Pyridinethiones. XV. 3-Methylthio-2-pentene-1,5-diones as Synthons for 4-Methylthio-2(1*H*)-pyridinethiones, and Synthesis of 4-Methylene-1,4-dihydropyridines

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Starting from α-oxoketene dithioacetals the 3-methylthio-1,5-pentenedione enolates **4** obtained from ketones **3** give 4-methylthio-2(1*H*)-pyridinethiones with isothiocyanates. Enolates **4** can be alkylated with methyl iodide at C-2, giving 5-methyl-4-methylthio-2-(1*H*)-pyridinethiones with isothiocyanates. The *S*-alkylated pyridinethiones react with the anion of malodinitrile, giving 4-(1,1-dicyanomethylene)-1,4-dihydropyridines.

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1,5-Pentenediones and especially the stable 1,3,5-triaryl-1,5-pentenediones are usually prepared from pyrylium salts [1]. The anions of such 1,5-pentenediones react with isothiocyanates yielding 3-acyl-2(1*H*)-pyridinethiones in a general [4 + 2]-pyridine synthesis [2]. Methylthio substituted pyridines are of interest as the methylthio moiety may, in some cases, be displaced by nucleophiles making further functionalization within the pyridine ring possible [3]. Interestingly it has been reported [4] that 3-methoxy-4-methylthio-2-piperidinethione which is a reduced 4-methylthiopyridine is a natural product and a constituent in the sukurajima radish.

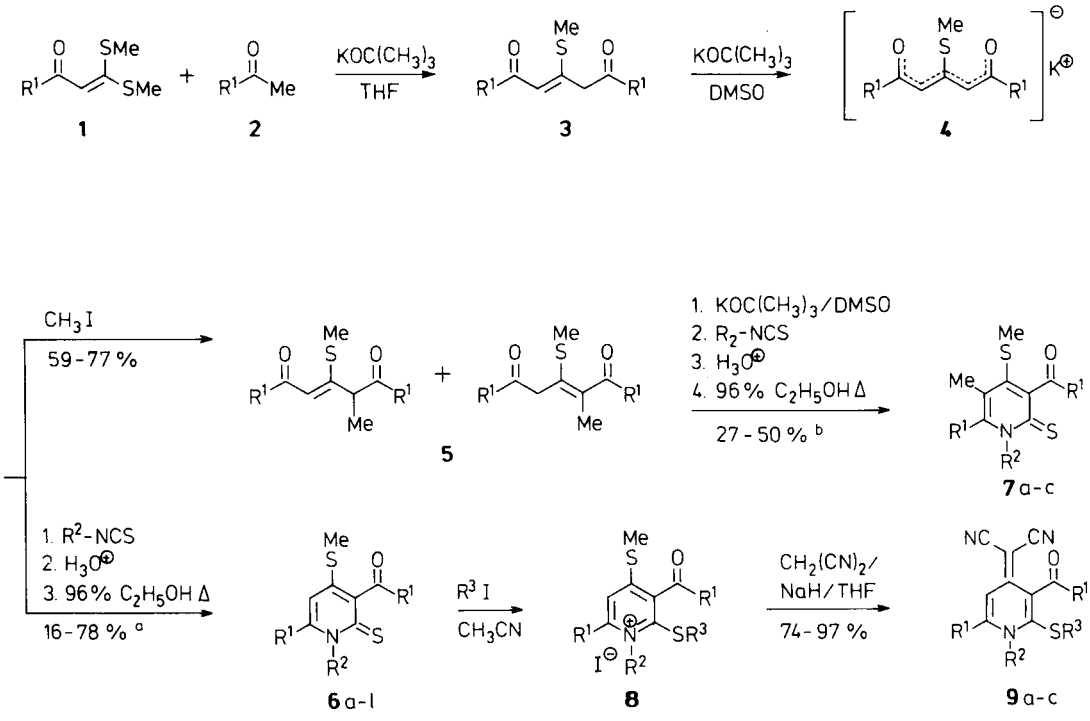
However, in general sulfide groups in pyridines are not readily displaced by nucleophiles [5] without additional activation of the pyridine ring facilitated by one or a combined action of the following effects; electron withdrawing substituents, quarternization and complex formation [6].

