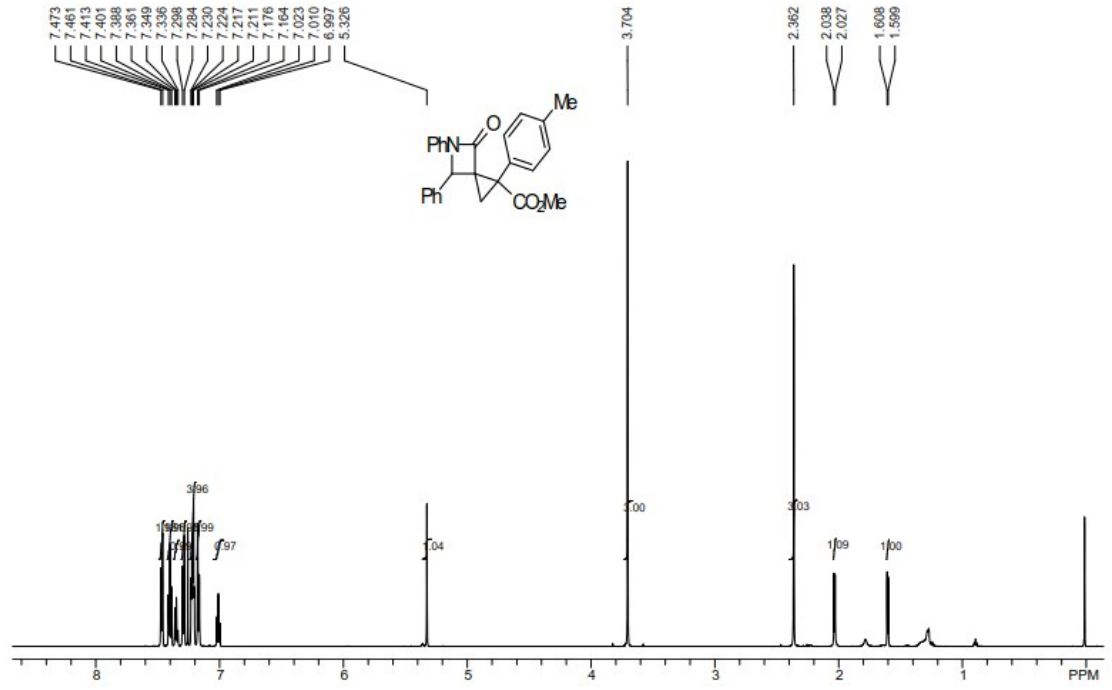
NMR spectra for compounds 3 and 4

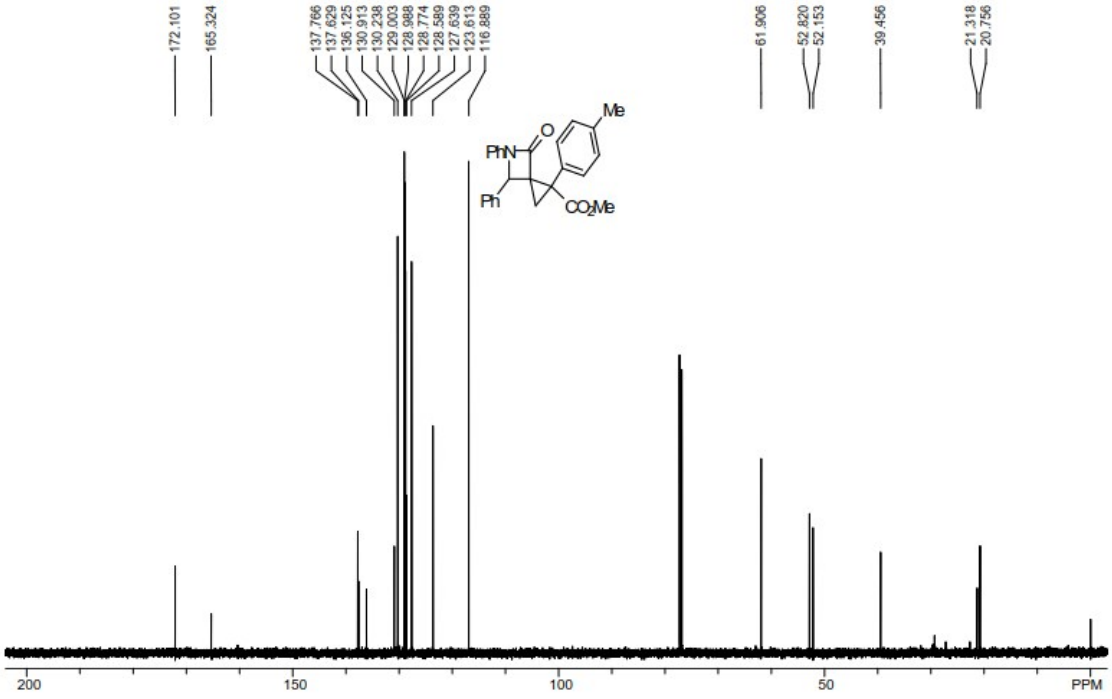
trans-methyl 4-oxo-1,5,6-triphenyl-5-azaspiro[2.3]hexane-1-carboxylate (_trans_-3a)



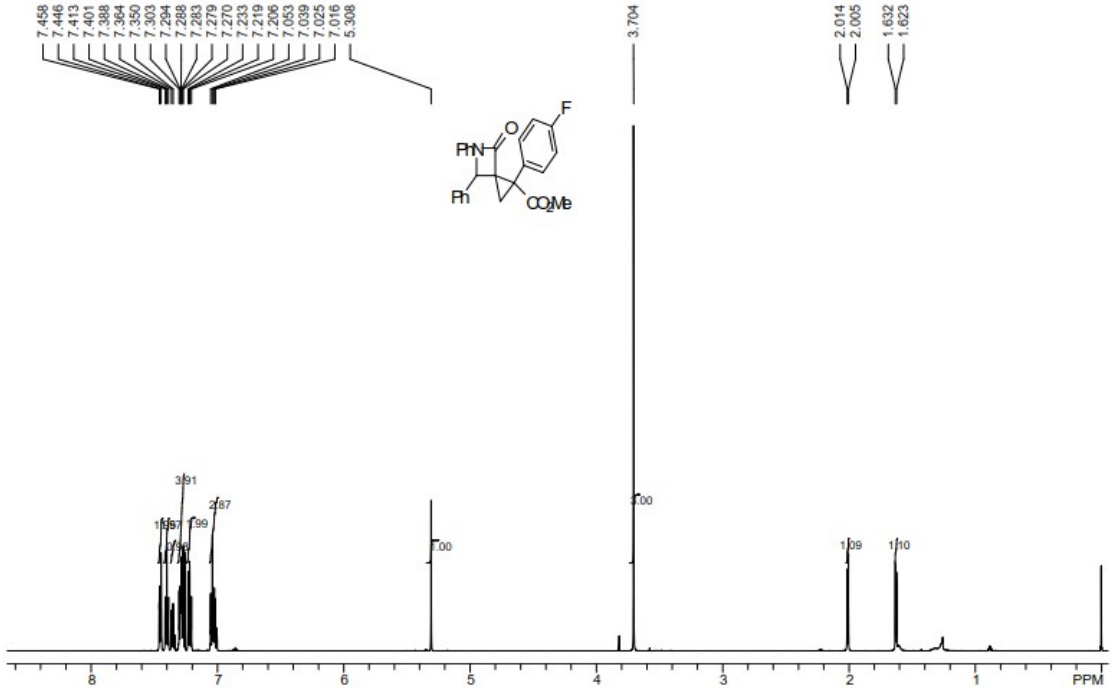


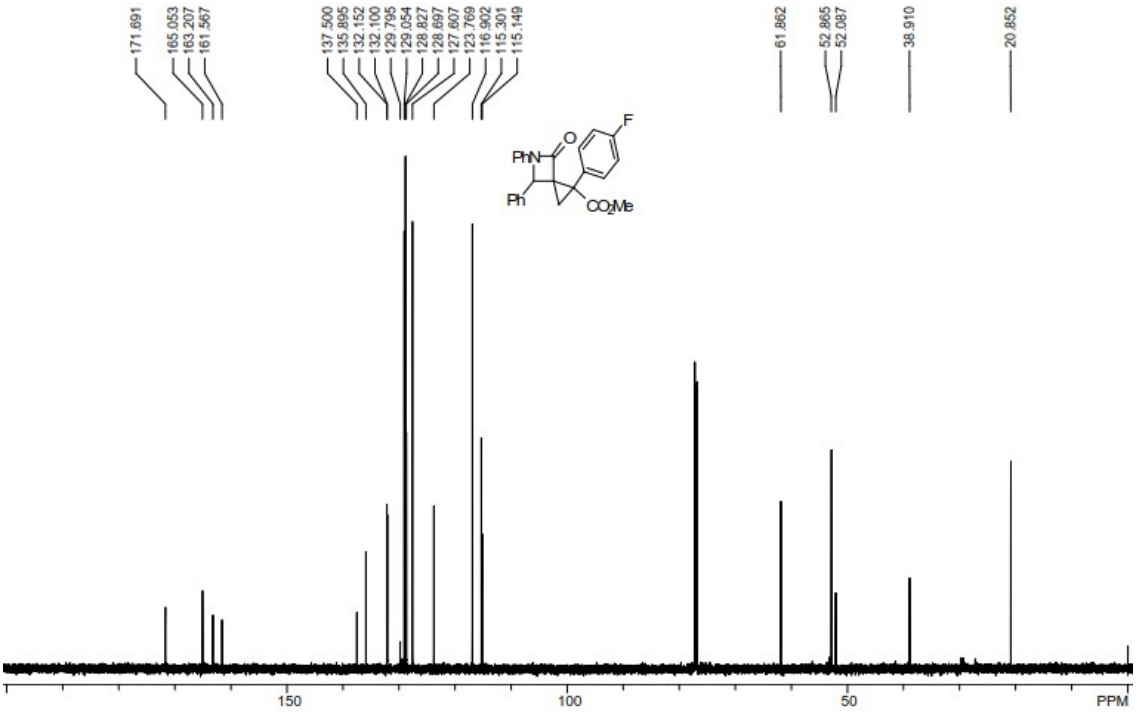
***trans*-methyl 4-oxo-5,6-diphenyl-1-(p-tolyl)-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3b)**



