# Synthesis of novel salicylaldimine Schiff bases with a pendant benzo-10-aza-15-crown

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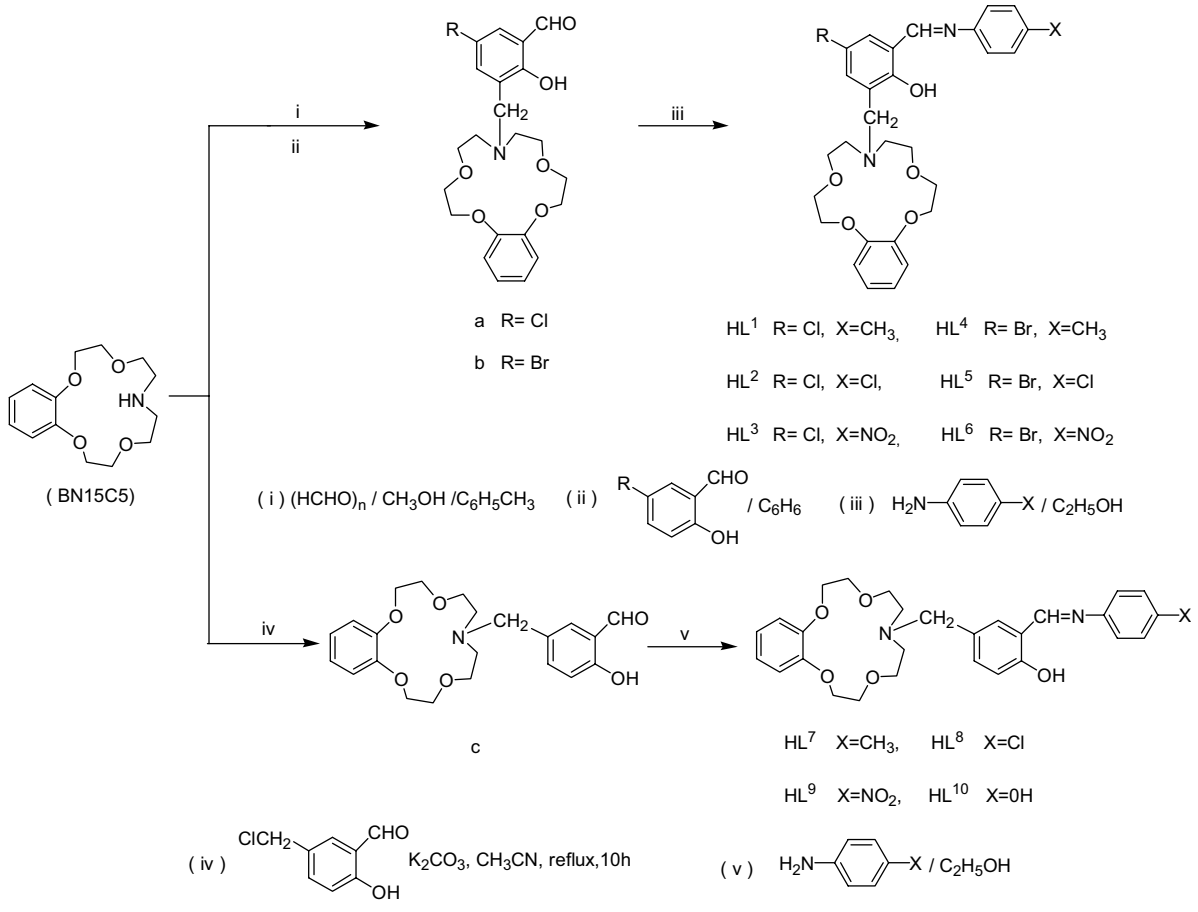
Novel salicylaldimine mono-Schiff bases with aza-crown pendant have been synthesised via condensation of 3-[(benzo-10-aza-15-crown-5)methyl] salicylaldehyde with substituted aniline and characterised by $^1$H NMR, IR, mass spectroscopy and elemental analysis. The crystal structure of *N*-(4-hydroxy-3- formylbenzyl)benzo-10-aza-15-crown-5 aldimine with 4-aminophenol ($HL^{10}$) has been determined from X-ray diffraction data.

