N–N Ring Opening of Diazabicyclo[3.1.0]hexanes with Aryl Isocyanates and Isothiocyanates

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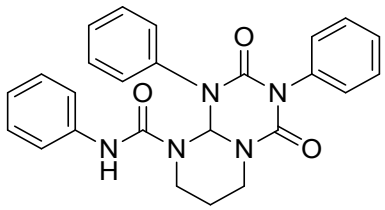
General information

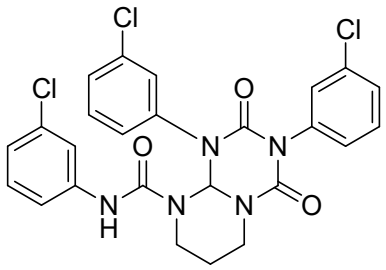
All the reactions were performed in anhydrous solvents under an argon atmosphere. Benzene was distilled over sodium. Reaction progress was monitored using thin layer chromatography (TLC) on precoated Silufol UV–254 plates. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 using a Bruker Avance 400 spectrometer, chemical shifts are given in ppm and normalized by the residual signals $CHCl_3$ (7.26) and DMSO-d5 (2.50) for proton spectra, and by the solvent signals $CDCl_3$ (77.16) and DMSO-d6 (39.52) for spectra on ^{13}C. HRMS spectra were obtained with a Bruker-maXis (QTOF). Xcalibur, Eos diffractometer was used for X-ray analysis. 1,5-Diazabicyclo[3.1.0]hexanes **1a,b** and azides **4a-c** were prepared using known procedures [1,2].

General procedure for synthesis of compounds 4

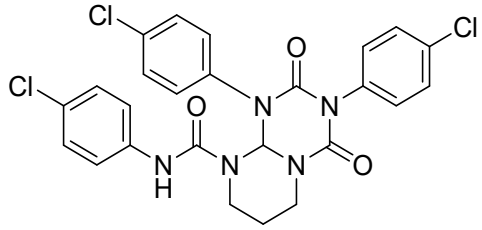
Diazabicyclohexane **1** (1 mmol) and isocyanate **2** (2.4 mmol) were dissolved in 5 ml benzene and molecular sieves (200 mg, MS 4A) were added. The solution was refluxed while stirring for several hours. After boiling, the solution was cooled to room temperature and diluted with diethyl ether, the precipitate along with the sieves was separated by filtration and dissolved in methylene chloride or acetone to separate the sieves. The solvent was removed using a rotary evaporator to obtain a pure product. The obtained product was recrystallized from a mixture of acetone and benzene if required.



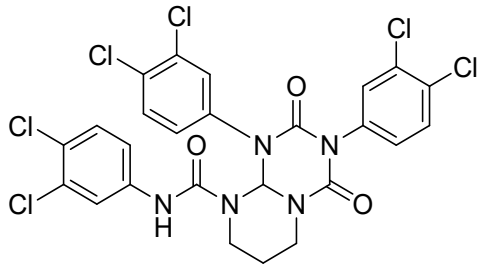
2,4-Dioxo-*N*,1,3-triphenylhexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3a was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 285 mg (2.4 mmol) of phenyl isocyanate **2a**, reaction time: 7 hours. Yield 241 mg (68%). White solid, m.p. 190–191 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.16 (s, 1H, NH), 7.50–7.26 (m, 14H, Ph), 7.04–6.97 (m, 1H, Ph), 6.45 (s, 1H, CH), 4.43–4.32 (m, 1H, CH_2), 3.92–3.80 (m, 1H, CH_2), 3.57–3.44 (m, 1H, CH_2), 3.30–3.18 (m, 1H, CH_2), 1.74–1.57 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.5, 151.0, 150.1, 139.5, 138.3, 136.6, 129.7, 128.9, 128.6, 128.4, 127.8, 127.6, 127.5, 122.5, 119.4, 78.3, 47.1, 41.3, 24.1. HRMS (ESI) m/z Calcd for $C_{25}H_{23}N_5O_3$ $[M+Na]^+$: 464.1693. Found: 464.1684.



***N*,1,3-Tris(3-chlorophenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3b** was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 368 mg (2.4 mmol) of 3-chlorophenyl isocyanate **2b**, reaction time: 5 hours. Yield 281 mg (65%). White solid, m.p. 124–125 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.41 (s, 1H, NH), 7.70–7.66 (m, 1H, Ar), 7.56–7.28 (m, 10H, Ar), 7.11–7.05 (m, 1H, Ar), 6.59 (s, 1H, CH), 4.43–4.32 (m, 1H, CH_2), 3.94–3.81 (m, 1H, CH_2), 3.64–3.52 (m, 1H, CH_2), 3.32–3.21 (m, 1H, CH_2), 1.78–1.60 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.3, 150.7, 149.7, 140.9, 139.3, 137.7, 133.0, 132.9, 132.5, 130.5, 130.2, 130.0, 129.6, 128.7, 127.9, 127.8, 127.6, 126.6, 122.3, 119.00, 117.8, 78.9, 46.4, 41.2, 24.0. HRMS (ESI) m/z Calcd for $C_{25}H_{20}Cl_3N_5O_3$ $[M+Na]^+$: 566.0524. Found: 566.0533.

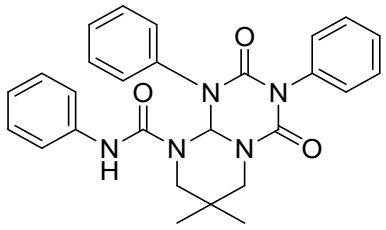


***N*,1,3-Tris(4-chlorophenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3c** was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 368 mg (2.4 mmol) of 4-chlorophenyl isocyanate **2c**, reaction time: 5 hours. Yield 345 mg (79%). White solid, m.p. 145–146 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.27 (s, 1H, NH), 7.53–7.45 (m, 6H, Ar), 7.44–7.39 (m, 2H, Ar), 7.38–7.30 (m, 4H, Ar), 6.51 (s, 1H, CH), 4.41–4.31 (m, 1H, CH_2), 3.90–3.79 (m, 1H, CH_2), 3.59–3.47 (m, 1H, CH_2), 3.30–3.17 (m, 1H, CH_2), 1.74–1.59 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.3, 150.7, 149.7, 138.4, 136.9, 135.3, 132.3, 132.1, 131.5, 129.6, 128.9, 128.5, 128.4, 126.3, 121.1, 79.0, 46.5, 41.2, 24.0. HRMS (ESI) m/z Calcd for $C_{25}H_{20}Cl_3N_5O_3$ $[M+Na]^+$: 566.0524. Found: 566.0525.

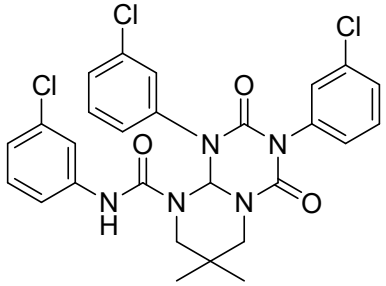


***N*,1,3-Tris(3,4-dichlorophenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3d** was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 451 mg (2.4 mmol) of 3,4-dichlorophenyl isocyanate **2d**, reaction time: 5 hours. Yield 333 mg (63%). White solid, m.p. 175–176 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.44 (s, 1H, NH), 7.79 (d, 1H, J = 2.3 Hz, Ar), 7.75–7.68 (m, 3H, Ar), 7.67 (d, 1H, J = 2.3 Hz, Ar), 7.54 (d, 1H, J = 8.8 Hz, Ar), 7.43–

7.33 (m, 3H, Ar), 6.67 (s, 1H, CH), 4.39–4.28 (m, 1H, CH_2), 3.88–3.76 (m, 1H, CH_2), 3.68–3.54 (m, 1H, CH_2), 3.28–3.16 (m, 1H, CH_2), 1.80–1.65 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.0, 150.6, 149.5, 139.5, 137.6, 136.1, 131.6, 131.1, 130.9, 130.85, 130.80, 130.7, 130.4, 130.2, 129.6, 128.2, 124.2, 120.8, 119.6, 78.5, 45.4, 40.8, 23.8. HRMS (ESI) m/z Calcd for $C_{25}H_{17}Cl_6N_5O_3$ $[M+Na]^+$: 669.9325. Found: 669.9329.

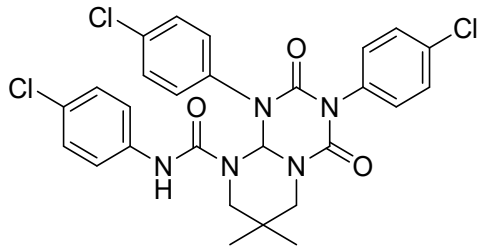


7,7-Dimethyl-2,4-dioxo-*N*,1,3-triphenylhexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3e was obtained from 112 mg (1 mmol) of diazaalkane **1b** and 285 mg (2.4 mmol) of phenyl isocyanate **2a**, reaction time: 7 hours. The obtained product was recrystallized from a mixture of acetone and benzene. Yield 310 mg (83%). White solid, m.p. 188–190 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.14 (s, 1H, NH), 7.52–7.24 (m, 14H, Ph), 7.04–6.95 (m, 1H, Ph), 6.38 (broad s, 1H, CH), 4.13–4.03 (m, 1H, CH_2), 3.63–3.48 (m, 1H, CH_2), 3.18–2.90 (m, 1H, CH_2), 0.97 (s, 3H, CH_3), 0.87 (s, 3H, CH_3). ^{1}H NMR (400 MHz, Acetone-*d*6) δ 8.31 (s, 1H, NH), 7.61 – 7.14 (m, 14H, Ph), 7.01 (t, *J* = 7.4 Hz, 1H, Ph), 6.46 (s, 1H, CH), 4.23 (d, *J* = 13.3 Hz, 1H, CH_2), 3.64 (d, *J* = 14.5 Hz, 1H, CH_2), 3.42 (d, *J* = 14.7 Hz, 1H, CH_2), 3.06 (d, *J* = 13.3 Hz, 1H, CH_2), 1.10 (s, 3H, CH_3), 0.95 (s, 3H, CH_3). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.7, 151.0, 150.3, 139.7, 138.3, 136.6, 129.7, 128.9, 128.6, 128.4, 128.3, 127.63, 127.62, 127.58, 122.3, 119.1, 78.9, 52.7, 33.6, 24.4, 23.0. HRMS (ESI) m/z Calcd for $C_{27}H_{27}N_5O_3$ $[M+Na]^+$: 492.2006. Found: 492.2023.

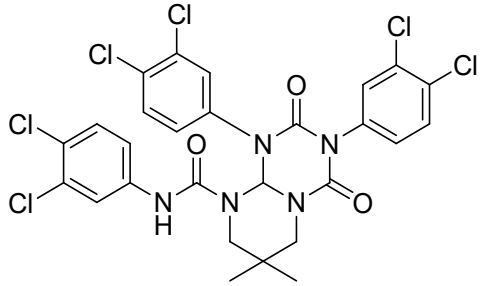


***N*,1,3-Tris(3-chlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3f** was obtained from 112 mg (1 mmol) of diazaalkane **1b** and 368 mg (2.4 mmol) of 3-chlorophenyl isocyanate **2b**, reaction time: 5 hours. Yield 365 mg (77%). White solid, m.p. 187–189 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.39 (s, 1H, NH), 7.65–7.24 (m, 11H, Ar), 7.05 (s, 1H, Ar), 6.49 (broad s, 1H, CH), 4.05 (d, 1H, *J* = 13.2 Hz, CH_2), 3.62–3.48 (m, 1H, CH_2), 3.15–3.00 (m, 1H, CH_2), 0.94 (s, 3H, CH_3), 0.87 (s, 3H, CH_3). ^{1}H NMR (400 MHz, Acetone-*d*6) δ 8.59 (s, 1H, NH), 7.66 (s, 1H, Ar), 7.61 – 7.19 (m, 10H, Ar), 7.05 (d, *J* = 7.9 Hz, 1H, Ar), 6.55 (s, 1H, CH), 4.22 (d, *J* = 13.3 Hz, 1H, CH_2), 3.69 (d, *J* = 14.6 Hz, 1H, CH_2), 3.49 (d, *J* = 14.7 Hz, 1H, CH_2), 3.10 (d, *J* = 13.5 Hz, 1H, CH_2), 1.09 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.6, 150.7, 149.9, 141.0, 139.3, 137.7, 133.05, 133.00, 132.5, 130.5, 130.3, 130.0, 129.6, 128.7, 128.0, 127.8, 127.5, 126.3, 122.1, 118.5, 117.5, 78.5,

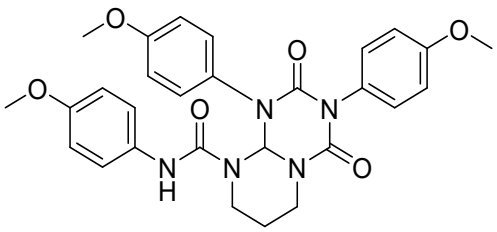
52.6, 33.8, 30.5, 24.3, 23.0. HRMS (ESI) m/z Calcd for $C_{27}H_{24}Cl_3N_5O_3$ [M+Na]$^+$: 596.0809. Found: 596.0831.



***N*,1,3-Tris(4-chlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1*H*-pyrimido[1,2-*a*][1,3,5]triazine-9(2*H*)-carboxamide 3g** was obtained from 112 mg (1 mmol) of diazaalkane **1b** and 368 mg (2.4 mmol) of 4-chlorophenyl isocyanate **2c**, reaction time: 5 hours. The obtained product was recrystallized from a mixture of acetone and benzene. Yield 327 mg (71%). White solid, m.p. 141–142 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.26 (s, 1H, NH), 7.56–7.28 (m, 12H, Ar), 6.42 (broad s, 1H, CH), 4.05 (d, 1H, *J* = 13.2 Hz, CH_2), 3.53 (d, 1H, *J* = 13.2 Hz, CH_2), 3.06 (d, 1H, *J* = 13.2 Hz, CH_2), 0.93 (s, 3H, CH_3), 0.86 (s, 3H, CH_3). ^{1}H NMR (400 MHz, Acetone-*d*6) δ 8.51 (s, 1H, NH), 7.56 (d, *J* = 8.8 Hz, 1H, Ar), 7.51 – 7.26 (m, 11H, Ar), 6.47 (s, 1H, CH), 4.22 (d, *J* = 13.3 Hz, 1H, CH_2), 3.66 (d, *J* = 14.6 Hz, 1H, CH_2), 3.44 (d, *J* = 14.6 Hz, 1H, CH_2), 3.07 (d, *J* = 13.3 Hz, 1H, CH_2), 1.08 (s, 3H, CH_3), 0.95 (s, 3H, CH_3). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.5, 152.5, 150.7, 149.9, 138.7, 138.5, 136.9, 135.3, 132.3, 132.1, 131.5, 129.4, 129.0, 128.6, 126.1, 125.3, 120.7, 119.8, 78.6, 52.7, 33.7, 30.7, 24.3, 22.9. HRMS (ESI) m/z Calcd for $C_{27}H_{24}Cl_3N_5O_3$ [M-H]$^+$: 570.0823. Found: 570.0815.



