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Supplementary Materials

Exploring 2-Tetradecanoylimino-3-aryl-4-methyl-1, 3-thiazolines derivatives as Alkaline Phosphatase Inhibitors: Biochemical Evaluation and Computational Analysis

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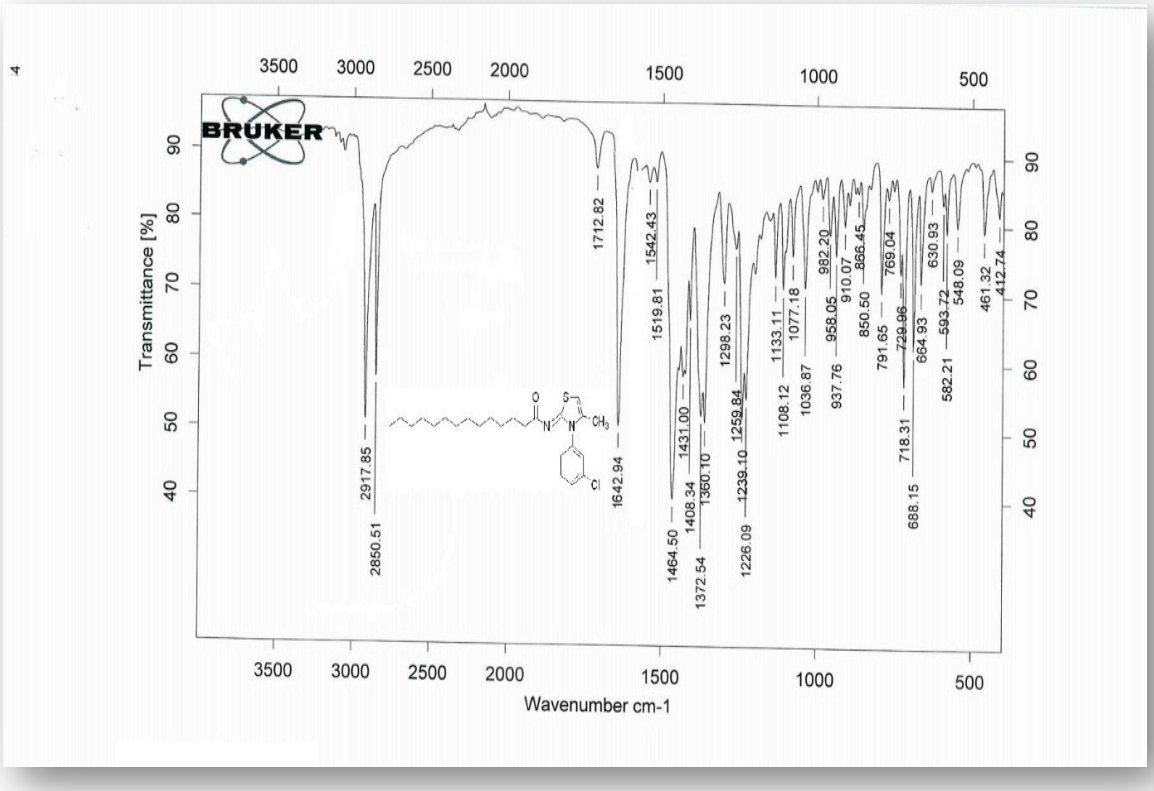

Figure S1. showing IR Spectra 2f.

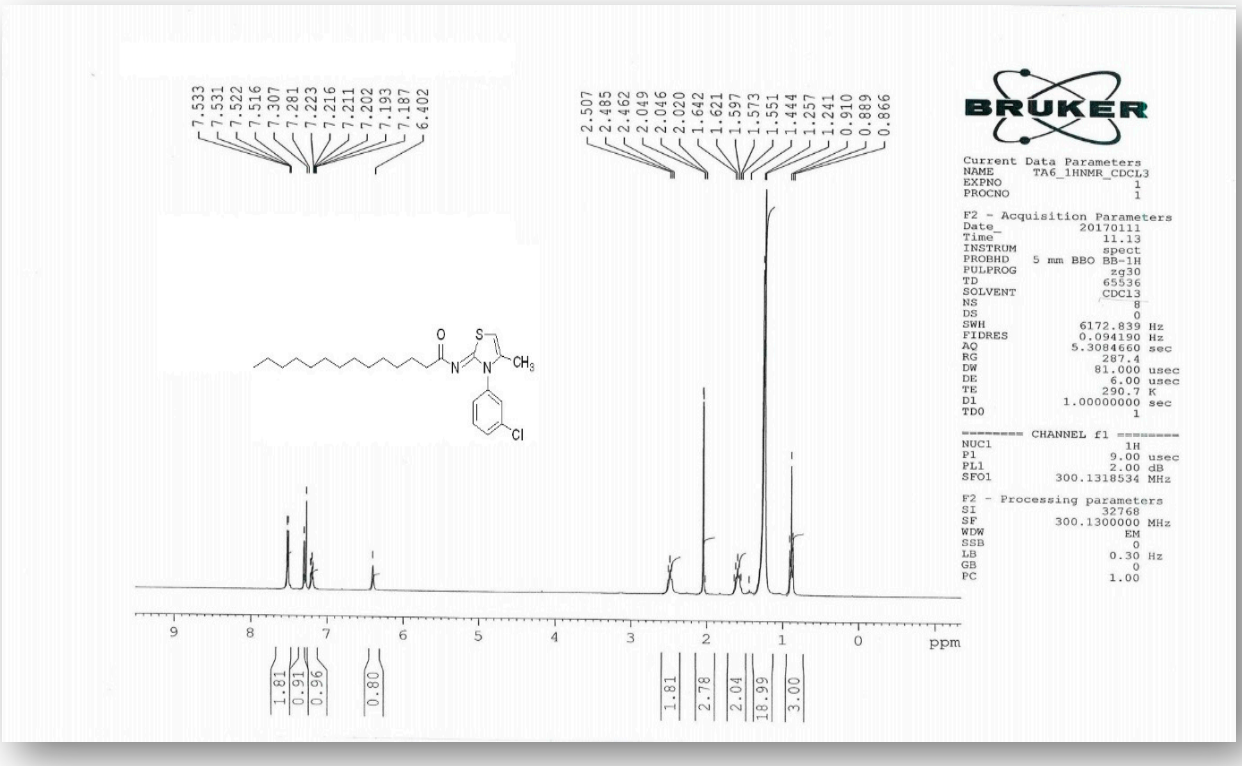

Figure S2. showing Proton NMR spectra 2f.