**Keywords:** synthesis, condensation, benzo-10-aza-15-crown-5, salicylaldimine mono-Schiff base

Salicylaldimine Schiff bases, an important class of metal chelators, were widely applied in the field of coordination chemistry,[1] analytical chemistry[2] and catalytic chemistry.[3] In recent years, there has been considerable interest in the research of salicylaldimine Schiff bases transition-metal complexes as oxygen carriers[4] and enzyme catalysis mimetics.[5,6] It was known that introduction of substituents to the Schiff base ligands would favour the complexes to form stable dioxygen adducts and avoid dimerising and losing activity.[7] Especially, crown ethers employed as the substituents have received much attention[8,9] because of their binding ability to alkali ions and special configuration due to the hydrophobicity of the outer ethylene groups and orderly arrangement of the inner oxygen atoms.[10,11] Crown ether ring with special configuration will endow crowned functional molecular with novel performance and character. For example, our recent works have shown that dioxygen affinities and biomimetic catalytic performance of crown ether substituted salicylaldimine Schiff bases transition-metal complexes are better in comparison with crown-free analogues.[12,13] Aza crown ether bearing salicylaldimine Schiff base ligands are good receptors for alkali and transition-metal guest cations.[14] Herein, as part of a further research program aimed at studying the effects of the bonded aza-crown ether ring possessing special stereo configuration and function on several important properties, namely, the ability for complexation with metal ions and biomimetic catalytic performance, we have designed and synthesised novel aza-crowned salicylaldimine mono-Schiff bases $HL^1$–$HL^{10}$ (see Scheme 1). Their route for the synthesis and the structure are shown in Scheme 1.




**Scheme 1** The synthetic route and structure of salicylaldimine mono-Schiff bases with benzo-10-aza-crown pendant

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## Experimental

*General methods and materials*

Melting points were determined on a Yanaco MP-500 micro-melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet-1705X spectrometer. $^1$H NMR spectra were recorded on a Bruker AC-200 MHz spectrometer using $Me_4Si$ as internal standard. Mass spectra were obtained on a Finnigan LCQ$^{DECA}$ spectrometer. The halogen analysis was measured using mercury titration method.[15,16] Other elementary analyses were performed on a Carlo Erba 1106 elemental analyser. X-ray diffraction were measured on a Enraf-Nornius CAD-4 diffractometer using graphite monochromated Mo Kα radiation λ = 0.071073nm.

5-Chlorosalicylaldehyde was obtained from Aldrich Co. The following compounds were prepared according to the literature: 5-chloromethylsalicylaldehyde,[17] 5-bromosalicylaldehyde;[18] benzo-10-aza-15-crown-5(BN15C5).[19] Other reagents were of analytical grade and were used without further purification. Silica gel (60H for TLC, Qingdao, China) was used for flash column chromatography.

*Synthesis of (benzo-10-aza-15-crown-5) salicylaldehydes*

*N-(2-hydroxy-3-formyl-5-chlorobenzyl)benzo-10-aza-15-crown-5 (a)*: A solution of benzo-10-aza-15-crown-5(5.32 g, 0.02 mol), paraformaldehyde (2.0 g) in MeOH(25 cm$^3$) and toluene (80 cm$^3$) was stirred under $N_2$ atmosphere and 25°C for 12 h. After the solvent was removed by evaporation, 5-chlorosalicylaldehyde (3.03 g, 0.02 mol) and benzene (80 cm$^3$) were added. The mixture was boiled under $N_2$ atmosphere and reflux for 12 h, cooled and then filtered. The solvent was removed by evaporation and the residual mass was chromatographed on a silica gel column using $CH_2Cl_2$ as an eluent to give the pure product as white solid, 7.40 g, 85% yield, m.p.139–140°C. $^1$H NMR($CDCl_3$) δ: 10.41 (s, 1H, OH, $D_2O$ exchangeable), 9.89 (s, 1H, CHO), 7.57–6.89 (m, 6H, ArH), 4.16–3.79 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.84 (t, $J$ = 5.3 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3455, 2944, 2851,1658, 1601, 1500, 1256, 1128, 1051; ESI-MS *m/z*: 437 ($M^+$); Anal. calcd. for $C_{22}H_{26}ClNO_6$: C 60.62, H 5.97, N 3.21, Cl 8.15; found C 60.45, H 6.15, N 3.41, Cl 7.98%.