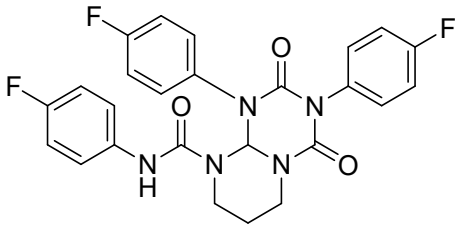
***N*,1,3-Tris(3,4-dichlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3h** was obtained from 112 mg (1 mmol) of diazaalkane **1b** and 451 mg (2.4 mmol) of 3,4-dichlorophenyl isocyanate **2d**, reaction time: 5 hours. Yield 314 mg (58%). White solid, m.p. 150–151 °C. ^{1}H NMR (400 MHz, Acetone-*d*6): δ 8.70 (broad s, 1H, NH), 7.79 (d, 1H, J = 2.4, Ar), 7.71 (d, 1H, *J* = 2.4, Ar), 7.68 (d, 1H, *J* = 2.3, Ar), 7.65 (d, 1H, *J* = 8.5, Ar), 7.59 (d, 1H, *J* = 8.6, Ar), 7.50–7.38 (m, 3H, Ar), 7.35 (s, 1H, Ar), 6.61 (s, 1H, CH), 4.21 (dd, 1H, J = 13.4, 1.6, CH_2), 3.69 (d, 1H, *J* = 14.8 Hz, CH_2), 3.51 (d, 1H, *J* = 14.8 Hz, CH_2), 3.09 (d, 1H, *J* = 13.4 Hz, CH_2), 1.08 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). ^{1}H-NMR (400 MHz, DMSO-*d*6): δ 9.46 (s, 1H, NH), 7.78–7.64 (m, 5H, Ar), 7.53 (d, *J* = 8.8 Hz, 1H, Ar), 7.43–7.30 (m, 3H, Ar), 6.58 (s, 1H, CH), 4.03 (d, *J* = 13.3 Hz, 1H, CH_2), 3.68–3.41 (m, 2H, CH_2), 3.16–2.97 (m, 1H, CH_2), 0.94 (s, 3H, CH_3), 0.88 (s, 3H, CH_3). ^{13}C NMR (100 MHz DMSO-*d*6): δ 156.4, 151.7, 150.5, 149.6, 139.6, 137.6, 136.1, 131.6, 131.2, 130.9, 130.8, 130.7, 130.6, 130.5, 130.4, 130.3, 129.4, 128.1, 124.0, 120.3, 119.2, 118.5, 78.1, 52.4, 34.0, 24.3, 23.1. HRMS (ESI) m/z Calcd for $C_{27}H_{21}Cl_6N_5O_3$ [M+Na]$^+$: 697.9639. Found: 697.9612.



***N*,1,3-Tris(4-methoxyphenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3i** was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 358 mg (2.4 mmol) of 3,4-methoxyphenyl isocyanate **2d,** reaction time: 5 hours. The obtained product was recrystallized from a mixture of diethyl ether and benzene. Yield 237 mg (56%). White solid. ^{1}H NMR (400 MHz, Acetone-*d6*) δ 8.15 (s, 1H, NH), 7.43 – 7.24 (m, 6H, Ar), 6.95 – 6.82 (m, 6H, Ar), 6.46 (s, 1H, CH), 4.50 (dd, *J* = 13.5, 5.8 Hz, 1H, CH_2), 3.87 (dt, *J* = 14.5, 4.6 Hz, 1H, CH_2), 3.81 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 3.61 – 3.52 (m, 1H, CH_2), 3.21 (td, *J* = 13.1, 4.5 Hz, 1H, CH_2), 1.91 – 1.81 (m, 1H, CH_2), 1.78 – 1.66 (m, 1H, CH_2). ^{13}C NMR (126 MHz, Acetone) δ 159.8 (2C), 157.2, 156.7, 152.7, 151.7, 133.4, 132.4, 131.7, 130.7, 130.3, 129.1, 122.4, 114.8, 114.6, 114.2, 80.7, 55.72, 55.66 (2C), 46.5, 41.8, 24.8. HRMS (ESI) m/z Calcd for $C_{28}H_{29}N_5O_6$ $[M+Na]^+$: 532.2191. Found: 532.2184.

General procedure for the synthesis of compounds 3 using azides

Benzoyl azide **4** (2.6 mmol, 2.6 equivalents) was dissolved in 5 ml of benzene, molecular sieves (200 mg, MS 4A) were added and boiled for 6 hours until the starting azide disappeared (monitored by TLC). After completion of the reaction, the solution was filtered, 84 mg (1 mmol) of diazabicyclohexane **1** and a new portion of molecular sieves (200 mg, MS 4A) were added. The solution was refluxed with stirring for 6 hours. After boiling, the solution was cooled to room temperature and diluted with diethyl ether, the precipitate along with the sieves was separated by filtration and dissolved in methylene chloride to separate the sieves. The solvent was distilled off using a rotary evaporator.

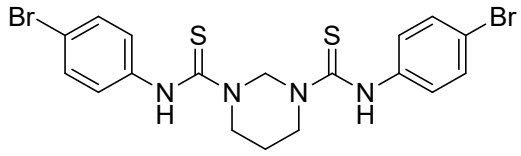


***N*,1,3-Tris(4-fluorophenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3j** was obtained from 84 mg (1 mmol) of diazaalkane **1a** and 430 mg (2.4 mmol) of 3,4-fluorobenzoyl azide **4b**. Yield 229 mg (53%). White solid, m.p. 133–134 °C. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 9.18 (s, 1H, NH), 7.52–7.39 (m, 4H, Ar), 7.38–7.33 (m, 2H, Ar), 7.31–7.20 (m, 4H, Ar), 7.17–7.08 (m, 2H, Ar), 6.48 (s, 1H, CH), 4.43–4.30 (m, 1H, CH_2), 3.90–3.78 (m, 1H, CH_2), 3.59–3.47 (m, 1H, CH_2), 3.28–3.16 (m, 1H, CH_2), 1.75–1.60 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d6*): δ 161.2 (d, $^{1}J_{C\text{-}F}$ = 242.0 Hz), 161.1 (d, $^{1}J_{C\text{-}F}$ = 243.0 Hz), 157.8 (d, $^{1}J_{C\text{-}F}$ = 239.2 Hz), 156.4 (s), 151.1 (s), 150.0 (s), 135.7 (d, $^{4}J_{C\text{-}F}$ = 2.4 Hz), 134.3 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 132.7 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 131.6 (d, $^{3}J_{C\text{-}F}$ = 8.7 Hz), 130.1 (d, $^{3}J_{C\text{-}F}$ = 8.9 Hz), 121.4 (d, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 115.7

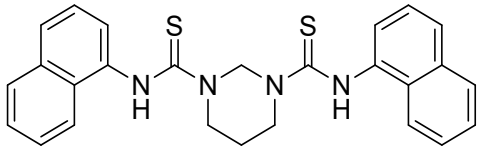
(d, $^2J_{C\text{-}F}$ = 22.6 Hz), 115.2 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 115.1 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 79.1 (s), 46.3 (s), 41.1 (s), 23.9 (s). HRMS (ESI) m/z Calcd for $C_{25}H_{20}F_3N_5O_3$ $[M+Na]^+$: 518.1410. Found: 518.1425.

General procedure for synthesis of compounds 8

Diazabicyclohexane **1** (1 mmol, 1 equivalent) and isothiocyanate **5** (1.8 mmol, 1.8 equivalent) were dissolved in benzene (5 ml), molecular sieves (200 mg, MS 4A) were added and mixtures refluxed for 12 hours with stirring. The solution was cooled to room temperature, the precipitate together with the sieves was separated by filtration, washed with diethyl ether and dissolved in methylene chloride to separate the sieves. The solvent was removed using a rotary evaporator to obtain a pure product.



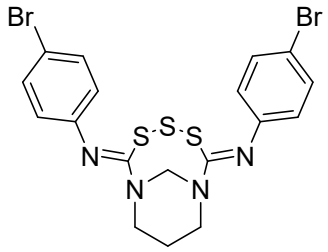
***N*^{1},*N*^{3}-Bis(4-bromophenyl)dihydropyrimidine-1,3(2*H*,4*H*)-bis(carbothioamide) 8a** was obtained from 84 mg (1 mmol) diazabicyclohexane **1a** and 385 mg (1.8 mmol) 4-bromophenyl isothiocyanate **5a**. Product yield 45 mg (11%). Yellow solid, m.p. 162–165 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.84 (s, 2H, NH), 7.54–7.46 (m, 4H, Ar), 7.38–7.26 (m, 4H, Ar), 5.87 (s, 2H, CH_2), 4.08–3.96 (m, 4H, CH_2), 1.95–1.84 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 180.7, 139.9, 131.0, 127.0, 116.9, 62.2, 47.5, 23.6,. HRMS (ESI) m/z Calcd for $C_{18}H_{18}Br_2N_4S_2$ $[M+H]^+$: 514.9392. Found: 514.9398.



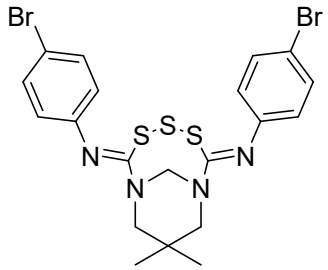
***N*^{1},*N*^{3}-Bis(naphthalen-1-yl)dihydropyrimidine-1,3(2*H*,4*H*)-bis(carbothioamide) 8b** was obtained from 84 mg (1 mmol) diazabicyclohexane **1a** and 333 mg (1.8 mmol) naphtalen-1-yl isothiocyanate **5a**. Product yield 45 mg (19%). Yellow solid, m.p. 181–182 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 9.96 (s, 2H, NH), 8.10–7.20 (m, 14H, Ar), 6.06 (s, 2H, CH_2), 4.35–4.05 (m, 4H, CH_2), 2.15–1.90 (m, 2H, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 182.1, 137.0, 133.8, 130.3, 127.9, 126.5, 125.9, 125.8, 125.7, 125.5, 123.7, 62.5, 47.6, 23.9. HRMS (ESI) m/z Calcd for $C_{26}H_{24}N_4S_2$ $[M+Na]^+$: 457.1515. Found: 457.1522.

General procedure for synthesis of compounds 9

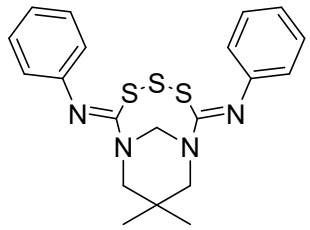
Diazabicyclohexane (1 equiv.) and isothiocyanate (1.5 equiv.) were dissolved in benzene (5 ml), 16 mole % of boron trifluoride etherate was added. The reactions was stirred until complete conversion of the initial isothiocyanate (TLC control). The reaction mixture was separated by column chromatography on silica gel (hexane: ethyl acetate 4:1) to give the product.



(*N,N′Z,N,N′Z*)-*N,N′*-(3,4,5-Trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)bis(4-bromoaniline) 9a was obtained from 42 mg (0.5 mmol) of diazabicyclohexane **1** and 160 mg (0.75 mmol) of 4-bromophenyl isothiocyanate **5a**. Product yield 61 mg (45%). Yellow crystals, m.p. 115–117 °C. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 7.42 (d, 4H, *J* = 8.7 Hz, Ar), 6.68 (d, 4H, *J* = 8.4 Hz, Ar), 6.16 (d, 1H, *J* = 14.9 Hz, CH_2), 4.84 (dd, 1H, *J* = 14.6, 3.2 Hz, CH_2), 4.40 (d, 2H, *J* = 13.1 Hz, CH_2), 3.50–3.38 (m, 2H, CH_2), 2.17–2.00 (m, 1H, CH_2), 1.73 (d, 1H, *J* = 13.3 Hz, CH_2). ^{13}C NMR (100 MHz DMSO-*d*6): δ 151.5, 148.4, 131.4, 124.4, 115.1, 65.3, 46.0, 25.0. HRMS (ESI) m/z Calcd for $C_{18}H_{16}Br_2N_4S_3$ $[M+H]^+$: 544.8956. Found: 544.8974.



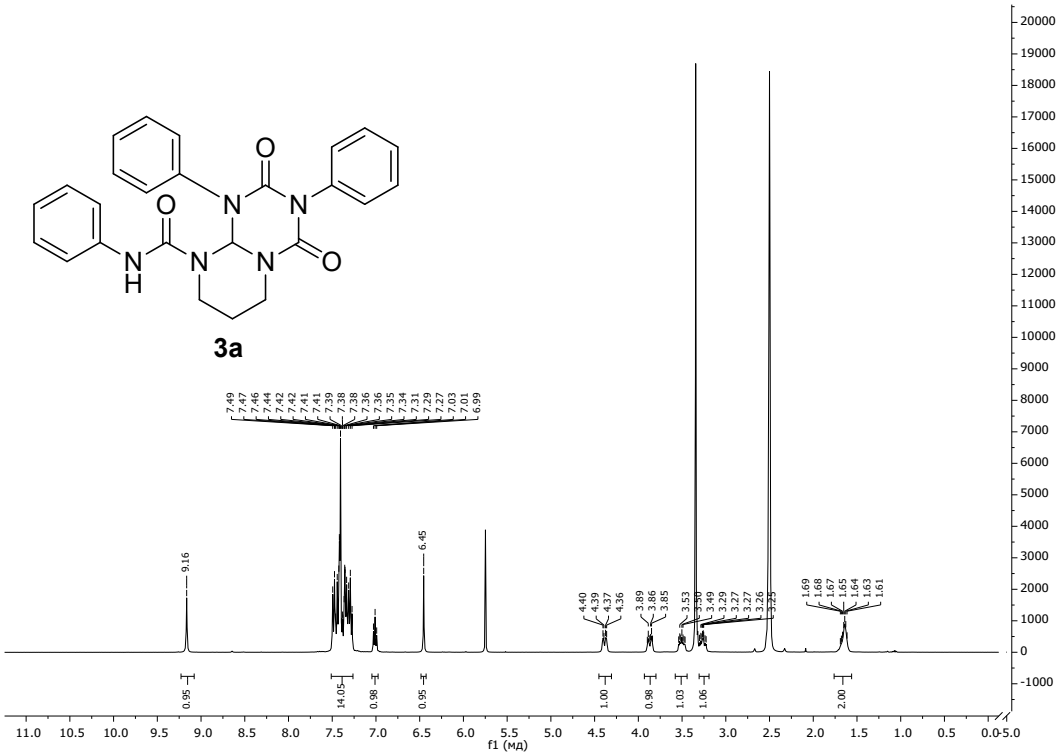
(*N,N′Z,N,N′Z*)-*N,N′*-(9,9-Dimethyl-3,4,5-trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)bis(4-bromoaniline) 9b was obtained from 56 mg (0.5 mmol) 3,3-dimethyldiazabicyclohexane and 160 mg (0.75 mmol) 4-bromophenyl isothiocyanate. Product yield 36 mg (25%). Yellow amorphous substance. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 7.40–7.33 (m, 4H, Ar), 6.53 (m, 4H, Ar), 6.47–6.39 (m, 1H, CH_2), 4.48 (d, 1H, *J* = 14.4 Hz, CH_2), 4.37 (d, 2H, *J* = 13.2 Hz, CH_2), 3.07 (d, 2H, *J* = 13.3 Hz, CH_2), 1.34 (s, 3H, CH_3), 1.01 (s, 3H, CH_3),. ^{13}C NMR (100 MHz DMSO-*d*6): δ 152.5, 148.3, 131.9, 124.2, 116.4, 65.5, 57.4, 35.6, 25.4, 22.8. HRMS (ESI) m/z Calcd for $C_{20}H_{20}Br_2N_4S_3$ $[M+H]^+$: 570.9290. Found: 570.9302.