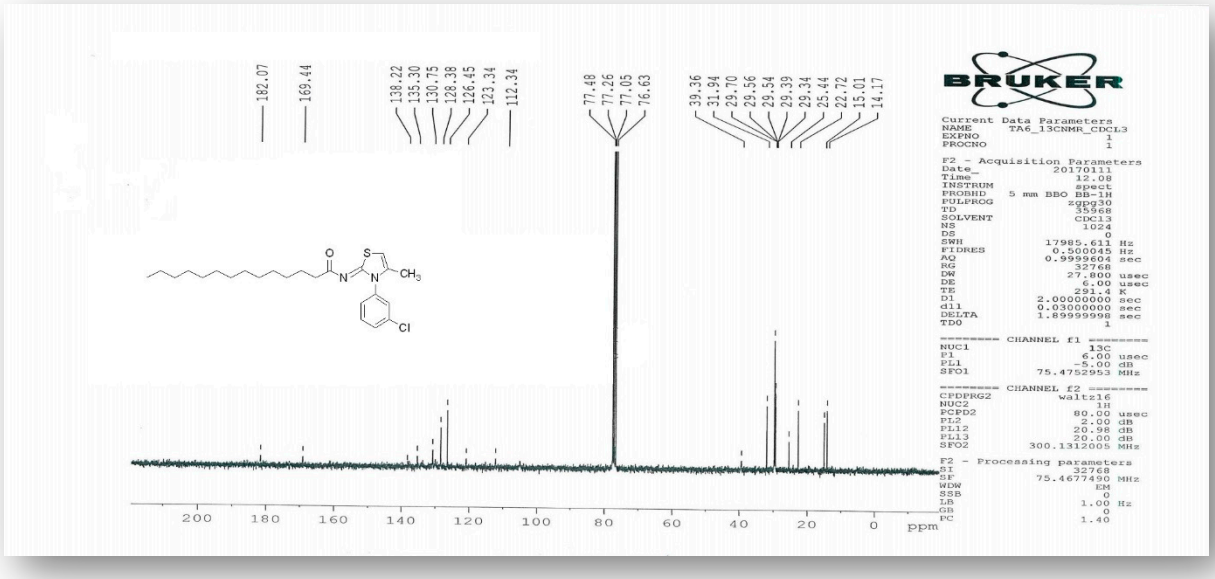

Figure S3. showing ^{13}C NMR spectra 2f.

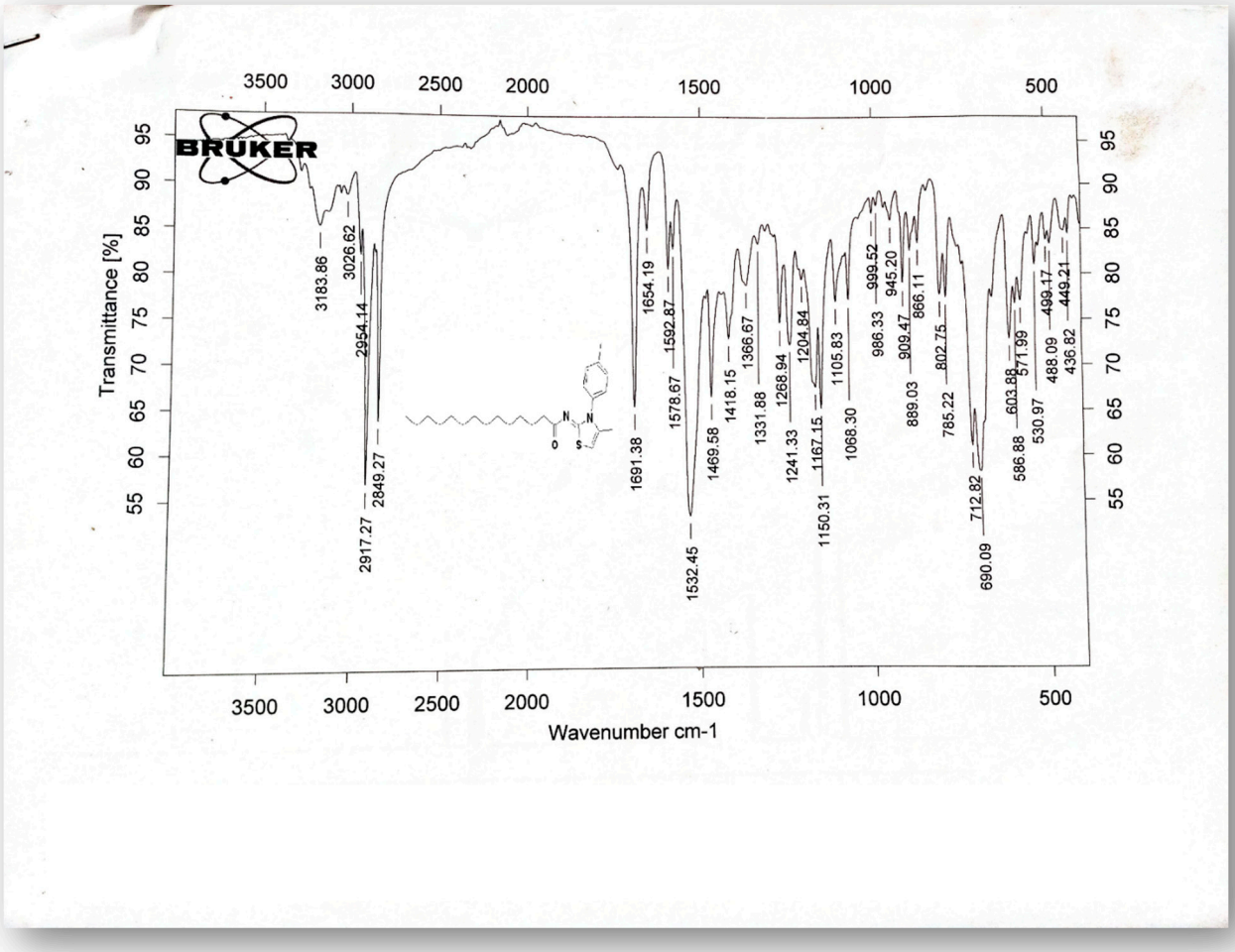

Figure S4. showing IR Spectra 2k.