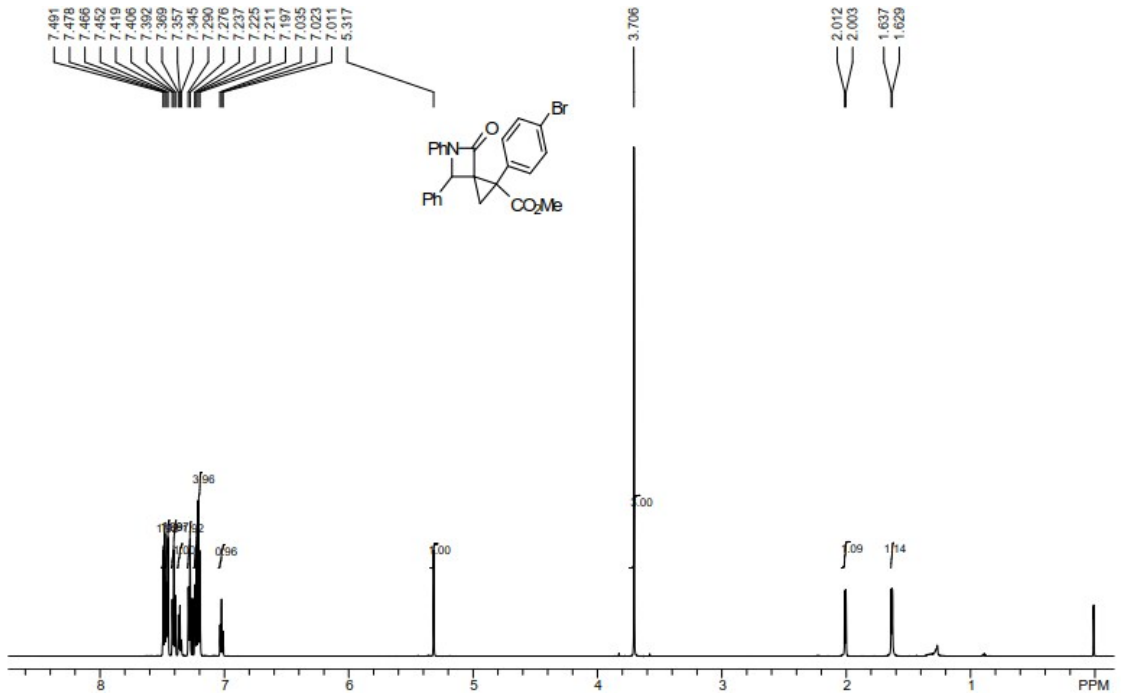


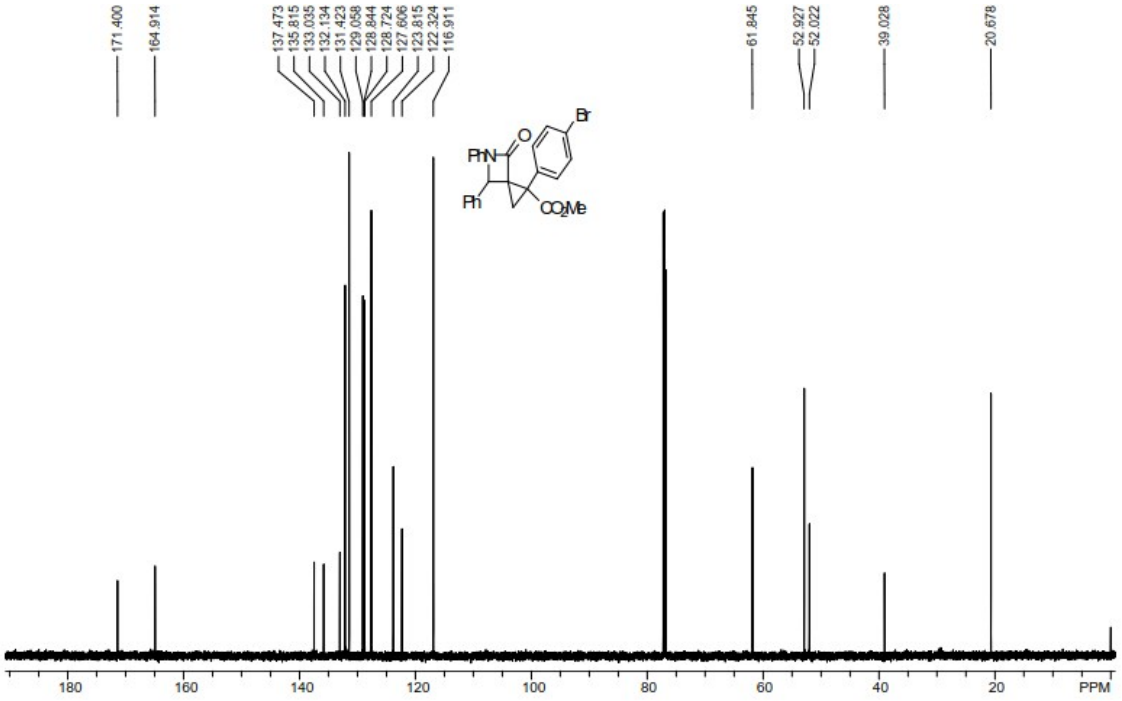
***trans*-methyl 1-(4-fluorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3c)**



