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Tris(8-methoxy-2-quinolylmethyl)amine (8-MeOTQA) as a highly fluorescent Zn^{2+} probe prepared by convenient C_3-symmetric tripodal amine synthesis†

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A convenient synthesis of C_3-symmetric tribenzylamine (TBA) derivatives has been investigated. The reaction of benzyl chlorides with acetaldehyde ammonia trimer (**1**) in the presence of base afforded tribenzylamines in high yields. This efficient method allows the diverse synthesis of TPA (tris(2-pyridylmethyl)amine) and TQA (tris(2-quinolylmethyl)amine) derivatives. Among the TQA compounds prepared, tris(8-methoxy-2-quinolylmethyl)amine (8-MeOTQA, **4**) exhibited superior properties as a fluorescent zinc probe with high quantum yield (ϕ_{Zn} = 0.51) and high sensitivity (limit of detection (LOD) = 3.4 nM). The X-ray crystallographic analysis of $[Zn(8\text{-MeOTQA})]^{2+}$ revealed that the steric and electronic effect of 8-methoxy substituents kicks out the solvent and counterion molecules from the metal coordination sphere, resulting in short $Zn-N_{quinoline}$ coordination distances (2.04–2.07 Å). The pseudo hexacoordinate complex of 6-methoxy derivative, $[Zn(6\text{-MeOTQA})(DMF)(ClO_4)]^+$, exhibited longer $Zn-N_{quinoline}$ distances (2.07–2.19 Å) and much smaller fluorescence intensity (ϕ_{Zn} = 0.027). The replacement of one of the three 8-methoxyquinolines with pyridine also afforded much less fluorescent zinc complex (ϕ_{Zn} = 0.095) due to the solvent coordination ($Zn-N_{quinoline}$ = 2.05–2.18 Å for $[Zn(8\text{-MeOBQPA})(CH_3OH)]^{2+}$).

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Introduction

Tris(2-pyridylmethyl)amine (TPA), prepared by Wenk in 1967,[1] is a versatile tetradentate ligand for many metal ions, including Li, Mn, Fe, Co, Ni, Cu, Zn, Ru, Tl, *etc*.[2–4] Resultant metal complexes with TPA and its derivatives have been developed as catalysts for molecular transformations,[5,6] dioxygen binding motifs[7,8] and molecular recognition platforms.[2,9,10] Introduction of electron withdrawing/donating substituents on the pyridine ring(s) can modulate the metal binding ability of the TPA ligand and properties of the resultant metal complexes.[11–13] Addition of coordinating substituents, as well as steric hindrance, also perturbs the structure, stability and reactivity of the metal complexes.[14]

In spite of its simple structure with C_3-symmetry, previously reported preparation methods of TPA derivatives frequently adopt multistep reaction *via* primary amine synthesis.[1,11,15–19] Although several one-step syntheses of TPA or tribenzylamine (TBA) derivatives from corresponding benzyl halides[20–22] or benzyl alcohol[23,24] utilizing ammonia or urea as nitrogen sources have been reported, they require transition metal catalysts such as Ru or Ir, high reaction temperature (~140 °C) or high pressure (~60 psi) with prolonged reaction period (12 hours–1 week), resulting in low yield in several cases. There is a great need for convenient and efficient synthesis of TPA derivatives under mild conditions such as ambient pressure and moderate temperature, use of common organic solvents (bp = ~80 °C for conventional removal *via* evaporation), short reaction period and easy work-up.

In our program developing quinoline–amine conjugates as TPA-derived ligands,[18,25] here we report a high-yield synthesis of TQA (tris(2-quinolylmethyl)amine) derivatives utilizing acetaldehyde ammonia trimer (**1**) as an easy-handled, solid ammonia equivalent. This four-component condensation including three halides and an ammonia derived from **1** proceeds under ambient pressure *via* reflux in acetonitrile for 2 hours. This method is applicable in preparation of versatile TBA/TPA/TQA derivatives.

