

Supporting Information

Base mediated spirocyclization of quinazoline: one-step synthesis of spiro-isoindolinone dihydroquinazolinones

Rapolu Venkateshwarlu,^{a,b} V. Narayana Murthy,^a Krishnaji Tadiparthi,^c Satish P. Nikumbh,^a Rajesh Jinkala,^a Vidavalur Siddaiah,^b M. V. Madhu babu,^a Hindupur Ramamohan,^a Akula. Raghunadh^{a*}

^a*Technology Development Centre, Custom Pharmaceutical Services, Dr. Reddy's Laboratories Ltd, Hyderabad 500049, India*

^b*Department of Organic Chemistry and FDW, Andhra University, Visakhapatnam 530045, India.*

^c*Department of Chemistry, Christ deemed to be University, Hosur road, Bangalore 560029, India*

E-mail: raghunadha@drreddys.com

General information.....	S2
Experimental Procedures and Characterization data.....	S2
¹ H and ¹³ C NMR Spectra.....	S3

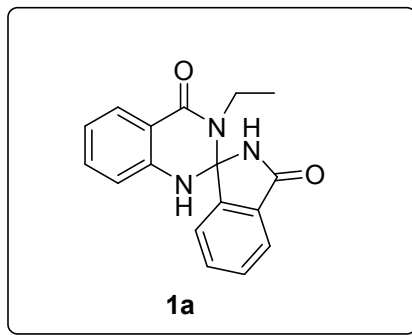
General information

Unless stated otherwise, solvents and chemicals were obtained from commercial sources and used without further purification. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254) using EtOAc-Hexane as eluent and visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230-400 mesh) using hexane and ethyl acetate. ^1H and ^{13}C NMR spectra were recorded in $\text{DMSO-}d_6$ solution by using a 400 MHz spectrometer. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, $\delta = 0.00$) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (J) are given in hertz. Infrared spectra were recorded on a FT-IR spectrometer. Melting points were determined using melting point B-540 apparatus and are uncorrected. HRMS was determined using waters LCT premier XETOF ARE-047 apparatus.

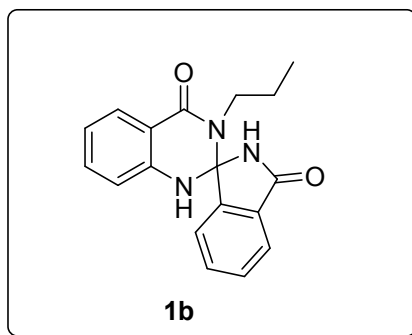
Experimental Procedures and Characterization data

General Procedure:

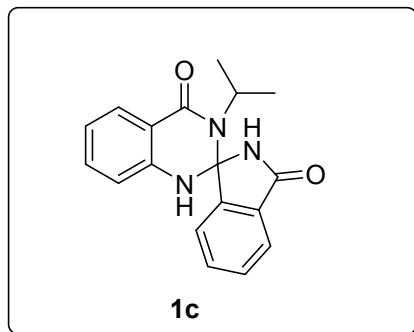
KHMDS (1M, 1.5 mmol) was added slowly to a solution of 2-aminobenzamide (1 mmol) and methyl-2-cyanobenzoate (1.5 mmol) in 1,4-dioxane (10 mL) under nitrogen atmosphere at 25-35°C and stirred for 4-5h. The reaction was monitored by TLC and after the completion of reaction, the reaction mass was diluted with water (5 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was washed with 5% HCl (5 mL) followed by water (2 x 10 mL). The combined organic layer was dried over anhydrous sodium sulphate and the solvent was evaporated to get the crude residue which was purified by column chromatography (EtOAc-Hexane) to get pure compound.



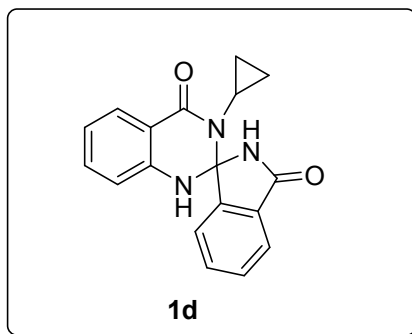
3'-Ethyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1a): Light brown color solid; Yield: 48%; ^1H NMR (400 MHz, CDCl_3): δ 8.28 (d, $J = 8.4$ Hz, 1H), 8.22 (bs, 1H), 8.01 (d, $J = 7.6$ Hz, 1H), 7.94 (d, $J = 7.2$ Hz, 1H), 7.83-7.74 (m, 3H), 7.51 (d, $J = 7.6$ Hz, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 1H), 3.47-3.40 (m, 2H), 1.17 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.7, 165.4, 149.8, 144.9, 135.5, 133.9, 133.1, 131.9 (2C), 131.1, 126.7, 125.8, 124.1, 121.9, 120.5, 34.5, 14.7; ESMS-Mass: 294.1 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_2$ (M+H) $^+$ 294.1243, found 294.1232.



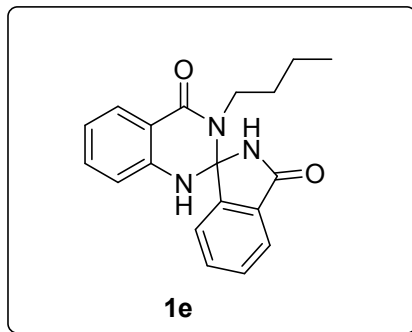
3'-Propyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1b): Light brown color solid; Yield: 55%; ^1H NMR (400 MHz, CDCl_3): δ 8.57 (bs, 1H), 8.24 (bs, 1H), 8.17 (d, $J = 7.6$ Hz, 1H), 7.98 (d, $J = 7.2$ Hz, 1H), 7.91 (d, $J = 7.2$ Hz, 1H), 7.83-7.72 (m, 2H), 7.45 (t, $J = 7.2$ Hz, 1H), 7.35 (t, $J = 7.2$ Hz, 1H), 6.99-6.91 (m, 1H), 3.34 (q, $J_1 = 6.8$ Hz, $J_2 = 6.0$ Hz, 2H), 1.55-1.46 (m, 2H), 0.88 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 168.2, 165.6, 150.2, 145.1, 135.5, 133.8, 132.9, 131.8, 131.6, 131.3, 126.5, 125.6, 123.9, 121.9, 120.8, 41.5, 22.6, 11.6; HRMS (ESI): Anal. calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2$ (M+H) $^+$ 308.1399, found 308.1407.



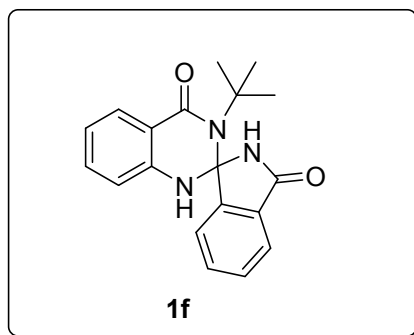
3'-Isopropyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1c): Light brown color solid; Yield: 58%; ^1H NMR (400 MHz, CDCl_3): δ 8.24 (d, $J = 7.6$ Hz, 1H), 8.13 (bs, 1H), 8.00 (d, $J = 7.2$ Hz, 2H), 7.93 (d, $J = 7.2$ Hz, 1H), 7.83-7.74 (m, 2H), 7.49 (t, $J = 7.2$ Hz, 1H), 7.32 (t, $J = 7.6$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 1H), 4.22-4.13 (m, 1H), 1.16 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.8, 164.7, 149.8, 144.9, 135.4, 133.8, 133.0, 131.8, 131.8, 131.1, 126.9, 125.8, 124.1, 121.8, 120.5, 41.4, 22.9 (2C); HRMS (ESI): Anal. calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 308.1399, found 308.1413.



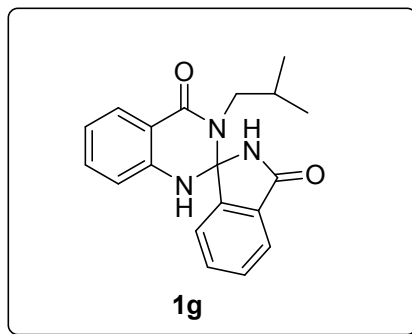
3'-Cyclopropyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione(1d): Off white color solid; Yield: 58%; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 10.89 (bs, 1H), 8.34 (d, $J = 3.6$ Hz, 1H), 8.02 (d, $J = 7.2$ Hz, 1H), 7.86-7.74 (m, 3H), 7.65-7.62 (m, 1H), 7.48-7.44 (m, 1H), 7.27-7.20 (m, 1H), 7.04-7.01 (m, 1H), 2.80-2.70 (m, 1H), 0.66-0.57 (m, 2H), 0.42-0.37 (m, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ 169.1, 164.6, 150.6, 145.3, 135.5, 133.7, 132.8, 131.1, 130.9, 129.5, 127.4, 124.4, 123.1, 122.1, 121.7, 50.1, 28.5 (2C); HRMS (ESI): Anal. calcd for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 306.1243, found 306.1253.



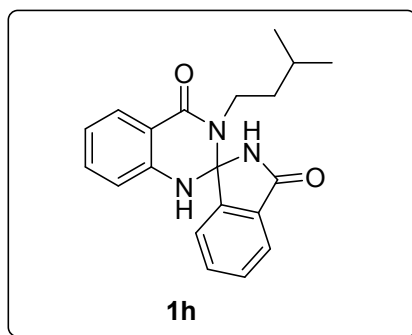
3'-Butyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1e): Off white color solid; Yield: 62%; ^1H NMR (400 MHz, CDCl_3): δ 8.22 (d, J = 7.2 Hz, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.82-7.73 (m, 2H), 7.29-7.25 (m, 1H), 6.99 (d, J = 7.6 Hz, 1H), 3.40 (t, J = 6.4 Hz, 2H), 1.51-0.1.43 (m, 2H), 1.34-1.24 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.9, 165.6, 150.1, 145.1, 135.5, 133.8, 133.0, 131.9, 131.8, 131.2, 126.6, 125.7, 123.9, 122.0, 120.7, 39.5, 31.5, 20.2, 13.6; HRMS (ESI): Anal. calcd for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 322.1556, found 322.1550.



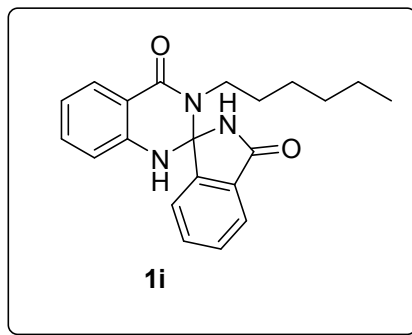
3'-(tert-Butyl)-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1f): Off white color solid; Yield: 62%; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 8.13 (s, 1H), 8.04 (d, J = 3.2 Hz, 1H), 7.88-7.85 (m, 3H), 7.82-7.78 (m, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.28-7.22 (m, 1H), 7.21-7.03 (m, 1H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.8, 164.6, 149.8, 144.8, 135.3, 133.8, 133.0, 131.7, 131.6, 131.1, 127.6, 125.8, 124.0, 122.1, 120.6, 51.0, 28.9(3C); ESMS-Mass: 322.1($\text{M}+\text{H}$); HRMS (ESI): Anal. calcd for $\text{C}_{19}\text{H}_{19}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 322.1556, found 322.1544.



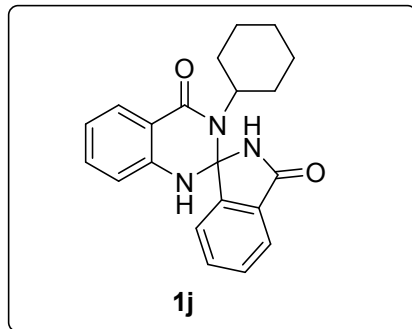
3'-Isobutyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1g): Off white color solid; Yield: 60%; ^1H NMR (400 MHz, CDCl_3): δ 8.26-8.21 (m, 2H), 8.19 (bs, 1H), 8.00 (d, $J = 7.2$ Hz 1H), 7.92 (d, $J = 6.8$ Hz, 1H), 7.86-7.77 (m, 2H), 7.33-7.26 (m, 1H), 7.49-7.46 (m, 1H), 6.99 (d, $J = 7.6$ Hz, 1H), 3.24-3.21 (t, $J = 6.0$ Hz, 2H), 1.80-1.74 (m, 1H), 0.89-0.88 (d, $J = 4.4$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.8, 165.6, 150.2, 145.1, 135.4, 133.7, 133.0, 131.9, 131.4, 125.9, 125.8, 123.9, 122.1, 120.7, 47.3, 28.4, 20.3; ESMS-Mass: 350.18 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_4$ (M+H) $^+$ 322.1556, found 322.1544.