*N-(2-hydroxy-3-formyl-5-bromobenzyl)benzo-10-aza-15-crown-5 (b)*: *b* was prepared as described for *a* to give white crystal, yield 82%, m.p.166–168°C. $^1$H NMR ($CDCl_3$) δ: 10.44(s, 1H, OH, $D_2O$ exchangeable), 9.86 (s, 1H, CHO), 7.71–6.88 (m, 6H, ArH), 4.16–3.75 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.84 (t, $J$ = 5.2 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3448, 2949, 2856,1656,1600,1501, 1255, 1130, 1050; ESI-MS *m/z*: 480 ($M^+$ + 1); Anal. calcd. for $C_{22}H_{26}BrNO_6$: C 55.00, H 5.42, N 2.92, Br 16.67; found C 55.15, H 5.25, N 2.73, Br 16.78%.

*N-(3-formyl-4-hydroxybenzyl)benzo-10-aza-15-crown-5(c)*: To a stirred mixture of benzo-10-aza-15-crown-5 (5.32 g, 0.02 mol) and $K_2CO_3$ (3.04 g, 0.022 mol) in acetonitrile (80 cm$^3$), a solution of 5-chloromethylsalicylaldehyde (3.42 g, 0.02 mol) in acetonitrile (20 cm$^3$) was added dropwise within 1 h. the mixture was refluxed for 10 h. Then the reaction mixture was filtered and the solvent was evaporated. The residual mass was chromatographed on a silica gel column using ethyl acetate as an eluent to give the pure product as white solid, 7.90 g, 89% yield, m.p. 80–82°C. $^1$H NMR($CDCl_3$) δ: 10.78 (s, 1H, OH, $D_2O$ exchangeable), 9.95 (s, 1H, CHO), 7.42–6.81 (m, 7H, ArH), 4.15–3.76 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.85 (t, $J$ = 5.5 Hz, 4H, $CH_2N$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3247, 1652, 1257, 1225, 1128; ESI-MS *m/z*: 401 ($M^+$); Anal. calcd for $C_{22}H_{27}NO_6$: C 65.84, H 6.73, N 3.49; found C 65.59, H 6.57, N 3.61%.

*Synthesis of mono-Schiff base ligands HL$^1$–HL$^{10}$*

*Ligand HL$^1$*: A solution of compound *a* (1.74 g, 4 mmol) and *p*-toluidine (0.43 g, 4 mmol) in EtOH(20 cm$^3$) was stirred for 4 h under $N_2$ atmosphere at 80°C, and then the mixture was cooled. The yellow precipitate was filtered and washed with EtOH. After recrystallisation from EtOH, yellow crystal (1.72 g, yield 82%) was obtained. M.p. 88–90°C. $^1$H NMR ($CDCl_3$) δ: 9.95 (s, 1H, OH, $D_2O$ exchangeable), 8.22 (s, 1H, N=CH), 7.57–6.42 (m, 10H, ArH), 4.21–3.71 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.84 (t, $J$ = 5.3 Hz, 4H, $NCH_2$), 2.27 (s, 3H, $CH_3$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3428, 2968, 2862, 1624, 1596, 1503, 1257, 1130, 1050; ESI-MS *m/z*: 526 ($M^+$); Anal. calcd. for $C_{29}H_{33}ClN_2O_5$: C 66.35, H 6.29, N 5.34, Cl 6.77. found C 66.17, H 6.45, N 5.18, Cl 6.89%.

*Ligand HL$^2$*: *HL$^2$* was prepared as described for *HL$^1$* except staring with 4-chloroaniline instead of *p*-toluidine to give yellow solid, yield 72%, m.p.95–97°C. $^1$H NMR ($CDCl_3$) δ: 9.98 (s, 1H, OH, $D_2O$ exchangeable), 8.19 (s, 1H, N=CH), 7.54–6.42 (m, 10H, ArH), 4.19–3.67 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.82 (t, $J$ = 5.1 Hz, 4H, $NCH_2$); IR (KBr, film) $\nu_{max}$: 3442, 2933, 2858, 1623, 1600,1500, 1252, 1131, 1050 cm$^{-1}$; ESI-MS *m/z*: 546 ($M^+$); Anal. calcd. for $C_{28}H_{30}Cl_2N_2O_5$: C 61.65, H 5.50, N 5.14, Cl 13.03. found C 61.83, H 5.32, N 5.29, Cl 13.28%.

