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Synthesis, characterization of some new 1-aroyl-3-(4-aminosulfonylphenyl)thioureas and crystal structure of 1-(3,4,5-trimethoxybenzoyl)- 3-(4-aminosulfonylphenyl)thiourea

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Synthesis, characterization of some new 1-aroyl-3-(4-aminosulfonylphenyl)thioureas and crystal structure of 1-(3,4,5-trimethoxybenzoyl)-3-(4-aminosulfonylphenyl)thiourea

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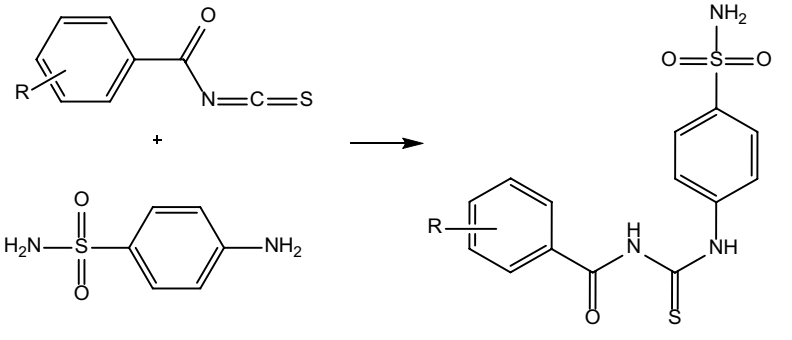
A small library of novel 1-aroyl-3-(4-aminosulfonylphenyl)thiourea derivatives was synthesized by the reaction of sulfanilamide with substituted aroyl isothiocyanates in dry acetonitrile. The scope of the reaction was indicated by the synthesis of 1-undecanoyl-3-(4-aminosulfonylphenyl)thiourea, an acyl derivative involving alkanoyl isothiocyanate. All the compounds have been characterized by analytical and spectroscopic methods and in one case by single-crystal X-ray diffraction data.



Keywords: 1-aroyl-3-(4-aminosulfonylphenyl)thioureas; sulfonamides; aryl/acyl isothiocyanates

1. Introduction

Since its first synthesis in 1908, sulfanilamide and its derivatives have extensively been used in chemotherapy due to their efficacy against a broad range of microorganisms. These are true anti-metabolites as they block a specific step in the biosynthetic pathway of the folic acid important in cell division due to its structural similarity with *para*-aminobenzoic acid. Sulfonyl

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ureas are among the most familiar sulfanilamide derivatives and over 12,000 are known, some of them being very potent hypoglycemic agents due to their ability to stimulate the release of insulin from the pancreatic islets. Carbutamide, tolbutamide, chlorpropamide and tolazamide belong to the first generation of sulfonylureas while those of second generation include glyburide and glipizide (*1–4*). Besides antibacterial and hypoglycemic activities, sulfonamides exhibit diuretic (*5*), anti-carbonic anhydrase (*6*), anti-thyroid (*7*) and anti-tumor activities (*8*). Some other sulfonamides used as drugs include the protease inhibitor and antiretroviral fosamprenavir, the non-steroidal anti-inflammatory drug celecoxib and sumatriptan, used to treat migraine headaches. Sulfonamides are found to exhibit remarkable antimalarial activity (*9–11*). Thus, 4-(3,4-dichlorophenylureido)thioureidobenzenesulfonamide possessing a thiourea scaffold was an effective *in vitro* inhibitor of carbonic anhydrase; repressed the *ex vivo* growth of *Plasmodium falciparum* with an IC_{50} of 1 μM. Sulfonamides inhibit the first step of pyrimidine nucleotide biosyntheses, that is, the carbonic anhydrase-mediate carbamoyl phosphate biosynthesis, sulfonamide thus have potential for the development of novel therapies for human malaria (*12*). Several antiplasmodial 7-chloro-4-aminoquinolyl-derived sulfonamides, ureas, thioureas and amides, have been synthesized and tested against chloroquine resistant and chloroquine sensitive *P. falciparum* (*13*).