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† Electronic supplementary information (ESI) available: Tables S1–S5, Chart S1, Fig. S1–S46 and crystallographic data in CIF format. CCDC 1017795–1017798, 1032611, 1046752 and 1046753. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5dt00514k

Zinc is indispensable element in living systems and its concentration is strictly controlled.[26–28] To visualize the Zn^{2+} distribution in the cell and living system, many fluorescent Zn^{2+} probes have been reported.[29–32] Thus, new fluorescent technology and molecular design based on new synthetic approach are of still continuing interest. Although the utility of TQA as a Zn^{2+}-selective fluorescent probe has been previously reported,[33] its improvement *via* appropriate substituent arrangement to enhance the fluorescence quantum yield and Zn^{2+} selectivity is lacking. To demonstrate the potential use of the present synthetic procedure for convenient construction of a compound library for C_3-symmetric TBA/TPA/TQA derivatives, the fluorescent zinc sensing property of the newly synthesized TQA compounds were investigated.

The TQA derivatives obtained in the present study include 8-MeOTQA (tris(8-methoxy-2-quinolylmethyl)amine, **4**), which exhibits extremely high fluorescence intensity upon zinc binding. The position and number of methoxy substituents on TQA are crucial for the fluorescence quantum yield, which is elucidated *via* X-ray crystallography of zinc complexes with 8-MeOTQA and 6-MeOTQA (**3**), as well as mono pyridine analog, 8-MeOBQPA (bis(8-methoxy-2-quinolylmethyl)(2-pyridylmethyl)amine, **8**).

Experimental

General

All reagents and solvents used for synthesis were from commercial sources and used as received. *N*,*N*-Dimethylformamide (DMF, Dojin) was spectral grade (Spectrosol). All aqueous solution was prepared using Milli-Q water (Millipore). ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on a Varian GEMINI 2000 spectrometer and referenced to internal $Si(CH_3)_4$ or solvent signals. UV-vis and fluorescence spectra were measured on a Jasco V-660 spectrophotometer and Jasco FP-6300 spectrofluorometer, respectively. Fluorescence quantum yields were measured on a HAMAMATSU photonics C9920–02 absolute PL quantum yield measurement system. *CAUTION: Perchlorate salts of metal complexes with organic ligands are potentially explosive. All due precautions should be taken*.

General procedures for preparation of tribenzylamines (TBAs), tris(2-pyridylmethyl)amine (TPA) and tris(2-quinolylmethyl)-amines (TQAs)

A mixture of benzyl chlorides (4.5 mmol), acetaldehyde ammonia trimer trihydrate (**1**·3H_2O) (1.0 mmol), potassium carbonate (4.5 mmol), potassium iodide (4.5 mmol) and acetonitrile (30 mL) was refluxed for 2 h. The resultant reaction mixture was cooled to room temperature and the solvent was evaporated. The residue was extracted with $CHCl_3$–water, dried and evaporated. The crude product was purified by silica gel column chromatography. Yields are shown in Table 1.

Tris(2,4,6-trimethylbenzyl)amine (2). ^{1}H NMR ($CDCl_3$): δ 6.74 (s, 6H), 3.45 (s, 6H), 2.22 (s, 9H), 2.07 (s, 18H). ^{13}C NMR ($CDCl_3$): δ 138.0, 135.8, 131.9, 128.5, 51.6, 21.1, 19.8. Anal. calcd for $C_{30}H_{39}N$ (**2**): H, 9.50; C, 87.11; N, 3.39. Found: H, 9.58; C, 86.80; N, 3.36.

Tris(6-methoxy-2-quinolylmethyl)amine (6-MeOTQA, 3). ^{1}H NMR ($CDCl_3$): δ 7.98 (d, J = 8.5 Hz, 3H), 7.94 (d, J = 9.2 Hz, 3H), 7.65 (d, J = 8.5 Hz, 3H), 7.31 (dd, J = 2.7, 9.2 Hz, 3H), 7.01 (d, J = 2.7 Hz, 3H), 4.06 (s, 6H), 3.90 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 157.2, 157.1, 143.2, 134.9, 130.2, 128.0, 121.7, 121.4, 105.0, 61.0, 55.6. Anal. calcd for $C_{33}H_{32}N_4O_4$ (**3**·H_2O): H, 5.88; C, 72.24; N, 10.21. Found: H, 5.79; C, 71.84; N, 9.86. ESI-MS m/z: 553.2 ($[M + Na]^+$).

