Synthesis of 2,4,6-Triaryl-1,3,5-dithiazines and *N*-Arylmethylene-1-thioacylamino-1-arylmethylamines from *N*,*N'*-Diarylmethylenearylmethanediamines and Thioamides

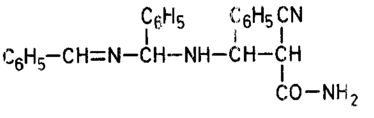
Tokiharu TAKAJO*, Satoshi KAMEE

Oyama National College of Technology, Oyama-shi, Tochigi, 323, Japan

Wataru ANDO

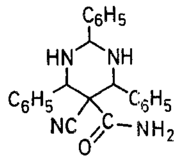
Department of Chemistry, University of Tsukuba, Sakura-mura, Niiharigun, Ibaraki, 305, Japan

The reaction of *N*,*N'*-dibenzylidenephenylmethanediamine (**1a**) with α-cyanoacetamide was reported[1] in 1936 to give tribenzaldiiminomalonic amide nitrile (**3**). Recently we found[2] that the crystalline product formed is not **3**, but the perhydropyrimidine derivative **4**. The condensation of *N*,*N'*-diarylmethylenearylmethanediamine **1** with formamide or acetamide is known to yield *N*-arylmethylene-1-acylamino-1-arylmethylamine[3] (**5**; Ar = C_6H_5, 4—H_3CO—C_6H_4; R = H, CH_3).



$C_6H_5{-}CH{=}N{-}\overset{C_6H_5}{\overset{|}{C}}H{-}NH{-}\overset{C_6H_5}{\overset{|}{C}}H{-}\underset{CO-NH_2}{\underset{|}{\overset{CN}{\overset{|}{C}}}}H$

3



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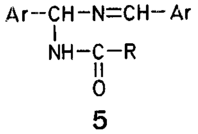


$Ar{-}\underset{NH-\underset{O}{\underset{\|}{C}}-R}{\underset{|}{C}}H{-}N{=}CH{-}Ar$

5

It has been shown[4–7] that 1,3,5-dithiazines can be formed by the action of halomethanes on thiourea, monoarylthiourea, or 1,5-diaryldithiobiuretes, and by the action of hydrogen sulfide on aldehyde + ammonia, or on *N*-alkyl derivatives obtained from alkylamine and thioacetic acids.