In our previous paper [2] we have shown that in the case

Table 1

Reaction Conditions and Spectral Data for Pyridinethiones **6a-l**

Product **6**	Reaction time/hours (temperature 0°)	IR (KBr) [cm^{-1}] ν (C=O)	UV (CH_3CN) λ [nm] (log ε)	^{1}H-NMR [ppm] (DMSO-d_6/TMS int) δ
6a	see Experimental	1650	258 (4.34), 296 (4.56), 413 (3.89)	2.58 (s, 3H, SCH_3), 7.09 (s, 1H, CH), 6.9-8.0 (m, 11H, H arom)
6b	3(60)	1650	258 (4.21), 296 (4.43), 414 (3.73)	2.58 (s, 3H, SCH_3), 7.10 (s, 1H, CH), 7.0-8.0 (m, 10H, H arom)
6c	3(40)	1640	261 (4.33), 414 (3.85)	2.58 (s, 3H, SCH_3, 3.76 (s, 3H, OCH_3), 7.08 (s, 1H, CH) 6.9-8.0 (m, 10H, H arom)
6d	1½(60)	1650	301 (4.57), 428 (3.86)	2.61 (s, 3H, SCH_3), 7.30 (s, 1H, CH), 6.5-8.0 (m, 10H, H arom)
6e	3(40)	1660	245 (4.71), 289 (4.78), 397 (4.17)	2.51 (s, 3H, SCH_3), 6.92 (s, 1H, CH), 7.15-7.95 (m, 15H, H aryl)
6f	1½(60)	1660	244 (4.39), 290 (4.47), 398 (3.93)	2.52 (s, 3H, SCH_3), 6.94 (s, 1H, CH), 7.25-7.95 (m, 14H, H aryl)
6g	3(40)	1670	246 (4.42), 290 (4.49), 396 (3.89)	2.03 (s, 3H, CH_3), 2.53 (s, 3H, SCH_3), 6.93 (s, 1H, CH), 7.09-7.90 (m, 14H, H aryl)
6h	3(45)	1670	260 (4.70), 290 (4.64), 402 (4.06)	2.52 (s, 3H, SCH_3), 6.97 (s, 1H, CH), 7.23-7.87 (m, 13H, H aryl)
6i	2(40)	1665	253 (4.73), 298 (4.83), 399 (4.22)	2.20 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.49 (s, 3H, SCH_3), 6.85 (s, 1H, CH), 7.01-7.83 (m, 13H, H aryl)
6j	2(40)	1660	260 (4.66), 290 (4.77), 400 (4.14)	2.24 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.50 (s, 3H, SCH_3), 6.87 (s, 1H, CH), 7.07-7.83 (m, 12H, H aryl)
6k	3(40)	1660	287 (4.70), 400 (4.00)	2.50 (s, 3H, SCH_3), 3.68 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.84 (s, 1H, CH), 6.75-7.88 (m, 13H, H aryl)
6l	3(40)	1660	287 (4.64), 398 (3.96)	2.51 (s, 3H, SCH_3), 3.69 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.85 (s, 1H, CH), 6.76-7.82 (m, 12H, H aryl)



a, **6a** was prepared without isolating **3**
b, **7c** was prepared without isolating **5**

Compound	R^1	R^2
6a	2-thienyl	C_6H_5
6b	2-thienyl	4-Cl-C_6H_4
6c	2-thienyl	4-CH_3O-C_6H_4
6d	2-furyl	4-Cl-C_6H_4
6e	C_6H_5	C_6H_5
6f	C_6H_5	4-Cl-C_6H_4
6g	C_6H_5	2-CH_3-C_6H_4
6h	C_6H_5	4-Br-C_6H_4
6i	4-CH_3-C_6H_4	C_6H_5
6j	4-CH_3-C_6H_4	4-Cl-C_6H_4
6k	4-CH_3O-C_6H_4	C_6H_5
6l	4-CH_3O-C_6H_4	4-Cl-C_6H_4

Compound	R^1
5a	C_6H_5
5b	2-thienyl
5c	2-furyl

Compound	R^1	R^2
7a	C_6H_5	C_6H_5
7b	2-furyl	4-Cl-C_6H_4
7c	4-Me-C_6H_4	C_6H_5

Compound	R^1	R^2	R^3
9a	2-thienyl	4-Cl-C_6H_4	Me
9b	C_6H_5	C_6H_5	Et
9c	C_6H_5	C_6H_5	Me

of 3-acyl-2,4-di(methylthio)pyridinium salts, nucleophiles such as the malodinitrile anion reacts regioselectively at the pyridine C-4 position.

In order to enable the preparation of other 2,4-di(methylthio)pyridines we now report the use of ketenedithioacetals for the synthesis of 2(1*H*)-pyridinethiones.

Ketene dithioacetal derivatives are versatile starting materials for the synthesis of numerous alkylthio substituted heterocycles [7].

Potts *et al.* [8] have shown that the ketones **3** and anions **4** are readily available and hence we can report the convenience of these starting materials for a general synthesis of 3-acyl-4-methylthio-2(1*H*)-pyridinethiones. This method is advantageous since the required 1,5-pentenedione anions **4** can be prepared directly from acyclic compounds without previous formation of a pyrylium ring.