Tris(8-methoxy-2-quinolylmethyl)amine (8-MeOTQA, 4). ^{1}H NMR (CD_2Cl_2): δ 8.11 (d, J = 8.5 Hz, 3H), 7.3–7.5 (m, 9H), 7.13 (d, J = 7.0 Hz, 3H), 4.20 (s, 9H), 4.08 (s, 6H). ^{13}C NMR (CD_2Cl_2): δ 157.1, 154.0, 138.9, 136.2, 127.8, 125.9, 121.5, 119.4, 108.1, 61.2, 56.3. Anal. calcd for $C_{33}H_{30}N_4O_3$ (**4**): H, 5.70; C, 74.70; N, 10.56. Found: H, 5.53; C, 74.35; N, 10.50. ESI-MS m/z: 553.2 ($[M + Na]^+$).

6,8-Dimethoxy-2-quinolinecarbaldehyde. A mixture of 6,8-dimethoxyquinaldine (2.60 g, 12.8 mmol) and SeO_2 (1.70 g, 15.4 mmol) in 1,4-dioxane (50 mL) was refluxed for 2 h. After cooling, the reaction mixture was filtered through celite, evaporated and purified by silica gel column chromatography (eluent: chloroform) to give 6,8-dimethoxy-2-quinolinecarbaldehyde (2.53 g, 11.6 mmol) in 91% yield.

^{1}H NMR ($CDCl_3$): δ 10.25 (d, J = 0.6 Hz, 1H), 8.13 (dd, J = 0.6, 8.5 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.73 (d, J = 2.4 Hz, 1H), 4.12 (s, 3H), 3.96 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 193.0, 160.5, 156.7, 149.1, 136.4, 135.4, 132.3, 118.5, 102.1, 97.0, 56.5, 55.8. Anal. Calcd for $C_{12}H_{11}NO_3$: H, 5.10; C, 66.35; N, 6.45. Found: H, 5.00; C, 65.93; N, 6.41.

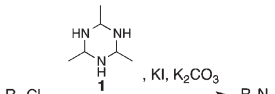
6,8-Dimethoxy-2-hydroxymethylquinoline. An ethanol solution (50 mL) of 6,8-dimethoxy-2-quinolinecarbaldehyde (1.03 g, 4.76 mmol) was added sodium borohydride (41.0 mg, 1.08 mmol) and stirred overnight at room temperature. After addition of water, the product was extracted with dichloromethane, dried and evaporated to give 6,8-dimethoxy-2-hydroxymethylquinoline (768 mg, 3.50 mmol) in 74% yield.

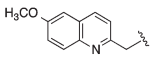
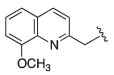
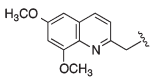
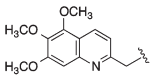
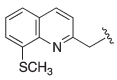
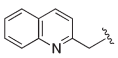
^{1}H NMR ($CDCl_3$): δ 8.01 (d, J = 8.2 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 6.73 (d, J = 2.1 Hz, 1H), 6.67 (d, J = 2.1 Hz, 1H), 4.92 (s, 2H), 4.03 (s, 3H), 3.92 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 157.7, 155.7, 155.5, 135.4, 135.2, 129.5, 101.5, 96.9, 65.0, 56.1, 55.6. Anal. Calcd for $C_{12}H_{13}NO_3$: H, 5.98; C, 65.74; N, 6.39. Found: H, 5.96; C, 65.57; N, 6.37.

6,8-Dimethoxy-2-chloromethylquinoline. A dichloromethane solution (50 mL) of 6,8-dimethoxy-2-hydroxymethylquinoline (1.11 g, 5.24 mmol) and thionyl chloride (0.38 mL, 5.2 mmol) was stirred overnight at room temperature. After addition of aqueous sodium hydrogen carbonate, the product was extracted with dichloromethane, dried and evaporated to give 6,8-dimethoxy-2-chloromethylquinoline (912 mg, 3.84 mmol) in 73% yield.

