Synthesis of *N,N'*-Bis[2-hydroxybenzylidene]arylmethanediamines

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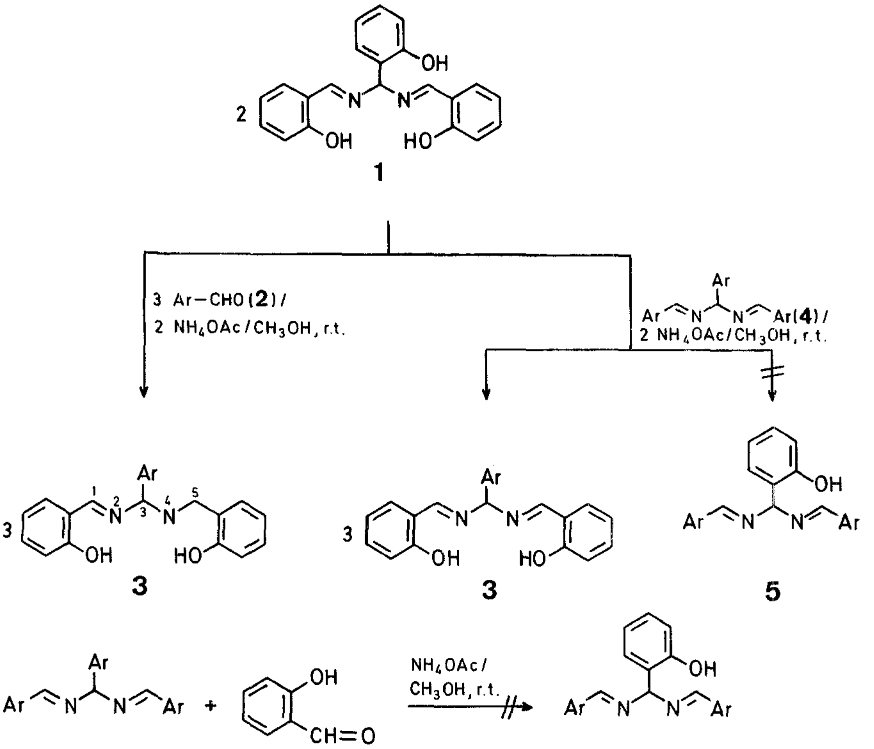
Since it was noted as early as 1837[1] that benzaldehyde reacts with ammonia to afford the unique trimeric product, *N,N'*-dibenzylidenephenylmethanediamine, a number of analogous double Schiff bases have been reported[2-12]. Recently, some of them were used for the synthesis of nitrogen-containing heterocyclic compounds[13]. We now report that the condensation product of salicylaldehyde and ammonia, *N,N'*-bis[2-hydroxybenzylidene]-2-hydroxyphenylmethanediamine (**1**) reacts with several different arylaldehydes **2** or other *N,N'*-diarylmethylenearylmethanediamines **4** to give the new *N,N'*-bis[2-hydroxybenzylidene]arylmethanediamines **3**.

When a mixture of 2 mol of **1** and 3 mol of an arylaldehyde **2** is allowed to react in the presence of 2 mol of ammonium acetate in methanol, 3 mol of the *N,N'*-bis[2-hydroxybenzylidene]arylmethanediamine **3** are formed in good yields (Table 1). Compounds **3** can also be prepared under the same conditions from **1** and *N,N'*-diarylmethylenearylmethanediamine **4**. In this reaction none of *N,N'*-diarylmethylene-2-hydroxyphenylmethanediamine **5** could be detected. Compound **5** is also not obtained from **4** and salicylaldehyde.



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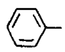
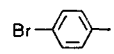
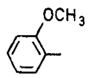
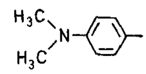
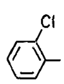
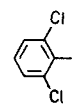
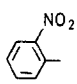
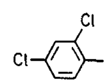
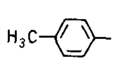
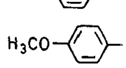
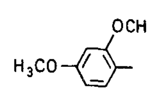
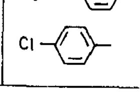
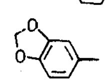
a		h	
b		i	
c		j	
d		k	
e			
f		l	
g		m	

All the compounds prepared are characterized by spectral data (Table 2).

