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TETRAHEDRON

SYNTHESIS OF NEW 2*H*-1,4-THIAZINES AND THEIR DERIVATIVES UTILIZING *N,N*-(DI-*N*-ALKYL)-*N'*-ARYLTHIOCARBAMOYLAMIDINES

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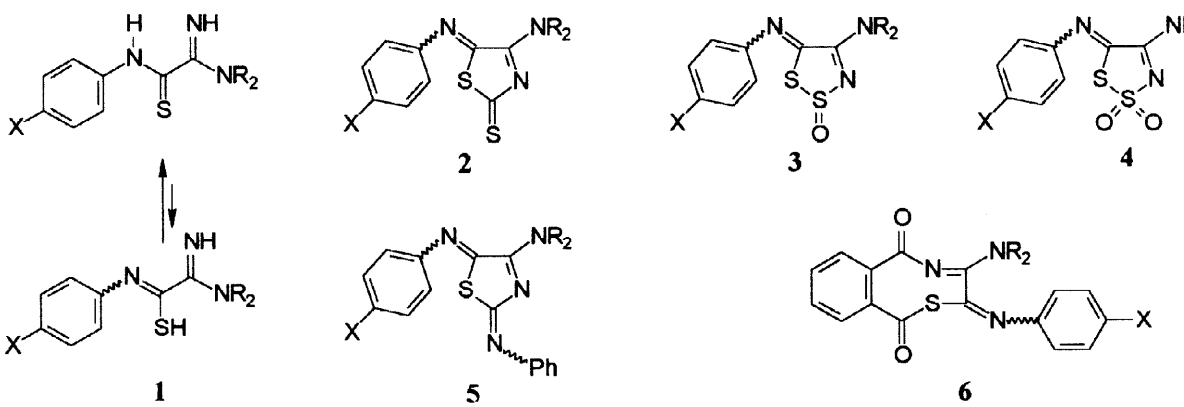
Abstract: The reactions of *N,N*-(di-*n*-alkyl)-*N'*-arylthiocarbamoylamidines (**1**) with 2-bromo-1-phenylethanone in the presence of K_2CO_3 in THF at reflux gave 3-(di-*n*-alkylamino)-2-arylimino-5-phenyl-2*H*-1,4-thiazines (**7**) in 32 to 62 % yields. Treatment of compounds **1** with bromoacetyl bromide in the presence of pyridine in CH_2Cl_2 at 0 °C afforded 5-(di-*n*-alkylamino)-6-arylimino-2*H*-1,4-thiazin-3-ones (**12**) in 41 to 84 % yields, whereas the same reactions of **1** with 2-bromopropionyl bromide under the same conditions gave 4-(di-*n*-alkylamino)-5-arylimino-2-(1-bromoethylidene)-2*H*-thiazolines (**17**) as minor compounds in addition to thiazin-3-ones **16**, analogous to compounds **12**. The reactions of **1** with ethyl bromoacetate in CH_2Cl_2 at room temperature, however, gave [(arylimino)(S-ethoxycarbonylmethyl)]methyl-*N,N*-(di-*n*-propyl)amidine hydrobromides (**19**) in 71 to 88 % yields. Compounds **7**, **12**, **16**, **17**, and **19** are all new and the mechanisms of their formations are proposed.

We have previously described the synthesis of *N,N*-(di-*n*-alkyl)-*N'*-arylthiocarbamoylamidines (**1**)[1] and demonstrated their synthetic utilities by preparing 4-dialkylamino-5-aryliminothiazoline-2-thiones (**2**), 4-dialkylamino-5-arylimino-5*H*-2-oxo-1,2,3-dithiazoles (**3**), 4-dialkylamino-5-arylimino-5*H*-2,2-dioxo-1,2,3-dithiazoles (**4**), 4-dialkylamino-5-arylimino-2-phenyliminothiazolines (**5**), and 4-dialkylamino-3-arylimino-2,5-benzothiazocine-1,6-diones (**6**).[2] All of these compounds **2-5**, having a five-membered cyclic skeleton except for compound **6**, were prepared from compounds **1**, which have four-atom unit as nucleophiles, reacting with one-atom unit such as thiophosgene, thionyl chloride, sulfuryl chloride, and *N*-phenylimidoyl dichloride as electrophiles.



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In a connection with the study to explore the potential synthetic utilities of compounds **1**, it was our aim to prepare 1,4-thiazine derivatives, which have attracted much attention due to the potential biological activities such as antibacterial[3] and cardiotonic[4] activities, by the cyclization of compounds **1** with two-carbon atom unit.

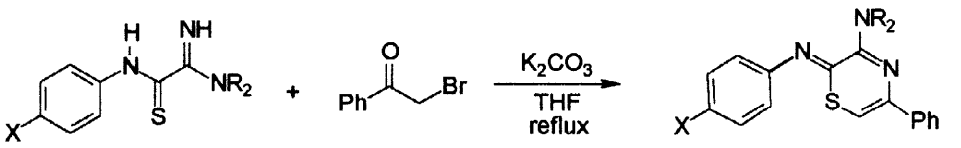
Of the 1,4-thiazines, 2*H*-1,4-thiazines have been most extensively studied.[5] However, the methods of synthesis are rather limited. Treatment of bis(aroylmethyl)sulfide with ammonia gas gave 3,5-diaryl-2*H*-1,4-thiazines.[6] 2-(Dialkylhydrazono)thioacetophenones react with acetylenic dienophiles such as methyl propiol-ate or dimethyl acetylenedicarboxylate to give 2-amino-2*H*-1,4-thiazines after amino group transposition.[7] Similarly, 2-hydrazonothioacetophenones are cyclized with methyl vinyl ketones in benzene with a few crystals of hydroquinone added, to afford 3-acetyl-3,4-dihydro-2*H*-1,4-thiazines, which undergo thermal elimination reaction at 60°C to give the corresponding 2*H*-1,4-thiazines.[8] In the presence of silica, 4-dimethylamino-3,4-dihydro-2*H*-1,4-thiazines afford 2*H*-1,4-thiazines.[9]

We have studied the reactions of compounds **1** with α-monohaloketones, α-monohaloacyl halides, and α-monobromo ester in order to prepare new 2*H*-1,4-thiazine derivatives. The results are described herein.

RESULTS AND DISCUSSION

Reactions with α-Monohaloketones

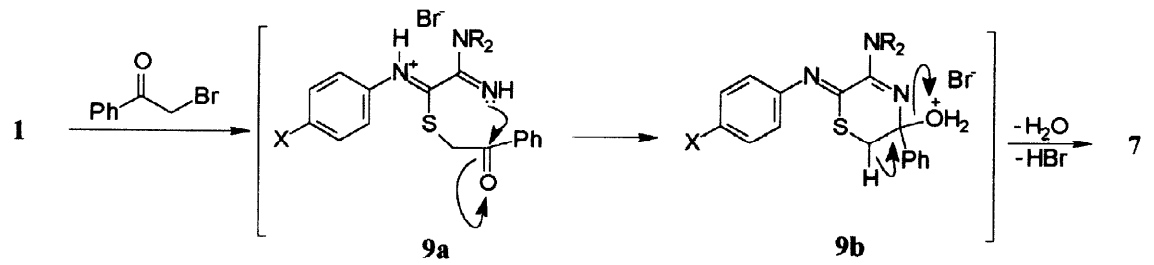
The reactions of **1** with 2-bromo-1-phenylethanone in the presence of K_2CO_3 in THF at reflux gave 3-(di-*n*-alkylamino)-2-arylimino-5-phenyl-2*H*-1,4-thiazines **7** as major products. Reaction conditions, yields, and physical properties of compounds **7** are summarized in Table 1 and their analytical and spectroscopic data in Table 2. Treatment of compound **1c** (X = Me, R = *n*-Pr) with pyridine (2 equiv.) in CH_2Cl_2 for 12 days at reflux gave **7c** in 52 %yield, which was lower than the yield obtained under the foregoing condition.



1 **7**

The structures of compounds **7a-i** were determined on the basis of the spectroscopic data and elemental analyses. A vinyl proton signal of componds **7** appears at δ 6.08 - 6.22 ppm, which is close to that (δ 6.45 ppm) of the analogous type of the compound, 3,5-diphenyl-2*H*-1,4-thiazine.[10] The stereochemistry of the arylimino group at C-2 was determined on the basis of *X*-ray analysis of **7i** (X = Cl, R = Et). ORTEP drawing of **7i** shows clearly that the 4-chlorophenyl group is directed toward S-1 (Fig. 1).

The formation of compounds **7** can be explained by a nucleophilic displacement of the bromine atom of 2-bromo-1-phenylethanone by the thione sulfur of compouds **1** to give an intermediate **9a**, followed by an intramolecular nucleophilic attack of the imino nitrogen of **9a** to the carbonyl carbon atom to give a cyclized intermediate **9b**, which loses a water molecule concomitant with loss of a HBr molecule to give **7** (Scheme 1).