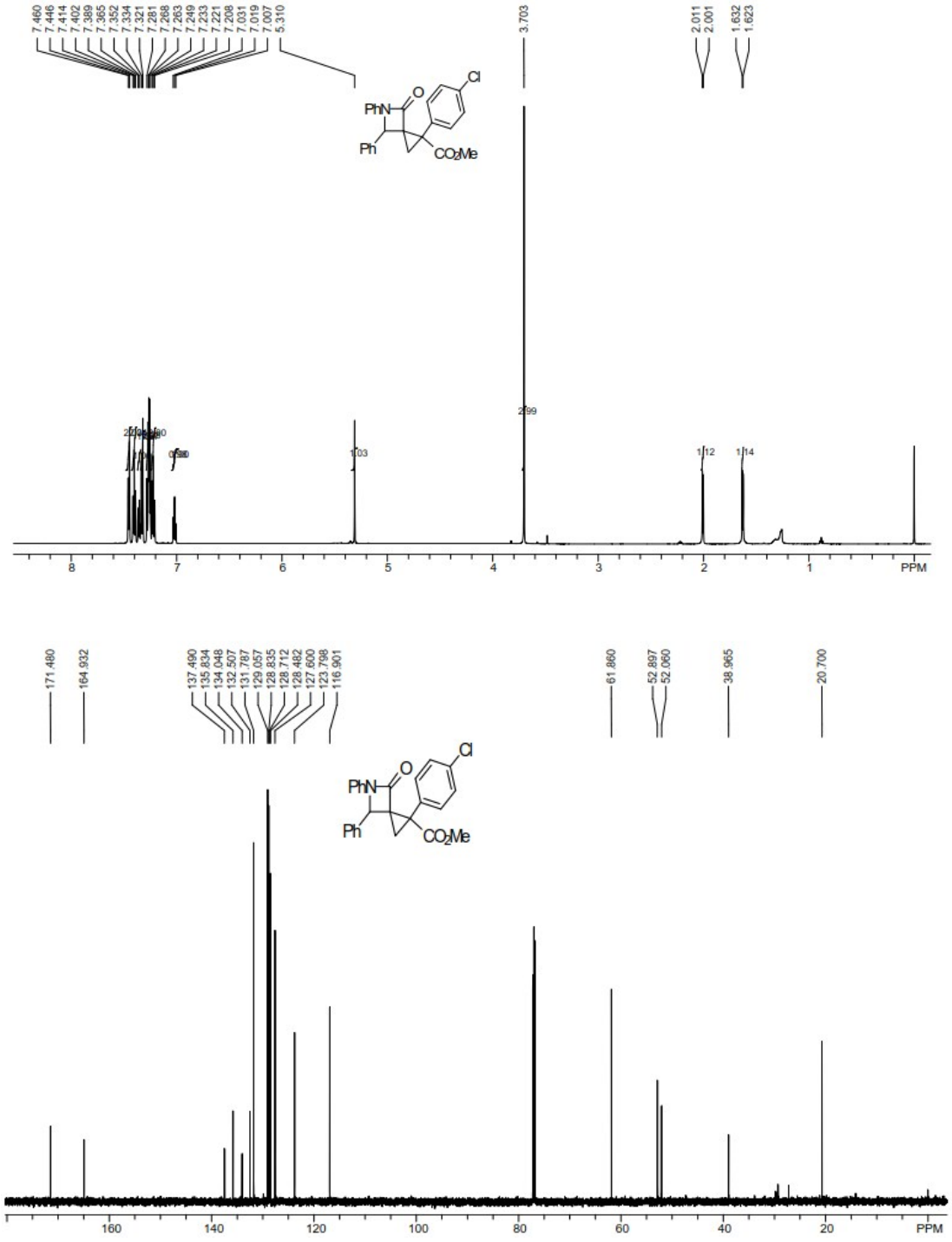


***trans*-methyl 1-(4-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3d)**

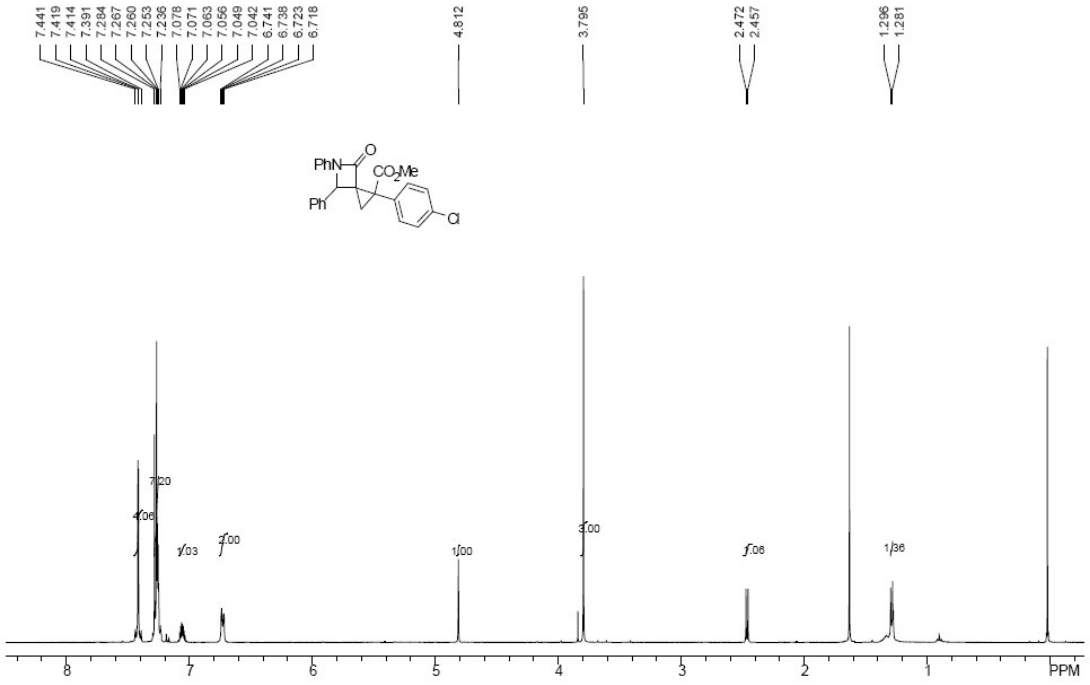


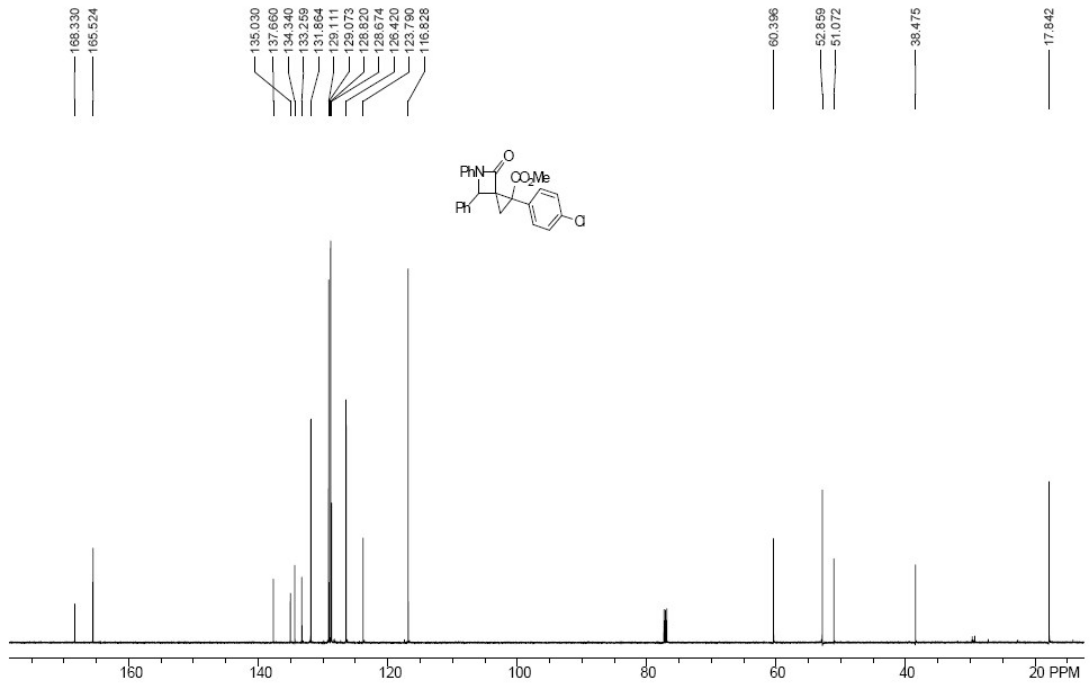


***trans*-methyl 1-(4-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3e)**

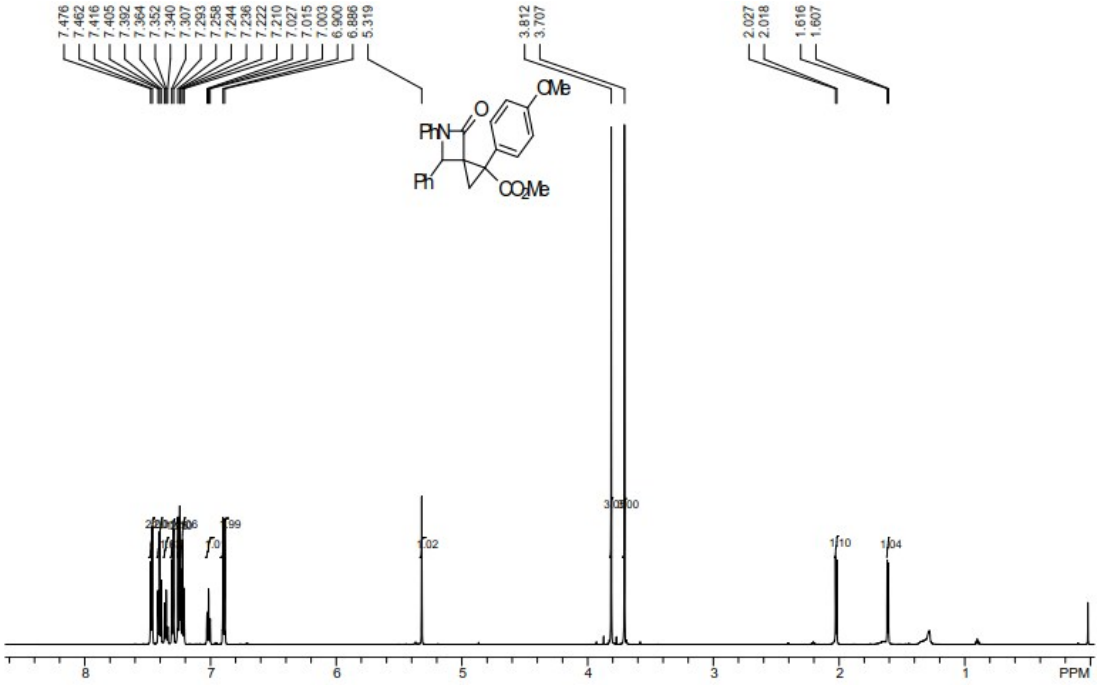


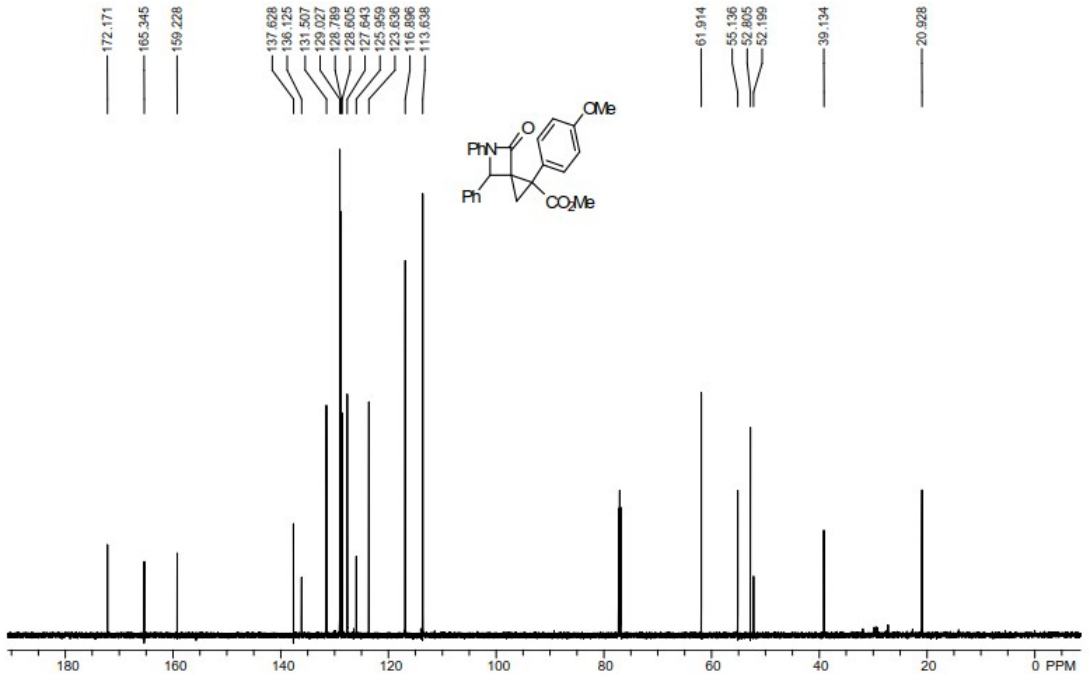
***cis*-methyl 1-(4-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*cis*-3e)**



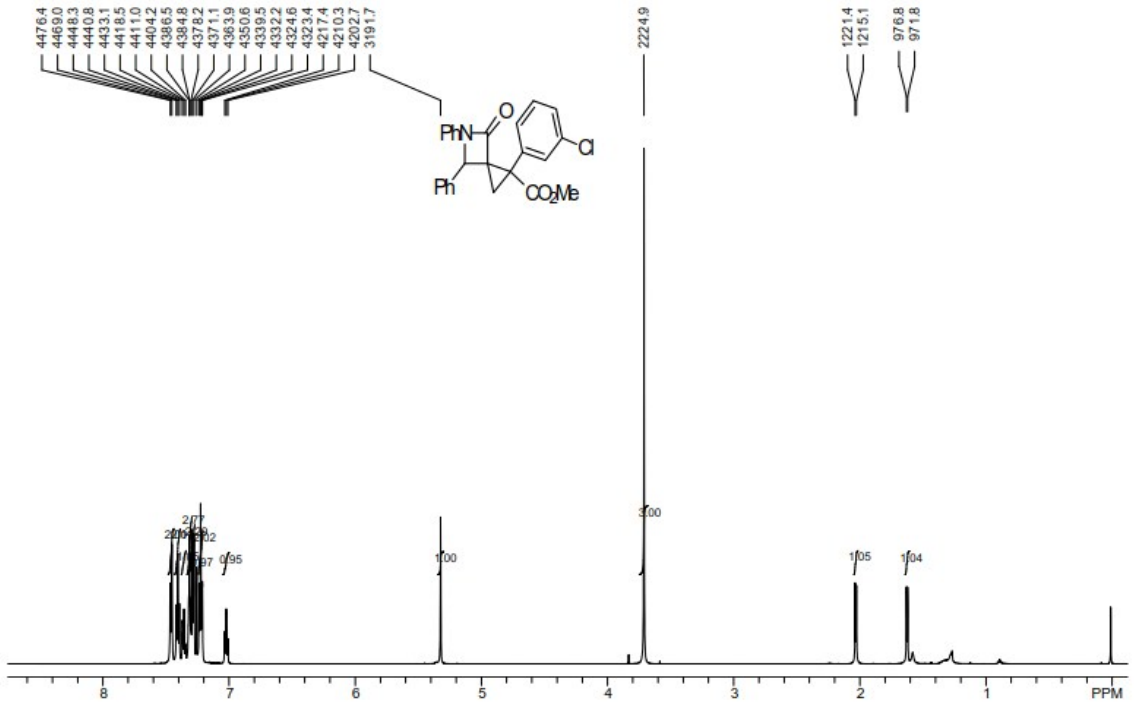


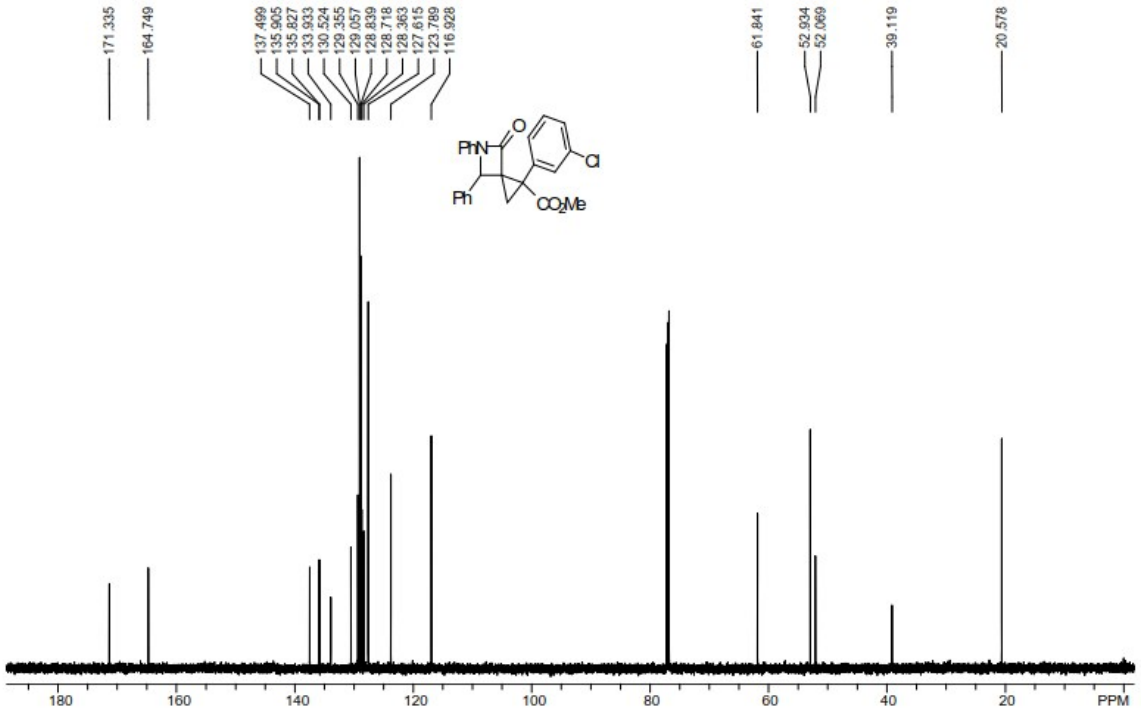
***trans*-methyl 1-(4-methoxyphenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3f)**



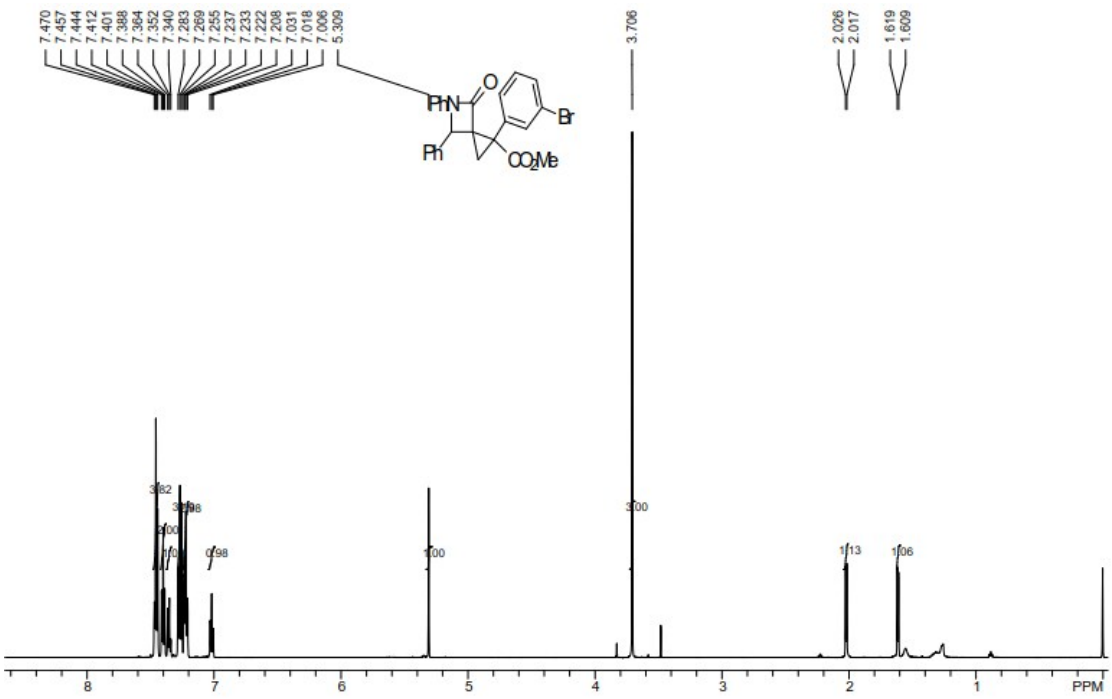


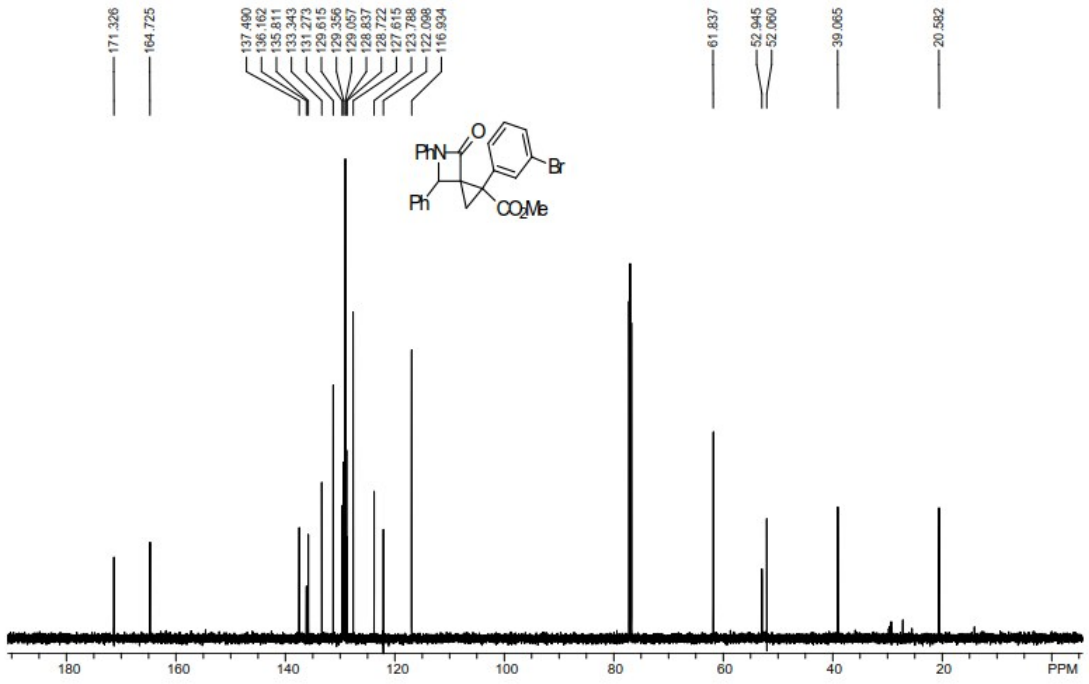
***trans*-methyl 1-(3-chlorophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3g)**