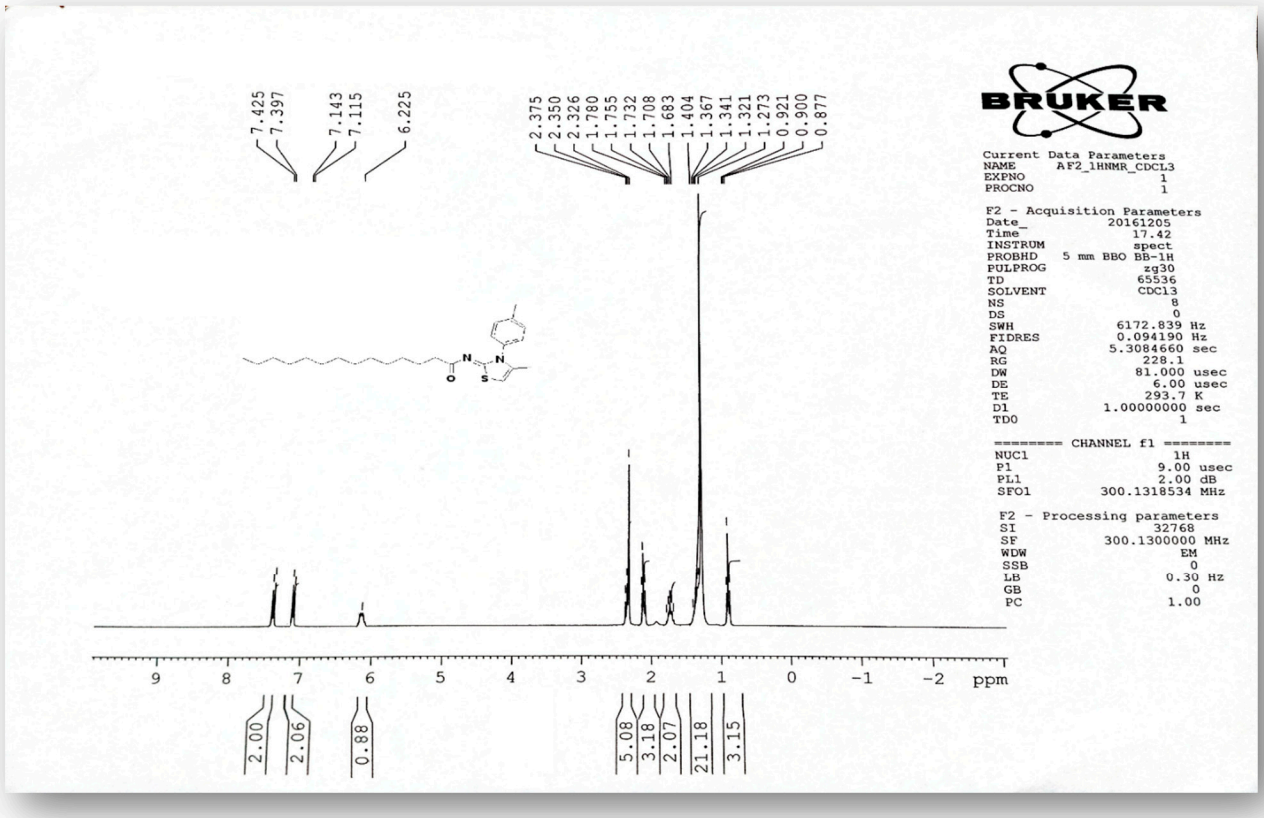

Figure S5. showing Proton NMR spectra 2k.

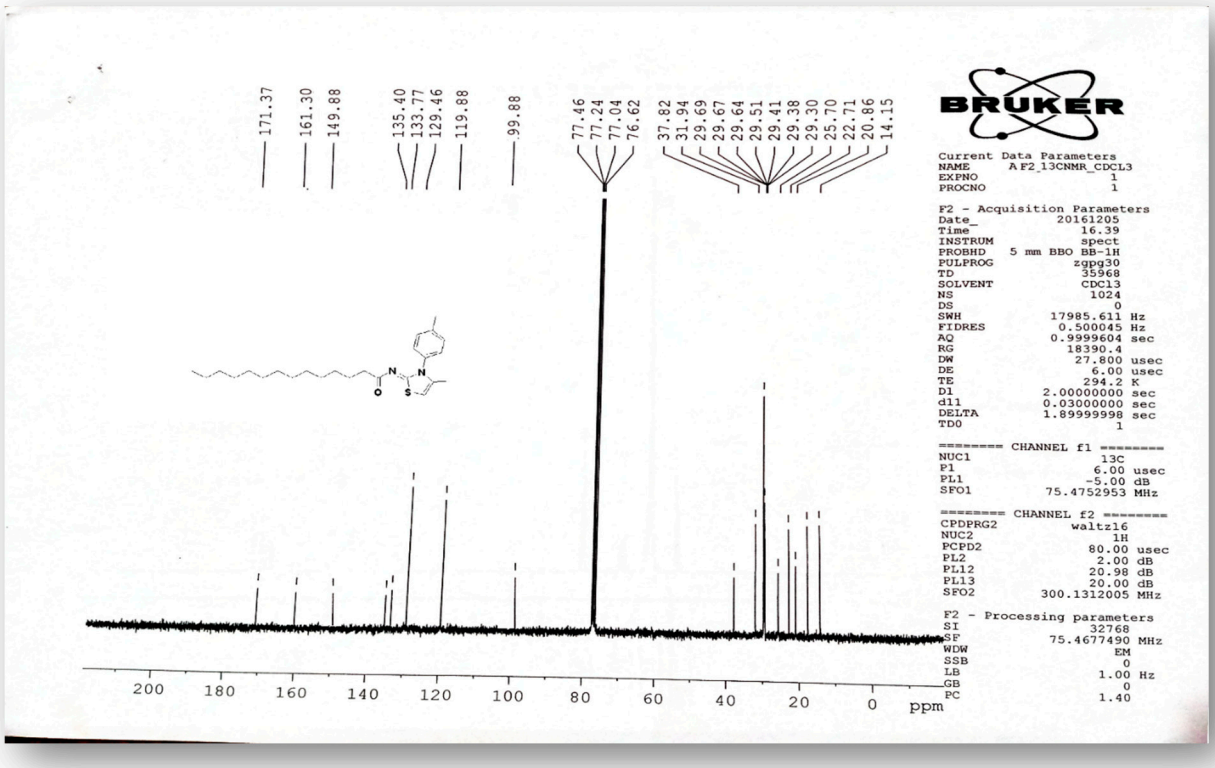

Figure S6. showing ^{13}C NMR spectra 2k.