Table 1. Compounds **6** and **7** prepared

Compound[a]	Reaction conditions	Yield [%]	m.p. [°C] (solvent)	Molecular formula[b]	I.R. (Nujol) ν[cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$/TMS) δ[ppm]
	Method/time					
6a	A/7 days	95	138–139° (ethanol)	$C_{21}H_{19}NS_2$ (349.4)	3300 (NH); 1600, 1582, 1150, 1026, 921, 806, 756, 731, 715, 700, 630	1.68 (t, 1H, J = 12.0 Hz, NH); 5.4 (d, 2H, J = 12.0 Hz, 2C$\underline{H}$—NH)[c]; 5.58 (s, 1H, S—C$\underline{H}$—S); 7.4 (m, 15H$_{\text{arom}}$)
6b	A/10 days	59	176–177° (THF/ethanol)	$C_{24}H_{25}NS_2$ (391.6)	3320 (NH); 1512, 1186, 1161, 1116, 829, 798, 761, 747, 724, 661	1.62 (t, 1H, J = 13.0 Hz, NH); 2.32 (s, 9H, 3CH$_3$); 5.38 (d, 2H, J = 13.0 Hz, 2C$\underline{H}$—NH)[c]; 5.53 (s, 1H, S—C$\underline{H}$—S); 7.12, 7.37 (2d, J = 8 Hz, 6H$_{\text{arom}}$ each)
6c	A/10 days	56	125–126° (THF/methanol)	$C_{24}H_{25}NO_3S_2$ (439.6)	3320 (NH); 1606, 1581, 1506, 1306; 1242 (C—O); 1170, 1029, 842, 771, 750	1.55 (t, 1H, J = 13.0 Hz, NH); 3.78 (s, 9H, 3OCH$_3$); 5.37 (d, 2H, J = 13.0 Hz, 2C$\underline{H}$—NH)[c]; 5.52 (s, 1H, S—C$\underline{H}$—S); 6.88, 7.44 (2d, J = 9 Hz, 6H$_{\text{arom}}$ each)
6d	A/4 days	42	169–170° (THF/methanol)	$C_{21}H_{16}Cl_3NS_2$ (452.7)	3300 (NH); 1591, 1489, 1158, 1084, 1016, 832, 790, 762	1.56 (t, 1H, J = 13.0 Hz, NH)[c]; 5.37 (d, 2H, J = 13.0 Hz); 5.54 (s, 1H, S—C$\underline{H}$—S); 7.38 (s, 12H$_{\text{arom}}$)
6e	A/3 days	50	167–168° (CH$_3$CN)	$C_{24}H_{25}NO_3S_2$ (439.6)	3360 (NH); 1600, 1585, 1495, 1292; 1255 (C—O); 1100, 1050, 1025, 787, 760, 752	2.7 (t, 1H, J = 12.5 Hz, NH); 5.83 (d, 2H, J = 12.5 Hz, 2C$\underline{H}$—NH)[c]; 6.2 (s, 1H, S—C$\underline{H}$—S); 6.8–7.75 (m, 12H$_{\text{arom}}$)
6f	A/7 days	84	176–177° (THF/methanol)	$C_{21}H_{16}Cl_3NS_2$ (452.7)	3320 (NH); 1593, 1570, 1187, 1156, 1087, 1043, 1034, 800, 753, 710, 684	1.88 (t, 1H, J = 12.5 Hz, NH); 3.86 (s, 9H, 3OCH$_3$); 5.93 (d, 2H, J = 12.5 Hz, 2C$\underline{H}$—NH)[c]; 6.19 (s, 1H, S—C$\underline{H}$—S); 7.4 (m, 12H$_{\text{arom}}$)
7aa	D/6 h	47	106–107° (ethanol/*n*-hexane)	$C_{16}H_{16}N_2S$ (268.4)	3180 (NH); 1640 (C=N); 1580; 1515, 1370, 1310 (C=S, NH—CS); 1180, 1065, 1040, 760, 695	2.51 (s, 3H, CH$_3$); 7.02 (d, 1H, J = 7.9 Hz, C$\underline{H}$—NH)[c]; 7.45 (m, 8H$_{\text{arom}}$); 7.8 (m, 2H$_{\text{arom}}$); 8.22 (br. d, 1H, NH); 8.59 (s, 1H, C$\underline{H}$=N)
7ba	D/6 h	59	104–105° (ethanol/*n*-hexane)	$C_{18}H_{20}N_2S$ (296.4)	3199 (NH); 1632 (C=N); 1606; 1538, 1515 (C=S, NH—CS); 1180, 1075, 1053, 808, 730	2.36, 2.4, 2.54 (3s, 3H each, CH$_3$); 6.97 (d, 1H, J = 7.9 Hz, C$\underline{H}$—NH)[c]; 7.21, 7.24, 7.44, 7.7 (4d, 2H$_{\text{arom}}$ each); 8.4 (br. d, 1H, NH); 8.52 (s, 1H, C$\underline{H}$=N)
7ca	D/7 h	60	138–139° (ethanol/*n*-hexane)	$C_{18}H_{20}N_2O_2S$ (328.4)	3190 (NH); 1625 (C=N); 1600, 1580; 1515, 1370, 1310 (C=S, NH—CS); 1367, 1265, 1020, 830, 730	2.56 (s, 3H, CH$_3$); 3.74, 3.78 (2s, 3H each, OCH$_3$); 6.88, 7.71 (2d, 2H$_{\text{arom}}$ each, J = 8.8 Hz); 6.91, 7.46 (2d, 2H$_{\text{arom}}$ each, J = 8.6 Hz); 6.91 (d, 1H, C$\underline{H}$—NH)[c]; 8.4 (br. d, 1H, NH); 8.48 (s, 1H, C$\underline{H}$=N)
7ga	A/2 days	97	142–143° (THF/methanol)	$C_{18}H_{20}N_2S$ (296.4)	3160 (NH); 1632 (C=N); 1600; 1530, 1327, 1298 (C=S, NH—CS); 1180, 1065, 985, 747, 730	2.43 (s, 6H, 2CH$_3$); 2.50 (s, 3H, CH$_3$); 7.02 (d, 1H, J = 8.3 Hz, C$\underline{H}$—NH)[c]; 7.25 (m, 6H$_{\text{arom}}$); 7.8 (m, 2H$_{\text{arom}}$); 8.05 (br. d, 1H, NH); 8.91 (s, 1H, C$\underline{H}$=N)
7ab	D/7 h	54	102–103° (ethanol-*n*-hexane)	$C_{17}H_{18}N_2S$ (282.4)	3190 (NH); 1640 (C=N); 1580; 1515, 1405, 1310 (C=S, NH—CS); 1035, 955, 755, 690	1.27 (t, 3H, J = 7.5 Hz, C$\underline{H}_3$—CH$_2$); 2.67 (q, 2H, J = 7.5 Hz, CH$_3$—C$\underline{H}_2$); 7.04 (d, 1H, J = 7.8 Hz, C$\underline{H}$—NH)[c]; 7.45 (m, 8H$_{\text{arom}}$); 7.8 (m, 2H$_{\text{arom}}$); 7.98 (br. d, 1H, NH); 8.59 (s, 1H, C$\underline{H}$=N)
7ac	A/2 days	97	128–129°[d]	$C_{21}H_{18}N_2S$ (330.4)	3180 (NH); 1626 (C=N); 1595, 1577; 1515, 1342, 1235 (C=S, NH—CS); 1020, 957, 748, 687	7.12 (d, 1H, J = 8.0 Hz, C$\underline{H}$—NH)[c]; 7.55 (m, 15H$_{\text{arom}}$); 8.34 (br. d, 1H, NH); 8.64 (s, 1H, C$\underline{H}$=N)

