PREPARATION OF NEW THIOHYDROXAMIC ACID DERIVATIVES: SYNTHESIS OF SUBSTITUTED 1-HYDROXY-1,2-DIHYDROIMIDAZOLE-2-THIONES

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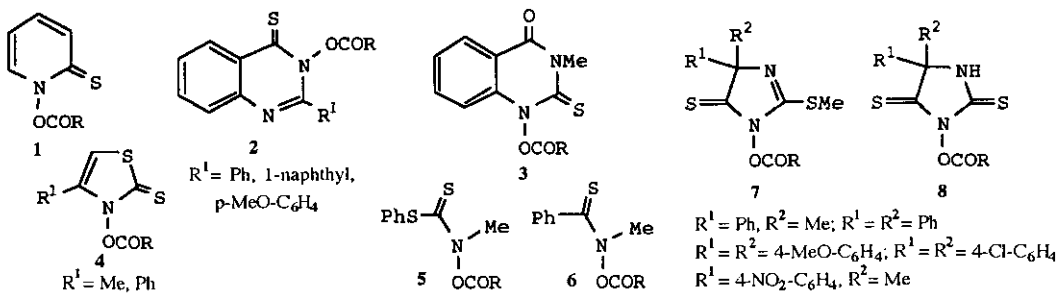
Abstract- A general method for the synthesis of the title compounds is reported. The *N*-phenacylarylamines (**11**), prepared from the corresponding phenacyl bromides (**9**) and arylamines (**10**), give the thiono (or dithio) carbamates (**12**) on treatment with phenoxythionocarbonyl or thiophenoxythionocarbonyl chlorides and potassium carbonate in dichloromethane. The desired thiohydroxamic acids (**13**) are obtained by heating compounds (**12**) with hydroxylamine hydrochloride in pyridine/ethanol.

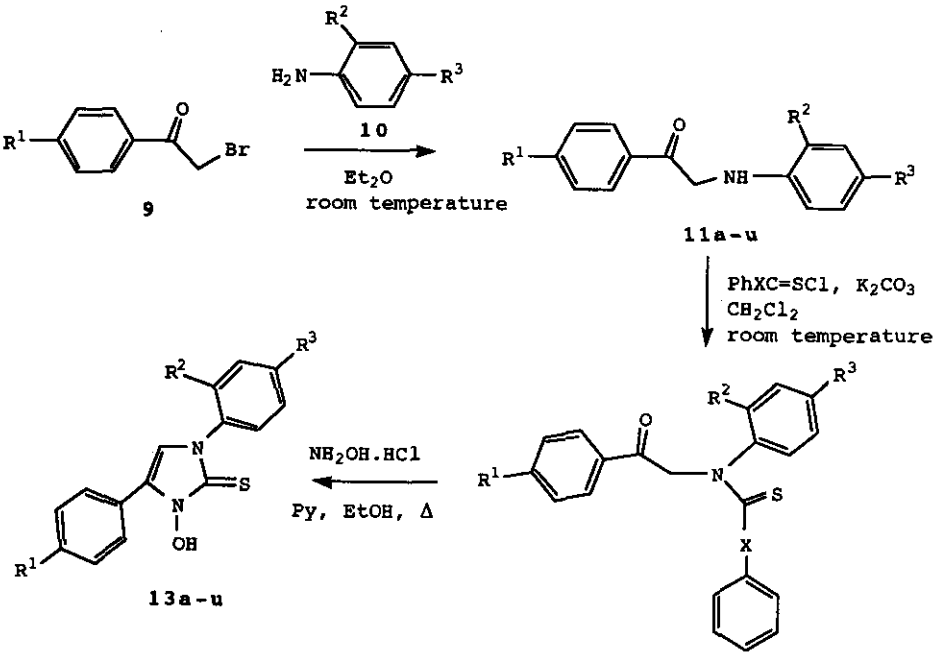
Since a decade the acyl derivatives of *N*-hydroxy-2-thiopyridone (**1**) have been widely used for the mild generation of carbon centered radicals under mild conditions.[2] More recently its application was also extended to the efficient generation of nitrogen[3] and oxygen[4] centered radicals. A number of other thiohydroxamic acids have been prepared (Scheme 1) and the photochemistry of their *O*-acyl derivatives has been investigated.[5-7]



Scheme 1

Dedicated to Professor Alan R. Katritzky on the occasion of his 65th Birthday--with anticipation of many more to come.

Despite their similar radical behavior, the rate of radical chain propagation varies greatly depending on the parent thiohydroxamic acids structure. Some of them such as the acyl derivatives of (**2**)[5] and (**7**)[6] are more light sensitive than the thiopyridone derivative. In contrast the acyl derivatives of (**8**) show a slower rate when photolyzed under identical conditions.[6] Others such as the thiohydroxamic acid derivatives (**3**, **4**, **5** and **6**) require the use of a UV lamp.[7] As a part of our ongoing research on thiohydroxamic acids we describe in the present paper the preparation of novel substituted 1-hydroxy-1,2-dihydroimidazoline-2-thiones. A number of analogs have been synthesized following a three step synthesis starting from the commercially available substituted phenacyl bromides (**9**) and arylamines (**10**) (Scheme 2).

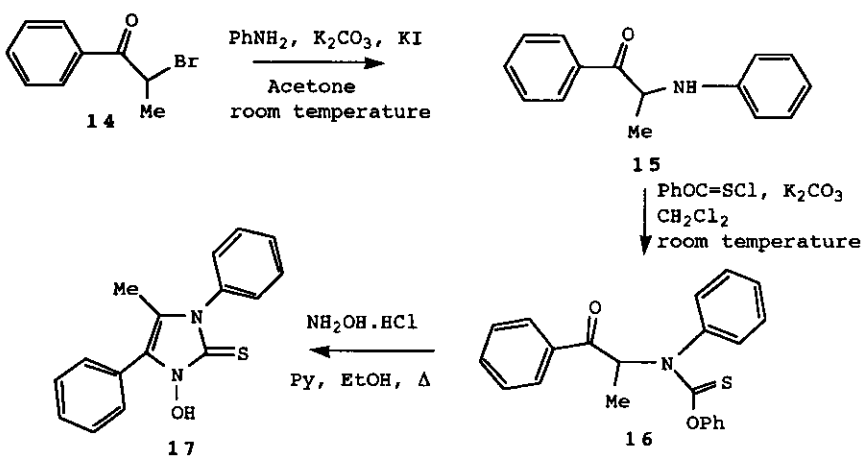


a: R^1=R^2=R^3=H **b**: R^1=R^2=H R^3=Me **c**: R^1=R^2=H R^3=OMe **d**: R^1=R^2=H R^3=OPh
e: R^1=H R^2=R^3=Me **f**: R^1=Me R^2=R^3=H **g**: R^1=R^3=Me R^2=H **h**: R^1=Me R^2=H R^3=OMe
i: R^1=Me R^2=H R^3=OPh **j**: R^1=OMe R^2=R^3=H **k**: R^1=OMe R^2=H R^3=Me **l**: R^1=R^3=OMe R^2=H
m: R^1=OMe R^2=H R^3=OPh **n**: R^1=OMe R^2=R^3=Me **o**: R^1=Br R^2=R^3=H **p**: R^1=Br R^2=H R^3=Me
q: R^1=Br R^2=H R^3=OMe **r**: R^1=Br R^2=H R^3=OPh **s**: R^1=Cl R^2=R^3=H **t**: R^1=Cl R^2=H R^3=Me
u: R^1=Cl R^2=H R^3=OMe