^{1}H NMR ($CDCl_3$): δ 8.03 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 4.88 (s, 2H), 4.05 (s, 3H), 3.90 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 158.3, 155.7, 152.9, 135.8, 135.4, 129.1, 121.4, 101.5, 96.8,

Table 1 Preparation of tribenzylamines (TBAs), tris(2-pyridylmethyl)amine (TPA) and tris(2-quinolylmethyl)amines (TQAs) using acetaldehydeammonia trimer (**1**)



Entry	R–	Product	Yield[a] (%)	Entry	R–	Product	Yield[a] (%)
1	$C_6H_5CH_2$–	TBA	95 (89)[b]	11		**3**	90
2	4-CH_3O–$C_6H_4CH_2$–	4-CH_3OTBA	97	12		**4**	92
3	4-F–$C_6H_4CH_2$–	4-FTBA	97	13		**5**	95
4	4-NO_2–$C_6H_4CH_2$–	4-NO_2TBA	100	14		**6**	100
5	2,4,6-$(CH_3)_3$–$C_6H_2CH_2$–	**2**	84 (84)[b]	15		**7**	94
6	C_6H_5–		0				
7	CH_2=$CHCH_2$–		0				
8	$C_6H_5CH_2CH_2CH_2$–		0				
9		TPA	98				
10		TQA	93				

[a] Based on R-Cl. Condition: R-Cl/**1**/KI/K_2CO_3 = 9/2/9/9, unless otherwise indicated. [b] R-Cl/**1**/KI/K_2CO_3 = 9/1/9/9.

56.2, 55.5, 47.7. Anal. Calcd for $C_{12}H_{12}ClNO_2$: H, 5.09; C, 60.64; N, 5.89. Found: H, 5.13; C, 60.69; N, 5.87.

Tris(6,8-dimethoxy-2-quinolylmethyl)amine (6,8-DiMeOTQA, 5). ^{1}H NMR ($CDCl_3$): δ 7.99 (d, J = 8.5 Hz, 3H), 7.85 (d, J = 8.5 Hz, 3H), 6.67 (d, J = 2.4 Hz, 3H), 6.62 (d, J = 2.4 Hz, 3H), 4.16 (s, 6H), 4.02 (s, 9H), 3.89 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 158.3, 155.7, 152.9, 135.8, 135.4, 129.1, 121.4, 101.5, 96.8, 56.2, 55.5, 47.7. Anal. Calcd for $C_{36}H_{38}N_4O_7$ (**5**·H_2O): H, 6.00; C, 67.70; N, 8.77. Found: H, 6.03; C, 67.65; N, 8.67. ESI-MS m/z: 643.3 ([M + Na]$^+$).

Tris(5,6,7-trimethoxyl-2-quinolylmethyl)amine (5,6,7-TriMeOTQA, 6). ^{1}H NMR ($CDCl_3$): δ 8.31 (d, J = 8.5 Hz, 3H), 7.60 (d, J = 8.5 Hz, 3H), 7.19 (s, 3H), 4.03 (s, 15H), 3.98 (s, 9H), 3.96 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 159.1, 155.4, 146.6, 144.9, 140.3, 130.4, 118.6, 117.9, 103.8, 99.9, 61.6, 61.2, 56.1. Anal. Calcd for $C_{39}H_{43.2}N_4O_{9.6}$ (**6**·0.6H_2O): H, 6.03; C, 64.92; N, 7.76. Found: H, 6.03; C, 64.75; N 7.68. ESI-MS m/z: 733.3 ([M + Na]$^+$).

8-Methylthio-2-quinolinecarbaldehyde. A mixture of 8-methylthioquinaldine (2.17 g, 11.5 mmol) and SeO_2 (1.53 g, 13.8 mmol) in 1,4-dioxane (30 mL) was refluxed for 1 h. After cooling, the reaction mixture was filtered through celite, evaporated and purified by silica gel column chromatography (eluent: chloroform) to give 8-methylthio-2-quinolinecarbaldehyde (1.76 g, 8.63 mmol) in 75% yield.

