# A Direct Synthesis of *N*,*N'*-Bis(2-hydroxybenzylidene)-1,1-diaminoalkanes by a Three-Component Reaction

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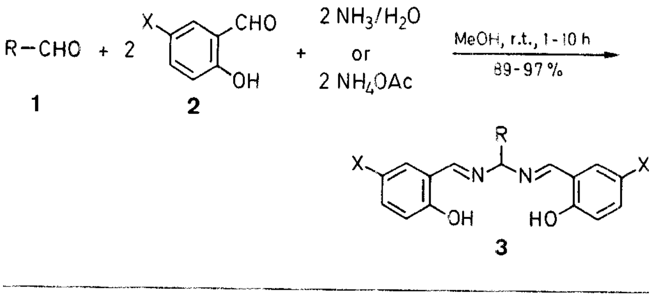
The direct synthesis of new double Schiff bases with an alkane-1,1-diamine unit is achieved in good yields through a three-component reaction of salicylaldehyde or 5-bromosalicylaldehyde, aliphatic aldehydes, and ammonium acetate or aqueous ammonia in methanol.

In our study of the three-component reaction of two different aldehydes and ammonium, we have developed an efficient and direct method for the synthesis of a large number of new mixed double Schiff bases possessing an active alkane-1,1-diamine unit. We have hitherto reported the reactions of salicylaldehyde and 5-bromosalicylaldehyde with aromatic aldehydes,[1,2] and of salicylaldehyde or its analogues with ferrocenealdehyde.[3] We now report the direct synthesis of the new *N*,*N'*-bis(2-hydroxybenzylidene)-1,1-diaminoalkanes **3** by reaction of salicylaldehyde or 5-bromosalicylaldehyde **(2)** with aliphatic aldehydes **1** and ammonia.

When 1 mol of an aliphatic aldehyde **1** and 2 mol of salicylaldehyde **2** or 5-bromosalicylaldehyde were allowed to react with aqueous ammonia or ammonium acetate in methanol at room



| 3 | R | X | 3 | R | X |
|---|---|---|---|---|---|
| **a** | $C_2H_5$ | H | **h** | $n$-$C_3H_7$ | Br |
| **b** | $n$-$C_4H_9$ | H | **i** | $n$-$C_4H_9$ | Br |
| **c** | $n$-$C_5H_{11}$ | H | **j** | $n$-$C_5H_{11}$ | Br |
| **d** | $n$-$C_6H_{13}$ | H | **k** | $n$-$C_6H_{13}$ | Br |
| **e** | $n$-$C_7H_{15}$ | H | **l** | $n$-$C_7H_{15}$ | Br |
| **f** | $n$-$C_8H_{17}$ | H | **m** | $n$-$C_8H_{17}$ | Br |
| **g** | $n$-$C_{10}H_{21}$ | H | **n** | $n$-$C_{10}H_{21}$ | Br |