Scheme 1

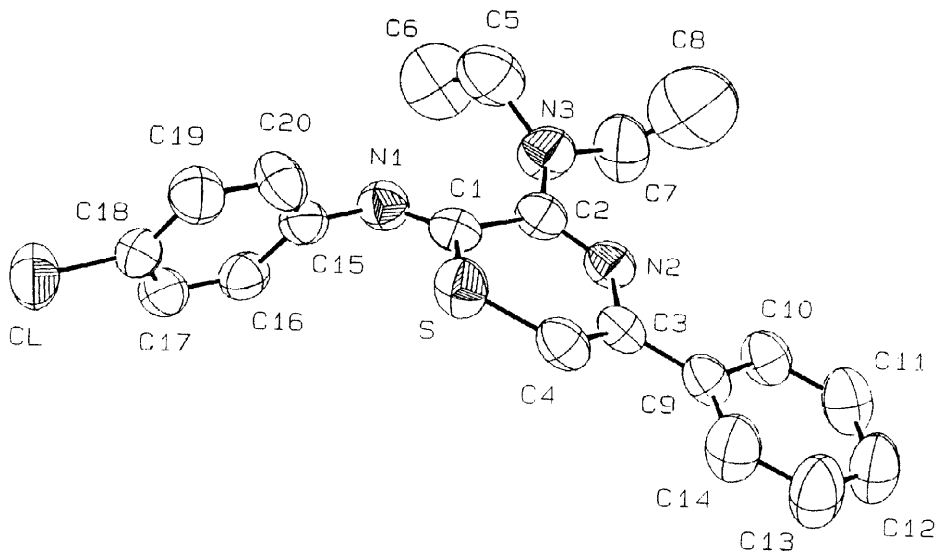


Fig. 1. ORTEP drawing of **7i**.

Selected bond lengths (Å): S-C4 1.714(4), S-C1 1.757(4), N1-C1 1.263(5), N1-C15 1.412(5), N2-C2 1.301(5), C3-C4 1.342(5). Selected bond angles (deg): C4-S-C1 103.3(2), C1-N1-C15 120.2(4), C2-N2-C3 125.1(3), C4-C3-N2 123.5(4), C3-C4-S 124.1(3), C2-C1-S 115.6(3).

Table 1. Reaction conditions, yields, and physical properties of compounds 7

Compounds	X	R	1 mmol	$PhCOCH_2Br$ mmol	Time h	Yield [a] %	mp [b] °C	Color
7a	NO_2	*n*-Pr	0.535	0.819	51	37	79-80	red
7b	Cl	*n*-Pr	0.588	0.588	40	43	89-90	yellow
7c	Me	*n*-Pr	0.624	0.944	41	62	80-81	yellow
7d	MeO	*n*-Pr	0.538	0.819	68	60	79-81	yellow
7e	NO_2	*n*-Bu	0.517	0.779	18	51	55-56	red
7f	Cl	*n*-Bu	0.491	0.754	46	51	69-71	yellow
7g	Me	*n*-Bu	0.517	0.794	20	62	64-66	yellow
7h	MeO	*n*-Bu	0.526	0.809	41	32	74-76	yellow
7i	Cl	Et	0.693	1.04	29	49	129-130	yellow

[a] Isolated yields. [b] Recrystallized from EtOH except for **7i** (from *n*-hexane).

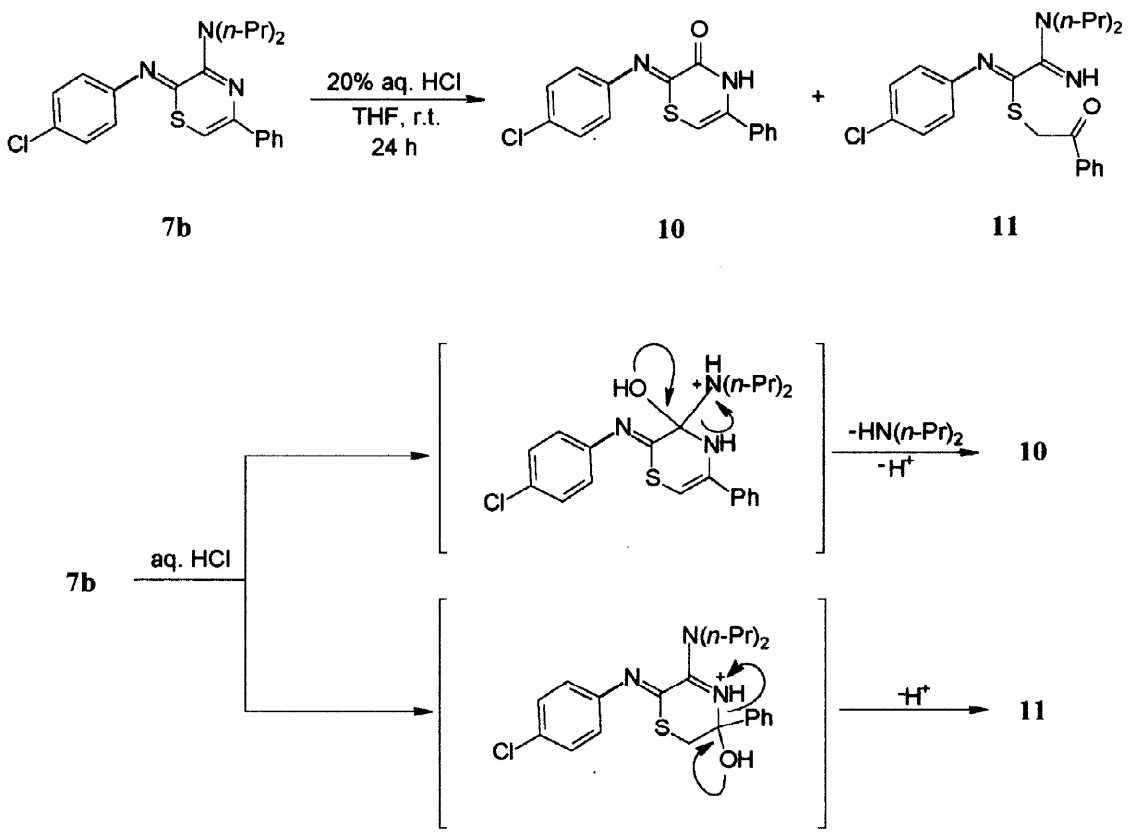
Table 2. Analytical, ^{1}H NMR, and IR data of compounds 7

Compounds	Molecular Formula	Analytical Calcd / Found	IR (neat) cm^{-1}	^{1}H NMR ($CDCl_3$) δ, ppm
7a	$C_{22}H_{24}N_4O_2S$	C, 64.68 / 64.59 H, 5.92 / 5.99 N, 13.71 / 13.63 S, 7.85 / 7.91	2944, 1570, 1509, 1478, 1453, 1413, 1366, 1331, 1248, 1210, 1162, 1102, 1074, 1006, 853, 715	0.60-1.12 (m, 6H, $2CH_3$), 1.55-1.96 (m, 4H, $2CH_2$), 3.51-3.87 (m, 4H, $2NCH_2$), 6.22 (s, 1H, SCH=), 6.95 (d, 2H, J = 8.0 Hz, ArH), 7.21-7.45 (m, 3H, ArH), 7.58-7.88 (m, 2H, ArH), 8.27 (d, 2H, J = 8.0 Hz, ArH)
7b	$C_{22}H_{24}ClN_3S$	C, 66.40 / 66.46 H, 6.08 / 6.15 N, 10.56 / 10.48 S, 8.06 / 8.17	2944, 1571, 1520, 1474, 1411, 1366, 1326, 1291, 1250, 1202, 1157, 1085, 1010, 714	0.60-1.09 (m, 6H, $2CH_3$), 1.48-1.94 (m, 4H, $2CH_2$), 3.55-3.82 (m, 4H, $2NCH_2$), 6.15 (s, 1H, SCH=), 6.78 (d, 2H, J = 8.0 Hz, ArH), 7.22-7.48 (m, 3H, ArH), 7.33 (d, 2H, J = 8.0 Hz, ArH), 7.64-7.82 (m, 2H, ArH)
7c	$C_{23}H_{27}N_3S$	C, 73.17 / 73.09 H, 7.21 / 7.24 N, 11.13 / 11.09 S, 8.49 / 8.58	2944, 1571, 1523, 1493, 1451, 1411, 1366, 1326, 1293, 1248, 1094, 1067, 1029, 1003, 915, 770, 714, 688	0.74-1.06 (m, 6H, $2CH_3$), 1.40-1.92 (m, 4H, $2CH_2$), 2.26 (s, 3H, CH_3), 3.45-3.84 (m, 4H, $2NCH_2$), 6.08 (s, 1H, SCH=), 6.76 (d, 2H, J = 8.0 Hz, ArH), 7.03-7.35 (m, 3H, ArH), 7.18 (d, 2H, J = 8.0 Hz, ArH), 7.53-7.85 (m, 2H, ArH)
7d	$C_{23}H_{27}N_3OS$	C, 70.20 / 70.10 H, 6.91 / 6.94 N, 10.68 / 10.71 S, 8.15 / 8.21	2944, 1570, 1523, 1491, 1451, 1410, 1366, 1326, 1285, 1240, 1094, 1066, 1027, 1006, 914, 830, 770, 718, 688	0.78-1.08 (m, 6H, $2CH_3$), 1.55-1.84 (m, 4H, $2CH_2$), 3.52-3.87 (m, 4H, $2NCH_2$), 3.80 (s, 3H, CH_3O), 6.10 (s, 1H, SCH=), 6.89 (s, 4H, ArH), 7.17-7.46 (m, 3H, ArH), 7.56-7.85 (m, 2H, ArH)
7e	$C_{24}H_{28}N_4O_2S$	C, 66.03 / 66.09 H, 6.46 / 6.50 N, 12.83 / 12.76 S, 7.34 / 7.42	2928, 1570, 1510, 1478, 1448, 1413, 1365, 1328, 1230, 1160, 1101, 1018, 998, 944, 853, 712, 693	0.77-1.06 (m, 6H, $2CH_3$), 1.06-1.88 (m, 8H, $2CH_2CH_2$), 3.55-3.86 (m, 4H, $2NCH_2$), 6.20 (s, 1H, SCH=), 6.92 (d, 2H, J = 8.0 Hz, ArH), 7.18-7.44 (m, 3H, ArH), 7.56-7.89 (m, 2H, ArH), 8.29 (d, 2H, J = 8.0 Hz, ArH)
7f	$C_{24}H_{28}ClN_3S$	C, 67.66 / 67.73	2936, 1571, 1523,	0.79-1.09 (m, 6H, $2CH_3$), 1.09-