*Ligand HL$^3$*: *HL$^3$* was prepared as described for *HL$^1$* except staring with *p*-nitroaniline instead of *p*-toluidine to give yellow solid, yield 78%, m.p.131–132°C. $^1$H NMR ($CDCl_3$) δ: 9.91 (s, 1H, OH, $D_2O$ exchangeable), 8.22 (s, 1H, N=CH), 7.57–6.48 (m, 10H, ArH), 4.20–3.71 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.81 (t, $J$ = 5.8 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3441, 2932, 2861,1622, 1601,1500, 1252, 1127, 1052; ESI-MS *m/z*: 557 ($M^+$); Anal. calcd. for $C_{28}H_{30}ClN_3O_7$: C 60.49, H 5.40, N 7.56, Cl 6.39. found C 60.65, H 5.26, N 7.39, Cl 6.52%.

*Ligand HL$^4$*: *HL$^4$* was prepared as described for *HL$^1$* except staring with *b* instead of *a* to give yellow solid, yield 82%, m.p.92–93°C. $^1$H NMR ($CDCl_3$) δ: 9.98 (s, 1H, OH, $D_2O$ exchangeable), 8.26 (s, 1H, N=CH), 7.59–6.46 (m, 10H, ArH), 4.25–3.76 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.81 (t, $J$ = 5.6 Hz, 4H, $NCH_2$), 2.31(s, 3H, $CH_3$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3435, 2966, 2856,1626,1600,1502,1255,1131,1049; ESI-MS *m/z:* 570 ($M^+$); Anal. calcd. for $C_{29}H_{33}BrN_2O_5$: C 61.16, H 5.80, N 4.92, Br 14.06. found C 61.03, H 5.65, N 4.78, Br 14.19%.

*Ligand HL$^5$*: *HL$^5$* was prepared as described for *HL$^2$* except staring with *b* instead of *a* to give yellow solid, yield 76%, m.p.99–101°C. $^1$H NMR ($CDCl_3$) δ: 9.96 (s, 1H, OH, $D_2O$ exchangeable), 8.24 (s, 1H, N=CH), 7.60–6.46 (m, 10H, ArH), 4.19–3.67 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.82 (t, $J$ = 5.1 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3444, 2932, 2860, 1623, 1600,1500, 1252, 1132, 1052; ESI-MS *m/z*: 590 ($M^+$); Anal. calcd. for $C_{28}H_{30}BrN_2O_5Cl$: C 57.00, H 5.09, N 4.75, Cl 6.02, Br 13.57. found C 57.16, H 5.23, N 5.59, Cl 6.18, Br 13.39%.

*Ligand HL$^6$*: *HL$^6$* was prepared as described for *HL$^3$* except staring with *b* instead of *a* to give yellow solid, yield 72%, m.p.146–147°C. $^1$H NMR ($CDCl_3$) δ: 9.99 (s, 1H, OH, $D_2O$ exchangeable), 8.27 (s, 1H, N=CH), 7.59–6.43 (m, 10H, ArH), 4.17–3.64 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.83 (t, $J$ = 5.8 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3440, 2930, 2863, 1624, 1601, 1500, 1250, 1129, 1053; ESI-MS *m/z*: 601 ($M^+$); Anal. calcd. for $C_{28}H_{30}BrN_3O_7$: C 56.00, H 5.00, N 7.00, Br 13.33. found C 16.15, H 4.83, N 7.19, Br 13.15%.

*Ligand HL$^7$*: *HL$^7$* was prepared as described for *HL$^1$* except staring with *c* instead of *a* to give yellow solid, yield 82%, m.p.97–98°C. $^1$H NMR ($CDCl_3$) δ: 13.12 (s, 1H, OH, $D_2O$ exchangeable), 8.34 (s, 1H, N=CH), 7.57–6.42 (m, 11H, ArH), 4.21–3.71 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.81 (t, $J$ = 5.7 Hz, 4H, $NCH_2$), 2.22 (s, 3H, $CH_3$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3228, 2968, 2862, 1624, 1596, 1503, 1257, 1130, 1050; ESI-MS *m/z*: 491 ($M^+$); Anal. calcd. for $C_{29}H_{34}N_2O_5$: C 71.02, H 6.94, N 5.71. found C 71.15, H 6.75, N 6.91%.