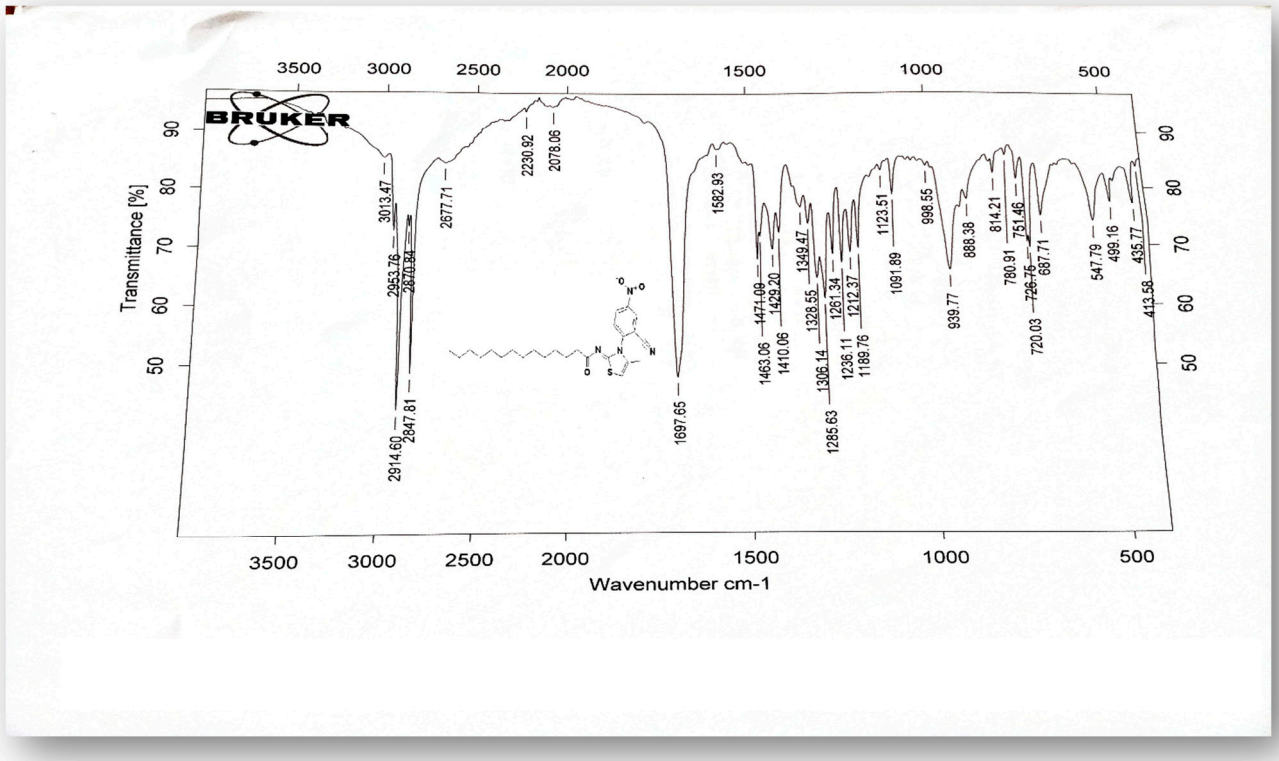

Figure S7. showing IR Spectra 2a.

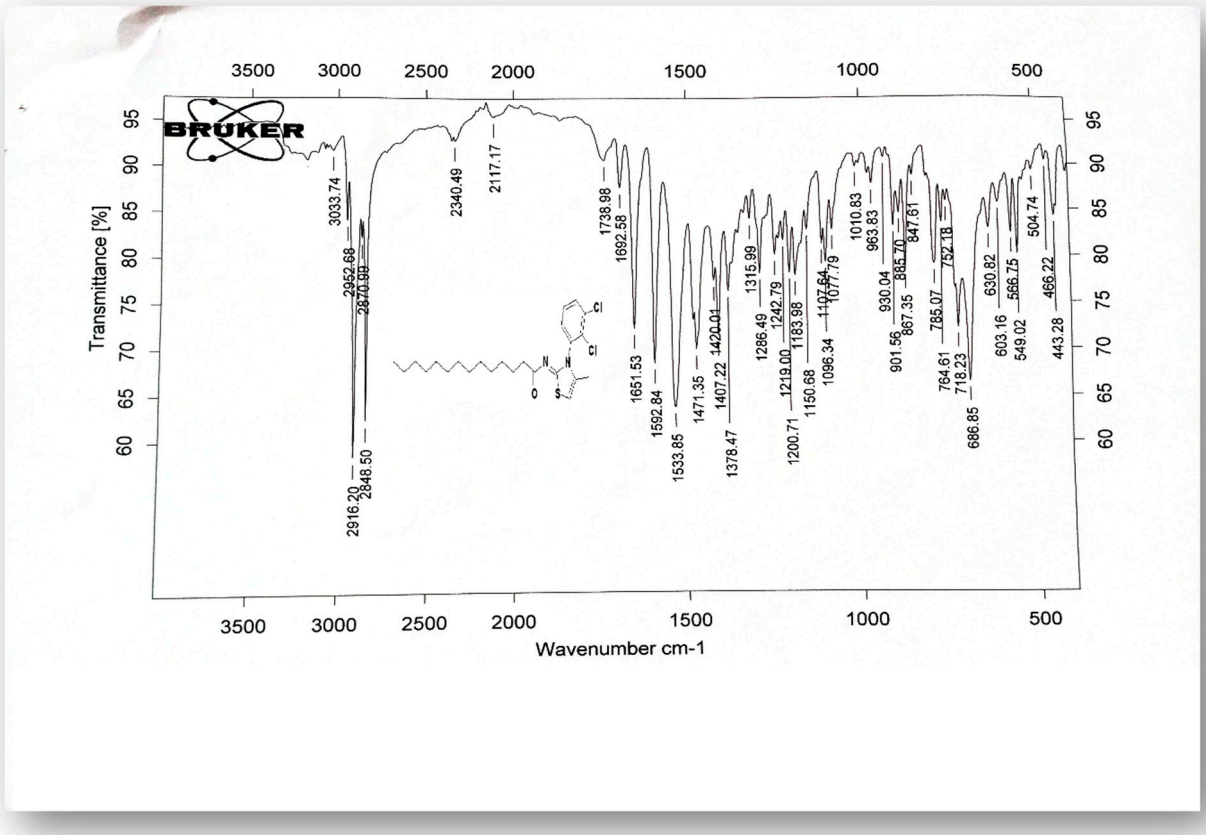

Figure S8. showing IR Spectra 2c.

