SUPPLEMENTARY MATERIAL

1*H*-Indole-2,3-dione 3-thiosemicarbazones carrying a 4-sulfamoylphenyl moiety with selective antiviral activity against Reovirus-1

Füsun Göktaş [a], Gizem Nur Duran [b], Mehmet Özbil [c], Özge Soylu-Eter [a,*], Nilgün Karalı [a]

[a] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Istanbul University, Istanbul, Turkey
[b] Department of Chemistry, Institute of Science and Technology, Marmara University, Istanbul, Turkey
[c] Department of Biotechnology, Institute of Biotechnology, Gebze Technical University, Kocaeli, Turkey

*** Corresponding author:** Ö. Soylu-Eter, **E-mail:** ozge.soylu@istanbul.edu.tr
Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Istanbul University, 34116, Fatih, Istanbul, Turkey.

Table of Contents **Page**

1. Spectral data of the compounds 6a-j

1*H*-Indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6a)
Yellow powder (1.18 g, 90%): mp 268ºC; IR (KBr): ν 3374, 3274, 3182 (NH), 1674 (C=O), 1337, 1154 (S=O), 1207 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 6.94 (1H, d, *J*: 7.80 Hz, ind. C_7-H), 7.10 (1H, dt, *J*: 7.80, 7.32 Hz, ind. C_5-H), 7.36 (2H, s, SO_2NH_2, D_2O exch.), 7.37 (1H, t, *J*: 7.80 Hz, ind. C_6-H), 7.76 (1H, d, *J*: 7.32 Hz, ind. C_4-H), 7.85 (4H, s, phen.), 10.94 (1H, s, N_4-H, D_2O exch.), 11.25 (1H, s, ind. NH, D_2O exch.), 12.89 (1H, s, N_2-H, D_2O exch.). HSQC-2D (DMSO-d_6/125 MHz): 111.87 (ind. C_7), 120.49 (ind. C_{3a}), 122.17 (ind. C_4), 123.11 (ind. C_6), 125.98 (phen. $C_{2,6}$), 126.67 (phen. $C_{3,5}$), 132.34 (ind. C_5), 133.55 (ind. C_3), 141.79 (ind. C_{7a}), 142.14 (phen. C_4), 143.34 (phen. C_1), 163.41 (ind. C_2), 177.09 (C=S). LCMS-ESI (-): m/z (%) 374 (M-H-, 100). Anal. Calcd for $C_{15}H_{13}N_5O_3S_2$ (375.42542): C, 47.99; H, 3.49; N, 18.65 Found: C, 47.68; H, 3.56; N, 18.17.

5-Methyl-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6b)
Yellow powder (1.27 g, 93%): mp 258-260ºC; IR (KBr): ν 3296, 3269, 3173 (NH), 1685 (C=O), 1329, 1153 (S=O), 1212 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 2.30 (3H, s, CH_3), 6.83 (1H, d, *J*: 8.33 Hz, ind. C_7-H), 7.18 (1H, d, *J*: 8.33 Hz, ind. C_6-H), 7.36 (2H, s, SO_2NH_2), 7.59 (1H, s, ind. C_4-H), 7.87 (4H, s, phen.), 10.93 (1H, s, N_4-H), 11.15 (1H, s, ind. NH), 12.88 (1H, s, N_2-H). Anal. Calcd for $C_{16}H_{15}N_5O_3S_2$ (389.452): C, 49.34; H, 3.88; N, 17.98 Found: C, 49.12; H, 3.89; N, 17.85.

5-Trifluoromethoxy-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6c)
Light yellow powder (1.45 g, 90%): mp 246-248ºC; IR (KBr): ν 3339, 3237, 3115 (NH), 1693 (C=O), 1326, 1153 (S=O), 1204 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 7.03 (1H, d, *J*: 8.32 Hz, ind. C_7-H), 7.35 (1H, dd, *J*: 8.32, 1.60 Hz, ind. C_6-H), 7.37 (2H, s, SO_2NH_2, D_2O exch.), 7.78 (1H, d, *J*: 1.60, Hz, ind. C_4-H), 7.84 (2H, s, phen. C_2-H, C_6-H), 7.85 (2H, s, phen. C_3-H, C_5-H), 11.01 (1H, s, N_4-H, D_2O exch.), 11.41 (1H, s, ind. NH, D_2O exch.), 12.75 (1H, s, N_2-H, D_2O exch.). Anal. Calcd for $C_{16}H_{12}F_3N_5O_4S_2$ (459.4227896): C, 41.83; H, 2.63; N, 15.24 Found: C, 41.49; H, 2.52; N, 15.16.

5-Fluoro-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6d)
Red powder (1.27 g, 92%): mp 260-262ºC; IR (KBr): ν 3338, 3236, 3115 (NH), 1693 (C=O), 1326, 1154 (S=O), 1205 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 6.94 (1H, dd, *J*: 8.30, 3.91 Hz, ind. C_7-H), 7.20 (1H, dd, *J*: 8.78, 2.44 Hz, ind. C_6-H), 7.36 (2H, s, SO_2NH_2), 7.62 (1H, dd, *J*: 8.30, 2.44 Hz, ind. C_4-H), 7.85 (4H, s, phen.), 10.96 (1H, s, N_4-H), 11.25 (1H, s, ind. NH), 12.77 (1H, s, N_2-H); HMBC-2D (DMSO-d_6/ 125 MHz): 109.06 (d, *J*: 25.88 Hz, ind. C_4), 112.96 (d, *J*: 8.14 Hz, ind. C_7), 118.56 (d, *J*: 24.44 Hz, ind. C_6), 121.92 (d, *J*: 9.58 Hz, ind. C_{3a}), 125.98 (phen. $C_{2,6}$), 126.73 (phen. $C_{3,5}$), 132.91 (d, *J*: 2.87 Hz, ind. C_3), 139.60 (d, *J*: 1.91 Hz, ind. C_{7a}), 141.94 (phen. C_4), 141.95 (phen. C_1), 158.98 (d, *J*: 237.71 Hz, ind. C_5), 163.49 (ind. C_2), 177.04 (C=S). LCMS-ESI (-): m/z (%) 392 (M-H-, 100). Anal. Calcd for $C_{15}H_{12}FN_5O_3S_2$ (393.4158832): C, 45.79; H, 3.07; N, 17.80 Found: C, 45.46; H, 3.26; N, 17.33.