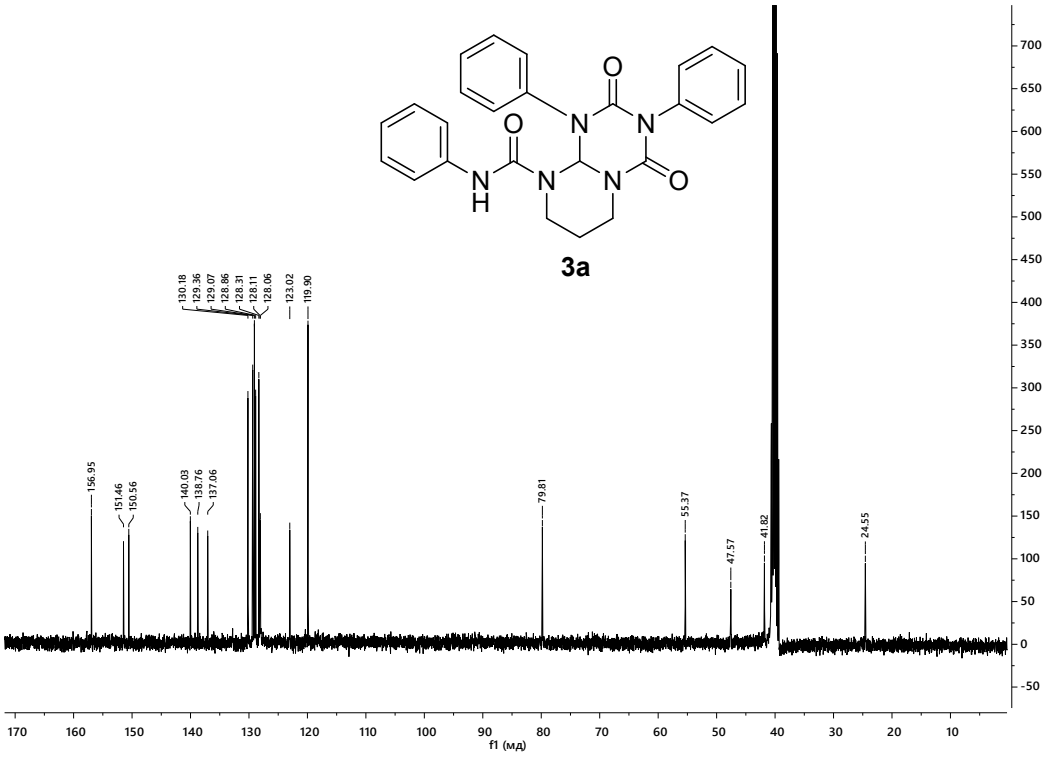
(*N,N′Z,N,N′Z*)-*N,N′*-(9,9-Dimethyl-3,4,5-trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)dianiline 9c was obtained from 56 mg (0.5 mmol) 3,3-dimethyldiazabicyclohexane and 67.5 mg (0.5 mmol) phenyl isothiocyanate. Product yield 36 mg (52%). Yellow amorphous substance. ^{1}H NMR (400 MHz, DMSO-*d*6): δ 7.35–7.24 (m, 4H, Ar), 7.07 (td, *J* = 7.3, 1.3 Hz, 2H, Ar), 6.79–6.70 (m, 4H, Ar), 6.48 (dt, *J* = 14.4, 2.2 Hz, 1H, CH_2), 4.51 (d, *J* = 14.4 Hz, 1H, CH_2), 4.44 (d, *J* = 13.2 Hz, 2H, CH_2), 3.11 (d, *J* = 13.2 Hz, 2H, CH_2), 1.41 (s, 3H, CH_3), 1.05 (s, 3H, CH_3). ^{13}C NMR (100 MHz DMSO-*d*6): δ 152.3, 149.4, 128.9, 123.4, 122.4, 65.6, 57.4, 35.4, 25.4, 22.9. HRMS (ESI) m/z Calcd for $C_{20}H_{22}N_4S_3$ $[M+H]^+$: 415.1079. Found: 415.1087.

2,4-Dioxo-*N*,1,3-triphenylhexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide
3a

^{1}H NMR, 400 MHz, DMSO-*d*6

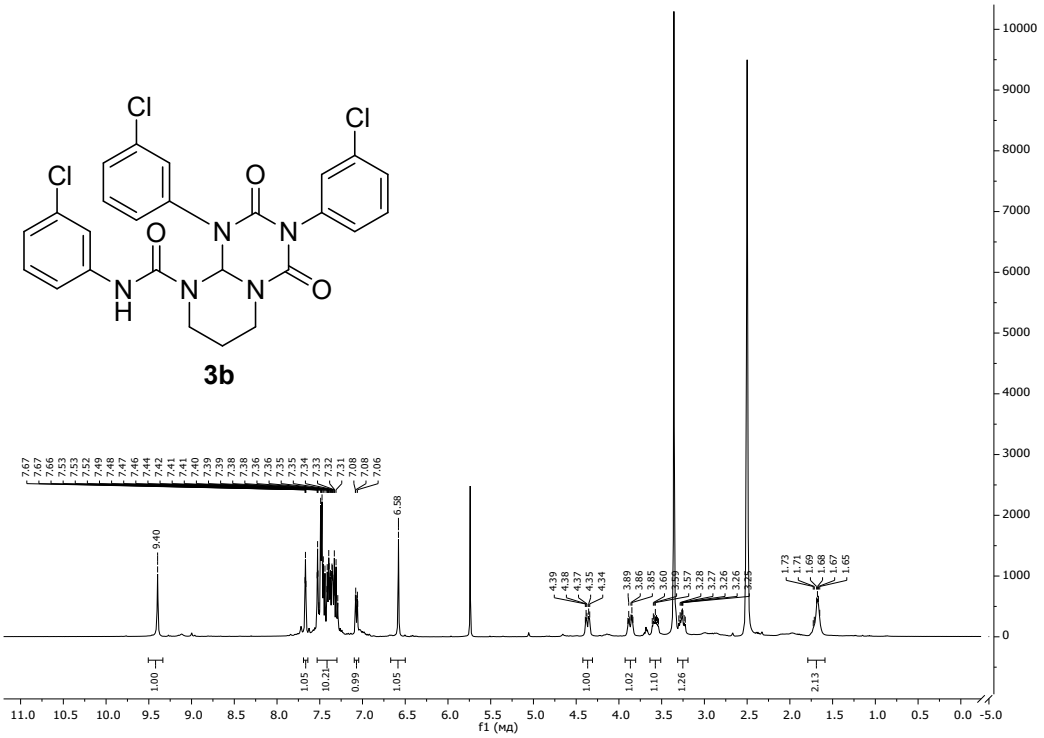


^{13}C NMR, 100 MHz DMSO-*d*6

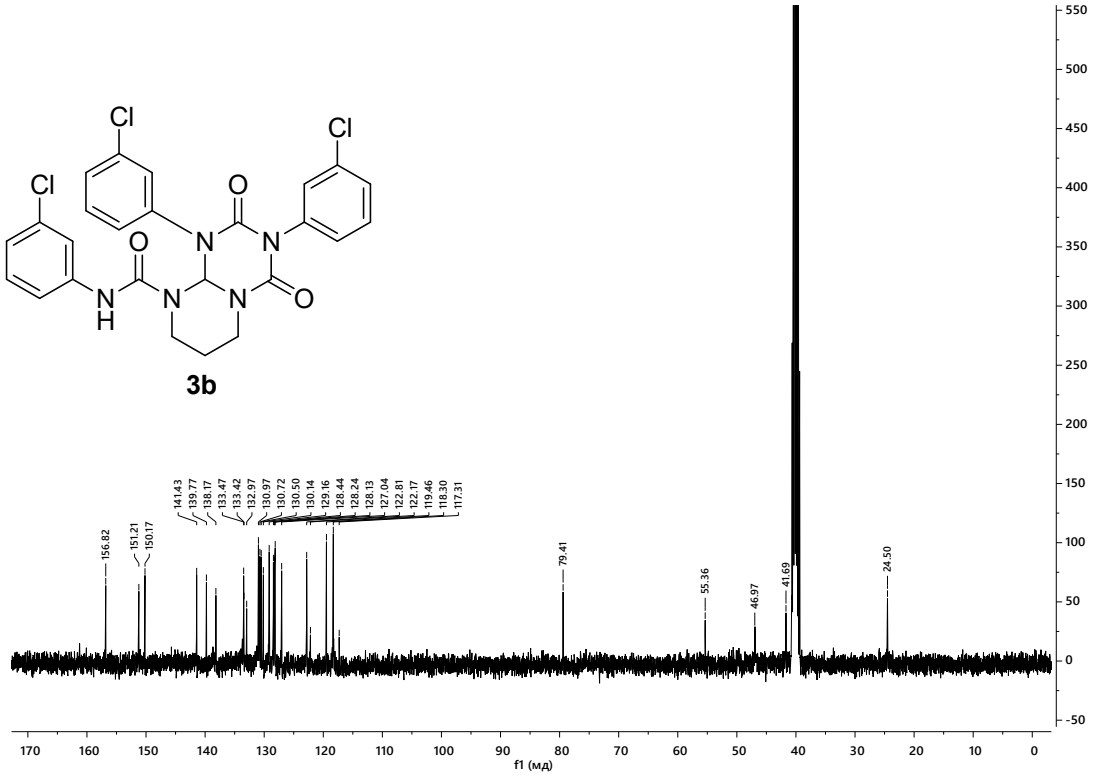


_N_,1,3-Tris(3-chlorophenyl)-2,4-dioxohexahydro-1_H_-pyrimido[1,2-a][1,3,5]triazine-9(2_H_)-carboxamide 3b

^{1}H NMR, 400MHz, DMSO-*d*6

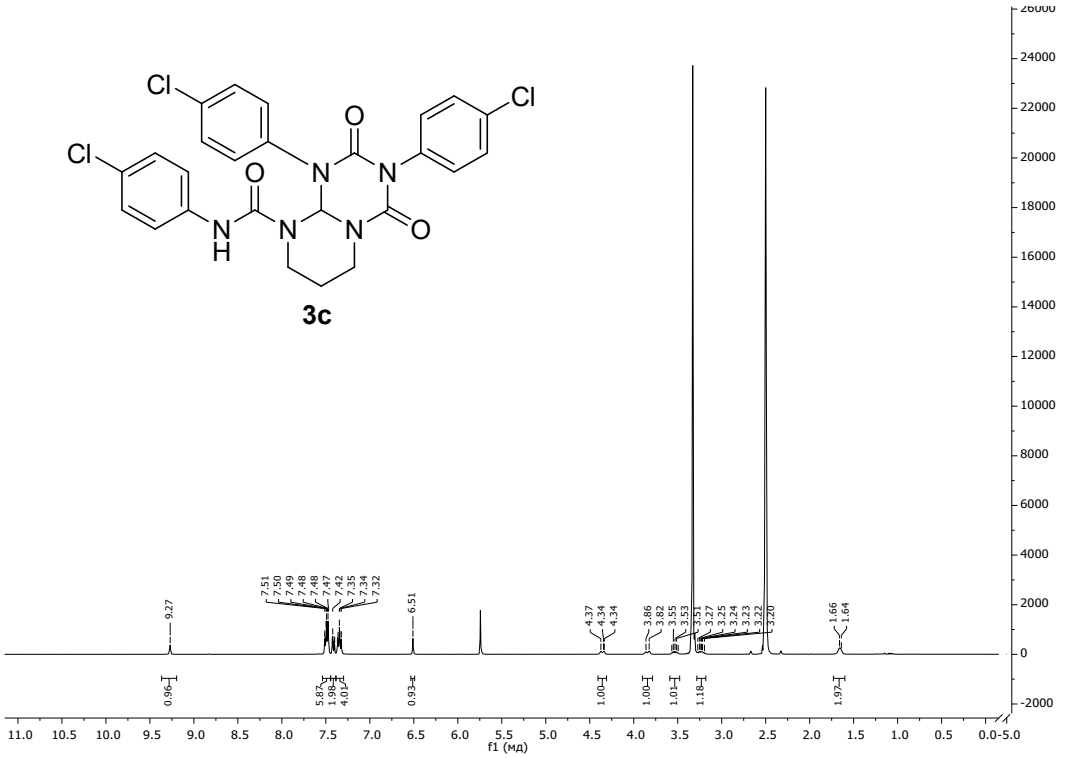


^{13}C NMR, 100 MHz, DMSO-*d*6

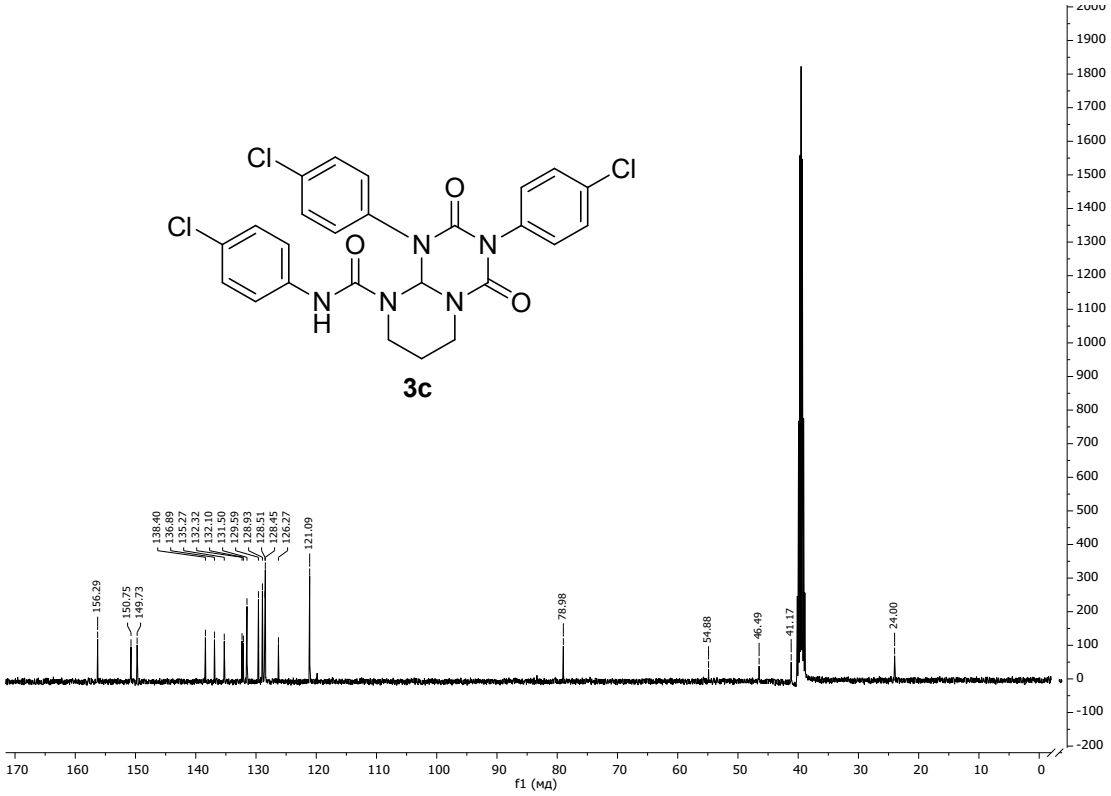


_N_,1,3-Tris(4-chlorophenyl)-2,4-dioxohexahydro-1_H_-pyrimido[1,2-a][1,3,5]triazine-9(2_H_)-carboxamide 3c