N,N'-Bis[2-hydroxybenzylidene]phenylmethanediamine (3a); Typical Procedure:

Method A: A mixture of 1 (1.73 g, 5 mmol), benzaldehyde (1.06 g, 10 mmol), and ammonium acetate (1.2 g, 15 mmol) in methanol (5 ml) is magnetically stirred at ambient temperature for two days. The pale yellow precipitate is collected, washed with methanol (3×5 ml), and air-dried to give almost pure (^{1}H-N.M.R.) 3a; yield: 2.45 g (99%); m.p. 117–119°C. The precipitate is recrystallized from methanol (25 ml) and benzene (5 ml) to give 3a as pale yellow crystals; yield: 1.6 g (65%); m.p. 123–124°C.

Table 1. N,N'-Bis[2-hydroxybenzylidene]arylmethanediamines 3a–m prepared

Product	Yield[a] [%] (reaction time) by Method A	by Method B	m.p. [°C] (solvent)	Molecular formula[b]	I.R. (Nujol) ν [cm^{-1}] C=N	Ar$_{ring}$	C—O	δ_{CH}
3a	65 (2 d)	67 (2 h)	123–124° (C_6H_6/CH_3OH)	$C_{21}H_{18}N_2O_2$ (330.4)	1620	1580	1280	760
3b	72 (1 d)	76 (10 h)	152–153° (CH_3CN)	$C_{22}H_{20}N_2O_3$ (360.4)	1620	1580	1280	760
3c	57 (3 d)	69 (7 h)	152–153° (C_6H_6/CH_3OH)	$C_{21}H_{17}ClN_2O_2$ (364.8)	1620	1580	1283	755
3d	53 (1 d)	— (—)	141–142° (THF/CH_3OH)	$C_{21}H_{17}N_3O_4$ (375.4)	1618	1580	1280	755[d]
3e	43 (4 d)	53 (1 d)	100–101° (C_6H_6/CH_3OH)	$C_{22}H_{20}N_2O_2$ (344.4)	1618	1575	1280	755
3f	58 (1 d)	73 (8 h)[c]	151–152° (CH_3CN)	$C_{22}H_{20}N_2O_3$ (360.4)	1620	1578	1260	755
3g	52 (3 h)	67 (1 d)	139–140° (C_6H_6/CH_3OH)	$C_{21}H_{17}ClN_2O_2$ (364.8)	1620	1575	1280	760
3h	55 (5 h)	— (—)	145–146° (CH_3CN)	$C_{21}H_{17}BrN_2O_2$ (409.3)	1622	1570	1275	755
3i	46 (1 d)[c]	46 (5 h)	137–138° (CH_3CN)	$C_{23}H_{23}N_3O_2$ (373.4)	1620	1575	1280	758
3j	87 (15 h)	85 (8 h)	158–159° (CH_3CN)	$C_{21}H_{16}Cl_2N_2O_2$ (399.3)	1620	1580	1275	755
3k	51 (4 d)	47 (1 d)	114–115° (CH_3CN)	$C_{21}H_{16}Cl_2N_2O_2$ (399.3)	1620	1585	1280	760
3l	45 (1 d)	— (—)	121–122° (THF/CH_3OH)	$C_{23}H_{22}N_2O_4$ (390.4)	1620	1590	1280	760
3m	45 (5 d)	58 (10 h)	108–109° (C_6H_6/CH_3OH)	$C_{22}H_{18}N_2O_4$ (374.4)	1620	1580	1285	765

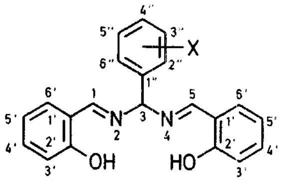
[a] Yield of recrystallized product.