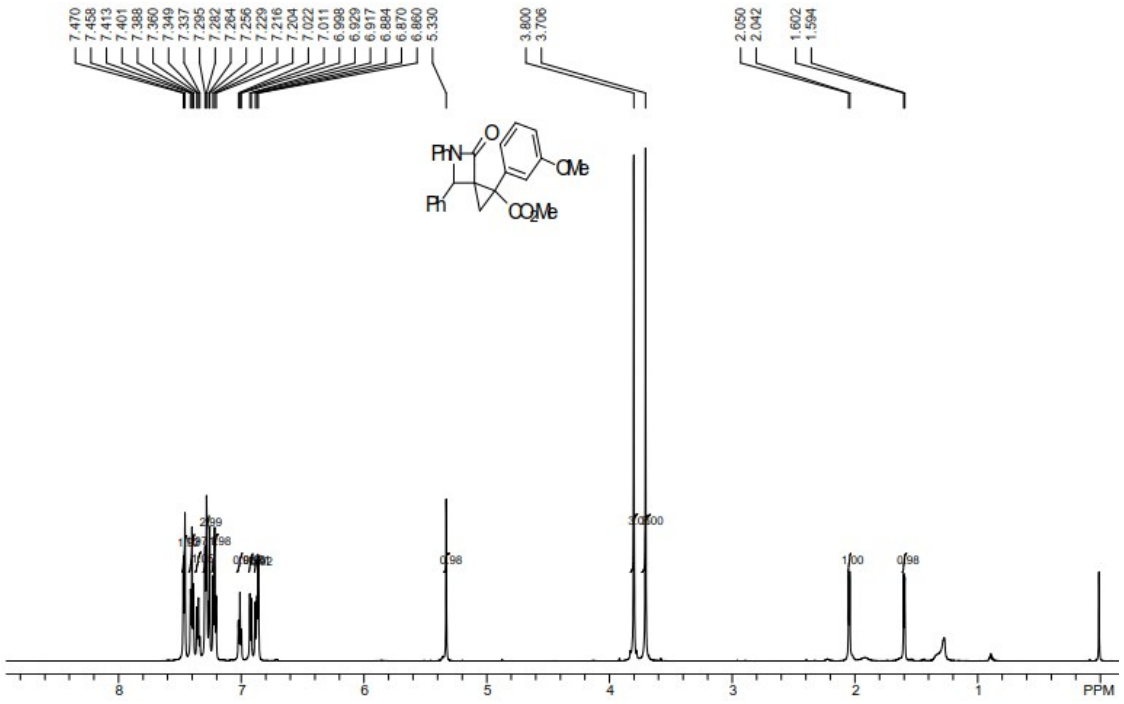


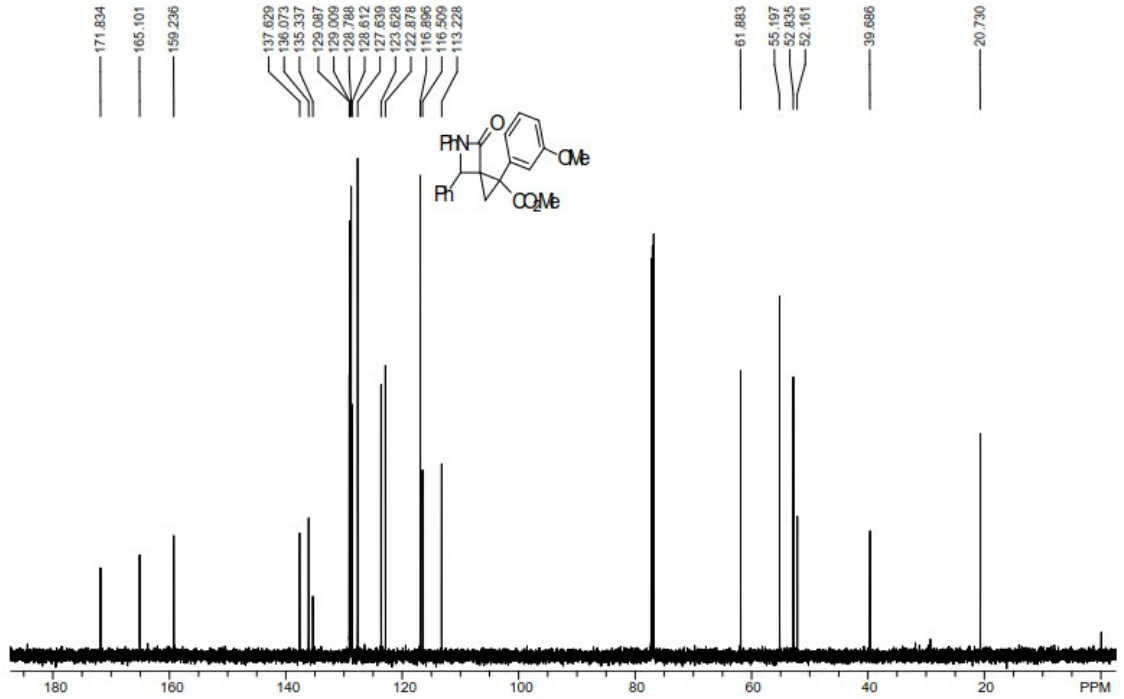
***trans*-methyl 1-(3-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3h)**



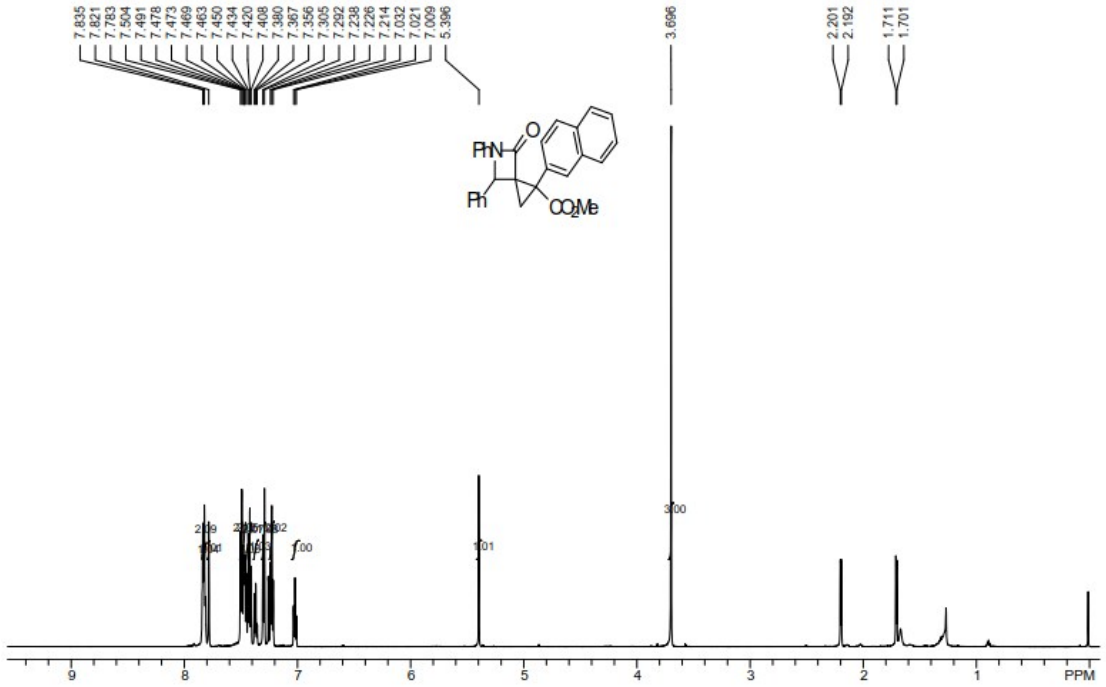


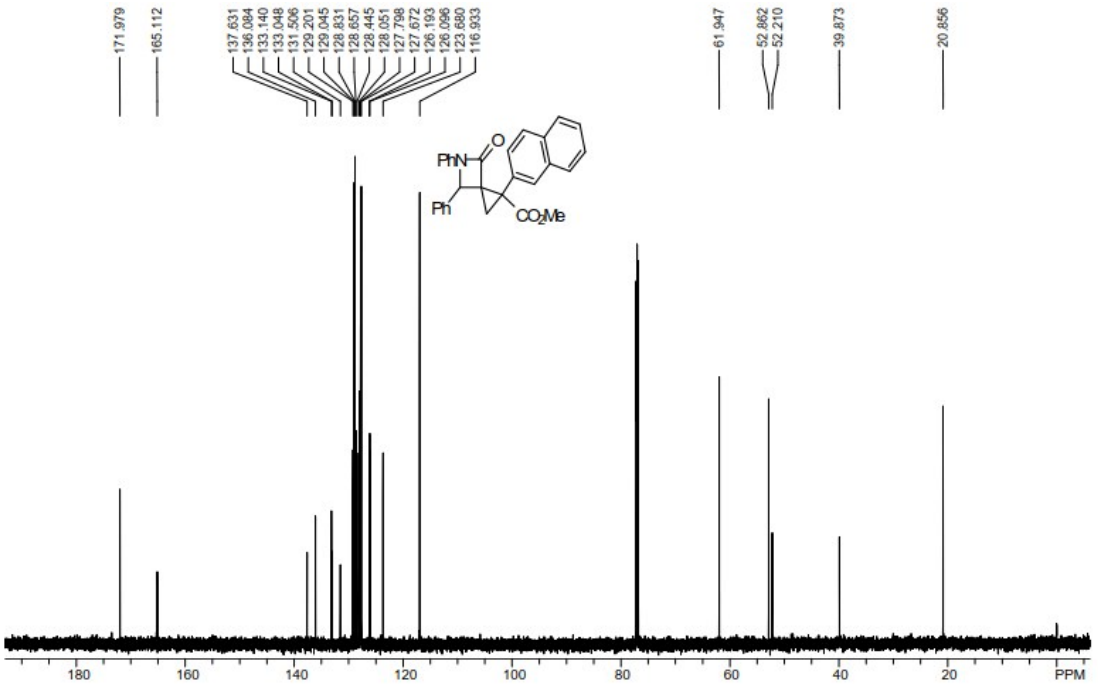
***trans*-methyl 1-(3-methoxyphenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3i)**



