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Supplementary Information

Improved Synthesis of 1,3,4-Thiadiazolium-2-phenylamines Using Microwave and Ultrasound Irradiation and Investigation of their Cytotoxic Activity

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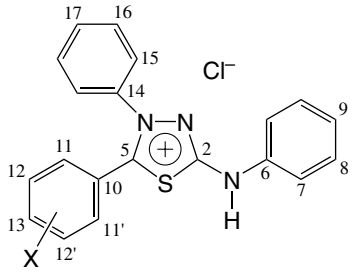
Characterization data



X = H (**1**), 4'-OCH_3 (**2**), 4'-NO_2 (**3**), 3',4'-OCH_2O (**4**)

*4,5-Diphenyl-1,3,4-thiadiazolium-2-phenylamine chloride (**1**)*

Pale yellow solid; mp 356-358 °C (lit.[21] mp 358 °C); IR (KBr) ν_{max}/cm^{-1} 3419, 3047, 2723, 1569, 1542, 1494, 1444, 1319, 755, 690; ^1H NMR ($CDCl_3$) δ 12.50 (s, N–H), 7.08-7.72 (m, H_{arom}); ^{13}C NMR (DMSO-d_6 δ 163.84 (C-5), 160.48 (C-2), 138.56 (C-14), 138.28 (C-10), 138.00 (C-6), 137.46 (C-17), 135.80 (C-13), 134.07 (C-11), 132.98 (C-16), 131.19 (C-8), 130.19 (C-12), 129.88 (C-15), 129.61 (C-9), 118.33 (C-7).

*4-Phenyl-5-(4'-methoxy-phenyl)-1,3,4-thiadiazolium-2-phenylamine chloride (**2**)*

Yellow solid; mp 242-243 °C (lit.[21] mp 238 °C); IR (KBr) ν_{max}/cm^{-1} 3425, 3048, 2935, 2665, 1602, 1542, 1448, 1567, 1309, 1175, 1024, 827, 752, 692; ^1H NMR ($CDCl_3$) δ 12.90 (s, N–H), 7.70 (d, H-12,H-12'), 6.90 (d, H-11, H-11'), 7.63-7.08 (m, H_{arom}), 3.86 (s, CH_3O); ^{13}C NMR (DMSO-d_6) δ 163.00 (C-5), 159.48 (C-2), 138.34 (C-14), 137.74 (C-6), 131.89 (C-10), 131.07 (C-17), 129.40 (C-12), 129.73 (C-16), 125.79 (C-8), 126.10 (C-9, C-13), 123.64 (C-11), 118.18 (C-15), 114.69 (C-7), 55.54 (OCH_3).

*4-Phenyl-5-(4'-nitrophenyl)-1,3,4-thiadiazolium-2-phenylamine chloride (**3**)*

Orange solid; mp 138-139 °C (lit.[21] mp 138-139 °C); IR (KBr) ν_{max}/cm^{-1} 3434, 3043, 2721, 1573, 1537, 1454, 1348, 854, 746, 694; ^1H NMR ($CDCl_3$) δ 12.75 (s, N–H), 8.21 (d, H-12,H-12'), 8.16 (d, H-11, H-11'), 7.71-7.00 (m, H_{arom}); ^{13}C NMR (DMSO-d_6) δ 163.84 (C-5), 159.20 (C-2), 137.95 (C-13), 136.95 (C-10), 131.43 (C-14), 131.25 (C-6), 129.46 (C-17), 128.85 (C-16), 126.00 (C-9), 125.67 (C-8), 124.90 (C-12), 123.79 (C-11), 123.33 (C-15), 118.24 (C-7).

*4-Phenyl-5-(3',4'-methylenedioxyphenyl)-1,3,4-thiadiazolium-2-phenylamine chloride (**4**)*

Pale yellow solid; mp 290-293 °C (lit.[6] mp 286-287 °C); IR (KBr) ν_{max}/cm^{-1} 3438, 3050, 2902, 2642, 1604, 1540, 1450, 1567, 1311, 1243, 1105, 1037, 754, 694; ^1H NMR ($CDCl_3$) δ 11.76 (s, N–H), 7.60-7.20 (m, H_{arom}), 7.17 (d, H-11'), 7.10 (d, H-12'), 7.02 (d, H-11), 6.08 (s, OCH_2O); ^{13}C NMR (DMSO-d_6) δ 163.05 (C-5), 160.05 (C-2), 150.70 (C-12), 148.00 (C-13), 140.50 (C-14), 138.80 (C-6), 133.45 (C-17), 130.95 (C-8), 129.75 (C-16), 126.13 (C-11'), 127.57 (C-15), 127.42 (C-9), 117.56 (C-7), 115.12 (C-10), 115.46 (C-11), 110.42 (C-12'), 103.86 (OCH_2O).