Table 2

Spectral Data for 5-Methyl-2(1*H*)-Pyridinethiones **7a-c**

Product 7	IR (KBr) [cm^{-1}] ν (C=O)	UV (CH_3CN) λ [nm] (log ϵ)	^{1}H-NMR [ppm] (DMSO-d_6/TMS int) δ [ppm]
7a	1665	239 (4.40) 2.94 (4.24) 412 (3.89)	2.01 (s, 3H), 2.28 (s, 3H), 7.08-7.96 (m, 15H)
7b	1660	277 (4.53) 297 (4.51) 4.20 (3.97)	2.14 (s, 3H), 2.33 (s, 3H), 6.4-8.1 (m, 10H), 1.99 (s, 3H), 2.19 (s, 3H)
7c	1660	249 (4.61) 296 (4.49) 413 (4.14)	2.27 (s, 3H), 2.29 (s, 3H), 2.39 (s, 3H), 7.03-7.83 (m, 13H)

Table 3

Spectral Data for 4-(1,1-Dicyanomethylene)-1,4-Dihydropyridines **9a-c**

Product 9	IR (KBr) [cm^{-1}] ν (C=N) ν (C=O)	UV (CH_3CN) λ [nm] (log ϵ)	^{1}H-NMR [ppm] (TFA/TMS int)
9a	2180, 1635	a	1.62 (s, 3H), 7.00-8.30 (m, 11H)
9b	2200, 1655	250 (4.30) 385 (4.44)	0.42 (m, 3H), 1.40-2.10 (m, 2H), 6.90-8.10 (m, 16H)
9c	2195, 2205, 1680	250 (4.27) 384 (4.42)	1.29 (s, 3H), 6.90-8.10 (m, 16H)

[a] Compound **9a** was insoluble in acetonitrile.

Table 4

^{13}C-NMR Spectral Data for Pyridinethiones **6a-k** [a] and **7a-c** in DMSO-d_6/TMS int δ [ppm]

Product	C=O	C=S	CH	S-CH_3	Others
6a	184.00	175.76	111.88	13.75	
6b	184.00	175.70	112.04	13.78	
6c	183.93	176.15	111.61	13.75	55.21 (OCH_3)
6d	178.75	175.83	—	13.76	
6e	191.41	175.07	111.30	13.70	
6f	191.41	174.03	111.35	13.21	
6g	191.26	174.21	111.63	13.68	17.43 (CH_3-aryl)
6h	190.38	175.03	111.52	13.75	
6i	191.06	175.14	111.29	13.65	20.59, 21.17 (CH_3-aryl)
6j	191.06	175.06	111.39	13.68	20.64, 21.19 (CH_3-aryl)
6k	190.13	175.12	111.28	13.59	54.98, 55.38 (OCH_3-aryl)
7a	178.42	176.14		16.52	18.01 (CH_3)
7b	190.85	174.92		16.99	17.95 (CH_3)
7c	190.57	174.97		17.03	17.94 (CH_3) 20.66, 21.17 (CH_3-aryl)

[a] Compound **6l** was insoluble in DMSO-d_6.

Thus, the anion **4** [8] was dissolved in dimethylsulfoxide with one equivalent of the required isothiocyanate followed by stirring at 40-60° for approximately 3 hours. Addition of water and hydrochloric acid to neutrality followed by reflux of the precipitated crystals in ethanol gave the new pyridines **6** in acceptable yields.

In contrast to previous reports [8] we found that it was in fact possible to alkylate [2] the anions **4** with methyl iodide, thus anions **4** gave diketones **5**. For the diketone **3** (R = C_6H_5) the ^{1}H-nmr spectrum showed the presence of a (4:1) mixture of 1,5-diphenyl-4-methyl-3-methylthio-2-pentene-1,5-dione and 1,5-diphenyl-2-methyl-3-methylthio-2-pentene-1,5-dione in compound **5a**. When R was a heteryl group, nearly 100% of the methylated diketone appeared as the 4-methyl-3-methylthio-2-pentene-1,5-dione isomer (**5b-c**). Treatment of these diketones with potassium *t*-butanolate followed by isothiocyanate as described above gave the 5-methylpyridinethiones **7**.

In order to observe regioselectively effects within the nucleophilic reactions of the 2,4-di(methylthio)pyridinium system the *S*-alkylated pyridinium iodides **8** were prepared in high yields from the 2(1*H*)-pyridinethiones **6** with an appropriate alkyl iodide in acetonitrile. The resulting salts were found to be slightly unstable and the crude products were therefore used directly in the next step without purifying, giving the 4-(1,1-dicyanomethylene)-1,4-dihydropyridines **9** in high yields.

