3,7-Diazabicyclo[3.3.1]nonan-9-ones, Octahydropyrido[4,3-*d*]pyrimidines, and 1,3,7-Triazabicyclo[3.3.1]non-3-enes from *N*,*N*′-Dibenzylidenephenylmethanediamines and Alkyl Methyl Ketones

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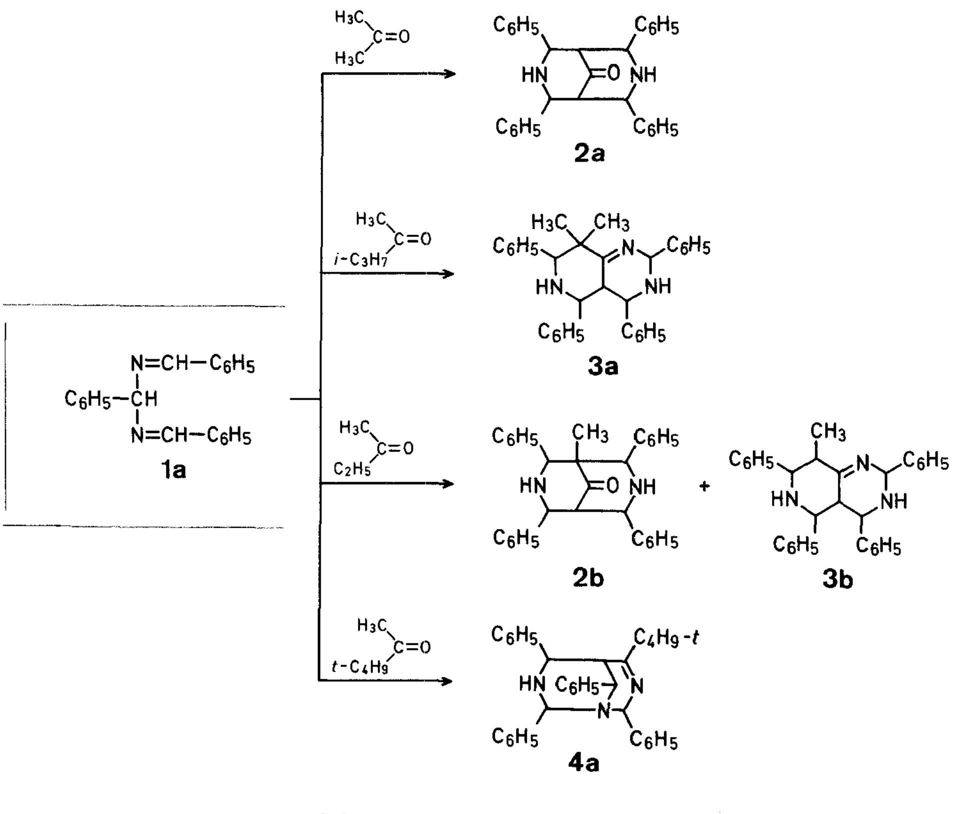
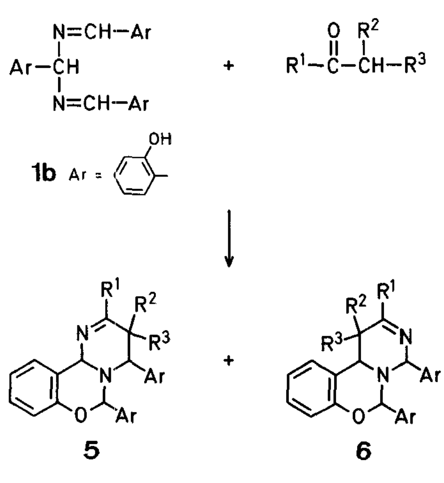
As a result of their unique structure as benzylideneamine type Schiff bases containing two azomethine groups, *N*,*N*′- dibenzylidenephenylmethanediamines **1** have potential as reagents for the synthesis of nitrogen-containing heterocyclic compounds[1-5].

In this paper, we report on the formation of e.g. 2,4,6,8-tetraphenyl-3,7-diazabicyclo[3.3.1]nonan-9-one[6] (**2a**), 8,8-dimethyl-2,4,5,7-tetraphenyl-2,3,4,4a,5,6,7,8-octahydropyrido[4,3-*d*]pyrimidines (**3a**) and 4-*t*-butyl-2,6,8,9-tetraphenyl-1,3,7-triazabicyclo[3.3.1]non-3-ene (**4a**) from the reaction of **1a** with acetone, isopropyl methyl ketone, or *t*-butyl methyl ketone, respectively, and ammonium acetate in methanol at 25–35 °C. With ethyl methyl ketone, a mixture of products **2b** and **3b** is obtained (Scheme **A**).