1-Aroyl-3-arylthioureas containing both carbonyl and thiocarbonyl groups can coordinate with metals using both sulphur and oxygen atoms; the presence of these hard and soft donor sites offer a huge bonding potential (*13, 14*). Thiourea derivatives are versatile precursors towards novel heterocycles such as benzo- and naphthothiazolediones (*15, 16*), 3-aryl-2,5,6-triphenylpyrimidin-4-ones

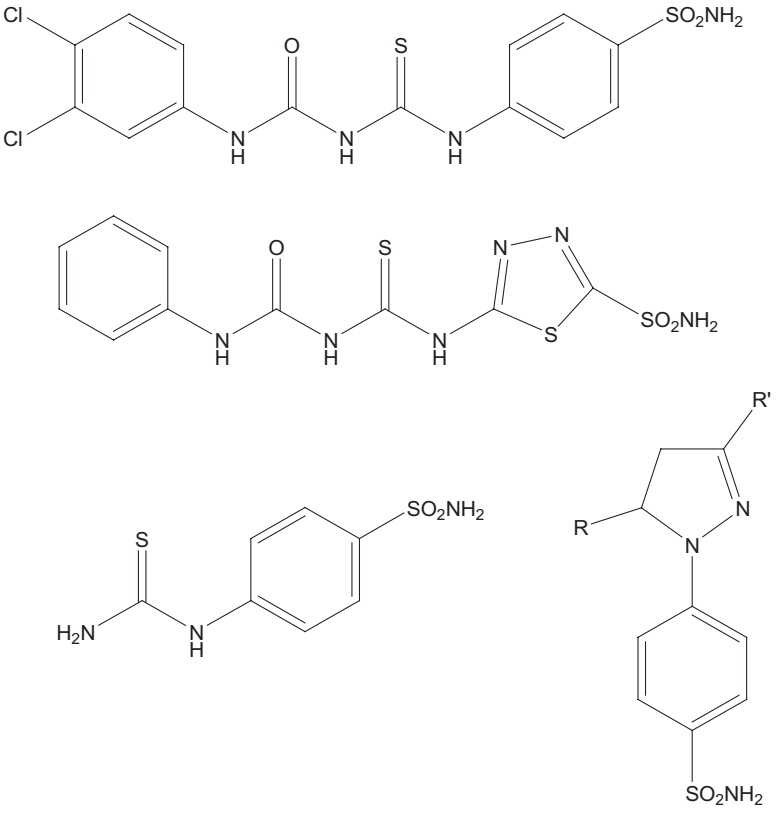


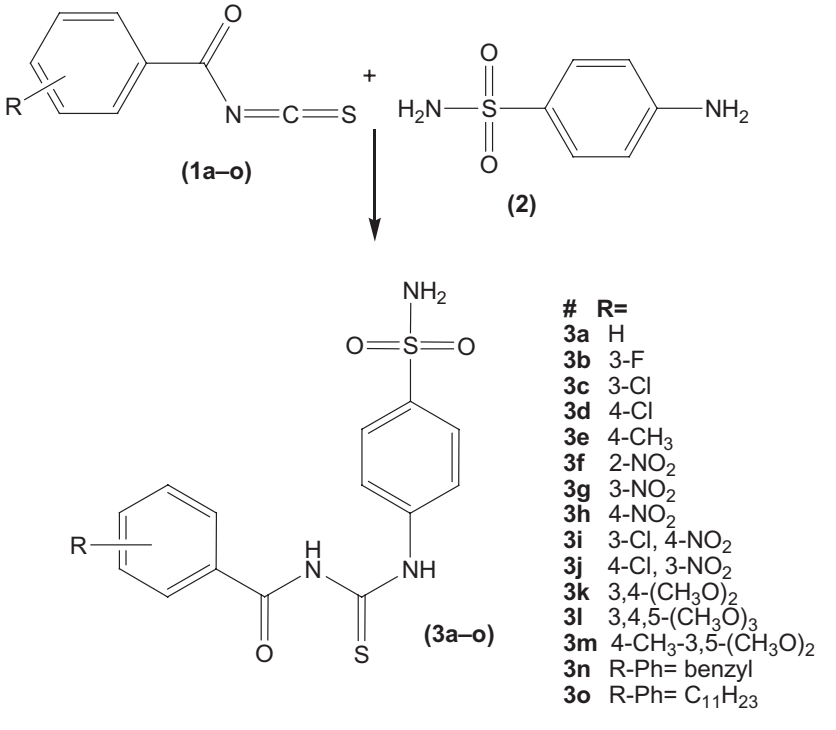
Figure 1. Some structurally related bio-active compounds.

(*17*) and *N*-4-amino-1-aryl-5-cyano-6-oxo-1*H*-indeno-thiazepin-2-ylidene)-4-arylamides (*18*). Thioureas exhibit potent anti-trypanosomal (*19*), influenza virus neuraminidase inhibitor (*20*), antifungal against plant pathogenic fungi (*21*), herbicidal (*22*) and anticancer activities (*23*).

In light of the above literature reports, it was thought of considerable interest to synthesize title compounds by appending the sulfanilamide moiety to thiourea nucleus in order to combine their beneficial effects in a single structural unit with expected bioactivities, especially the antimalarial and enzyme inhibitory activities. The aim of the synthesis is to reduce the toxicity of the parent compound and improve the therapeutic effect. The title compounds constitute a unique class of thioureas in which the free anilino nitrogen of sulfanilamide has been incorporated in the thiourea nucleus in contrast to most of the known sulfonyl urea/thiourea derivatives in which the sulfonamide amino group is a part of the urea/thiourea moiety (*24, 25*). Some of the structurally related compounds are presented (Figure 1).