The ^{1}H and ^{13}C-nmr spectra of the new methylenepyridines **9** corresponded well with the data reported [3] previously for related compounds, but clear indication of regioselectivity was obtained only when the 2(1*H*)-pyridinethione **6e** was reacted with ethyliodide followed by reaction with the malodinitrile anion. In this case the resulting 4-methylenepyridine **9b** contained the 2-ethylthio group, and thus confirmed the high regioselectivity in this type of reaction which probably is a result of a combination of steric and electronic effects.

EXPERIMENTAL

Microanalyses were carried out by NOVO A/S Bagsvaerd, Denmark. The ir spectra were obtained on a Perkin-Elmer 580; the uv spectra were obtained on a Varian CARY 219; ^{1}H and ^{13}C-nmr spectra were obtained on a 250 MHz Bruker AC 250 spectrometer. The ms spectra were obtained on a Varian MAT 311 A. Melting points are uncorrected, and were obtained with a Büchi apparatus. Yields are given for analytical pure products.

The required α-oxoketene dithioacetals **1** and 2-pentene-1,5-diones **3**, were prepared as described by Potts *et al.* [8].

1,5-Bis(2-furyl)-3-methylthio-2-pentene-1,5-dione **3**, (R^1 = 2-furyl).

Potassium *t*-butoxide (100 mmoles) and 2-acetylfuran (50 mmoles) were stirred in tetrahydrofuran (125 ml, 20°) for 10 minutes. 3,3-Bis(methylthio)-1-(2-furyl)-2-propen-1-one (50 mmoles) was added, and the stirring continued for 75 minutes. Water (300 ml, 0°) and glacial acetic acid (70 ml) were added to the precipitated salt, and the resulting mixture was poured into water (1750 ml, 0°). The precipitated compound was iso-

lated, dried and recrystallized from absolute ethanol, yield, 10.4 g (75%), mp 127-128°; ms: m/z (relative intensity %) 276 (9), 261 (8), 229 (8), 95 (100); ir (potassium bromide): ν = 1680, 1625 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform/TMS): 2.51 (s, 3H, SCH_3), 4.46 (s, 2H, CH_2), 6.7-7.6 ppm (m, 6H, H arom).

Anal. Calcd. for $C_{14}H_{12}O_2S$: C, 60.86; H, 4.38. Found: C, 61.17; H, 4.38.

4-Methylthio-1-phenyl-3-(2-thenoyl)-6-(2-thienyl)-2-thioxo-1,2-dihydropyridine [4-Methylthio-1-phenyl-3-(2-thenoyl)-6-(2-thienyl)-2(1*H*)-pyridinethione] (**6a**).

Sodium 2-methyl-2-butanolate (1.5 molar in toluene, 30 ml) was dropped into a cold (0°) solution of 2-acetylthiophene (20 mmoles) in anhydrous tetrahydrofuran (100 ml) with stirring for 10 minutes. 3,3-Bis(methylthio)-1-(2-thienyl)-2-propen-1-one (20 mmoles) was added, and the stirring continued for 20 hours. The precipitated red sodium salt was collected, washed with ether (300 ml), dried *in vacuo*, and dissolved in dry dimethylsulfoxide (60 ml, 22°). Phenylisothiocyanate (19.2 mmoles) was added, and the mixture was stirred for 2 hours (42°). The resulting dark red solution was poured into water (600 ml, 0°) and treated with 1 molar hydrochloric acid (to *p*H = 6). The precipitate was isolated, washed with water and dried. The crude product was refluxed in toluene (350 ml, 1 hour) and the yellow crystals were filtered from the hot solution and recrystallized from acetonitrile, yield, 4.4 g (52%), mp >260°; ms: m/z (relative intensity, %) 425 (100), 410 (6), 396 (98), 350 (18), 111 (50), 77 (54).

Anal. Calcd. for $C_{21}H_{15}NOS_4$: C, 59.26; H, 3.55; N, 3.29. Found: C, 59.50; H, 3.56; N, 3.20.

General Procedure for the Preparation of 2-(1*H*)-Pyridinethiones **6b-l**.

Potassium *t*-butoxide (10 mmoles) and 1,5-bis(aryl or 2-heteryl)-3-methylthio-2-pentene-1,5-dione (**3**) (10 mmoles) were stirred in dry dimethylsulfoxide (40 ml, 22°) for 10 minutes. The required arylisothiocyanate (10 mmoles) (4-chlorophenylisothiocyanate was dissolved in 5 ml dimethylsulfoxide before addition) was added to the red solution, and the stirring was continued for the time and temperature indicated in Table 1. The reaction mixture was poured into water (400 ml, 0°) with stirring, and treated with 1 molar hydrochloric acid (to *p*H = 7). The precipitate was collected, dried, and triturated in 96% ethanol (50 ml, 60°) for 4 hours, and the resulting suspension filtered hot. The yellow crystals were recrystallized from acetonitrile or toluene.