5-Chloro-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6e)
Orange powder (1.33 g, 93%): mp 266-268ºC; IR (KBr): ν 3323, 3291, 3165 (NH), 1691 (C=O), 1311, 1161 (S=O), 1204 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 6.95 (1H, d, *J*: 8.30 Hz, ind. C_7-H), 7.40 (1H, dd, *J*: 8.30, 2.44 Hz, ind. C_6-H), 7.84 (1H, d, *J*: 2.44 Hz, C_4-H), 7.36 (2H, s, SO_2NH_2), 7.85 (4H, s, phen.), 10.99 (1H, s, N_4-H), 11.34 (1H, s, ind. NH), 12.71

(1H, s, N_2-H). Anal. Calcd for $C_{15}H_{12}ClN_5O_3S_2$ (409.87048): C, 43.96; H, 2.95 N, 17.09 Found: C, 43.64; H, 2.86; N, 17.09.

5-Bromo-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6f)
Dark yellow powder (1.53 g, 96%): mp 254-255ºC; IR (KBr): ν 3306, 3245, 3172 (NH), 1687 (C=O), 1326, 1151 (S=O), 1204 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 6.90 (1H, d, *J*: 8.33, Hz, ind. C_7-H), 7.58 (1H, dd, *J*: 8.33, 2.25 Hz, ind. C_6-H), 7.36 (2H, s, SO_2NH_2), 7.99 (1H, d, *J*: 2.25, Hz, ind. C_4-H), 7.85 (4H, s, phen.), 11.00 (1H, s, N_4-H), 11.35 (1H, s, ind. NH.), 12.70 (1H, s, N_2-H). Anal. Calcd for $C_{15}H_{12}BrN_5O_3S_2$ (454.32148): C, 39.65; H, 2.66; N, 15.41 Found: C, 39.72; H, 2.66; N, 15.09.

Sodium 1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone]-5-sulfonate (6g)
Dark yellow powder (1.10 g, 66%): mp >300ºC; IR (KBr): ν 3271, 3234 (NH), 1712 (C=O), 1313, 1153 (S=O), 1220 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 6.89 (1H, d, *J*: 8.40 Hz, ind. C_7-H), 7.38 (2H, s, SO_2NH_2), 7.65 (1H, dd, *J*: 8.00, 1.60 Hz, ind. C_6-H), 7.84 (4H, s, phen.), 8.16 (1H, d, *J*: 1.60 Hz, ind. C_4-H), 11.20 (1H, s, N_4-H), 11.33 (1H, s, ind. NH.), 12.86 (1H, s, N_2-H); Anal. Calcd for $C_{15}H_{12}N_5NaO_6S_3.4H_2O$ (549.531569): C, 32.78; H, 3.85; N, 12.74 Found: C, 32.86; H, 3.69; N, 12.78.

7-Fluoro-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6h)
Yellow powder (1.18 g, 86%): mp 271-273ºC; IR (KBr): ν 3394, 3277, 3136 (NH), 1681 (C=O), 1338, 1149 (S=O), 1220 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 7.14 (1H, dd (t), *J*: 7.80, 4.88 Hz, ind. C_5-H), 7.31 (1H, dd, *J*: 8.29, 1.95 Hz, ind. C_6-H), 7.39 (2H, s, SO_2NH_2, D_2O exch.), 7.63 (1H, d, *J*: 7.32 Hz, ind. C_4-H), 7.85 (4H, s, phen.), 11.04 (1H, s, N_4-H, D_2O exch.), 11.81 (1H, s, ind. NH, D_2O exch.), 12.86 (1H, s, N_2-H, D_2O exch.); Anal. Calcd for $C_{15}H_{12}FN_5O_3S_2$ (393.4158832): C, 45.79; H, 3.07; N, 17.80 Found: C, 45.64; H, 2.89; N, 17.52.

7-Chloro-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6i)
Yellow powder (1.25 g, 87%): mp 288-289ºC; IR (KBr): ν 3331, 3271, 3130 (NH), 1693 (C=O), 1334, 1138 (S=O), 1224 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 7.15 (1H, t, *J*: 7.80 Hz, ind. C_5-H), 7.46 (1H, d, *J*: 7.80 Hz, ind. C_6-H), 7.39 (2H, s, SO_2NH_2, D_2O exch.), 7.75 (1H, d, *J*: 7.32 Hz, ind. C_4-H), 7.85 (4H, s, phen.), 11.04 (1H, s, N_4-H, D_2O exch.), 11.79 (1H, s, ind. NH, D_2O exch.), 12.83 (1H, s, N_2-H, D_2O exch.); Anal. Calcd for $C_{15}H_{12}ClN_5O_3S_2$ (409.87048): C, 43.96; H, 2.95; N, 17.09 Found: C, 44.08; H, 3.34; N, 16.93.