^{1}H NMR, 400 MHz, DMSO-*d*6



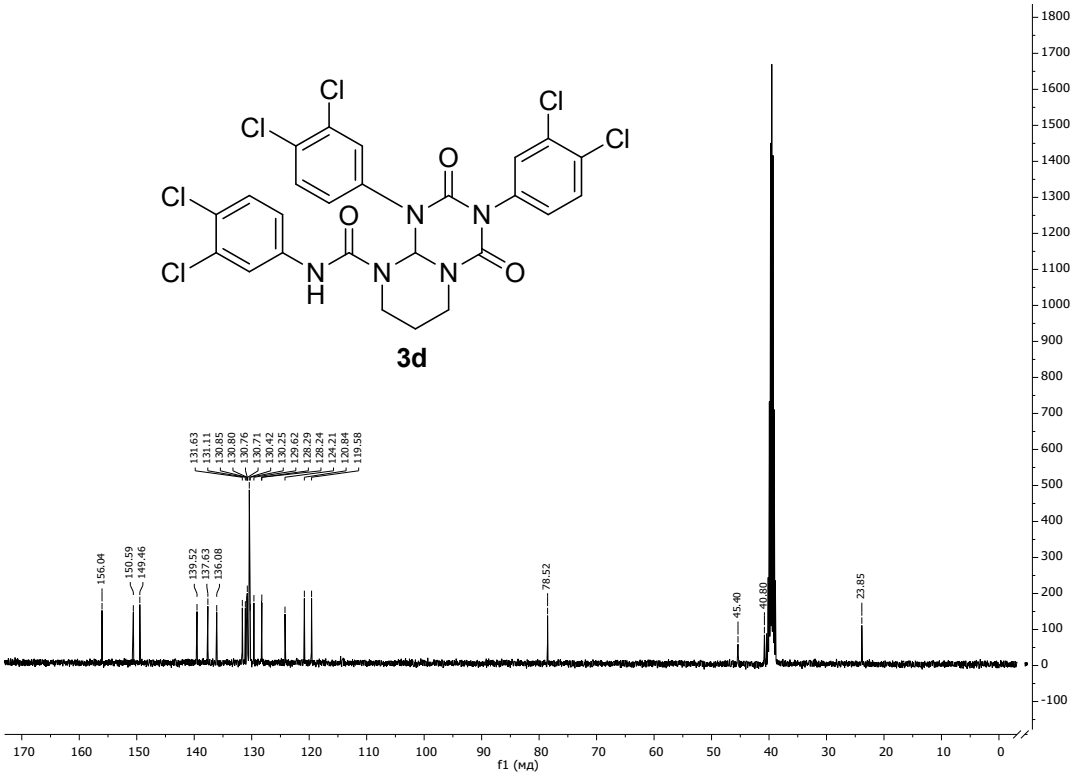
^{13}C NMR, 100 MHz, DMSO-*d*6



***N*,1,3-Tris(3,4-dichlorophenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3d**

^{1}H NMR, 400 MHz, DMSO-*d*6

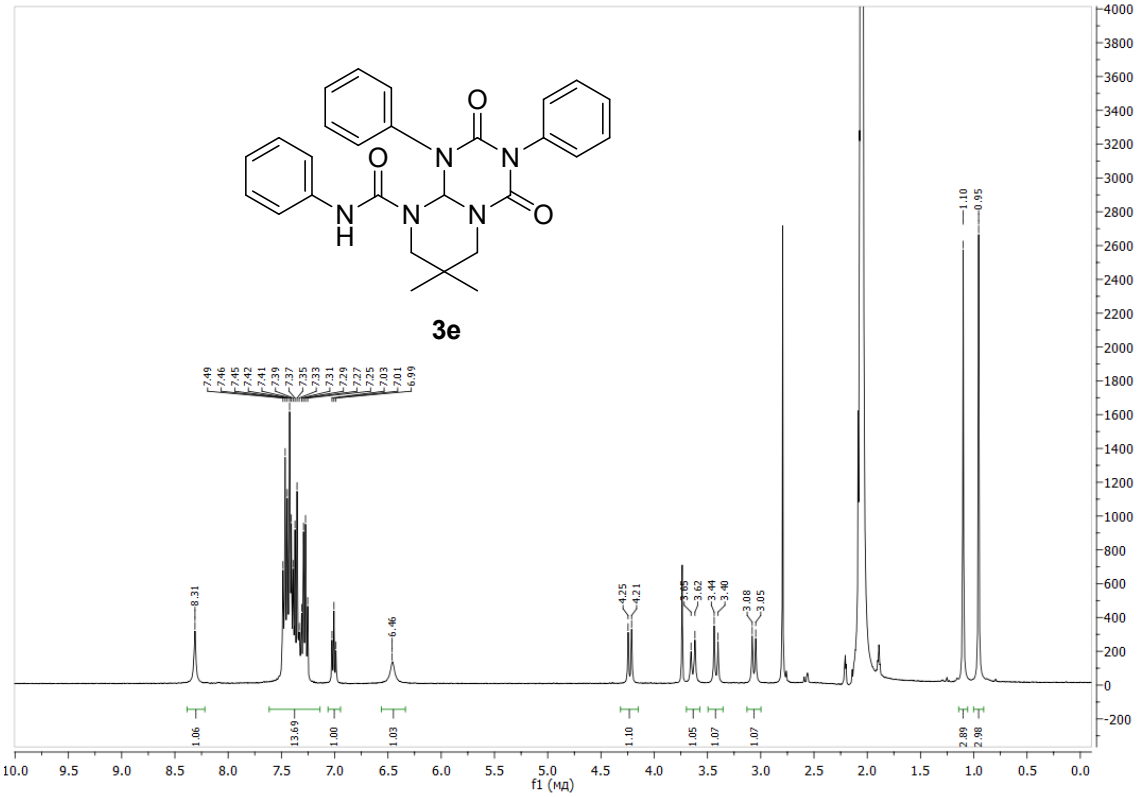
^{13}C NMR, 100 MHz, DMSO-*d*6



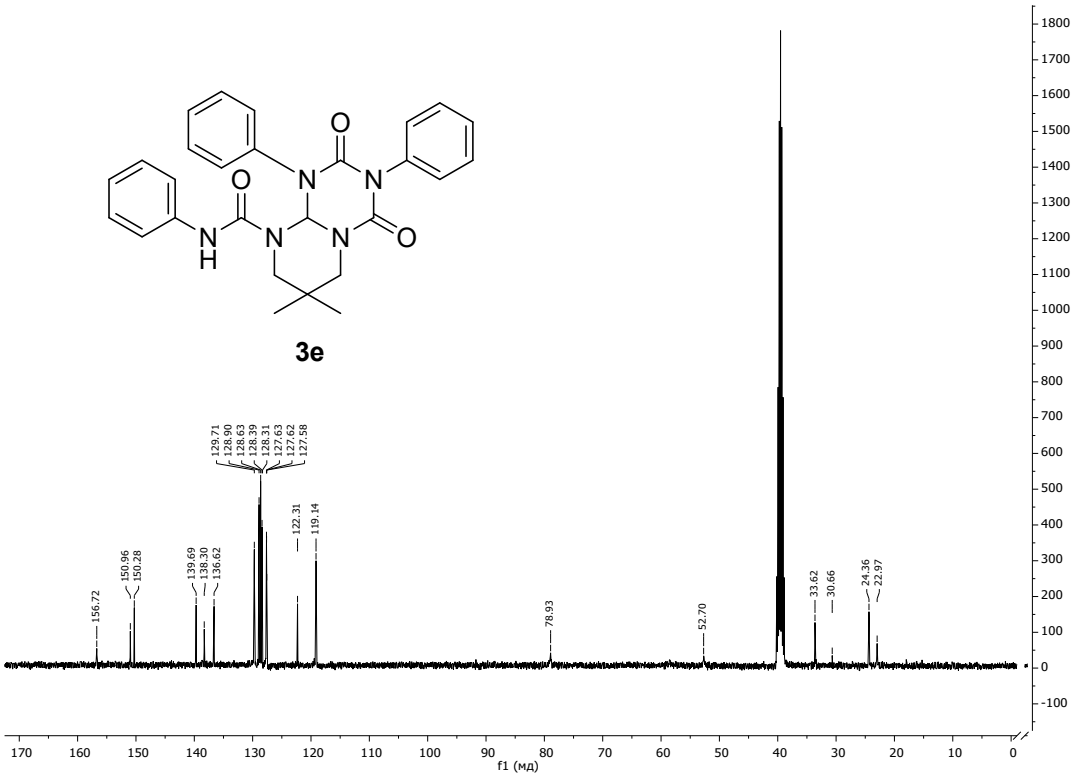
7,7-Dimethyl-2,4-dioxo-*N*,1,3-triphenylhexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3e

