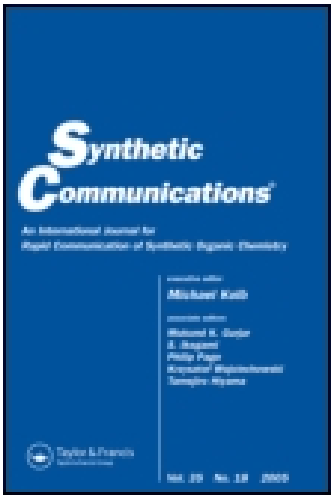

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A Convenient Procedure to Prepare 1, 4-Dithioaroyl Piperazines

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A CONVENIENT PROCEDURE TO PREPARE 1, 4- DITHIOAROYL PIPERAZINES

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ABSTRACT A simple, convenient and high-yield synthetic method for 1,4-dithioaroyl piperazines is reported. Aromatic aldehydes, anhydrous piperazine and elementary sulfur were used as starting synthetic materials. The reaction condition was mild.

Derivatives of piperazines have wide biological activities. However, only a few 1,4-dithioaroyl piperazines were prepared[1], some compounds exhibited antisecretory and antiulcer activities[2]. They were synthesized from corresponding 1,4-dibenzoyl piperazines[3], but the operation was difficult and the yield was unsatisfactory.

We were interested in the kind of compounds as medicines and corrosion inhibitors, and also as ligands possessing both hard and soft donor atoms. In connection with our before work[4], we now report a convenient and highly efficient synthesis of 1,4-dithioaroyl piperazines.

The synthetic route is outlined as Scheme 1. Aromatic aldehydes, anhydrous piperazines and elementary sulfur were used as starting synthetic materials. The anhydrous piperazine was obtained from hexahydrate piperazine by dehydrating with dried benzene. The reactions were carried out at 70~90°C for 2~3 h. The target compounds were easily obtained in 63~91% yield. The

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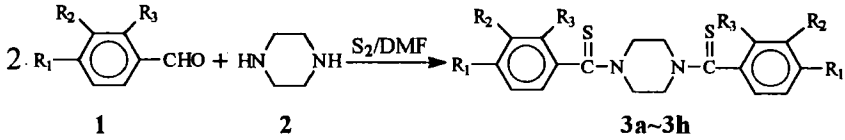
reaction conditions were listed in Table 1. The structures of all target products were confirmed by IR, ^{1}HNMR and elementary analysis (Table 2). The IR spectra of all products showed C=S absorption at 1202~1232 cm^{-1}.

Thus, We provide a simple, convenient synthetic method for 1,4-dithioaroyl piperazines. The biological activities of the products are to be tested.



Scheme 1 Synthetic route of 1,4-dithioaroyl piperazines

General procedure for preparation of 1,4-dithioaroyl piperazines: The aromatic aldehyde (10 mmol), anhydrous piperazine (5 mmol), elementary sulfur (5 mmol) and DMF (10 ml) were placed in a flask fitted a reflux condenser and magnetic stirrer. The mixture was stirred at the temperature indicated in Table 1, and the reaction was monitored by TLC. After cooled to room temperature, the crude product was filtered, washed with several drops of DMF and dried. The pure product was obtained after the crude product was refluxed in CS_2 for 30 min, cooled and filtered.

Table 1 Preparation of 1,4-dithioaroyl piperazines

Product	R_1, R_2, R_3	Reaction Time/Temp	yield (%)
3a	R_1=R_2=R_3=H	2h/80°C	86
3b	R_1,R_2=OCH_2O,R_3=H	3h/70°C	79
3c	R_1=OCH_3,R_2=R_3=H	2h/80°C	86
3d	R_1=R_2=OCH_3,R_3=H	3h/80°C	90
3e	R_1=OH,R_2=R_3=H	2h/80°C	88
3f	R_1=OH,R_2=OCH_3,R_3=H	2h/80°C	91
3g	R_1=NO_2,R_2=R_3=H	2h/90°C	77
3h	R_1=R_3=NO_2,R_2=H	3h/90°C	63

Table 2 Physical and Chemical data of Compound 3a~3h

Comp.	mp (°C)	molecular formula	Analysis(%) Calcd. (Found) C	H	N	IR(KBr) υ(cm^{-1})		^{1}HNMR (DMSO/TMS) δ(ppm)
3a	276~278	$C_{18}H_{18}N_2S_2$	66.22 (66.34)	5.56 (5.43)	8.58 (8.39)	1500 1300 760	1490 1220 700	3.66, 3.88, 4.24, 4.49 (m, 8H, $4CH_2N$), 7.29~7.44 (m, 10H,Ar-H)
3b	302~304	$C_{20}H_{18}N_2O_4S_2$	57.95 (57.98)	4.38 (4.53)	6.76 (6.34)	1492 1300 864	1438 1214 814	3.72, 3.91, 4.19, 4.40 (m,8H, $4CH_2N$), 5.97,6.09(s,4H, $2OCH_2O$), 6.86~6.97(m,6H, Ar-H)
3c	272~274	$C_{20}H_{22}N_2O_2S_2$	62.14 (62.24)	5.74 (5.58)	7.25 (7.23)	1600 1300 814	1480 1218	3.73, 3.93, 4.21, 4.44 (m,8H, $4CH_2N$), 3.77,3.80(s,6H, $2OCH_3$), 6.90~7.38(m, 8H, Ar-H)
3d	260~262	$C_{22}H_{26}N_2O_4S_2$	59.17 (59.50)	5.87 (5.88)	6.27 (6.12)	1600 1478 1232	1519 1290 820	3.72, 3.75, 3.78, 3.82 (s,12H, $4OCH_3$), 3.84, 3.93, 4.21, 4.42 (m,8H, $4CH_2N$), 6.93~6.97 (m, 6H,Ar-H)

(continued)

Table 2 Continued

Comp.	mp (°C)	molecular formula	Analysis(%) Calcd. (Found) C	H	N	IR(KBr) υ(cm^{-1})		^{1}HNMR (DMSO/TMS) δ(ppm)
3e	321~323	$C_{18}H_{18}N_2O_2S_2$	60.31 (60.45)	5.06 (5.12)	7.82 (7.43)	3218 1480 1202	1608 1300 831	3.74, 3.93, 4.19, 4.40 (m,8H, $4CH_2N$), 6.72~6.74 (m,4H,Ar-H), 7.23~7.24(m,4H,Ar-H), 9.96 (s,2H,2OH)
3f	334~336	$C_{20}H_{22}N_2O_4S_2$	57.39 (57.53)	5.30 (5.12)	6.70 (6.89)	3394 1483 1210	1602 1308 809	3.76, 3.80 (s,6H,$2OCH_3$), 3.82, 3.95,4.20, 4.41 (m,8H, $4CH_2N$), 6.75~6.96 (m,6H, Ar-H)
3g	133~135	$C_{18}H_{16}N_4O_4S_2$	51.92 (51.68)	3.87 (3.94)	13.46 (13.64)	3420 1408 1212	1598 1350 854	3.12~4.51 (m,8H,$4CH_2N$), 7.53~7.64 (m,4H,Ar-H), 8.22~8.31(m,4H,Ar-H)
3h	200~202	$C_{18}H_{14}N_6O_8S_2$	42.68 (42.95)	2.79 (2.63)	16.60 (16.31)	3422 1522 820	1627 1349 739	2.66~4.10 (m,8H,$4CH_2N$), 7.22~8.84 (m,6H,Ar-H)

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