New Synthesis of Dimethyl *N*-Aroylcarbimidodithioates and 3-Aryl-5-methylthio-1*H*-1,2,4-triazoles

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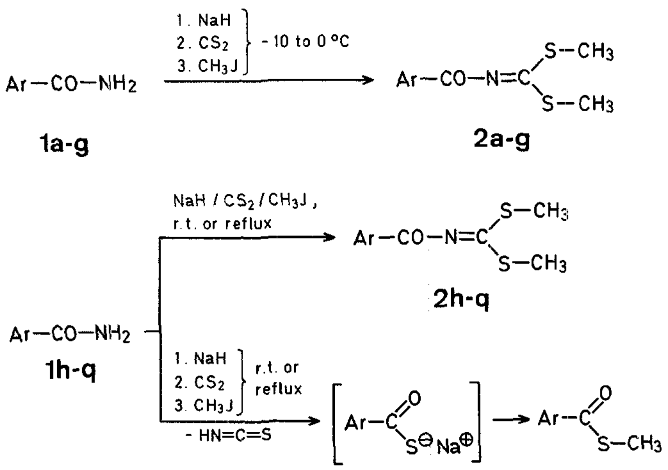
We have previously reported[1] the reaction of cyclic amides and related compounds with carbon disulfide in the presence of sodium hydride, and the isolation of free *N*-acyl- and *N*-carbamoyldithiocarbamic acids. In the case of α,β-unsaturated amides, the reaction led to cyclization to give 2-thioxoperhydro-1,3-thiazin-4-ones[2]. We report here a new general synthesis of dimethyl *N*-aroylcarbimidodithioates **2** and 3-aryl-5-methylthio-1*H*-1,2,4-triazoles **6** from aromatic amides **1**.

The unsubstituted dimethyl *N*-benzoylcarbimidodithioate (**2j**) was previously prepared[3] by methylation of methyl *N*-benzoyldithiocarbamate, obtained from thiobenzoic acid and methyl thiocyanate; dialkyl or diaryl *N*-benzoylcarbimidodithioates were also prepared by the reaction of *N*-benzoylcarbimidic dichloride with sodium thiolates[4]. However, the



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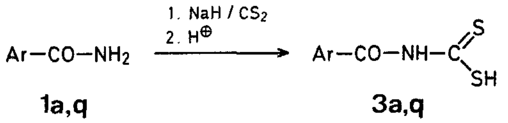
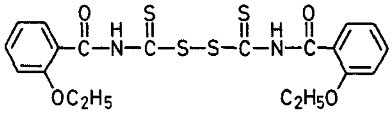
method reported here is more convenient. Of the aromatic amides **1a–q**, **1a–g** reacted with carbon disulfide in the presence of sodium hydride, followed by methylation to give esters **2a–g**. The procedure was carried out stepwise with cooling. In the case of **2h–q**, the starting materials were mixed from the start, and the reaction was conducted at room or reflux temperature. If carried out stepwise, the reaction resulted in the formation of an *S*-methyl arenethiocarboxylate. Shahak and Sasson[5] have reported the cleavage of an amide bond of a primary or secondary amide by treatment with sodium hydride and carbon disulfide, giving a thioacid and an isothiocyanate.

Attempts to isolate the free *N*-aroyldithiocarbamic acids in two cases gave, *N*-(2-ethoxybenzoyl)-dithiocarbamic acid (**3a**) and *N*-(2-furoyl)-dithiocarbamic acid (**3q**). Acid **3a**, obtained by the reaction of **1a** with carbon disulfide with cooling and then acidification, easily changed on keeping in a solvent into the oxidatively coupled product, bis[*N*-(2-ethoxybenzoyl)-thiocarbamoyl] disulfide (**4**). Disulfide **4** was warmed in pyridine to give bis[2-ethoxybenzoyl] disulfide (**5**). The relatively stable dithio-acid **3q** was obtained by refluxing of the reactants in tetrahydrofuran and then acidification. Both **3a** and **3q** were exceedingly sensitive to nickel(II) ion, giving purple-red precipitates.





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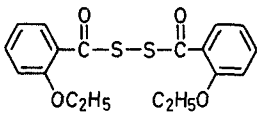

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Esters **2a–q** reacted with hydrazine hydrate on refluxing in ethanol to give the 1*H*-1,2,4-triazoles **6a–q** in good yields. Some synthetic methods of the triazoles **6** have been reported previously, which involve cyclization of thiosemicarbazide derivatives[6–15]. Our method is simpler and has the advantage that substituted aromatic amides are readily available.