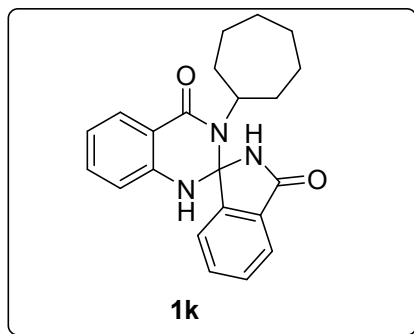
3'-Isopentyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1h): Off white color solid; Yield: 60%; ^1H NMR (400 MHz, CDCl_3): δ 8.25 (d, $J = 8.0$ Hz, 1H), 8.13 (bs, 1H), 8.03-7.99 (m, 2H), 7.93 (d, $J = 7.2$ Hz, 1H), 7.80-7.77 (m, 2H), 7.49-7.45 (m, 1H), 7.31 (t, $J = 7.2$ Hz, 1H), 6.98 (d, $J = 7.6$ Hz, 1H), 3.43-3.38 (m, 2H), 1.59-1.53 (m, 1H), 1.40-1.35 (m, 2H), 0.82 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.8, 165.5, 150.1, 145.1, 135.4, 133.8, 133.1, 131.9, 131.9, 131.1, 126.6, 125.8, 124.0, 122.1, 120.6, 38.3, 37.9, 25.7, 22.3 (2C); ESMS-Mass: 350.18 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_4$ (M+H) $^+$ 336.1712, found 336.1697.



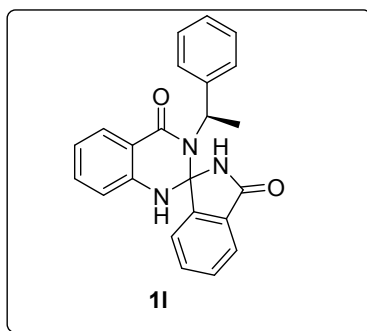
3'-Hexyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1i): Light brown color solid; Yield: 62% ; ^1H NMR (400 MHz, CDCl_3): δ 8.30 (bs, 1H), 8.21-8.17 (m, 2H), 8.00 (d, J = 6.8 Hz, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.81-7.73 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 3.39-3.34 (m, 2H), 1.51-1.43 (m, 2H), 1.24-1.18 (m, 2H), 1.14-1.12 (m, 4H), 0.81 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.9, 165.5, 150.1, 145.0, 135.5, 133.8, 133.0, 131.9, 131.8, 131.1, 126.5, 125.7, 123.9, 121.9, 120.7, 39.8, 31.5, 29.4, 26.8, 22.4, 13.9; HRMS (ESI): Anal. Calc. Mass for $\text{C}_{21}\text{H}_{24}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 350.1869, found 350.1885.



3'-Cyclohexyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1j): Light brown color solid; Yield: 61%; ^1H NMR (400 MHz, CDCl_3): δ 8.20 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.82-7.73 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 3.91-3.87 (m, 1H), 1.91-1.87 (m, 2H), 1.65-1.55 (m, 3H), 1.40-1.37 (m, 2H), 1.18-1.09 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.9, 164.7, 149.9, 144.9, 135.4, 133.8, 133.0, 131.8, 131.8, 131.2, 126.8, 125.7, 123.9, 121.9, 120.6, 48.2, 32.9 (2C), 25.6, 24.6 (2C); HRMS (ESI): Anal. Calc. Mass $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 348.1712, found 348.1721.

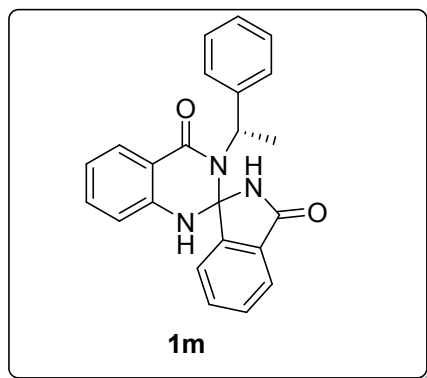


3'-(Cycloheptyl)-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1k): Light brown color solid; Yield: 62%; ^1H NMR (400 MHz, CDCl_3): δ 8.12-8.05 (m, 2H), 8.02 (bs, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.82-7.74 (m, 2H), 7.47 (t, J = 6.8 Hz, 1H), 7.33-7.26 (m, 1H), 6.98 (d, J = 8.0 Hz, 1H), 4.10-4.07 (m, 1H), 1.93-1.89 (m, 2H), 1.68-1.50 (m, 4H), 1.45-1.25 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.8, 164.3, 149.9, 144.9, 135.4, 133.7, 133.0, 131.8, 131.8, 131.2, 126.8, 125.7, 124.0, 122.1, 120.6, 50.4, 35.0 (2C), 28.2 (2C), 23.9 (2C); ESMS-Mass: 362.18 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2$ (M+H) $^+$ 362.1869, found 362.1874.

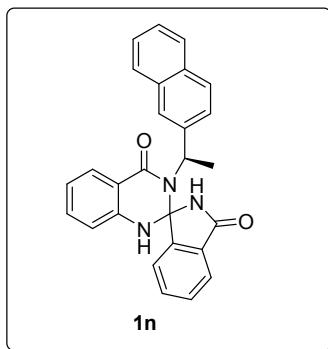


3'-(*R*)-1-Phenylethyl-1'*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'*H*)-dione (1l): Light brown color solid; Yield: 55%; ^1H NMR (400 MHz, CDCl_3): δ 8.64 (bs, 1H), 8.28 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 7.2 Hz, 1H), 7.84-7.80 (m, 1H), 7.75-7.72 (m, 1H), 7.71-7.61 (m, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.36-7.26 (m, 3H), 7.21-7.16 (m, 3H), 6.98 (d, J = 8.0 Hz, 1H), 5.27-5.19 (m, 1H), 1.53 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.7, 164.7, 143.4, 135.2, 133.9, 132.9, 132.1 (2C), 130.9, 128.6 (3C), 127.2, 126.7, 126.3 (3C), 125.9, 123.9, 122.2, 120.6, 49.3,

21.8; ESMS-Mass:370.15 (M+H); HRMS (ESI): Anal. calcd for C₂₃H₁₉N₃O₂ (M+H)⁺ 370.1556, found 370.1567.

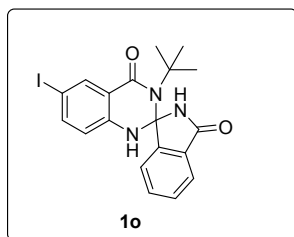


3'-(S)-1-Phenylethyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1m): Light brown color solid; Yield: 55%; ¹H NMR (400 MHz, CDCl₃): δ 8.64 (bs, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.05 (bs, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.73 (t, *J* = 6.8 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.36-7.26 (m, 3H), 7.22-7.17 (m, 3H), 6.98 (d, *J* = 8.0 Hz, 1H), 5.26-5.19 (m, 1H), 1.52 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 167.8, 164.7, 143.3, 135.2, 133.8, 132.8, 132.1 (2C), 130.9, 128.6 (3C), 127.2, 126.6, 126.3 (3C), 125.8, 123.8, 122.1, 120.6, 49.3, 21.8; ESMS-Mass:370.15 (M+H); HRMS (ESI): Anal. calcd for C₂₃H₁₉N₃O₂ (M+H)⁺ 370.1556, found 370.1554.



3'-[(*R*)-1-(Naphthalen-2-yl)ethyl]-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione

(1n): Light brown color solid; Yield: 60%; ^1H NMR (400 MHz, CDCl_3): δ 8.56 (bs, 1H), 8.33 (d, $J = 7.6$ Hz, 1H), 7.90 (d, $J = 8.4$ Hz, 1H), 7.67 (d, $J = 7.6$ Hz, 1H), 7.60-7.51 (m, 4H), 7.46-7.41 (m, 2H), 7.39-7.35 (m, 3H), 7.33-7.26 (m, 1H), 7.24-7.19 (m, 1H), 6.89 (d, $J = 7.6$ Hz, 1H), 6.84 (d, $J = 7.6$ Hz, 1H), 5.98 (t, $J = 7.2$ Hz, 1H), 1.75 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.5, 164.6, 149.8, 145.2, 137.9, 134.4, 133.7, 133.6, 132.3, 132.2, 132.0, 131.0, 130.4, 128.5, 128.4, 126.2, 126.1, 125.8, 125.5, 124.8, 123.5, 123.2, 122.7, 121.3, 120.5, 45.2, 19.9; ESMS-Mass: 420.17 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{27}\text{H}_{21}\text{N}_3\text{O}_2$ (M+H) $^+$ 420.1712, found 420.1711.



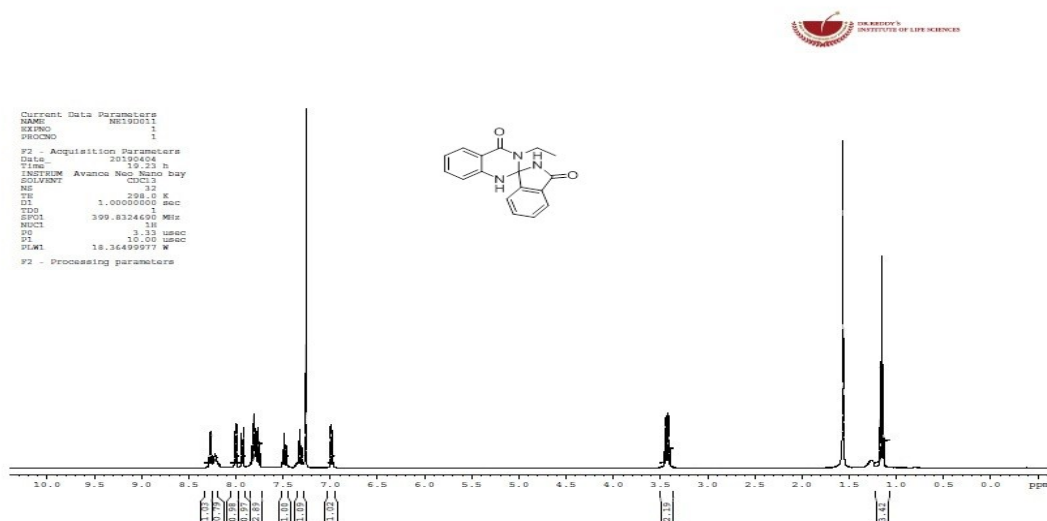
3'-(tert-butyl)-6'-iodo-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1o): Light

brown white color solid; Yield: 70%; ^1H NMR (400 MHz, CDCl_3): δ 8.57 (s, 1H), 8.46-8.45 (d, $J = 8.4$ Hz, 1H), 8.15 (s, 1H), 7.97-7.792 (m, 1H), 7.80-7.70 7.28-7.22 (m, 1H), 6.75-6.72 (m, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 166.4, 162.0, 148.9, 143.4, 139.5, 139.4, 134.4, 133.1, 132.9, 132.2, 128.1, 123.1, 121.4, 121.1, 88.9, 50.1, 27.8 (3C); ESMS-Mass: 447.28 (M+H); HRMS (ESI): Anal. calcd for $\text{C}_{19}\text{H}_{19}\text{IN}_3\text{O}_2$ (M+H) $^+$ 448.0522, found 448.0516.