5,7-Dibromo-1*H*-indole-2,3-dione 3-[N-(4-sulfamoylphenyl)thiosemicarbazone] (6j)
Yellow powder (1.77 g, 95%): mp 283ºC; IR (KBr): ν 3328, 3255, 3215 (NH), 1694 (C=O), 1329, 1151 (S=O), 1205 (C=S). ^{1}H NMR (DMSO-d_6/ 500 MHz) ppm: 7.37 (2H, s, SO_2NH_2), 7.80 (1H, d, *J*: 1.92 Hz, ind C_6-H), 7.84 (2H, s, phen. C_2-H, C_6-H), 7.86 (2H, s, phen. C_3-H, C_5-H), 8.01 (1H, d, *J*: 1.92 Hz, ind. C_4-H), 11.04 (1H, s, N_4-H), 11.69 (s, 1H, ind. NH.), 12.65 (s, 1H, N_2-H). 13C-NMR (DEPT) (DMSO-d_6/ 125MHz) ppm: 124.00 (ind. C_4), 126.17 (phen. C_2, C_6), 126.75 (phen. C_3, C_5), 138.00 (ind. C_6). LCMS-ESI (-): m/z (%) 530, 532, 534 (M-H-, 43, 100, 52). Anal. Calcd for $C_{15}H_{11}Br_2N_5O_3S_2$ (533.21754): C, 33.79; H, 2.08; N, 13.13 Found: C, 33.85; H, 2.65; N, 13.20.

2. Spectra of the compound 7a-c

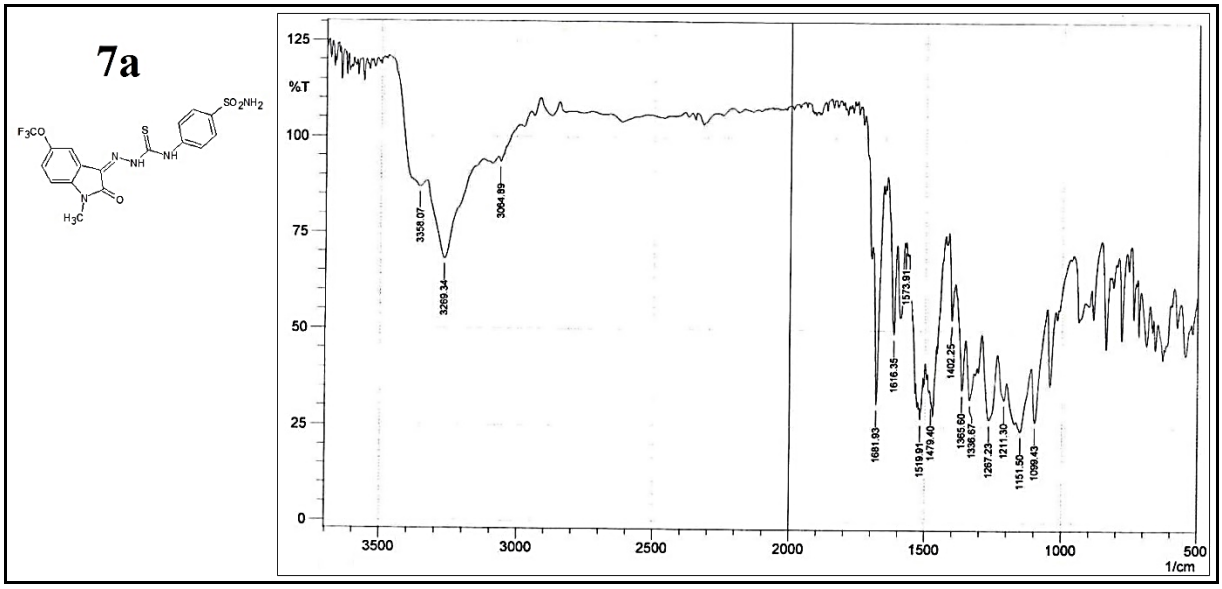

Figure S1: IR (KBr) spectrum of the compound **7a**

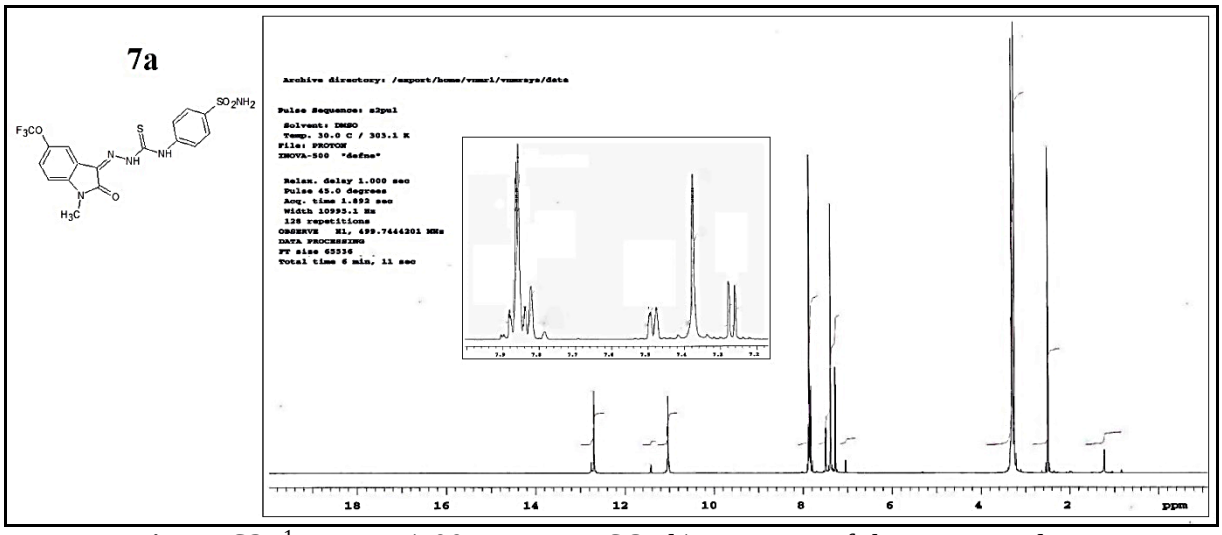

Figure S2: ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of the compound **7a**