		H, 6.62 / 6.58 N, 9.86 / 9.81 S, 7.53 / 7.64	1474, 1451, 1413, 1365, 1326, 1288, 1227, 1083, 1018, 946, 853, 829, 768, 722, 646	1.82 (m, 8H, $2CH_2CH_2$), 3.48-3.87 (m, 4H, $2NCH_2$), 6.12 (s, 1H, SCH=), 6.75 (d, 2H, J = 8.0 Hz, ArH), 7.05-7.40 (m, 3H, ArH), 7.32 (d, 2H, J = 8.0 Hz, ArH), 7.55-7.85 (m, 2H, ArH)
7g	$C_{25}H_{31}N_3S$	C, 74.03 / 73.96 H, 7.70 / 7.75 N, 10.36 / 10.33 S, 7.90 / 7.85	2944, 1571, 1523, 1494, 1450, 1413, 1365, 1328, 1288, 1277, 1101, 1016, 944, 858, 819, 770, 714, 688	0.70-1.09 (m, 6H, $2CH_3$), 1.09-1.89 (m, 8H, $2CH_2CH_2$), 2.35 (s, 3H, CH_3), 3.50-3.85 (m, 4H, $2NCH_2$), 6.11 (s, 1H, SCH=), 6.78 (d, 2H, J = 8.0 Hz, ArH), 7.02-7.45 (m, 3H, ArH), 7.24 (d, 2H, J = 8.0 Hz, ArH), 7.58-7.85 (m, 2H, ArH)
7h	$C_{25}H_{31}N_3OS$	C, 71.22 / 71.13 H, 7.41 / 7.47 N, 9.97 / 9.92 S, 7.60 / 7.71	2920, 1570, 1523, 1491, 1450, 1411, 1366, 1285, 1242, 1178, 1160, 1099, 1077, 1026, 998, 966, 944, 857, 830, 770, 720, 688, 630	0.78-1.06 (m, 6H, $2CH_3$), 1.06-1.86 (m, 8H, $2CH_2CH_2$), 3.51-3.91 (m, 4H, $2NCH_2$), 3.84 (s, 3H, CH_3O), 6.10 (s, 1H, SCH=), 6.88 (s, 4H, ArH), 7.10-7.78 (m, 3H, ArH), 7.61-7.85 (m, 2H, ArH)
7i	$C_{20}H_{20}ClN_3S$	C, 64.94 / 64.70 H, 5.45 / 5.52 N, 11.36 / 11.39 S, 8.67 / 8.75	2952, 2912, 1563, 1518, 1472, 1418, 1365, 1346, 1326, 1274, 1080, 1014, 834, 717, 642	1.28 (t, 6H, J = 8.0 Hz, $2CH_3$), 3.75 (q, 4H, J = 8.0 Hz, $2NCH_2$), 6.14 (s, 1H, SCH=), 6.81 (d, 2H, J = 8.0 Hz, ArH), 7.20-7.45 (m, 3H, ArH), 7.35 (d, 2H, J = 8.0 Hz, ArH), 7.64-7.83 (m, 2H, ArH)

For the chemical reactivities of compounds **7**, compoud **7b** was treated with 20 % agueous hydrochloric acid in THF for 24 h at room temperature. From the reaction mixture were isolated 2-(4-chlorophenylimino)-5-phenyl-4*H*-1,4-thiazin-3-one (**10**) and [*S*-(benzoylmethyl)(4-chlorophenylimino)]methyl-*N*,*N*-(di-*n*-propyl)amidine (**11**) in 53 % and 18 % yields, respectively. The result indicates that **7b** undergoes hydrolysis *via* two pathways: A nucleophilic attack of water to an imino carbon bearing a di-*n*-propylamino group of **7b** may result in the formation of compound **10**. On the other hand, protonation of an olefinic carbon, followed by a nucleophilic attack of water would lead to compound **11**, which is identical with deprotonated compound **9a** (X = Cl, R = *n*-Pr) (Scheme 2).

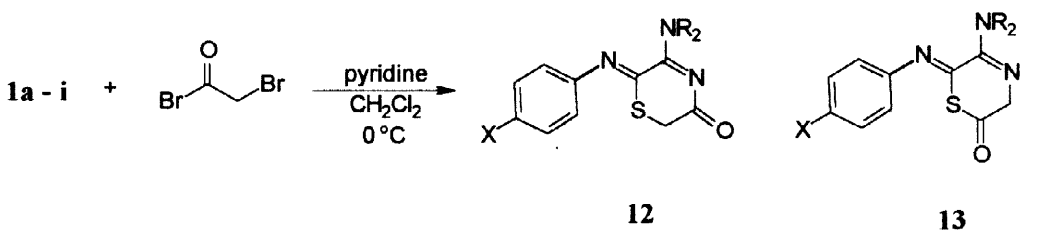
Reduction of compound **7b** with $LiAlH_4$ in THF at either room or reflux temperature did not proceed and **7b** was recovered in 87 % yield. On the other hand, treatment of compound **7b** with *m*-chloroperbenzoic acid (*m*-CPBA) in CH_2Cl_2 at room temperature gave a complex mixture from which **7b** (27 %) was isolable.



Scheme 2

Reactions with α-monobromoacyl bromides

The reactions of compounds **1** with bromoacetyl bromide in the presence of pyridine (2 equiv.) at 0 °C gave a mixture showing two spots on TLC (R_f = 0.90-0.95 and 0.10-0.50, *n*-hexane : EtOAc = 1 : 1), which were separated by column chromatography. The former was unidenifiable complex mixture and the latter was identified as 5-(di-*n*-alkylamino)-6-arylimino-2*H*-1,4-thiazin-3-ones (**12**). Reaction conditions, yields, and melting points of compounds **12** are summarized in Table 3 and their analytical and spetroscopic data in Table 4.



The structures of compouds **12** were determined on the basis of the spectroscopic data and elemental analyses. The stereochemistry of arylimino group of **12** was determined based on *X*-ray analysis of **12i**, which showed that the arylimino group was directed toward S-1 (Fig. 2).The possible formation of regioisomer **13** was eliminated in view of the chemical shift of the methylene protons appeared in the range of δ 3.53-3.59 ppm. The chemical shift of the corresponding proton NMR signal of the isomer **13** would be expected to

appear at further downfield because of the presence of two electron-withdrawing groups (a carbonyl group and an imino nitrogen atom) directly bonded to the methylene carbon.[11] However, even crude compounds isolated from chromatography did not show absorptions of methylene protons below the range foregoing up to around δ 6.5 ppm. Furthermore, according to the principle of hard and soft acids and bases (HSAB principle) concept,[12] it is reasonable to expect the bond formations between the imino nitrogen (hard base) and the acyl carbon atom (hard acid), and the thione sulfur (soft base) and the carbon atom (soft acid) of the bromomethyl group.