1-(4-Chlorophenyl)-4-methylthio-3-(2-thenoyl)-6-(2-thienyl)-2-thioxo-1,2-dihydropyridine [1-(4-Chlorophenyl)-4-methylthio-3-(2-thenoyl)-6-(2-thienyl)-2 (1*H*)-pyridinethione] (**6b**).

This compound was recrystallized from acetonitrile, yield, 3.6 g (78%), mp >260°; ms: m/z (relative intensity, %) 461 (52), 459 (99), 444 (6), 432 (46), 430 (87), 384 (15), 111 (100), 83 (11), 75 (13).

Anal. Calcd. for $C_{21}H_{14}ClNOS_4$: C, 54.83; H, 3.07; N, 3.04. Found: C, 55.20; H, 3.04; N, 2.98.

1-(4-Methoxyphenyl)-4-methylthio-3-(2-thenoyl)-6-(2-thienyl)-2-thioxo-1,2-dihydropyridine [1-(4-Methoxyphenyl)-4-methylthio-3-(2-thenoyl)-6-(2-thienyl)-2(1*H*)-pyridinethione] (**6c**).

This compound was recrystallized from acetonitrile, yield, 0.73 g (16%), mp >260°; ms: m/z (relative intensity, %), 455 (100), 440 (5), 426 (68), 380 (10), 111 (75), 92 (16), 77 (17).

Anal. Calcd. for $C_{22}H_{17}NO_2S_4$: C, 57.99; H, 3.76; N, 3.07. Found: C, 58.39; H, 3.76; N, 3.15.

1-(4-Chlorophenyl)-3-(2-furoyl)-6-(2-furyl)-4-methylthio-2-thioxo-1,2-dihydropyridine [1-(4-Chlorophenyl)-3-(2-furoyl)-6-(2-furyl)-4-methylthio-2(1*H*)-pyridinethione] (**6d**).

The crude product gave a satisfactory analysis, yield, 2.9 g (68%), mp >260°; ms: m/z (relative intensity, %), 429 (23), 427 (50), 414 (45), 412 (100), 399 (63), 368 (38), 366 (84), 111 (38), 95 (48).

Anal. Calcd. for $C_{21}H_{14}ClNO_3S_2$: C, 58.94; H, 3.30; N, 3.27. Found: C, 58.90; H, 3.24; N, 3.16.

3-Benzoyl-1,6-diphenyl-4-methylthio-2-thioxo-1,2-dihydropyridine [3-Benzoyl-1,6-diphenyl-4-methylthio-2(1*H*)-pyridinethione] (**6e**).

This compound was recrystallized from acetonitrile, yield, 2.57 g (62%), mp 259-260°; ms: m/z (relative intensity, %), 413 (52), 398 (2), 384 (100), 368 (9), 105 (12), 77 (57).

Anal. Calcd. for $C_{25}H_{19}NOS_2$: C, 72.60; H, 4.63; N, 3.39. Found: C, 72.93; H, 4.65; N, 3.37.

3-Benzoyl-1-(4-chlorophenyl)-4-methylthio-6-phenyl-2-thioxo-1,2-dihydropyridine [3-Benzoyl-1-(4-chlorophenyl)-4-methylthio-6-phenyl-2(1*H*)-pyridinethione] (**6f**).

This compound was recrystallized from acetonitrile, yield, 2.2 g (49%), mp 258-259°; ms: m/z (relative intensity, %), 449 (23), 447 (50), 432 (3), 420 (44), 418 (100), 105 (24), 77 (49).

Anal. Calcd. for $C_{25}H_{16}ClNOS_2$: C, 67.02; H, 4.05; N, 3.13. Found: C, 67.06; H, 4.04; N, 3.11.

3-Benzoyl-1-(2-methylphenyl)-4-methylthio-6-phenyl-1,2-thioxo-1,2-dihydropyridine [3-Benzoyl-1-(2-methylphenyl)-4-methylthio-6-phenyl-2(1*H*)-pyridinethione] (**6g**).

This compound was recrystallized from toluene, yield, 3.2 g (74%), mp >260°; ms: m/z (relative intensity, %), 427 (31), 412 (16), 398 (44), 322 (100), 105 (29), 91 (37), 77 (67), 65 (21).

Anal. Calcd. for $C_{26}H_{21}NOS_2$: C, 73.03; H, 4.95; N, 3.28. Found: C, 73.29; H, 5.01; N, 3.11.