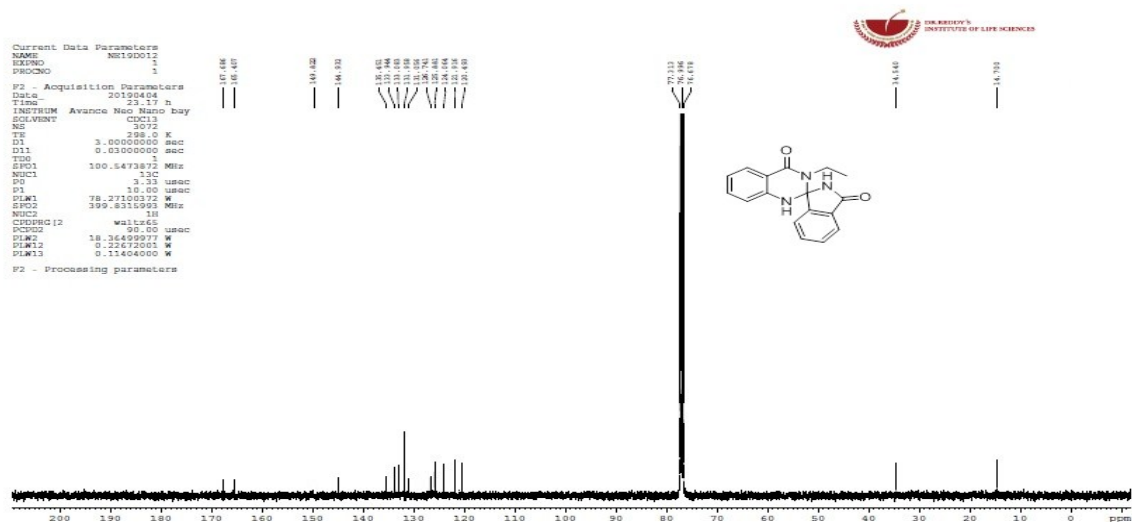
Spectra Data

^1H and ^{13}C NMR Spectra

^1H NMR of 3'-Ethyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1a):



^{13}C NMR of 3'-Ethyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1a):



HRMS of 3'-Ethyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1a):

Elemental Composition Report

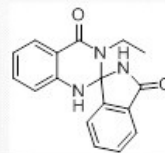
Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3



Monoisotopic Mass, Even Electron Ions

149 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

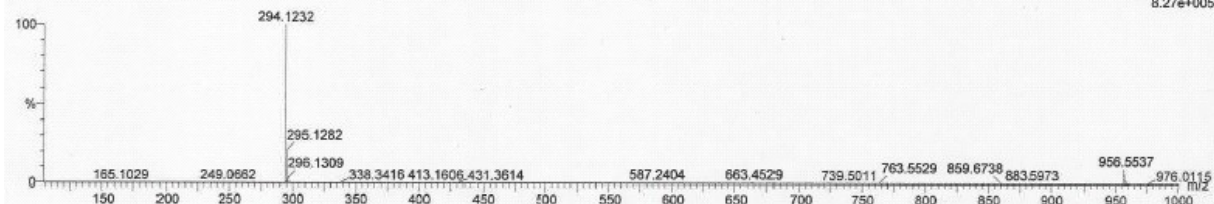
Elements Used:

C: 0-28 H: 0-37 N: 0-5 O: 0-7

SR/RV-012-0328993

190315001 21 (0.262) Cm (21.23-(33.36+5.6))

1: TOF MS ES+
8.27e+005

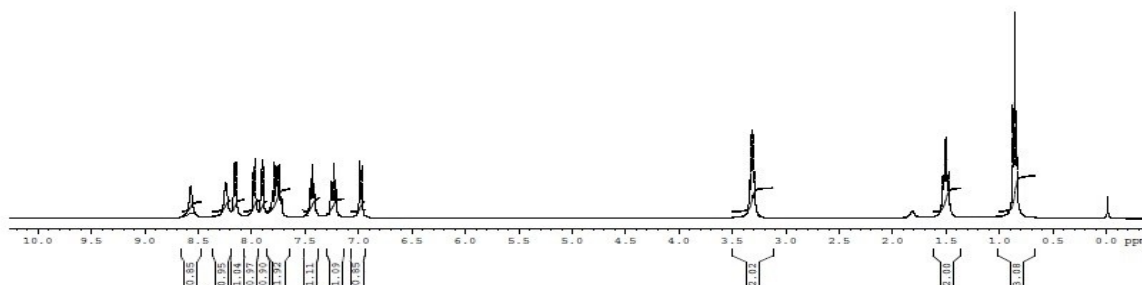
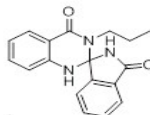


Minimum:				-1.5		
Maximum:	5.0	5.0		80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
294.1232	294.1243	-1.1	-3.7	11.5	292.0	C17 H16 N3 O2

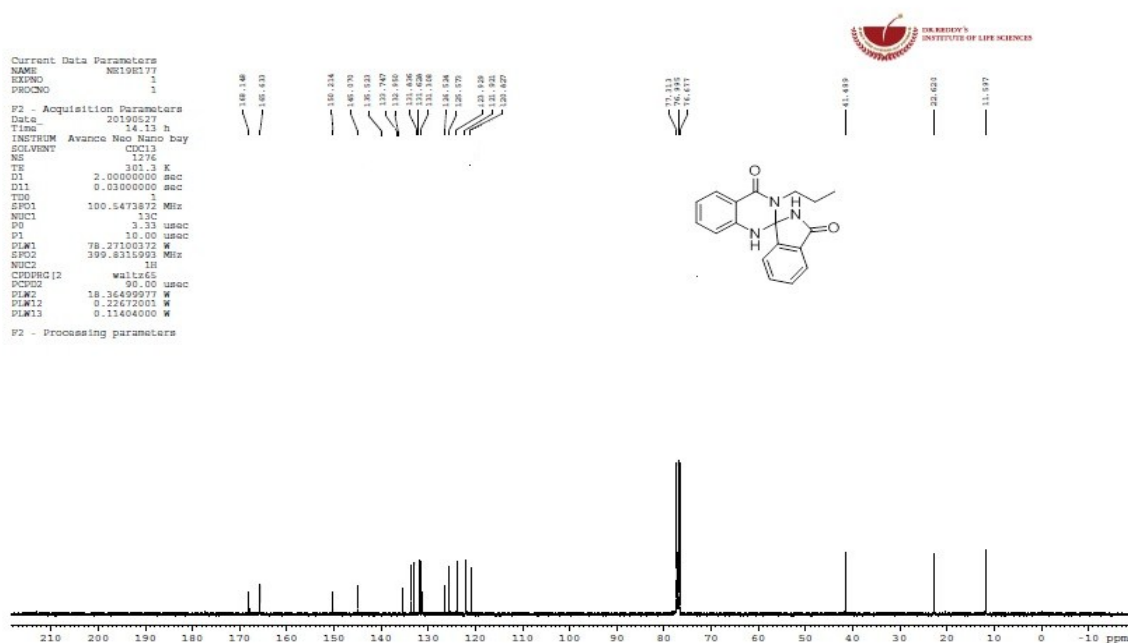
f 3'-Propyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1b):



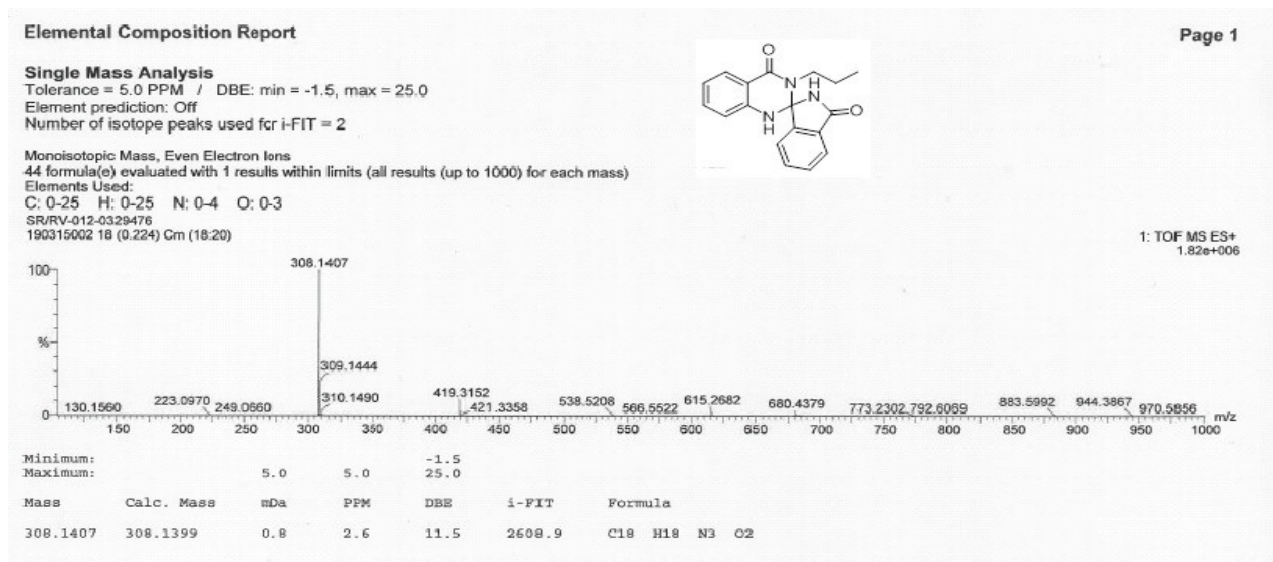
Current Data Parameters
NAME: N198176
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190527
Time: 12.58 h
INSTRUM: Avance Neo-Mag
SOLVENT: CDCl3
NS: 16
TE: 301.1 K
D1: 1.00000000 sec
TDO: 1
SFO1: 399.8324690 MHz
NUC1: 1H
P1: 3.33 usec
PL1: 10.00 usec
PLW1: 10.36499977 W
F2 - Processing parameters



¹³C NMR of 3'-Propyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4'(3'H)-dione (1b):



HRMS of 3'-Propyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4'(3'H)-dione (1b):



HRMS of 3'-Isopropyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1c):

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

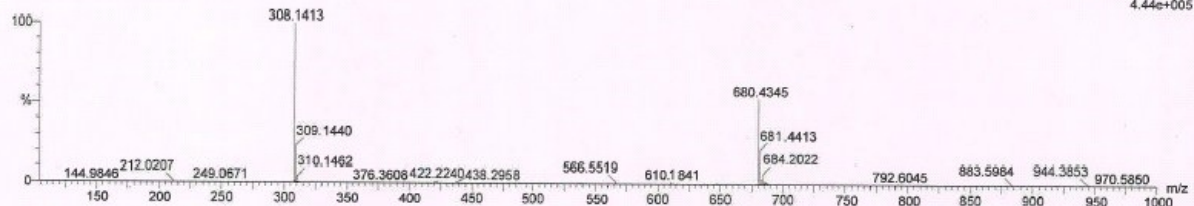
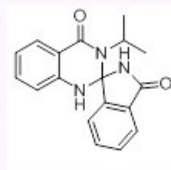
152 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-28 H: 0-37 N: 0-5 O: 0-7

SR/RV-012-0329476

190315002 20 (0.241) Cm (20:23-45:50)



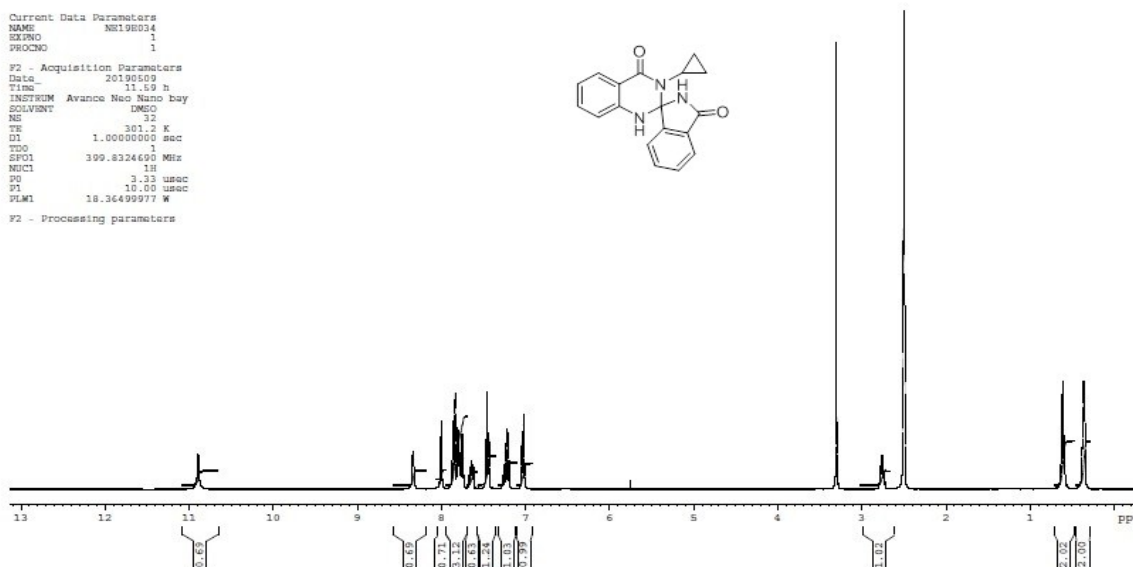
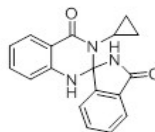
1: TOF MS ES+
4.44e+005