*Ligand HL$^8$*: *HL$^8$* was prepared as described for *HL$^2$* except staring with *c* instead of *a* to give yellow solid, yield 72%, m.p.105–107°C. $^1$H NMR ($CDCl_3$) δ: 13.05 (s, 1H, OH, $D_2O$ exchangeable), 8.41 (s, 1H, N=CH), 7.66–6.49 (m, 11H, ArH), 4.18–3.68 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.82 (t, $J$ = 5.4 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3236, 2927, 2861, 1624, 1600,1502, 1256, 1128, 1052; ESI-MS *m/z*: 512 ($M^+$); Anal. calcd. for $C_{28}H_{31}ClN_2O_5$: C 65.82, H 6.07, N 5.48, Cl 6.95. found C 65.96, H 6.26, N 5.29, Cl 6.78%.

*Ligand HL$^9$*: *HL$^9$* was prepared as described for *HL$^3$* except staring with *c* instead of *a* to give yellow solid, yield 72%, m.p.120–122°C. $^1$H NMR ($CDCl_3$) δ: 13.11 (s, 1H, OH, $D_2O$ exchangeable), 8.43 (s, 1H, N=CH), 7.68–6.81 (m, 11H, ArH), 4.16–3.74 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.85 (t, $J$ = 5.2 Hz, 4H, $NCH_2$); IR (KBr, cm$^{-1}$) $\nu_{max}$: 3232, 2929, 2859, 1623, 1600,1501, 1254, 1129, 1050; ESI-MS *m/z*: 522 ($M^+$); Anal. calcd. for $C_{28}H_{31}N_3O_7$: C 64.49, H 5.95, N 8.06. found C 64.68, H 5.76, N 8.19%.

*Ligand HL$^{10}$:* *HL$^{10}$* was prepared as described for *HL$^8$* except staring with 4-aminophenol instead of 4-chloroaniline to give yellow solid, yield 85%. m.p. 95–97°C. $^1$H NMR ($CDCl_3$) δ: 13.65 (s, 1H, OH, $D_2O$ exchangeable), 10.29 (s, 1H, OH, $D_2O$ exchangeable), 8.55 (s, 1H, N=CH), 7.41–6.85 (m, 11H, Ar-H), 4.16–3.77 (m, 14H, $OCH_2$, $NCH_2Ar$), 2.83 (t, $J$ = 5.7 Hz, 4H, $CH_2N$), 1.63 (brs, 2H, $H_2O$). IR (KBr) $\nu_{max:}$ 3446, 3225, 1622, 1258, 1126 cm$^{-1}$; ESI-MS *m/z*: 492 ($M^+$); Anal. calcd for $C_{28}H_{34}N_2O_7$($HL^{10}$·$H_2O$): C 65.88, H 6.67, N 5.49; found C 65.97, H 6.49, N 5.56%.

## Results and discussion

*Synthesis*

The Schiff base ligands (HL$^1$–HL$^{10}$) were conveniently prepared by the reaction of aromatic amines with crown ether-functionalised salicylaldehyde and characterised by IR, $^1$H NMR, mass spectroscopy and elemental analysis. In the IR spectra of Schiff base ligands HL$^1$–HL$^6$, the characteristic frequency of Ar–OH at 3444–3428 cm$^{-1}$ was observed, as was