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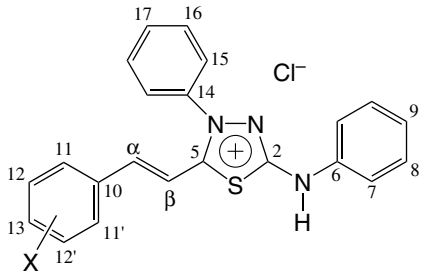

X = H (**5**), 2'-OCH_3 (**6**), 4'-NO_2 (**7**), 4'-$N(CH_3)_2$ (**8**)

*4-Phenyl-5-styryl-1,3,4-thiadiazolium-2-phenylamine chloride (**5**)*

Yellow solid; mp 264-265 °C (lit.[12] mp 266-267 °C); IR (KBr) ν_{max}/cm^{-1} 3432, 3056, 2670, 1604, 1567, 1538, 1498, 1448, 1330, 954, 746, 690; ^{1}H NMR ($CDCl_3$) δ 12.58 (s, N–H), 7.95 (d, H_α), 7.19-7.83 (m, H_{arom}), 7.06 (d, H_β); ^{13}C NMR (DMSO-d_6) δ 164.90 (C-5), 160.30 (C-2), 149.84 (C-α), 138.00 (C-14), 137.82 (C-6), 135.35 (C-10), 135.90 (C-17), 134.89 (C-13), 132.30 (C-11), 131.95 (C-16), 133.64 (C-8), 130.56 (C-12), 129.20 (C-15), 127.28 (C-9), 120.79 (C-7), 115.67 (C-β).

*4-Phenyl-5-(2'-methoxy-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**6**)*

Yellow solid; mp 198-200 °C (lit.[12] mp 195-196 °C); IR (KBr) ν_{max}/cm^{-1} 3423, 3054, 2925, 2786, 1604, 1594, 1540, 1444, 1565, 1295, 1249, 1110, 1031, 966, 836, 754, 690; ^{1}H NMR ($CDCl_3$) δ 11.90 (s, N–H), 7.92 (d, H_α), 7.84-6.90 (m, H_{arom}), 6.97 (d, H_β), 3.81 (s, CH_3O); ^{13}C NMR (DMSO-d_6) δ 162.29 (C-11), 159.15 (C-5), 158.57 (C-2), 144.58 (C-α), 138.26 (C-14), 136.87 (C-6), 133.94 (C-11'), 131.70 (C-13), 130.51 (C-17), 130.07 (C-16), 128.89 (C-8), 125.56 (C-15), 124.04 (C-9), 122.11 (C-10), 118.89 (C-7), 111.40 (C-β), 55.46 (OCH_3).

*4-Phenyl-5-(4'-nitro-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**7**)*

Orange solid; mp 234-236 °C (lit.[12] mp 232-233 °C); IR (KBr) ν_{max}/cm^{-1} 3432, 3048, 2721, 1616, 1571, 1519, 1450, 1342, 956, 840, 746, 688; ^{1}H NMR ($CDCl_3$) δ 12.74 (s, N–H), 8.33 (d, H-12, H-12'), 8.25 (d, H_α), 8.04 (d, H-11, H-11'), 7.96-7.39 (m, H_{arom}), 7.33 (d, H_β); ^{13}C NMR (DMSO-d_6) δ 165.10 (C-5), 162.38 (C-2), 151.00 (C-13), 147.55 (C-α), 142.99 (C-10), 140.20 (C-14), 139.05 (C-6), 132.92 (C-17), 131.98 (C-16), 130.50 (C-8), 129.68 (C-11), 127.20 (C-15), 126.33 (C-9), 125.25 (C-12), 117.71 (C-7), 114.81 (C-β).