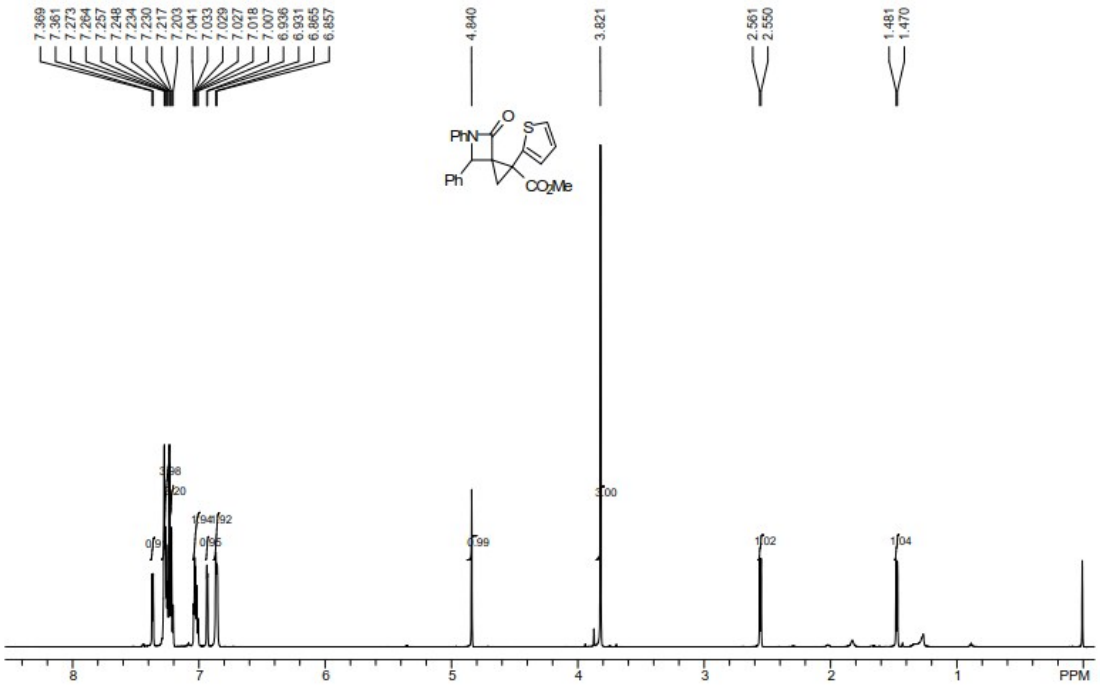


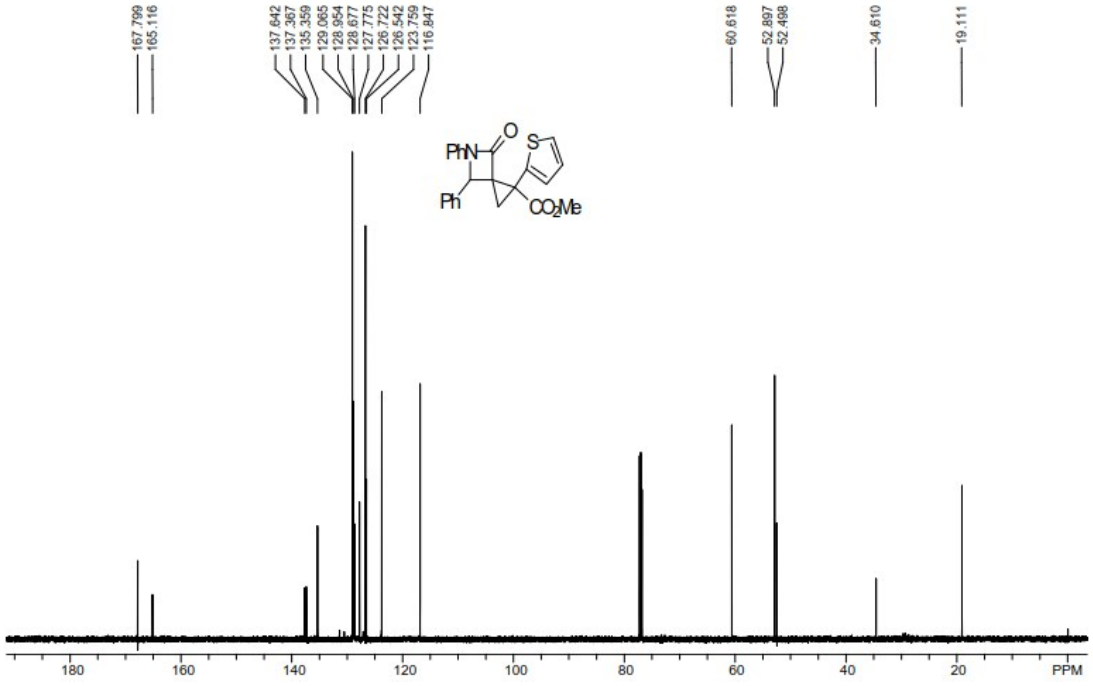
***trans*-methyl 1-(naphthalen-2-yl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3j)**



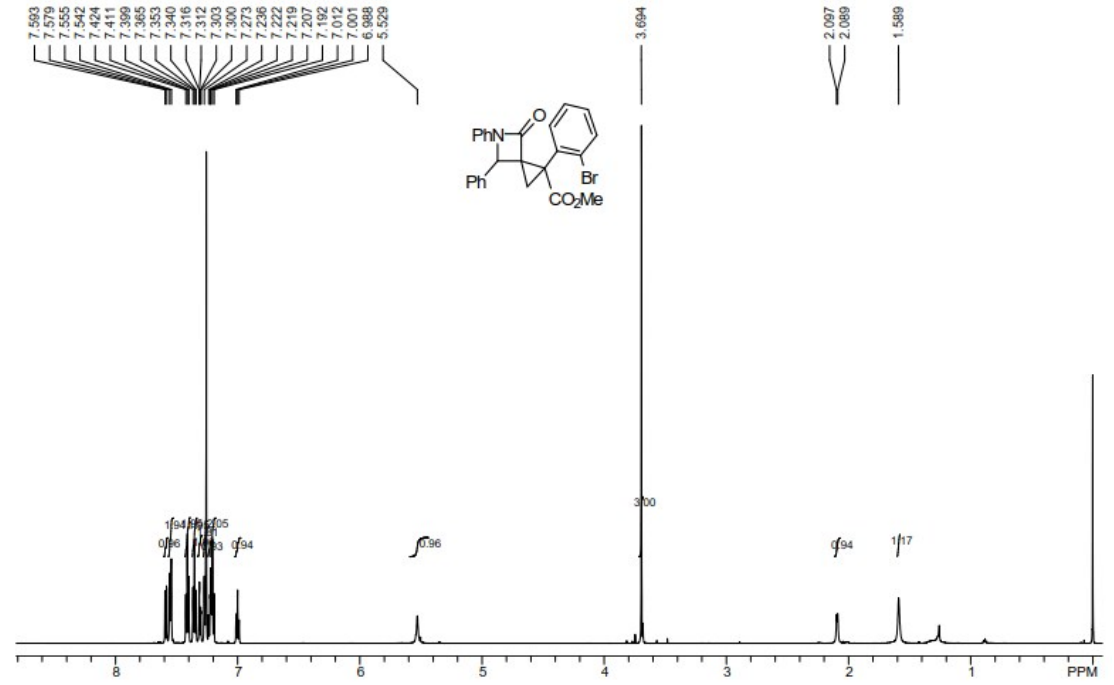


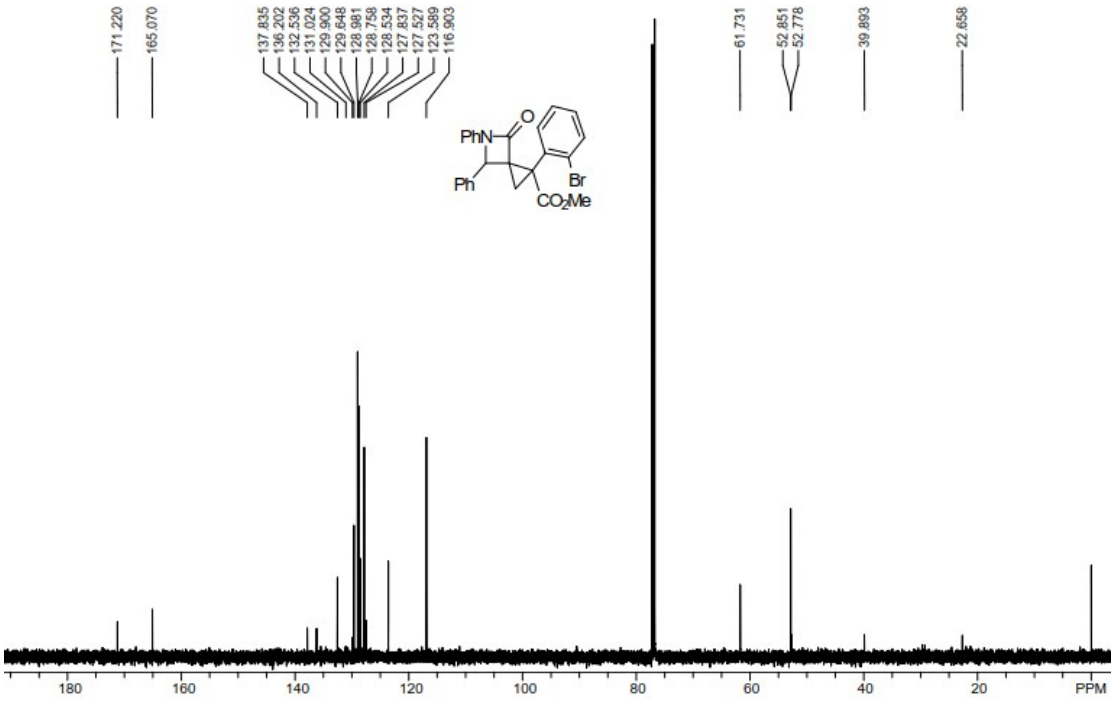
***trans*-methyl 4-oxo-5,6-diphenyl-1-(thiophen-2-yl)-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3k)**



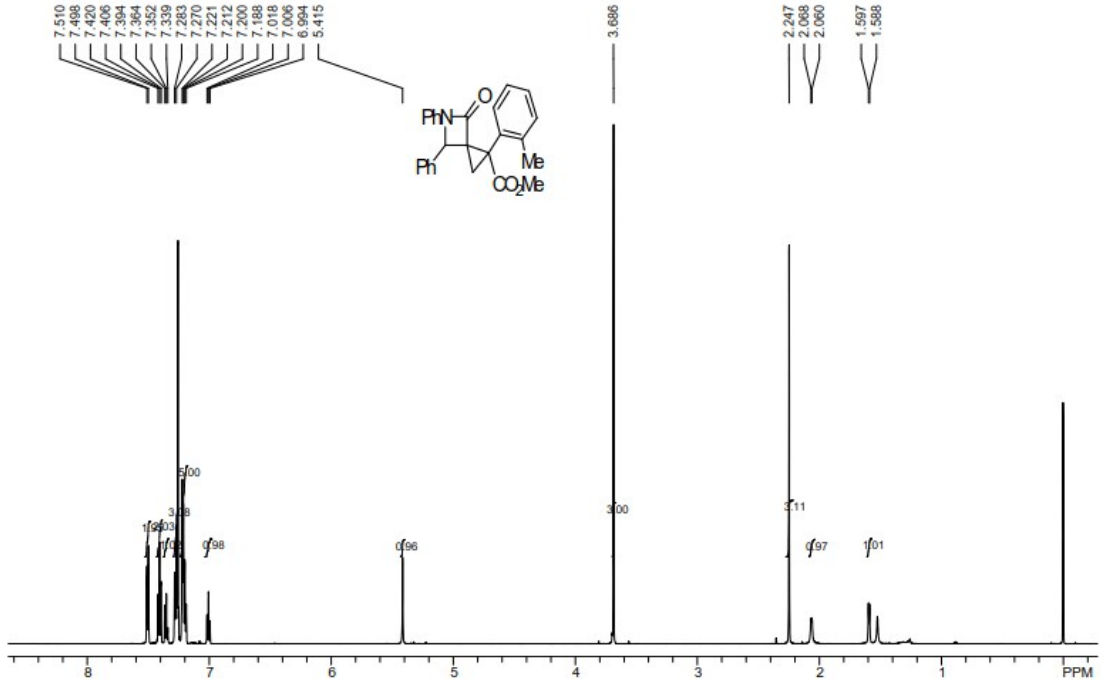


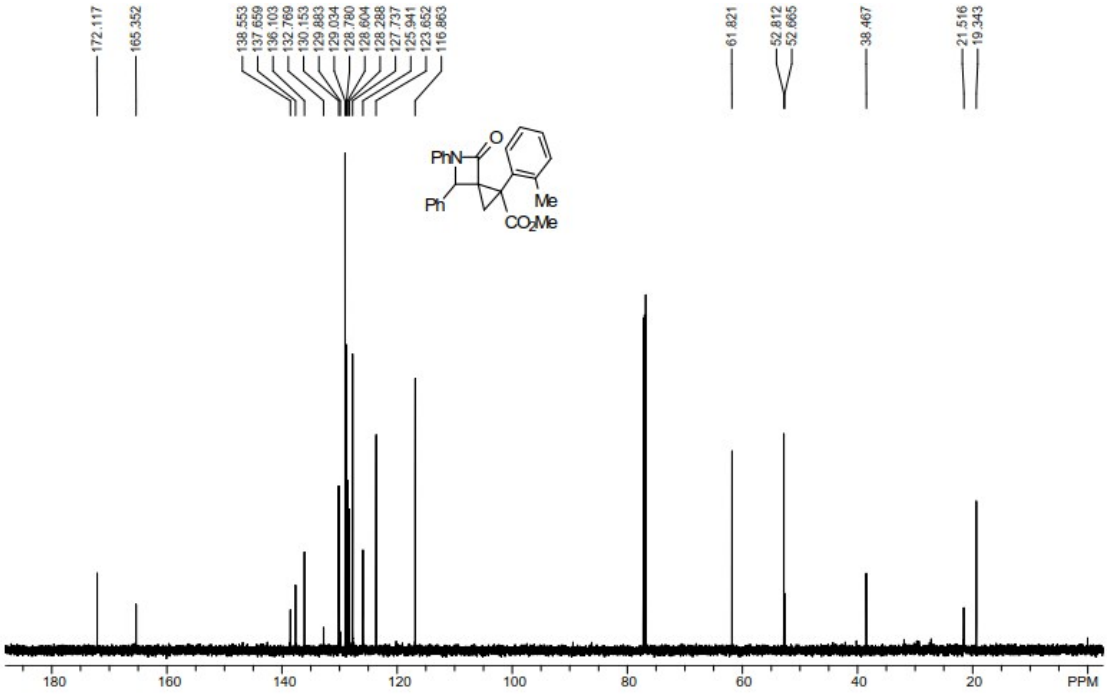
***trans*-methyl 1-(2-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3l)**