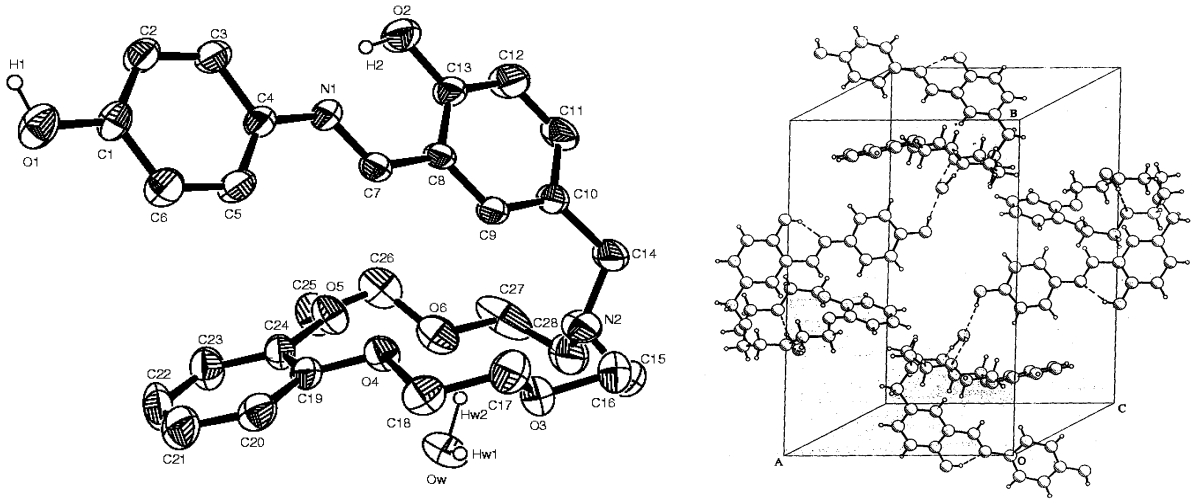


**Fig. 1** The X-ray structure of $HL^{10}$

that for CH=N at 1626–1622 $cm^{-1}$. However, in the IR spectra of Schiff base ligands $HL^7$–$HL^{10}$, the characteristic frequency of Ar–OH at 3236–3225 $cm^{-1}$ was observed, as was that for CH=N at 1624–1622 $cm^{-1}$. $^1H$ NMR spectra of Schiff base ligands $HL^1$–$HL^{10}$ show the aromatic protons as multiplet in the range 7.60–6.42 ppm. However, the chemical shifts O–H protons of the phenolic groups are in the range 9.99–9.91 ppm for $HL^1$–$HL^6$, in the range 13.65–13.05 ppm for $HL^7$–$HL^{10}$, respectively.

*Crystal structure*

Single crystals of $HL^{10}$ were obtained by volatilisation of a $CH_3COOC_2H_5$ solution of $HL^{10}$. The perspective drawing of $HL^{10}$ with atomic numbering is depicted in Fig. 1. Single crystal data were collected using a CAD-4 four-circle automated diffractometer, which utilised graphite monochromated Mo Kα radiation with DIFRAC. The structure was solved using the direct method and refined on $F^2$ using a full matrix least-squares procedure. All non-hydrogen atoms were refined anisotropically. Positions of all hydrogen atoms for $HL^{10}$ were calculated based on geometrical factors. These hydrogens were allowed to ride on their neighboring heavy atoms during refinement, and the rest hydrogen atoms of $HL^{10}$ were refined isotropically. The structure was solved, refined and displayed using NRCVAX and SHELXS 97 program package. The data for the crystal structure of *N*-(4-hydroxy-3-formylbenzyl)benzo-10-aza-15-crown-5 aldimine with 4-aminophenol ($HL^{10}$) are presented in Table 1. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC No 296082).

**Table 1** Crystal data and structure refinement of $HL^{10}\cdot H_2O$

| Empirical formula | ($HL^{10}$) $C_{28}$ $H_{34}$ $N_2O_7$ |
|---|---|
| Formula weight | 510.57 |
| Crystal system | Monoclinic |
| Space group | P 21/n |
| Unit cell dimensions | *a* = 12.424(7) Å deg.<br>α = 90.00(4) deg.<br>*b* = 19.945(7) Å deg.<br>β = 116.45(5) deg.<br>*c* = 12.556(7) Å deg.<br>γ = 90.00(4) deg. |
| Volume | 2783(2) $Å^3$ |
| Z | 4 |
| Density (calculated) | 1.218 $Mg/m^3$ |
| Absorption coefficient | 0.088 $mm^{-1}$ |
| *F*(000) | 1088 |
| Crystal size | 0.20 × 0.25 × 0.30 mm |
| θ range for data collection | 1.92 to 22.51 deg. |
| Index ranges | –13<=*h*<=11,<br>0<=*k*<=21, 0<=*l*<=13 |
| Reflections collected | 3785 |
| Independent reflections | 3629 [R(int) = 0.0000] |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 3629/0/335 |
| Goodness-of-fit on $F^2$ | 0.850 |
| Final R indices [$I>2\sigma(I)$] | $R_1$ = 0.0606, $wR_2$ = 0.1446 |
| R indices (all data) | $R_1$ = 0.1917, $wR_2$ = 0.1837 |

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