2. Results and discussion

A variety of aroyl isothiocyanates (**1a**–**n**) and an acyl isothiocyanate (**1o**) were prepared *in situ* by reaction of suitably substituted acid chlorides with an equimolar quantity of potassium thiocyanate in dry acetonitrile. Treatment of isothiocyanates with sulfanilamide (**2**) in acetonitrile in 1:1 molar ratio furnished the corresponding 1-aroyl/alkanoyl-3-(4-aminosulfonyl phenyl)thioureas (**3a**–**o**) in 80–91% yield (Scheme 1) (*14*).



Scheme 1. Synthetic pathway of 1-aroyl-3-(4-aminosulfonylphenyl)thioureas.

Typically, in the IR spectra of the aroyl substituted thiourea's stretching vibrations attributable to free and associated NH at 3212–3350 cm^{-1}, C=O at 1655–1675 cm^{-1}, C=S at 1244–1263 cm^{-1}

Table 1. Physical and IR data of 1-aroyl-3-(4-aminosulfonylphenyl)thioureas (**3a**–**n**).

Compound	R	Yield (%)	m.p. (°C)	IR (cm^{-1})
3a	H	86	209–210	3270 (NH), 1655 (C=O), 1592 (C=C), 1470 (thioamide I) 1326 (C−S), 1299 (thioamide II), 1159, 1080 (thioamide III), 750 ((thioamide IV)
3b	3-F	90	143–144	3290 (NH), 1661 (C=O), 1590 (C=S), 1531 (thioamide I), 1334 (C−S), 1244 (thioamide II), 1154, 1097 (thioamide III), 750 (thioamide IV)
3c	3-Cl	87	240–241	3293 (NH), 1665 (C=O), 1591 (C=C), 1542 (thioamide I), 1332 (C−S), 1245 (thioamide II), 1158, 1091 (thioamide III), 750 (thioamide IV)
3d	4-Cl	71	190–191	3287 (NH), 1665 (C=O), 1590 (C=C), 1525 (thioamide I), 1325 (C−S), 1254 (thioamide II), 1158, 1011 (thioamide III), 754 (thioamide IV)
3e	4-CH_3	64	210–211	3317 (NH), 1665 (C=O), 1595 (C=C), 1500 (thioamide I), 1334 (C−S), 1263 (thioamide II), 1158, 1110 (thioamide III), 747 (thioamide IV)
3f	2-NO_2	85	178–179	3350 (NH), 1680 (C=O), 1593 (C=C), 1471 (thioamide I), 1328 (C−S), 1257 (thioamide II), 1154, 1091 (thioamide III), 747 (thioamide IV)
3g	3-NO_2	85	190–191	3382 (NH), 1671 (C=O), 1598 (C=S), 1471 (thioamide I), 1328 (C−S), 1268 (thioamide II), 1156, 1092 (thioamide III), 746 (thioamide IV)
3h	4-NO_2	88	180–181	3350 (NH), 1670 (C=O), 1594 (C=C), 1462 (thioamide I), 1326 (C−S), 1257 (thioamide II), 1155, 1072 (thioamide III), 750 (thioamide I (thioamide V)
3i	3-Cl-4-NO_2	84	192–193	3350 (NH), 1670 (C=O), 1594 (C=C), 1465 (thioamide I), 1326 (C−S), 1257 (thioamide II), 1155, 1079 (thioamide III), 749 (thioamide IV)
3j	4-Cl-3-NO_2	88	211–212	3310 (NH), 1677 (C=O), 1594 (C=C), 1478 (thioamide I), 1320 (C−S), 1250 (thioamide II), 1151, 1081 (thioamide III), 750 (thioamide IV)
3k	3,4-$(CH_3O)_2$	90	165–166	3317 (NH), 1665N (C=O), 1595 (C=C), 1481 (thioamide I), 1334 (C−S), 1263 (thioamide II), 1158, 1098 (thioamide III), 757 (thioamide IV)
3l	3,4,5-$(CH_3O)_3$	79	202–203	3311 (NH), 1660 (C=O), 1591 (C=C), 1481 (thioamide I), 1313 (C−S), 1259 (thioamide II), 1158, 1098 (thioamide III), 756 (thioamide IV)
3m	4-CH_3-3,5-$(CH_3O)_2$	77	210–211	3317 (NH), 1665 (C=O), 1590 (C=C), 1482 (thioamide I), 1331 (C−S), 1261 (thioamide II), 1158, 1089 (thioamide III), 755 (thioamide VI)
3n	R-Ph=Ph-CH_2-	62	145–146	3212 (NH), 1661 (C=O), 1591 (C=C), 1482 (thioamide I), 1334 (C−S), 1263 (thioamide II), 1158, 1082 (thioamide III), 749 (thioamide IV)
3o	$C_{11}H_{23}$-	70	133–135	3269 (NH), 2915, 2849, 1697 (C=O), 1593 (C=C), 1522, 1466 (thioamide I), 1309 (C−S), 1263 (thioamide II), 1150, 903 (thioamide III), 753 (thioamide IV), 632