^{1}H NMR, 400 MHz, DMSO-*d*6

^{1}H NMR, 400 MHz, Acetone-*d*6

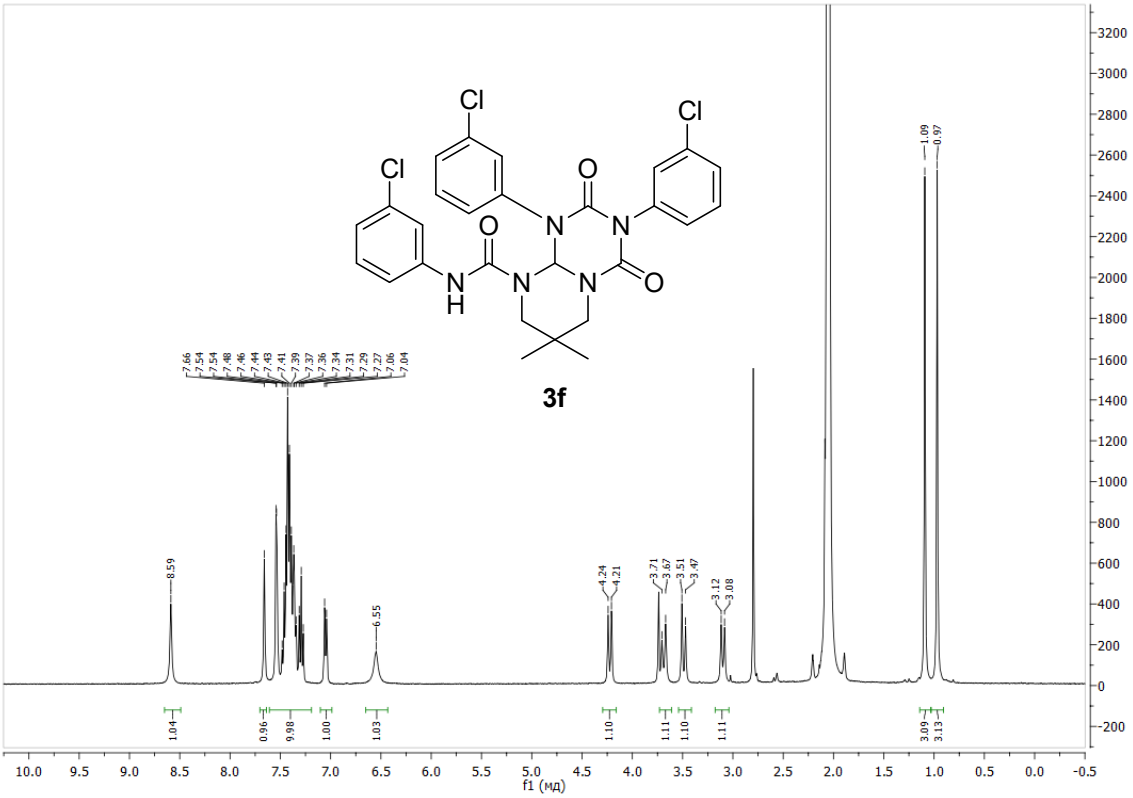


^{13}C NMR, 100 MHz, DMSO-*d*6

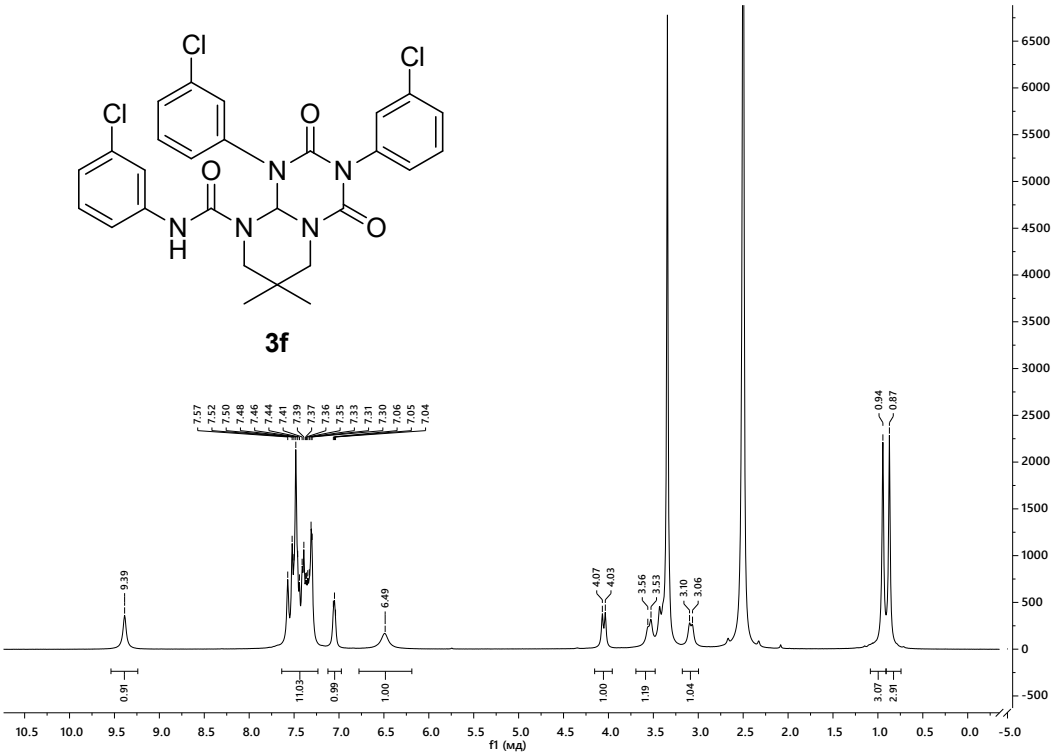


***N*,1,3-Tris(3-chlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3f**

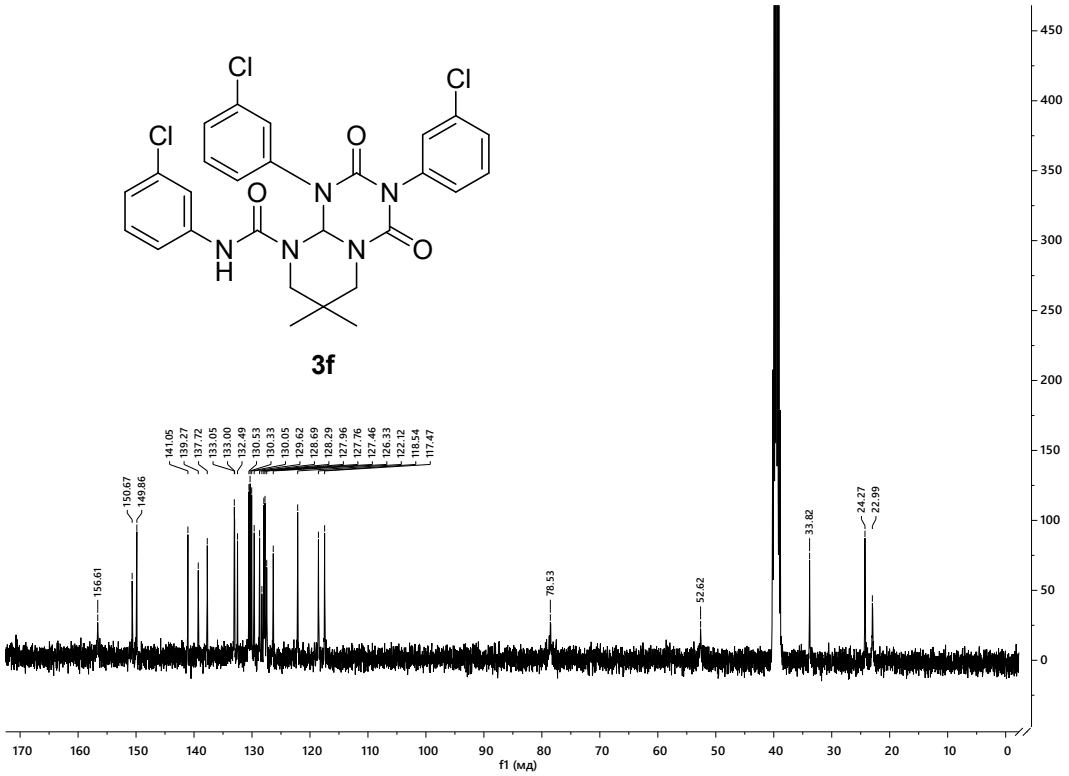
^{1}H NMR, 400 MHz, Acetone-*d*6



^{1}H NMR, 400 MHz, DMSO-*d*6

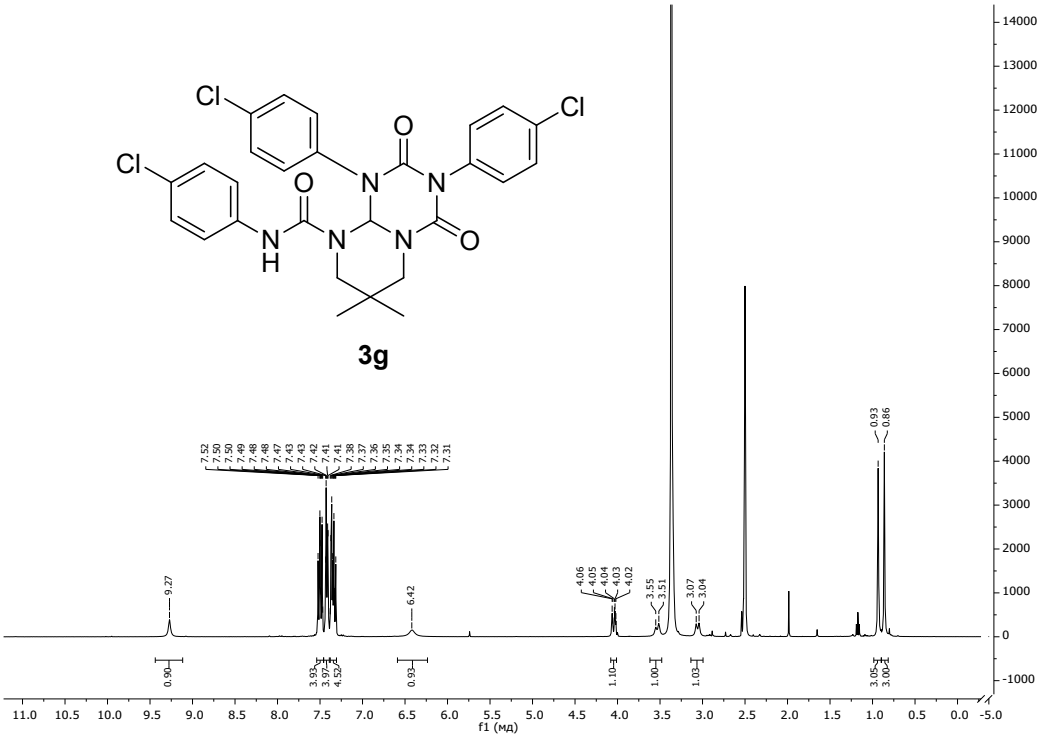


^{13}C NMR, 100 MHz DMSO-*d*6

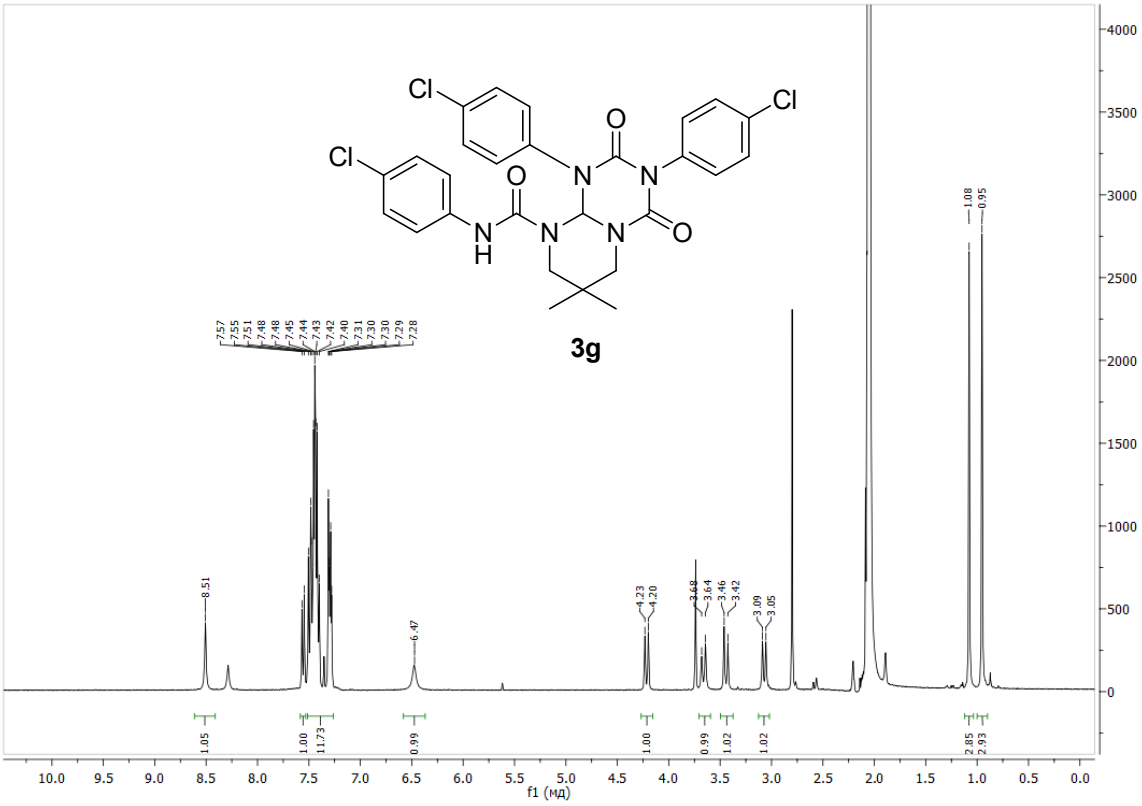


_N_,1,3-Tris(4-chlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1_H_-pyrimido[1,2-a][1,3,5]triazine-9(2_H_)-carboxamide 3g

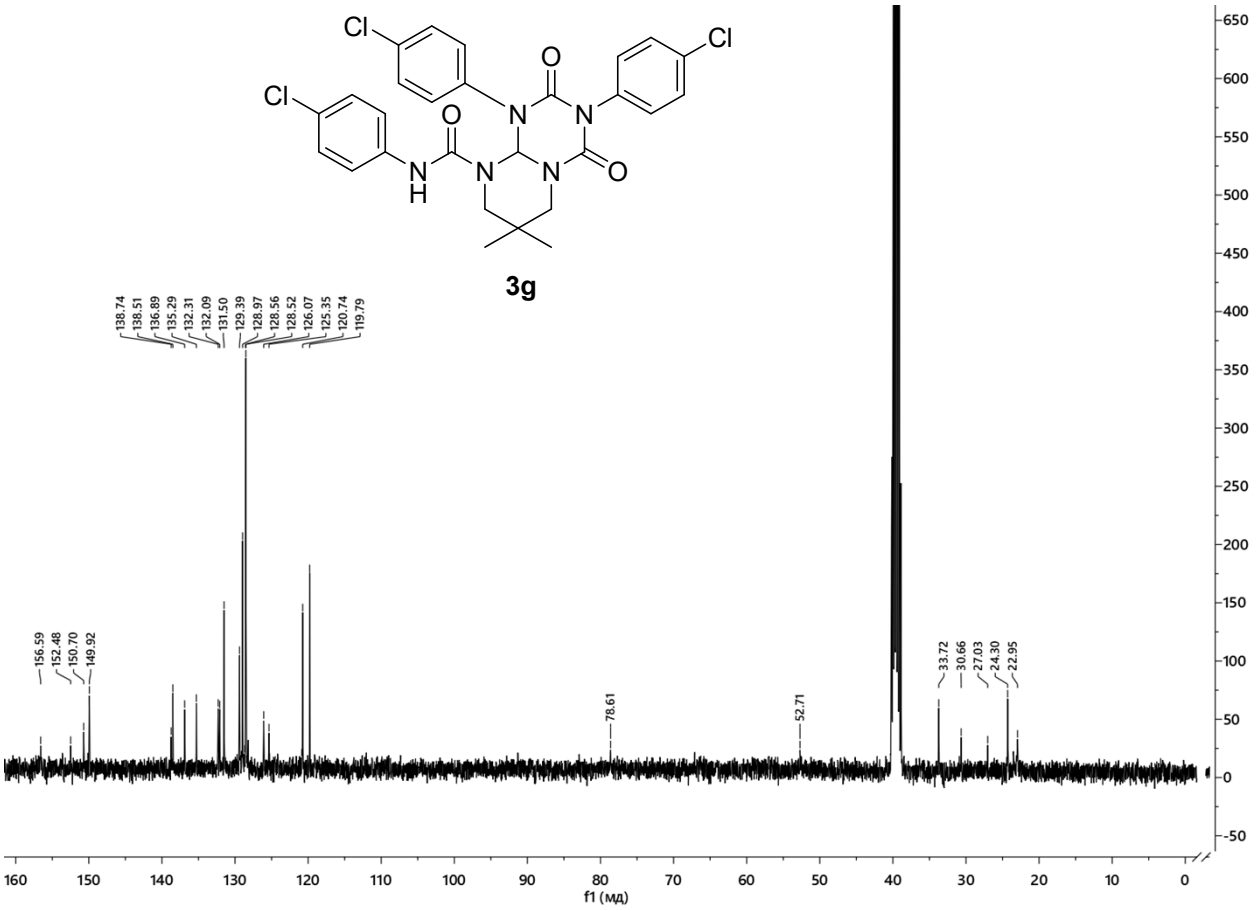
^{1}H NMR, 400 MHz, DMSO-*d6*



^{1}H NMR, 400 MHz, Acetone-*d6*

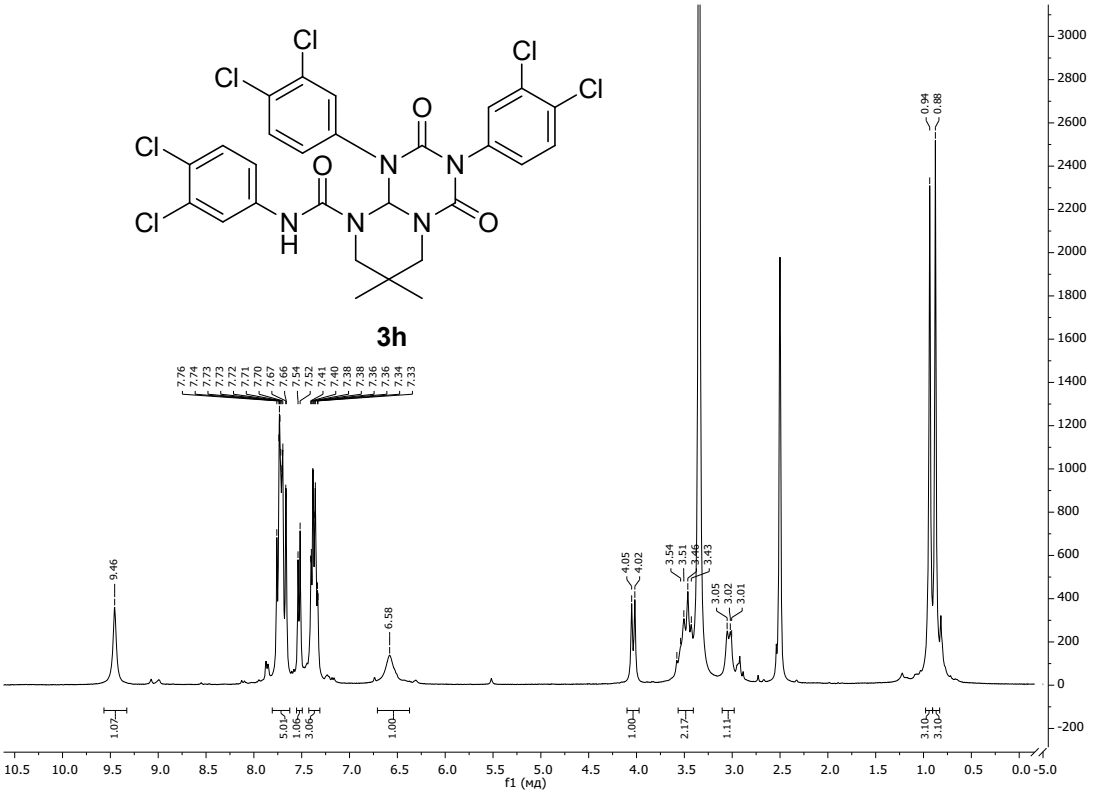


^{13}C NMR, 100 MHz, DMSO-*d*6

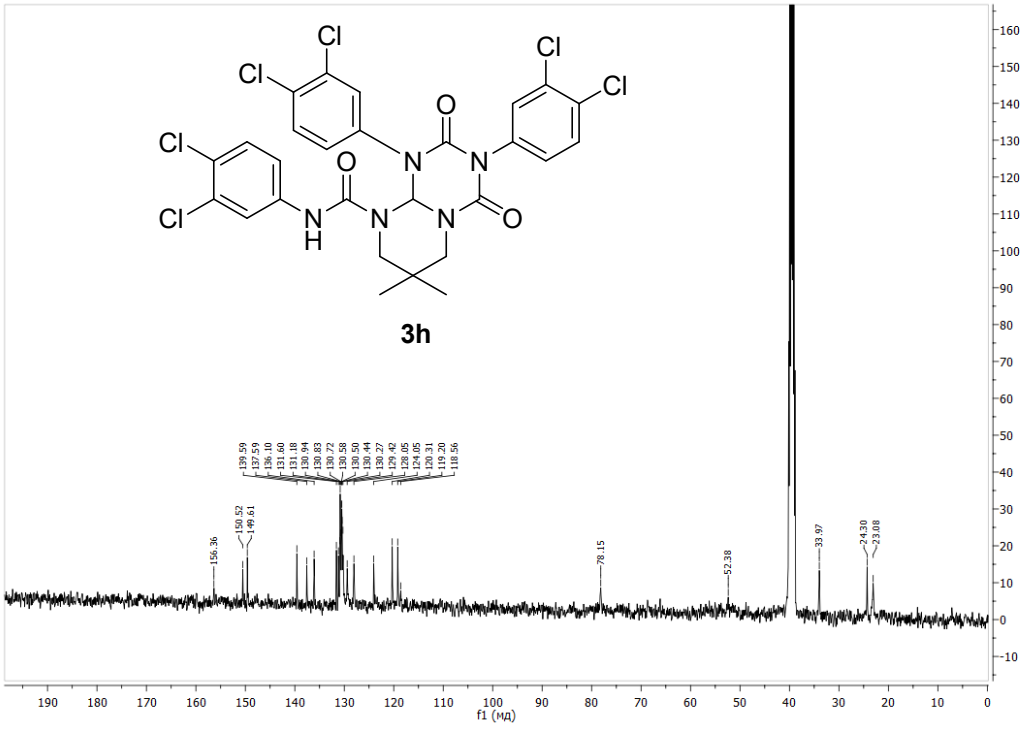


_N_,1,3-Tris(3,4-dichlorophenyl)-7,7-dimethyl-2,4-dioxohexahydro-1_H_-pyrimido[1,2-a][1,3,5]triazine-9(2_H_)-carboxamide 3h