[a] The appearance of **7ac** is yellow, all others are colorless.

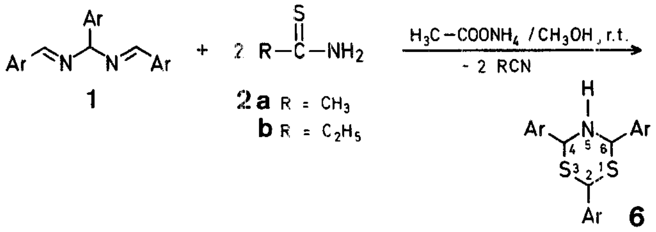
[b] Satisfactory microanalyses obtained: C ±0.19, H ±0.2, N ±0.17.

[c] A singlet was observed for C$\underline{H}$—ND (after treatment with D$_2$O).

[d] Product **7ac** is satisfactorily pure without recrystallization.

We present here the synthesis of 2,4,6-triaryl-5,6-dihydro-2*H*, 4*H*-1,3,5-dithiazines **6** and *N*-arylmethylene-1-thioacylamino-1-arylmethylamines **7** from **1** and thioamides **2**. The reaction of **1** with thioacetamide (**2a**) or thiopropionamide (**2b**) in the presence of ammonium acetate in methanol gives **6**, whereas the reaction of **1** with thioamides in an aprotic solvent such as benzene or acetonitrile at 70 °C yields **7** as major product (Tables 1 and 2).