Scheme **A**

In these reactions of **1a** with alkyl methyl ketone, the addition of acetic acid facilitates the formation of **2** and disturbs the formation of **3** and **4**. When the reaction with ethyl methyl ketone was carried out in the presence of acetic acid, the yield of **2b** increased from 0.7% to 39% and the yield of **3b** decreased from 44% to 3%. In contrast, a similar reaction of *N*,*N*′-bis[2-hydroxybenzylidene]-2-hydroxyphenylmethanediamine (**1b**) with aliphatic ketones gives the pale yellow substances **5** and **6**[4] (Scheme **B**).



Scheme **B**

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Table 1. Compounds **2**, **3**, and **4** prepared

Product[a] No.	R^1	R^2	R^3	Ar	Yield [%][b] (reaction time)[c] by Method A	by Method B	m.p. [°C][d]	Molecular formula[e] or Lit. m.p. [°C]	
2a	H	H	H	C_6H_5	15 (7 day)	26 (7 day)	255–256°	250–252°[6]	
2b	CH_3	H	H	C_6H_5	0.7 (4 day)	39 (12 h)	240.5–242°	$C_{32}H_{30}N_2O$	(458.6)
2c	H	H	H	4-H_3C—C_6H_4	9.0 (2 day)	26 (2 day)	224–225°	$C_{35}H_{36}N_2O$	(500.7)
2d	CH_3	H	H	4-H_3C—C_6H_4	16 (104 day)	36 (1 day)	219–220°	$C_{36}H_{38}N_2O$	(514.7)
2e	H	H	H	4-H_3CO—C_6H_4	8.0 (2 day)	17 (1 day)	222–224°	226–228°[6]	
2f	H	H	H	4-Cl—C_6H_4	31 (7 day)	34 (1 day)	236–237°	239–241°[6]	
3a	CH_3	H	H	C_6H_5	44 (4 day)	3.0 (12 h)	183–184°	$C_{32}H_{31}N_3$	(457.6)
3b	CH_3	CH_3	H	C_6H_5	50 (6 day)	—	186–187°	$C_{33}H_{33}N_3$	(471.6)
3c	CH_3	CH_3	H	4-H_3C—C_6H_4	51 (4 day)	—	168–169°	$C_{37}H_{41}N_3$	(527.7)
4a	CH_3	CH_3	CH_3	C_6H_5	76 (5 day)	—	188–190°	$C_{34}H_{35}N_3$	(485.6)
4b	CH_3	CH_3	CH_3	4-H_3C—C_6H_4	60 (27 day)	—	185–187°	$C_{38}H_{43}N_3$	(541.8)
4c	CH_3	CH_3	CH_3	4-Cl—C_6H_4	60 (14 day)	—	218–219°	$C_{34}H_{31}Cl_4N_3$	(623.4)

[a] For location of substituents, see Scheme **D**.

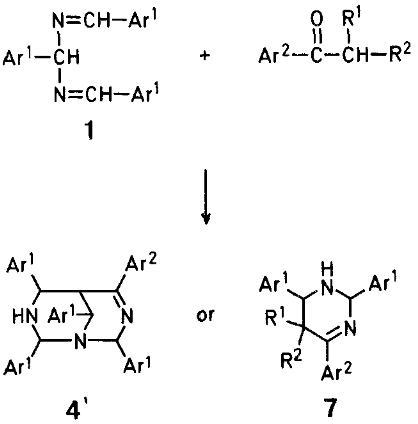
[b] Yield of isolated product.

[c] Time for the solid to separate.

[d] Recrystallized from tetrahydrofuran/methanol.

[e] Satisfactory microanalyses obtained: C ±0.32, H ±0.37, N ±0.20.

A strikingly parallel example to the formation of **4a** is the formation of **4′** from the following condensation of **1** with alkyl aryl ketones[5] (Scheme C).



Scheme C

The above results suggest the following modes of formation of **2**, **3**, and **4**, and hence, it should be recognized that acetic acid functions as a promotor for the deamination and as an inhibitor for the dehydration in this reaction (Scheme **D**).