in addition to those for the aromatic ring at 1581–1590 cm^{-1} could be identified; however, the presence of sulfonamido group leads to further complexity. In compounds containing the thioamide group (HNCS), a set of fundamentals involving the N−C and C=S bonds are identified known as "thioamide" bands: I, II, III and IV. These bands have a large contribution from C–N stretching and (N−H) deformation (I), C−N and C−S stretchings (II and III) and C−S (IV) stretching and they usually appear around 1470, 1250, 1080 and 750 cm^{-1}, respectively (*14*, *26*). The structures were further supported by ^1H and ^{13}C NMR data (Tables 1 and 2). In ^1H NMR, the characteristic broad singlets at δ 9.19 and 12.76 for protons of N_1 and N_3, respectively, besides the signals for aromatic protons are observed. ^{13}C NMR showed the peaks around δ 170 and 179 for C=O and

Table 2. ^{1}H NMR and ^{13}C NMR data of the 1-aroyl-3-(4-aminosulfonylphenyl)thioureas (**3a**–**n**).

Compound	R	^{1}H NMR (δ ppm, J Hz)	^{13}C NMR (δ ppm)	CHNS analysis (calcd; obs.)	EI-MS m/z(%)
3a	H	12.84 (s, 1H, NH), 11.68 (s, 1H, NH), 7.1–7.6 (m, 5H, Ar), 7.62 (d, 2H, Ar, $J = 5.6$), 6.5 (d, 2H, Ar, $J = 5.5$)	179 (C=S), 171 (C=O), 139 (C−N), 136 (C−S), 133 (C−CO), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 124 (Ar), 122 (Ar), 121 (Ar)	C (50.13), H (3.91), N (12.53), (19.21); C (50.74), H (4.1), N (12.99), S (19.9)	335 [M^{+}], 214 (2), 171 (32), 105 (100), 77 (11), 52 (16)
3b	3-F	12.81 (s, 1H, NH), 11.7 (s, 1H, NH), 7.9 (d, 2H, Ar, $J = 6.1$), 7.15 (d, 2H, Ar, $J = 6.5$), 7.62 (d, 2H, Ar, $J = 6.3$), 6.5 (d, 2H, Ar, $J = 5.9$)	180 (C=S), 173 (C=O), 157 (C−F), 139 (C−N), 136 (C−CO), 133 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar),124 (Ar), 122 (Ar), 121 (Ar),	C (47.83), H (3.42), N (11.89), S (18.15); C (48.1), H (3.91), N (12.2), S (19.1)	353 [M^{+}], 214 (5), 171 (37), 123 (100), 95 (44), 70 (54)
3c	3-Cl	12.2 (s, 1H, NH), 10.9 (s, 1H, NH), 7.7 (s, 1H, Ar), 7.69 (s, 1H, Ar), 7.62 (d, 2H, Ar,$J = 5.9$), 7.4 (s, 1H, Ar), 6.9 (s, 1H, Ar)	179 (C=S), 171 (C=O), 139 (C−N), 136 (C−CO), 133 (Ar), 132 (C−Cl), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar),124 (Ar), 122 (Ar)	C (45.46), H (3.27), N (11.37), S (17.34); C (45.88), H (3.87), N (11.89), S (17.54)	369, 371 [M^{+}], 214 (10), 171 (55), 138 (100), 111 (31), 85 (4)
3d	4-Cl	12.8 (s, 1H, NH), 11.3 (s, 1H, NH), 7.9 (d, 2H, Ar), 7.11 (d, 2H, Ar, $J = 5.5$), 7.62 (d, 2H, Ar, $J = 5.9$), 6.45 (d, 2H, Ar, $J = 4.5$)	179 (C=S), 171 (C=O), 139 (C-S), 138.1 (C−Cl), 136 (C−CO), 133 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar),124 (Ar), 122 (Ar), 121 (Ar)	C (45.46), H (3.27), N (11.37), S (17.34); C (45.88), H (3.87), N (11.89), S (17.54)	369, 371 [M^{+}], 214 (9), 138 (100), 111 (34), 85 (12)
3e	4-CH_3	12.2 (s, 1H, NH), 11 (s, 1H, NH), 7.62 (d, 2H, Ar, $J = 5.2$), 6.45 (d, 2H, Ar, $J = 5.5$), 6.3 (d, 2H, Ar, $J = 5.9$), 6.2 (d, 2H, Ar, $J = 5.6$), 2.3 (s, 3H, CH_3)	179 (C=S), 171 (C=O), 141 (C−CH_3), 139 (C−S), 136 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 124 (Ar), 122 (Ar), 121 (Ar), 32 (CH_3)	C (51.56), H (4.33), N (12.03), S (18.37); C (52.3), H (4.88), N (12.91), S (18.99)	349 [M^{+}], 214 (1), 171 (56), 119 (100), 91 (65)
3f	2-NO_2	13.1 (s, 1H, NH), 11.9 (s, 1H, NH), 8.6 (d, 1H, Ar), 7.7 (d, H, Ar, $J = 5.6$), 7.5 (d, 1H, Ar, $J = 5.1$), 7.5 (d, 1H, Ar, $J = 5.9$), 7.4 (d, 2H, Ar, $J = 5.9$), 6.5 (d, 2H, Ar $J = 5.3$)	179 (C=S), 171 (C=O), 147 (C−NO_2), 139 (C−S), 136.1 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar),124 (Ar), 122 (Ar)	C (44.20), H (3.18), N (14.73), S (16.86); C (44.92), H (3.8), N (15.2), S (17.1)	380 [M^{+}], 214 (6), 171 (42), 165 (33), 150 (100), 122 (11), 97 (21)
3g	3-NO_2	12.9 (s, 1H, NH), 11.1 (s, 1H, NH),7.7 (s, 1H, Ar), 7.69 (d, 1H, Ar, $J = 6.1$), 7.67 (d, 2H, Ar, $J = 5.3$), 7.42 (s, d, H, Ar, $J = 5.4$), 6.6 (d, 1H, Ar, $J = 5.1$)	179 (C=S), 171 (C=O), 146.3 (C−NO_2), 139 (C−S), 136 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar),124 (Ar), 122 (Ar)	C (44.20), H (3.18), N (14.73), S (16.86); C (44.92), H (3.8), N (15.2), S (17.1)	380 [M^{+}], 214 (7), 171 (47), 150 (100), 122 (27), 97 (5)