Table 3. Reaction conditions, yields, and melting points of compounds **12**

Compounds	X	R	**1** mmol	$BrCOCH_2Br$ mmol	Time min	Yield [a] %	mp[b] °C
12a	NO_2	*n*-Pr	0.511	0.57	95	62	129-130
12b	Cl	*n*-Pr	0.630	0.69	90	75	104-107
12c	Me	*n*-Pr	0.609	1.09	80	41	86-89
12d	MeO	*n*-Pr	0.518	0.57	105	47	109-110
12e	NO_2	*n*-Bu	0.482	0.57	110	66	140-141
12f	Cl	*n*-Bu	0.490	0.57	105	84	109-110
12g	Me	*n*-Bu	0.540	0.57	85	59	99-100
12h	MeO	*n*-Bu	0.514	0.57	115	50	101-103
12i	NO_2	Et	0.31	0.34	130	47	180-183 (dec.)

[a] Isolated yields. [b] Recrystallized from a mixture of *n*-hexane and dichloromethane except for **12f** (from *n*-hexane) and **12i** (from ethyl acetate).

Table 4. Analytical, ^1H NMR, and IR data of compounds **12**

Comp-ounds	Molecular Formula	Analytical Calcd / Found	IR (KBr) cm^{-1}	^1H NMR ($CDCl_3$) δ, ppm
12a	$C_{16}H_{20}N_4O_3S$	C, 55.16 / 55.09 H, 5.79 / 5.84 N, 16.08 / 16.14 S, 9.20 / 9.29	2936, 1651, 1574, 1541, 1509, 1456, 1426, 1334, 1045	0.60-1.14 (m, 6H, $2CH_3$), 1.32-2.03 (m, 4H, $2CH_2$), 3.13-3.90 (m, 4H, $2NCH_2$), 3.59 (s, 2H, CH_2), 6.99 (d, 2H, J = 8.0 Hz, ArH), 8.25 (d, 2H, J = 8.0 Hz, ArH)
12b	$C_{16}H_{20}ClN_3OS$	C, 56.88 / 56.94 H, 5.97 / 6.00 N, 12.44 / 12.41 S, 9.49 / 9.54	2944, 1648, 1595, 1539, 1477, 1469, 1434, 1370, 1320, 1286, 1083, 1053, 920	0.60-1.14 (m, 6H, $2CH_3$), 1.37-2.03 (m, 4H, $2CH_2$), 3.12-3.89 (m, 4H, $2NCH_2$), 3.57 (s, 2H, CH_2), 6.95 (d, 2H, J = 8.0 Hz, ArH), 7.35 (d, 2H, J = 8.0 Hz, ArH)
12c	$C_{17}H_{23}N_3OS$	C, 64.32 / 64.27	2944, 1662, 1589,	0.69-1.12 (m, 6H, $2CH_3$), 1.54-1.94

		H, 7.30 / 7.32 N, 13.24 / 13.27 S, 10.10 / 10.17	1533, 1496, 1454, 1426, 1365, 1309, 1283, 1250, 1043	(m, 4H, $2CH_2$), 2.35 (s, 3H, CH_3), 3.45-3.81 (m, 4H, $2NCH_2$), 3.56 (s, 2H, CH_2), 6.84 (d, 2H, J = 8.0 Hz, ArH), 7.22 (d, 2H, J = 8.0 Hz, ArH)
12d	$C_{17}H_{23}N_3O_2S$	C, 61.24 / 61.29 H, 6.95 / 6.98 N, 12.60 / 12.64 S, 9.61 / 9.67	2944, 1653, 1595, 1573, 1530, 1496, 1458, 1371, 1320, 1288, 1248, 1048, 1029	0.60-1.15 (m, 6H, $2CH_3$), 1.36-2.01 (m, 4H, $2CH_2$), 3.17-3.92 (m, 4H, $2NCH_2$), 3.56 (s, 2H, CH_2), 3.80 (s, 3H, CH_3O). 6.92 (s, 4H, ArH)
12e	$C_{18}H_{24}N_4O_3S$	C, 57.43 / 57.46 H, 6.43 / 6.47 N, 14.88 / 14.91 S, 8.52 / 8.58	2936, 1662, 1600, 1586, 1552, 1504, 1458, 1430, 1341, 1320, 1275, 1221, 1160, 1099, 1056, 862, 699	0.60-1.10 (m, 6H, $2CH_3$), 1.10-2.03 (m, 8H, $2CH_2$), 3.20-3.90 (m, 4H, $2NCH_2$), 3.57 (s, 2H, CH_2), 6.97 (d, 2H, J = 8.0 Hz, ArH), 8.26 (d, 2H, J = 8.0 Hz, ArH)
12f	$C_{18}H_{24}ClN_3OS$	C, 59.08 / 59.13 H, 6.61 / 6.59 N, 11.48 / 11.50 S, 8.76 / 8.80	2944, 1650, 1598, 1542, 1472, 1430, 1370, 1320, 1277, 1054	0.60-1.08 (m, 6H, $2CH_3$), 1.08-2.20 (m, 8H, $2CH_2$), 3.19-3.90 (m, 4H, $2NCH_2$), 3.56 (s, 2H, CH_2), 6.83 (d, 2H, J = 8.0 Hz, ArH), 7.35 (d, 2H, J = 8.0 Hz, ArH)
12g	$C_{19}H_{27}N_3OS$	C, 66.05 / 66.11 H, 7.88 / 7.90 N, 12.16 / 12.19 S, 9.28 / 9.36	2936, 1672, 1595, 1555, 1494, 1453, 1432, 1366, 1314, 1274, 1043	0.60-1.10 (m, 6H, $2CH_3$), 1.10-2.00 (m, 8H, $2CH_2$), 2.34 (s, 3H, CH_3), 3.14-3.93 (m, 4H, $2NCH_2$), 3.53 (s, 2H, CH_2), 6.80 (d, 2H, J = 8.0 Hz, ArH), 7.19 (d, 2H, J = 8.0 Hz, ArH)
12h	$C_{19}H_{27}N_3O_2S$	C, 63.13 / 63.19 H, 7.53 / 7.50 N, 11.62 / 11.60 S, 8.87 / 8.95	2944, 1651, 1576, 1526, 1494, 1456, 1371, 1318, 1283, 1250, 1050	0.60-1.07 (m, 6H, $2CH_3$), 1.07-1.98 (m, 8H, $2CH_2$), 3.18-3.91 (m, 4H, $2NCH_2$), 3.55 (s, 2H, CH_2), 3.78 (s, 3H, CH_3O), 6.90 (s, 4H, ArH)
12i	$C_{14}H_{16}N_4O_3S$	C, 52.49 / 52.56 H, 5.03 / 5.06 N, 17.49 / 17.44 S, 10.01 / 10.10	3088, 2968, 2920, 1651, 1598, 1574, 1536, 1504, 1466, 1438, 1333, 1309, 1096, 1042, 981	1.31 (t, 3H, J = 7.1 Hz, CH_3), 1.37 (t, 3H, J = 7.1 Hz, CH_3), 3.62 (s, 2H, CH_2), 3.72 (q, 2H, J = 7.1 Hz, NCH_2), 3.77 (q, 2H, J = 7.1 Hz, NCH_2), 7.03 (d, 2H, J = 8.9 Hz, ArH), 8.30 (d, 2H, J = 8.9 Hz, ArH)

For comparison, **1c** (X = Me, R = *n*-Pr) was treated with K_2CO_3 (2 equiv.) in THF at 0°C for 150 min. However, **12c** was obtained in 28 % yield together with the recovery of the starting material **1c** (35 %). The

same reaction carried out at room temperature for 24 h gave **12c** (12 %) together with an unknown complex mixture.