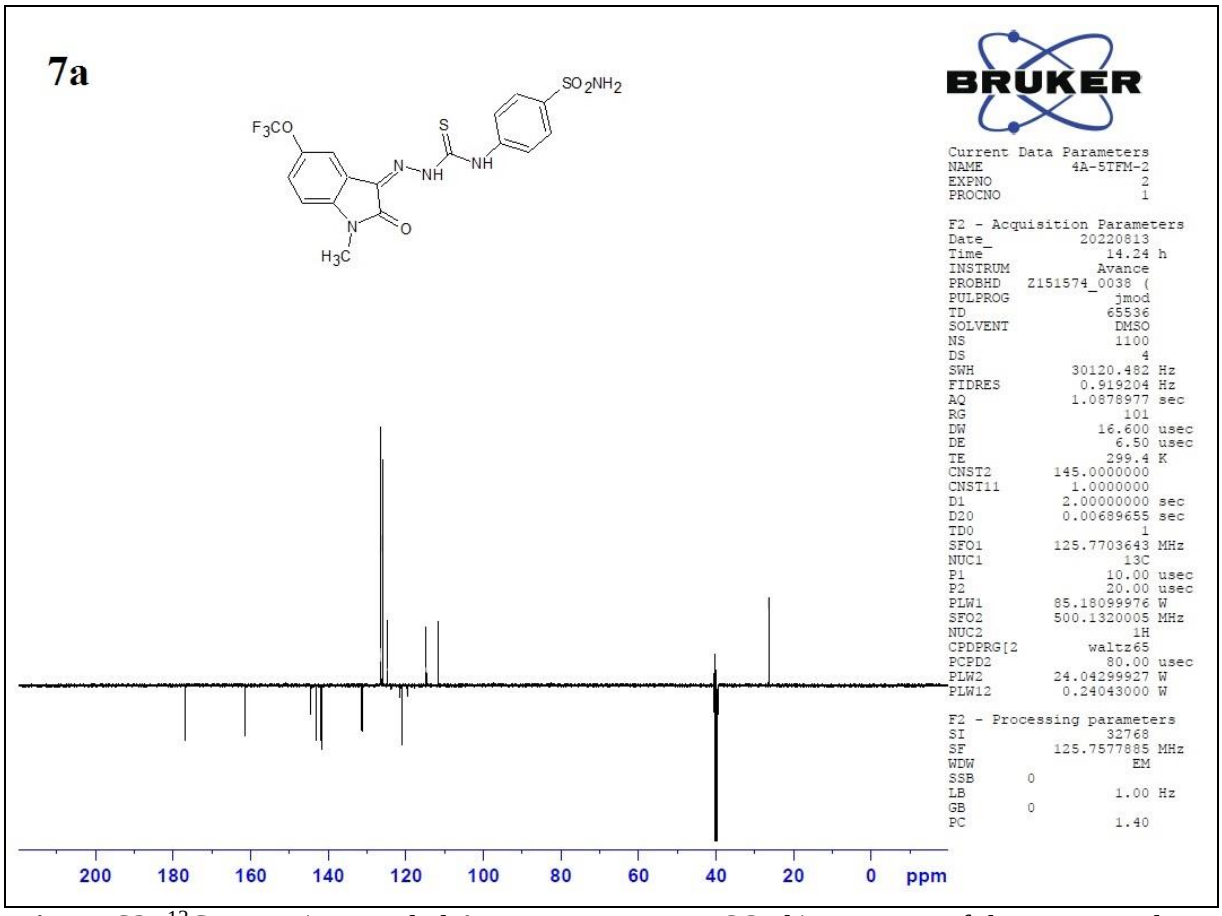

Figure S3: ^{13}C NMR (Decoupled APT, 125 MHz, DMSO-d_6) spectrum of the compound **7a**