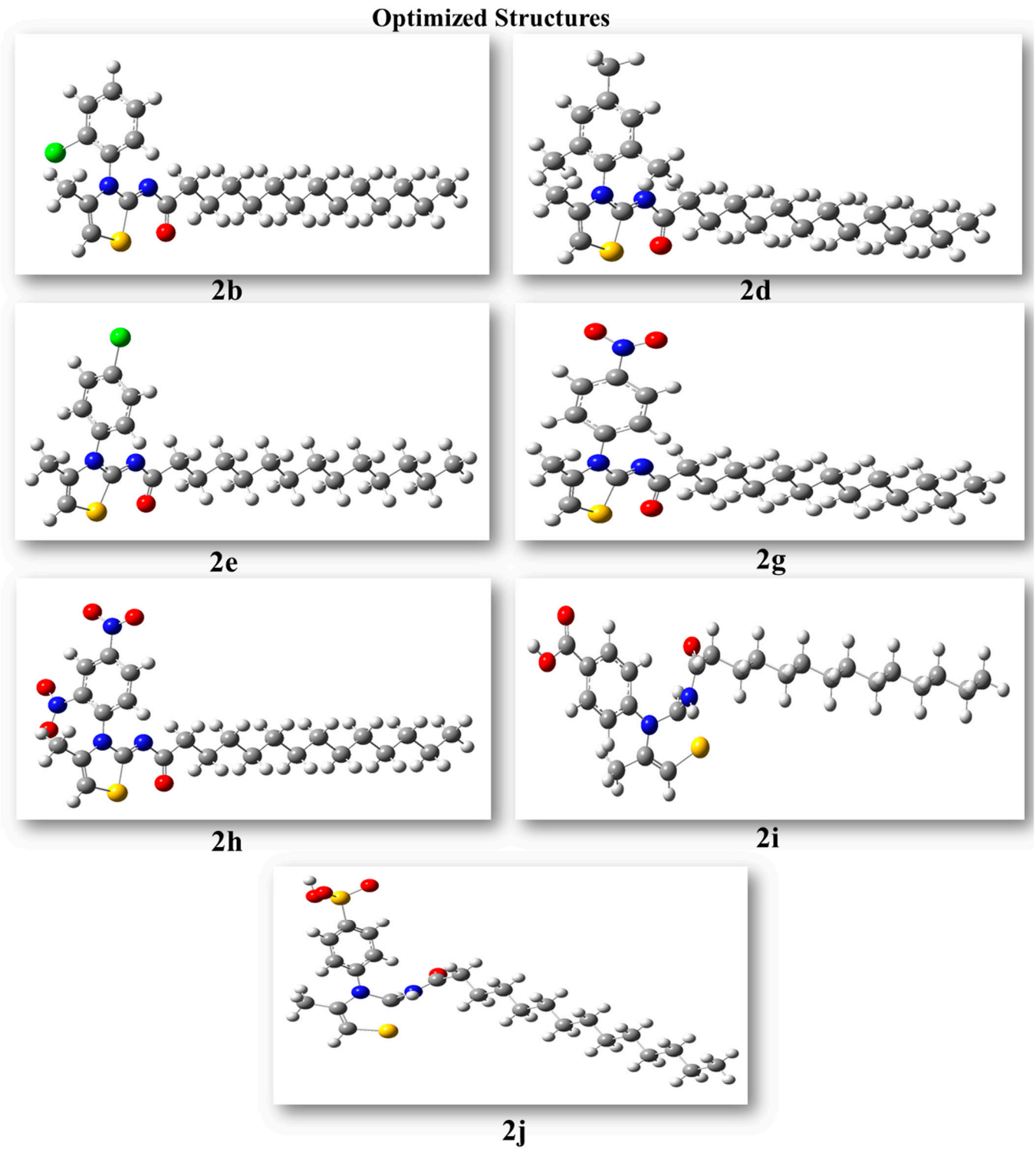

Figure S9. showing the optimized structures.

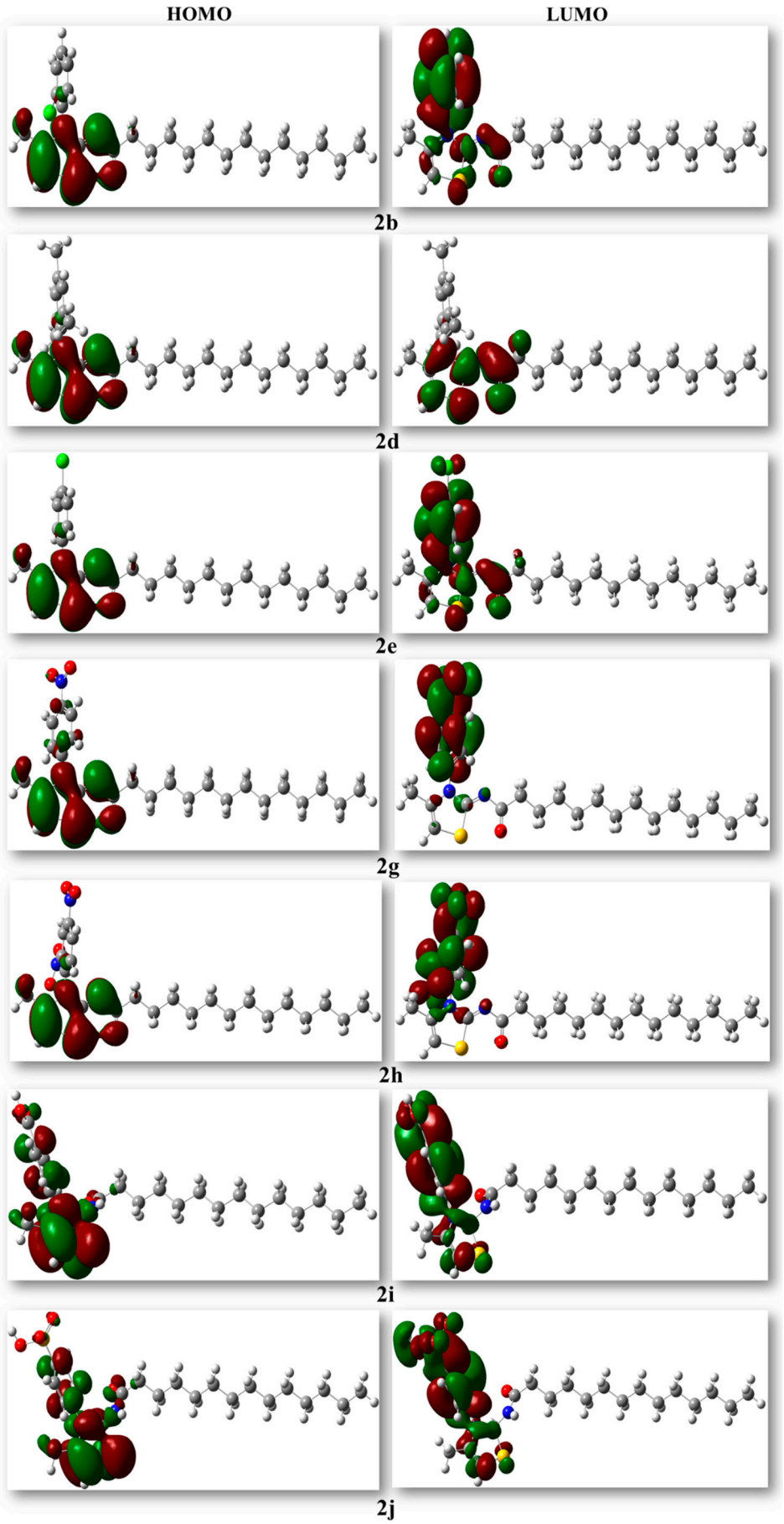

Figure S10. showing HOMO LUMO orbitals of synthesized derivatives.