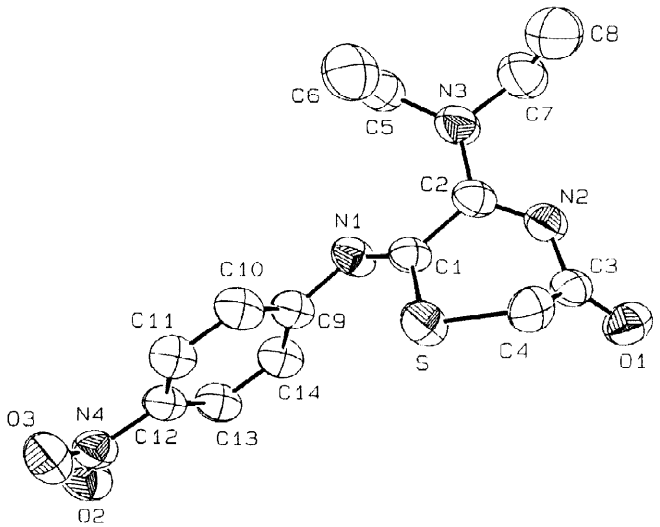
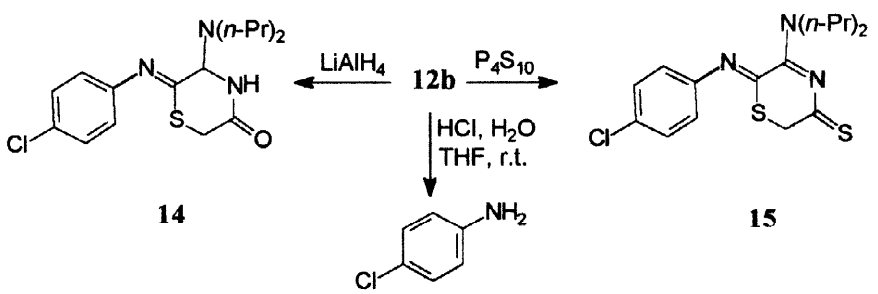


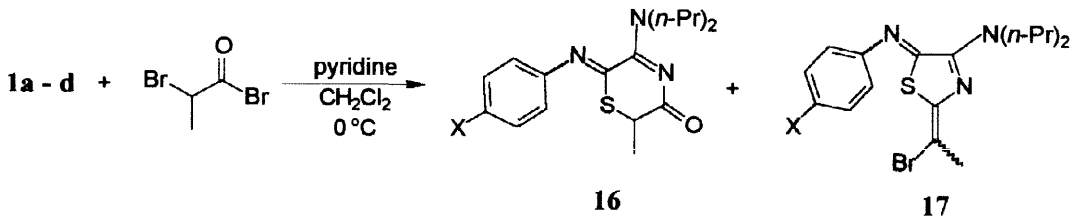
Fig. 2. ORTEP drawing of **12i**.

Selected bond lengths (Å): S-C1 1.748(3), S-C4 1.809(4), C1-C2 1.503(5), C3-C4 1.495(5), N2-C2 1.303(4), N2-C3 1.366(5), N1-C1 1.273(4). Selected bond angles (deg): C1-S-C4 100.6(2), C1-N1-C9 122.2(3), C2-N2-C3 121.8(3), N2-C3-C4 116.8(3), C3-C4-S 111.5(2), N1-C1-C2 119.6(3).

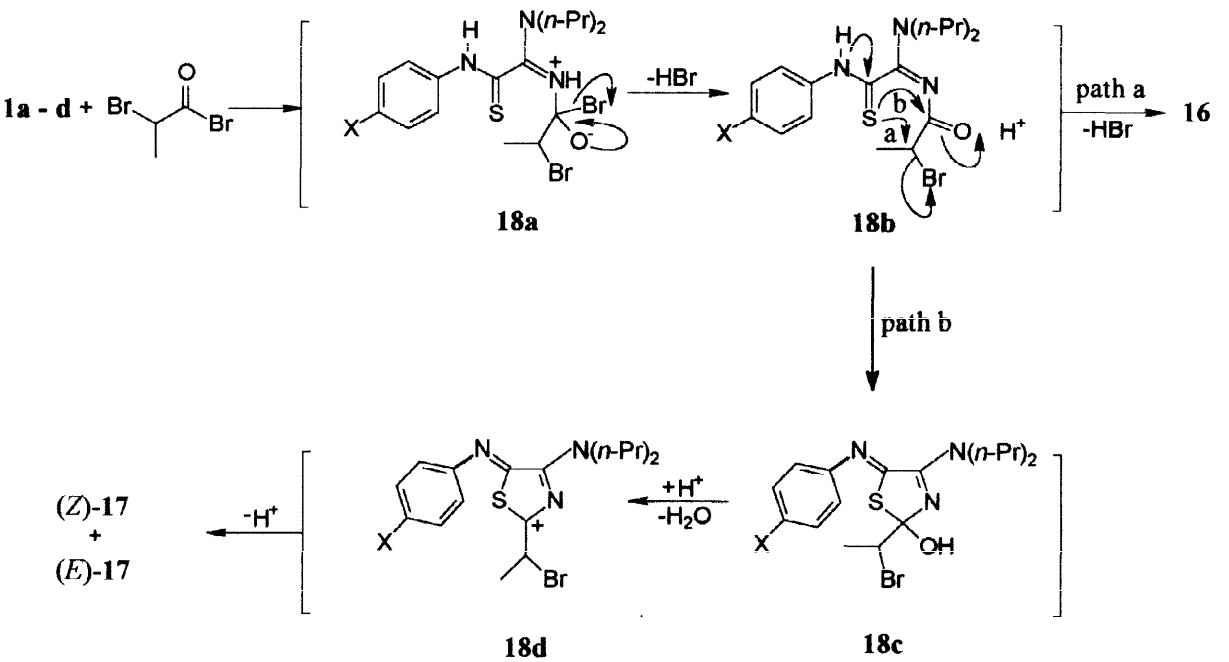
In contrast with the reaction of **7b**, the reduction of compound **12b** with $LiAlH_4$ in THF at room temperature gave 2-(4-chlorophenylimino)-5-oxo-3-(di-*n*-propylamino)thiomorpholine (**14**) in 87 % yield. Treatment of **12b** with P_4S_{10} in benzene gave the corresponding 5-thioxothiazine **15** in 46 % yield. However, only 4-chloroaniline and a complex mixture were isolated by treatment of **12b** with 20 % aqueous hydrochloric acid in THF at room temperature. Treatmement of **12b** with *m*-CPBA gave a complex mixture from which the starting **12b** was recovered in 51 % yield.



The reactions of **1** (R = *n*-Pr) with 2-bromopropionyl bromide in the presence of pyridine (2 equiv.) in CH_2Cl_2 at 0 °C gave 6-arylimino-2-methyl-5-(di-*n*-propylamino)-2*H*-1,4-thiazin-3-ones (**16**) as major products and 5-(arylimino)-2-(1-bromoethylidene)-4-(di-*n*-propylamino)thiazolines (**17**) as minor products. Reaction conditions, yields, and melting points of compounds **16** and **17** are summarized in Table 5. Analytical and spectroscopic data of compounds **16** and **17** are summarized in Table 6 and 7, respectively.



The formation of compounds **16** can be explained by the same mechanism as proposed for compounds **12**. We prefer the pathway in which a bromine atom of acyl bromide is displaced by the imino nitrogen of **1** to give an intermediate **18a**, which loses HBr to give an intermediate **18b** (HSAB principle, vide supra). Nucleophilic displacement of a bromine atom of **18b** by the thione sulfur (path a) concomitant with loss of HBr can give compounds **16**. However, when the thione sulfur attacks the carbonyl carbon atom in the presence of acid catalyst (HBr) (path b), the formation of bromohydrin **18c** would be expected. Dehydration of **18c** in the presence of HBr can give rise to a cation **18d**, which undergoes deprotonation reaction to give a mixture of (*Z*)- and (*E*)-**17** (Scheme 3).



Scheme 3

Table 5. Reaction conditions, yields, and melting points of compounds **16** and **17**

Compounds	**1** mmol	$CH_3CHBrCOBr$ mmol	Time min	Yield [a] %	mp [b] °C	Yield [a] %
16a	0.564	0.65	90	60	99-101	**17a** 21 (76:24) [c]
16b	0.541	0.65	90	63	79-81	**17b** 12 (69:31) [c]
16c	0.743	0.93	90	45	77-79	**17c** 12 (75:25) [c]

16d	0.709	0.75	90	48	109-110	**17d**	0

[a] Isolated yields. [b] Recrystallized from a mixture of *n*-hexane and dichloromethane. [c] The numbers in the parenthesis represent the ratio of the geometrical isomers, calculated on the basis of the integral values of methyl protons of the ethylidene group.