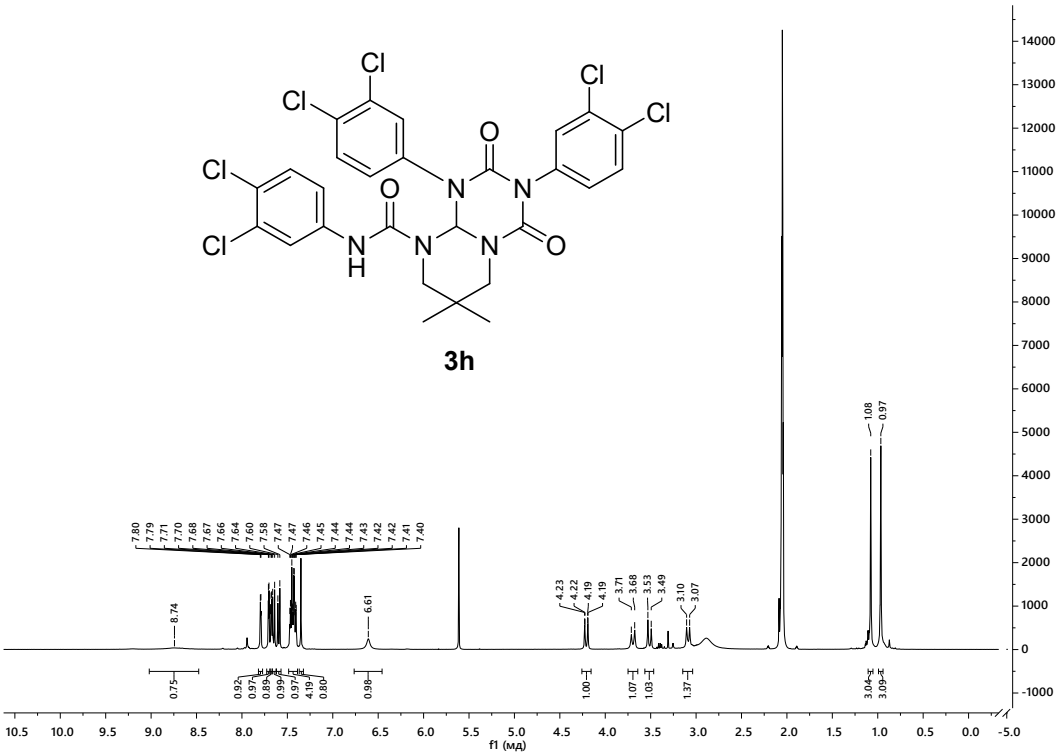
^{1}H NMR, 400 MHz, DMSO-*d*6



^{13}C NMR, 100 MHz, DMSO-*d*6

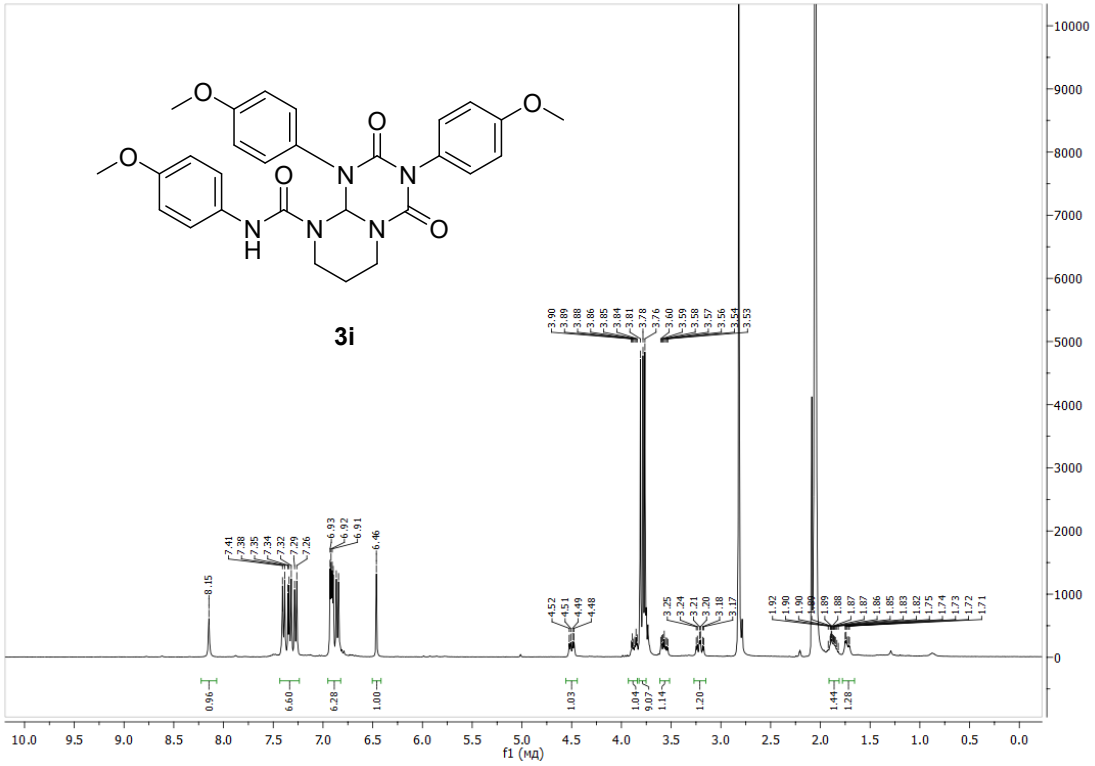


^{1}H NMR, 400 MHz, acetone-*d*6

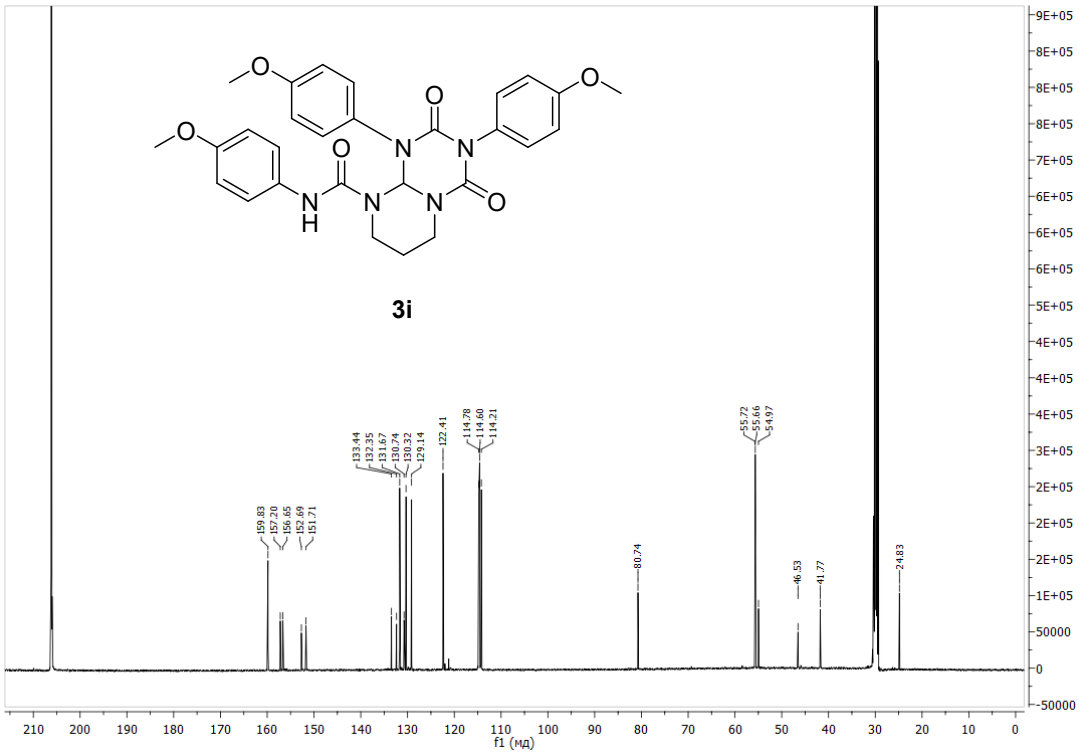


***N*,1,3-Tris(4-methoxyphenyl)-2,4-dioxohexahydro-1*H*-pyrimido[1,2-a][1,3,5]triazine-9(2*H*)-carboxamide 3i**

^{1}H NMR, 400 MHz, Acetone-*d*6

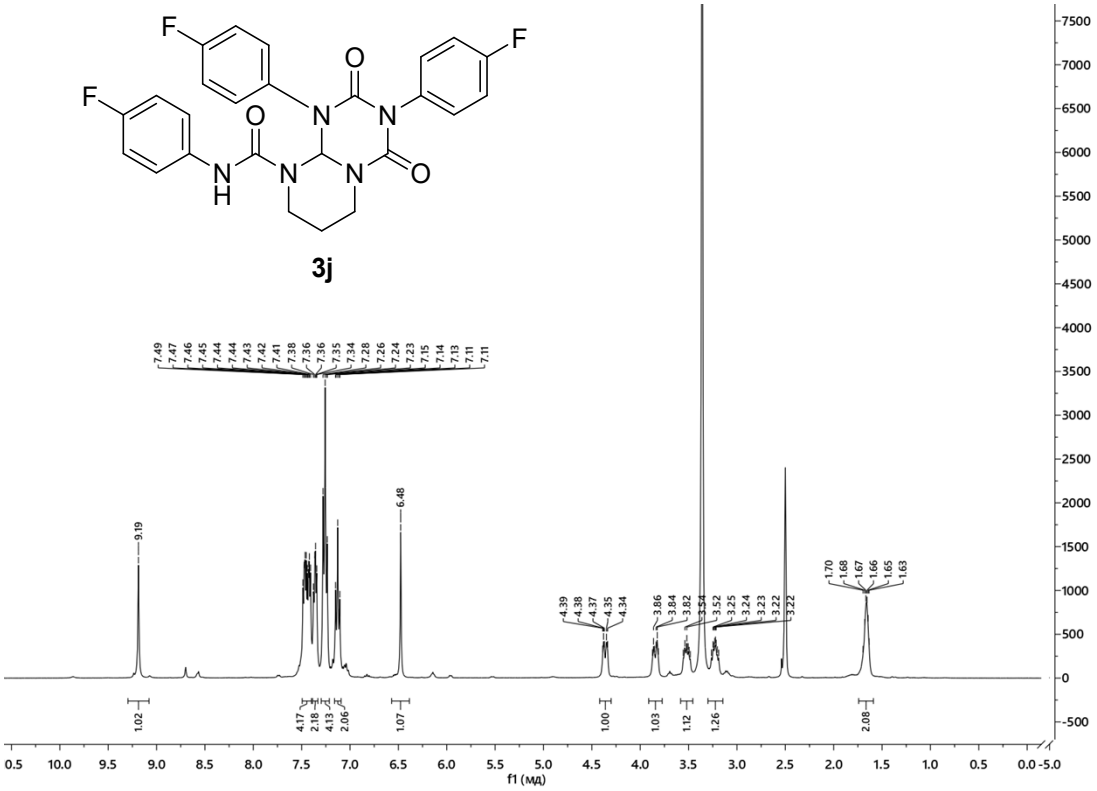


^{13}C NMR, 126 MHz, Acetone-*d*6

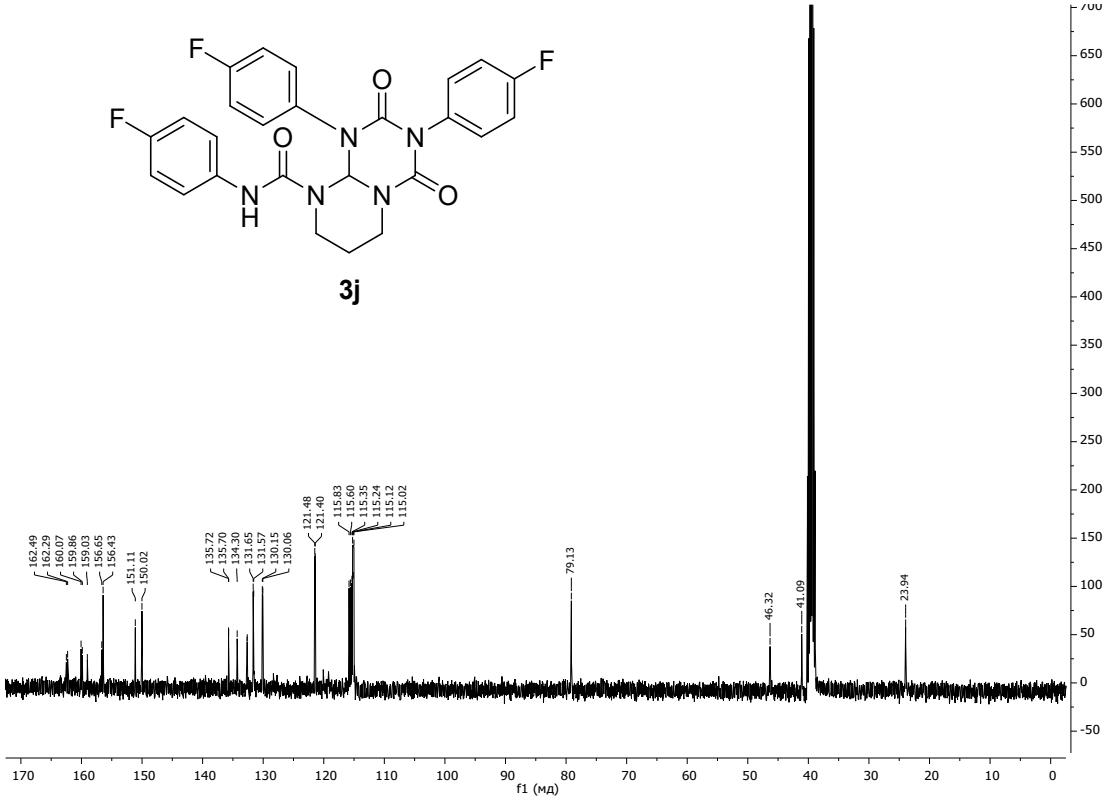


_N_,1,3-Tris(4-fluorophenyl)-2,4-dioxohexahydro-1_H_-pyrimido[1,2-a][1,3,5]triazine-9(2_H_)-carboxamide 3j