Scheme 2

Several procedures are reported in the literature for the preparation of substituted *N*-phenacylarylamines. Low yields of (**11**) were obtained when the reaction was carried in refluxing ethanol in the presence of potassium carbonate.[8] We found that the best method consists in treating the substituted phenacyl bromide (**9**) with 2 equivalent of the arylamine (**10**) in ether at room temperature.[9] Compounds (**11**) are quite instable but can be stored as crystals for a long period of time. The introduction of the thiocarbonyl moiety was successfully achieved by reacting (**11a-u**) with phenyl chlorothiono (or dithio) formate and potassium carbonate in dichloromethane at room temperature. The use of pyridine instead of K_2CO_3 gave also a good yield of (**12**). However it was difficult in this case to obtain the pure product even after crystallization. The cyclization step leading to the thiohydroxamic acids (**13a-u**) was effected by refluxing (**12a-u**) with hydroxylamine hydrochloride in a mixture of pyridine-ethanol.

We have also investigated the possibility of introducing a methyl substituent at position C-4 of the ring. The *N*-phenacylamine (**15**) was found to be quite difficult to obtain in good yield using the standard procedure described previously. Phenacyl bromide (**14**) was finally converted to the desired (**15**) on treatment with aniline in presence of K_2CO_3 and excess of KI in acetone at room temperature for 24 h (Scheme 3). Treatment of (**15**) with phenyl chlorothionoformate as usual gave (**16**) in 95 % yield. The cyclization step was also more difficult to realize on this derivative and was finally achieved by the use of a large excess of hydroxylamine hydrochloride and pyridine. Nevertheless we were able to get the thiohydroxamic (**17**) in 65% yield.



Scheme 3

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage melting point apparatus and are uncorrected. Ir spectra were recorded on a Perkin Elmer 881 spectrophotometer. ^{1}H Nmr were recorded using a Varian Gemini 200 or a Varian XL 200E (200 MHz) and tetramethylsilane as internal reference. ^{13}C Nmr were determined on Varian Gemini 200 or a Varian XL 200E (50 MHz) spectrometer. Microanalyses were performed by Atlantic Microlab Inc., Norcross, GA. Solvents were used either as purchased or dried and purified by standard methods.

General Procedure for the Preparation of Compounds (11):

A solution of the phenacyl bromide (**9**) (5 mmol) and arylamine (**10**) (10 mmol) in ether (10 ml) was stirred overnight at room temperature. The precipitate was filtered off and the filtrate evaporated under reduced pressure at 20°C. The residue was dissolved in dichloromethane and washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to give the *N*-arylphenacylamine (**11**) which crystallized from CH_2Cl_2/hexanes to form yellow crystals.

11a: Yield 70%, mp 97°C {lit.,[9] 95-97°C}, ^{1}H nmr ($CDCl_3$) δ 4.58 (2H, s), 4.90 (1H, s), 6.70 (3H, m), 7.20 (2H, t), 7.50 (3H, m), 8.00 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 50.3, 113.0, 117.8, 127.7, 128.9, 129.4, 133.8, 134.9, 147.1, 195.0.

11b:Yield 71%, mp 129°C {lit.,[9] 126-128°C}, ir (KBr) 3390, 1674, 1608, 1514 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.20 (3H, s), 4.50 (2H, s), 4.65 (1H, br), 6.60 (2H, d, J= 8.5 Hz), 7.00 (2H, d, J= 8.5 Hz), 7.50 (3H, m), 7.90 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 20.1, 50.5, 113.2 , 127.0, 127.8, 128.9, 129.9, 133.8, 135.1, 145.0, 195.6.

11c: Yield 85%, mp 89-90°C {lit.,[10] 90.5-91.5°C}, ir (CH_2Cl_2) 3397, 1689, 1510, 1216 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 3.75 (3H, s), 4.40 (1H, br), 4.55 (2H, s), 6.65 (2H, d, J= 9.0 Hz), 6.80 (2H, d, J= 9.0 Hz), 7.40-7.60 (3H, m), 8.00 (2H, d, J= 8.1 Hz), ^{13}C nmr ($CDCl_3$) δ 51.2, 55.7, 114.2, 115.0, 127.7, 127.8, 128.8, 133.7, 135.0, 141.4, 152.2, 195.4.

11d:Yield 82%, mp 120-122°C, ir ($CHCl_3$) 3378, 1676, 1591, 1216, 1160, 1060 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 4.57 (2H, s), 4.75 (1H, br), 6.65 (2H, d, J= 8.9 Hz), 6.89-7.05 (5H, m), 7.25 (2H, m), 7.50 (3H, m), 8.00 (2H, J= 8.0 Hz). ^{13}C nmr ($CDCl_3$) δ 50.7, 114.1, 117.2, 121.4, 122.1, 127.9, 129.0, 129.6, 134.0, 135.0, 143.9, 148.2, 159.2, 195.4.

11e: Yield 90%, mp 149°C, ir (CH_2Cl_2) 3417, 3055, 2986, 1689, 1592, 1504, 1420, 1261, 1023 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.25 (3H, s), 2.27 (3H, s), 4.60 (2H, s), 6.00 (1H, bs), 6.70 (1H, d, J= 7.8 Hz), 6.9-7.1 (2H, m), 7.50-7.70 (3H, m), 8.10 (2H, d, J= 8.1 Hz), ^{13}C nmr ($CDCl_3$) δ 17.3, 20.3, 50.6, 110.1, 122.5, 126.5, 127.2, 127.7, 128.8, 131.1, 133.7, 134.9, 142.7, 195.3.

11f: Yield 73%, mp 120°C, ir (KBr) 3390, 1671, 1599 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.40 (3H, s), 4.55 (2H, s), 4.80 (1H, br), 6.70 (3H, m), 7.15-7.35 (4H, m), 7.90 (2H, d, J= 8.1 Hz). ^{13}C nmr ($CDCl_3$) δ 21.6, 50.1, 113.0, 117.7, 127.8, 129.3, 129.5, 132.4, 144.7, 147.1, 194.5.

11g: Yield 81%, mp 130~133°C {lit.,[11] 120-121°C}, ir (CH_2Cl_2) 3404, 3055, 2987, 1686, 1605, 1512, 1420, 1261, 1178 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.30 (3H, s), 2.40 (3H, s), 4.60 (2H, s), 4.70 (1H, bs), 6.70 (2H, d, J= 8.6

Hz), 7.10 (2H, d, J= 8.1 Hz), 7.30 (2H, d, J= 8.6 Hz), 7.90 (2H, d, J= 8.1 Hz), ^{13}C nmr ($CDCl_3$) δ 20.3, 21.6, 50.5, 113.1, 126.9, 127.7, 129.4, 129.7, 132.4, 144.6, 144.8, 194.7.