Minimum:							
Maximum:	5.0	5.0	-1.5				
			80.0				
Mass	Calc. Mass	mDa	PFM	DBE	i-FIT	Formula	
308.1413	308.1399	1.4	4.5	11.5	751.2	C18	H18 N3 O2

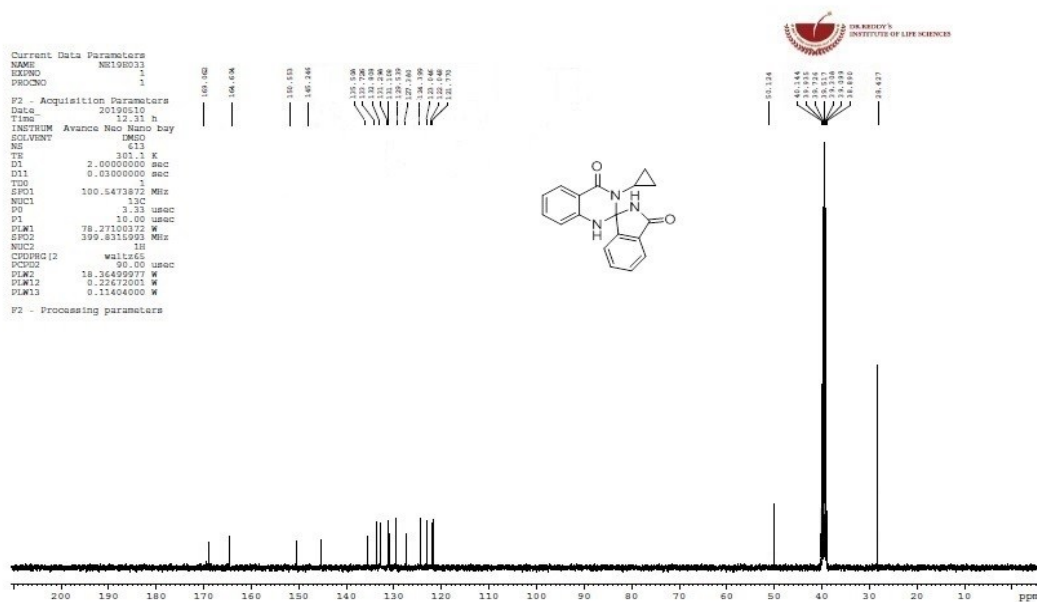
¹H NMR of 3'-Cyclopropyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1d)



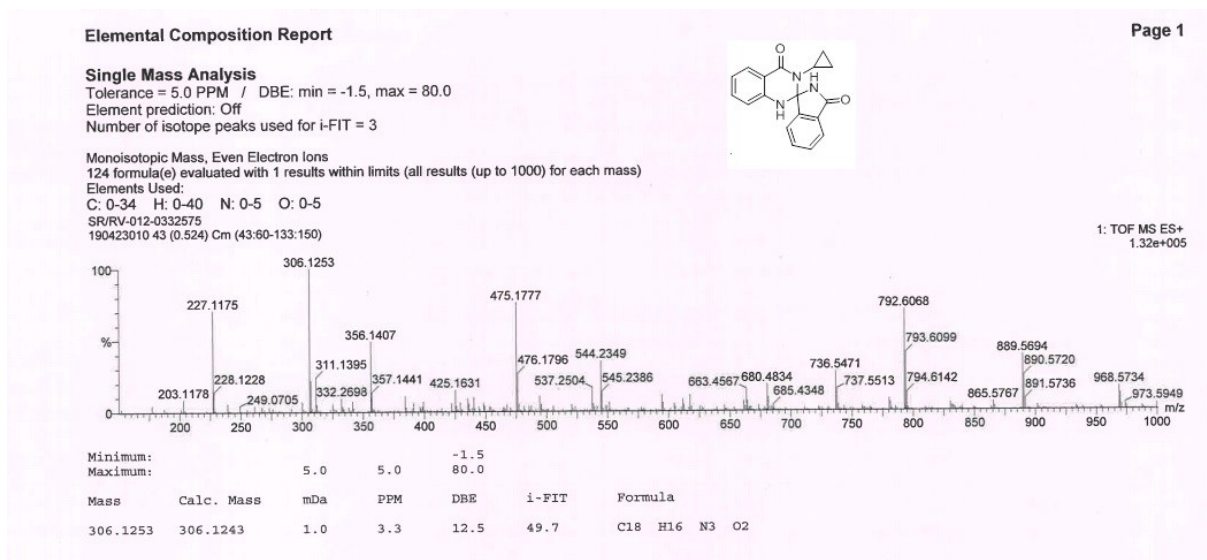
Current Data Parameters
NAME: NS19B034
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190509
Time: 11:59 h
INSTRUM: Avance Neo Nano bay
SOLVENT: DMSO
NS: 32
TE: 301.2 K
D1: 1.00000000 sec
TDO: 1
SFO1: 300.8324690 MHz
NUC1: 1H
P0: 3.33 usec
P1: 10.00 usec
PLM1: 18.36499977 W
F2 - Processing parameters



¹³C NMR of 3'-Cyclopropyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione(1d)

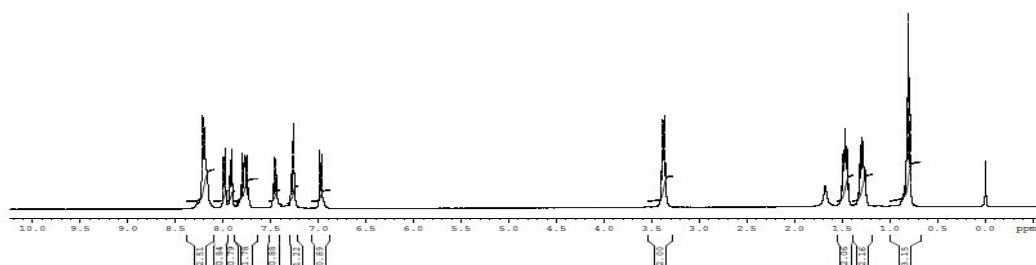
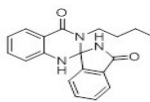


HRMS of 3'-cyclopropyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1d)



¹H NMR of 3'-Butyl-1'H-spiro[isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione(1e):

Current Data Parameters
NAME NE19P004
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190604
Time 13.02 h
INSTRUM Avance Neo Nano buy
SOLVENT CDCl3
NS 16
DS 301.1 K
D1 1.00000000 sec
SFO1 399.8324690 MHz
NUC1 1H
P1 3.33 usec
PL1 18.36499977 W
F2 - Processing parameters



¹³C NMR of 3'-Butyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1e):

Current Data Parameters
NAME NE19P005
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190604
Time 14.53 h
INSTRUM Avance Neo Nano buy
SOLVENT CDCl3
NS 16
DS 301.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TDS 100.5473872 MHz
SFO1 100.6261155 MHz
NUC1 13C
P1 10.00 usec
PL1 78.27100372 W
SFO2 399.8315993 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 90.00 usec
PLM2 18.36499977 W
PLM3 0.22672003 W
PLM13 0.11404000 W
F2 - Processing parameters

167.805
167.146

150.128
148.086

135.707
135.104
134.104
133.104
132.104
131.104
130.104
129.104
128.104
127.104
126.104
125.104
124.104
123.104
122.104
121.104
120.104
119.104
118.104
117.104
116.104
115.104
114.104
113.104
112.104
111.104
110.104
109.104
108.104
107.104
106.104
105.104
104.104
103.104
102.104
101.104
100.104
99.104
98.104
97.104
96.104
95.104
94.104
93.104
92.104
91.104
90.104
89.104
88.104
87.104
86.104
85.104
84.104
83.104
82.104
81.104
80.104
79.104
78.104
77.104
76.104
75.104
74.104
73.104
72.104
71.104
70.104
69.104
68.104
67.104
66.104
65.104
64.104
63.104
62.104
61.104
60.104
59.104
58.104
57.104
56.104
55.104
54.104
53.104
52.104
51.104
50.104
49.104
48.104
47.104
46.104
45.104
44.104
43.104
42.104
41.104
40.104
39.104
38.104
37.104
36.104
35.104
34.104
33.104
32.104
31.104
30.104
29.104
28.104
27.104
26.104
25.104
24.104
23.104
22.104
21.104
20.104
19.104
18.104
17.104
16.104
15.104
14.104
13.104
12.104
11.104
10.104
9.104
8.104
7.104
6.104
5.104
4.104
3.104
2.104
1.104
0.104

77.313
77.000
76.697
76.394



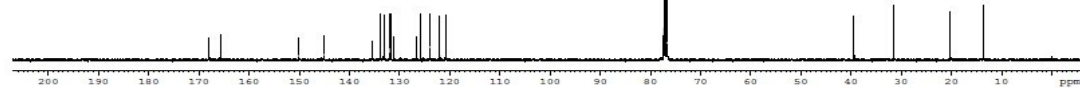
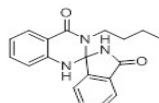
31.447

31.443

26.443

14.438

-1.032



HRMS of 3'-Butyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1e):

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 25.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

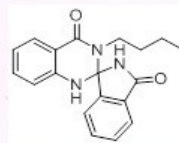
41 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

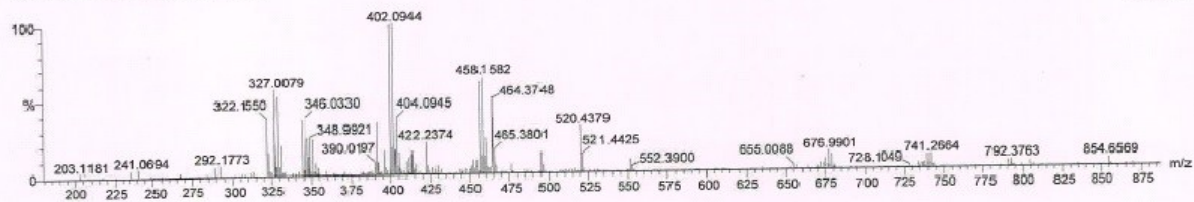
C: 0-25 H: 0-25 N: 0-4 O: 0-3

SR/RV-012-0345502

190727004 96 (1.163) Cm (95:102-151:158)



1: TOF MS ES+
8.73e+003



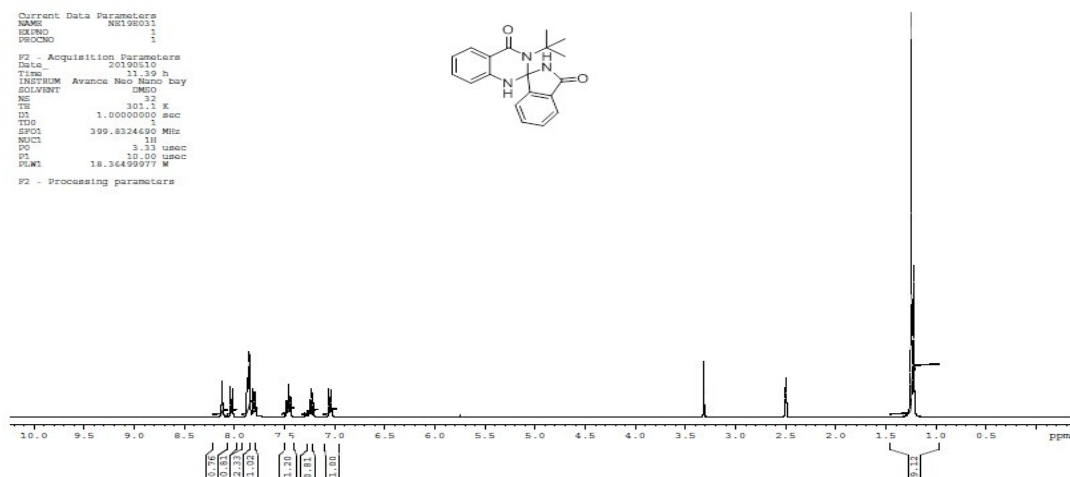
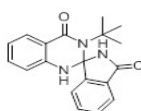
Minimum:				-1.5		
Maximum:	5.0	10.0	25.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
322.1550	322.1556	+0.6	+1.9	11.5	127.5	C19 H20 N3 O2