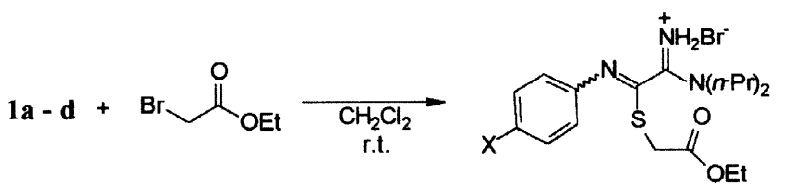
Table 6. Analytical, ^{1}H NMR, and IR data of compounds **16**

Comp-ounds	Molecular Formula	Analytical Calcd / Found	IR (neat) cm^{-1}	^{1}H NMR ($CDCl_3$) δ, ppm
16a	$C_{17}H_{22}N_4O_3S$	C, 62.22 / 62.27 H, 7.25 / 7.23 N, 12.09 / 12.06 S, 9.23 / 9.29	2952, 1670, 1576, 1542, 1509, 1456, 1432, 1366, 1336, 1275, 1230, 1160, 1099, 1050, 997, 853, 734, 694	0.60-1.10 (m, 6H, $2CH_3$), 1.45 (d, 3H, J = 8.0 Hz, CH_3), 1.40-2.00 (m, 4H, $2CH_2$), 3.20-4.00 (m, 4H, $2NCH_2$), 3.90 (q, 1H, J = 8.0 Hz, CH), 7.00 (d, 2H, J = 8.0 Hz, ArH), 8.27 (d, 2H, J = 8.0 Hz, ArH).
16b	$C_{17}H_{22}ClN_3OS$	C, 65.22 / 65.18 H, 7.60 / 7.63 N, 12.68 / 12.72 S, 9.67 / 9.74	2952, 1669, 1595, 1541, 1470, 1430, 1366, 1318, 1270, 1230, 1197, 1157, 1085, 1046, 830, 739	0.60-1.10 (m, 6H, $2CH_3$), 1.45 (d, 3H, J = 8.0 Hz, CH_3), 1.40-1.95 (m, 4H, $2CH_2$), 3.20-3.90 (m, 4H, $2NCH_2$), 3.85 (q, 1H, J = 8.0 Hz, CH), 6.85 (d, 2H, J = 8.0 Hz, ArH), 7.30 (d, 2H, J = 8.0 Hz,ArH).
16c	$C_{18}H_{25}N_3OS$	C, 58.03 / 58.07 H, 6.30 / 6.32 N, 11.94 / 11.99 S, 9.11 / 9.18	2952, 1669, 1590, 1539, 1496, 1453, 1429, 1368, 1318, 1274, 1230, 1147, 1045, 1026, 998, 915, 899, 867, 818, 758, 718	0.60-1.20 (m, 6H, $2CH_3$), 1.45 (d 3H, J = 8.0 Hz, CH_3), 1.40-1.95 (m, 4H, $2CH_2$), 2.35 (s, 3H, CH_3), 3.20-3.90 (m, 4H, $2NCH_2$), 3.80 (q, 1H, J = 8.0 Hz, CH), 6.80 (d, 2H, J = 8.0 Hz, ArH), 7.15 (d, 2H, J = 8.0 Hz, ArH).
16d	$C_{18}H_{25}N_3O_2S$	C, 56.34 / 56.30 H, 6.12 / 6.15 N, 15.46 / 15.50 S, 8.85 / 8.92	2952, 1666, 1579, 1539, 1493, 1450, 1366, 1320, 1285, 1246, 1157, 1098, 1045, 1026, 995, 910, 894, 832, 758, 696, 598	0.60-1.20 (m, 6H, $2CH_3$), 1.45 (d 3H, J = 8.0 Hz, CH_3), 1.50-1.95 (m, 4H, $2CH_2$), 3.20-3.85 (m, 4H, $2NCH_2$), 3.80 (s, 3H, CH_3O), 3.82 (d, 1H, J = 8.0 Hz, CH), 6.95 (s, 4H, ArH).

Table 7. Analytical, ^{1}H NMR, and IR data of compounds **17**

Compounds	Molecular Formula	Analytical Calcd / Found	IR (neat) cm^{-1}	^{1}H NMR ($CDCl_3$) δ, ppm
17a	$C_{17}H_{21}BrN_4O_2S$	C, 48.01 / 48.07 H, 4.98 / 4.95 N, 13.17 / 13.20 S, 7.54 / 7.60	2952, 1603, 1574, 1549, 1506, 1451, 1333, 1261, 1224, 1162, 1099, 1077, 1042, 1022, 915, 890, 830, 738, 699	0.60-1.10 (m, 6H, $2CH_3$), 1.40-1.92 (m, 4H, $2CH_2$), 2.31, 2.60 (major) (2s, 3H, CH_3), 3.40-3.95 (m, 4H, $2NCH_2$), 7.10 (d, 2H, J = 8.0 Hz, ArH), 8.27 (d, 2H, J = 8.0 Hz, ArH).
17b	$C_{17}H_{21}BrClN_3S$	C, 49.23 / 49.28 H, 5.10 / 5.13 N, 10.13 / 10.16 S, 7.73 / 7.79	2952, 1598, 1574, 1549, 1474, 1451, 1424, 1370, 1222, 1085, 1042, 1026, 1010, 827	0.60-1.10 (m, 6H, $2CH_3$), 1.35-2.00 (m, 4H, $2CH_2$), 2.32, 2.56 (major) (2s, 3H, CH_3), 3.40-3.90 (m, 4H, $2NCH_2$), 6.95 (d, 2H, J = 8.0 Hz, ArH), 7.35 (d, 2H, J = 8.0 Hz, ArH)
17c	$C_{18}H_{24}BrN_3S$	C, 54.82 / 54.87 H, 6.13 / 6.10 N, 10.65 / 10.63 S, 8.13 / 8.20	2952, 1605, 1586, 1547, 1494, 1450, 1424, 1370, 1221, 1096, 1075, 1042, 1024, 818	0.70-1.10 (m, 6H, $2CH_3$), 1.36-2.00 (m, 4H, $2CH_2$), 2.32, 2.56 (major) (2s, 6H, $2CH_3$), 3.50-3.90 (m, 4H, $2NCH_2$), 6.92 (d, 2H, J = 8.0 Hz, ArH), 7.20 (d, 2H, J = 8.0 Hz, ArH).

In the meantime, the reaction of **1a - d** with ethyl bromoacetate in CH_2Cl_2 at room temperature gave [(arylimino)(*S*-ethoxycarbonylmethyl)]methyl-*N,N*-(di-*n*-propyl)amidine hydrobromides **19** in good yields. Reaction conditions, yields, and melting points of compounds **19** are summarized in Table 8 and their analytical and spectroscopic data in Table 9.



19

Attempted purification of compouds **19** by the repeated column chromatography failed but it was successful by employing HPLC using CH_3CN as a solvent.

The structures of compounds **19** were determined on the basis of the spectroscopic data and elemental anayses. It is evident for the amidines to be protonated on the imino nitrogen atom rather than on the amino

nitrogen atom because imino nitrogens are generally more basic than amino nitrogens in amidines.[13] ^{1}H NMR spetra of compounds **19** exhibited a broad singlet at δ 4.86 to 6.17 ppm, corresponding to the two protons of the protonated imines.

Table 8. Reaction conditions and yields of compounds **19**

Compounds	**1** mmol	$BrCH_2CO_2Et$ mmol	Time h	Yield [a] %
19a	0.334	0.34	24	84
19b	0.447	0.46	1.5	82
19c	0.411	0.42	1	88
19d	0.321	0.34	0.5	71

[a] Isolated yields.

Table 9. Analytical, ^{1}H NMR, and IR data of compounds **19**

Comp-ounds	Molecular Formula	Analytical Calcd / Found	IR (neat) cm^{-1}	^{1}H NMR ($CDCl_3$) δ, ppm
19a	$C_{18}H_{27}BrN_4O_4S$	C, 45.48 / 45.55 H, 5.72 / 5.69 N, 11.79 / 11.84 S, 6.74 / 6.81	3312, 2968, 1734, 1582, 1510, 1480, 1458, 1376, 1338, 1294, 1262, 1213, 1171, 1110, 1050, 1026, 859	0.56-0.95 (m, 6H, $2CH_3$), 1.12-1.85 (m, 7H, $2CH_2$ + CH_3), 2.76-3.41 (m, 4H, $2NCH_2$), 3.85 (s, 2H, $COCH_2$), 4.22 (q, 2H, *J* = 8.0 Hz, OCH_2), 4.86 (s, br, 2H, $=^+NH_2$), 6.97 (d, 2H, *J* = 8.0 Hz, ArH), 8.16 (d, 2H, *J* = 8.0 Hz, ArH)
19b	$C_{18}H_{27}BrClN_3O_2S$	C, 46.51 / 46.47 H, 5.85 / 5.88 N, 9.04 / 9.09 S, 6.90 / 6.98	3296, 2952, 1739, 1605, 1579, 1478, 1370, 1288, 1202, 1179, 1150, 1117, 1085, 1050, 1026, 830	0.59-1.12 (m, 6H, $2CH_3$), 1.12-2.00 (m, 7H, $2CH_2$ + CH_3), 2.76-3.41 (m, 4H, $2NCH_2$), 3.85 (s, 2H, $COCH_2$), 4.20 (q, 2H, *J* = 8.0 Hz, OCH_2), 5.80 (s, br, 2H, $=^+NH_2$), 6.87 (d, 2H, *J* = 8.0 Hz, ArH), 7.25 (d, 2H, *J* = 8.0 Hz, ArH)
19c	$C_{19}H_{30}BrN_3O_2S$	C, 51.35 / 51.39 H, 6.80 / 6.83 N, 9.45 / 9.42 S, 7.21 / 7.26	3296, 2952, 1731, 1648, 1606, 1578, 1474, 1451, 1370, 1288, 1149, 1112,	0.55-1.18 (m, 6H, $2CH_3$), 1.18-1.95 (m, 7H, $2CH_2$ + CH_3), 2.25 (s, 3H, CH_3), 2.76-3.41 (m, 4H, $2NCH_2$), 3.82 (s, 2H, $COCH_2$),