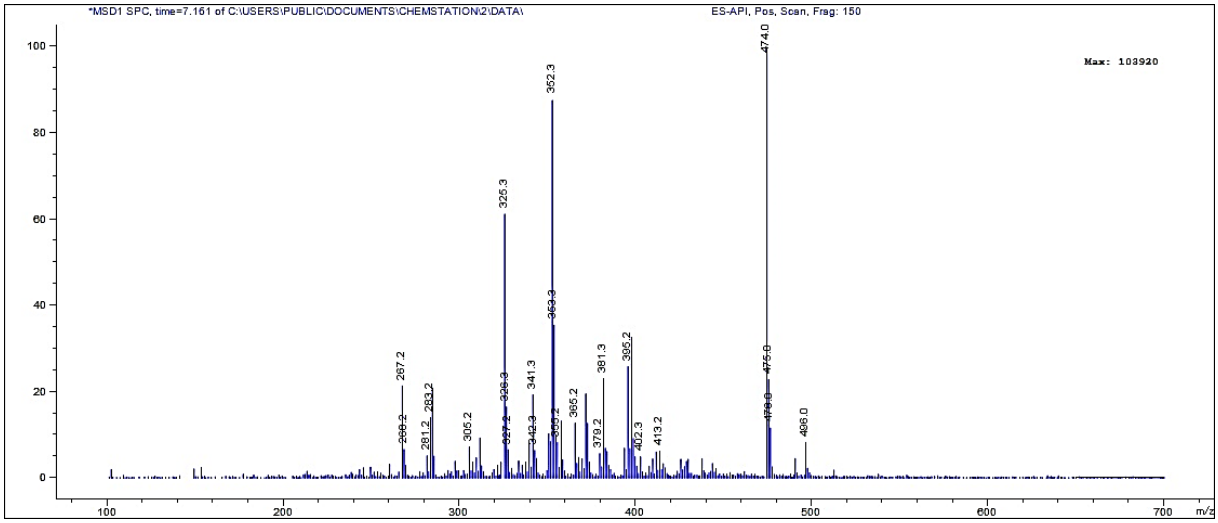

Figure S4: LCMS (ESI+) spectrum of the compound **7a**

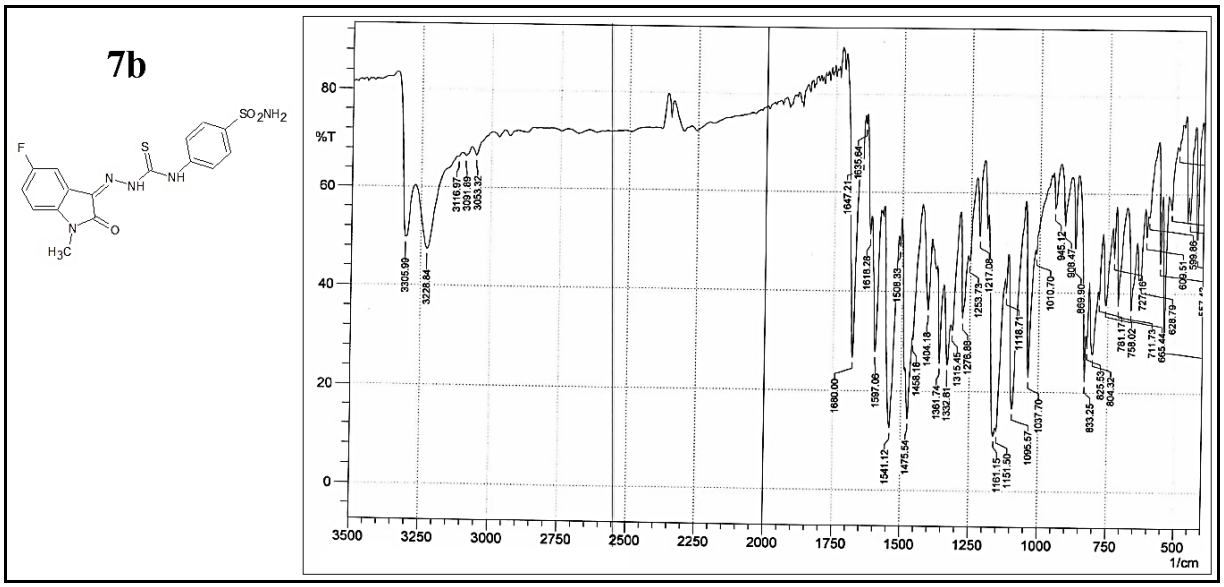

Figure S5: IR (KBr) spectrum of the compound **7b**

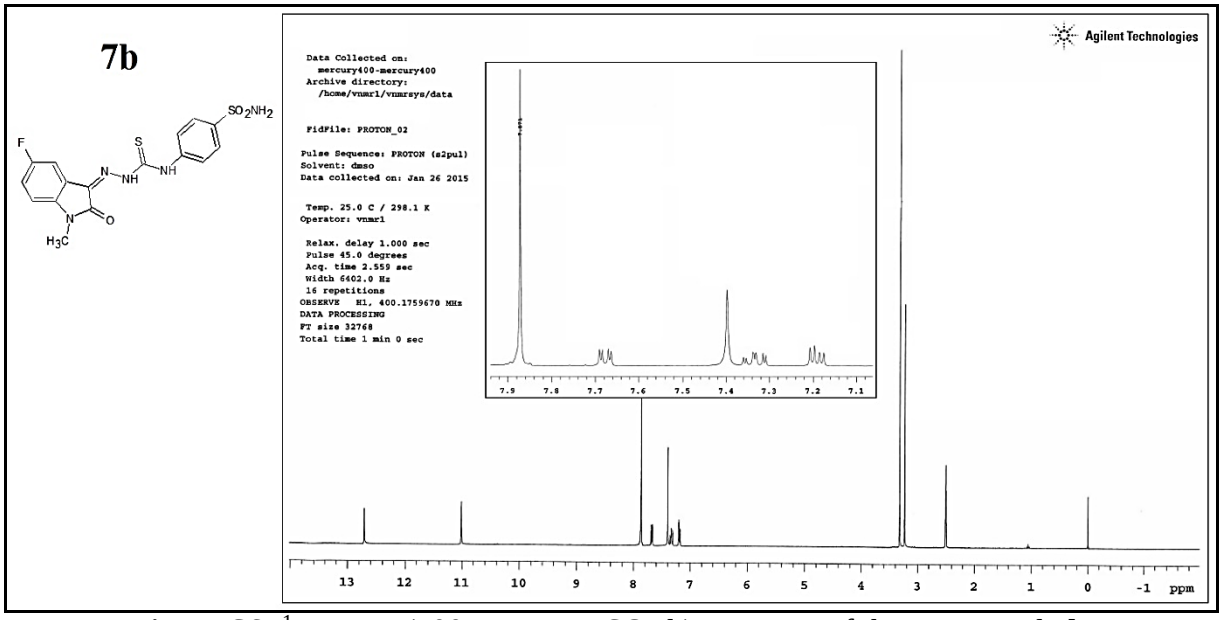

Figure S6: ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of the compound **7b**