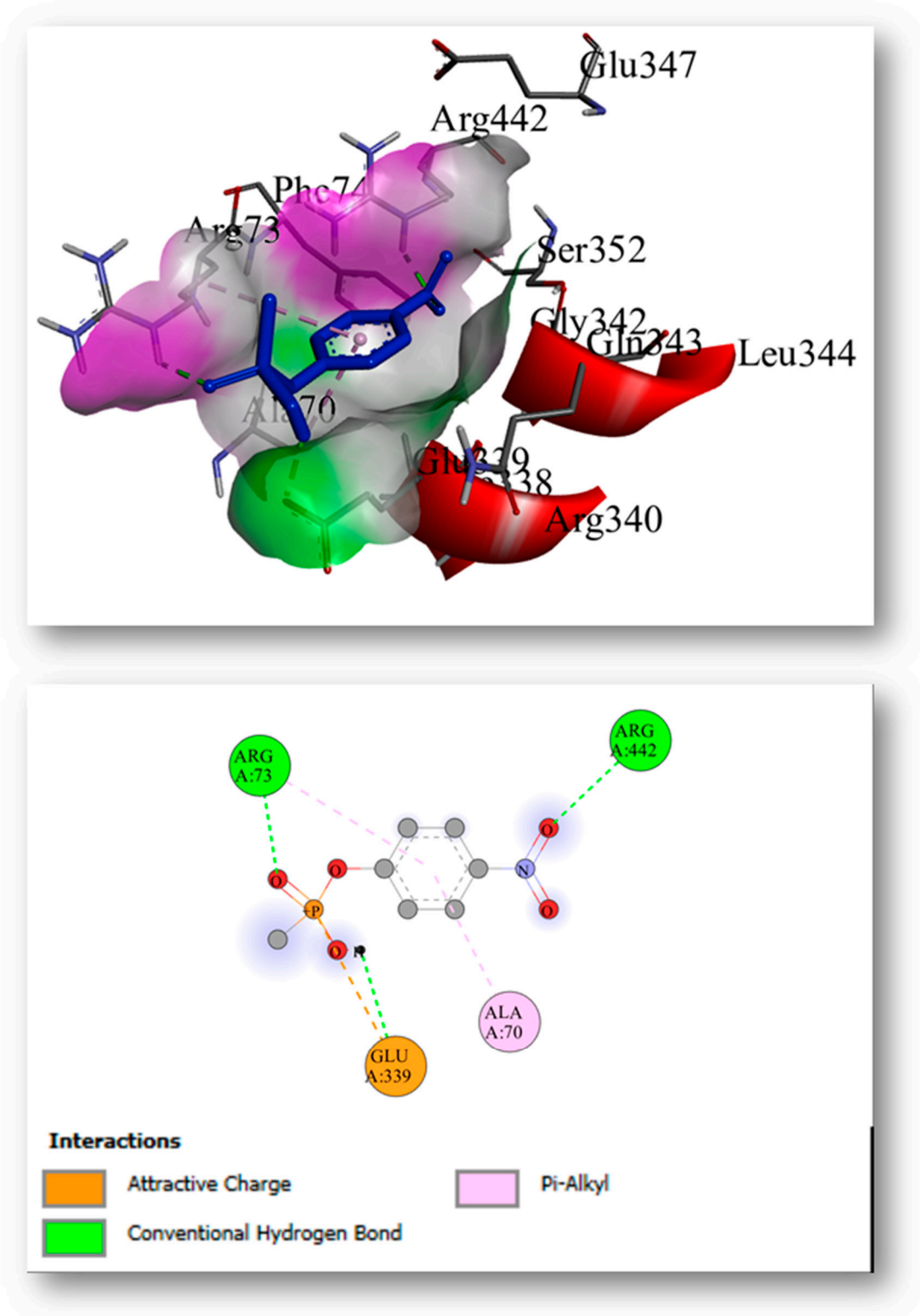

Figure S11. showing 2D and 3D interaction of Alkaline Phaosphatase with reference ligand Para Nitrophenyl Phosphonate.

Characterization Data of Synthesized Compound (2a-2k)

2-Tetradecanoylimino-3-(2-cyano-4-nitrophenyl)-4-methyl-1,3-thiazoline (2a)

Brown solid, Yield; 73%, m.p: 164oC, Rf = 0.39 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 3013.4 (Sp^2 CH stretching) 2953.7 (Sp^3 CH stretching) 1697.6 (C=O), 1582.9 (Ar-C=C), 1471.0 (C=N), 1261.3 (C-S), 1189.7 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 8.19 (1H, d, Ar-H, J=6.5 Hz), 7.63 (d, 1H, Ar-H, J=3.9Hz), 7.43 (d, 1H, Ar-H, J= 4.1Hz), 6.48 (s, 1 H, CH=C), 2.31 (t, 2H, J=3.2Hz), 2.14 (quint, 2H), 2.05 (quint, 2H), 2.03 (quint, 2H),1.87 (quint, 2H), 1.81 (quint, 2H), 1.78 (quint, 2H), 1.63 (quint, 2H), 1.50 (quint, 2H), 1.42 (quint, 2H), 1.33 (quint, 2H), 1.26 (sex, 2H), 1.05 (s, 3H), 0.95 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 177.3(C=O), 168.3, 138.6, 136.5, 134.6, 132.7, 131.3, 130.4 129.8, 118.3 (Ar-C), 117.3, 32.5, 31.2, 28.6, 27.4, 25.8, 23.7, 20.3, 19.8, 17.7, 16.3, 15.6, 13.2, 12.4, 11.3 Anal. Calcd. For C25H34N4O3S: C, 63.59; H, 7.38; N, 11.74; S, 6.71 found: C, 63.27; H, 7.17; N, 11.63; S, 5.50.

2-Tetradecanoylimino-3-(2-chlorophenyl)-4-methyl-1,3-thiazoline (2b)

Light blue solid, Yield; 76%, m.p: 163oC, Rf = 0.43 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1654.9 (C=O), 1572.4 (Ar-C=C), 1464.3 (C=N), 1249.1 (C-S), 1153.2 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 7.73 (1H, d, Ar-H, J=7.2 Hz), 7.63 (d, 1H, Ar-H, J=5.53Hz), 7.55 (d, 1H, Ar-H, J= 7.25Hz), 7.30 (d, 1H, Ar-H, J= 5.53Hz), 6.63 (s, 1 H, CH=C), 2.31 (t, 2H, J=3.1Hz), 2.28 (quint, 2H), 2.13 (quint, 2H), 2.02 (quint, 2H),1.89 (quint, 2H), 1.77 (quint, 2H), 1.69 (quint, 2H), 1.68(quint, 2H), 1.59 (quint, 2H), 1.46 (quint, 2H), 1.39 (quint, 2H), 1.32 (sex, 2H), 1.19 (s, 3H), 0.98 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 176.7(C=O), 164.3, 137.5, 136.5, 135.4, 133.5, 131.3, 130.7, 128.3, 118.8 (Ar-C), 34.6, 32.1, 27.6, 25.4, 23.7, 21.8, 19.7, 18.1, 16.7, 15.1, 14.6, 13.9, 12.4, 11.8 Anal. Calcd. For C24H35ClN2OS: C, 66.02; H, 7.98; N, 6.34; S, 7.26 found: C, 65.93; H, 7.72; N, 6.23; S, 7.14

2-Tetradecanoylimino-3-(2,3-dichlorophenyl)-4-methyl-1,3-thiazoline (2c)

Light yellow crystalline solid, Yield; 71%, m.p: 195oC, Rf = 0.45 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 3033.7 (Sp^2 CH stretching) 2916.2 (Sp^3 CH stretching) 1692 (C=O), 1592 (Ar-C=C), 1471 (C=N), 1286 (C-S), 1183 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 7.31-6.26 (3H, m, Ar-H), 6.73 (s, 1 H, CH=C), 2.25 (t, 2H, J=3Hz), 2.16 (quint, 2H), 2.10 (quint, 2H), 1.96 (quint, 2H),1.87 (quint, 2H), 1.75 (quint, 2H), 1.64 (quint, 2H), 1.59(quint, 2H), 1.54 (quint, 2H), 1.48 (quint, 2H), 1.38 (quint, 2H), 1.27 (sex, 2H), 1.16 (s, 3H), 1.08 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 175.7(C=O), 167.5, 138.5, 137.5, 136.6, 135.8, 134.6, 129.7, 126.6, 117.9 (Ar-C), 34.6, 33.6, 29.3, 26.6, 24.7, 23.8, 20.4, 19.5, 18.4, 17.1, 15.3, 13.6, 12.4, 11.8 Anal. Calcd. For C24H34Cl2N2OS: C, 61.30; H, 7.15; N, 5.86; S, 6.73 found: C, 61.20; H, 7.07; N, 5.63; S, 6.54.