			1024, 818	4.20 (q, 2H, J = 8.0 Hz, OCH_2), 6.17 (s, br, 2H, $=^+NH_2$), 6.83 (d, 2H, J = 8.0 Hz, ArH), 7.05 (d, 2H, J = 8.0 Hz, ArH)
19d	$C_{19}H_{30}BrN_3O_3S$	C, 49.56 / 49.51 H, 6.57 / 6.59 N, 9.13 / 9.16 S, 6.96 / 6.75	3296, 2952, 1734, 1603, 1576, 1496, 1454, 1368, 1285, 1240, 1027, 830	0.58-1.09 (m, 6H, $2CH_3$), 1.09-1.99 (m, 7H, $2CH_2$ + CH_3), 2.76-3.41 (m, 4H, $2NCH_2$), 3.76 (s, 3H, CH_3O), 3.87 (s, 2H, $COCH_2$), 4.20 (q, 2H, J = 8.0 Hz, OCH_2), 5.08 (s, br, 2H, $=^+NH_2$), 6.68-6.97 (m, 4H, ArH)

EXPERIMENTAL

N,N-(di-*n*-alkyl)-*N'*-Arylthiocarbamoylamidines were prepared by the literature method.[2] 2-Bromo-1-phenylethanone, 3-chloro-2-propanone, bromoacetyl bromide, 2-bromopropionyl bromide, and ethyl bromoacetate were obtained from Aldrich Chemical Co. Inc.. Thin layer chromatography was carried out on Merck Chromatogram sheet (Kiesel gel 60 F254). Chromatogram was visualized by a mineral UV lamp. Column chromatography was performed using silica gel (Merck, 70-230 mesh) unless otherwise specified. ^1H NMR spetra were obtained with a Brucker AC-80 at 80 MHz, using tetramethylsilane as an internal standard. Infrared (IR) spetra were obtained using a Shimazu IR-470. Mass spectra (MS) were obtained by a VG 12-250 mass spectrometer at 70 eV. HPLC was performed with a C-18 column (μBondpak C18, 10 μm, 7.8 × 300 mm i.d.) and a differential refractometer, using CH_3CN as eluent (flow rate = 0.8 ml / min). Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

General Procedure for the Synthesis of 3-(Di-*n*-alkylamino)-2-arylimino-5-phenyl-2*H*-1,4-thiazines (7).

To a soluton of *N,N*-(di-*n*-alkyl)-*N'*-arylthiocarbamoylamidines **1** (0.49-0.62 mmol) in THF (70 ml) was added K_2CO_3 (0.99-1.27 mmol). A solution of 2-bromo-1-phenylethanone (0.49-0.62 mmol) in THF (50 ml) was dropwise added to the mixture at reflux. Heating was continued for an appropriate time and the reaction mixture was quenched by adding water (50 ml). Evaporation of THF under reduced pressure, followed by extraction with $CHCl_3$ (3 × 20 ml) gave a residue, which was chromatographed on a silica gel column (2 × 13 cm). Elution with a mixture of *n*-hexane and CH_2Cl_2 (1 : 1) gave compounds **7**, unreacted 2-bromo-1-phenylethanone and a complex mixture. Consult Table **1** for reaction conditions, yields, and physical properties and Table **2** for the analytical and spectroscopic data of compounds **7**.

Hydrolysis of 2-(4-Chlorophenylimino)-5-phenyl-3-(di-*n*-propylamino)-2*H*-1,4-thiazine (7b) with Aqueous Hydrochloric Acid.

To a solution of **7b** (152 mg, 0.382 mmol) in THF (30 ml) was added 20 % aqueous hydrochloric acid (30 ml). The mixture was stirred for 24 h at room temperature. Neutralization of the mixture with aqueous NaOH (5%), followed by evaporation of THF *in vacuo* gave an aqueous solution, which was extracted with

$CHCl_3$ (3 × 30 ml). The extracts were dried over $MgSO_4$. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel column (2 × 12 cm). Elution with CH_2Cl_2 gave 2-(4-chlorophenylimino)-5-phenyl-4*H*-1,4-thiazin-3-one (**10**) (64 mg, 53 %): white solid; mp 199-200 °C (*n*-hexane-CH_2Cl_2); IR (KBr) 3336, 3088, 2912, 1670, 1582, 1518, 1478, 1426, 1390, 1301, 1274, 1229, 1168, 1110, 1094, 1066, 1026, 1010, 910, 878, 856, 822, 750, 736, 675, 643, 498, 456, 430 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 7.35 (d, 2H, J = 8.0 Hz, ArH), 7.20-7.62 (m, 3H, ArH), 7.90 (d, 2H, J = 8.0 Hz, ArH), 8.00-8.20 (m, 2H, ArH), 8.23 (s, 1H, CH=), 10.47 (s, br, 1H, NH), MS (m/z) 314 (M^+, 100), 279 (24.5), 272 (15.3), 188 (18.5), 161 (40.9), 102 (84.2). Anal. Calcd for $C_{16}H_{11}ClN_2OS$: C, 61.05; H, 3.52; N, 8.90; S, 10.18. Found: C, 61.09; H,3.54; N, 8.87; S, 10.23.

Elution with CH_2Cl_2 gave [*S*-(benzoylmethyl)(4-chlorophenylimino)]methyl-*N*,*N*-(di-*n*-propyl)amidine (**11**) (28 mg, 18 %): colorless liquid; IR (neat) 3320, 2944, 1696, 1586, 1502, 1445, 1389, 1298, 1085, 1051, 1011, 960, 923, 827, 787, 758, 730, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.60-1.05 (m, 6H, $2CH_3$), 1.25-1.90 (m, 4H, $2CH_2$), 2.32-2.70 (m, 4H, $2NCH_2$), 4.44 (s, 2H, CH_2), 7.28 (d, 2H, J = 8.0 Hz, ArH), 7.20-7.54 (m, 3H, ArH), 7.55(d, 2H, J = 8.0 Hz, ArH), 7.71-7.95 (m, 2H, ArH), 9.04 (s, br, 1H, NH). Anal. Calcd for $C_{22}H_{26}ClN_3OS$: C, 63.52; H, 6.30; N, 10.10; S, 7.71. Found: C, 63.47; H, 6.32; N, 10.12; S, 7.77.

Elution with CH_2Cl_2 gave an unknown mixture (31 mg).

Reaction of 7b with Lithium Aluminum Hydride ($LiAlH_4$).

To a solution of **7b** (144 mg, 0.362 mmol) in THF (30 ml) was added $LiAlH_4$ (17 mg, 0.45 mmol). The mixture was stirred for 1.5 h at room temperature and then worked up as usual. Only **7b** (125 mg, 98 %) was isolable. The reaction did not proceed at reflux temperature.

Reaction of 7b with *m*-Chloroperbenzoic Acid (*m*-CPBA).

To a solution of **7b** (153 mg, 0.384 mmol) in CH_2Cl_2 (30 ml) was added *m*-CPBA (116 mg, 71.5 %). The color of the solution turned immediately from yellow to dark red. The mixture was stirred for 9 h at room temperature and then washed with aqueous $NaHCO_3$ solution. The solution was evaporated and the residue was chromatographed on a silica gel column (2 × 15 cm). Elution with a mixture of *n*-hexane and dichloromethane (1 : 1) gave unreacted **7b** (41 mg, 27 %) and a complex mixture, which showed many spots on TLC (silica gel, *n*-hexane - CH_2Cl_2).

General Procedure for the Sythesis of 5-(Di-*n*-alkylamino)-6-arylimino-2*H*-1,4-thiazin-3-ones (12).

To a solution of a mixture of **1** (0.49-0.63 mmol) and pyridine (0.99-1.5 mmol) in CH_2Cl_2 (50 ml) at 0 °C was added dropwise a solution of bromoacetyl bromide (0.57-1.1 mmol) in CH_2Cl_2 (40 ml) for 65 min to 85 min. The mixture was additionally stirred for an appropriate time, followed by washing with water (5 × 150 ml). Drying over $MgSO_4$, followed by removal of the solvent in *vacuo* gave a residue, which was chromatographed on a silica gel column (2 × 13 cm). Elution with a mixture of *n*-hexane and EtOAc (1 : 1) gave a mixture of deep blue color. Elution next with the same solvent mixture (1 : 2) gave compounds **12**. Consult Table **3** for reaction conditions, yields, and melting points of compounds **12** and Table **4** for their analytical and spectroscopic data.