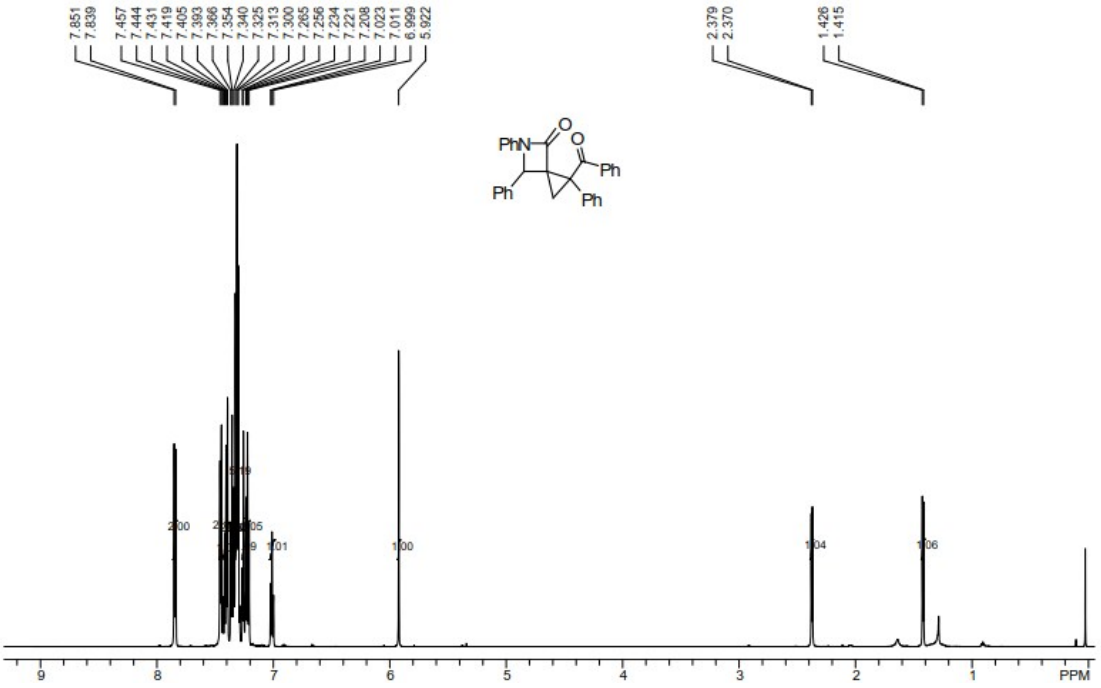


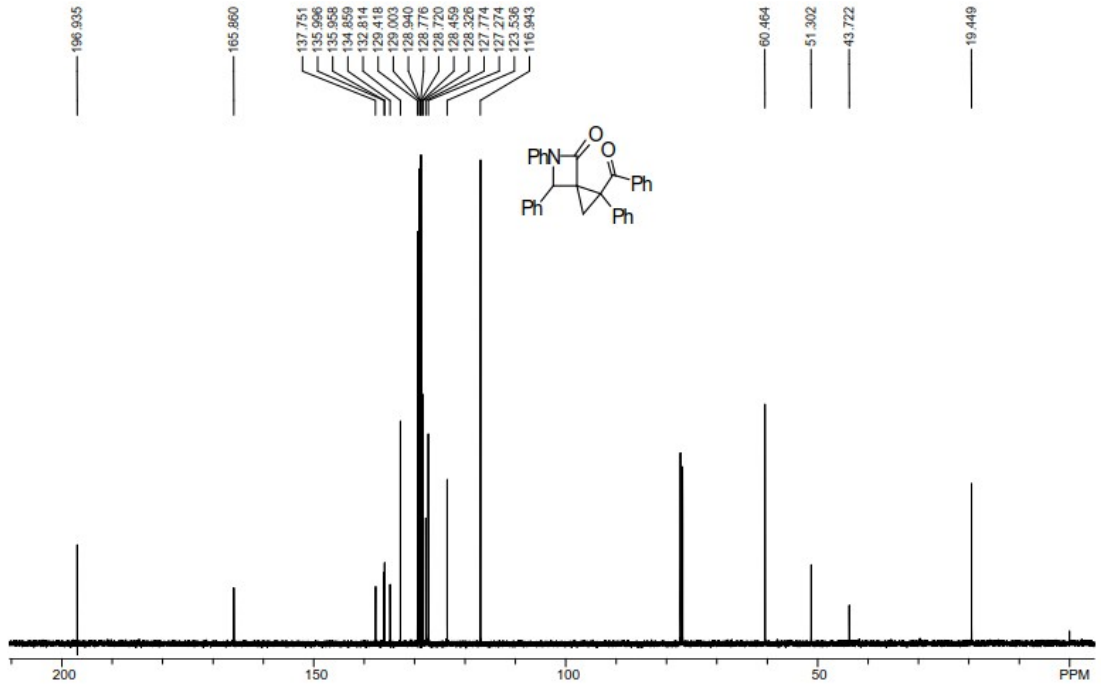
***trans*-methyl 4-oxo-5,6-diphenyl-1-(o-tolyl)-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3m)**



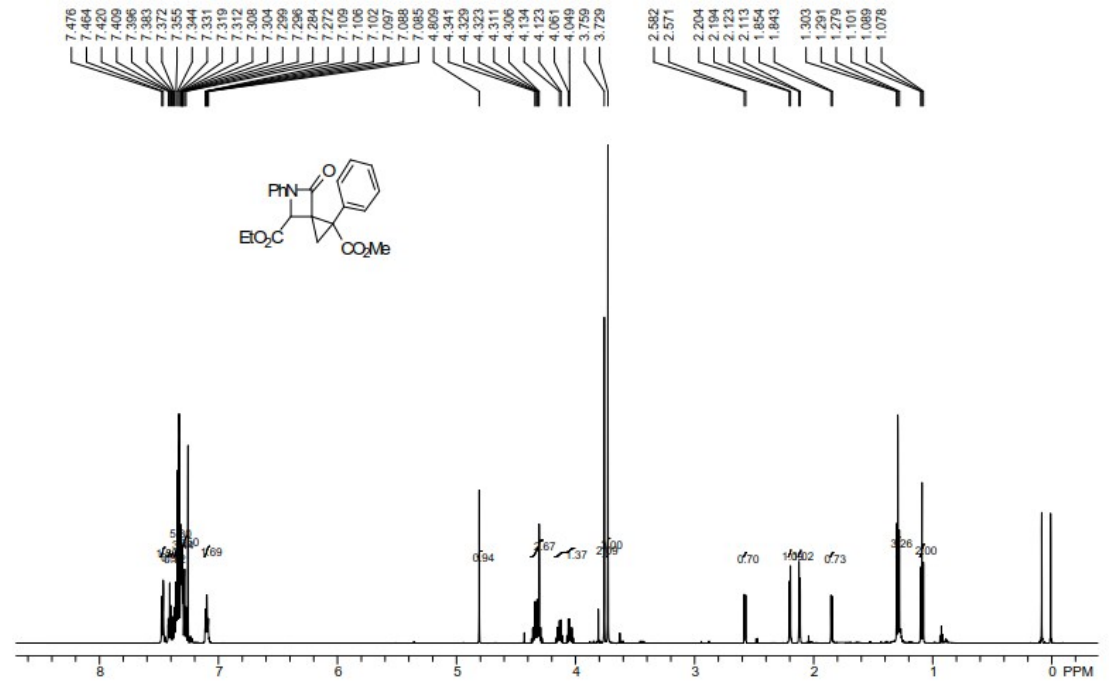


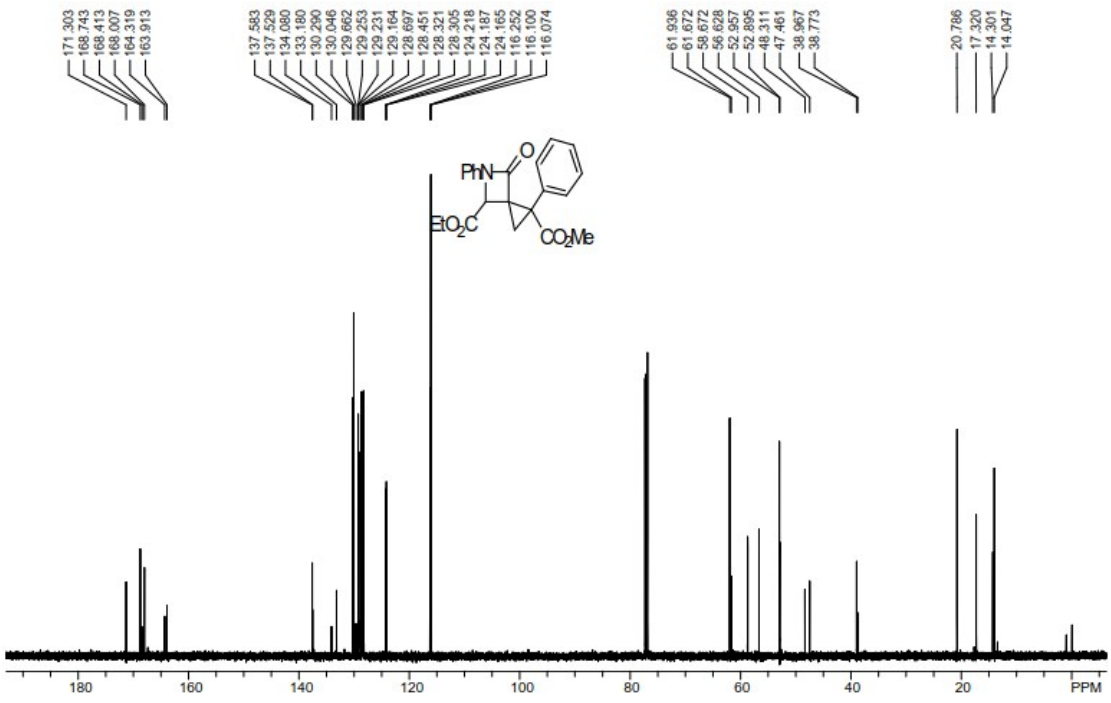
***trans*-1-benzoyl-1,5,6-triphenyl-5-azaspiro[2.3]hexan-4-one (*trans*-3n)**