The former reaction in protic solvent can be regarded as the condensation of **1** with hydrogen sulfide produced by the decomposition of thioamides **2a** and **2b**. In fact, **1** also reacts with hydrogen sulfide to give **6**. Thiobenzamide being unable to split off hydrogen sulfide does not give **6**, but **7** in both the procedures mentioned above.



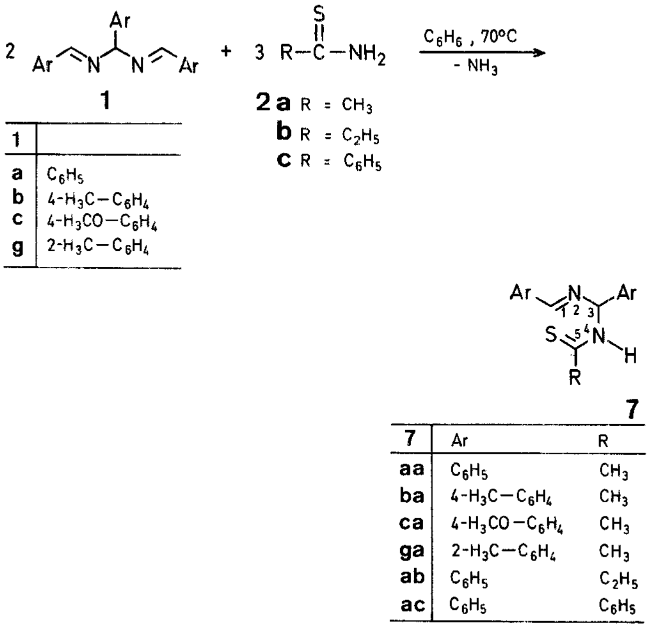
1,6	Ar
a	C_6H_5
b	$4\text{-}H_3C\text{-}C_6H_4$
c	$4\text{-}H_3CO\text{-}C_6H_4$
d	$4\text{-}Cl\text{-}C_6H_4$
e	$2\text{-}H_3CO\text{-}C_6H_4$
f	$2\text{-}Cl\text{-}C_6H_4$

Table 2. ^{13}C-N.M.R. Spectral Data of Compound **6** and **7**

Chemical shifts [δ ppm], ($CDCl_3/TMS_{int}$)