1

H-NMR of 3'-(tert-butyl)-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1f):



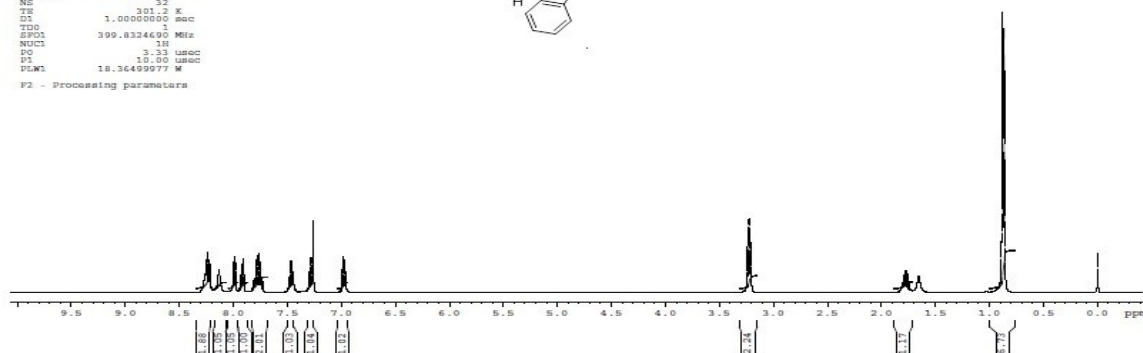
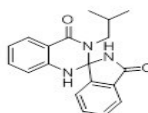
Current Data Parameters
NAME: NS198031
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190510
Time: 11:39 h
INSTRUM: Avance Neo Nano buy
SOLVENT: DMSO
NS: 12
TS: 101.1 K
DT: 1.0000000 sec
TD: 399.832460 MHz
SFO2: 1H
NUC1: 1H
PC: 3.33 usec
P1: 10.00 usec
PL1: 18.36499977 W
F2 - Processing parameters



¹H-NMR of 3'-isobutyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1g):



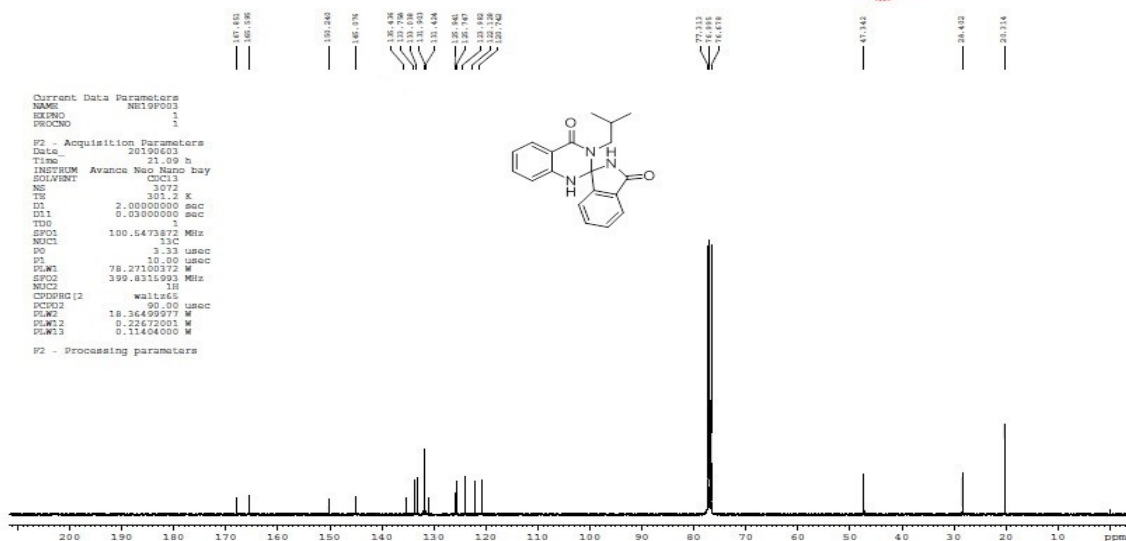
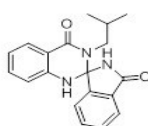
Current Data Parameters
NAME: NH19P002
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190603
Time: 17.58 h
INSTRUM: Avance Neo Nano buy
SOLVENT: CDCl3
NS: 32
DS: 1
TE: 301.2 K
D1: 1.00000000 sec
TDO: 399.8324690 MHz
SFO: 1H
NUC1: 1H
P1: 3.33 usec
PL1: 18.00 usec
PL12: 18.36499977 W
F2 - Processing parameters



¹³C NMR of 3'-Isobutyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1g):



Current Data Parameters
NAME: NH19P003
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190603
Time: 21.09 h
INSTRUM: Avance Neo Nano buy
SOLVENT: CDCl3
NS: 1072
DS: 1
TE: 301.2 K
D1: 2.00000000 sec
D11: 0.03000000 sec
TDO: 100.5473879 MHz
SFO: 13C
NUC1: 13C
P1: 3.33 usec
PL1: 10.00 usec
PL12: 78.27100372 W
SFO: 399.8315993 MHz
NUC2: 1H
CROSSPO2: waltz16
PCPO2: 90.00 usec
PL12: 18.36499977 W
PL12: 0.22672001 W
PL13: 0.11404000 W
F2 - Processing parameters



HRMS of 3'-Isobutyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1g):

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 25.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

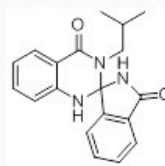
41 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

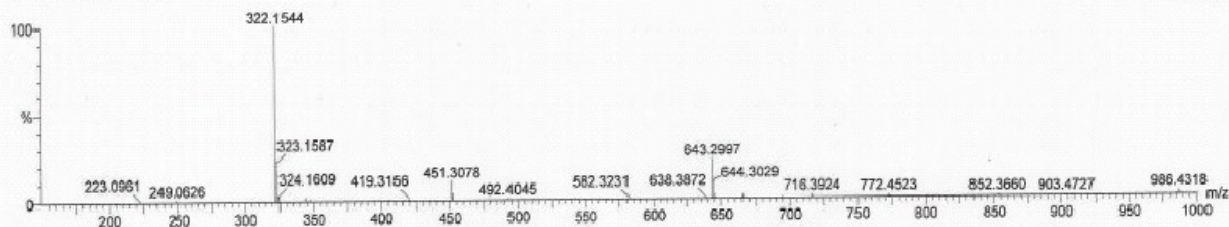
C: 0-25 H: 0-25 N: 0-4 O: 0-3

SR/RV-012-0358457

190723004 98 (1.194) Cm (98:101)

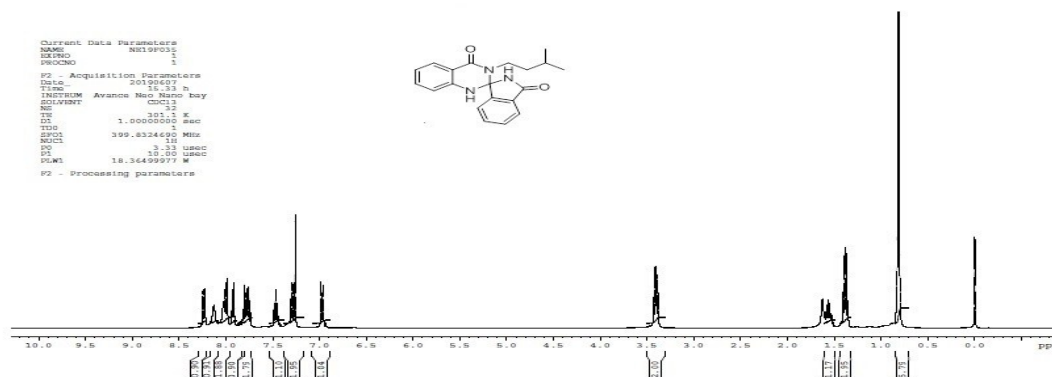


1: TOF MS ES+
5.44e+005

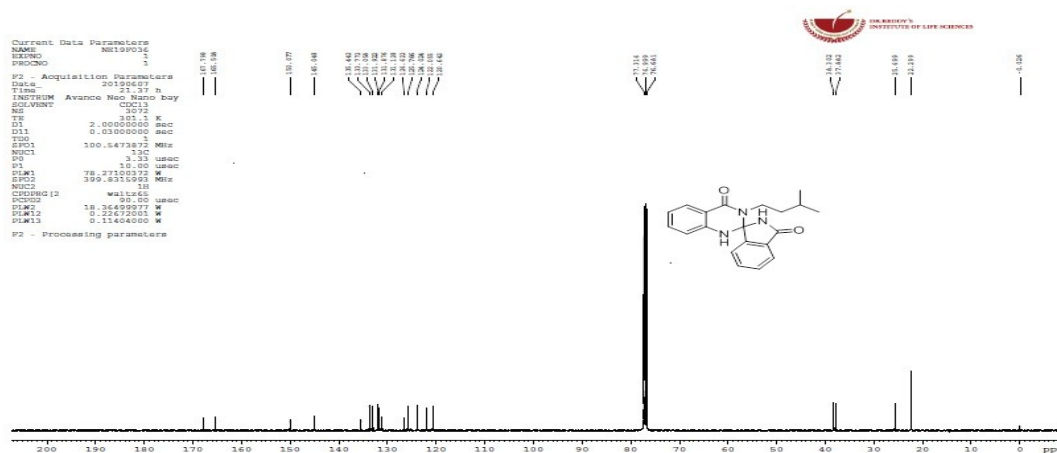


Minimum:				-1.5		
Maximum:	5.0	5.0		25.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
322.1544	322.1556	-1.2	-3.7	11.5	26.6	C19 H20 N3 O2

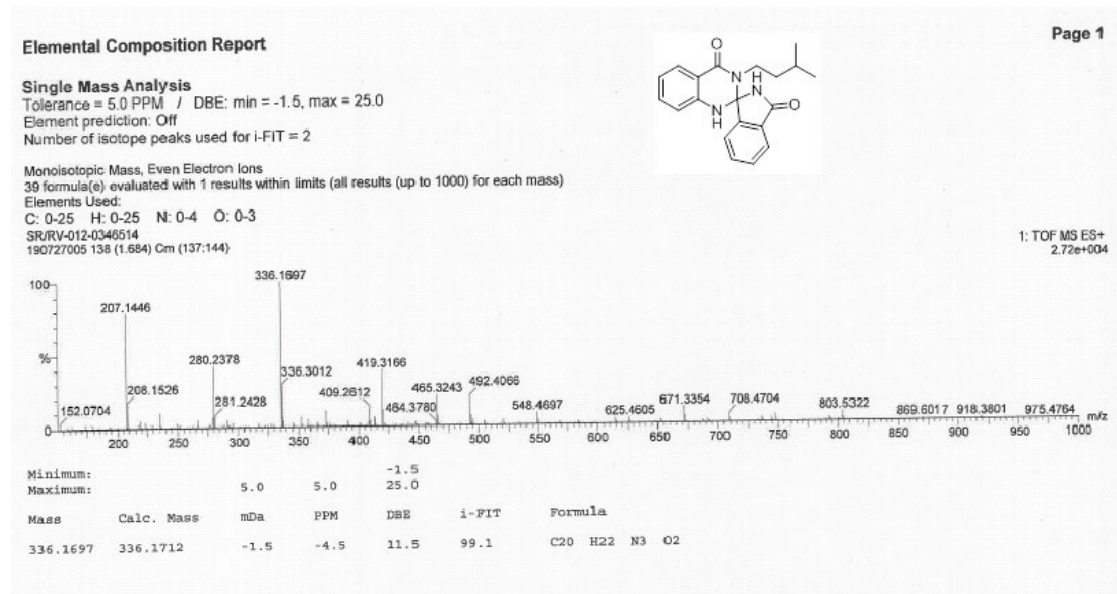
¹H-NMR of 3'-isopentyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1h):