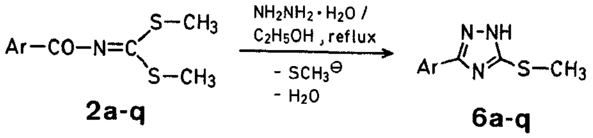

Table 1. Dimethyl *N*-Aroylcarbimidodithioates **2a–q**

Compound	Ar	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a] or Lit. m.p. [°C]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	U.V. (C_2H_5OH) λ [nm] (ε)	M.S. m/e (M^+)
2a	2-C_2H_5O—C_6H_4	70	oil	$C_{12}H_{15}NO_2S_2$ (269.3)	1645[b]	249 (15500); 302 (7700)	269
2b	2-Cl—C_6H_4	86	88–89° (C_2H_5OH/C_2H_5OAc)	$C_{10}H_{10}ClNOS_2$ (259.8)	1620	252 (5900); 291 (7600)	259
2c	2-O_2N—C_6H_4	83	99–100° (C_2H_5OH)	$C_{10}H_{10}N_2O_3S_2$ (270.2)	1618	232 sh (5200); 252 (6500); 292 sh (10600); 300 (10900)	270
2d	3-O_2N—C_6H_4	96	116–118° (C_2H_5OH)	$C_{10}H_{10}N_2O_3S_2$ (270.2)	1630	237 (12800); 301 (10600); 308 sh (10200)	270
2e	4-O_2N—C_6H_4	95	102–103° (C_2H_5OH)	$C_{10}H_{10}N_2O_3S_2$ (270.2)	1618	245 sh (9800); 267 (14000); 307 (14800)	270
2f	3-pyridyl	53	77–78° (hexane)	$C_9H_{10}N_2OS_2$ (226.2)	1622	236 (6500); 300 (8800); 306 sh (8500)	226
2g	2-thienyl	22	60–62° (acetone/hexane)	$C_8H_9NOS_3$ (231.2)	1610	279 (11000); 307 sh (12900); 318 (15000)	231
2h	2-H_3C—C_6H_4	55	68–69° (C_2H_5OH/hexane)	$C_{11}H_{13}NOS_2$ (239.2)	1620	250 (11800); 290 (9800)	239
2i	1-naphthyl	58	73–75° (acetone/hexane)	$C_{14}H_{13}NOS_2$ (275.3)	1645	215 (39700); 242 (16700); 320 sh (10100); 326 (10200)	275
2j	C_6H_5	43	46–47° (acetone/hexane)	46°[3]	1620	248 (15100); 285 (14200); 305 sh (13000)	225
2k	3-H_3C—C_6H_4	77	oil	$C_{11}H_{13}NOS_2$ (239.2)	1635[b]	253 (12300); 290 (12300); 307 sh (10100)	239
2l	4-H_3C—C_6H_4	61	60–61° (hexane)	$C_{11}H_{13}NOS_2$ (239.2)	1620	259 (12100); 281 sh (11000); 305 sh (10200)	239
2m	2-H_3CO—C_6H_4	47	85–87° (acetone/hexane)	$C_{11}H_{13}NO_2S_2$ (255.2)	1630	249 (11900); 300 (8600)	255
2n	4-Cl—C_6H_4	87	78–79° (ether/hexane)	$C_{10}H_{10}ClNOS_2$ (259.8)	1645	259 (13100); 288 (12000); 305 (12600)	259
2o	4-H_3CO—C_6H_4	64	65–66° (hexane)	$C_{11}H_{13}NOS_2$ (255.2)	1620	220 sh (5600); 284 (7800); 309 (7200)	255
2p	4-C_2H_5O—C_6H_4	50	63–64° (ether/hexane)	$C_{12}H_{15}NO_2S_2$ (269.3)	1610	221 (8100); 285 (11700); 310 (10800)	269
2q	2-furyl	55	114–115° (C_2H_5OH)	$C_8H_9NO_2S_2$ (215.2)	1625	285 sh (9200); 315 (13600)	215

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[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.28, H ±0.19, N ±0.23, S ±0.48).

[b] Film.