2,4,6,8-Tetrakis[4-methylphenyl]-3,7-diazabicyclo[3.3.1]nonan-9-one (2c; 4-H_3C—C_6H_4 in place of C_6H_5 in 2a); Typical Procedure:

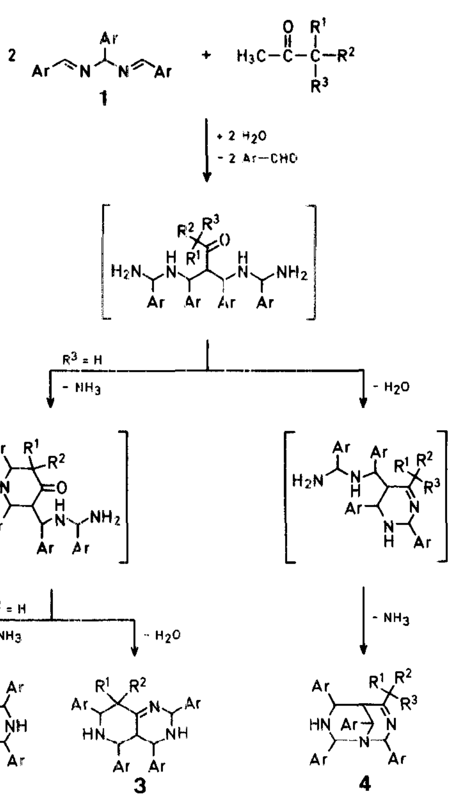
Method A: A mixture of *N,N′*-bis[4-methylbenzylidene]-4-methylphenylmethanediamine (**1c**; 3.40 g, 10 mmol), acetone (0.58 g, 10 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (5 ml) is magnetically stirred at ambient temperature (25–35 °C) for 24 h, then methanol (15 ml) is added, and stirring is continued for a further 24 h. The deposited precipitate is collected and washed with methanol to give **2c**: yield: 0.32 g (9%).

Method B: An equimolar (10 mmol) mixture of **1c**, acetone, and ammonium acetate in solution of methanol (2.5 ml) and acetic acid (2.5 ml) is similarly treated to give **2c**; yield: 0.98 g (26%).

1-Methyl-2,4,6,8-tetraphenyl-3,7-diazabicyclo[3.3.1]nonan-9-one (2b) and 8-methyl-2,4,5,7-tetraphenyl-2,3,4,4a,5,6,7,8-octahydropyrido[4,3-*d*]pyrimidine (3b); Typical Procedure:

Method A: A mixture of **1a** (3.58 g, 12 mmol), ethyl methyl ketone (0.65 g, 9 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (5 ml) is magnetically stirred at ambient temperature for two days and then allowed to stand for two days. The resultant precipitate is collected and washed with hot methanol (30 ml) to give a white crystalline matter (2.5 g) consisting of a mixture of **2b** and **3b** (~3:97 molar ratio). The former product is not sufficiently soluble in tetrahydrofuran and is thus easily removed from the latter by dissolving the major part of **3b** in a minimum amount of tetrahydrofuran (~5 ml) and recrystallizing from tetrahydrofuran/methanol to give **2b**; yield: 0.03 g (0.7%) and **3b**; yield: 1.8 g (44%).

Method B: A mixture of **1a** (3.58 g, 12 mmol), ethyl methyl ketone (9 mmol), ammonium acetate (10 mmol), acetic acid (2.5 ml), and methanol (2.5 ml) is magnetically stirred at ambient temperature for 12 h and al-