11h: Yield 89%, mp 93°C, ir (CH_2Cl_2) 3404, 3000, 2953, 2834, 1683, 1605, 1568, 1509, 1459, 1347, 1236, 1178, 1141, 1034 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.40 (3H, s), 3.80 (3H, s), 4.50 (2H, s), 4.70 (1H, bs), 6.70 (2H, d, J= 9.1 Hz), 6.80 (2H, d, J= 9.1 Hz), 7.30 (2H, d, J= 8.1 Hz), 7.90 (2H, d, J= 8.1 Hz), ^{13}C nmr ($CDCl_3$) δ 21.6, 51.0, 55.7, 114.1, 114.9, 127.7, 129.4, 132.4, 141.5, 144.6, 152.2, 194.9.

11i: Yield 89%, mp 138~140°C, ir (CH_2Cl_2) 3402, 3055, 2986, 1685, 1605, 1507, 1486, 1420, 1348, 1262, 1179, 1071 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.40 (3H, s), 4.60 (2H, s), 4.80 (1H, bs), 6.70 (2H, d, J= 9.0 Hz), 6.90-7.10 (5H, m), 7.20-7.40 (4H, m), 7.90 (2H, d, J= 8.3 Hz), ^{13}C nmr ($CDCl_3$) δ 21.7, 50.5, 113.9, 117.0, 121.3, 121.9, 127.8, 129.4, 129.5, 132.3, 143.8, 144.8, 147.7, 159.0, 194.6.

11j: Yield 85%, mp 105-106°C {lit.,[11] 108-109°C}, ir (CH_2Cl_2) 3400, 1679, 1600, 1503, 1350, 1223, 1172 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 3.88 (3H, s), 4.53 (1H, s), 4.63 (1H, br), 6.71 (3H, m), 6.95 (2H, d, J= 8.9 Hz), 7.21 (2H, m), 7.98 (2H, d, J= 8.9 Hz), ^{13}C nmr ($CDCl_3$) δ 49.8, 55.5, 113.0, 117.6, 127.8, 129.3, 130.0, 147.1, 164.0, 193.4.

11k: Yield 58%, mp 119°C, ir (KBr) 3398, 1672, 1592, 1504 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.27 (3H, s), 3.89 (3H, s), 4.54 (2H, s), 4.60 (1H, br), 6.65 (2H, d, J= 8.5 Hz), 7.00 (2H, d, J= 8.5 Hz), 7.05 (2H, d, J= 8.9 Hz), 8.00 (2H, d, J= 8.9 Hz), ^{13}C nmr ($CDCl_3$) δ 20.3, 50.3, 55.5, 113.9, 126.8, 129.8, 129.9, 144.9, 163.9, 193.6.

11l: Yield 82%, mp 125-126°C {lit.,[10] 127-128°C}, ir ($CHCl_3$) 3405, 1679, 1589, 1509, 1348, 1260, 1235, 1172, 1032 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 3.75 (3H, s), 3.89 (3H, s), 4.54 (2H, s), 6.73 (2H, d, J= 8.9 Hz), 6.85 (2H, d, J= 9.0 Hz), 6.95 (2H, J= 8.9 Hz), 8.00 (2H, d, J= 9.0 Hz). ^{13}C nmr ($CDCl_3$) δ 51.0, 55.5, 55.7, 114.1, 114.7, 115.1, 130.2, 132.1, 141.1, 152.8 , 164.3, 194.0.

11m: Yield 85%, mp 75 °C, ir (CH_2Cl_2) 3395, 3055, 2985, 1687, 1592, 1487, 1421, 1251, 1166, 1108, 1027 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 3.90 (3H, s), 4.60 (2H, s), 6.10 (1H, bs), 6.70 (2H, d, J= 8.9 Hz), 6.90-7.00 (6H, m), 7.2-7.3 (3H, m), 8.00 (2H, d, J= 9.0 Hz), ^{13}C nmr ($CDCl_3$) δ 50.5, 55.4, 113.9, 114.2, 117.0, 118.5, 119.6, 121.1, 121.8, 127.6, 129.3, 129.6, 129.9, 143.4, 147.9, 158.7, 163.9, 193.3.

11n: Yield 89%, mp 114°C, ir (CH_2Cl_2) 3413, 3052, 2983, 1679, 1599, 1509, 1420, 1347, 1309, 1258, 1167, 1028 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.30 (6H, s), 3.90 (3H, s), 4.60 (2H, s), 4.70 (1H, bs), 6.70 (1H, d, J= 7.8 Hz), 6.90-7.00 (4H, m), 8.00 (2H, d, J= 8.8 Hz), ^{13}C nmr ($CDCl_3$) δ 17.3, 20.3, 50.2, 55.5, 110.1, 114.0, 122.6, 126.3, 127.2, 127.9, 130.0, 131.1, 142.9, 163.9, 193.7.

11o: Yield 89%, mp 119°C {lit.,[11] 124 °C}, ir (CH_2Cl_2) 3405, 1694, 1601, 1502, 1437, 1398, 1349, 1316, 1217, 1145, 1090 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 4.55 (2H, s), 4.80 (1H, bs), 6.60-6.80 (3H, m), 7.20 (2H, m), 7.60 (2H, d, J= 8.8 Hz), 7.90 (2H, d, J= 8.8 Hz), ^{13}C nmr ($CDCl_3$) δ 50.3, 113.0, 117.9, 129.0, 129.1, 129.3, 132.1, 133.6, 146.9, 194.1.

11p: Yield 86%, mp 146-147°C {lit.,[8] 154°C}, ir (CH_2Cl_2) 3409, 2923, 1687, 1614, 1583, 1517, 1347, 1215, 1142, 1071 cm^{-1}, ^{1}H nmr ($CDCl_3$) δ 2.30 (3H, s), 4.50 (2H, s), 4.70 (1H, bs), 6.60 (2H, d, J= 8.5 Hz), 7.00 (2H, d, J= 8.5 Hz), 7.60 (2H, d, J= 8.5 Hz), 7.80 (2H, d, J= 8.5 Hz), ^{13}C nmr ($CDCl_3$) δ 20.4, 50.7, 113.1, 127.1, 129.0, 129.2, 129.8, 132.1, 133.6, 144.7. 194.4.

11q: Yield 93%, mp 124-125°C, ir (CH_2Cl_2) 3406, 1687, 1584, 1510, 1464, 1386, 1347, 1236, 1215, 1142, 1070, 1035 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.75 (3H, s), 4.50 (2H, s), 4.70 (1H, bs), 6.70 (2H, d, J= 9.0 Hz), 6.80 (2H, d, J= 9.0 Hz), 7.70 (2H, d, J= 8.7 Hz), 7.90 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 51.2, 55.7, 114.3, 115.1, 129.1, 129.3, 132.3, 133.8, 141.4, 152.6, 194.9.

11r: Yield 89%, mp 138-139°C, ir (CH_2Cl_2) 3392, 1678, 1577, 1499, 1478, 1388, 1341, 1225, 1050, 1026 cm^{-1}, ^1H nmr ($CDCl_3$) δ 4.60 (2H, s), 4.80 (1H, bs), 6.70 (2H, d, J= 8.9 Hz), 6.90-7.10 (5H, m), 7.40 (2H, t, J= 8.5 Hz), 7.70 (2H, d, J= 8.8 Hz), 7.90 (2H, d, J= 8.8 Hz), ^{13}C nmr ($CDCl_3$) δ 50.6, 113.8, 116.9, 121.0, 121.8, 128.8, 129.0, 129.3, 132.0, 133.3, 143.4, 147.7, 158.7, 194.0.