Table 2. 3-Aryl-5-methylthio-1*H*-1,2,4-triazoles **6a–q**

Compound	Ar	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a] or Lit. m.p. [°C]	U.V. (C_2H_5OH) λ [nm] (ε)	M.S. *m/e* (M^+)
6a	2-$C_2H_5O—C_6H_4$	71	142–143° (acetone/hexane)	$C_{11}H_{13}N_3OS$ (235.3)	241 (10400); 264 (6200); 267 sh (5800); 297 (6800); 302 sh (6200)	235
6b	2-$Cl—C_6H_4$	81	109–111° (acetone/hexane)	—[15]	232 sh (10200); 257 sh (5300)	225
6c	2-$O_2N—C_6H_4$	78	125–126° (acetone/hexane)	$C_9H_8N_4O_2S$ (236.2)	235 sh (10700)	236
6d	3-$O_2N—C_6H_4$	93	149–150° (acetone/hexane)	$C_9H_8N_4O_2S$ (236.2)	226 (15300); 255 (13600)	236
6e	4-$O_2N—C_6H_4$	65	215–216° (C_2H_5OH)	200–202°[14]	225 sh (4600); 272 sh (5100); 313 (8200)	236
6f	3-pyridyl	45	174–175° (C_2H_5OH/H_2O)	$C_8H_8N_4S$ (192.2)	225 (12700); 260 sh (6000)	192
6g	2-thienyl	81	172–173° (acetone/hexane)	$C_7H_7N_3S_2$ (197.3)	248 (10500); 255 sh (9800); 279 (11800)	197
6h	2-$H_3C—C_6H_4$	95	77–78° (acetone/hexane)	$C_{10}H_{11}N_3S$ (205.3)	232 sh (9100); 248 sh (6600)	205
6i	1-naphthyl	72	186–188° (C_2H_5OH)	$C_{13}H_{11}N_3S$ (241.3)	224 (69200); 295 (12400)	241
6j	C_6H_5	85	158–159° (acetone/hexane)	162°[10]	236 (13500); 260 sh (8300)	191
6k	3-$H_3C—C_6H_4$	63	100–101° (acetone/hexane)	$C_{10}H_{11}N_3S$ (205.3)	240 (12900); 263 sh (8700)	205
6l	4-$H_3C—C_6H_4$	91	155–156° (acetone/hexane)	$C_{10}H_{11}N_3S$ (205.3)	242 (6600); 260 sh (5000)	205
6m	2-$H_3CO—C_6H_4$	95	201–202° (acetone/hexane)	—[15]	241 (15000); 265 (9400); 275 (8800); 297 (10500); 304 sh (9600)	221
6n	4-$Cl—C_6H_4$	95	153–154° (acetone/hexane)	154°[8]	242 (17100); 265 sh (12600)	225
6o	4-$H_3CO—C_6H_4$	77	128–129° (acetone/hexane)	126°[7]	255 sh (15300); 266 (15800)	221
6p	4-$C_2H_5O—C_6H_4$	98	183–184° (acetone/hexane)	—[11]	255 sh (12500); 267 (13300)	235
6q	2-furyl	85	153–154° (H_2O)	147–148°[12]	218 (6100); 257 (11800); 264 sh (11400)	181

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.29, H ±0.23, N ±0.27, S ±0.43).

Dimethyl *N*-Aroylcarbimidodithioates 2a–g; General Procedure:

A mixture of amide **1a–g** (0.01 mol), sodium hydride (1 g; 50% dispersion in oil; 0.02 mol), and tetrahydrofuran (40 ml) is stirred at −10 to 0 °C for 0.5 to 1 h, and then carbon disulfide (2.5 g, 0.033 mol) is added. After an additional 0.5 to 1 h of stirring, a solution of methyl iodide (4.5 g, 0.032 mol) in tetrahydrofuran (10 ml) is added and the mixture is stirred at −10 to 0 °C for 3 h. Ice and water (~100 g) are added and the aqueous solution is extracted with benzene (30×2 ml). The benzene extract is dried with magnesium sulfate. After removal of solvents, the yellow solid product is collected and recrystallized (Table 1). In the case of **2a**, the yellow oil is purified by column chromatography on silica gel (80% benzene/20% ethyl acetate as eluent).

Dimethyl *N*-Aroylcarbimidodithioates 2h–q; General Procedure:

A mixture of amide **1h–q** (0.01 mol), tetrahydrofuran (40 ml), carbon disulfide (3 g, 0.039 mol), methyl iodide (4.5 g, 0.32 mol), and sodium hydride (1 g; 50% dispersion in oil; 0.02 mol) is stirred at room temperature for 1–4 h (**1h–n**) or refluxed for 4 h (**1o–q**) (Table 1). The reaction mixture is worked up as described for the preparation of **2a–g**. In the case of **2k**, the yellow oil is worked up as described for the preparation of **2a**.