Scheme D

Table 2. Spectral Data of Compounds **2**, **3**, and **4**

Product No.	I.R. (nujol) ν [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$) δ [ppm]	M.S. (70 eV, 200 °C) *m/e* (relative intensity %)
2a	3340 (NH); 1717 (C=O); 771, 705 (δ_{C-H})	7.7–6.5 (m, 20 H_{arom}); 4.75, 4.40 (d, 2H, N—C$\underline{H}$—CH)[a]; 2.90 (q, 2H, CH—C$\underline{H}$—CH)[a]; 2.1, 1.7 (br, 1H, NH)	444 (M$^+$, 1), 250 (86), 233 (32), 208 (62), 195 (53), 194 (76), 131 (84), 105 (49), 104 (100), 103 (57), 77 (56)
2b	3330 (NH); 1712 (C=O); 765, 704 (δ_{C-H})	7.9–6.6 (m, 20 H_{arom}); 5.28, 3.84 (s, 1H, N—CH); 4.74, 4.34 (d, 1H, N—C$\underline{H}$—CH)[a]; 3.00 (q, 1H, CH—C$\underline{H}$—CH)[a]; 2.1, 1.6 (br, 1H, NH); 0.64 (s, 3H, CH$_3$)	458 (M$^+$, 1.2), 264 (76), 222 (26), 195 (48), 194 (100), 131 (47), 105 (27), 104 (46), 103 (30), 91 (32), 77 (30)
2c	3325 (NH); 1729 (C=O); 812, 802, 730, 718 (δ_{C-H})	7.45, 7.16, 6.84, 6.56 (d, 4 H_{arom})[b]; 4.63, 4.25 (d, 2H, N—C$\underline{H}$)[a]; 2.78 (q, 2H, CH—C$\underline{H}$—CH)[a]; 2.37, 2.18 (s, 6H, CH$_3$); 2.0, 1.5 (br, 1H, NH)	—
2d	3325 (NH); 1710 (C=O); 815, 712 (δ_{C-H})	7.6–6.5 (m, 16 H_{arom}); 5.21, 3.76 (s, 1H, N—CH); 4.68, 4.27 (d, 1H, N—C$\underline{H}$—CH)[a]; 2.94 (q, 1H, CH—C$\underline{H}$—CH)[a]; 2.42, 2.38, 0.63 (s, 3H, CH$_3$); 2.19 (s, 6H, CH$_3$); 2.0, 1.4 (br, 1H, NH)	—
2e	3350, 3320 (NH); 1715 (C=O); 1256, 1247 (C—O); 839, 830, 723 (δ_{C-H})	7.48, 6.92 (d, 4 H_{arom})[b]; 6.63 (s, 8 H_{arom}); 4.60, 4.25 (d, 2H, N—C$\underline{H}$—CH)[a]; 3.83, 3.63 (s, 6H, CH$_3$); 2.76 (q, 2H, CH—C$\underline{H}$—CH)[a]; 2.0, 1.5 (br, 1H, NH)	—
2f	3340 (NH); 1711 (C=O); 1490; 822, 793, 720 (δ_{C-H})	7.43 (s, 8 H_{arom}); 7.09, 6.64 (d, 4 H_{arom})[b]; 4.59, 4.31 (d, 2H, N—C$\underline{H}$—CH)[a]; 2.75 (q, 2H, CH—C$\underline{H}$—CH)[a]; 2.1, 1.5 (br, 1H, NH)	—
3a	3330 (NH); 1662 (C=N); 752, 722, 700 (δ_{C-H})	7.7–6.6 (m, 20 H_{arom}); 5.44 (t, 1H, CH—N=)[a]; 3.83 [d, 1H, C$\underline{H}$—CH(CH$_3$)—][b]; 3.75, 3.69 (d, 1H, N—C$\underline{H}$—CH)[b]; 3.1 (m, 1H, CH—C$\underline{H}$—CH); 2.7 [m, 1H, C$\underline{H}$(CH$_3$)—]; 1.7 (br, 2H, NH); 1.01 (d, 3H, CH$_3$)[c]	247 (27), 246 (43), 194 (17), 118 (19), 115 (16), 105 (39), 104 (54), 77 (28), 32 (22), 28 (100)
3b	3320 (NH); 1652 (C=N); 788, 753, 703 (δ_{C-H})	7.5–6.7 (m, 20 H_{arom}); 5.46 (d, 1H, CH—N=)[a]; 3.87 (s, 1H, N—CH); 3.75, 3.67 (d, 1H, N—C$\underline{H}$—CH)[b]; 3.3 (m, 1H, CH—C$\underline{H}$—CH); 1.5 (br, 2H, NH); 1.34, 1.14 (s, 3H, CH$_3$)	471 (M$^+$, 0.7), 262 (28), 261 (100), 194 (70), 193 (32), 132 (62), 117 (24), 106 (38), 105 (27), 104 (45), 91 (32)
3c	3300 (NH); 1655 (C=N); 810, 721 (δ_{C-H})	7.5–6.7 (m, 12 H_{arom}); 6.63 (s, 4 H_{arom}); 5.40 (d, 1H, CH—N=)[a]; 3.81 (s, 1H, N—CH); 3.68, 3.60 (d, 1H, N—C$\underline{H}$—CH)[b]; 3.4 (m, 1H, CH—C$\underline{H}$—CH); 2.28, 2.14 (s, 6H, CH$_3$); 1.6 (br, 2H, NH); 1.29, 1.10 (s, 3H, CH$_3$)	—
4a	3320 (NH); 1643 (C=N); 763, 755, 697 (δ_{C-H})	8.0–7.1 (m, 20 H_{arom}); 5.91 (s, 1H, CH—N=); 5.30 (d, 1H, HN—CH—N)[c]; 4.59 (q, 1H, HN—C$\underline{H}$—CH)[a,c]; 4.09 (d, 1H, N—C$\underline{H}$—CH)[a]; 3.52 (t, CH—C$\underline{H}$—CH)[a]; 1.77 (q, 1H, NH)[c]; 0.77 (s, 9H, CH$_3$)	485 (M$^+$, 0.2); 429 (21); 428 (57), 291 (38), 276 (48), 195 (37), 194 (100), 193 (32), 104 (30), 91 (46), 77 (37)
4b	3310 (NH); 1642 (C=N); 810, 720 (δ_{C-H})	7.9–6.6 (m, 16 H_{arom}); 5.88 (s, 1H, CH—N=); 5.31 (d, 1H, HN—C$\underline{H}$—N)[c]; 4.55 (q, 1H, HN—C$\underline{H}$—CH)[a,c]; 4.04 (d, 1H, N—C$\underline{H}$—CH)[c]; 3.46 (t, 1H, CH—C$\underline{H}$—CH)[c]; 2.34, 0.76 (s, 9H, CH$_3$); 2.27 (s, 3H, CH$_3$); 1.7 (br, 1H, NH)	—
4c	3320 (NH); 1641 (C=N); 1090; 833, 818, 732 (δ_{C-H})	7.8–7.0 (m, 16 H_{arom}); 5.76 (s, 1H, CH—N=); 5.2 (br, 1H, HN—C$\underline{H}$—N); 4.5 (br, 1H, HN—C$\underline{H}$—CH); 3.92 (d, 1H, N—C$\underline{H}$—CH)[a]; 3.43 (t, 1H, CH—C$\underline{H}$—CH)[a]; 1.8 (br, 1H, NH); 0.76 (s, 9H, CH$_3$)	—