11s: Yield 93%, mp 114-115°C {lit.,[11] 114°C}, ir (CH_2Cl_2) 3407, 3052, 2985, 1688, 1600, 1261 cm^{-1}, ^1H nmr ($CDCl_3$) δ 4.56 (2H, s), 4.85 (1H, bs), 6.70-6.80 (3H, m), 7.20 (2H, m), 7.50 (2H, d, J= 8.7 Hz), 7.90 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 50.3, 113.0, 117.9, 129.1, 129.2, 129.4, 133.2, 140.3, 146.9, 193.9.

11t: Yield 84%, mp 133-135°C (lit.,[8] 130°C), ir (CH_2Cl_2) 3407, 1686, 1615, 1517, 1216, 1143, 1092 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.20 (3H, s), 4.50 (2H, s), 4.60 (1H, bs), 6.60 (2H, d, J= 8.5 Hz), 7.00 (2H, d, J= 8.5 Hz), 7.50 (2H, d, J= 9.0 Hz), 8.00 (2H, d, J= 9.0 Hz), ^{13}C nmr ($CDCl_3$) δ 20.3, 50.6, 113.1, 127.1, 129.1, 129.1, 129.8, 133.2, 140.1, 144.6, 194.1.

11u: Yield 91%, mp 118-120°C, ir (CH_2Cl_2) 3403, 3053, 1687, 1589, 1510, 1462, 1392, 1347, 1262, 1237, 1216, 1092, 1035 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.75 (3H, s), 4.50 (2H, s), 4.70 (1H, bs), 6.70 (2H, d, J= 9.1 Hz), 6.80 (2H, d, J= 9.1 Hz), 7.50 (2H, d, J= 8.8 Hz), 7.90 (2H, d, J= 8.8 Hz), ^{13}C nmr ($CDCl_3$) δ 51.2, 55.6, 114.3, 115.1, 129.2, 129.3, 133.4, 140.3, 141.4, 152.6, 194.6.

General Procedure for the Preparation of Compounds (12a-u and 16):

Phenoxythionocarbonyl or thiophenoxythionocarbonyl chlorides (11 mmol) and K_2CO_3 (1.52 g, 11 mmol) were added to a solution of (**11a-u**) or (**15**) (10 mmol) in dichloromethane (20 ml). The reaction mixture was stirred for 12 h at room temperature and the salt which precipitated was filtered. The solution was then washed successively with 1% aqueous sodium hydrogen carbonate, water and brine and dried over $MgSO_4$. After filtration and evaporation of the solvent under vacuum, the resulting solid was crystallized to give the corresponding thiocarbamates (**12a-u**) or (**16**).

12a: Yield 90%, white crystals, mp 143°C (CH_2Cl_2/ EtOH), ir (CH_2Cl_2) 1702, 1444, 1220, 1202, 1180 cm^{-1}, ^1H nmr ($CDCl_3$) δ 5.60 (2H, s), 7.00-7.50 (13 H, m), 8.00 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 62.4, 122.4 , 122.6, 125.8, 126.5, 127.8, 128.0, 128.7, 129.1, 129.3, 133.6, 135.1, 142.7, 154.1, 189.3, 192.0. Anal. Calcd for $C_{21}H_{17}NO_2S$: C,72.59; H, 4.93; N, 4.03; S, 9.23. Found: C, 72.68; H, 4.94; N, 4.04; S, 9.16.

12b: Yield 69 %,white crystals, mp 105°C (CH_2Cl_2/hexanes) ir (KBr) 1690, 1441, 1198, 1173 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.36 (3H, s), 5.42 and 5.63 (2H, 2s, 0.5:1.5), 7.00 -7.60 (12H, m), 8.00 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 20.1, 65.2, 122.0 to 129.9 (CH), 133.6, 135.1, 137.9, 140.1, 154.2, 189.5, 195.6.

12c: Yield 92%, yellow crystals, mp 50°C, ir (CH_2Cl_2) 1700, 1592, 1508, 1445, 1221, 1203, 1181 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.78 (3H, s), 5.60 (2H, s), 6.90 (2H, m), 7.10-7.60 (10 H, m), 7.95 (2H, d, J= 8.0 Hz), ^{13}C nmr

($CDCl_3$) δ 55.4, 62.6, 114.4 to 129.0 (CH), 133.6, 135.1, 135.4, 154.0, 159.0, 189.7, 192.2. Anal. Calcd for $C_{22}H_{19}NO_3S$: C,70.00; H, 5.07; N, 3.71; S, 8.49. Found: C, 70.08; H, 5.11; N, 3.74; S, 8.42.

12d: Yield 92%, yellow crystals, mp 57-58°C (ether/hexanes), ir ($CHCl_3$) 3065, 2924, 1699, 1589, 1426, 1443, 1382, 1348, 1288, 1222, 1018 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.34 (3H, s), 3.85 (3H, s), 5.40 and 5.60 (2H, 2s, 0.5:1.5), 6.90-7.60 (17H, m), 7.95 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 62.5, 118.7 to 129.8 (CH), 133.7, 134.9, 137.4, 154.1, 156.2, 157, 189.6, 192.0.

12e: Yield 93%, white crystals, mp 58°C (ether/hexanes), ir (CH_2Cl_2) 3053, 2984, 1700, 1592, 1492, 1443, 1381, 1298, 1184, 1020 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.40 (3H, s), 2.60 (3H, s), 5.00 (1H, d, J= 17.5 Hz), 6.30 (1H, d, J= 17.5 Hz), 7.10-7.70 (11H, m), 8.10 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 17.4, 20.7, 61.4, 122.1, 125.5, 126.6, 127.6, 128.4, 128.7, 128.8, 131.3, 133.3, 133.6, 134.7, 137.9, 134.0, 153.8, 189.2, 191.6.

12f: Yield 98%, white crystals, mp 118°C (ether/hexanes), ir (KBr) 1686, 1585, 1439, 1375, 1289, 1224, 1169 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.40 (3H, s), 5.40 and 5.60 (2H, 2s, 0.5:1.5), 7.05 (1H, d, J= 8.1 Hz), 7.10-7.40 (8H, m), 7.55 (2H, d, J= 8.1 Hz), 7.90 (2H, d, J= 8.0 Hz). ^{13}C nmr ($CDCl_3$) δ 21.6, 62.3, 122.4 to 129.5 (CH), 132.5, 142.8, 144.6, 154.1, 189.4, 191.5.

12g: Yield 91%, yellow crystals, mp 57°C (ether/hexanes), ir (CH_2Cl_2) 3005, 2986, 1701, 1587, 1490, 1381, 1296, 1154, 1026 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.38 (3H, s), 2.40 (3H, s), 5.70 and 5.40 (2H, 2s, 1.6:0.4), 7.10-7.50 (11H, m), 8.00 (2H, d, J= 9.0 Hz), ^{13}C nmr ($CDCl_3$) δ 20.9, 21.5, 62.3, 122.2, 126.1, 127.8, 128.9, 129.2, 129.7, 130.0, 132.4, 137.7, 140.1, 144.4, 154.0, 189.3, 191.5.