***N*-(2-Ethoxybenzoyl)-dithiocarbamic Acid (3a):**

The reaction of 2-ethoxybenzamide (**1a**) with sodium hydride and then carbon disulfide is conducted as described for the preparation of **2a–g**. Ice and water (~100 g) are added to the reaction mixture, and the whole is washed with benzene (40 ml). The aqueous portion is separated and acidified with 2 normal hydrochloric acid (~15 ml) with cooling in ice. The yellow precipitate is collected, washed with water, and dried; yield: 0.85 g (35%); m.p. 122–123 °C.

$C_{10}H_{11}NO_2S_2$	calc.	C 49.77	H 4.59	N 5.80	S 26.57
(241.3)	found	49.62	4.42	5.64	26.31

I.R. (KBr): ν=3240 (NH); 2460 (SH); 1680 cm^{-1} (C=O).

U.V. (C_2H_5OH): λ_{max}=266 (ε=15300); 315 nm (11600).

***N*-(2-Furoyl)-dithiocarbamic Acid (3q):**

A mixture of 2-furoyl amide (**1q**; 1.1 g, 0.01 mol), tetrahydrofuran (40 ml), and sodium hydride (1 g; 50% dispersion in oil; 0.02 mol) is refluxed for 30 min, and to this carbon disulfide (5 g, 0.066 mol) is added. The mixture is refluxed for 3 h and worked up as described for the preparation of **3a**. The orange precipitate is collected [yield: 0.9 g (48%)], and recrystallized from ether/hexane to give yellow crystals; m.p. 77–79 °C (dec.).

$C_6H_5NO_2S_2$	calc.	C 38.49	H 2.69	N 7.48	S 34.25
(187.2)	found	38.69	2.65	7.29	34.48

I.R. (KBr): ν=3330 (NH); 1695 cm^{-1} (C=O).

U.V. (C_2H_5OH): λ_{max}=253 (ε=9100); 286 (16900); 315 (sh) nm (9300).

Bis[*N*-(2-ethoxybenzoyl)-thiocarbamoyl] Disulfide (4):

A solution of **2a** (0.65 g, 0.0027 mol) in tetrahydrofuran (30 ml)/ethanol (10 ml) is kept for 2 days at room temperature. The yellow crystals are collected and washed with ethanol; yield: 0.38 g (59%); m.p. 137–138 °C.

$C_{20}H_{20}N_2O_4S_4$	calc.	C 49.98	H 4.19	N 5.83	S 26.68
(480.6)	found	50.21	4.33	5.55	27.00

I.R. (KBr): ν=3240 (NH); 1652 cm^{-1} (C=O).

U.V. ($CHCl_3$): λ_{max}=272 (ε=21700); 295 (16000); 321 nm (15700).

Bis[2-ethoxybenzoyl] Disulfide (5):

A solution of **4** (0.65 g, 0.0014 mol) in pyridine (6 ml) is warmed at 60 °C for ~5 min until the color changes from yellow to colorless. Water (14 ml) is added and the solution is cooled. The white precipitate is collected [yield: 0.38 g (78%)] and recrystallized from ethanol/ethyl acetate; m.p. 137–139 °C.

$C_{18}H_{18}O_4S_2$	calc.	C 59.65	H 5.01	S 17.69
(362.5)	found	59.62	5.00	17.84

I.R. (KBr): $\nu = 1665, 1647\ cm^{-1}$ (C=O).

U.V. (C_2H_5OH): $\lambda_{max} = 256$ ($\varepsilon = 19000$); 316 nm (12000).

3-Aryl-5-methylthio-1*H*-1,2,4-triazoles 6a–q; General Procedure:

A mixture of **2** (0.002 mol), ethanol (20 ml), and 80% hydrazine hydrate (0.5 g, 0.008 mol) is refluxed for 3 h. To the reaction mixture ice and water (~100 g) and then 2 normal hydrochloric acid (~5 ml) are added with cooling in ice. The white precipitate is collected and recrystallized. In the case of **6c** or **6f**, the acidic solution is extracted with chloroform (30 ml) and then ethyl acetate (30 ml), and the combined extracts are concentrated (Table 2).

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