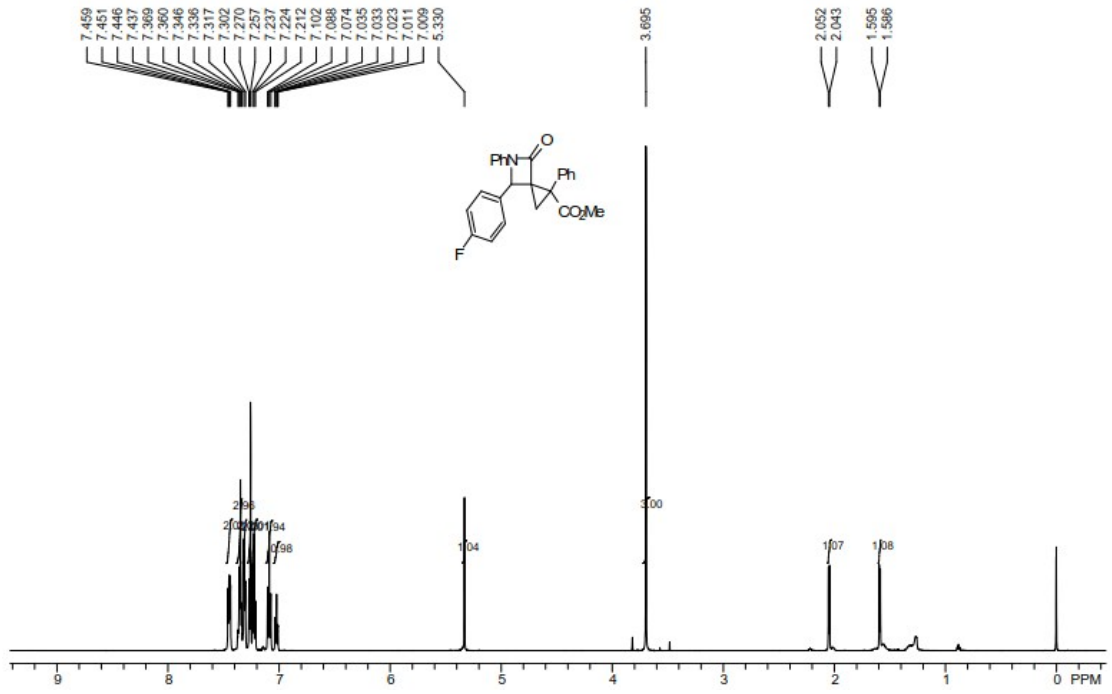


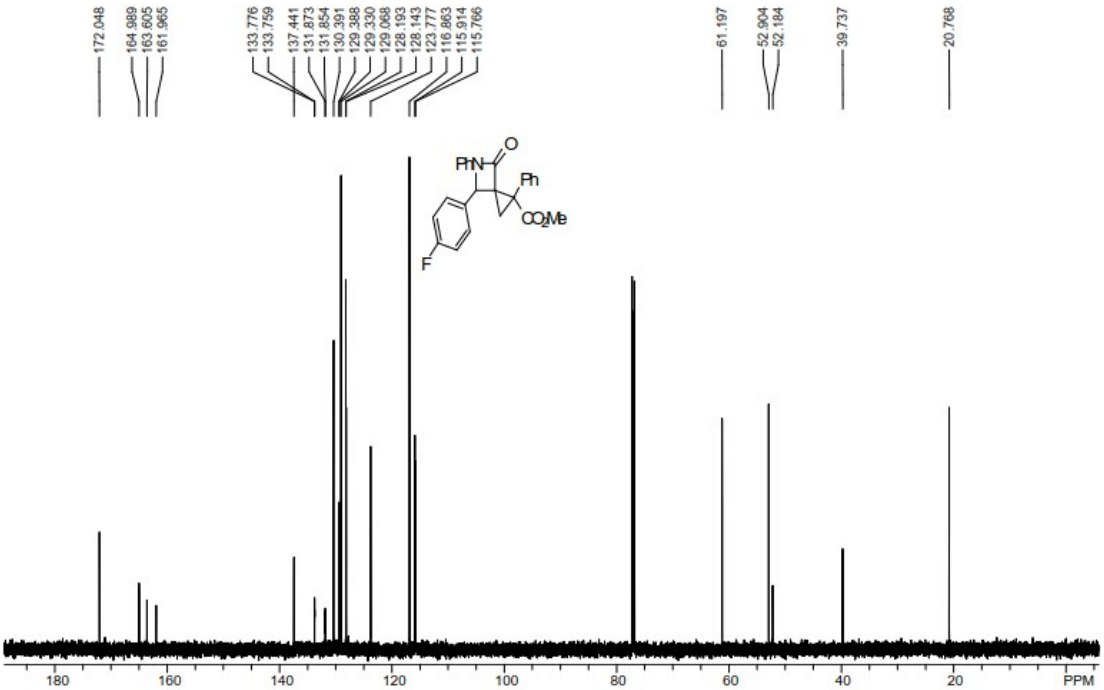
4-ethyl 1-methyl 6-oxo-1,5-diphenyl-5-azaspiro[2.3]hexane-1,4-dicarboxylate (3ab)



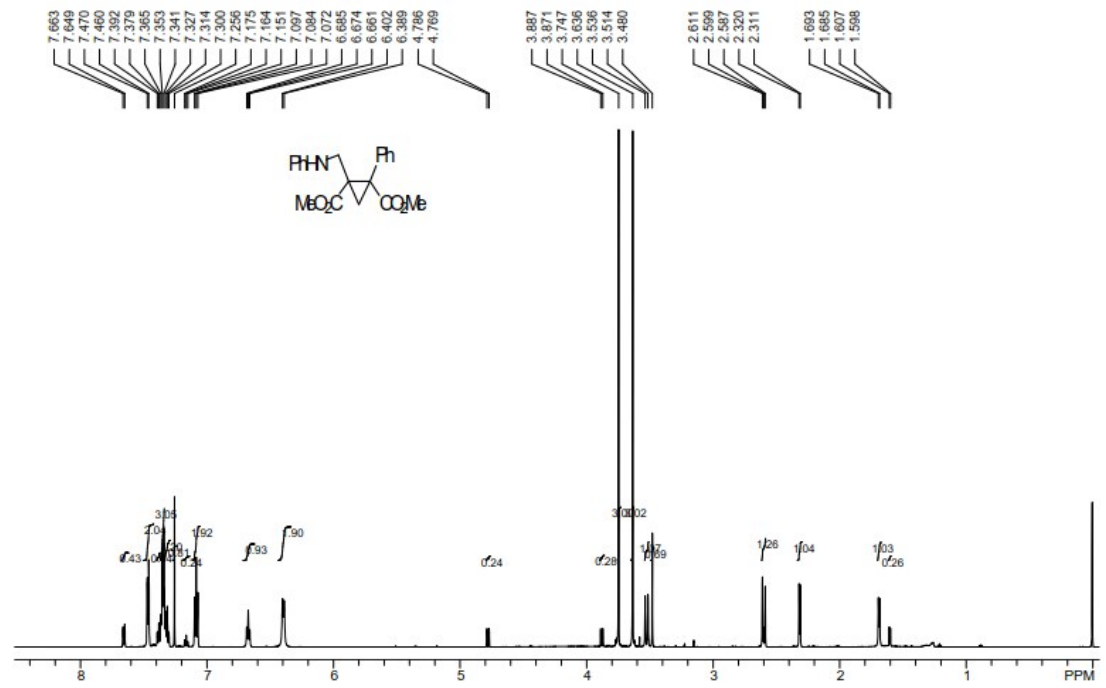


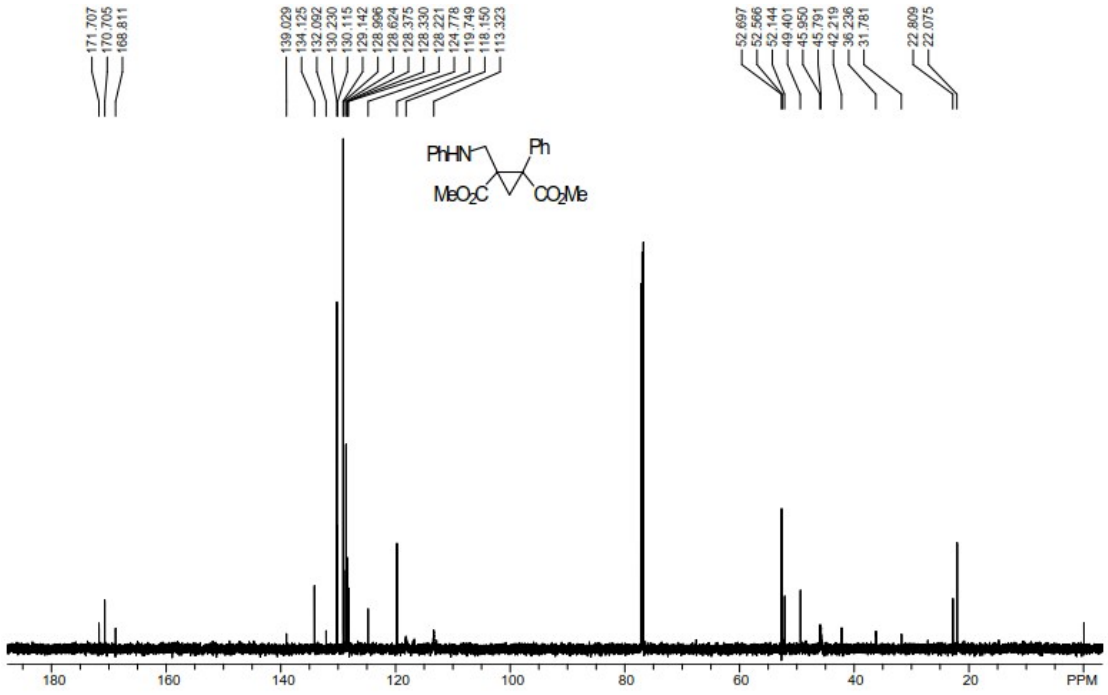
***trans*-methyl 4-(4-fluorophenyl)-6-oxo-1,5-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3ac)**



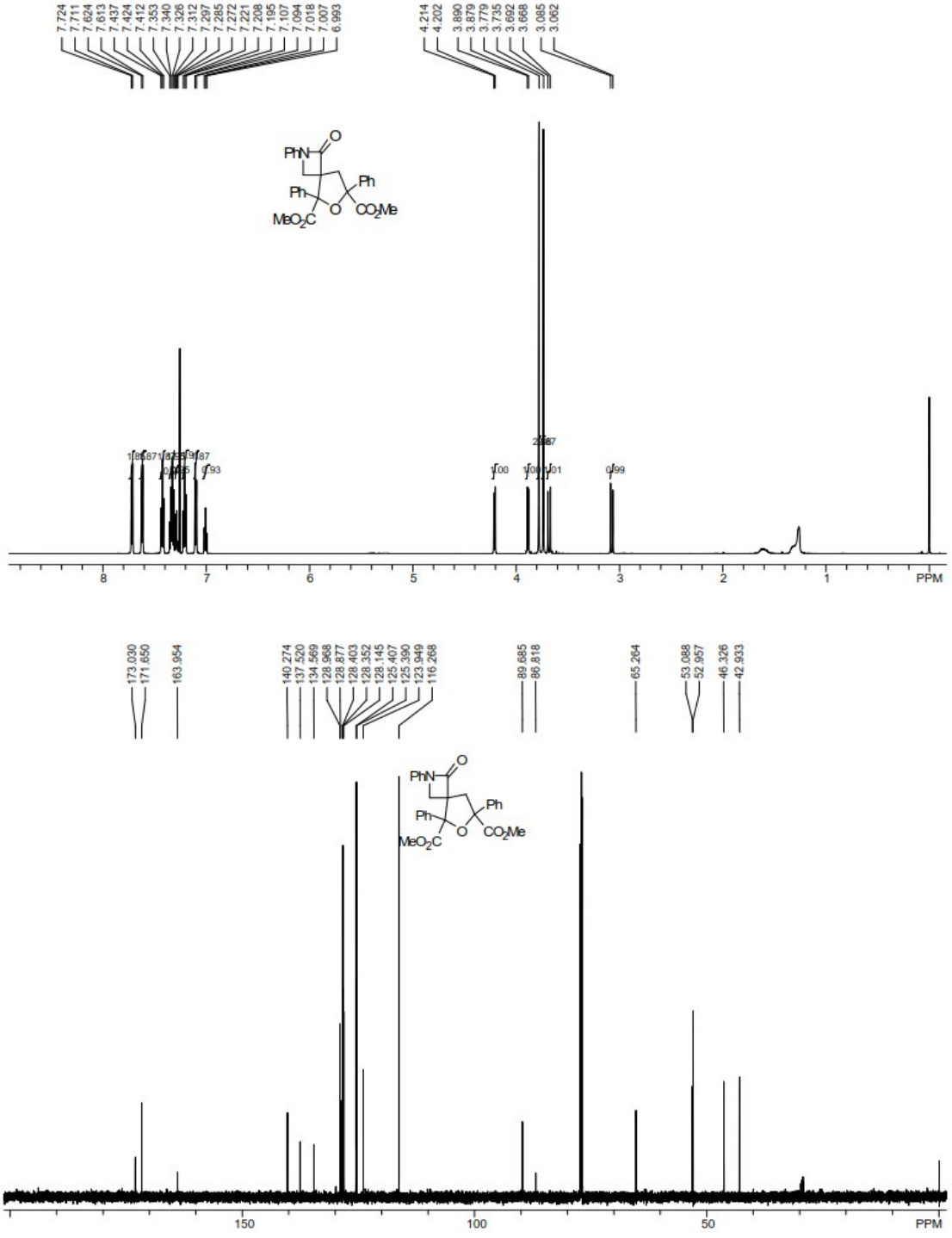


Dimethyl 1-phenyl-2-((phenylamino)methyl)cyclopropane-1,2-dicarboxylate (3ad)