12h: Yield 98%, white crystals, mp 55-58°C (ether/hexanes), ir (CH_2Cl_2) 3006, 2960, 1688, 1603, 1493, 1444, 1383, 1295, 1206, 1104, 1030 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.40 (3H, s), 3.80 (3H, s), 5.60 and 5.40 (2H, s, 1.4:0.6), 6.90 (2H, d, J= 8.7 Hz), 7.00-7.40 (7H, m), 7.30 (1H, m), 7.50 (2H, d, J= 8.0 Hz), 7.90 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 21.5, 55.2, 62.4, 114.3, 122.3, 125.7, 127.5, 127.9, 128.9, 129.3, 132.4, 135.4, 144.5, 154.1, 158.7, 189.5, 191.6.

12i: Yield 94%, white crystals, mp 58°C (ether/hexanes), ir (CH_2Cl_2) 3053, 2986, 1692, 1589, 1487, 1446, 1421, 1262, 1226, 1181, 1070 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.60 (3H, s), 5.80 and 5.60 (2H, 2s, 1.6:0.4), 7.20-7.60 (14H, m), 7.70 (2H, d, J= 8.6 Hz), 8.10 (2H, d, J= 8.6 Hz), ^{13}C nmr ($CDCl_3$) δ 21.7, 62.5, 118.7, 119.5, 122.4, 122.6, 123.9, 125.9, 128.0, 129.1, 129.4, 129.8, 132.6, 137.9, 144.8, 154.2, 156.3, 157.0, 189.6, 191.6.

12j: Yield 61%, pale yellow crystals, mp 175°C (decomp) (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 1687, 1598, 1368, 1218, 1169, 1112 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.83 (3H, s), 5.68 (2H, s), 6.90 (2H, d, J= 8.9 Hz), 7.43 (8H, m), 7.65 (2H, m), 7.94 (2H, d, J= 8.9 Hz), ^{13}C nmr ($CDCl_3$) δ 55.4, 63.3, 113.8, 128.0, 128.9, 129.4, 129.6, 129.8, 130.2, 132.5, 136.6, 144.2, 163.7, 190, 201.1.

12k: Yield 92%, pale yellow crystals, mp 125°C (ether/hexanes), ir (KBr) 1684, 1592, 1437, 1380, 1292, 1166 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.34 (3H, s), 3.85 (3H, s), 5.38 and 5.52 (2H, 2s, 0.5:1.5), 6.80 (2H, d, J= 8.5 Hz), 7.10 (2H, d, J= 8.5 Hz), 7.20 (3H, m), 7.32 (2H, d, J= 8.0 Hz), 7.40 (2H, d, J= 8.7 Hz), 7.95 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 21.0, 55.5, 62.2, 113.9, 122.4, 128.5 to 130 (CH), 137.9, 140.3, 154.2, 163.8, 189.5, 190.5.

12l: Yield 93%, pale yellow crystals, mp 55-56°C (CH_2Cl_2/hexanes), ir (KBr) 1699, 1589, 1505, 1444, 1383, 1294 cm^{-1}; ^1H nmr ($CDCl_3$) δ 3.78 (3H, s); 3.85 (3H, s); 5.38 and 5.57 (2H, 2s, 0.6:1.4); 6.80-7.50 (12H, m); 7.95 (2H, d, J= 8.0 Hz), ^{13}C nmr ($CDCl_3$) δ 55.2, 55.3, 62.3, 113.9 to 130.3 (CH), 135.7, 154.4, 159.1, 164.1, 189.9, 190.8.

12m: Yield 95%, white crystals, mp 138°C (ether/hexanes), ir (CH_2Cl_2) 3055, 2987, 1686, 1596, 1487, 1445, 1420, 1260, 1171 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.80 (3H, s), 5.60 and 5.40 (2H, 2s, 1.6:0.4), 6.90-7.40 (14H, m), 7.60 (2H, d, J= 8.7 Hz), 8.00 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 55.3, 62.1, 113.8, 118.5, 119.3, 119.4, 122.2, 123.7, 125.7, 127.8, 128.9, 129.7, 130.1, 137.4, 154.0, 156.1, 156.8, 163.7, 189.4, 190.4.

12n: Yield 99%, white crystals, mp 64-65°C (ether/hexanes), ir (CH_2Cl_2) 1687, 1598, 1493, 1451, 1384, 1348, 1262, 1230, 1173, 1026 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.30 (3H, s), 2.40 (3H, s), 3.90 (3H, s), 4.90 (1H, d, J= 17.1 Hz), 6.10 (1H, d, J= 17.1 Hz), 7.00 (2H, d, J= 9.0 Hz), 7.00-7.50 (8H, m), 8.00 (2H, d, J= 9.0 Hz), ^{13}C nmr ($CDCl_3$) δ 17.7, 21.0, 55.5, 61.3, 113.90, 122.5, 125.8, 127.0, 127.7, 128.2, 129.0, 130.2, 131.6, 133.9, 138.3, 139.3, 154.1, 163.8, 189.6, 190.3.

12o: Yield96 %, yellow crystals, mp 111°C (ether/hexanes), ir (CH_2Cl_2) 3050, 2923, 1703, 1590, 1487, 1440, 1382, 1349, 1294, 1262, 1203, 1090 cm^{-1}, ^1H nmr ($CDCl_3$) δ 5.60 and 5.40 (2H, 2s, 1.4:0.6), 7.10-7.60 (12H, m), 7.90 (2H, m), ^{13}C nmr ($CDCl_3$) δ 62.2, 122.3, 125.9, 126.5, 127.6, 128.1, 128.8, 129.1, 129.3, 132.0, 133.7, 142.6, 154.0, 189.3, 191.2.

12p: Yield 96%, white crystals, mp 69°C (ether/hexanes), ir (CH_2Cl_2) 1703, 1585, 1507, 1487, 1445, 1383, 1204, 1069 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.30 (3H, s), 5.50 and 5.30 (2H, 2s, 1.5:0.5), 7.10 (2H, m), 7.20 (3H, m), 7.30-7.40 (4H, m), 7.60 (2H, d, J= 8.5 Hz), 7.90 (2H, d, J= 8.6 Hz), ^{13}C nmr ($CDCl_3$) δ 21.1, 62.4, 122.4, 125.9, 126.3, 129.1, 129.4, 129.98, 132.1, 133.9, 138.06, 140.13, 154.2, 189.5, 191.4.

12q: Yield 98%, white crystals, mp 119-120°C (ether/hexanes), ir (CH_2Cl_2) 1700, 1584, 1505, 1444, 1293, 1260, 1205, 1183, 1069 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.80 (3H, s), 5.60 and 5.40 (2H, 2s, 1.4:0.6), 7.00 (2H, d, J= 9.0 Hz), 7.10 (2H, d, J= 7.5 Hz), 7.30 (1H, m), 7.40 (2H, d, J= 7.8 Hz), 7.70 (2H, d, J= 8.6 Hz), 7.90 (2H, d, J= 8.6 Hz), ^{13}C nmr ($CDCl_3$) δ 55.4, 62.5, 114.6, 122.5, 126.1, 127.8, 129.3, 129.6, 132.3, 132.4, 134.1, 135.6, 154.4, 159.3, 189.8, 191.8.