(*Continued*)

Table 2. Continued

Compound	R	^{1}H NMR (δ ppm, J Hz)	^{13}C NMR (δ ppm)	CHNS analysis (calcd; obs.)	EI-MS m/z(%)
3h	4-NO_2	12.2 (s, 1H, NH), 11 (s, 1H, NH), 7.69 (d, 2H, Ar, $J = 6.2$), 6.54 (d, 2H, Ar, $J = 5.2$), 6.42 (d, 2H, Ar, $J = 4.9$), 6.2 (d, 2H, Ar, $J = 5.9$)	179 (C=S), 171 (C=O), 150.8 (C-NO_2), 139 (C-S), 136 (C-CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 124 (Ar), 122 (Ar)	C (44.20), H (3.18), N (14.73), S (16.86) C (44.92), H (3.8), N (15.2), S (17.1)	380 [M^+], 214 (6), 171 (54), 150 (100), 122 (41), 97 (11)
3i	3-Cl-4-NO_2	12.9 (s, 1H, NH), 10.7 (s, 1H, NH),8.1 (s, 1H, Ar), 7.69 (d, 1H, Ar), 6.54 (d, 1H, Ar), 6.42 (d, 2H, Ar), 6.2 (d, 2H, Ar)	179 (C=S), 171 (C=O), 144 (C−NO_2), 141 (C−Cl), 139 (C−S), 136 (C−C), 133 (Ar), 132 (Ar), 131 (Ar), 128 (Ar), 127 (Ar), 124 (Ar), 121 (Ar)	C (40.53), H (2.67), N (13.51), S (15.46); C (41.2), H (3.1), N (13.68), S (15.90)	413, 415 [M^+], 214 (19), 183 (100)
3j	4-Cl-3-NO_2	12.5 (s, 1H, NH), 11.5 (s, 1H, NH), 7.69 (d, 1H, Ar, $J = 5.7$), 6.54 (d, 1H, Ar, $J = 5.9$), 6.42 (d, 2H, Ar, $J = 5.5$), 6.2 (d, 2H, Ar, $J = 5.6$)	178 (C=S), 172 (C=O), 144.3 (C−NO_2), 141 (C−Cl), 139 (C−S), 136.2 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 128 (Ar), 127 (Ar), 124 (Ar), 122 (Ar), 121 (Ar)	C (40.53), H (2.67), N (13.51), S (15.46); C (41.2), H (3.1), N (13.68), S (15.90)	413, 415 [M^+], 214 (11), 183 (100), 171 (28)