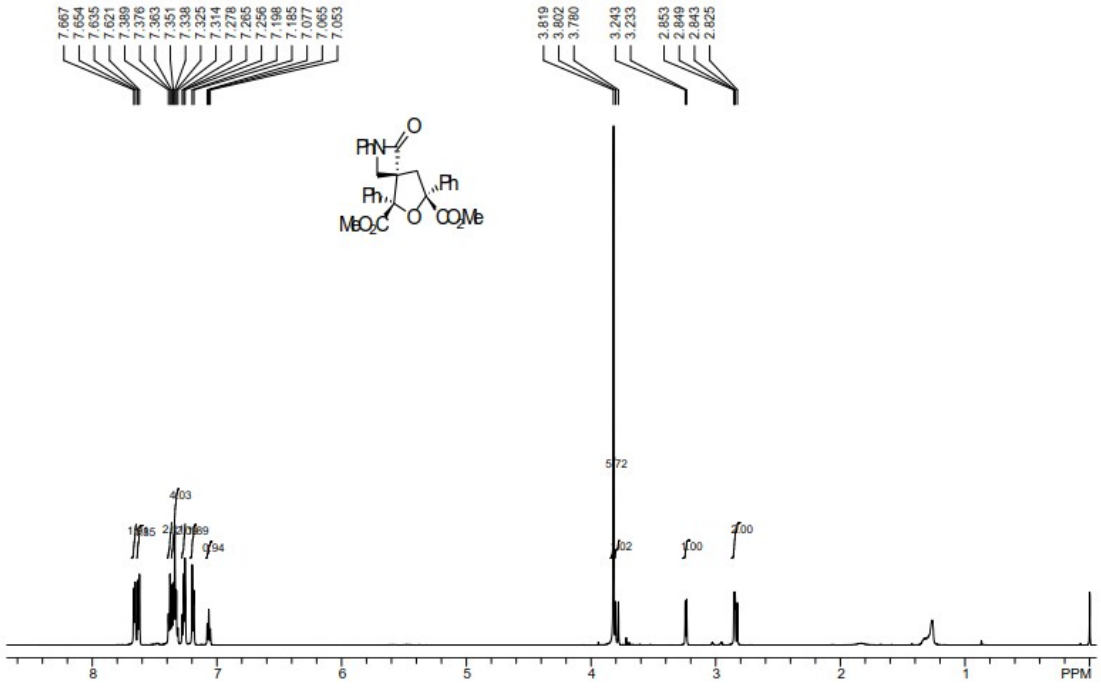


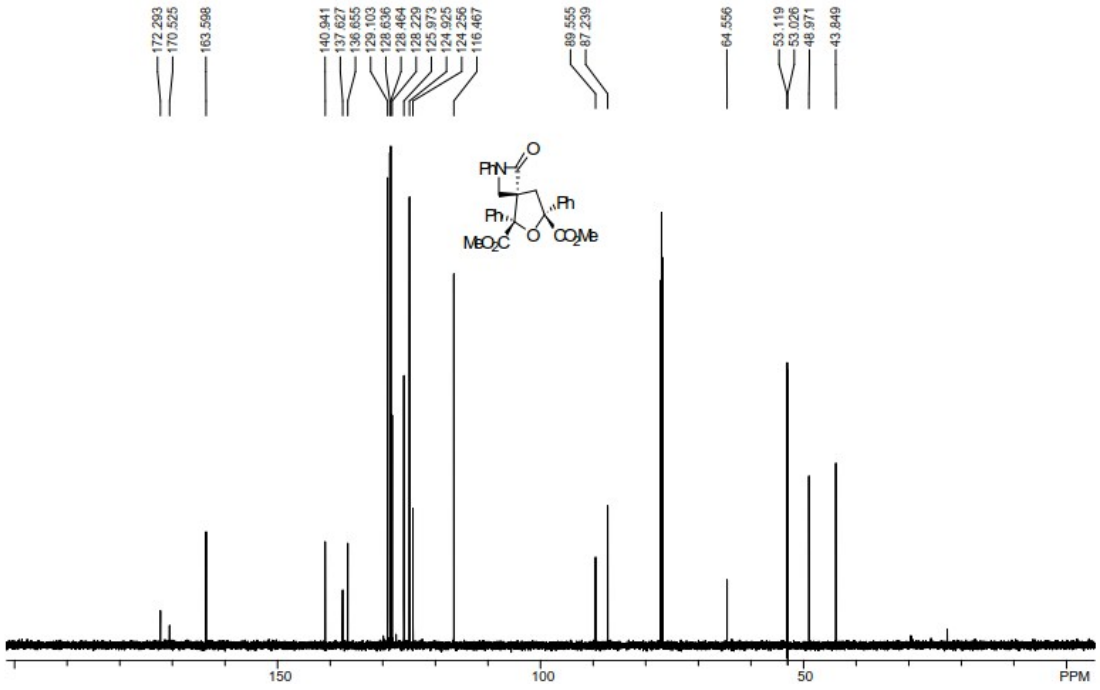


Dimethyl 1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4a)

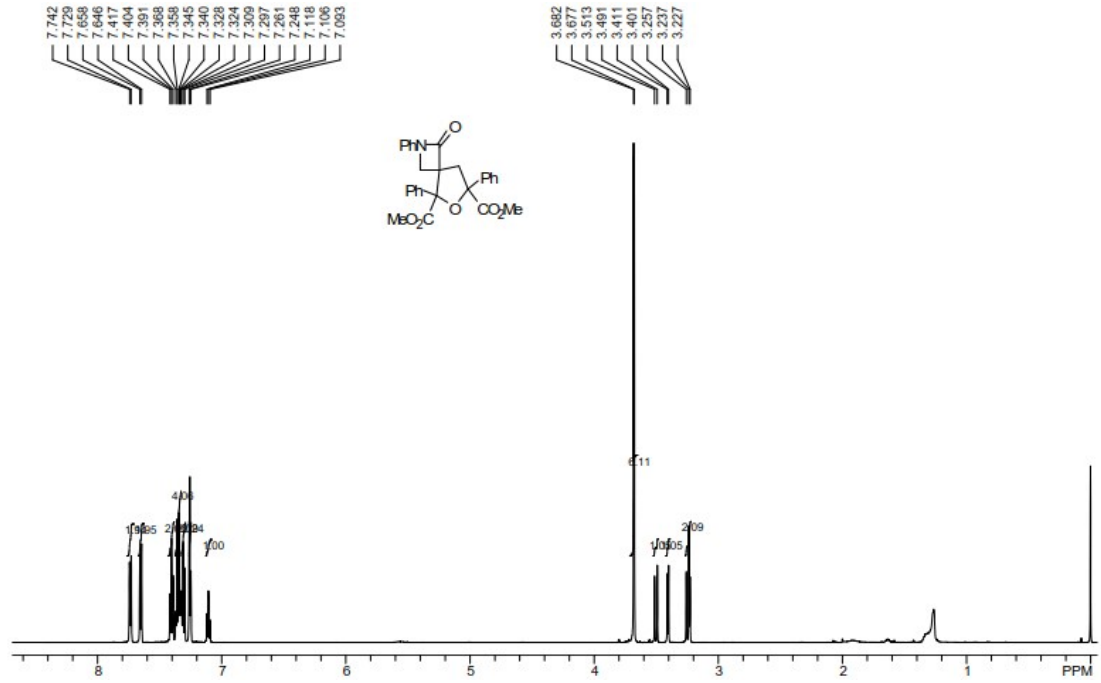


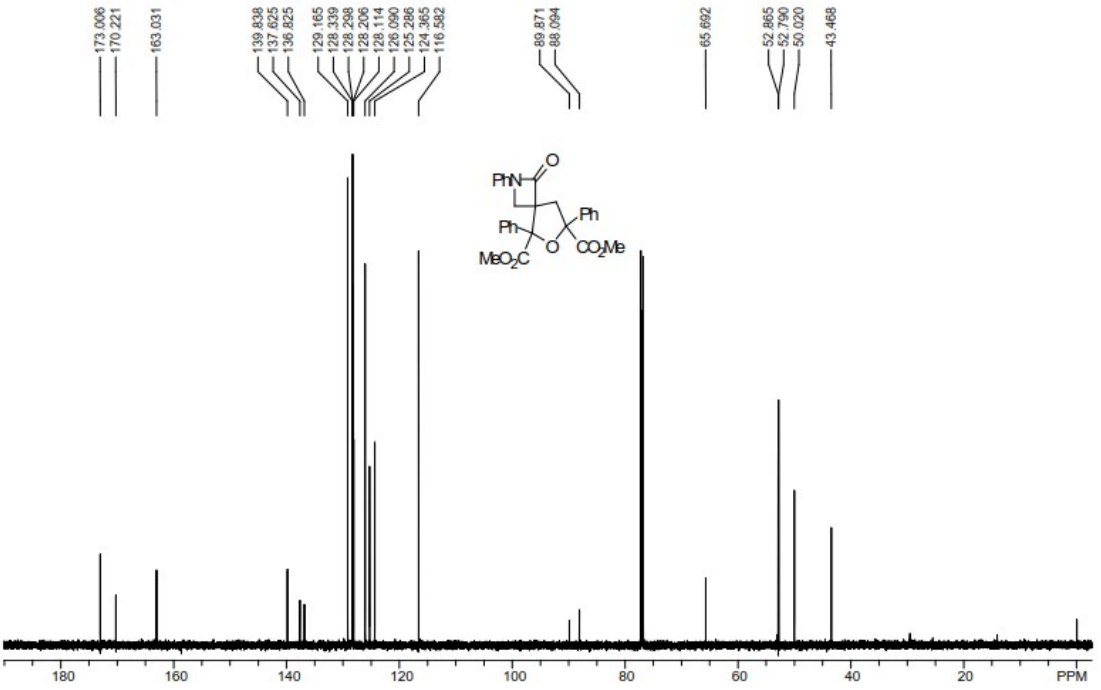
Dimethyl (4*S,5*R**,7*R**)-1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4b)**





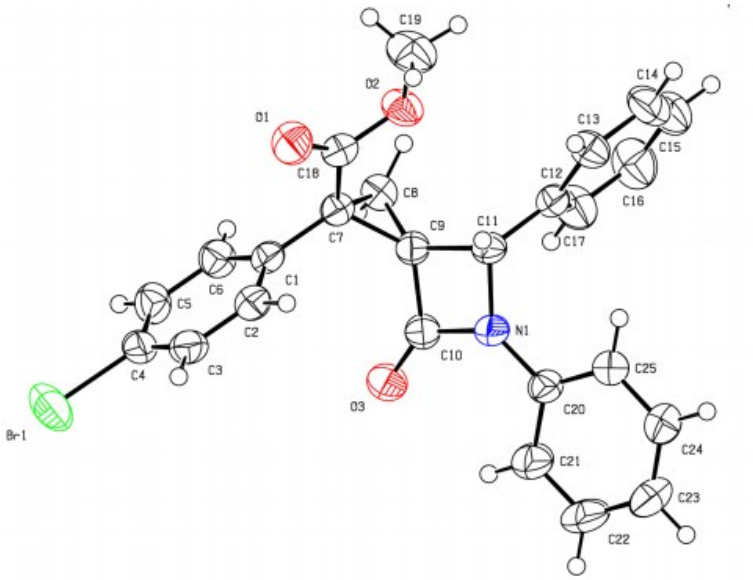
Dimethyl 1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4c)

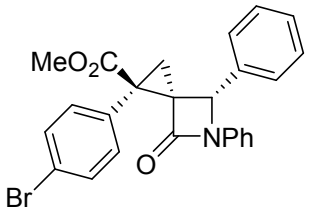




X-ray crystal structure for methyl 1-(4-bromophenyl)-4-oxo-5,6-diphenyl-5-azaspiro[2.3]hexane-1-carboxylate (*trans*-3d)

$C_{25}H_{20}BrNO_3$, MW = 462.33, Triclinic, space group P-1, R1 = 0.0318, wR2 = 0.0680, a = 9.6348(5) Å, b = 10.2842(5) Å, c = 11.5040(5) Å, α = 103.149(4)°, β = 104.108(4)°, γ = 94.618(4)°, V = 1065.30(9) Å^3, Crystal size 0.20×0.15×0.11 mm^3, T = 293 K, Z = 2, Z' = 0, μ(MoK$_\alpha$) = 2.843, The final wR_2 was 0.0952 (all data) and R_1 was 0.0377. Further information is contained in the CIF file.

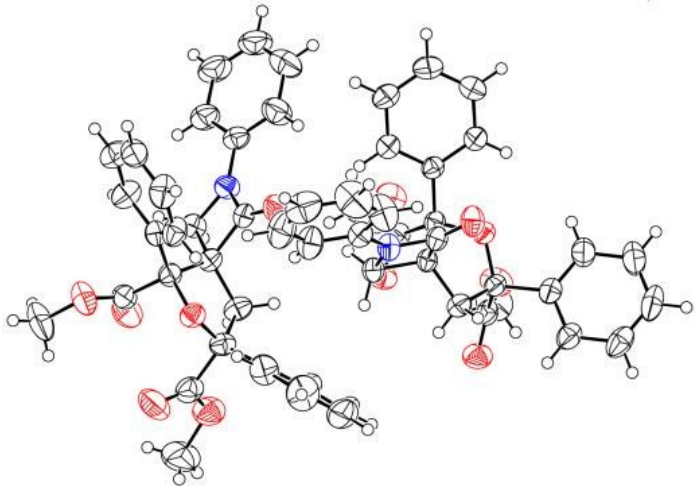


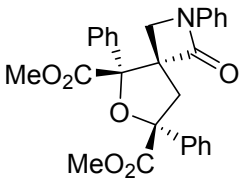


trans-**3d**

X-ray crystal structure for dimethyl 1-oxo-2,5,7-triphenyl-6-oxa-2-azaspiro[3.4]octane-5,7-dicarboxylate (4b)

$C_{28}H_{25}NO_6$, MW = 471.49, Triclinic, space group P-1, R1 = 0.0526, wR2 = 0.1479, a = 10.6091(5) Å, b = 11.9396(5) Å, c = 20.1405(8) Å, α = 103.598(4)°, β = 99.511(4)°, γ = 95.686(4)°, V = 2420.12(18) Å^3, Crystal size 0.13 x 0.09 x 0.07 mm^3 T = 292 K, Z = 4, 8518 reflections measured, 0 restraints, 635 parameters. Further information is contained in the CIF file.





4b