*4-Phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**)*

Purple solid; mp 201-203 °C; IR (KBr) ν_{max}/cm^{-1}: 3425, 3062, 2923, 2852, 1612, 1565, 1577, 1525, 1444, 1378, 1268, 941, 808, 750, 692; ^{1}H NMR ($CDCl_3$) δ 12.39 (s, N–H), 7.85 (d, H_α), 7.81 (d, H-12, H-12'), 7.73 (d, H-11, H-11'), 7.71- 6.71 (m, H_{arom}), 6.70 (d, H_β), 3.02 (m, $N(CH_3)_2$); ^{13}C NMR (DMSO-d_6) δ 163.27 (C-13), 157.14 (C-5), 153.01 (C-2), 149.47 (C-α), 138.81 (C-14), 137.15 (C-6), 131.76 (C-11, 11'), 131.20 (C-17), 130.12 (C-16), 129.33 (C-8), 126.16 (C-15), 123.66 (C-9), 121.08 (C-10), 118.30 (C-7), 111.88 (C-12, 12'), 103.81 (C-β), 39.75 ($N(CH_3)_2$); Elemental analysis: Found: C, 66.38; H, 5.15; N, 12.94. Calc. for $C_{24}H_{23}N_4SCl$: C, 66.27; H, 5.33; N, 12.88%.

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Same as cited in the Article

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IR, ^{13}C NMR, DEPT-Q and ^{1}H, spectra of compound ***8***

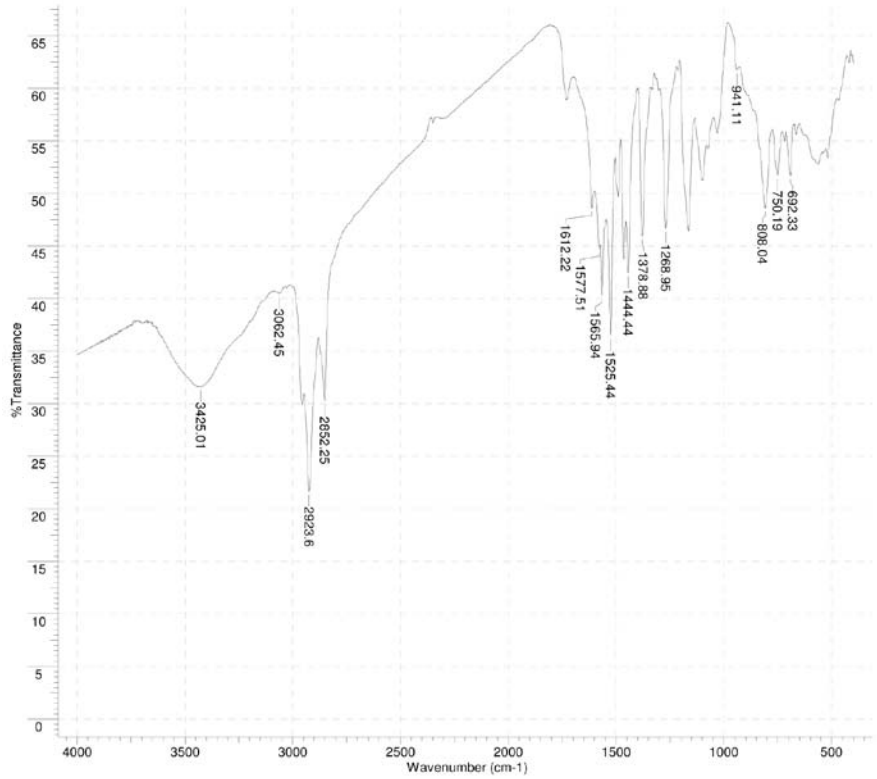

Figure S1. IR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4- thiadiazolium-2-phenylamine chloride (**8**).