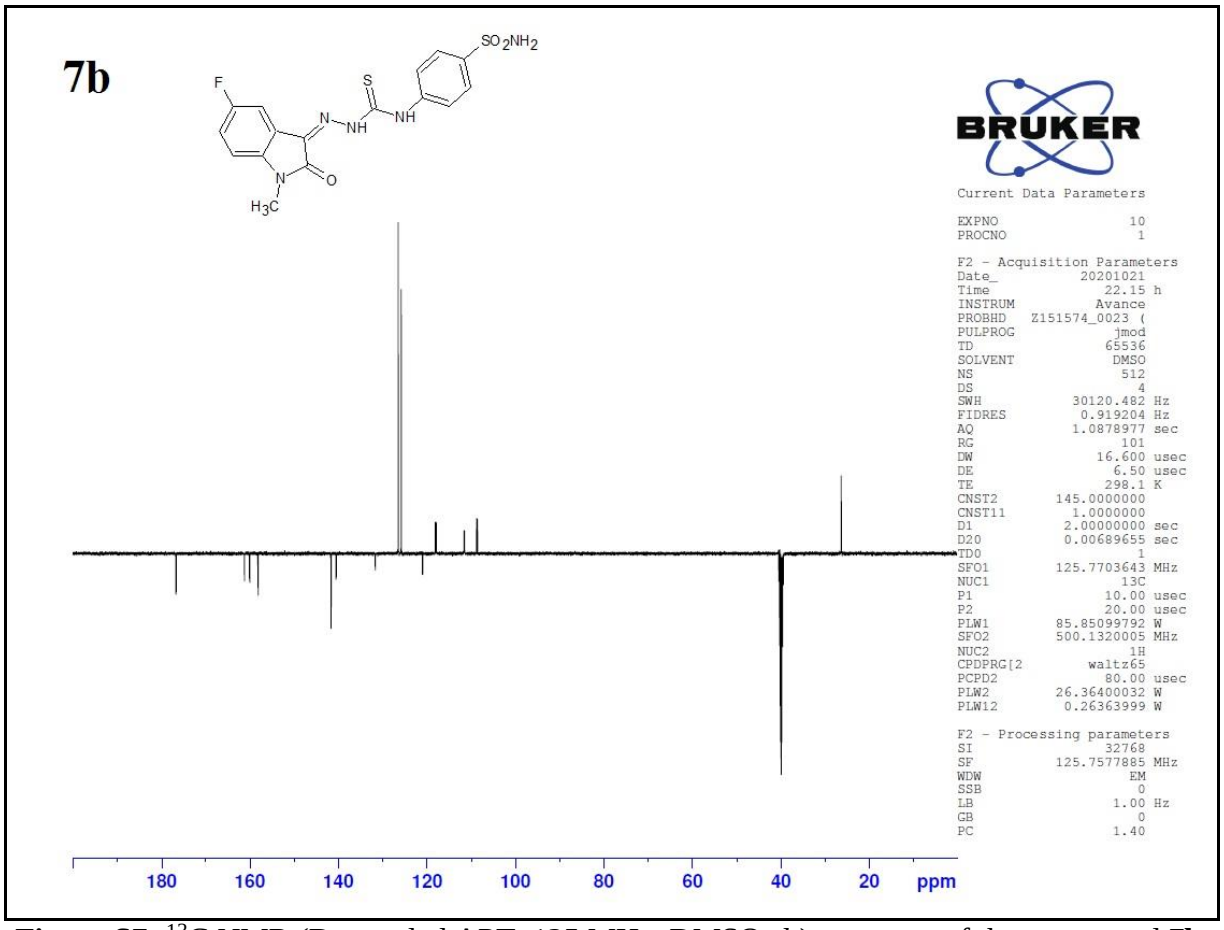

Figure S7: ^{13}C NMR (Decoupled APT, 125 MHz, DMSO-d_6) spectrum of the compound **7b**