2-Tetradecanoylimino-3- mesityl -4-methyl-1,3-thiazoline (2d)

Black solid, Yield; 77%, m.p: 174oC, Rf = 0.36 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1645.6 (C=O), 1562.7 (Ar-C=C), 1434.5 (C=N), 1269.7 (C-S), 1143.2 (C-N); 1H NMR (DMSO-d6, 300MHz,); δ (ppm) 7.53 (2H, s, Ar-H), 6.68 (s, 1 H, CH=C), 3.20 (s, 9H, -CH3), 2.32 (t, 2H, J=2Hz), 2.28 (quint, 2H), 2.16 (quint, 2H), 1.97 (quint, 2H), 1.81 (quint, 2H), 1.76 (quint, 2H), 1.67 (quint, 2H), 1.61(quint, 2H), 1.57 (quint, 2H), 1.44 (quint, 2H), 1.32 (quint, 2H), 1.21 (sex, 2H), 1.19 (s, 3H), 1.13 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 176.7(C=O),

169.6, 138.6, 138.3, 135.6, 133.3, 130.6, 128.7, 128.2, 117.3 (Ar-C), 35.9, 34.6, 31.3, 29.9, 27.7, 26.7, 24.2, 22.5, 20.7, 18.4, 17.8, 16.4, 15.4, 14.6, 13.3, 12.4, 11.3 Anal. Calcd. For C27H42N2OS: C, 73.12; H, 9.35; N, 6.21; S, 7.15 found: C, 72.97; H, 9.24; N, 6.13; S, 7.02.

2-Tetradecanoylimino-3-(4-chlorophenyl)-4-methyl-1,3-thiazoline (2e)

Light brown solid, Yield; 81%, m.p: 187oC, Rf = 0.41 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1646.9 (C=O), 1569.4 (Ar-C=C), 1484.5 (C=N), 1253.1 (C-S), 1154.2 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 7.76 (d, 2H, Ar-H, J=8.35 Hz), 7.43 (d, 2H, Ar-H, J=8.03Hz), 6.83 (s, 1 H, CH=C), 2.21 (t, 2H, J=3.0Hz), 2.19 (quint, 2H), 2.17 (quint, 2H), 2.08 (quint, 2H), 1.97 (quint, 2H), 1.85 (quint, 2H), 1.79 (quint, 2H), 1.67 (quint, 2H), 1.61 (quint, 2H), 1.45 (quint, 2H), 1.36 (quint, 2H), 1.23 (sex, 2H), 1.13 (s, 3H), 1.09 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 177.7(C=O), 166.8, 136.5, 135.5, 133.4, 131.9, 131.3, 128.7, 128.2, 117.2 (Ar-C), 34.6, 32.1, 29.6, 27.4, 25.7, 23.8, 21.7, 19.1, 17.7, 16.9, 14.6, 13.7, 12.8, 11.6 Anal. Calcd. For C24H35ClN2OS: C, 66.16; H, 8.01; N, 6.34; S, 7.21 found: C, 66.05; H, 7.91; N, 6.23; S, 7.10.

2-Tetradecanoylimino-3-(3-chlorophenyl)-4-methyl-1,3-thiazoline (2f)

Light yellow solid, Yield; 85%, m.p: 195oC, Rf = 0.34 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 3020 at C-H aromatic 2917 at C-H thiazoline, 1642.9 (C=O), 1542.4 (Ar-C=C), 1464.5 (C=N), 1239.1 (C-S), 1133.2 (C-N); 1H NMR ($CDCl_3$, 300 MHz,); δ (ppm) 7.53 (dd, 1H, J = 7.5, 7.2 Ar-H), 7.51 (d, 1H, J =7.5, Ar-H), 7.30 (d, 1H, J = 7.1, Ar-H), 7.21 (d, 1H, J =7.2, Ar-H), 6.40 (s, 1 H, CH=C), 2.50 (t, 2H, J=3.0Hz), 2.40 (quint, 2H), 2.17 (quint, 2H), 2.09 (quint, 2H),1.95 (quint, 2H), 1.83 (quint, 2H), 1.75 (quint, 2H), 1.63 (quint, 2H), 1.54 (quint, 2H), 1.51 (quint, 2H), 1.41 (quint, 2H), 1.11 (sex, 2H), 0.88 (s, 3H), 0.86 (t, 3H) ; 13C NMR (75 MHz $CDCl_3$) δ (ppm) 182.1(C=O), 169.4, 138.1, 135.71, 130.3, 128, 126.5, 124.3, 123.4, 112.4, (Ar-C), 39.4, 39.1, 29.6, 27.3, 25.6, 24.7, 23.8, 21.5, 19.7, 18.3, 17.6, 16.9, 15.0, 14.2, Anal. Calcd. For C24H35ClN2OS: C, 66.13; H, 8.01; N, 6.31; S, 7.11 found: C, 65.97; H, 7.91; N, 6.23; S, 6.95.

2-Tetradecanoylimino-3-(4-nitrophenyl)-4-methyl-1,3-thiazoline (2g)

Black solid, Yield; 79%, m.p: 174oC, Rf = 0.34 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1682.6 (C=O), 1553.3 (Ar-C=C), 1463.7 (C=N), 1236.3 (C-S), 1136.9 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 7.65 (d, 2H, Ar-H, J=8.01 Hz), 7.43 (d, 2H, Ar-H, J=7.43Hz), 6.38 (s, 1 H, CH=C), 2.23 (t, 2H, J=3Hz), 2.16 (quint, 2H), 2.13 (quint, 2H), 2.08 (quint, 2H),1.94 (quint, 2H), 1.84 (quint, 2H), 1.71 (quint, 2H), 1.63 (quint, 2H), 1.58 (quint, 2H), 1.44 (quint, 2H), 1.35 (quint, 2H), 1.28 (sex, 2H), 1.16 (s, 3H), 1.08 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 176.7(C=O), 168.3, 138.5, 137.5, 135.8, 133.4, 132.2, 130.8, 129.2, 118.1 (Ar-C), 35.6, 34.1, 32.4, 29.4, 28.7, 25.8, 23.7, 20.5, 18.7, 17.9, 15.5, 14.6, 12.3, 11.9 Anal. Calcd. For C24H35N3O3S: C, 64.53; H, 7.76; N, 9.31; S, 7.11 found: C, 64.37; H, 7.65; N, 9.23; S, 7.01.