[a] $J = 1-4$ Hz in the cases in which a doublet, triplet, or quartet was observed.
[b] $J = 8-10$ Hz in the cases in which a doublet was observed.
[c] $J = 6-7$ Hz in the cases in which a doublet, triplet, or quartet was observed.

lowed to stand overnight. The deposited precipitate is collected and washed with hot methanol (30 ml) to give **2b**; yield: 39%. From the washings, **3b** is obtained; yield: 0.12 g (2.9%).

8,8-Dimethyl-2,4,5,7-tetraphenyl-2,3,4,4a,5,6,7,8-octahydropyrido[4,3-*d*]pyrimidine (3a); Typical Procedure:

Method A: A mixture of **1a** (3.58 g, 12 mmol), isopropyl methyl ketone (0.78 g, 9 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (5 ml) is magnetically stirred at ambient temperature for three days, then methanol (5 ml) is added, stirring is continued for one day, and the mixture is allowed to stand for two days. The deposited precipitate is collected and washed with methanol (15 ml) to give **3a** as a white crystalline matter; yield: 2.13 g (50%).

4-*t*-Butyl-2,6,8,9-tetraphenyl-1,3,7-triazabicyclo[3.3.1]non-3-ene (4a); Typical Procedure:

Method A: A mixture of **1a** (4.17 g, 14 mmol), *t*-butyl methyl ketone (1.00 g, 10 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (7 ml) is magnetically stirred at ambient temperature for 5 days. The resultant precipitate is collected and washed with methanol (15 ml) to give crude **4a**; yield: 3.7 g (76%).

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[1] D. H. Hunter, S. K. Shim, *J. Am. Chem. Soc.* **91**, 6202 (1969).
[2] C. Shin, J. Yoshimura, *Tetrahedron Lett.* **1973**, 2615.
[3] C. Shin et al., *Nippon Kagaku Kaishi* **1976**, 1100; *C. A.* **86**, 5250 (1977).
[4] S. Kambe et al., *Synthesis* **1975**, 802.
[5] T. Takajo et al., *Synthesis* **1977**, 647.
[6] V. Baliah, R. Usha, *Indian J. Chem.* **10**, 319 (1972).