**Table 1.** *N,N'*-Bis(2-hydroxybenzylidene)-1,1-diaminoalkanes **3** Prepared

| Product | N Source | Reaction Time (h) | Yield[a] (%) | mp (°C)[b] (solvent) | Molecular Formula[c] |
|---|---|---|---|---|---|
| **3a** | $NH_4OAc/NH_3/H_2O$ | 8 | 91 | 94–96 ($C_6H_6$/MeOH) | $C_{17}H_{18}N_2O_2$ (282.3) |
| **3b** | $NH_3/H_2O$ | 6 | 97 | 84–85 ($C_6H_6$/MeOH) | $C_{19}H_{22}N_2O_2$ (310.4) |
| **3c** | $NH_4OAc/NH_3/H_2O$ | 1.5 | 93 | 72–74 ($C_6H_6$) | $C_{20}H_{24}N_2O_2$ (324.4) |
| **3d** | $NH_4OAc$ | 2 | 90 | 84–86 (MeOH) | $C_{21}H_{26}N_2O_2$ (338.4) |
| **3e** | $NH_3/H_2O$ | 2 | 92 | 64–65 (MeOH) | $C_{22}H_{28}N_2O_2$ (352.5) |
| **3f** | $NH_4OAc$ | 1 | 95 | 60–62 (MeOH) | $C_{23}H_{30}N_2O_2$ (366.5) |
| **3g** | $NH_3/H_2O$ | 6 | 95 | 52–54 ($C_6H_6$/MeOH) | $C_{25}H_{34}N_2O_2$ (394.5) |
| **3h** | $NH_3/H_2O$ | 8 | 90 | 98–100 ($CHCl_3$/MeOH) | $C_{18}H_{18}Br_2N_2O_2$ (454.2) |
| **3i** | $NH_3/H_2O$ | 8 | 92.5 | 109–111 ($CHCl_3/C_6H_6$) | $C_{19}H_{20}Br_2N_2O_2$ (468.2) |
| **3j** | $NH_4OAc/NH_3/H_2O$ | 10 | 92 | 192–194 ($CHCl_3$/MeOH) | $C_{20}H_{22}Br_2N_2O_2$ (482.2) |
| **3k** | $NH_4OAc/NH_3/H_2O$ | 8 | 89 | 87–89 ($C_6H_6$/MeOH) | $C_{21}H_{24}Br_2N_2O_2$ (496.2) |
| **3l** | $NH_3/H_2O$ | 6 | 91 | 94–96 ($C_6H_6$/MeOH) | $C_{22}H_{26}Br_2N_2O_2$ (510.3) |
| **3m** | $NH_4OAc/NH_3/H_2O$ | 8 | 92 | 104–105 ($C_6H_6$/MeOH) | $C_{23}H_{28}Br_2N_2O_2$ (524.3) |
| **3n** | $NH_3/H_2O$ | 6 | 93 | 96–98 (MeOH) | $C_{25}H_{32}Br_2N_2O_2$ (552.3) |

[a] Yield of isolated product, based on **2**.

[b] Uncorrected, measured with a Mettler-X6 apparatus.

[c] Satisfactory microanalyses: C ±0.03, H ±0.028, N ±0.03.