Reaction of 6-(4-Chlorophenylimino)-5-(di-*n*-propylamino)-2*H*-1,4-thiazin-3-one (12b) with $LiAlH_4$.

To a solution of **12b** (169 mg, 0.500 mmol) in THF (30 ml) was added a suspension of $LiAlH_4$ (25 mg, 0.66 mmol) in THF (30 ml) through a dropping funnel for 5 min. The mixture was stirred for 2 h and worked up as usual. Column chromatography (2 × 12 cm) of the mixture using a mixture of *n*-hexane and EtOAc(1 : 1) as an eluent gave 2-(4-chlorophenylimino)-5-oxo-3-(di-*n*-propylamino)thiomorpholine (**14**) (148 mg, 87 %): pale yellow liquid; IR (neat) 3218, 3096, 2952, 2856, 1682, 1616, 1589, 1478, 1466, 1387, 1294, 1181, 1134, 1083, 1038, 1011, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.64-1.06 (m, 6H, $2CH_3$), 1.32-1.80 (m, 4H, $2CH_2$), 2.48-2.90 (m, 4H, $2NCH_3$), 3.11 and 4.41 (d, 2H, J = 12.0 Hz, CH_2), 4.67 (d, 1H, J = 6.0 Hz, CH), 6.79 (d, 2H, J = 8.0 Hz, ArH), 7.28 (d, 2H, J = 8.0 Hz, ArH), 7.88 (d, br, 1H, J = 6.0 Hz, NH). MS (m/z) 339 (M^+, 11.7), 240 (65.5), 155 (100). Anal. Calcd for $C_{16}H_{22}ClN_3OS$: C, 56.54; H, 6.52; N, 12.36; S, 9.43. Found: C, 56.57; H, 6.50; N, 12.39; S, 9.49.

Reaction of 12b with Phosphorus Pentasulfide (P_4S_{10}).

To a solution of **12b** (110 mg, 0.326 mmol) in benzene (30 ml) was added P_4S_{10} (147 mg, 0.331 mmol). The mixture was vigorously stirred for 7 h, followed by washing with water (3 × 50 ml). The organic layer was dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue, which was chromatographed on a silica gel column (3 × 13 cm). Elution with a mixture of *n*-hexane and EtOAc (3 : 1) gave a complex mixture and 6-(4-chlorophenylimino)-5-(di-*n*-propylamino)-2*H*-1,4-thiazine-3-thione (**15**) (53 mg, 46 %): red liquid; IR (neat) 2952, 1586, 1542, 1454, 1427, 1360, 1325, 1248, 1224, 1182, 1142, 1085, 1037, 1022, 1010, 923, 829, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.60-1.20 (m, 6H, $2CH_3$), 1.40-2.00 (m, 4H, $2CH_2$), 3.40-3.86 (m, 4H, $2NCH_2$), 3.94 (s, 2H, CH_2), 6.89 (d, 2H, J = 8.0 Hz, ArH), 7.36 (d, 2H, J = 8.0 Hz, ArH); MS (m/z) 353 (M^+, 44.1), 323 (39.6), 291 (65.7), 262 (100), 220 (49.6). Anal. Calcd for $C_{16}H_{20}ClN_3S_2$: C, 54.30; H, 5.70; N, 11.87; S, 18.12. Found: C, 54.27; H, 5.72; N, 11.91; S, 18.17.

Hydrolysis of 12b with Aqueous Hydrochloric Acid

To a solution of **12b** (180 mg, 0.533 mmol) in THF (30 ml) was added 20 % hydrochloric acid (30 ml). The mixture was stirred for 24 h, followed by neutralization with aqueous NaOH (5%). The aqueous layer was extracted with $CHCl_3$ (3 × 20 ml). The organic extracts were dried over $MgSO_4$. Removal of the solvent *in vacuo* gave a residue, which was chromatographed on a silica gel column (2 × 8 cm). Elution with a mixture of *n*-hexane and EtOAc (1 : 1) gave 4-chloroaniline (58 mg, 85 %). Elution with ethanol gave a unknown compound (9 mg) which was insoluble in most of the organic solvents.

General Procedure for the Synthesis of 6-Arylimino-2-methyl-5-(di-*n*-propylamino)-2*H*-1,4-thiazin-3-ones (16) and 5-Arylimino-2-(1-bromoethylidene)4-(di-*n*-propylamino)thiazolines (17).

To a solution of a mixture of **1** (0.54-0.74 mmol) and pyridine (1.2-1.5 mmol) in CH_2Cl_2 (70 ml) at 0° C was added dropwise a solution of 2-bromopropionyl bromide (0.65-0.93 mmol) in CH_2Cl_2 (50 ml) for 1 h. The mixture was additionally stirred for an appropriate time and then washed with water (5 × 50 ml). The mixture was worked up as usual. The reaction mixture was chromatographed on a silica gel column (2 × 15 cm). Elution with a mixture of *n*-hexane and CH_2Cl_2 (4 : 1) gave compounds **17** and a complex mixture. Elution with a mixture of n-hexane and EtOAc (1 : 1) gave compounds **16**. Consult Table **5** for reaction conditions, yields,

and melting points of compounds **16** and **17**. Consult Table **6** and **7** for analytical, and spectroscopic data of compounds **16** and **17**, respectively.

General Procedure for the Synthesis of [(Arylimino)(*S*-ethoxycarbonylmethyl)]methyl-*N*,*N*-(di-*n*-propyl)amidine Hydrobromides (19).

To a solution of **1** (0.32-0.45 mmol) in CH_2Cl_2 (100 ml) was added ethyl bromoacetate (0.34-0.36 mmol). The mixture was stirred for an appropriate time at room temperature. Evaporation of the solvent *in vacuo* gave a crude product. TLC (silica gel) of each product showed one spot with a tail: **19a** (R_f = 0.7 - 0.9, CH_2Cl_2 : acetone = 2 : 1), **19b** (R_f = 0.4 - 0.6, CH_2Cl_2 : acetone = 5 : 1), **19c** (R_f = 0.2 - 0.4, EtOAc : acetone = 1 : 2), **19d** (R_f = 0.2 - 0.4, EtOAc : acetone = 2 : 7). The crude products were purified by employing HPLC using acetonitrile as an eluent, Consult Table **8** for reaction conditions and yields of compounds **19** and Table **9** for their analytical and spectroscopic data.

Single Crystal *X*-ray Analyses of 7i and 12i.

The data were collected on an Enraf-Nomius CAD 4 diffractometer using graphite-monochromated Mo-K_α radiation. The structures were solved by direct methods and subsequent Fourier maps. Refinements were carried out by full-matrix least-squares techniques. Non-hydrogen atoms were anisotropically refined. Atomic scattering factors were taken from International Tables for *X*-ray Crystallography, Vol IV, 1974. All calculations and drawings were performed using a Micro VAX II Computer with the SDP system.

Crystal and Refinement Parameters for Compounds **7i** and **12i**

	7i	**12i**
Molecular formula	$C_{20}H_{20}ClN_3S$	$C_{14}H_{16}N_4O_3S$
Molecular weight	370.91	320.37
Crystal system	monoclinic	monoclinic
Space group	P2 (1) / n	P2 (1) / c
a, Å	10.2568(12)	8.190(2)
b, Å	13.775(2)	7.586(2)
c, Å	13.679(2)	24.917(8)
α, deg	90.000(13)	90.00(2)
β, deg	98.659(12)	98.23(2)
γ, deg	90.00(2)	90.00(2)
V, Å^3	1910.7(4)	1532.3(7)
Z	4	4
ρ calc., g / cm^3	1.289	1.389
Crystal size, mm	0.20 × 0.45 × 0.55	0.25 × 0.25 × 0.45
Absorption coefficient, mm^{-1}	0.317	0.229
θ range, deg	2.11 - 24.98	1.65 - 23.45
Index ranges	$-12 \le h \le 12$, $0 \le k \le 16$, $0 \le l \le 16$	$0 \le h \le 9$, $0 \le k \le 8$, $-27 \le l \le 27$
N_b of measured reflections	3504	2070
N_b of reflections used $\{I > 2\sigma(I)\}$	3357	1927
Data to parameter ratio	3356 / 228	1927 / 199
Final R indices	R_1 = 0.0726, wR_2 = 0:2245	R_1 = 0.0761, wR_2 = 0.1952
R indices (all data)	R_1 = 0.1135, wR_2 = 0.2417	R_1 = 0.0763, wR_2 = 0.1957

Atomic coordinates, bond lengths, angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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