12r: Yield 89%, white crystals, mp 175 °C (ether/hexanes), ir (CH_2Cl_2) 3031, 1689, 1577, 1487, 1430, 1300, 1199 cm^{-1}, ^1H nmr ($CDCl_3$) δ 5.60 and 5.40 (2H, 2s, 1.6:0.4), 7.00-7.30 (8H, m), 7.30-7.50 (8H, m), 7.90 (2H, d, J= 8.8 Hz), ^{13}C nmr ($CDCl_3$) δ 62.4, 118.7, 119.5, 122.3, 123.9, 126.0, 127.9, 129.1, 129.2, 129.3, 129.8, 133.3, 137.2, 140.1, 154.1, 156.1, 157.1, 189.6, 191.1.

12s: Yield 96%, orange crystals, mp 98°C (ether/hexanes), ir (CH_2Cl_2) 1703, 1589, 1488, 1442, 1383, 1294, 1202, 1090 cm^{-1}, ^1H nmr ($CDCl_3$) δ 5.50 and 5.30 (2H, 2s, 1.4:0.6), 7.00-7.45 (10H, m), 7.50 (2H, d, J= 8.7 Hz), 8.00 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 62.2, 122.2, 125.9, 126.5, 128.0, 129.0, 129.2, 129.3, 129.5, 133.3, 140.0, 142.5, 154.0, 189.3, 190.9.

12t: Yield 94%, white crystals, mp 125°C (ether/hexanes), ir (CH_2Cl_2) 3050, 1700, 1589, 1439, 1251, 1224, 1202, 1089 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.40 (3H, s), 5.60 and 5.40 (2H, 2s, 1.5:0.5), 7.00-7.50 (11H, m), 7.90

(2H, m), ^{13}C nmr ($CDCl_3$) δ 21.0, 62.3, 122.3, 122.6, 125.9, 126.2, 129.1, 129.3, 129.9, 133.4, 135.4, 138.0, 140.1, 154.1, 189.4, 191.1.

12u: Yield 97%, white crystals, mp 96-97°C (ether/hexanes), ir (CH_2Cl_2) 1685, 1598, 1505, 1444, 1384, 1296, 1204, 1171, 1029 cm^{-1}, ^1H nmr ($CDCl_3$) δ 3.80 (3H, s), 5.60 and 5.40 (2H, 2s, 1.4:0.6), 7.00 (2H, d, J= 9.0 Hz), 7.10-7.40 (5H, m), 7.50 (4H, d, J= 9.2 Hz), 8.00 (2H, d, J= 8.7 Hz), ^{13}C nmr ($CDCl_3$) δ 55.4, 62.5, 114.6, 122.5, 126.1, 127.8, 129.3, 129.4, 129.5, 133.6, 135.57, 140.3, 154.4, 159.3, 189.8, 191.5.

16: Yield 95%, white crystals, mp 155°C (ether/hexanes), ir (CH_2Cl_2) 3050, 2978, 1676, 1583, 1479, 1440, 1394, 1287, 1198, 1173, 1112, 1065, 1018 cm^{-1}, ^1H nmr ($CDCl_3$) δ 1.30 (3H, d, J= 7.4 Hz), 6.80 (1H, q, J= 7.8 Hz), 7.00 (2H, d, J= 7.8 Hz), 7.10-7.60 (10H, m), 8.30 (2H, m), ^{13}C nmr ($CDCl_3$) δ 16.0, 62.7, 122.3, 125.8, 128.4, 128.5, 129.0, 129.0, 129.1, 133.4, 135.7, 138.8, 154.0, 189.2, 197.9.

General Procedure for the Preparation of Thiohydroxamic Acids (13a-u):

To a solution of compounds (**12a-u**) (10 mmol) in ethanol (15 ml) were added pyridine (3.25 ml, 40 mmol) and hydroxylamine hydrochloride (0.77 g, 11 mmol). The reaction mixture was refluxed for 8 h and the solvent was then evaporated. The residue was dissolved in dichloromethane and washed with water and brine. The solution was dried over $MgSO_4$, filtered and evaporated. The thiohydroxamic acids (**13a-u**) was obtained pure by crystallization in the appropriate system of solvents.

13a: Yield 80%, white crystals, mp 163°C (EtOH) (decomp.), ir (CH_2Cl_2) 2972, 1545, 1497, 1382, 1362, 1132, 1111 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 7.00 (1H, s), 7.40 (6H, m), 7.70 (4H, m), 11.40 (1H, br), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 110.6, 125.1, 126.1, 126.5, 127.7, 128, 128.1, 128.5, 137.4, 158.2. Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.13; H, 4.51; N, 10.44; S, 11.95. Found: C, 67.10; H, 4.53; N, 10.41; S, 11.87.

13b: Yield 49%, white crystals, mp 154-155 °C (CH_2Cl_2/hexanes), ir (KBr) 2611, 1347 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.39 (3H, s), 6.90 (1H, s), 7.28 (2H, d, J= 8.6 Hz), 7.40 (5H, m), 7.67 (2H, d, J= 8.6 Hz), 10.25 (1H, br), ^{13}C nmr ($CDCl_3$) δ 21.1, 111.0, 125.1, 126, 126.8 , 128.9, 129.9, 134.8, 138.7. Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.05; H, 4.99; N, 9.92; S, 11.35. Found: C, 67.90; H, 5.03 ; N, 9.96; S,11.43.

13c: Yield 46%, white crystals, mp 168°C (decomp.) (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 2800, 1756, 1510, 1383, 1361, 1241, 1133 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.82 (3H, s), 6.50 (2H, d, J= 8.9 Hz), 7.15 (1H, s), 7.40 (3H, m), 7.54 (2H, d, J= 8.8 Hz), 7.71 (2H, d, J= 8.1 Hz), 11.85 (1H, br), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 54.0, 110.6, 112.6 125.6, 125.7, 127.0, 127.2, 129.5, 157.6. Anal. Calcd for $C_{16}H_{14}N_2O_2S$: C, 64.40; H, 4.73; N, 9.39; S, 10.74. Found: C, 64.48; H, 4.74 ; N, 9.43 ; S, 10.68.

13d: Yield 51%, white crystals, mp 157°C (decomp.) (CH_2Cl_2/hexanes), ir (KBr) 3120, 1461, 1218 cm^{-1}, ^1H nmr ($CDCl_3$) δ 6.90 (1H, s), 6.94 (2H, d, J= 8.9 Hz), 7.00-7.20 (5H, m), 7.30-7.50 (5H, m), 7.60 (2H, d, J= 8.9 Hz), 10.00 (1H, br), ^{13}C nmr ($CDCl_3$) δ 110.9, 119.7, 124.2, 125.1, 126.7, 127.9, 128.9, 129, 129.9, 132, 156, 157.7. Anal. Calcd for $C_{21}H_{16}N_2O_2S$: C, 69.97; H, 4.47; N, 7.77. Found: C, 69.77; H, 4.50; N, 7.70.