[b] Satisfactory microanalyses obtained: C ±0.19, H ±0.15, N ±0.20.

[c] See experimental.

[d] A sharp band of medium intensity is observed at 1350 cm^{-1} (NO_2).

Table 2. N.M.R. Data for Compounds **3**



Product	^{1}H-N.M.R. (CDCl$_3$/TMS)[a] δ [ppm]				^{13}C-N.M.R. (CDCl$_3$/TMS)[e] δ [ppm] J [Hz]				
	OH[b]	N=CH[c]	N—CH—N[d]	Other signals	3-C ($^{1}J_{CH}$)	1'-C	2'-C	1,5-C ($^{1}J_{CH}$)	Other signals
3a	12.70	8.36	5.83	7.2 (m, 9H); 6.75 (m, 4H)	89.9 (145.2)	118.7	161.2	164.9 (161.3)	117.3, 119.0, 127.0, 129.1, 132.3, 133.2 (2C each); 128.6 (4''-C); 140.2 (1''-C)
3b	13.16	8.61	6.46	7.4 (m, 6H); 6.95 (m, 6H); 3.85 (s, 3H)	85.5 (146.2)	118.9	161.2	165.0 (162.1)	55.6 ($^{1}J_{CH}$=145 Hz, OCH$_3$); 110.9, 121.2, 128.0, 129.7 (1C each); 117.2, 118.9, 132.2, 133.0 (2C each); 133.3 (1''-C); 156.7 (2''-C)
3c	12.81	8.59	6.45	7.35 (m, 8H); 6.95 (m, 4H)	85.5 (148.2)	118.5	161.1	165.7 (160.4)	127.7, 129.0, 129.9, 130.0 (1C each); 117.2, 119.1, 132.4, 135.3 (2C each); 133.0 (2''-C); 137.3 (1''-C)
3d	12.65	8.66	6.68	7.6 (m, 8H); 6.9 (m, 4H)	83.8 (149.1)	118.4	161.1	166.6 (162.2)	124.7, 129.5, 129.8, 133.9 (1C each); 117.3, 119.3, 132.7, 133.6 (2C each); 133.9 (1''-C); 148.1 (2''-C)
3e	12.98	8.53	5.95	7.3 (m, 8H); 6.9 (m, 4H); 2.36 (s, 3H)	89.6 (146.5)	118.6	161.1	164.7 (160.4)	21.1 ($^{1}J_{CH}$=125.6 Hz, CH$_3$); 124.7, 129.5, 129.8, 133.9 (1C each); 117.2, 119.0, 129.6, 132.2, 133.1 (2C each); 137.2, 138.4 (1''-C, 4''-C)
3f	13.04	8.53	5.91	7.35 (m, 6H); 6.95 (m, 6H); 3.76 (s, 3H)	89.4 (148.2)	118.6	161.1	164.6	55.3 ($^{1}J_{CH}$=143.9 Hz, OCH$_3$); 114.2, 117.2, 119.0, 128.2, 132.3, 133.1 (2C each); 132.3 (1''-C); 159.8 (4''-C)
3g	12.79	8.58	5.96	7.35 (m, 8H); 7.0 (m, 4H)	89.1 (148.2)	118.4	161.1	165.2 (160.4)	117.2, 119.2, 128.3, 129.2, 132.4, 133.4 (2C each); 134.5 (4''-C); 138.7 (1''-C)
3h	12.80	8.55	5.91	7.4 (m, 8H); 6.95 (m, 4H)	89.2 (147.3)	118.4	161.1	165.3 (161.3)	117.3, 119.2, 128.6, 132.2, 133.5 (2C each); 122.7 (4''-C); 139.2 (1''-C)
3i	13.15	8.55	5.93	7.3 (m, 6H); 6.85 (m, 6H); 2.92 (s, 6H)	89.6 (145.6)	118.7	161.1	164.2 (160.4)	40.4 [$^{1}J_{CH}$=135.4 Hz, N(CH$_3$)$_2$]; 112.6, 117.1, 118.8, 127.9, 132.1, 132.9 (2C each); 127.6 (1''-C); 150.7 (4''-C)
3j	12.91	8.64	6.8–7.5	6.8–7.5 (m, 12H)	85.0 (146.5)[f]	118.5	161.0	165.9 (160.4)	117.2, 119.0, 129.7, 132.3, 133.3 (2C each); 130.2 (4''-C); 134.6 (1''-C); 135.2 (2''-C, 6''-C)
3k	12.70	8.62	6.40	7.4 (m, 7H); 6.95 (m, 4H)	85.1 (150.8)	118.4	161.1	166.0 (161.2)	128.0 (1C); 117.3, 119.2, 129.8, 132.5, 133.5 (2C each); 135.0 (1''-C); 136.0 (2''-C, 4''-C)
3l	13.12	8.58	6.38	7.4–6.4 (m, 11H); 3.78 (s, 3H); 3.83 (s, 3H)	83.0 (149.5)	118.8	161.2	164.6 (160.4)	55.4, 55.5 ($^{1}J_{CH}$=143.8 Hz, 2OCH$_3$); 98.8, 104.8, 128.7 (1C each); 117.1, 118.8, 132.1, 132.8 (2C each); 120.6 (1''-C); 157.7 (2''-C, 4''-C)
3m	12.85	8.51	5.88	7.3 (m, 4H); 6.9 (m, 7H); 5.93 (s, 2H)	89.6 (147.8)	118.6	161.1	164.8 (160.4)	101.3 ($^{1}J_{CH}$=173.5 Hz, O—CH$_2$—O); 117.2, 119.0, 132.3, 133.3 (2C each); 147.9, 148.3 (3''-C, 4''-C)