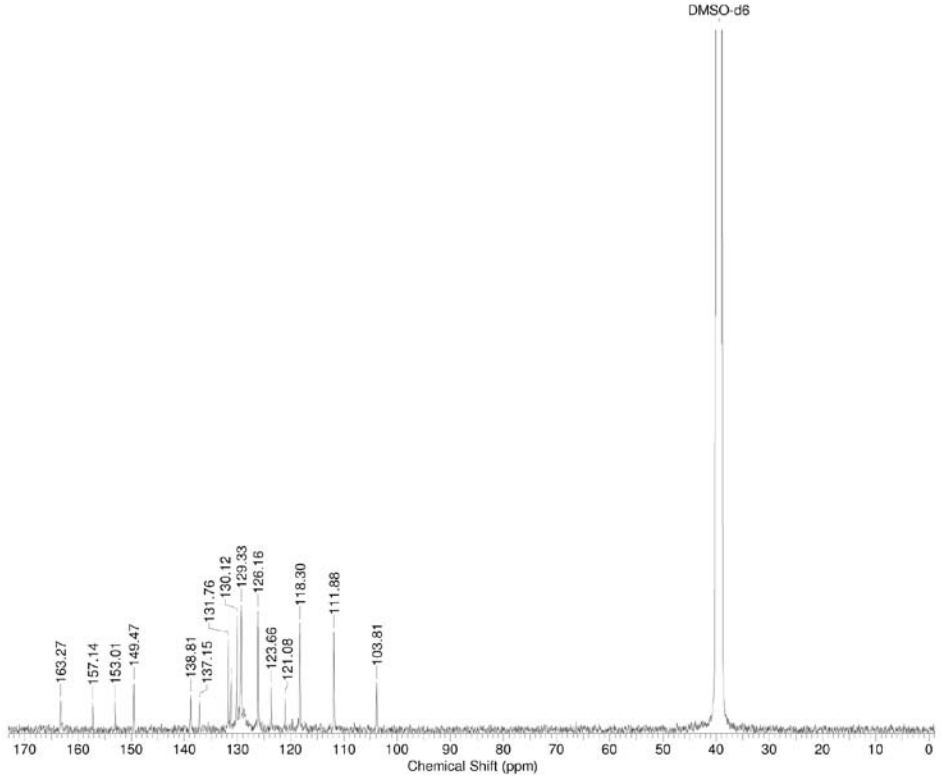

Figure S2. ^{13}C NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

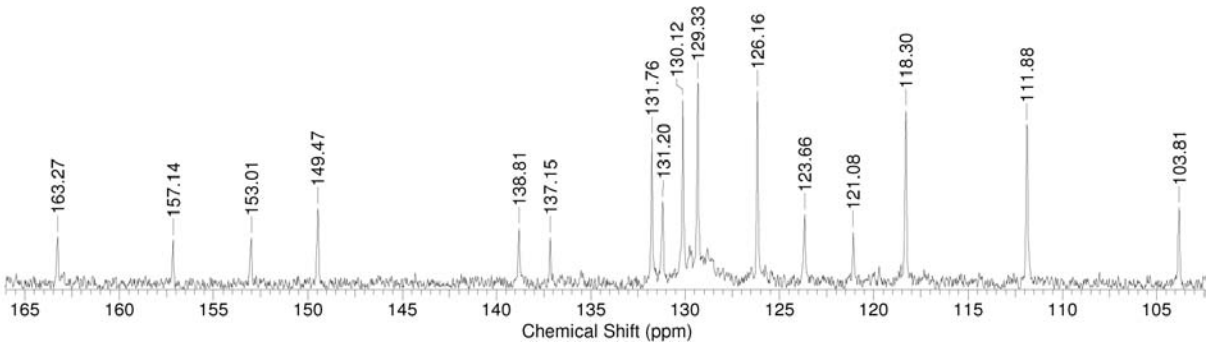

Figure S3. Expansion of ^{13}C NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