3-(4-Bromobenzoyl)-6-(4-bromophenyl)-4-methylthio-1-phenyl-2-thioxo-1,2-dihydropyridine [3-(4-Bromobenzoyl)-6-(4-bromophenyl)-4-methylthio-1-phenyl-2(1*H*)-pyridinethione] (**6h**).

This compound was recrystallized from toluene, yield, 2.2 g (39%), mp >260°; ms: m/z (relative intensity, %), 571 (54), 556 (2), 542 (100), 185 (12), 157 (14), 77 (41).

Anal. Calcd. for $C_{25}H_{17}Br_2NOS_2$: C, 52.55; H, 3.00; N, 2.45. Found: C, 52.36; H, 3.05; N, 2.31.

3-(4-Methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-1-phenyl-2-thioxo-1,2-dihydropyridine [3-(4-Methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-1-phenyl-2(1*H*)-pyridinethione] (**6i**).

This compound was recrystallized from toluene, yield, 2.3 g (52%), mp 259-261°; ms: m/z (relative intensity, %), 441 (67), 426 (3), 412 (100), 221 (17), 119 (8), 91 (14).

Anal. Calcd. for $C_{27}H_{23}NOS_2$: C, 73.44; H, 5.25; N, 3.17. Found: C, 73.81; H, 5.28; N, 3.03.

1-(4-Chlorophenyl)-3-(4-methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-2-thioxo-1,2-dihydropyridine [1-(4-Chlorophenyl)-3-(4-methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-2(1*H*)-pyridinethione (**6j**).

This compound was recrystallized from toluene, yield, 2.4 g (50%), mp >260°; ms: m/z (relative intensity, %), 475 (60), 460 (3), 446 (100), 237 (20), 119 (14), 91 (23).

Anal. Calcd. for $C_{27}H_{22}ClNOS_2$: C, 68.12; H, 4.66; N, 2.94. Found: C, 68.50; H, 4.71; N, 2.78.

3-(4-Methoxybenzoyl)-6-(4-methoxyphenyl)-4-methylthio-1-phenyl-2-thioxo-1,2-dihydropyridine [3-(4-Methoxybenzoyl)-6-(4-methoxyphenyl)-4-methylthio-1-phenyl-2(1*H*)-pyridinethione] (**6k**).

This compound was recrystallized from acetonitrile, yield, 2.1 g (45%), mp 257-258°; ms: m/z (relative intensity, %), 473 (58), 458 (4), 444 (100), 237 (12), 135 (21), 77 (21).

Anal. Calcd. for $C_{27}H_{23}NO_3S_2$: C, 68.47; H, 4.89; N, 2.96. Found: C, 68.33; H, 4.88; N, 3.02.

1-(4-Chlorophenyl)-3-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-4-methylthio-2-thioxo-1,2-dihydropyridine [1-(4-Chlorophenyl)-3-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-4-methylthio-2-(1*H*)-pyridinethione] (**6l**).

This compound was recrystallized from acetonitrile, yield, 3.5 g (71%), mp 252-253°; ms: m/z (relative intensity, %), 487 (29), 472 (18), 458 (33), 352 (100), 135 (32), 91 (14), 77 (18).

Anal. Calcd. for $C_{28}N_{25}NO_3S_2$: C, 68.96; H, 5.17; N, 2.87. Found: C, 68.81; H, 5.22; N, 3.14.

1,5-Bis(Aryl or 2-heteryl)-4-methyl-3-methylthio-2-pentene-1,5-dione or 1,5-Bis(aryl or heteryl)-2-methyl-3-methylthio-2-pentene-1,5-dione (**5**).

General Procedure.

The required 3-methylthio-2-pentene-1,5-dione **3** (10 mmoles) and potassium 2-methyl-2-butanolate (10 mmoles) were mixed in dry dimethyl sulfoxide (40 ml, 22°), with stirring for 15 minutes. Methyliodide (15 mmoles) was added, and the stirring continued for one hour (reaction temperature held nearly constant at 22°). The reaction mixture was poured into cold water (200 ml, 0°), from which an orange oil was precipitated. The water was decanted and the oil washed four times with water (4 × 100 ml), dissolved in methylene chloride (100 ml), dried with sodium sulphate, and concentrated *in vacuo*. The crude product was recrystallized from absolute ethanol, giving pale yellow crystals.

1,5-Diphenyl-4-methyl-3-methylthio-2-pentene-1,5-dione and 1,5-Diphenyl-2-methyl-3-methylthio-2-pentene-1,5-dione (**5a**).