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[a] Recorded on a Hitachi R-900 N.M.R. spectrometer at 90 MHz.

[b] s, 2H except for **3i** (br. s, 2H).

[c] s, 1H.

[d] s, 1H except for **3j** where the peak overlaps with that of aromatic protons.

[e] Recorded on a Hitachi R-900 FT-N.M.R. spectrometer at 22.6 MHz.

[f] $^{3}J_{CH}$=10.5 Hz.

Method B: A mixture of **1** (3.45 g, 10 mmol), *N,N'*-dibenzylidenephenylmethanediamine (**4a**; 1.49 g, 5 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (20 ml) is magnetically stirred at ambient temperature for 4 h. The resultant precipitate is collected by vacuum filtration, washed with methanol (3 x 5 ml), and dried at room temperature to give crude **3a**; yield: 4.95 g (99.9%); m.p. 108–110 °C. The precipitate is recrystallized from acetonitrile (30 ml) to give pale yellow crystals of **3a**; yields: 3.31 g (67%); m.p. 122–123 °C.

***N,N'*-Bis[2-hydroxybenzylidene]-4-methoxyphenylmethanediamine (3f):** A mixture of **1** (1.73 g, 10 mmol), *N,N'*-bis[4-methoxybenzylidene]-4-methoxyphenylmethanediamine (**4b**; 0.97 g, 2.5 mmol), and ammonium acetate (0.77 g, 10 mmol) in methanol (10 ml) is magnetically stirred at ambient temperature for 8 h, and worked up as described above to give crude **3f**; yield: 2.35 g (87%); m.p. 114–115 °C. The precipitate is recrystallized from acetonitrile (15 ml) to give **3f** as yellow crystals; yield: 1.98 g (73%); m.p. 151–152 °C.