3k	3,4-$(OCH_3)_2$	12.87 (s, 1H, NH), 11.68 ((s, 1H, NH), 7.9 (s, 1H, Ar), 7.88 (s, 2H, Ar), 6.7 (d, 1H, Ar, $J = 5.9$), 6.6 (d, 1H, Ar, $J = 6.1$), 6.5 (s, 2H, Ar), 3.9 (s, 6H, OCH_3)	179 (C=S), 171 (C=O), 141 (C−OCH_3), 139 (C−S), 138 (C−OCH_3), 136.1 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 121 (Ar), 65 (O*C*H_3)	C (52.87), H (4.71) N (11.56), S (17.64); C (53.1), H (4.77) N (11.72), S (17.89)	395 [M^+], 214 (53), 165 (100), 137 (42)
3l	3,4,5-$(OCH_3)_3$	12.87 (s, 1H, NH), 11.68 (s, 1H, NH), 7.9 (s, 2H, Ar), 7.88 (s, 2H, Ar), 6.5 (s, 2H, Ar), 3.9 (s, 9H, OCH_3)	179 (C=S), 171 (C=O), 147 (C−OCH_3), 141 (C−OCH_3), 139 (C−S), 136.3 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 65 (O*C*H_3)	C (48.60), H (4.33), N (10.63), S (16.22); C (49.20), H (4.77), N (11.3), S (16.87)	425 [M^+], 214 (48), 195 (100), 166 (11)
3m	4-CH_3-3,5-$(OCH_3)_2$	12.82 (s, 1H, NH), 11.7 (s, 1H, NH), 7.9 (s, 2H, Ar), 7.88 (s, 2H, Ar), 6.5 (s, 2H, Ar), 3.9 (s, 6H, OCH_3), 2.52 (s, 3H, CH_3)	180 (C=S), 170 (C=O), 141 (OCH_3), 139 (C−S), 136.1 (C−CO), 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 116 (C−CH_3), 65 (O*C*H_3), 21.3 (CH_3)	C (48.60), H (4.33), N (10.63), S (16.22); C (49.20), H (4.77), N (11.3), S (16.87)	409 [M^+], 214 (21), 179 (100), 171 (45), 151 (17)
3n	R-Ph=Ph-CH_2	12.9 (s, 1H, NH), 11.7 (s, 1H, NH), 7.1–7.6 (m, 5H, Ar), 7.62 (d, 2H, Ar, $J = 6.2$), 6.5 (d, 2H, Ar, $J = 5.9$), 4.3 (s, 2H, CH_2)	180 (C=S), 173 (C=O), 139 (C−S), 136.2 (C−CO), 135.4 (C−C) 133 (Ar), 132 (Ar), 131 (Ar), 129 (Ar), 128 (Ar), 127 (Ar), 126 (Ar), 59 (*C*H_2)	C (51.56), H (4.33), N (12.03), S (18.35); C (52.1), H (4.99), N (12.78), S (18.8)	349 [M^+], 214 (8), 171 (52), 91 (100)

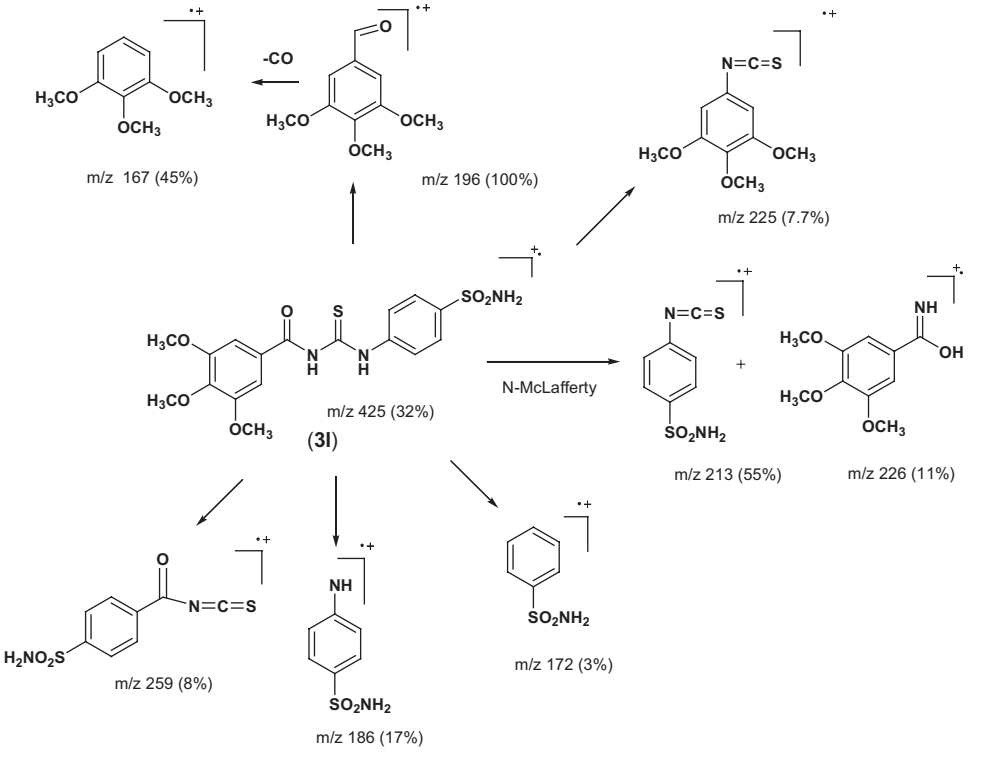
(*Continued*)