^{1}H NMR ($CDCl_3$): δ 10.24 (d, J = 0.9 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 4.3 Hz, 2H), 7.46 (dd, J = 4.3, 4.3 Hz, 1H), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 193.0, 150.8, 144.7, 137.3, 130.0, 129.0, 123.4, 123.0, 117.6, 14.4. Anal. Calcd for $C_{11}H_{9.2}NO_{1.1}S$ (+0.1H_2O): H, 4.52; C, 64.43; N, 6.83. Found: H, 4.60; C, 64.38; N, 6.78.

8-Methylthio-2-hydroxymethylquinoline. An ethanol solution (30 mL) of 8-methylthio-2-quinolinecarbaldehyde (228 mg, 1.12 mmol) was added sodium borohydride (41.0 mg, 1.08 mmol) and stirred overnight at room temperature. After addition of water, the product was extracted with dichloromethane, dried and evaporated to give 8-methylthio-2-hydroxymethylquinoline (231 mg, 1.12 mmol) in 100% yield.

^{1}H NMR ($CDCl_3$): δ 8.07 (d, J = 8.2 Hz, 1H), 7.53 (dd, J = 1.5, 7.9 Hz, 1H), 7.46 (dd, J = 7.3, 7.9 Hz, 1H), 7.37 (dd, J = 1.2, 7.3 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 4.92 (s, 2H), 4.51 (s, 1H), 2.55 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 157.5, 143.2, 139.0, 136.8, 127.0, 126.2, 123.0, 122.9, 118.6, 64.1, 14.3. Anal. Calcd for $C_{11}H_{11.2}NO_{1.1}S$ (+0.1H_2O): H, 5.45; C, 63.80; N, 6.76. Found: H, 5.37; C, 63.81; N, 6.68.

8-Methylthio-2-chloromethylquinoline. A dichloromethane solution (30 mL) of 8-methylthio-2-hydroxymethylquinoline (130 mg, 0.63 mmol) and thionyl chloride (0.050 mL, 0.70 mmol) was stirred overnight at room temperature. After

addition of aqueous sodium hydrogen carbonate, the product was extracted with dichloromethane, dried and evaporated to give 6,8-dimethoxy-2-chloromethylquinoline (142 mg, 0.63 mmol) in 100% yield.

^{1}H NMR ($CDCl_3$): δ 8.15 (d, J = 8.5 Hz, 1H), 7.65 (d, J = 8.5 Hz, 1H), 7.55 (dd, J = 1.5, 7.9 Hz, 1H), 7.48 (dd, J = 7.0, 8.2 Hz, 1H), 7.39 (dd, J = 1.5, 7.0 Hz, 1H), 4.88 (s, 2H), 2.56 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 155.3, 144.0, 139.6, 137.2, 127.0, 126.8, 123.00, 122.97, 120.8, 47.3, 14.4. Anal. Calcd for $C_{11}H_{10.2}ClNO_{0.1}S$ (+0.1H_2O): H, 4.56; C, 58.58; N, 6.21. Found: H, 4.51; C, 58.34; N, 6.06.

Tris(8-methylthio-2-quinolylmethyl)amine (8-MeSTQA, 7). ^{1}H NMR ($CDCl_3$): δ 8.09 (d, J = 7.9 Hz, 3H), 7.93 (d, J = 8.2 Hz, 3H), 7.51 (d, J = 7.3 Hz, 3H), 7.43 (dd, J = 7.6, 7.9 Hz, 3H), 7.35 (d, J = 6.7 Hz, 3H), 4.18 (s, 6H), 2.56 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 157.8, 144.6, 138.8, 136.0, 125.9, 125.5, 123.0, 122.39, 122.35, 25.6, 14.4. Anal. Calcd for $C_{33}H_{32}N_4OS_3$ (7·H_2O): H, 5.40; C, 66.41; N, 9.39. Found: H, 5.07; C, 65.97; N, 8.97. ESI-MS m/z: 601.2 ([M + Na]$^+$).