**Table 2.** Spectral Data of Compounds **3**

| Compound | UV ($CHCl_3$)[a] $\lambda_{max}$ (nm) | IR (KBr)[b] $\nu$ ($cm^{-1}$) | $^1$H-NMR ($CDCl_3$/TMS)[c] $\delta$, *J* (Hz) |
|---|---|---|---|
| **3a** | 320 (w), 260 (s) | 3000 (br, OH); 1621 (s, C=N); 1585, 1490, 1460 (m, Ar) | 1.02 (t, 3H, $CH_3$); 1.99 (m, 2H, $CH_2$); 4.81 (t, 1H, NCHN, *J* = 8); 7.36–6.91 (m, 8$H_{arom}$); 8.46 (s, 2H, 2CH=N); 12.70 (s, 2H, 2OH) |
| **3b** | 320 (w), 260 (s) | 3000 (br, OH); 1620 (s, C=N); 1575, 1490, 1460 (m, Ar) | 0.94 (m, 3H, $CH_3$); 1.44 [m, 4H, $(CH_2)_2$]; 1.98 (m, 2H, $CH_2$); 4.88 (t, 1H, NCHN); 6.82–7.36 (m, 8$H_{arom}$); 8.45 (s, 2H, 2CH=N); 12.83 (br s, 2H, 2OH) |
| **3c** | 320 (w), 260 (s), 242 (sh) | 2700 (br, OH); 1620 (s, C=N); 1575, 1490, 1460 (m, Ar) | 0.90 (t, 3H, $CH_3$); 1.39 [m, 6H, $(CH_2)_3$]; 1.92 (m, 2H, $CH_2$); 4.88 (t, 1H, NCHN); 6.81–7.45 (m, 8$H_{arom}$); 8.45 (s, 2H, 2CH=N); 12.31 (br, 2H, 2OH) |
| **3d** | 320 (w), 262 (s) | 2900 (br, OH); 1620 (s, C=N); 1575, 1490, 1460 (m, Ar) | 0.88 (t, 3H, $CH_3$); 1.33 [m, 8H, $(CH_2)_4$]; 1.97 (m, 2H, $CH_2$); 4.87 (t, 1H, NCHN); 6.81–7.44 (m, 8$H_{arom}$); 8.44 (s, 2H, 2CN=N); 12.56 (br, 2H, 2OH) |
| **3e** | 320 (w), 253 (s) | 3000 (br, OH); 1621 (s, C=N); 1575, 1494, 1460 (m, Ar) | 0.89 (t, 3H, $CH_3$); 1.34 [m, 10H, $(CH_2)_5$]; 1.93 (m, 2H, $CH_2$); 4.89 (t, 1H, NCHN); 6.92–7.37 (m, 8$H_{arom}$); 8.46 (s, 2H, 2CH=N); 12.00 (s, 2H, 2OH) |
| **3f** | 320 (w), 260 (s) | 3000 (br, OH); 1620 (s, C=N); 1578, 1492, 1460 (m, Ar) | 0.90 (m, 3H, $CH_3$); 1.33 [m, 12H, $(CH_2)_6$]; 1.93 (m, 2H, $CH_2$); 4.89 (t, 1H, NCHN); 6.84–7.41 (m, 8$H_{arom}$); 8.37 (s, 2H, 2CH=N); 12.85 (br, 2H, 2OH) |
| **3g** | 320 (w), 260 (s), 253 (m) | 2800 (br, OH); 1620 (s, C=N); 1576, 1492, 1458 (m, Ar) | 0.89 (t, 3H, $CH_3$); 1.28 [br, 16H, $(CH_2)_8$]; 1.95 (m, 2H, $CH_2$); 4.85 (t, 1H, NCHN): 7.00–7.36 (m, 8$H_{arom}$); 8.45 (s, 2H, 2CH=N); 13.10 (s, 2H, 2OH) |
| **3h** | 322 (w), 260 (m), 253 (s) | 2900 (br, OH); 1622 (s, C=N); 1565, 1472 (m, Ar) | 0.96–1.86 [m, 7H, $(CH_2)_2CH_3$]; 4.87 (t, 1H, NCHN); 6.81–7.45 (m, 8$H_{arom}$); 8.34 (s, 2CH=N); 12.50 (br, 2H, 2OH) |
| **3i** | 333 (w), 260 (m), 253 (s), 242 (vs) | 2900 (br, OH); 1620 (s, C=N); 1564, 1473 (m, Ar) | 0.92 (m, 3H, $CH_3$); 1.34 [m, 4H, $(CH_2)_2$]; 1.90 (m, 2H, $CH_2$); 4.75 (m, 1H, NCHN); 6.79–7.37 (m, 6$H_{arom}$); 8.32 (s, 2H, 2CH=N); 12.57 (br, 2H, 2OH) |
| **3j** | 323 (w), 256 (s), 245 (m) | 2900 (br, OH); 1628 (s, C=N); 1475 (m, Ar) | 0.91–1.94 [m, 11H, $(CH_2)_4CH_3$]; 4.56 (t, 1H); 6.70–6.27 (m, 6$H_{arom}$); 8.45 (s, 2H, 2CH=N); 12.32 (br, 2H, 2OH) |
| **3k** | 334 (w), 260 (s), 242 (m) | 3000 (br, OH); 1622 (s, C=N); 1565, 1475 (m, Ar) | 0.87 (m, 3H, $CH_3$); 1.30 [m, 8H, $(CH_2)_4$]; 1.80 (m, 2H, $CH_2$); 4.8 (t, 1H, NCHN); 6.5–7.43 (m, 6$H_{arom}$); 8.36 (s, 2H, 2CH=N); 13.0 (br, 2H, 2OH) |
| **3l** | 332 (w), 260 (s), 253 (m), 241 (vs) | 3000 (br, OH); 1622 (s, C=N); 1565, 1474 (m, Ar) | 0.88 (m, 3H, $CH_3$); 1.30 [m, 10H, $(CH_2)_5$]; 3.90 (m, 1H, NCHN); 6.95–7.50 (m, 6$H_{arom}$); 8.37 (s, 2H, 2CH=N); 13.11 (br, 2H, 2OH) |
| **3m** | 332 (w), 260 (s), 255 (m), 241 (vs) | 3000 (br, OH); 1620 (s, C=N); 1565, 1487 (m, Ar) | 0.89 (m, 3H, $CH_3$); 1.28 [m, 12H, $(CH_2)_6$]; 1.93 (m, 2H, $CH_2$); 4.80 (br, 1H, NCHN); 6.83–7.47 (m, 6$H_{arom}$); 8.35 (s, 2H, 2CH=N); 12.0 (br, 2H, 2OH) |
| **3n** | 332 (w), 253 (m), 240 (s) | 2800 (br, OH); 1621 (s, C=N); 1580, 1500, 1460 (m, Ar) | 1.00 (t, 3H, $CH_3$); 1.33 [m, 16H, $(CH_2)_8$]; 1.93 (m, 2H, $CH_2$); 4.91 (t, 1H, NCHN); 6.89–7.41 (m, 6$H_{arom}$); 8.37 (s, 2H, 2CH=N); 11.59 (br, 2H, 2OH) |

[a] Measured on a Shimadzu UV-240 spectrophotometer.