Table 2. Continued

Compound	R	^{1}H NMR (δ ppm, J Hz)	^{13}C NMR (δ ppm)	CHNS analysis (calcd; obs.)	EI-MS m/z(%)
3o	R-Ph=$C_{11}H_{23}$-	12.76 (s, 1H, NH), 9.03 (s, 1H, NH), 7.93 (d, 2H, Ar), 7.95 (d, 2H, Ar, J = 6.2), 2.41 (m, 2H, CH_2), 1.27 (br s, 16H), 1.66 (m, 2H, CH_2), 0.89 (t, 3H,J = 6.2), 8.74 (brs, NH_2)	174 (C=O), 182 (C=S), 140 (C−N), 136.2 (C−CO), 135.4 (C−C) 133 (Ar), 131 (Ar), 33.9 (C1′), 32.0 (C9′), 29.74, 29.72, 29.6, 29.55, 29.51, 29.4 (C4′−C8′), 26.9 (C2′), 24.7 (C3′), 22.8 (C10′), 14.2 (C11′)	C (55.18), H, (7.55) N (10.16), S, (15.51); C (55.11), H (7.46), N (10.08), S (15.41)	413 [M^+], 230 (35), 171 (52), 91 (100)

C=S, respectively (*13, 14*), except for the acyl derivative **3o** where these appear at δ 174 and 182, respectively. Table 1 gives the physical and IR data of thioureas (**3a**–**o**) while the ^{1}H NMR and ^{13}C NMR data are listed in Table 2.

In the mass spectra of the compounds, in addition to the molecular ion peaks, the major fragments are derived from the *N*-McLafferty rearrangement and the base peaks originate from the substituted benzoyl cation. The fragmentation pattern of (**3l**) is shown in Scheme 2.



Scheme 2. Mass fragmentation of 1-(3,4,5-trimethoxybenzoyl)-3-(4-aminosulfonylphenyl) thiourea (**3l**).

2.1. *X-ray structure*

ORTEP drawing of the molecular structure of compound **3l** as determined in the crystalline phase is depicted in Figure 2.

The *N*-(phenylcarbamothioyl)benzamide moiety is essentially planar with a maximum deviation of 0.1025(10) Å for atom C2 (Figure 2). The central N2/C7/S2/N3/C8/O3 plane makes dihedral angles of 6.55(5)° and 6.45(5)° with benzene C1–C6 and C9–C14 rings, respectively. The two benzene rings make a dihedral angle of 0.81(5)°. In the molecule, intramolecular N−H···O and C−H···S hydrogen bonds are observed. In the crystal structure, the molecules are connected by N−H···O hydrogen bonds to afford a double chain structure running along the [10-1] direction (Figure 3). The chains are further connected through water molecules to form a layer expanding parallel to the (111) plane.

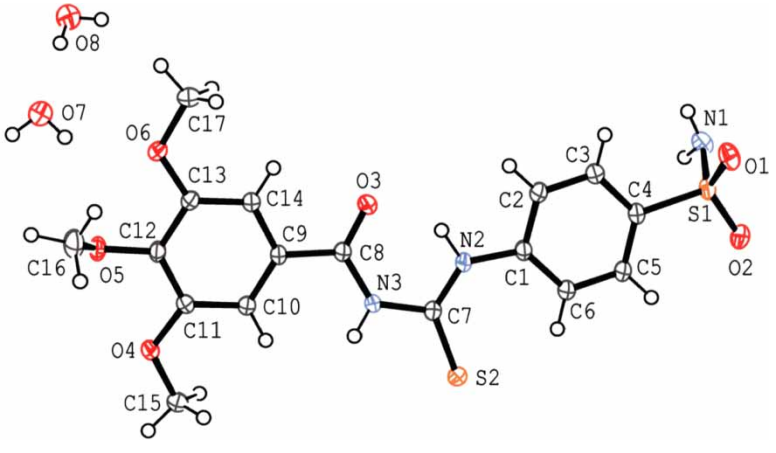


Figure 2. Molecular structure of **3l** with the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level.