Bis(8-methoxy-2-quinolylmethyl)(2-pyridylmethyl)amine (8-MeOBQPA, 8). To an acetonitrile solution (30 mL) of 8-methoxy-2-chloromethylquinoline (483 mg, 2.33 mmol) and 2-aminomethylpyridine (0.11 mL, 1.16 mmol) was added potassium carbonate (643 mg, 4.65 mmol) and potassium iodide (772 mg, 4.65 mmol). The resulting reaction mixture was refluxed for 2 days. The resulting solution was cooled to room temperature and the solvent was evaporated. The residue was extracted with $CHCl_3$–water, dried, evaporated and washed with acetonitrile to give 8-MeOBQPA as white powder (368 mg, 0.82 mmol) in 71% yield.

^{1}H NMR ($CDCl_3$): δ 8.53 (d, J = 4.9 Hz, 1H), 8.12 (d, J = 8.5 Hz, 2H), 7.91 (d, J = 8.5 Hz, 2H), 7.65–7.64 (m, 2H), 7.44–7.34 (m, 4H), 7.13 (dd, J = 4.9, 8.5 Hz, 1H), 7.02 (dd, J = 0.6, 7.3 Hz, 2H), 4.17 (s, 4H), 4.07 (s, 6H), 3.94 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 159.2, 159.1, 154.8, 148.9, 139.2, 136.2, 136.1, 128.2, 126.0, 122.9, 121.8, 121.0, 119.2, 107.6, 61.1, 60.5, 56.1. Anal. Calcd for $C_{28}H_{26}N_4O_2$ (8-MeOBQPA): H, 5.82; C, 74.64; N, 12.44. Found: H, 5.76; C, 74.61; N, 12.57. ESI-MS m/z: 473.2 ([M + Na]$^+$).

[Zn(6-MeOTQA)(DMF)(ClO_4)]ClO_4. A mixture of 6-MeOTQA (5.3 mg, 0.010 mmol) in $CHCl_3$ (0.20 mL) and $Zn(ClO_4)_2$·6H_2O (3.7 mg, 0.010 mmol) in methanol (1.0 mL) and DMF (0.1 mL) was stand at 4 °C for 1 day to give colorless crystals of [Zn(6-MeOTQA)(DMF)(ClO_4)]ClO_4 (5.0 mg, 0.0056 mmol) in 56% yield.

^{1}H NMR (CD_3CN): δ 8.56 (d, J = 9.2 Hz, 3H), 8.30 (d, J = 8.5 Hz, 3H), 7.85 (s, 1H), 7.55 (dd, J = 9.2, 2.4 Hz, 3H), 7.42 (d, J = 8.5 Hz, 3H), 7.30 (d, J = 2.4 Hz, 3H), 4.75 (s, 6H), 3.88 (s, 9H), 3.05 (s, 3H), 2.90 (s, 3H). ^{13}C NMR (CD_3CN): δ 165.0, 159.1, 155.1, 140.9, 140.4, 131.0, 128.1, 122.3, 107.6, 63.6, 56.7, 47.6, 37.9, 33.1. Anal. Calcd for $C_{36}H_{39}Cl_2N_5O_{13}Zn$ ([Zn(6-MeOTQA)(DMF)(ClO_4)]ClO_4·H_2O): H, 4.44; C, 48.80; N, 7.90. Found: H, 4.22; C, 49.00; N, 7.90.

[Zn(8-MeOTQA)](ClO_4)$_2$. A mixture of 8-MeOTQA (15.3 mg, 0.030 mmol) in $CHCl_3$ (0.03 mL) and $Zn(ClO_4)_2$·6H_2O (11.1 mg, 0.030 mmol) in methanol (15 mL) was stand at 4 °C for 1 day to give colorless crystals of [Zn(8-MeOTQA)](ClO_4)$_2$ (17.5 mg, 0.029 mmol) in 98% yield.

^{1}H NMR (CD_3CN): δ 8.66 (d, J = 8.2 Hz, 3H), 7.70–7.79 (m, 9H), 7.47 (dd, J = 1.8, 7.3 Hz, 3H), 4.71 (d, J = 17.9 Hz, 3H), 4.32 (d, J = 17.9 Hz, 3H), 3.73 (s, 9H). ^{13}C NMR (CD_3CN): δ 159.1, 150.8, 142.8, 136.3, 130.2, 129.5, 123.6, 122.3, 112.7, 59.0, 57.3. Anal. Calcd for $C_{33}H_{30}Cl_2N_4O_{11}Zn$ ([Zn(8-MeOTQA)]-(ClO_4)$_2$): H, 3.80; C, 49.86; N, 7.05. Found: H, 3.77; C, 49.61; N, 7.05.