***N,N'*-Bis[2-hydroxybenzylidene]-4-dimethylaminophenylmethanediamine (3i):**
A mixture of **1** (1.73 g, 5 mmol), 4-dimethylaminobenzaldehyde (1.12 g, 7.5 mmol), and ammonium acetate (1.54 g, 20 mmol) in methanol (5 ml) and concentrated aqueous ammonia solution (1 ml) is magnetically stirred at ambient temperature for one day, and worked up as described above to give crude **3i**; yield: 2.7 g (96%); m.p. 109–111 °C. The precipitate is recrystallized from acetonitrile (20 ml) to give pale yellow crystals of **3i**; yield: 1.29 g (46%); m.p. 137–138 °C.

Received: August 9, 1983

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[1] M. A. Laurent, *Liebigs Ann. Chem.* **21**, 130 (1837).

[2] L. B. Howard, G. E. Hilbert, *J. Am. Chem. Soc.* **54**, 3628 (1932).

[3] G. Dougherty, W. H. Taylor, *J. Am. Chem. Soc.* **55**, 1294 (1933).

[4] T. Tsumaki, Y. Muto, M. Tanaka, *J. Chem. Soc. Japan. Pure Chem. Sect.* **74**, 161 (1953).

[5] A. Kamal, A. Ahmad, A. A. Qureshi, *Tetrahedron* **19**, 869 (1963).

[6] Y. Ogata, A. Kawasaki, N. Okumura, *J. Org. Chem.* **29**, 1985 (1964).

[7] I. Nicholson, R. Poretz, *J. Chem. Soc.* **1965**, 3067.

[8] D. Korbonits, S. Holly, K. Harsanyl, *Chem. Ber.* **103**, 3605 (1970).

[9] R. H. Hasek, E. U. Flam, J. C. Martin, *J. Org. Chem.* **26**, 1822 (1961).

[10] B. Samuel, K. Wade, *J. Chem. Soc.* [A] **1969**, 1742.

[11] H. Böhme, A. Ingendoh, *Liebigs Ann. Chem.* **1978**, 1928.

[12] A. Sakurai, H. Midorikawa, *Bull. Chem. Soc. Jpn.* **49**, 837 (1979).

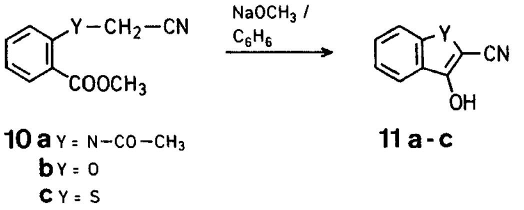
[13] T. Takajo, S. Kambe, W. Ando, *Synthesis* **1982**, 1080.

Errata and Addenda 1984

M. H. Elnagdi, M. R. H. Elmoghayar, G. E. H. Elgemeie, *Synthesis* **1984** (1), 1-26:

The second paragraph on page 2 should read:
Cyclic 3-oxoalkanenitriles **11** are obtained via cyclisation of methyl *N*-acetyl-*N*-cyanomethylanthranilate (**10a**)[61a], methyl 2-(cyanomethoxy)-benzoate (**10b**)[61b], or methyl 2-(cyanomethylthio)-benzoate (**10c**)[61] under basic conditions.

The formula scheme **10** → **11** (p. 3) should be:



10 a Y = N–CO–CH3
b Y = O
c Y = S

11 a-c

The experimental procedure for **11a** (p. 3) should read:

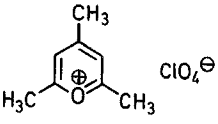
2-Cyano-3-hydroxyindole (11a; Y = NH)[61]:
A mixture of freshly prepared sodium methoxide (10 mmol) and methyl *N*-acetyl-*N*-cyanomethylanthranilate (**10a**; 10 mmol) in benzene (25 ml) is stirred for 2 h at room temperature then left for 12 h at room temperature. The mixture is poured into water. Carbon dioxide is bubbled into the resulting solution till no more solid separates. The product is collected and recrystallised; yield: 64%; m.p. 165–167 °C (dec.).