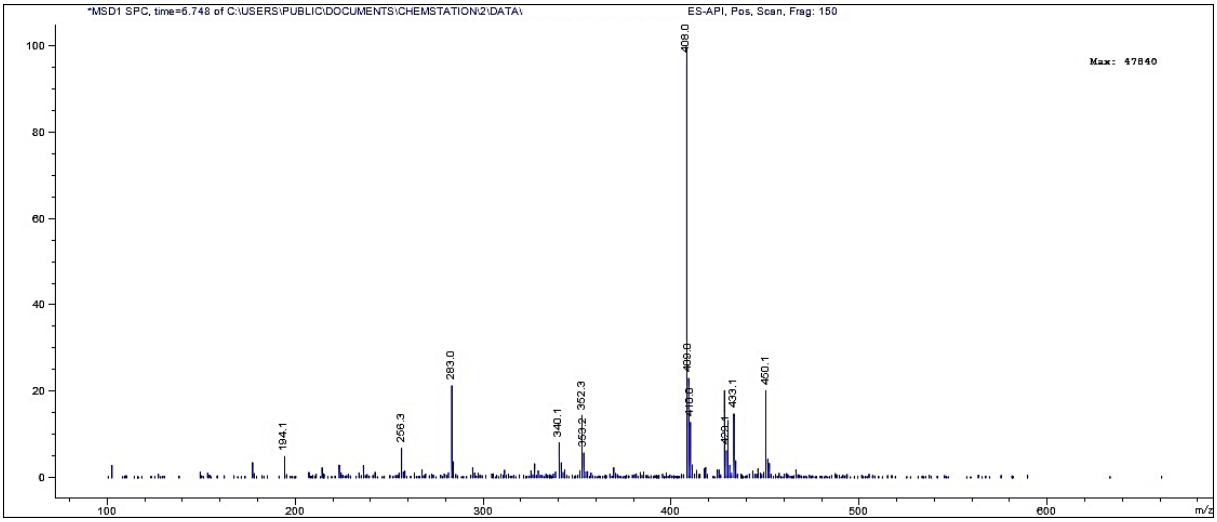

Figure S8: LCMS (ESI+) spectrum of the compound **7b**

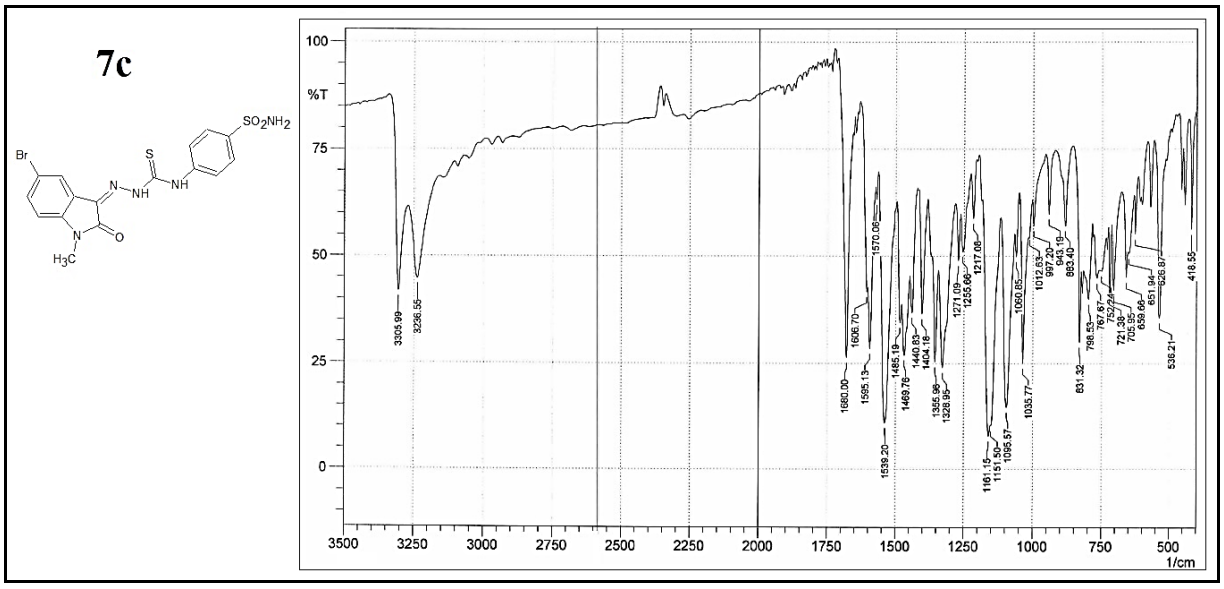

Figure S9: IR (KBr) spectrum of the compound **7c**

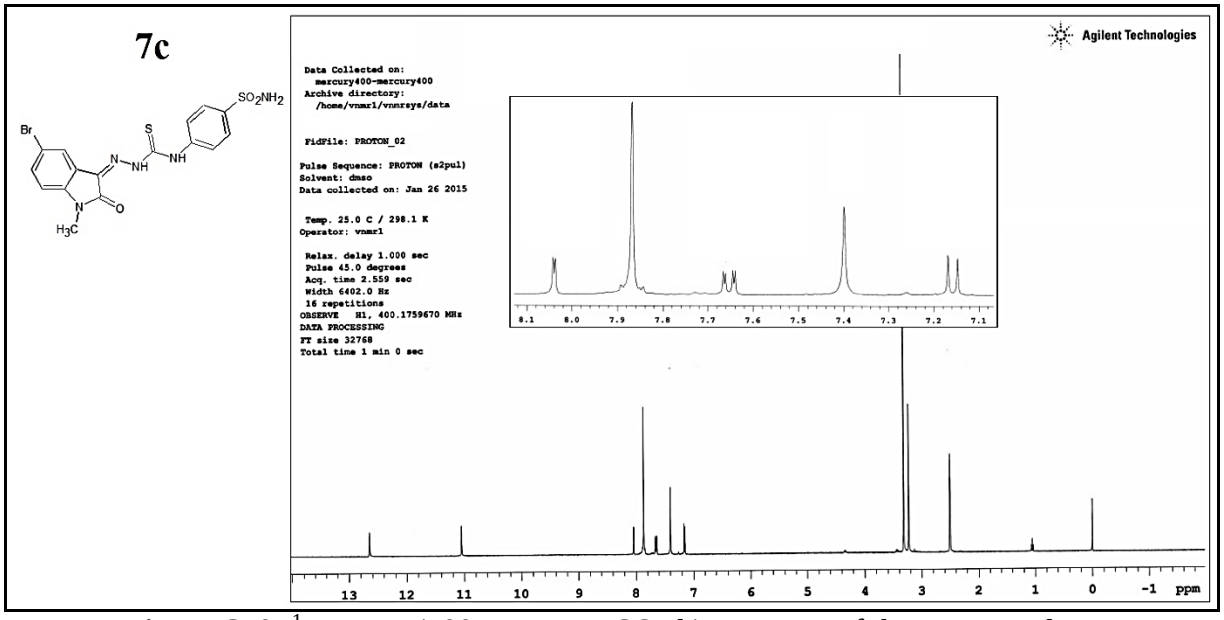

Figure S10: ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of the compound **7c**