[Cd(8-MeOTQA)](ClO_4)$_2$. A mixture of 8-MeOTQA (7.9 mg, 0.015 mmol) in $CHCl_3$ (0.03 mL) and $Cd(ClO_4)_2$·6H_2O (6.6 mg, 0.015 mmol) in methanol (0.5 mL) was stand at 4 °C for 1 day to give colorless crystals of [Cd(8-MeOTQA)](ClO_4)$_2$ (8.6 mg, 0.013 mmol) in 89% yield.

^{1}H NMR (CD_3CN): δ 8.59 (d, J = 8.5 Hz, 3H), 7.66–7.78 (m, 9H), 7.58 (dd, J = 1.5, 7.3 Hz, 3H), 4.45 (br., 6H), 4.10 (s, 9H). ^{13}C NMR (CD_3CN): δ 158.1–150.3, 141.9, 136.8, 130.0, 129.1, 124.0, 122.9, 113.2, 60.1, 58.1. Anal. Calcd for $C_{33}H_{30}CdCl_2N_4O_{11}$ ([Cd(8-MeOTQA)](ClO_4)$_2$): H, 3.59; C, 47.08; N, 6.65. Found: H, 3.61; C, 46.96; N, 6.62.

[Zn(8-MeOBQPA)(CH_3OH)](ClO_4)$_2$. To a chloroform solution (0.1 mL) of 8-MeOBQPA (4.5 mg, 0.010 mmol) was added $Zn(ClO_4)_2$·6H_2O (3.7 mg, 0.010 mmol) in methanol (0.8 mL) and the solution was stand at 4 °C to give [Zn(8-MeOBQPA)-(CH_3OH)](ClO_4)$_2$ as colorless crystals (5.3 mg, 0.0071 mmol) in 71% yield.

^{1}H NMR (CD_3CN): δ 8.86 (d, J = 5.2 Hz, 1H), 8.60 (d, J = 8.5 Hz, 2H), 8.04 (ddd, J = 7.8, 7.8, 1.5 Hz, 1H), 7.72–7.70 (m, 4H), 7.67–7.60 (m, 3H), 7.52 (d, J = 4.1 Hz, 1H), 7.42 (dd, J = 4.9, 4.3 Hz, 2H), 4.50 (d, J = 3.4 Hz, 4H), 4.25 (s, 2H), 3.90 (s, 6H). ^{13}C NMR (CD_3CN): δ 157.5, 155.4, 151.3, 148.6, 141.8, 141.6, 136.1, 130.0, 129.0, 125.8, 125.1, 122.7, 121.4, 111.6, 57.7, 57.4, 56.7. Anal. Calcd for $C_{28}H_{28}Cl_2N_4O_{11}Zn$ ([Zn(8-MeOBQPA)(H_2O)](ClO_4)$_2$): H, 3.85; C, 45.89; N, 7.65. Found: H, 3.62; C, 46.20; N, 7.54.

[Cd(8-MeOBQPA)(CH_3OH)](ClO_4)$_2$. To a chloroform solution (0.1 mL) of 8-MeOBQPA (4.5 mg, 0.010 mmol) was added $Cd(ClO_4)_2$·6H_2O (4.2 mg, 0.010 mmol) in methanol (0.8 mL) and the solution was stand at 4 °C to give [Cd(8-MeOBQPA)-(CH_3OH)](ClO_4)$_2$ as colorless crystals (6.2 mg, 0.0079 mmol) in 79% yield.