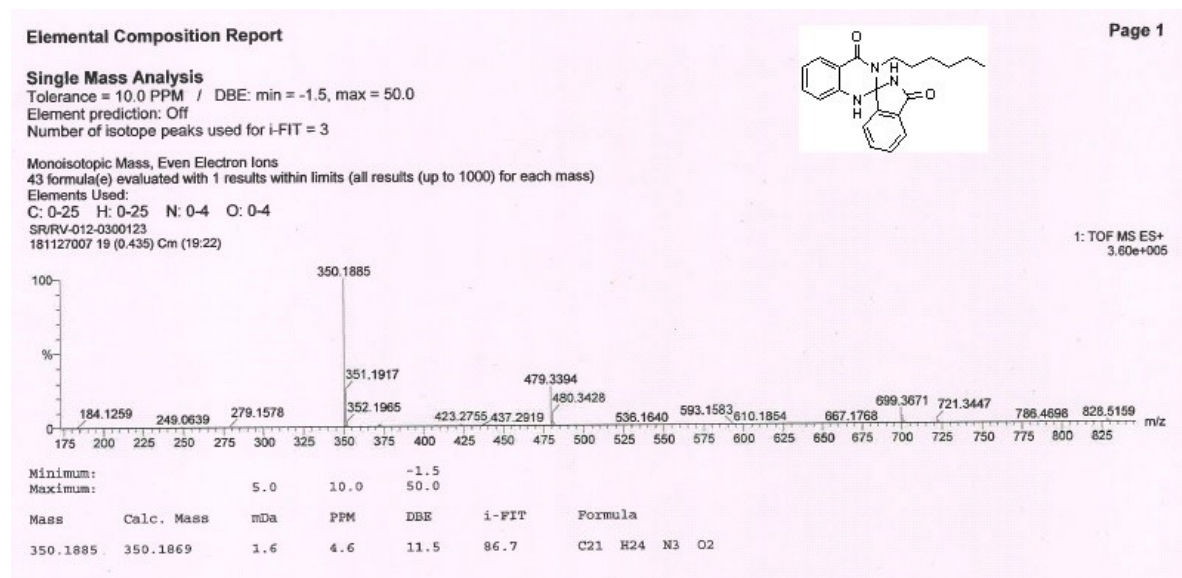
¹³C NMR of 3'-Isopentyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1h):



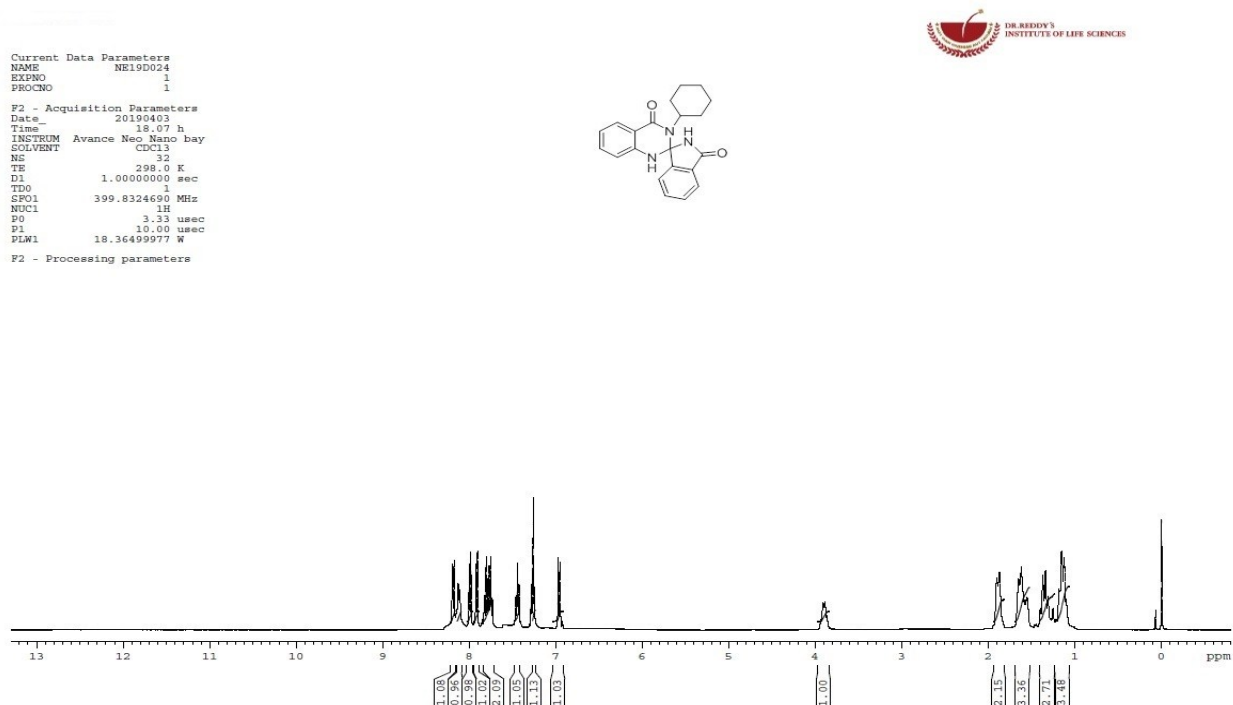
HRMS of 3'-isopentyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1h):



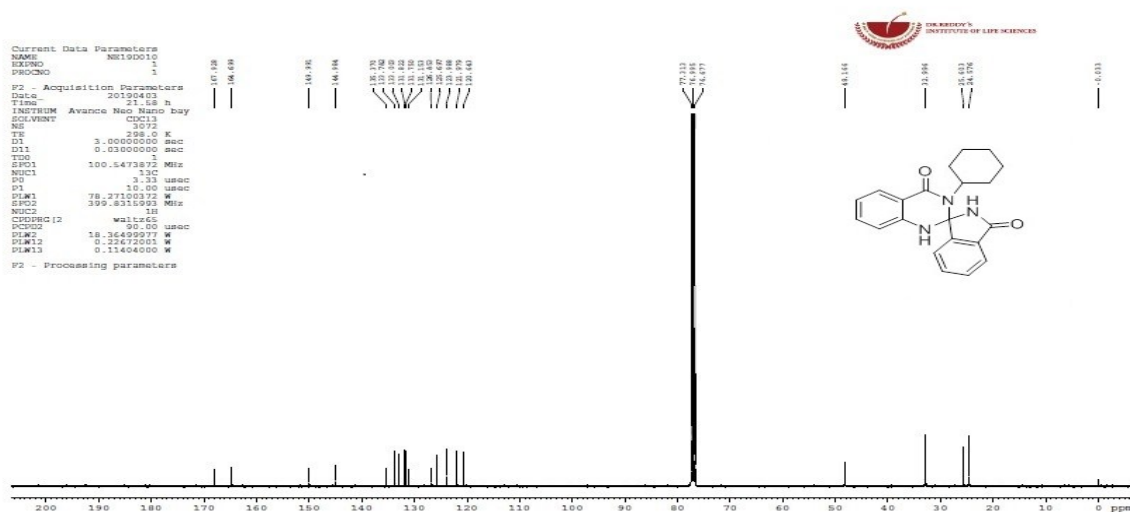
HRMS of 3'-hexyl-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1i):



¹H-NMR of 3'-cyclohexyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1j):



¹³C NMR of 3'-Cyclohexyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1j):



HRMS of 3'-cyclohexyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1j):

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

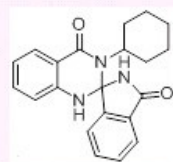
45 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

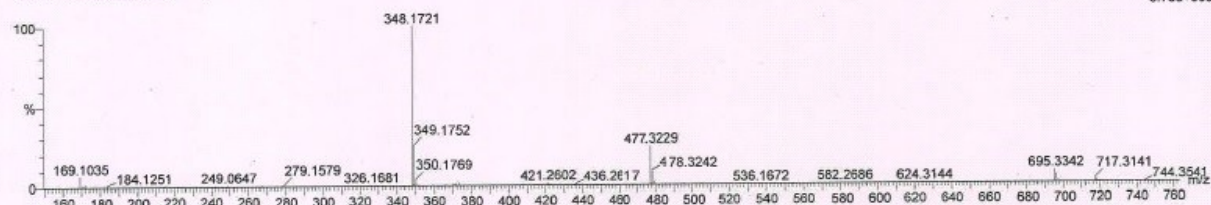
C: 0-25 H: 0-25 N: 0-4 O: 0-4

SRV-012-0300125

181127005 18 (0.416) Cm (18.22)



Page 1

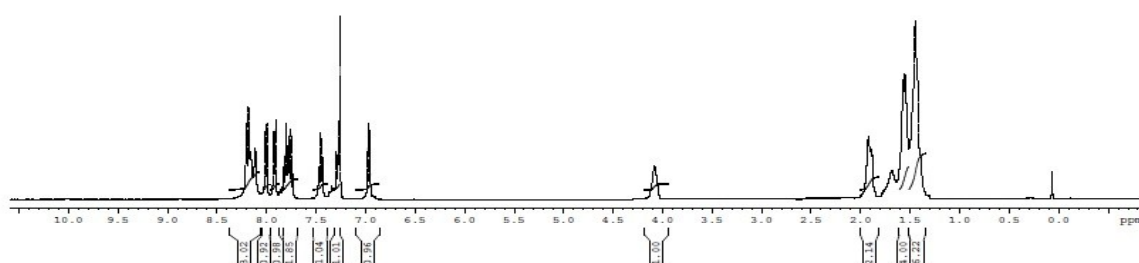
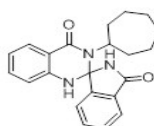


Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
348.1721	348.1712	0.9	2.6	12.5	215.5	C21 H22 N3 O2

¹H-NMR of 3'-cycloheptyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1k):



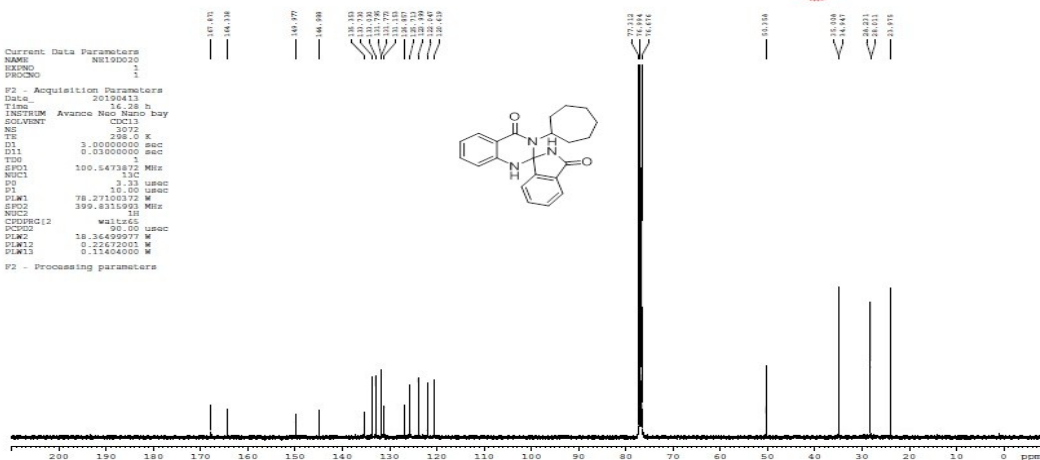
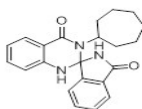
Current Data Parameters
NAME: N1100019
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190413
Time: 12.18 h
INSTRUM: Avance Neo Nano bay
SOLVENT: CDCl3
NS: 32
TE: 298.0 K
D1: 1.00000000 sec
TD0: 1
SFO1: 399.8324600 MHz
NUC1: 1H
P0: 3.33 usec
P1: 10.00 usec
PLW1: 18.36499977 W
F2 - Processing parameters



¹³C-NMR of 3'-cycloheptyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1k):