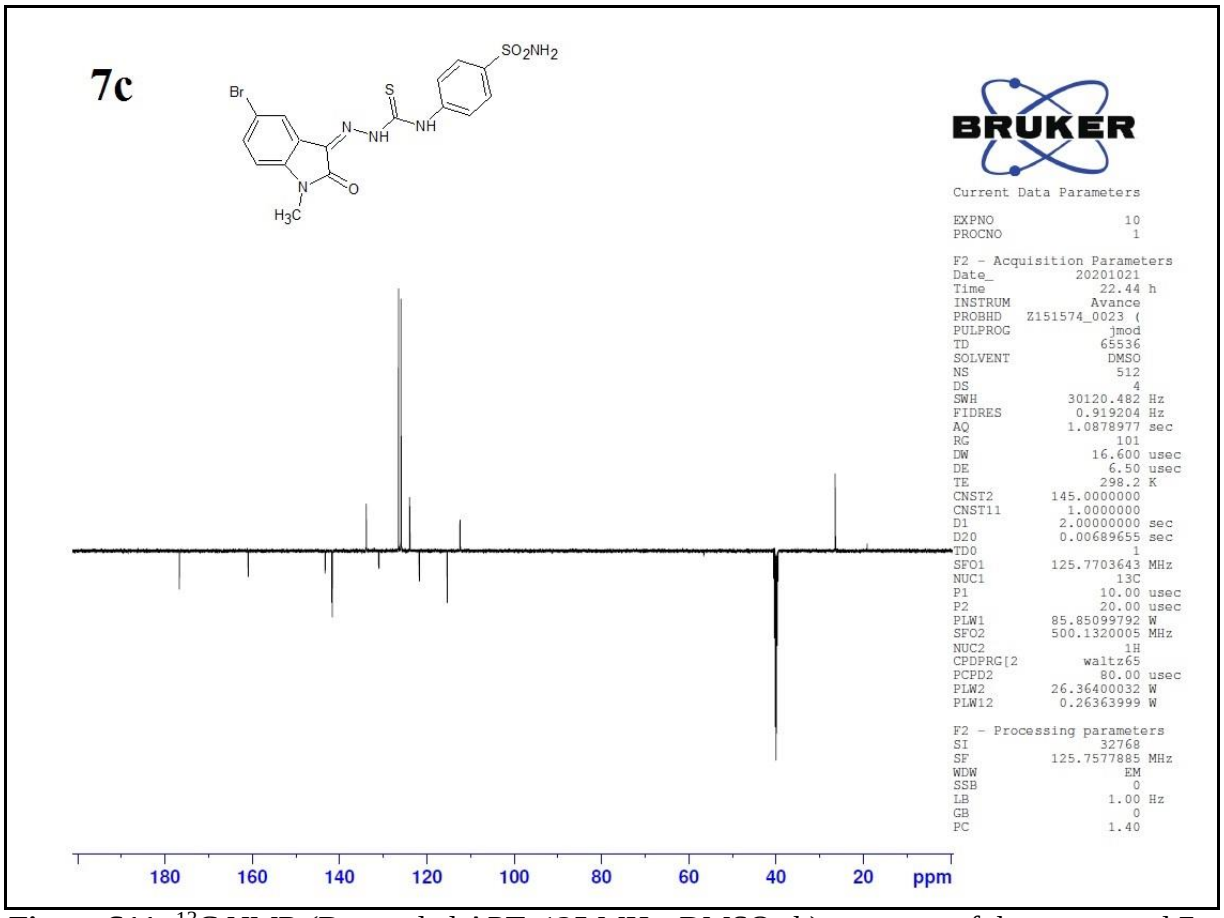

Figure S11: ^{13}C NMR (Decoupled APT, 125 MHz, DMSO-d_6) spectrum of the compound **7c**

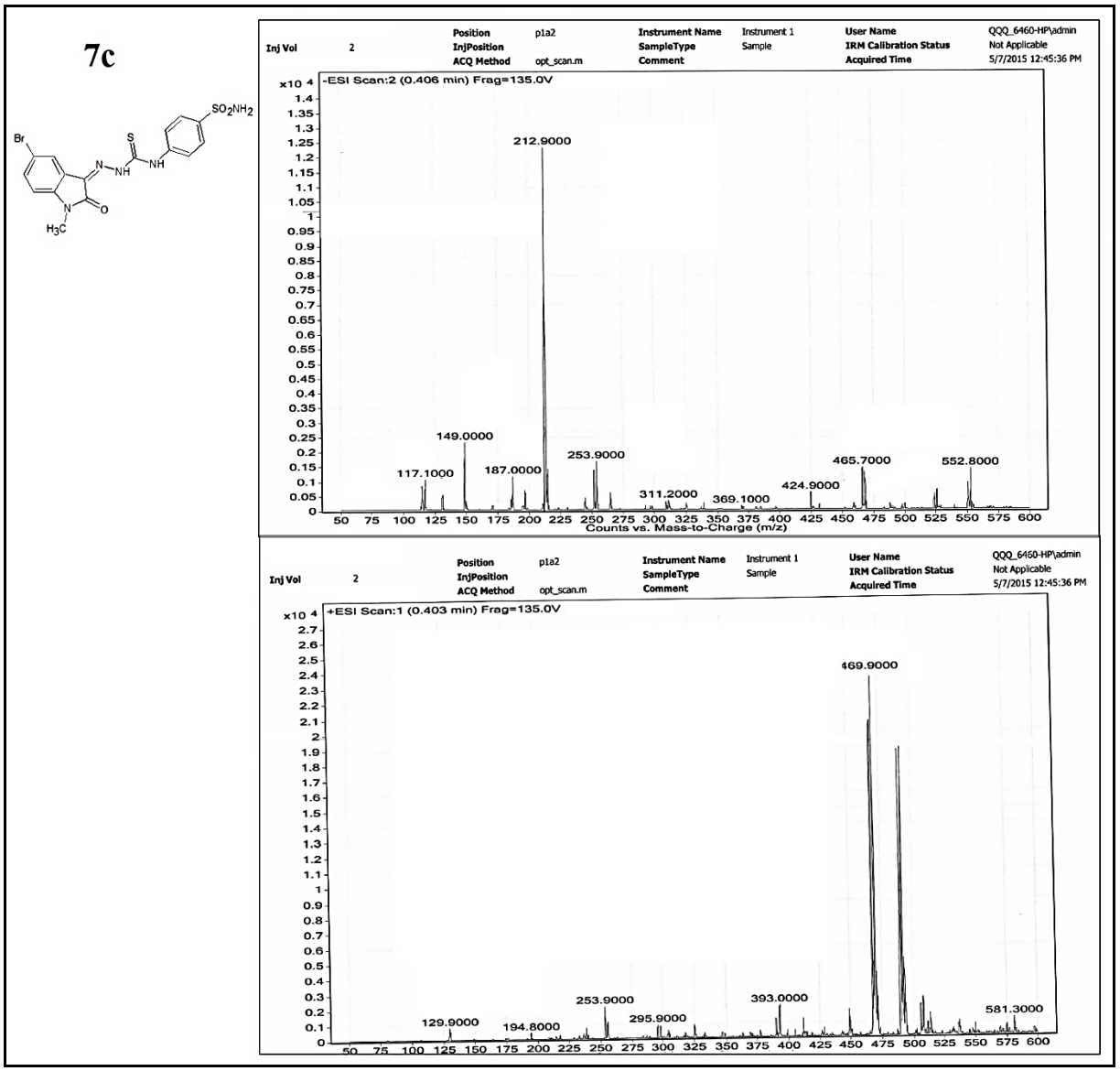

Figure S12: LCMS (ESI- and ESI+) spectra of the compound **7c**