[b] Recorded on a Shimadzu IR-408 spectrophotometer.

[c] Recorded on a Varian CFT-80 spectrometer.

temperature for several hours, $N,N'$-bis(2-hydroxybenzylidene)-1,1-diaminoalkanes **3** were obtained as pale yellow precipitates in high yields. The aliphatic aldehydes used in the study ranged from propanal to undecanal. Neither $N,N'$-dialkyl-1,1-diaminoalkanes[4] nor $N,N'$-bis(2-hydroxybenzylidene)-2-hydroxyarylmethanediamines[5,6] which might arise from the condensation of aliphatic aldehydes **1** or salicylaldehydes **2** and ammonia in the present reaction system, are isolated.

In all the cases, the products isolated contain one residue originating from the aliphatic aldehyde and two residues originating from the salicylaldehyde. The structures of compounds **3** are corroborated by microanalytic and spectral data. In the IR spectra, the characteristic Schiff base C=N stretching frequency is found in the region $\nu = 1600-1628\ \text{cm}^{-1}$ as a single strong band. The OH stretching frequency is found at $\nu \approx 3000\ \text{cm}^{-1}$ with particular width. The stretching vibrations of C–H in the alkyl groups appear at $\nu = 2800-2900\ \text{cm}^{-1}$ with sharp absorptions. In the $^1$H-NMR spectra, the broad signals around $\delta = 12-13$ are assigned to the protons of the phenoxy group, which can be exchanged by $D_2O$. The two protons of CH=N have the same chemical shifts ($\delta = 8.30-8.46$). The UV spectra show 2–4 absorptions dependent on the particular compound. Some compounds were also examined by mass spectrometry which in all cases shows that the molecular ion peaks have only a low relative intensity, but the fragments obtained are in agreement with the structures.

**$N,N'$-Bis(2-hydroxybenzylidene)-1,1-diaminopropane (3a); Typical Procedure:**

To a stirred mixture of salicylaldehyde (**2**, X=H; 2.44 g, 20 mmol) and propanal (**1**, R=$C_2H_5$; 0.58 g, 10 mmol) in MeOH (5 mL) under $N_2$ at room temperature is added $NH_4OAc$ (1.54 g, 20 mmol) in one portion and stirring is continued for 30 min. Then 30% aqueous $NH_3$ (5 mL) is slowly added dropwise and dropped. The intense stirring of the mixture is again continued for 8 h. The reaction is complete when no more pale yellow precipitate is formed. The solid product is isolated by suction, washed with cold MeOH (5 mL) and with cold EtOH (5 mL), and recrystallized from benzene/MeOH to give pure **3a**; yield: 1.86 g (91%); mp 94–96 °C.

| | | | | |
|---|---|---|---|---|
| $C_{17}H_{18}N_2O_2$ | calc. | C 72.32 | H 6.43 | N 9.92 |
| (282.3) | found | 72.03 | 6.36 | 9.65 |

**$N,N'$-Bis(2-hydroxybenzylidene)-1,1-diaminohexane (3d); Typical Procedure:**

To a stirred mixture of salicylaldehyde (**2**; X=H; 2.44 g, 20 mmol) and heptanal (**1**, R=$n$-$C_6H_{13}$; 0.86 g, 10 mmol) in MeOH (8 mL) under $N_2$ at room temperature is added $NH_4OAc$ (3.08 g, 40 mmol) in one portion and stirring under $N_2$ is continued for 2 h. The solid product is collected by suction, washed with EtOH (5 mL), and recrystallized from MeOH to give pure **3d**; yield: 2.79 g (90%); mp 84–86 °C.

| | | | | |
|---|---|---|---|---|
| $C_{21}H_{26}N_2O_2$ | calc. | C 74.53 | H 7.74 | N 8.27 |
| (338.4) | found | 74.24 | 7.58 | 8.21 |

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