Current Data Parameters
NAME: N1100020
EXPNO: 1
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20190413
Time: 12.28 h
INSTRUM: Avance Neo Nano bay
SOLVENT: CDCl3
TE: 298.0 K
D1: 3.00000000 sec
D11: 0.03000000 sec
TD0: 1
SFO1: 100.6278722 MHz
NUC1: 13C
P0: 3.33 usec
P1: 15.00 usec
PLW1: 78.27100372 W
SFO2: 399.8316993 MHz
NUC2: 1H
CHRG12: waltz16
PCPD0: 50.00 usec
PLW2: 18.36499977 W
PLW12: 0.22672003 W
PLW13: 0.11404000 W
F2 - Processing parameters



HRMS of 3'-cycloheptyl-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1k):

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

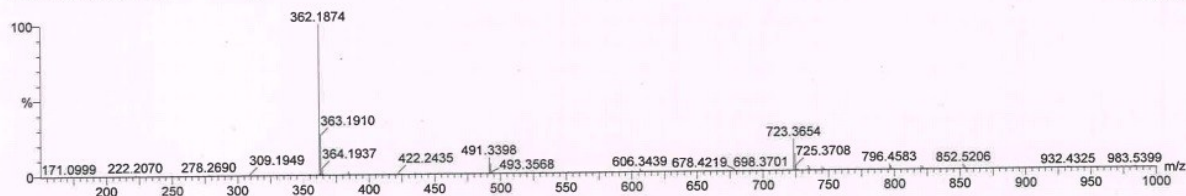
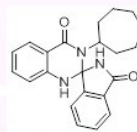
126 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-34 H: 0-40 N: 0-5 O: 0-5

SR/RV-012-0332554

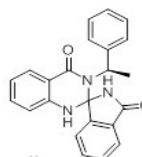
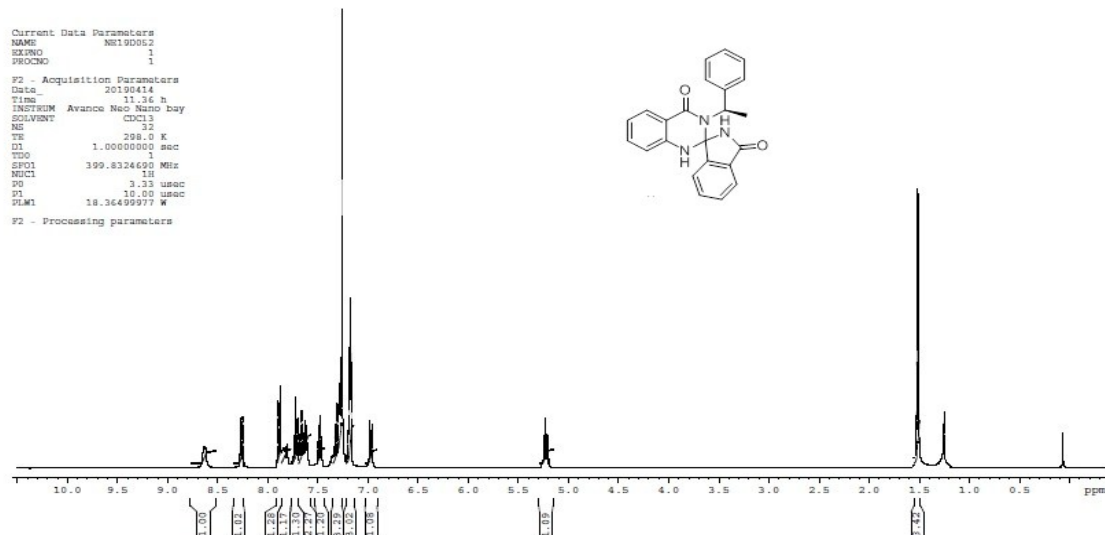
190423009 55 (0.670) Cm (52.60-121.136)



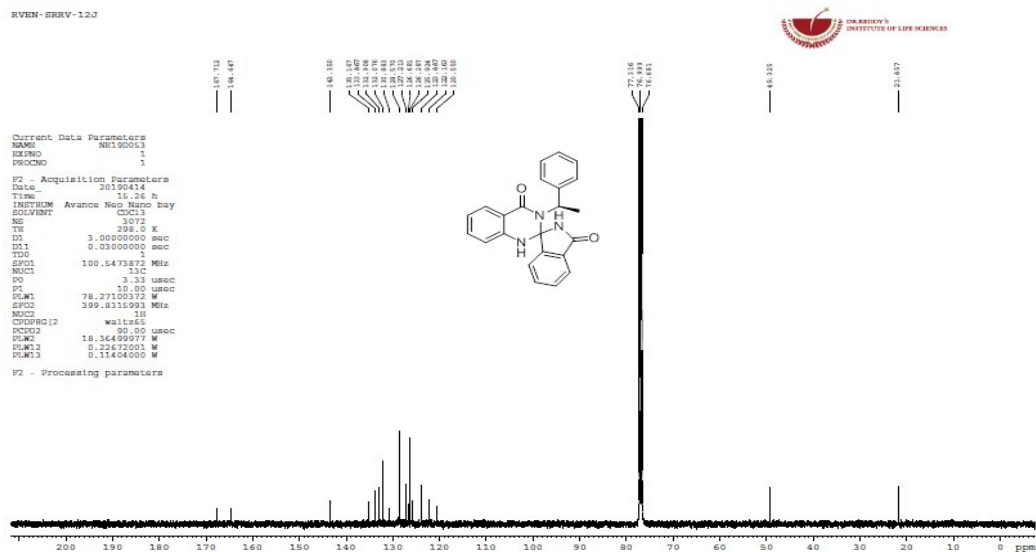
Minimum:				-1.5					
Maximum:		5.0	5.0	80.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula			
362.1874	362.1869	0.5	1.4	12.5	130.5	C22	H24	N3	O2

1: TOF MS ES+
3.00e+005

¹H-NMR of 3'-((R)-1-phenylethyl)-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1l):



¹³C-NMR of 3'-((R)-1-phenylethyl)-1'H-spiro[isindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1l):



HRMS of 3'-((R)-1-phenylethyl)-1'H-spiro[isindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1l):

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

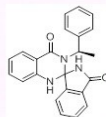
126 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

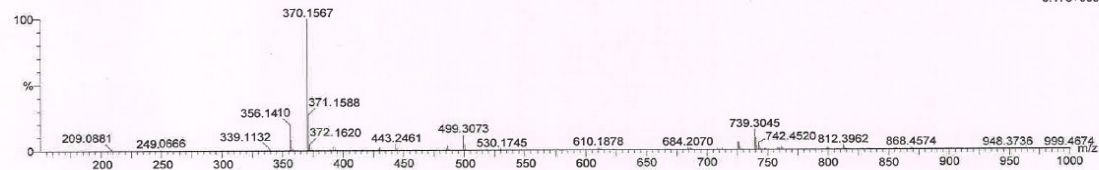
C: 0-34 H: 0-40 N: 0-5 O: 0-5

SR/RV-012-0335079

190423005 28 (0.339) Cm (28:39-103:113)



Page 1

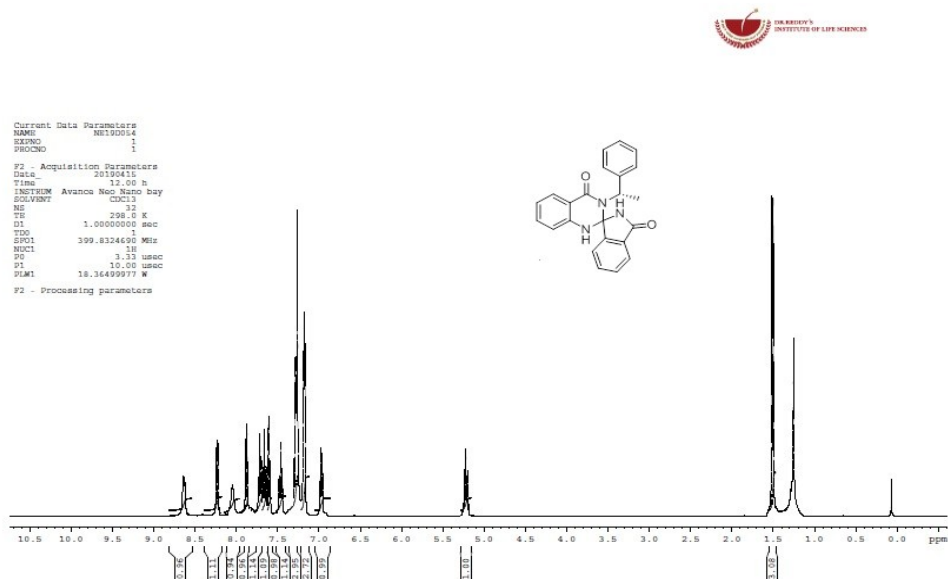


Minimum:

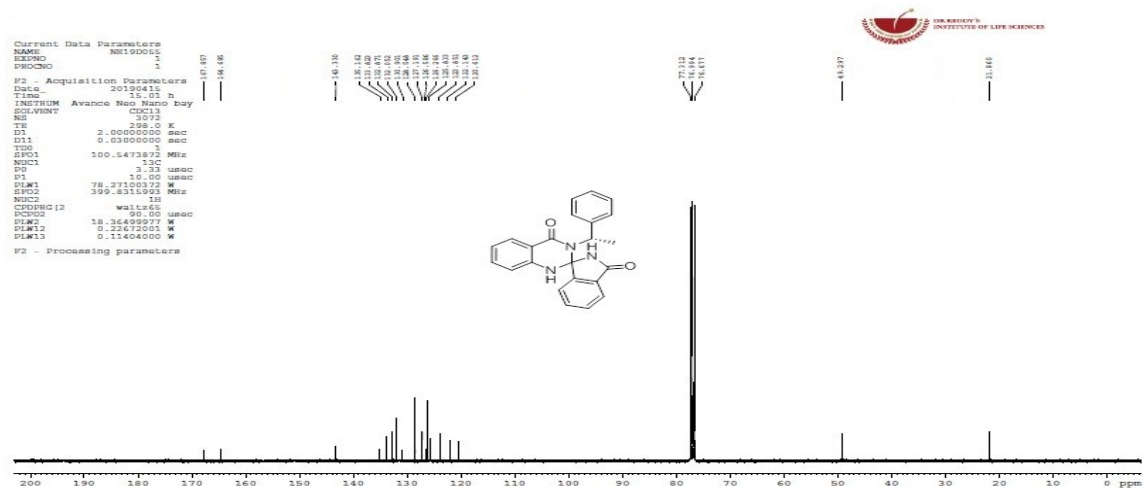
Maximum:

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
370.1567	370.1556	1.1	3.0	15.5	205.7	C23 H20 N3 O2

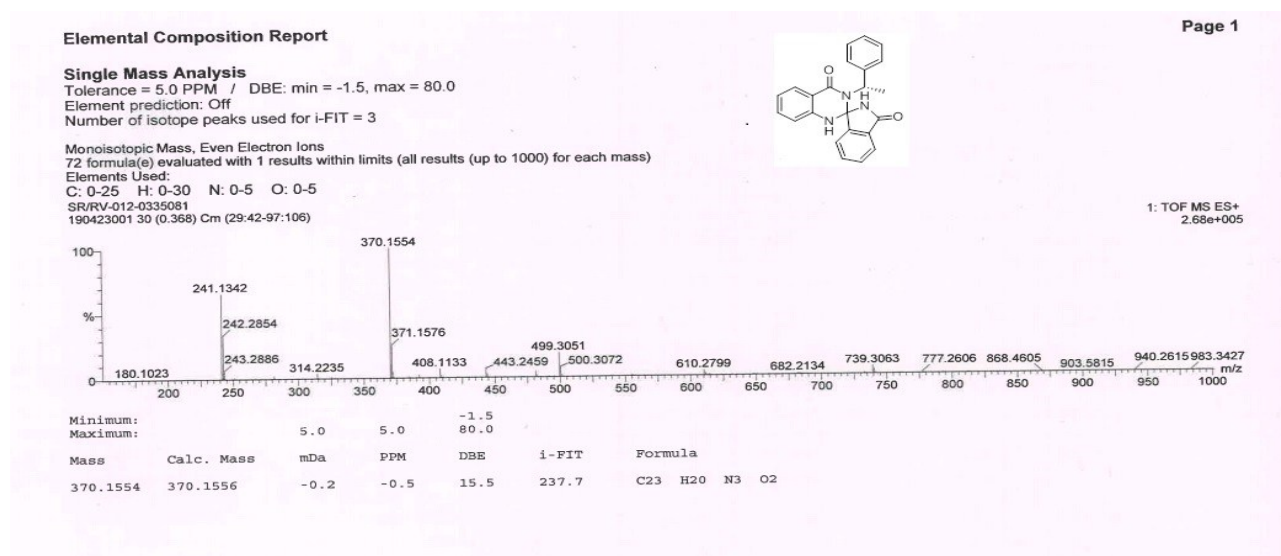
¹H-NMR of 3'-((S)-1-phenylethyl)-1'H-spiro[isindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1m):