This compound was obtained in a total yield of 2.4 g (77%), mp 78-82°; ms: m/z (relative intensity, %), 310 (2), 295 (13), 105 (100), 77 (43), ir (potassium bromide): ν 1685, 1630 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform/TMS): δ 1.42 (d, CH_3, J = 6.8 Hz), 2.02 (s, CH_3), 2.29 (s, SCH_3), 2.44 (s, SCH_3), 4.30 (s, CH_2), 6.10 (q, CH, J = 6.8 Hz), 6.79 (s, CH), 7.3-8.2 ppm (m, 10H, H arom).

Anal. Calcd. for $C_{19}H_{18}O_2S$: C, 73.52; H, 5.84. Found: C, 73.90; H, 5.93.

1,5-Bis(2-thienyl)-4-methyl-3-methylthio-2-pentene-1,5-dione (**5b**).

The general procedure gave **5b**, yield, 2.0 g (63%), mp 159-162°; ms: m/z (relative intensity, %), 322 (3), 307 (15), 275 (18), 111 (100), 83 (11), 39 (21); ir (potassium bromide): ν 1655, 1610 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform/TMS): δ 1.51 (d, 3H, CH_3, J = 6.9 Hz), 2.37 (s, 3H, SCH_3), 6.35 (q, 1H, CH, J = 6.9 Hz), 6.53 (s, 1H, CH, J = 6.9 Hz), 6.53 (s, 1H, CH), 7.0-7.9 ppm (m, 6H, H arom).

Anal. Calcd. for $C_{15}H_{14}O_2S_3$: C, 55.87; H, 4.38. Found: C, 56.08; H, 4.39.

1,5-Bis(2-furyl)-4-methyl-3-methylthio-2-pentene-1,5-dione (**5c**).

The general procedure gave **5c**, yield, 1.7 g (59%); ms 155-157°; ms: m/z (relative intensity, %), 290 (8), 275 (11), 243 (14), 95 (100); ir (potassium bromide): ν 1675, 1622 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform/TMS): δ 1.51 (d, 3H, CH_3, J = 7.0 Hz), 2.39 (s, 3H, SCH_3), 6.19 (q, 1H, CH, J = 7.0 Hz), 6.61 (s, 1H, CH), 6.4-7.6 ppm (m, 6H, H arom).

Anal. Calcd. for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86. Found: C, 62.28; H, 4.86.

3-Benzoyl-1,6-diphenyl-5-methyl-4-methylthio-2-thioxo-1,2-dihydropyridine [3-Benzoyl-1,6-diphenyl-5-methyl-4-methylthio-2(1*H*)-pyridinethione] (**7a**).

Potassium *t*-butoxide (3.2 mmoles) and **5a** (3.2 mmoles) was stirred in dry dimethylsulfoxide (20 ml) for 15 minutes. Phenylisothiocyanate (3.2 mmoles) was added, and the stirring was continued for one hour (40°). The reaction mixture was poured into water (200 ml, 0°) and treated with 1 molar hydrochloric acid (to *p*H = 7). The precipitated yellow compound was isolated, washed with water and triturated in 96% ethanol (25 ml) for two hours (60°), and the resulting suspension was filtered hot. The yellow crystals were recrystallized from ethanol:acetonitrile (1:1), yield, 0.7 g (50%), mp 231-232°; ms: m/z (relative intensity, %), 427 (60), 412 (3), 398 (100), 382 (13), 352 (17), 105 (11), 77 (27).

Anal. Calcd. for $C_{26}H_{21}NOS_2$: C, 73.03; H, 4.95; N, 3.28. Found: C, 73.24; H, 4.98; N, 3.22.

1-(4-Chlorophenyl)-3-(2-furoyl)-6-(2-furyl)-5-methyl-4-methylthio-2-thioxo-1,2-dihydropyridine [1-(4-Chlorophenyl-3-(2-furoyl)-6-(2-furyl)-5-methyl-4-methylthio-2(1*H*)-pyridinethione] (**7b**).

Potassium *t*-butoxide (1.7 mmoles) and **5c** (1.7 mmoles) were stirred in dry dimethylsulfoxide (25 ml) for 10 minutes. 4-Chlorophenylisothiocyanate (1.7 mmoles) dissolved in dimethylsulfoxide (3 ml), was added to the red solution, and the stirring was continued for two hours (45°). The reaction mixture was poured into cold water (200 ml, 0°) and treated with 1 molar hydrochloric acid (to *p*H = 7). The precipitate was washed with water and triturated in 96% ethanol for 16 hours (45°), and the resulting suspension filtered hot. The yellow crystals were recrystallized from acetonitrile, yield, 0.2 g (27%), mp >260°; ms: m/z (relative intensity, %), 441 (25), 426 (100), 412 (35), 380 (30), 111 (47), 95 (70), 39 (60).

Anal. Calcd. for $C_{22}H_{16}ClNO_3S_2$: C, 59.79; H, 3.65; N, 3.17. Found: C, 60.01; H, 3.60; N, 3.37.