13e: Yield 71%, white crystals, mp 153-155°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3405, 3050, 2984, 1420, 1225, 1128, 1020 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.10 (3H, s), 2.30 (3H, s), 6.70 (1H, s), 7.00-7.20 (3H, m), 7.30-7.40 (3H, m), 7.70 (2H, d, J= 7.7 Hz), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 17.4, 20.6,

111.1, 126.2, 126.4, 127.0, 127.1, 128.1, 128.2, 131.2, 133.7, 134.9, 138.9, 157.9. Anal. Calcd for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45; S, 10.82. Found: C, 68.95; H, 5.43; N, 9.49; S, 10.74.

13f: Yield 37%, white crystals, m p 167°C (decomp.) (CH_2Cl_2/hexanes) ir (KBr) 2657, 1372 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.41 (3H, s), 7.06 (1H, s), 7.24 (2H, d, J= 8.1 Hz), 7.53 (3H, m), 7.67 (4H, m), 11.60 (1H, br), ^{13}C nmr ($CDCl_3$) δ 20.8, 110.4, 123.4 , 125.3, 126.6, 127.6, 128.5, 128.7, 137.6, 138.0, 158.4. Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.05; H, 4.99; N, 9.92; S, 11.35. Found: C, 68.01; H, 5.05; N, 9.95; S, 11.41.

13g: Yield 71%, white crystals, mp 151-153°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3431, 3051, 2984, 1420, 1259, 1194, 1155 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.27 (3H, s), 2.30 (3H, s), 6.80 (1H, s), 7.10-7.20 (4H, m), 7.40-7.50 (4H, m), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 20.8, 20.1, 110.4, 124.3, 125.1, 125.4, 126.6, 129.1, 129.4, 138.0, 138.3, 135.1. Anal. Calcd for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45; S, 10.82. Found: C, 69.05; H, 5.49; N, 9.51; S, 10.78.

13h: Yield 69%, white crystals, mp 165-166°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3408, 3054, 2987, 1603, 1508, 1421, 1360, 1258, 1028 cm^{-1}; ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.30 (3H, s), 3.70 (3H, s), 6.90 (2H, d, J= 8.9 Hz), 7.10 (2H, d, J= 8.1 Hz), 7.40 (2H, d, J= 8.8 Hz), 7.50 (2H, d, J= 8.1 Hz), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 21.0, 55.2, 110.6, 113.9, 123.4, 126.6, 126.7, 129.1, 130.5, 138.3, 158.9. Anal. Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97; S, 10.26. Found: C, 65.47; H, 5.13; N, 8.95; S, 10.34.

13i: Yield 66%, white crystals, mp 160-161°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3419, 3050, 2985, 1484, 1421, 1260, 1128, 1011 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.40 (3H, s), 7.00-7.10 (4H, m), 7.15-7.30 (4H, m), 7.30-7.45 (2H, m), 7.50-7.70 (4H, m), 12.00 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 21.3, 110.6, 118.5, 119.6, 119.7, 124.2, 126.8, 129.5, 129.9, 139.0, 156.1, 157.5. Anal. Calcd for $C_{22}H_{18}N_2O_2S$: C, 70.56; H, 4.84; N, 7.48; S, 8.56. Found: C, 70.66; H, 4.89; N, 7.43; S, 8.65.

13j: Yield 79%, white crystals, mp 176°C (decomp.) (CH_2Cl_2/hexanes), ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.83 (3H, s), 6.98 (3H, m), 7.50 (3H, m), 7.66 (4H, m), 11.59 (1H, s), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 54.9, 110.1, 113.7, 118.7, 125.3, 127.6, 128.2 , 128.5, 137.7, 159.3. Anal. Calcd for $C_{16}H_{14}N_2O_2S$: C, 64.40; H, 4.73; N, 9.39; S, 10.74. Found: C, 64.14; H, 4.77; N, 9.27; S, 10.62.

13k: Yield 51%, white crystals, mp 153°C (decomp.) (CH_2Cl_2/hexanes) ir (KBr): 2594-1353-1247 cm^{-1}, ^1H nmr ($CDCl_3$) δ 2.39 (3H, s), 3.82 (3H, s), 6.80 (1H, s), 6.94 (2H, d, J= 8.8 Hz), 7.27 (2H, d, J= 8.3 Hz), 7.50 (2H, d, J= 8.8 Hz), 7.60 (2H, d, J= 8.8 Hz), 10.10 (1H, br), ^{13}C nmr ($CDCl_3$) δ 21.1, 55.3, 110.0, 114.3, 125.1, 128.4, 129.8, 138.6, 160. Anal. Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.96; S, 10.26. Found: C, 65.48; H, 5.22; N, 8.98; S, 10.28.

13l: Yield 69%, white crystals, mp 159-160°C (decomp.) (CH_2Cl_2/hexanes) ir (KBr) 2590, 1496, 1453, 1357, 1293, 1242, 1172, 1126, 1011 cm^{-1}; ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.41 (3H, s), 3.47 (3H, s), 6.90 (5H, m), 7.55 (2H, d, J= 8.8 Hz), 7.65 (2H, d, J= 8.8 Hz), 11.40 (1H, br), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 24.5, 54.7, 109.8, 113.3, 118.4, 126.3, 127.8, 130.2, 158.3, 158.9. Anal. Calcd for $C_{17}H_{16}N_2O_3S$: C, 62.17; H, 4.91; N, 8.53. Found: C, 62.42; H, 4.89; N, 8.57.

13m: Yield 69%, white crystals, mp 178 °C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3409, 3050, 2984, 1421, 1225, 1128, 1019 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.80 (3H, s), 7.00-7.10 (4H, m), 7.10-7.30 (4H, m), 7.30-7.40

(2H, m), 7.50-7.70 (4H, m), 11.5 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 55.3, 110.4, 118.6, 119.2, 119.8, 124.1, 126.6, 129.4, 129.9, 139.0, 156.0, 157.3. Anal. Calcd for $C_{22}H_{18}N_2O_3S$: C, 67.67; H, 4.65; N, 7.18; S, 8.21. Found: C, 67.40; H, 4.66; N, 7.06; S, 8.12.

13n: Yield 76%, white crystals, mp 155-157°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3405, 3050, 2984, 1421, 1220, 1126, 1020 cm^{-1}; ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.30 (3H, s), 2.40 (3H, s), 3.80 (3H, s), 6.70 (1H, s), 6.90 (2H, d, J= 9.0 Hz), 7.10 (3H, m), 7.60 (2H, d, J= 9.0 Hz), 10.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 17.9, 21.1, 55.3, 110.7, 114.2, 118.6, 127.4, 127.6, 128.5, 131.8, 133.8, 135.4, 139.7, 159.9. Anal. Calcd for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.56; N, 8.58; S, 9.82. Found: C, 66.58; H, 5.42; N, 8.40; S, 9.64.

13o: Yield 51%, white crystals, mp 240-246°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3405, 3050, 2985, 1598, 1511, 1420, 1330, 1251, 1150, 1013 cm^{-1}, ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 6.90 (1H, s), 7.20-7.50 (9H, m), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 111.0, 122.0, 125.1, 125.3, 125.6, 127.8, 128.0, 128.5, 128.6, 131.3, 131.5, 137.3. Anal. Calcd for $C_{15}H_{11}N_2OBrS$: C, 51.88; H, 3.19; N, 8.07; S, 9.23. Found: C, 51.73; H, 3.25; N, 7.96; S, 9.17.