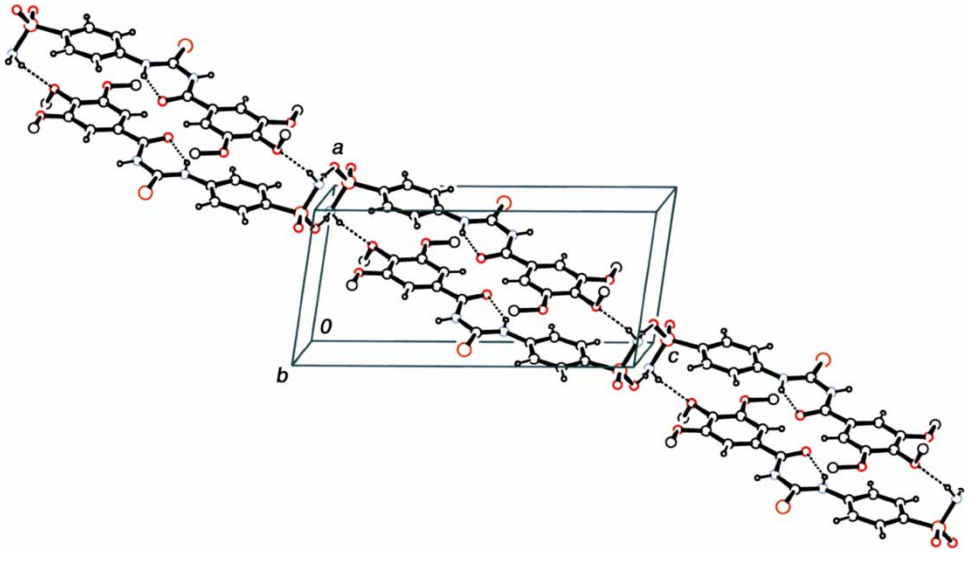


Figure 3. Crystal packing of **3l** with intra- and intermolecular hydrogen bonding pattern indicated as dashed lines.

3. Conclusion

Several 1-aroyl-3-(4-aminosulfonylphenyl)thioureas (**3a**–**n**) and one 1-acyl derivative (**3o**) have been synthesized, which differ from most of the known sulfonyl thiourea derivatives in having the free anilino nitrogen of sulfanilamide incorporated into the thiourea nucleus leaving the sulfonamide amino group intact, for detailed bioevaluation and comparison.

4. Experimental

4.1. *Instrumentation*

Melting points were recorded using a digital Gallenkamp (SANYO) model MPD.BM 3.5 apparatus and are uncorrected. ^{1}H NMR spectra were determined in $CDCl_3$ solution at 300 MHz using a Bruker AM-300 spectrophotometer using TMS as an internal reference and ^{13}C NMR spectra were determined at 75 MHz using a Bruker 75 MHz NMR spectrometer in $CDCl_3$ solution. FTIR spectra were recorded on an FTS 3000 MX spectrophotometer. Mass spectra (EI, 70 eV) were determined on a MAT 312 instrument, and elemental analyses were conducted using a LECO-183 CHNS analyzer.

Crystallographic data were collected on a Bruker-AXS SMART APEX CCD diffractometer. The crystal structure was solved by direct methods. H-atoms were located from different Fourier maps and then refined at idealized positions with the riding model.

4.2. *Synthesis of 1-aroyl-3-(4-aminosulfonylphenyl)thioureas: general procedure*

A solution of suitably substituted benzoyl/acyl chloride (10 mmol) in dry acetonitrile (50 ml) was added dropwise to a suspension of potassium thiocyanate (10 mmol) in acetonitrile (30 ml) and the reaction mixture was refluxed for 30 min to afford isothiocyanates (**1a**–**o**). After cooling to room temperature, a solution of sulfanilamide (**2**) (10 mmol) in dry acetonitrile (10 ml) was added and the resulting mixture refluxed for 1–3 h. The reaction mixture was poured into cold water and the precipitated thioureas (**3a**–**o**) were recrystallized using aqueous ethanol. The physicochemical and spectral data (IR, ^{1}H, ^{13}C NMR, EI-MS) of the products are given in Tables 1 and 2.

Supplementary material

CCDC 787098 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif or by e-mailing data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: +44 1223-336033.

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