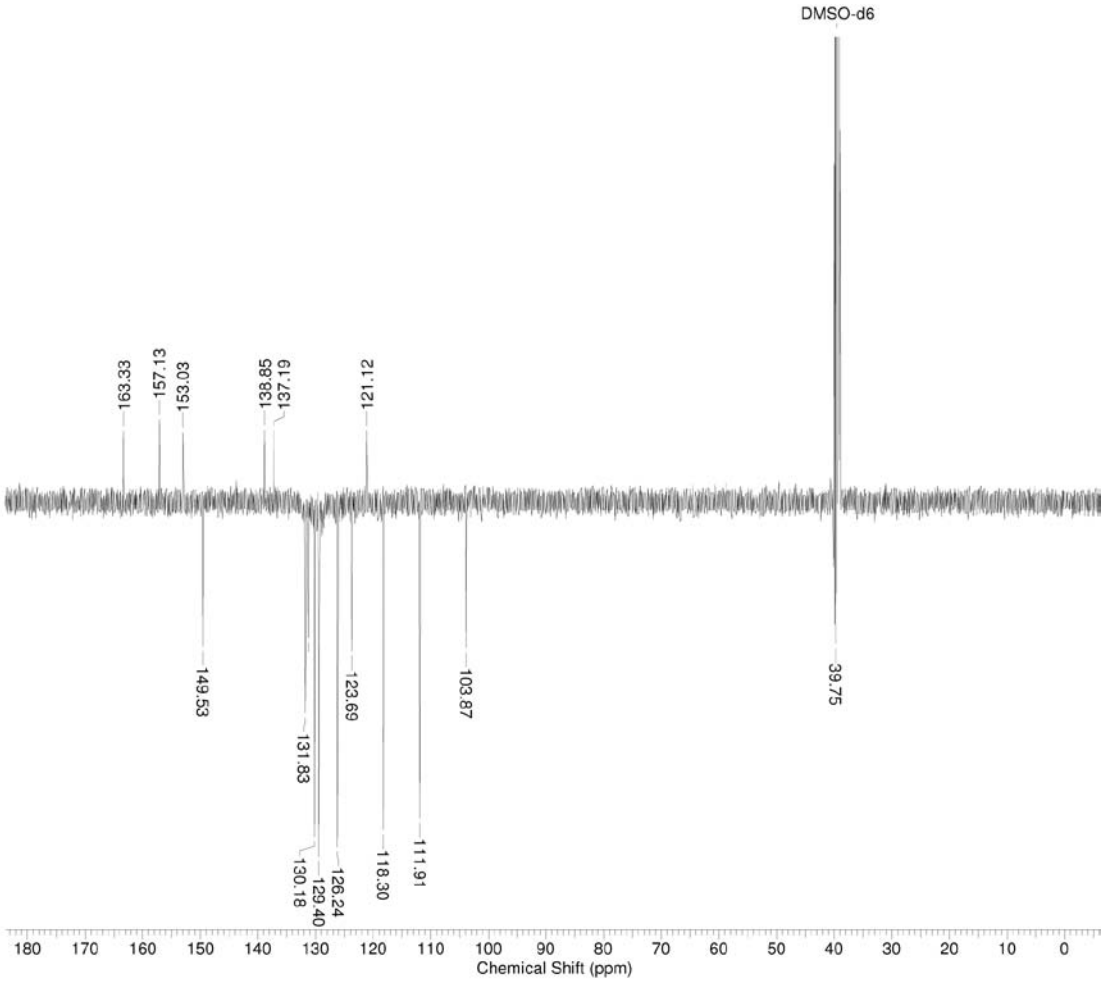

Figure S4. DEPT-Q spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

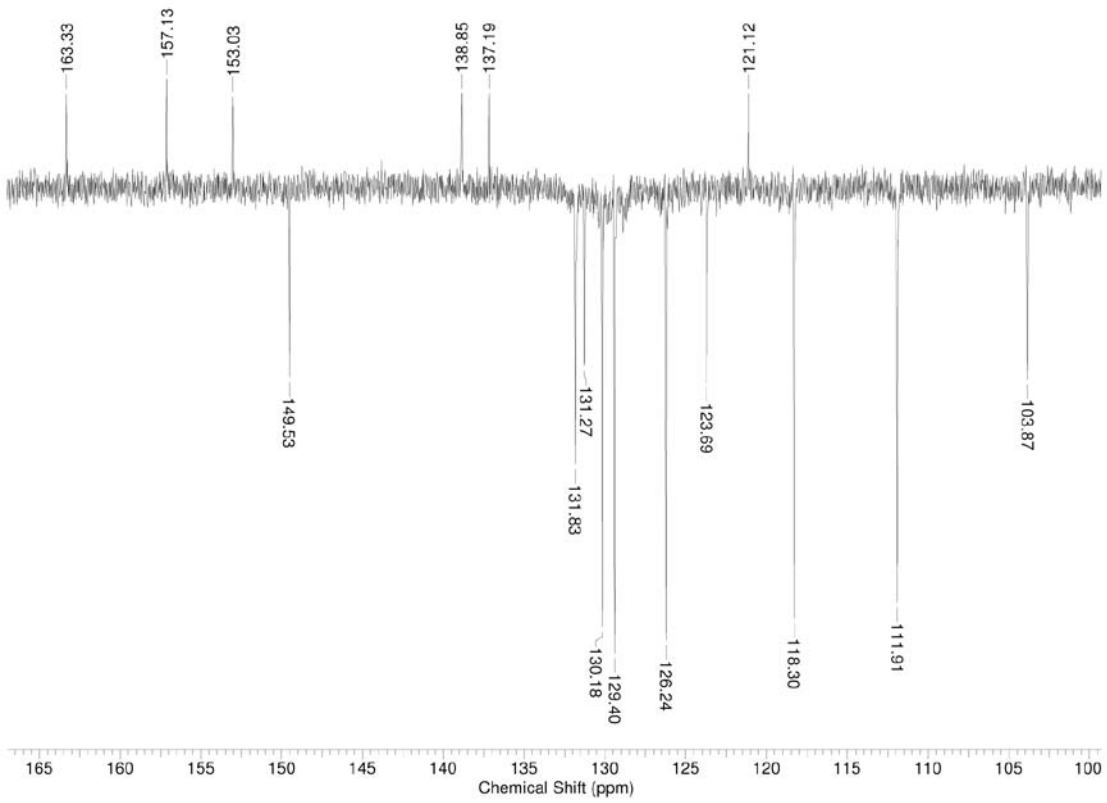

Figure S5. Expansion of DEPT-Q spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