Compound	C-4 and C-6 ($^{1}J_{CH}$, Hz)	C-2 ($^{1}J_{CH}$, Hz)	C_{arom}	Other
6a	70.2 (152)	55.1 (156)	126.6 (d, 3C, $^{1}J_{CH}$ = 157 Hz); 128.3 (d, 2C); 128.5 (d, 3C, $^{1}J_{CH}$ = 158 Hz); 128.9 (d, 7C, $^{1}J_{CH}$ = 159 Hz); 129.4 (s, C-1′ at C-2); 139.8 (s, C-1′ at C-4 and -6)	
6b	70.0 (153)	54.8 (154)	126.5 (d, C-2′ and 6′ at C-4 and -6, $^{1}J_{CH}$ = 158 Hz); 128.2 (d, C-2′ and -6′ at C-2, $^{1}J_{CH}$ = 159 Hz); 129.4 (d, C-3′ and -5′ at C-2, -4 and -6, $^{1}J_{CH}$ = 159 Hz); 136.6 (s, C-1′ at C-2); 137.1 (s, C-1′ at C-4 and -6); 138.2 (s, C-4′ at C-2, -4 and -6)	21.1 (q, 3C, CH_3, $^{1}J_{CH}$ = 127 Hz)
6c	69.7 (156)	54.4 (154)	114.3 (d, C-3′ and 5′ at C-2, -4 and -6, $^{1}J_{CH}$ = 160 Hz); 127.9 (d, C-2′ and -6′ at C-4 and -6, $^{1}J_{CH}$ = 166 Hz); 129.6 (d, C-2′ and -6′ at C-2); 131.8 (s, C-1′ at C-2); 132.4 (s, C-1′ at C-4 and -6); 159.8 (s, C-4′ at C-2, -4 and -6)	55.4 (q, 3C, OCH_3, $^{1}J_{CH}$ = 144 Hz)
6d	69.4 (153)	54.3 (154)	127.9 (d, C-2′ and 6′ at C-4 and -6); 129.1 (d, C-3′ and -5′ at C-2, -4 and -6, $^{1}J_{CH}$ = 167 Hz); 129.6 (d, C-2′ and -6′ at C-2); 134.6 (s, C-1′ at C-4 and -6); 137.3 (s, C-1′ at C-2); 137.8 (s, C-4′ at C-2, -4 and -6)	
6e	65.7 (158)	47.7 (157)	110.8 (d, C-3′ at C-2, $^{1}J_{CH}$ = 158 Hz); 111.6 (d, C-3′ at C-4 and -6, $^{1}J_{CH}$ = 159 Hz); 121.0 (d, C-5′ at C-2, -4 and -6, $^{1}J_{CH}$ = 163 Hz); 128.0 (d, 2C); 129.2 (d, 1C); 129.4 (d, 2C); 130.3 (d, 1C); 128.0 (s, C-1′ at C-2); 128.4 (s, C-1′ at C-4 and -6); 155.6 (s, C-2′ at C-2); 156.2 (s, C-2′ at C-4 and -6)	55.8 (q, 3C, OCH_3, $^{1}J_{CH}$ = 144 Hz)
6f	67.4 (156)	51.8 (158)	127.5, 128.0 (2d, 2C each); 129.8 (d, 5C, $^{1}J_{CH}$ = 163 Hz); 130.3 (d, 2C); 130.6 (d, 1C); 132.9 (s, C-2′ at C-2, -4 and -6); 136.4 (s, C-1′ at C-2); 137.0 (s, C-1′ at C-4 and -6)	

	C-3 ($^{1}J_{CH}$, Hz)	C-1 ($^{1}J_{CH}$, Hz)	C-5	C_{arom}	Other
7aa	79.8 (149)	164.7 (159)	201.0	127.0 (d, 2C, $^{1}J_{CH}$ = 162 Hz); 128.7 (d, 7C, $^{1}J_{CH}$ = 161 Hz); 131.7 (d, 1C, $^{1}J_{CH}$ = 161 Hz); 135.1, 139.6 (2s, 1C each)	34.2 (q, CH_3, $^{1}J_{CH}$ = 129 Hz)
7ba	79.9 (150)	164.5 (153)	200.7	126.9 (d, 2C, $^{1}J_{CH}$ = 161 Hz); 128.8 (d, 2C); 129.4 (d, C-3′ and 5′ at C-1 and -3, $^{1}J_{CH}$ = 157 Hz); 132.6, 136.9, 138.3, 142.2 (4s, 1C each)	21.1, 21.5 (2q, CH_3 at C-4′ of C-1 and -3, $^{1}J_{CH}$ = 126 Hz), 34.2 (q, CH_3 at C-5, $^{1}J_{CH}$ = 129 Hz)
7ca	79.7 (153)	163.7 (162)	200.5	114.1 (d, C-3′ and 5′ at C-1 and 3, $^{1}J_{CH}$ = 164 Hz); 128.2 (d, 2C, $^{1}J_{CH}$ = 163 Hz); 130.5 (d, 2C, $^{1}J_{CH}$ = 163 Hz); 128.2, 132.3 (2s, C-4′ at C-1 and -3); 159.8, 162.5 (2s, C-1′ at C-1 and -3)	34.2 (q, CH_3 at C-5, $^{1}J_{CH}$ = 129 Hz), 55.4 (q, 2C, OCH_3 at C-4′ of C-1 and -3, $^{1}J_{CH}$ = 144 Hz)
7ga	77.4 (147)	162.9 (161)	200.8	126.3 (d, 2C); 127.4, 127.6, 128.6 (3d, 1C each); 130.9 (d, 2C), 131.1 (d, 1C); 133.6, 136.6, 138.0, 138.7 (4s, 1C each)	19.4 (q, 2C, CH_3 at C-2′ of C-1 and -3, $^{1}J_{CH}$ = 127 Hz), 34.3 (q, CH_3 at C-5, $^{1}J_{CH}$ = 130 Hz)
7ab	79.5 (139)	164.3 (157)	206.8	127.0 (d, 2C, $^{1}J_{CH}$ = 158 Hz); 128.8 (d, 7C, $^{1}J_{CH}$ = 161 Hz); 131.6 (d, 1C, $^{1}J_{CH}$ = 161 Hz); 135.5, 140.0 (2s, C-1′ at C-1 and 3)	13.4 (q, CH_3, $^{1}J_{CH}$ = 128 Hz), 40.1 (t, CH_2, $^{1}J_{CH}$ = 128 Hz)
7ac	80.2 (157)	164.1 (158)	198.6	126.9, 127.1 (2d, 2C each); 128.5 (d, 2C); 128.7 (d, 4C); 128.9 (d, 3C); 131.3, 131.6 (2d, 1C each); 135.5, 140.0, 141.7 (3s, 1C each)	