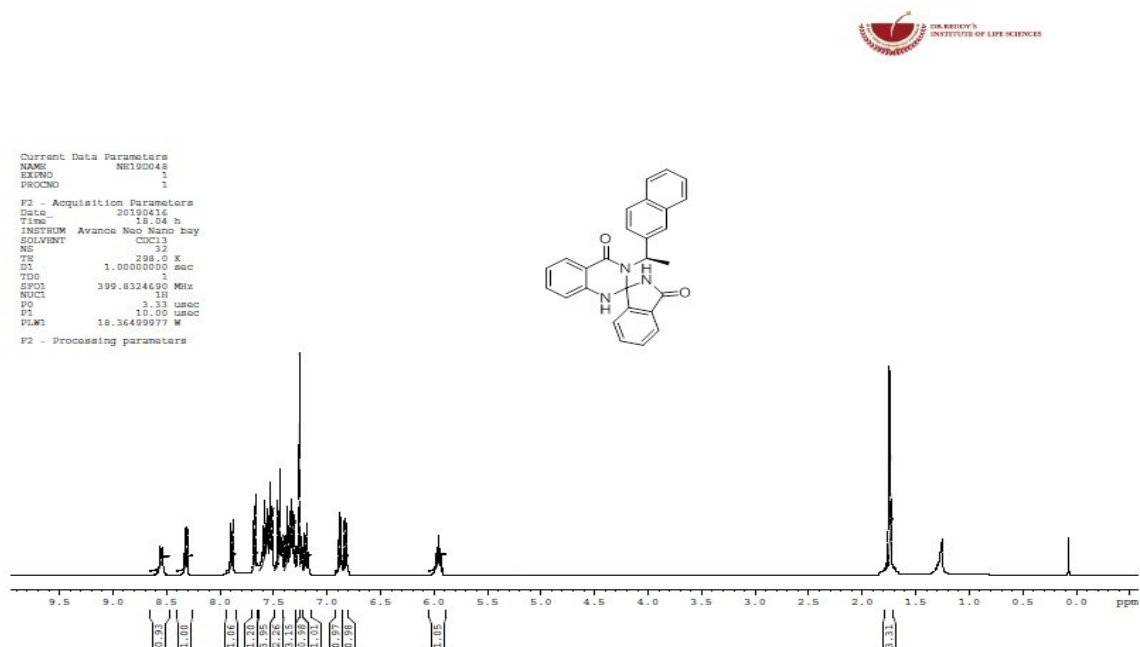
¹³C-NMR of 3'-((S)-1-phenylethyl)-1'H-spiro[isindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1m):



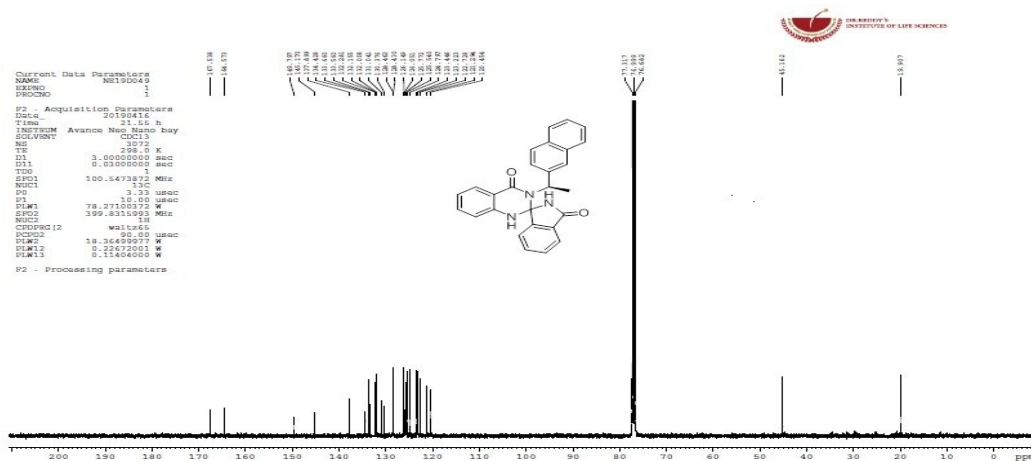
HRMS of 3'-((S)-1-phenylethyl)-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1m):



¹H NMR of 3'-((R)-1-(Naphthalen-2-yl)ethyl)-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione (1n):



¹³C-NMR of 3'-((R)-1-(naphthalen-2-yl) ethyl)-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1n):



HRMS of 3'-((R)-1-(naphthalen-2-yl)ethyl)-1'H-spiro [isoindoline-1, 2'-quinazoline]-3, 4' (3'H)-dione (1n):

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

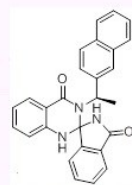
125 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

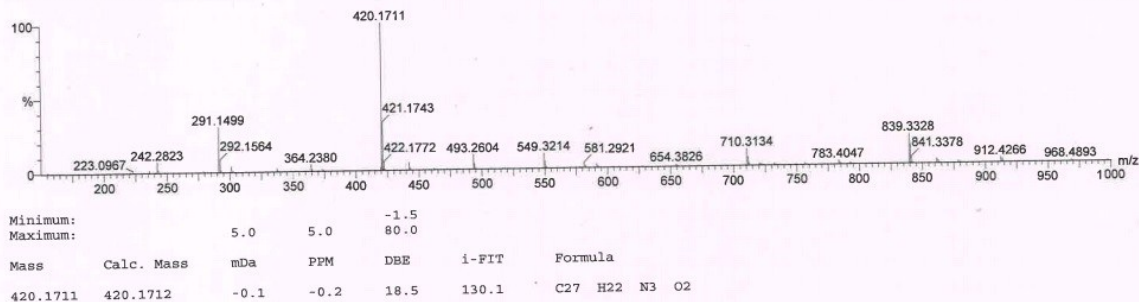
C: 0-34 H: 0-40 N: 0-5 O: 0-5

SR/RV-012-0335082

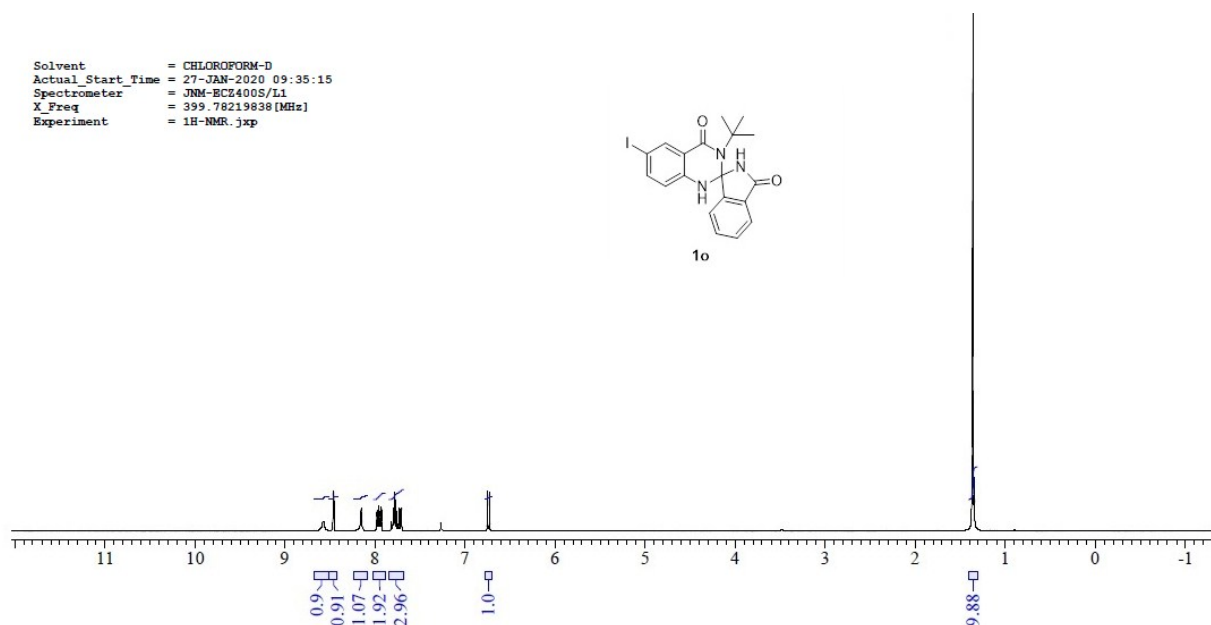
190423008 74 (0.907) Cm (73:83-141:145)



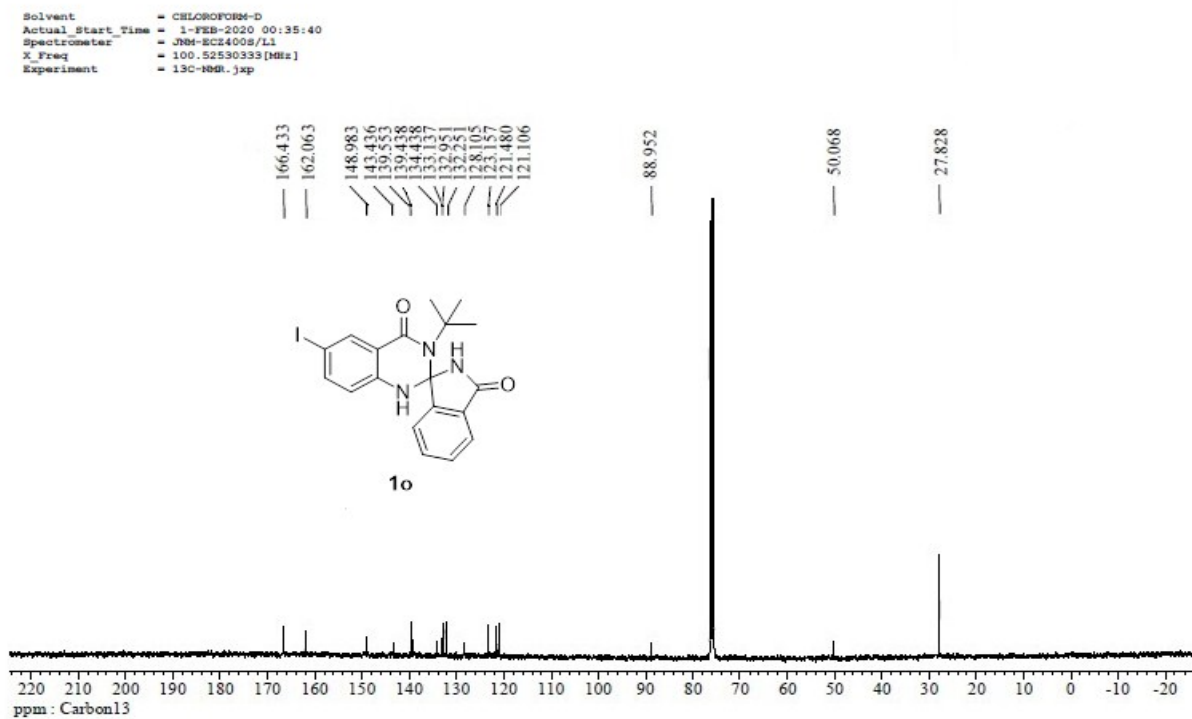
1: TOF MS ES+
4.09e+005



¹H NMR 3'-(tert-butyl)-6'-iodo-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1o):



¹³C-NMR of 3'-(tert-butyl)-6'-iodo-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1o):



HRMS of 3'-(tert-butyl)-6'-iodo-1'H-spiro[isoindoline-1,2'-quinazoline]-3,4'(3'H)-dione(1o):