The following references should be added (p. 23):

[61] (a) D. Vorländer, *Ber. Dtsch. Chem. Ges.* **35**, 1683, 1696 (1902).
(b) R. Bryant, D. L. Haslam, *J. Chem. Soc.* **1965**, 2361.

P. Molina, A. Tárraga, E. Romero, M. L. Peña, *Synthesis* **1984** (1), 71–73:

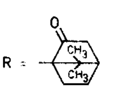
The structure of compound **6** (p. 71) should be:



6

Abstract 6803, *Synthesis* **1984** (1), 82:

The substituent R should be:

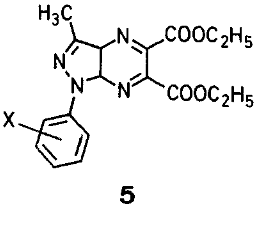


F. Pochat, *Synthesis* **1984** (2), 146–148:

Compounds **3c**, **5c**, and **5g** (p. 147 and 148) should be named as *N'*-acyl-*N'*-(methylthiomethyl)-hydrazones.

P. G. Baraldi, D. Simoni, V. Periotto, S. Manfredini, M. Guarneri, *Synthesis* **1984** (2), 148–149:

The structure of compound **5** (p. 149) should be:



5

S. C. W. Coltman, S. C. Eyley, R. A. Raphael, *Synthesis* **1984** (2), 150–152:

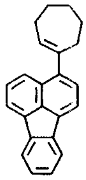
The first line of the experimental procedure for esters **4** should read: To a solution of **2** (0.1 mol) in absolute ethanol (30 ml) is added a 1

R. Lapouyade, A. Nourmamode, *Synthesis* **1984** (2), 161–164:

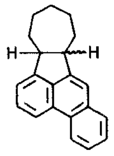
The title should read:
A New Synthesis of 6b,8,9,10,11,11a-Hexahydro-7*H*-cyclohepta[*a*]acenaphthylenes by Base-Catalyzed Photocyclization of 1-Arylcycloheptenes

The structures of products **1d**, **4b**, and **4c** in Tables 2 and 3 (p. 163) should be:

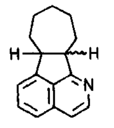
1d



4b

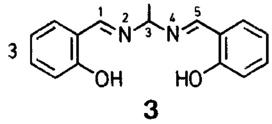


4c



T. Takajo, S. Kambe, W. Ando, *Synthesis* **1984** (3), 256–259:

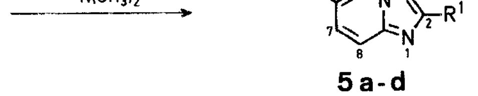
The structure of product **3** (p. 257, left) should be:



3

S. Podergajs, B. Stanovnik, M. Tišler, *Synthesis* **1984** (3), 263–265:

The structures of reagent **2** and products **5a–d** (p. 264) should be:



5a-d

U. Schöllkopf, U. Busse, R. Kilger, P. Lehr, *Synthesis* **1984** (3), 271–274:

The heading for the first experimental procedure (p. 274) should be: (3*S*,6*S*)-3,6-Diisobutyl-2,5-dioxohexahydropyrazine (**9**):

J. Cabré, A. L. Palomo, *Synthesis* **1984** (5), 413–417:

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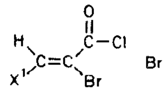
The formulae of Schemes **A** and **B** (p. 413) should be interchanged.
The following experimental procedure should be added:

Cyclohexylammonium Carboxylates (Tables 3); General Procedure:
To a solution of cyclohexylamine (1.15 ml, 10.0 mmol) in the solvent (20 ml, Table 3), the carboxylic acid is added at room temperature. The mixture is stirred for 15 min at room temperature and then cooled to 0–5 °C. The precipitate is filtered and washed with cold (0 to −5 °C) solvent (10 ml).

D. P. Stack, R. M. Coates, *Synthesis* **1984** (5), 434–436:

The structure of product **2e** (Table, p. 435) should be:

e



Br