2-Tetradecanoylimino-3-(2,4-dinitrophenyl)-4-methyl-1,3-thiazoline (2h)

Dark brown solid, Yield; 76%, m.p: 165oC, Rf = 0.37 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1647.2 (C=O), 1537.8 (Ar-C=C), 1473.9 (C=N), 1272.1 (C-S), 1173.6 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 8.63 (1H, d, Ar-H, J=6.8 Hz), 8.32 (d, 1H, Ar-H, J=4.5Hz), 7.63 (d, 1H, Ar-H, J= 4.2Hz), 6.37 (s, 1 H, CH=C), 2.36 (t, 2H, J=3Hz), 2.30 (quint, 2H), 2.16 (quint, 2H), 2.03 (quint, 2H),1.95 (quint, 2H), 1.62 (quint, 2H), 1.57 (quint, 2H), 1.52 (quint,

2H), 1.45 (quint, 2H), 1.38 (quint, 2H), 1.31 (quint, 2H), 1.23 (sex, 2H), 1.13 (s, 3H), 1.06 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 176.3 (C=O), 168.4, 138.9, 136.5, 135.3, 133.7, 132.6, 131.4, 127.9, 117.4 (Ar-C), 35.5, 33.2, 29.7, 27.8, 25.9, 24.7, 21.3, 19.7, 18.3, 16.9, 14.6, 12.7, 11.9, 11.6 Anal. Calcd. For C24H34N4O5S: C, 58.59; H, 6.83; N, 11.24; S, 6.34 found: C, 58.47; H, 6.67; N, 11.03; S, 6.24.

4-(4-Methyl-2-tetradecanamidothiazol-3(2H)-yl)benzoic acid (2i)

Light brown solid, Yield; 80%, m.p: 164oC, Rf = 0.33 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1672.8 (C=O), 1553.7 (Ar-C=C), 1457.5 (C=N), 1237.7 (C-S), 1154.2 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 11.89 (s, 1H, COOH), 7.85 (d, 2H, Ar-H, J=8.25 Hz), 7.43 (d, 2H, Ar-H, J=7.26Hz), 6.52 (s, 1 H, CH=C), 2.23 (t, 2H, J=3.0Hz), 2.12 (quint, 2H), 2.08 (quint, 2H), 1.98 (quint, 2H),1.86 (quint, 2H), 1.74 (quint, 2H), 1.69 (quint, 2H), 1.64 (quint, 2H), 1.57 (quint, 2H), 1.44 (quint, 2H), 1.32 (quint, 2H), 1.25 (sex, 2H), 1.15 (s, 3H), 1.09 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 178.7(C=O), 172.3, 169.7, 138.5, 137.5, 135.9, 134.6, 133.1, 129.7, 129.1, 117.7 (Ar-C), 33.6, 32.1, 29.5, 26.4, 25.7, 24.8, 21.7, 19.1, 17.7, 15.9, 14.6, 13.1, 12.8, 11.3 Anal. Calcd. For C25H36N2O3S: C, 67.43; H, 8.06; N, 6.20; S, 7.11 found: C, 67.33; H, 7.91; N, 6.13; S, 7.01.

4-(4-Methyl-2-tetradecanamidothiazol-3(2H)-yl)benzenesulfonic acid (2j)

Black solid, Yield; 87%, m.p: 166oC, Rf = 0.43 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 1682.1 (C=O), 1573.6 (Ar-C=C), 1434.8 (C=N), 1242.6 (C-S), 1163.4 (C-N); 1H NMR (DMSO-d6, 300 MHz,); δ (ppm) 7.76 (d, 2H, Ar-H, J=7.52 Hz), 7.58 (d, 2H, Ar-H, J=7.25Hz), 6.64 (s, 1 H, CH=C), 3.01 (s, 1H, SO3H), 2.22 (t, 2H, J=2.5Hz), 2.19 (quint, 2H), 2.10 (quint, 2H), 1.89 (quint, 2H),1.74 (quint, 2H), 1.65 (quint, 2H), 1.57 (quint, 2H), 1.52 (quint, 2H), 1.46 (quint, 2H), 1.41 (quint, 2H), 1.32 (quint, 2H), 1.24 (sex, 2H), 1.18 (s, 3H), 1.07 (t, 3H); 13C NMR (75 MHz DMSO-d6) δ (ppm) 177.8(C=O), 169.4, 138.5, 137.9, 136.6, 135.4, 133.8, 130.7, 129.1 117.6 (Ar-C), 34.6, 33.4, 31.6, 28.4, 26.7, 24.8, 22.7, 20.1, 18.7, 16.9, 14.6, 13.1, 12.6, 11.9, Anal. Calcd. For C24H36N2O4S2: C, 59.79; H, 7.45; N, 5.72; S, 13.21 found: C, 59.57; H, 7.31; N, 5.63; S, 13.10.

2-Tetradecanoylimino-3-p-tolyl-4-methyl-1,3-thiazoline (2k)

Yellow solid, Yield; 75%, m.p: 146oC, Rf = 0.45 (n-hexane: ethyl acetate, 1:1), FTIR υ (cm-1) 3026 (Sp^2 CH stretching) 2917 (Sp^3 CH stretching) 1691 (C=O), 1532 (Ar-C=C), 1418 (C=N), 1241 (C-S), 1167 (C-N); 1H NMR ($CDCl_3$ 300 MHz,); δ (ppm) 7.42 (d, 2H, Ar-H, J=7.5 Hz), 7.14 (d, 2H, Ar-H, J=7.2Hz), 6.22 (s, 1 H, CH=C), 2.37 (s, 1H, CH3), 2.35 (t, 2H, J=3Hz), 2.32 (quint, 2H), 1.78 (quint, 2H), 1.75 (quint, 2H),1.73 (quint, 2H), 1.70 (quint, 2H), 1.68 (quint, 2H), 1.40 (quint, 2H), 1.36 (quint, 2H), 1.34 (quint, 2H), 1.32 (quint, 2H), 1.27 (sex, 2H), 0.92 (s, 3H), 0.87 (t, 3H); 13C NMR (75 MHz $CDCl_3$) δ (ppm) 171.3(C=O), 161.1, 149.8, 135.4, 133.7, 129.4, 119.8, 99.8, (Ar-C), 37.8, 31.9, 29.6, 29.4, 29.3, 25.7, 22.7, 20.8, 14.1, Anal. Calcd. For C25H38N2OS: C, 72.32; H, 9.14; N, 6.65; S, 7.53 found: C, 72.23; H, 9.03; N, 6.53; S, 7.33.