^{1}H NMR, 400 MHz, DMSO-*d*6



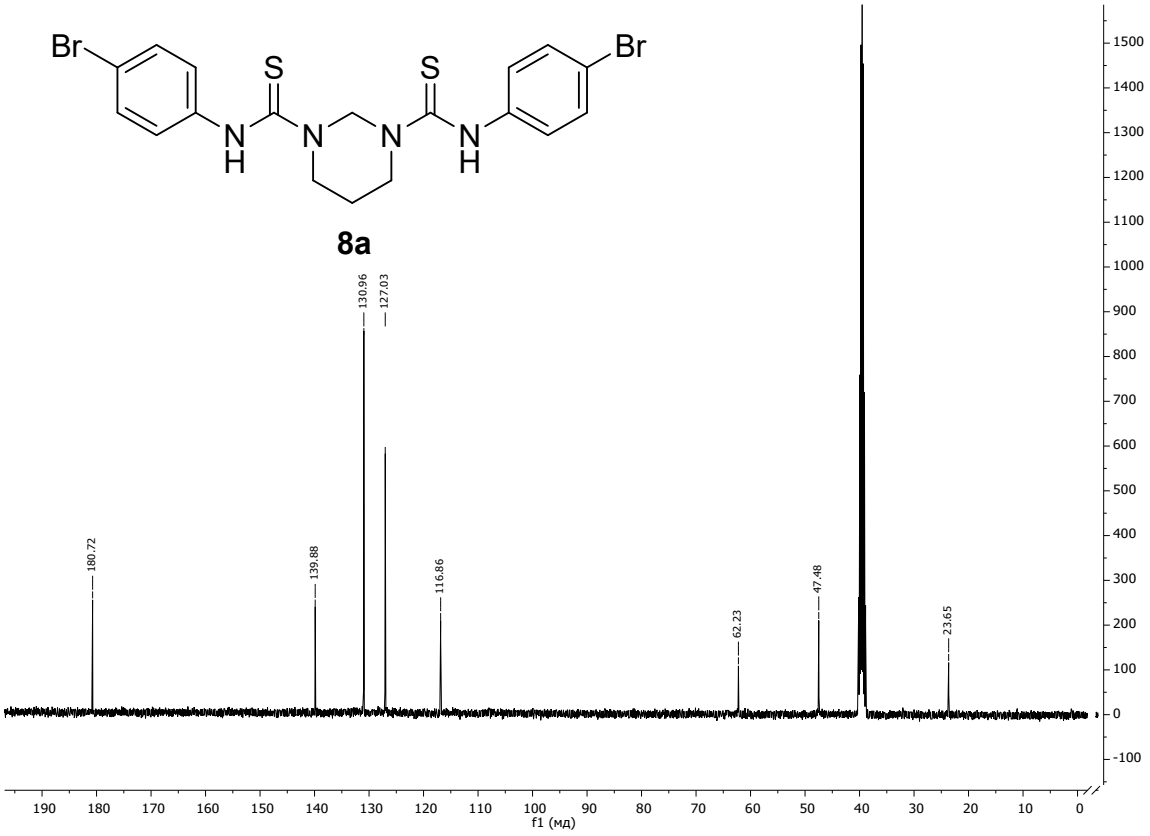
^{13}C NMR, 100 MHz, DMSO-*d*6



N^1,N^3-Bis(4-bromophenyl)dihydropyrimidine-1,3(2*H*,4*H*)-bis(carbothioamide) 8a

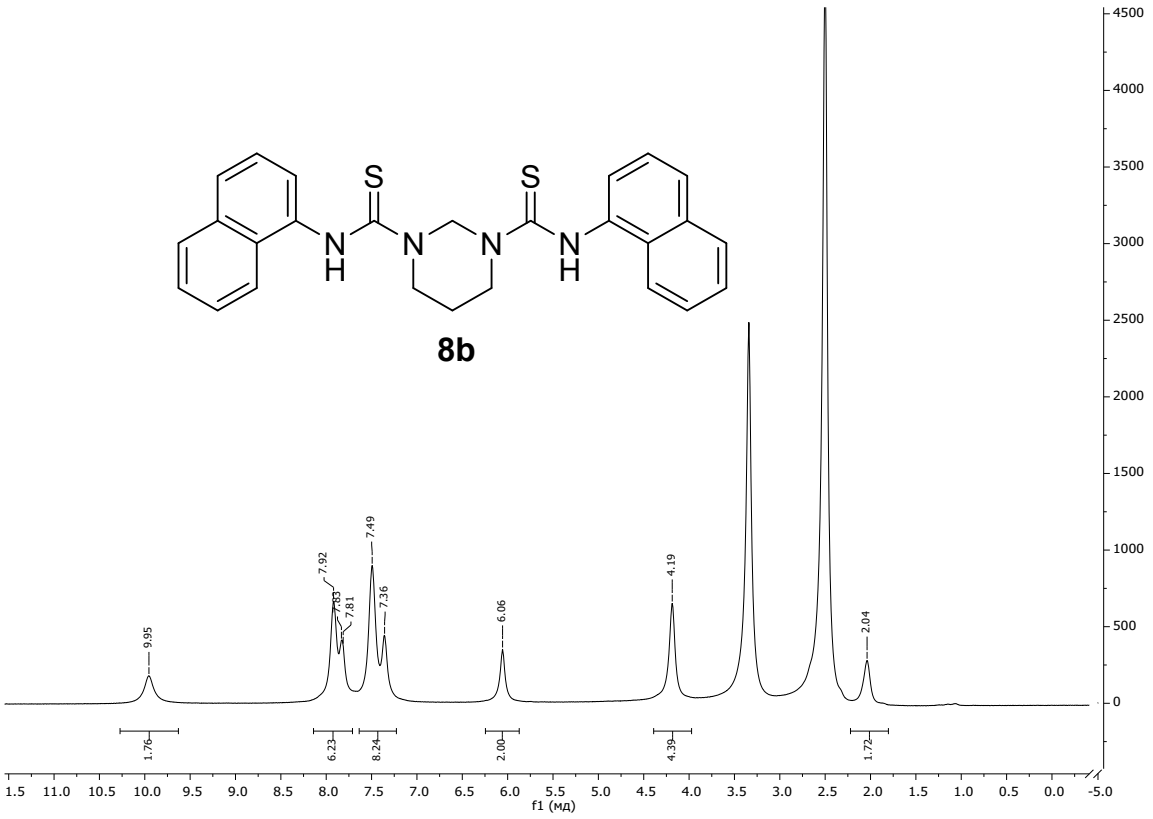
^{1}H NMR, 400 MHz, DMSO-*d*6

^{13}C NMR, 100 MHz, DMSO-*d*6

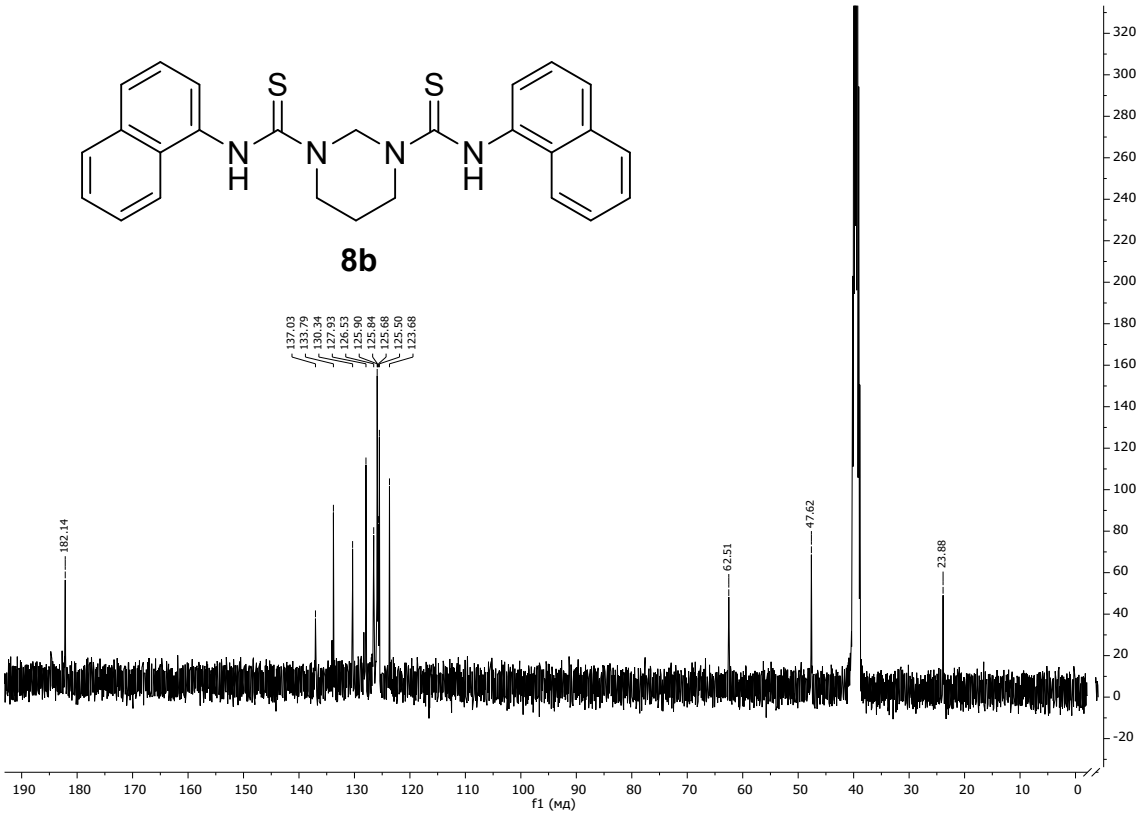


N^1,N^3-Di(naphthalen-1-yl)dihydropyrimidine-1,3(2*H*,4*H*)-bis(carbothioamide) 8b

^{1}H NMR, 400 MHz, DMSO-*d*6

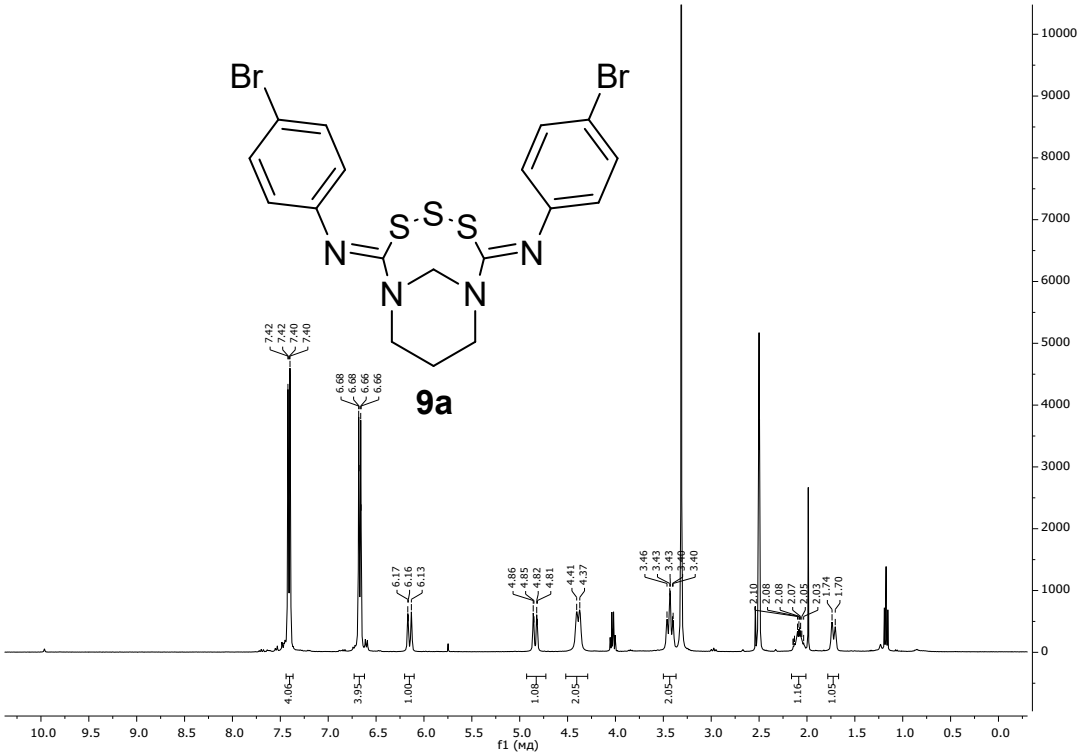


^{13}C NMR, 100 MHz, DMSO-*d*6

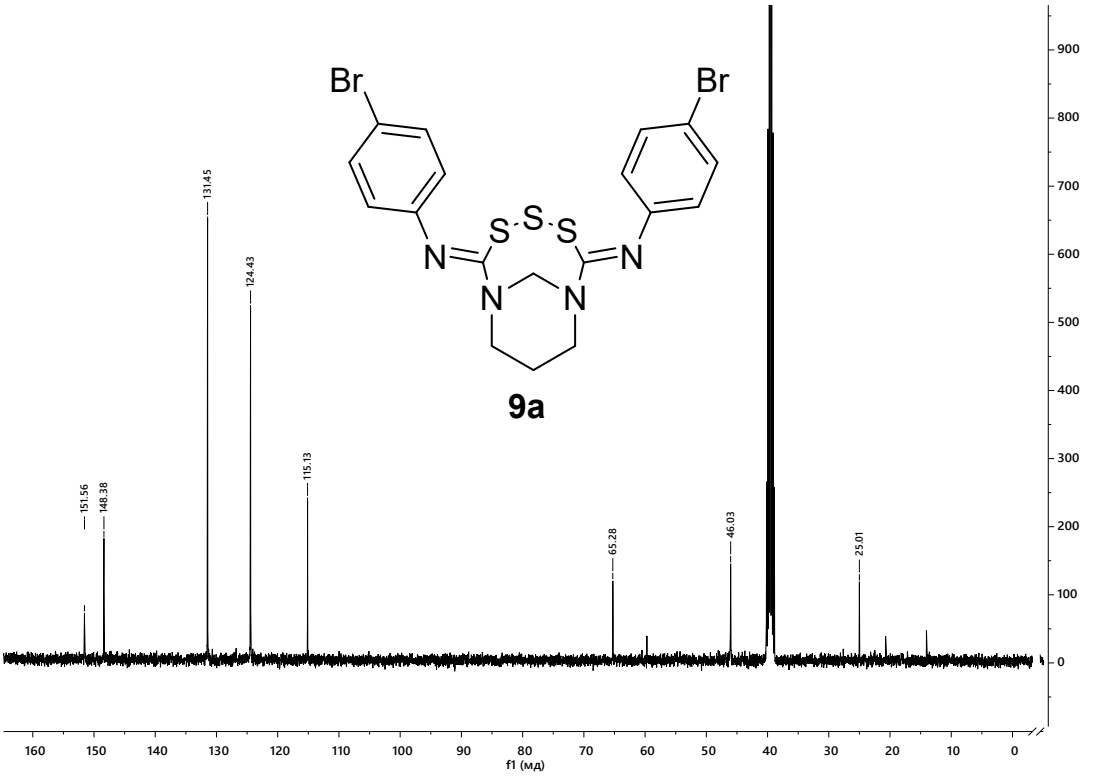


(*N,N'Z,N,N'Z*)-*N,N'*-(3,4,5-Trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)bis(4-bromoaniline) 9a