5-Methyl-3-(4-methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-1-phenyl-2-thioxo-1,2-dihydropyridine [5-Methyl-3-(4-methylbenzoyl)-6-(4-methylphenyl)-4-methylthio-1-phenyl-2(1*H*)-pyridinethione] (**7c**).

Potassium *t*-butoxide (13.8 mmoles) and 1,5-bis(4-methylphenyl)-3-methylthio-2-pentene-1,5-dione (13.8 mmoles) (**3**) (R = 4-methylphenyl) were mixed in dry dimethyl sulfoxide (50 ml) with stirring for 20 minutes. Methyl iodide (14 mmoles) was dropped into the red solution, and the stirring was continued for one hour (most of the colour disappeared). Another portion of potassium *t*-butoxide (15 mmoles) was added to the reaction mixture, and after 15 minutes with stirring, phenylisothiocyanate (15 mmoles) was added, and the stirring was continued for 2 hours (40°). The reaction mixture was poured into cold water (500 ml, 0°), treated with 1 molar hydrochloric acid (to *p*H = 7), and the precipitated yellow compound was collected, washed with water, triturated in 96% ethanol (30 ml, 60°) for one hour, filtered hot, and the resulting crystals were recrystallized from toluene (this compound crystallized with one mole of toluene), yield, 2.3 g (30%), mp 258-260°; ms: m/z (relative intensity, %), 455 (69), 441 (6), 426 (100), 380 (15), 228 (16), 119 (12), 91 (19).

Anal. Calcd. for $C_{28}H_{25}NOS_2$: C, 73.81; H, 5.33; N, 3.07. Found: C, 76.34; H, 5.99; N, 2.65. Calcd. for 1 mole of toluene: C, 76.74; H, 6.07; N, 2.55.

2-Alkylthio-3-(aroyl or heteroyl)-6-(aryl or heteryl)-4-methylthiopyridinium Iodides **8**. General Procedure.

The required pyridinethione (10 mmoles) and alkyl iodide (20 mmoles) were dissolved in dry acetonitrile (50 ml, 20°), and refluxed for 45 minutes. After cooling and concentration of the reaction mixture *in vacuo*, the precipitated iodides **8** were isolated by filtration, and used, without further purification, in the next step.

2-Alkylthio-1-aryl-3-(benzoyl or 2-thenoyl)-4-(1,1-dicyanomethylene)-6(phenyl or 2-thienyl)-1,4-dihydropyridine (**9**).

General Procedure.

Sodium hydride (5 mmoles) and malondinitrile (5 mmoles) were stirred in dry tetrahydrofuran (50 ml) at room temperature for 10 minutes, the pyridinium iodide **8** (5 mmoles) was added, and stirring was continued for 1 hour. The reaction mixture was poured into cold water (150 ml) and treated with dilute hydrochloric acid (1 molar). The precipitate was isolated and recrystallized in acetonitrile.

1-(4-Chlorophenyl)-4-(1,1-dicyanomethylene)-2-methylthio-3-(2-thenoyl)-6-(2-thienyl)-1,4-dihydropyridine (**9a**).

The general procedure gave **9a** as orange crystals, yield, 2.3 g (94%), mp >260°; ms: m/z (relative intensity, %), 493 (39), 491 (78), 476 (4), 125 (22), 111 (100).

Anal. Calcd. for $C_{24}H_{14}ClN_3OS_3$: C, 58.58; H, 2.87; N, 8.54. Found: C, 58.64; H, 2.84; N, 8.48.

3-Benzoyl-4-(1,1-dicyanomethylene)-1,6-diphenyl-2-ethylthio-1,4-dihydropyridine (**9b**).

The general procedure gave **9b** as yellow crystals, yield, 1.7 g (74%), mp >260°; ms: m/z (relative intensity, %), 459 (100), 445 (64), 430 (20), 416 (20), 402 (38), 105 (80), 77 (99).

Anal. Calcd. for $C_{29}H_{21}N_3OS$: C, 75.79; H, 4.61; N, 9.14. Found: C, 75.67; H, 4.52; N, 9.15.

3-Benzoyl-4-(1,1-dicyanomethylene)-1,6-diphenyl-2-methylthio-1,4-dihydropyridine (**9c**).

The general procedure gave **9c** as yellow crystals, yield, 2.2 g (97%), mp >260°, ms: m/z (relative intensity, %), 445 (96), 430 (4), 416 (44), 105 (46), 77 (100).

Anal. Calcd. for $C_{28}H_{19}N_3OS$: C, 75.48; H, 4.30; N, 9.43. Found: C, 75.81; H, 4.40; N, 9.37.

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