2 **1** + 3 **2**; $\xrightarrow[-NH_3]{C_6H_6,\ 70°C}$ **7**

1	
a	C_6H_5
b	$4\text{-}H_3C{-}C_6H_4$
c	$4\text{-}H_3CO{-}C_6H_4$
g	$2\text{-}H_3C{-}C_6H_4$

2a R = CH_3
b R = C_2H_5
c R = C_6H_5

7	Ar	R
aa	C_6H_5	CH_3
ba	$4\text{-}H_3C{-}C_6H_4$	CH_3
ca	$4\text{-}H_3CO{-}C_6H_4$	CH_3
ga	$2\text{-}H_3C{-}C_6H_4$	CH_3
ab	C_6H_5	C_2H_5
ac	C_6H_5	C_6H_5

2,4,6-Triphenyl-5,6-dihydro-2*H*,4*H*-1,3,5-dithiazine (6a); Typical Procedure:

Method A: A mixture of **1a** (2.98 g, 10 mmol), thioacetamide (**2a**; 0.75 g, 10 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (5 ml) is magnetically stirred at ambient temperature for 7 days. The precipitate obtained is collected and washed with methanol (15 ml) to give **6a** as a white crystalline matter, yield: 1.65 g (95%); m.p. 138–139 °C (C_2H_5OH).

Method B: A mixture of **1a** (0.75 g, 2.5 mmol), thiopropionamide (**2b**; 0.45 g, 5 mmol), and ammonium acetate (0.4 g, 5 mmol) in methanol (2 ml) is magnetically stirred at ambient temperature for 4 days. The precipitate formed is worked up as above to give **6a**; yield: 0.5 g (57%).

Method C: Hydrogen sulfide is bubbled through **1a** (1.49 g, 5 mmol) in methanol (5 ml) at ambient temperature for ~ 1 h until the methanol solution is tinged pale yellow, and then the mixture is further allowed to stir for 2 h. The precipitate deposited is worked up as above to give **6a**; yield: 1.08 g (62%).

N-Benzylidene-thioacetylamino-1-phenylmethylamine (7aa); Typical Procedure:

Method D: A mixture of **1a** (1.49 g, 5 mmol) and thioacetamide (**2a**; 0.56 g, 7.5 mmol) in benzene (5 ml) is magnetically stirred for 6 h at 70 °C. The solution is then concentrated at room temperature under vacuum, the precipitate collected by filtration, washed with hexane, aqueous ethanol, and dried to give the crude product (1.8 g), which is recrystallized from ethanol/hexane (1 : 1); yield: 0.95 g (47%); m.p. 106–107 °C.

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