^{1}H NMR, 400 MHz, DMSO-*d*6

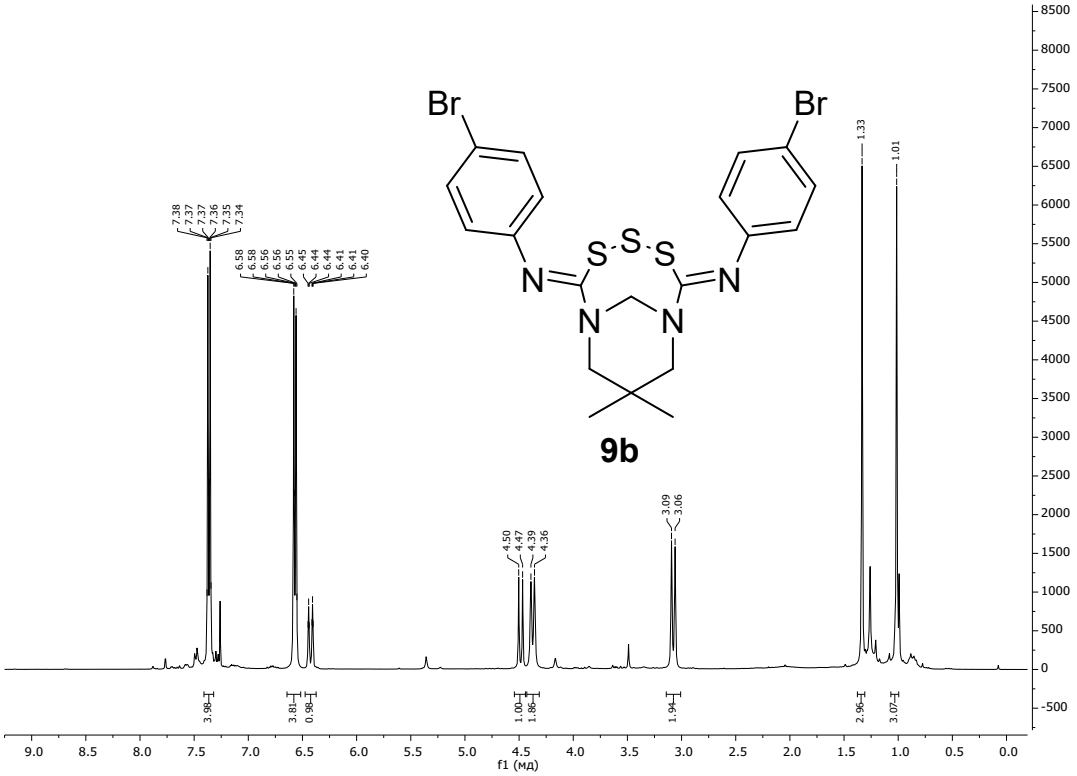


^{13}C, 400 MHz, DMSO-*d*6

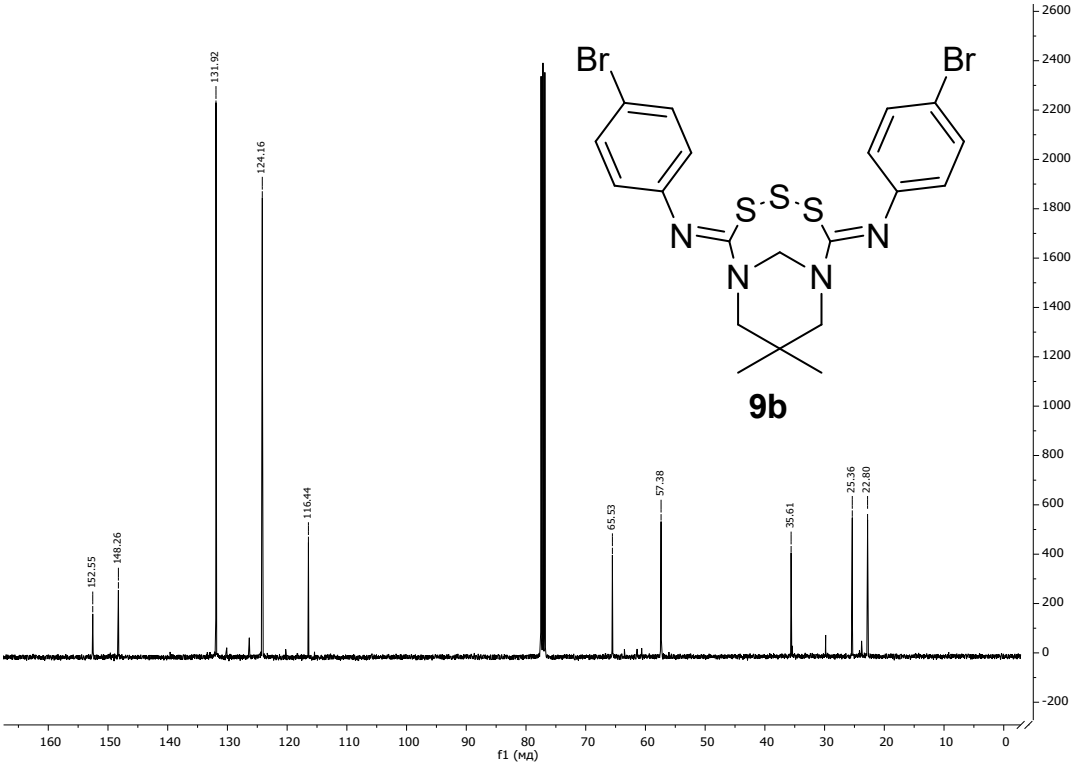


(*N,N'Z,N,N'Z*)-*N,N'*-(9,9-Dimethyl-3,4,5-trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)bis(4-bromoaniline) 9b

^{1}H NMR, 400 MHz, $CDCl_3$

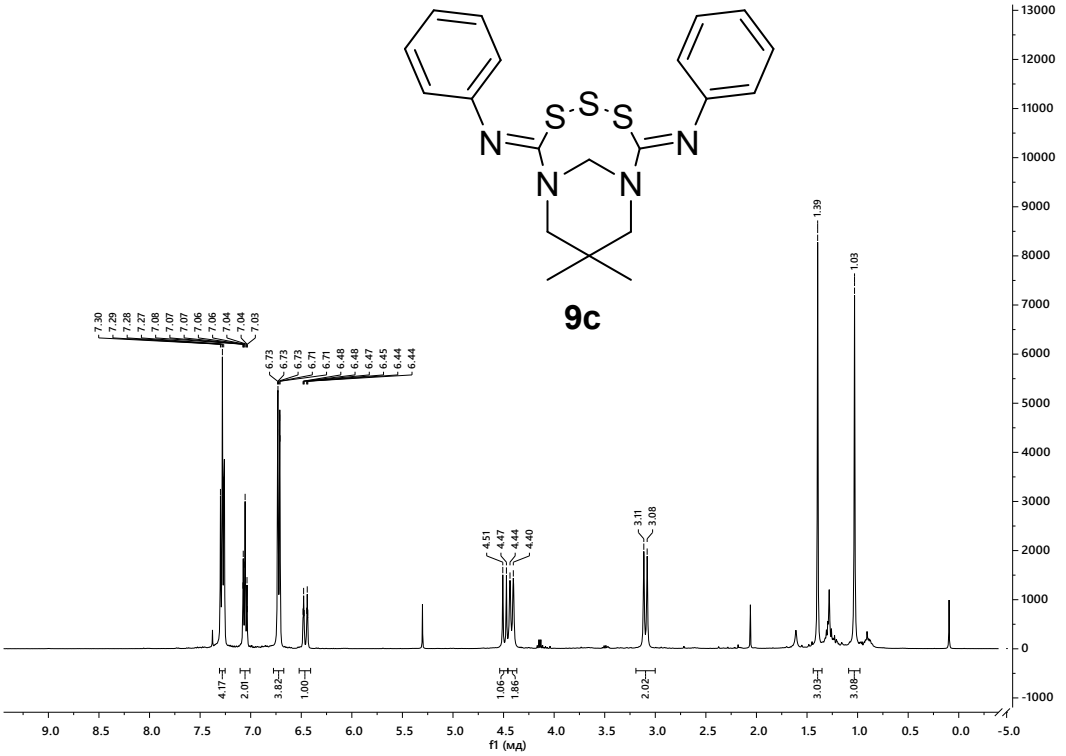


^{13}C NMR, 400 MHz, $CDCl_3$

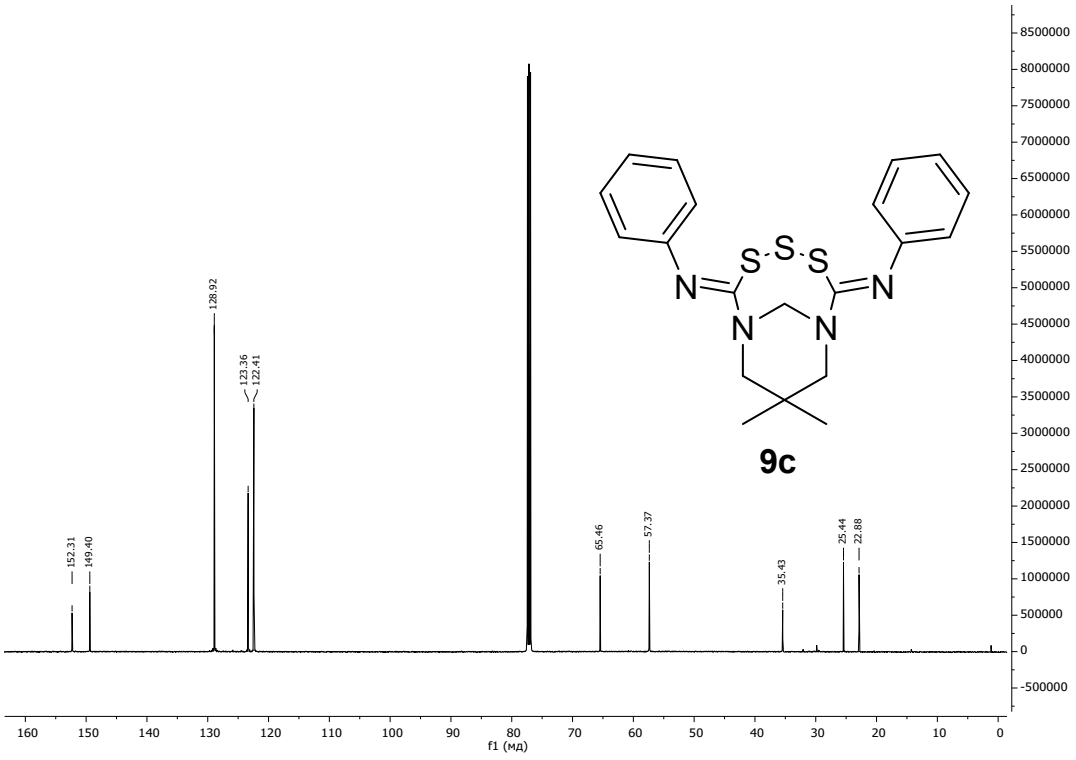


(*N,N′Z,N,N′Z*)-*N,N′*-(9,9-Dimethyl-3,4,5-trithio-1,7-diazabicyclo[5.3.1]undecane-2,6-diylidene)dianiline 9c

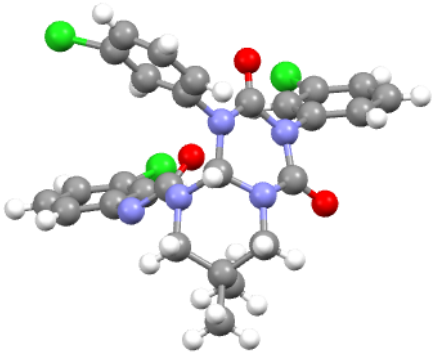
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 400 MHz, $CDCl_3$



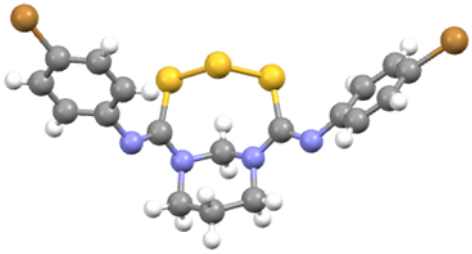
X-Ray diffraction analysis data



Single-crystal X-ray structure of compound **3f**.

Table 1 Crystal data and structure refinement for 032-017_MME28.

Identification code	032-017_MME28
Empirical formula	$C_{27}H_{23}Cl_3N_5O_3$
Formula weight	571.85
Temperature/K	100.00(10)
Crystal system	hexagonal
Space group	$P6_1$
a/Å	19.0210(3)
b/Å	19.0210(3)
c/Å	13.5011(2)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	4230.25(15)
Z	6
ρ_{calc}g/cm^3	1.347
μ/mm^{-1}	3.254
F(000)	1770.0
Crystal size/mm^3	0.07 × 0.05 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.364 to 139.986
Index ranges	$-23 \le h \le 16$, $-20 \le k \le 23$, $-16 \le l \le 16$
Reflections collected	17903
Independent reflections	5021 [R_{int} = 0.0464, R_{sigma} = 0.0450]
Data/restraints/parameters	5021/1/355
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0599, wR_2 = 0.1636
Final R indexes [all data]	R_1 = 0.0644, wR_2 = 0.1675
Largest diff. peak/hole / e Å^{-3}	0.99/-0.44
Flack parameter	0.030(13)



Single-crystal X-ray structure of compound **9a**.

Table 1 Crystal data and structure refinement for 13401_MME7.

Identification code	13401_MME7
Empirical formula	$C_{18}H_{16}Br_2N_4S_3$
Formula weight	544.35
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	5.82120(10)
b/Å	15.4764(4)
c/Å	22.0939(5)
α/°	90
β/°	91.022(2)
γ/°	90
Volume/Å^3	1990.15(8)
Z	4
ρ_{calc}g/cm^3	1.817
μ/mm^{-1}	8.207
F(000)	1080.0
Crystal size/mm^3	0.22 × 0.14 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.838 to 139.988
Index ranges	$-3 \leq h \leq 7$, $-18 \leq k \leq 18$, $-26 \leq l \leq 26$
Reflections collected	8113
Independent reflections	3755 [R_{int} = 0.0286, R_{sigma} = 0.0259]
Data/restraints/parameters	3755/0/245
Goodness-of-fit on F^2	1.117
Final R indexes [I>=2σ (I)]	R_1 = 0.0342, wR_2 = 0.0890
Final R indexes [all data]	R_1 = 0.0349, wR_2 = 0.0896
Largest diff. peak/hole / e Å^{-3}	0.87/-0.76

[1] Vishnevskiy Y.V., Schwabedissen J., Rykov A.N., Kuznetsov V.V., Makhova N.N. *Journal of Physical Chemistry* **2015**, 119, 10871-10881.

[2] Ikeda R., Kimura T., Tsutsumi T., Tamura S., Sakai N., Konakahara T. *Bioorg. Med. Chem. Lett.* **2012**, 22, 3506-3515.