13p: Yield 68%, white crystals, mp 154-156°C (CH_2Cl_2/hexanes), ir (KBr) 3406, 3078, 1471, 1364, 1286, 1262, 1123, 1063 cm^{-1}, ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.40 (3H, s), 7.00 (1H, s), 7.30 (2H, d, J= 8.5 Hz), 7.40-7.60 (6H, m), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 20.7, 111.1, 122.1, 125.0, 127.3, 128.0, 129.3, 131.4, 134.8, 138.0, 158.2. Anal. Calcd for $C_{16}H_{13}N_2OBrS$: C, 53.19; H, 3.63; N, 7.77; S, 8.87. Found: C, 53.31; H, 3.69; N, 7.82; S, 8.83.

13q: Yield 62%, white crystals, mp 160-165°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3436, 2981, 1598, 1420, 1258, 1028 cm^{-1}; ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.80 (3H, s), 6.90-7.00 (3H, m), 7.40-7.60 (6H, m), 11.10 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 54.9, 111.2, 113.5, 113.6, 121.8, 126.4, 126.5, 126.6, 127.0, 131.2,158.6. Anal. Calcd for $C_{16}H_{13}N_2O_2BrS$: C, 50.94, H, 3.47; N, 7.43; S, 8.50. Found: C, 50.94; H, 3.47; N, 7.38; S, 8.57.

13r: Yield 71%, white crystals, mp 196-198°C (CH_2Cl_2/hexane), ir (CH_2Cl_2) 3429, 3053, 2986, 1485, 1420, 1260, 1158, 1011 cm^{-1}; ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 6.80-7.00 (6H, m), 7.00-7.40 (8H, m), 12.00 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 111.0, 117.8, 119.0, 123.5, 125.5, 126.2, 126.9, 127.9, 129.4, 131.3, 155.6, 156.7. Anal. Calcd for $C_{21}H_{15}N_2O_2BrS$: C, 57.41; H, 3.44; N, 6.38; S, 7.30. Found: C, 57.19; H, 3.51; N, 6.44; S, 7.42.

13s: Yield 62%, white crystals, mp 230-240°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3405, 3049, 2985, 1598, 1512, 1421, 1338, 1258, 1150, 1013 cm^{-1}, ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 7.00 (1H, s), 7.30-7.50 (5H, m), 7.60-7.70 (4H, m), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 114.8, 125.7, 125.7, 126.2, 128.1, 128.4, 128.8, 129.0, 133.4, 137.6. Anal. Calcd for $C_{15}H_{11}N_2OClS$: C, 59.50; H, 3.66; N, 9.25; S, 10.59. Found: C, 59.29; H, 3.59; N, 9.17; S, 10.69.

13t: Yield 69%, white crystals, mp 155°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3406, 3084, 2904, 1475, 1364, 1263, 1082 cm^{-1}, ^{1}H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 2.40 (3H, s), 7.00 (1H, s), 7.30 (2H, d, J= 8.3 Hz), 7.40 (2H, d, J= 8.8 Hz), 7.50 (2H, d, J= 8.3 Hz), 7.70 (2H, d, J= 8.8 Hz), 11.50 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ

20.6, 111.0, 124.8, 125.0, 127.3, 127.7, 128.4, 129.1, 133.7, 134.8, 137.8, 158.5. Anal. Calcd for $C_{16}H_{13}ClN_2OS$: C, 60.66; H, 4.13; N, 8.84. Found: C, 60.61; H, 4.08; N, 8.86.

13u: *Yield 60%, white crystals, mp 141-144°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2)* 3408, 3018, 2983, 1421, 1259, 1023 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 3.80 (3H, s), 6.90 (1H, s), 7.00 (2H, d, J= 8.8 Hz), 7.40 (2H, d, J=8.6 Hz), 7.50 (2H, d, J= 8.8 Hz), 7.70 (2H, d, J= 8.6 Hz), 11.10 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 54.9, 111.2, 113.6, 124.7, 126.5, 127.1, 127.6, 128.2, 130.1, 133.5, 158.5, 158.6. Anal. Calcd for $C_{16}H_{13}N_2O_2ClS$: C, 57.74; H, 3.94; N, 8.42; S, 9.63. Found: C, 57.69; H, 3.92; N, 8.38; S, 9.70.

Preparation of Compound (15):

To a solution of 2-bromopropiophenone (**14**) (1.52 ml, 10 mmol) in acetone (20 ml) were added aniline (**2a**) (0.95 ml, 10.5 mmol), K_2CO_3 (1.45 g, 10.5 mmol) and KI (3. 32 g, 20 mmol). The reaction mixture was stirred for 24 h at room temperature. The acetone was then evaporated and the residue diluted with dichloromethane and washed with water and brine. The solution was dried over $MgSO_4$, filtered and evaporated under reduced pressure. Crystallization from CH_2Cl_2/hexanes afforded the desired (**15**) (1.91 g, 85%). This formed yellow crystals, mp 100°C {lit.,[12] 101°C}, ir (CH_2Cl_2) 3391, 3043, 2870, 1672, 1589, 1488, 1440, 1418, 1336, 1307, 1279, 1215, 1150, 1070 cm^{-1}, ^1H nmr ($CDCl_3$) δ 1.50 (3H, d, J= 6.9 Hz), 4.70 (1H, bs), 5.20 (1H, q, J= 6.9 Hz), 6.60-6.80 (3H, m), 7.20-7.30 (2H, m), 7.40-7.60 (3H, m), 8.00 (2H, d, J= 7.8 Hz), ^{13}C nmr ($CDCl_3$) δ 19.5, 53.2, 113.4, 117.8, 128.4, 128.8, 129.3, 133.5, 134.5, 146.4, 200.5.

Preparation of Thiohydroxamic acid (17):

To a solution of (**16**) (3.60 g, 10 mmol) in ethanol (15 ml) were added pyridine (16 ml, 200 mmol) and hydroxylamine hydrochloride (6.95 g, 100 mmol). The reaction mixture was refluxed for 24 h and the solvent removed under reduced pressure. The residue was dissolved in dichloromethane and washed with water and brine. The solution was dried over $MgSO_4$, filtered and evaporated. The thiohydroxamic acid (**17**) (1.84 g, 65%) was obtained pure after recrystallization from CH_2Cl_2/hexanes. This formed white crystals, mp 126-129°C (CH_2Cl_2/hexanes), ir (CH_2Cl_2) 3405, 3050, 2984, 1420, 1229, 1120, 1028 cm^{-1}, ^1H nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 1.90 (3H, s), 7.20 (5H, m), 7.40 (5H, m), 11.00 (1H, bs), ^{13}C nmr ($CDCl_3$:DMSO-d_6, 1:1) δ 10.2, 109.4, 119.4, 124.6, 126.4, 127.9, 128.0, 128.6, 128.9, 129.0, 135.6, 157.2. Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92; S, 11.36. Found: C, 67.94; H, 5.03; N, 9.82; S, 11.43.

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