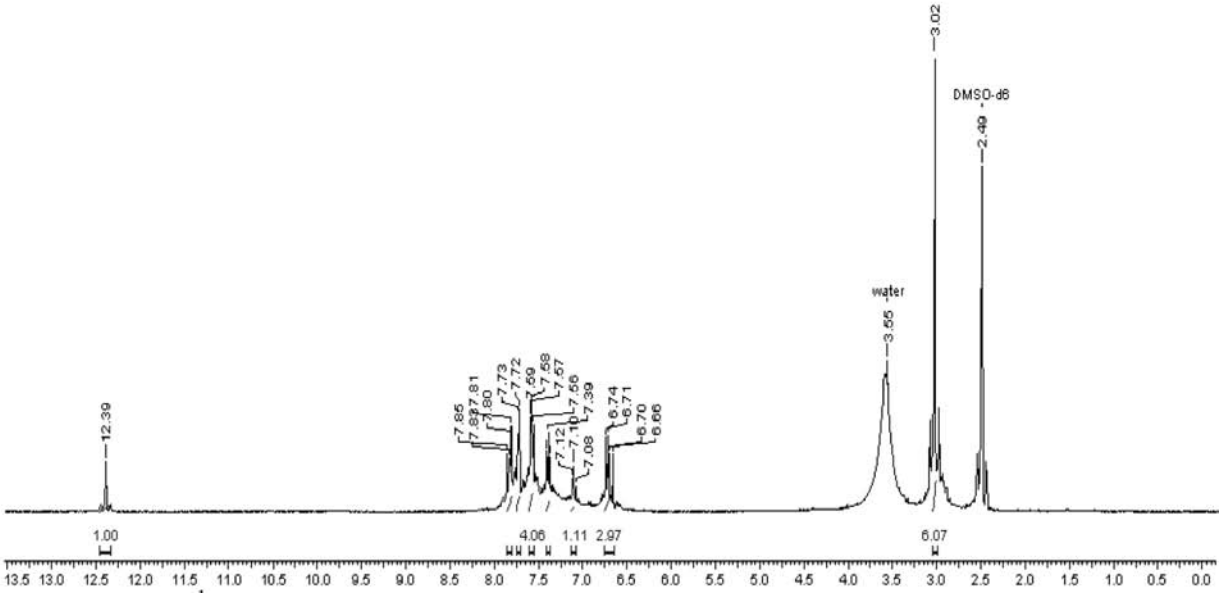

Figure S6. [1]H NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

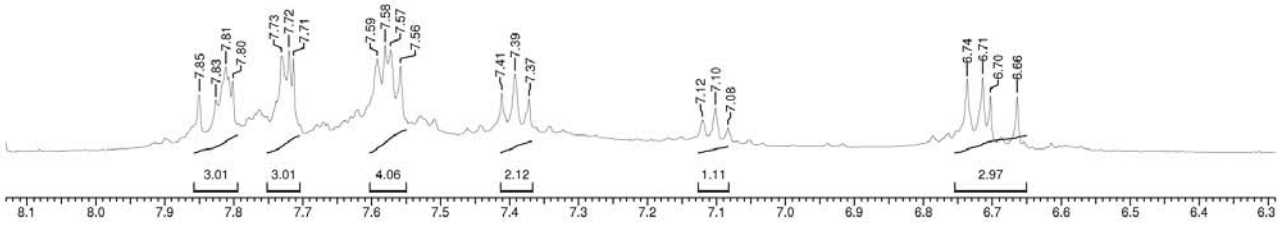

Figure S7. Expansion of ^{1}H NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in DMSO-d_6.

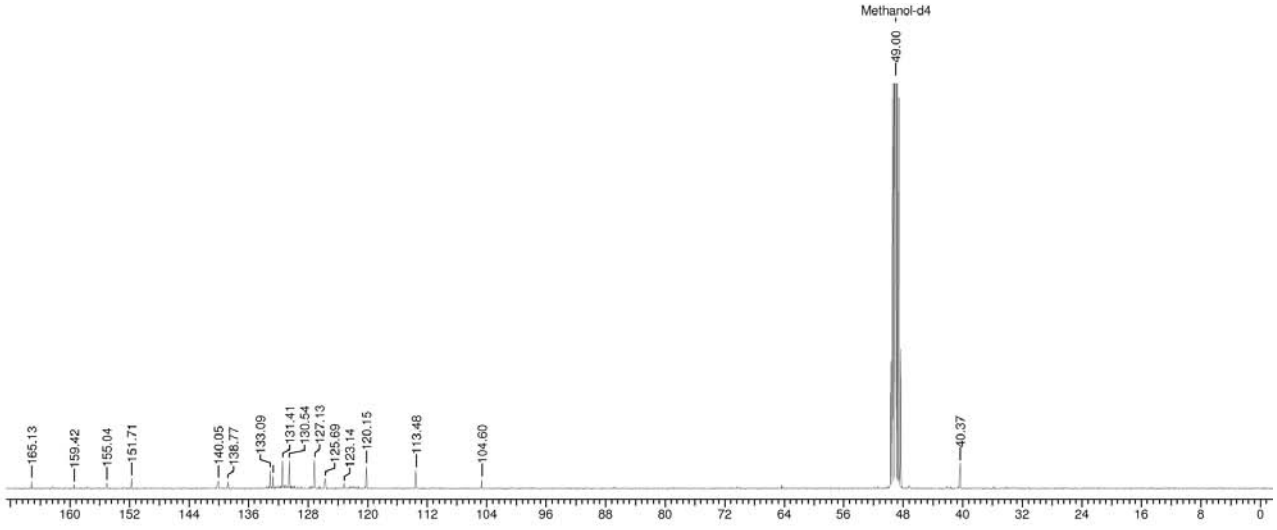

Figure S8. ^{13}C NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in MeOH-d_4.

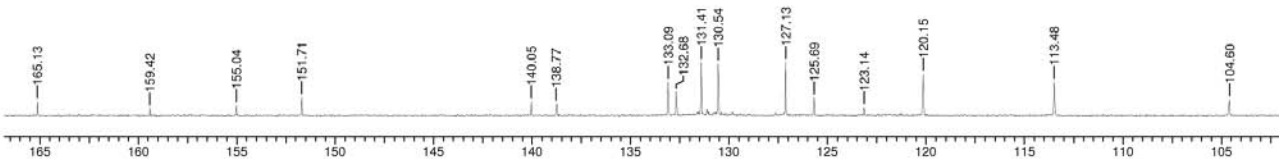

Figure S9. Expansion of ^{13}C NMR spectrum of 4-phenyl-5-(4'-dimethylamino-styryl)-1,3,4-thiadiazolium-2-phenylamine chloride (**8**) in MeOH-d_4.