^{1}H NMR (CD_3CN): δ 8.79 (d, J = 5.5 Hz, 1H), 8.56 (d, J = 8.5 Hz, 2H), 8.03 (dd, J = 6.7, 1.8 Hz, 1H), 7.74–7.58 (m, 7H), 7.53–7.48 (m, 3H), 4.39 (s, 4H), 4.15 (s, 8H). ^{13}C NMR (CD_3CN): δ 157.2, 155.5, 150.4, 149.5, 141.2, 136.3, 129.7, 128.7, 125.8, 123.3, 121.9, 111.8, 58.1, 57.8, 57.2. Anal. Calcd for $C_{28}H_{28}CdCl_2N_4O_{11}$ ([Cd(8-MeOBQPA)(H_2O)](ClO_4)$_2$): H, 3.64; C, 43.37; N, 7.23. Found: H, 3.33; C, 43.62; N, 7.19.

X-ray crystallography

Single crystals of **2**, 8-MeOTQA·0.5CH_2Cl_2 (**4**·0.5CH_2Cl_2), [Zn-(6-MeOTQA)(DMF)(ClO_4)]ClO_4·0.5H_2O, [Zn(8-MeOTQA)](ClO_4)$_2$, [Zn(8-MeOBQPA)(CH_3OH)](ClO_4)$_2$·0.5H_2O, [Cd(8-MeOTQA)]-(ClO_4)$_2$ and [Cd(8-MeOBQPA)(CH_3OH)](ClO_4)$_2$·CH_3OH were covered by paratone-N oil and mounted on a glass fibre. All data were collected at 153 K on Rigaku Mercury or Saturn CCD

detector, with monochromatic MoKα radiation, operating at 50 kV/40 mA (Mercury) or 50 kV/24 mA (Saturn). Data were processed on a PC using CrystalClear Software (Rigaku). Structures were solved by direct methods (SIR-92[34] or SIR2008[35]) and refined by full-matrix least-squares methods on F^2 (SHELXL-97).[36] Crystal data are summarized in Tables S1–S4.† CCDC-1017795–1017798, 1032611, 1046752 and 1046753 contain the supplementary crystallographic data for this paper.

Results and discussion

Ligand synthesis

The condensation of three halides with an ammonia derived from **1** in the presence of K_2CO_3 proceeds under ambient pressure *via* reflux in acetonitrile for 2 hours, with minimal work-up procedures, *i.e.*, filtration and evaporation. Very limited examples have utilized acetaldehyde ammonia trimer (**1**) for organic synthesis[37,38] and there has been no previous report for tertiary amine synthesis using **1**. Table 1 lists the scope and limitations of the present method. Benzyl chlorides (entries 1–5), 2-chloromethylpyridine (entry 9) and 2-chloromethylquinolines (entries 10–15) gave corresponding tertiary amines in high yield. However, the reaction did not proceed at all for chlorobenzene (entry 6), allyl chloride (entry 7) and alkyl chloride (entry 8).

Although the reaction stoichiometry can be reduced to 9 : 1 for benzyl chloride–**1**, under which condition the isolated yield of TBA was 89% and a small amount of starting material was recovered, the reactions listed in Table 1 are carried out under 9 : 2 conditions considering the halide conversion and acceleration of the reaction.

No secondary or primary amines were detected under the present conditions except for sterically hindered 2,4,6-trimethylbenzyl chloride (entry 5), in which secondary amine was formed in 9% yield and tertiary amine **2** was obtained in 84% yield. In this case, reducing the amount of **1** to 1/9 relative to halide prevented the secondary amine formation but did not improve the yield of **2** (84%) because of incomplete halide conversion as mentioned above. The structure of **2** was confirmed by X-ray crystallography (Fig. 1).

Zn^{2+}-induced absorbance and fluorescence spectral changes in TQA derivatives 3–5

The Zn^{2+}-induced fluorescence enhancement of unsubstituted TQA has been already reported.[33] But, the substituent effect on the quinoline ring was not studied due to the synthetic hurdle. To demonstrate the potential use of the present procedure as a convenient C_3-symmetric tertiary amine synthesis, the fluorescent zinc sensing property of the newly synthesized TQA compounds were investigated.

Among the TQA derivatives **3**–**7** prepared in this work, tris-(8-methoxy-2-quinolylmethyl)amine (8-MeOTQA (**4**), Fig. 2 for crystal structure) exhibits the most attractive Zn^{2+} sensing properties. Fig. 3 shows the absorbance and fluorescence spectral changes of 8-MeOTQA with increasing Zn^{2+} concentration.

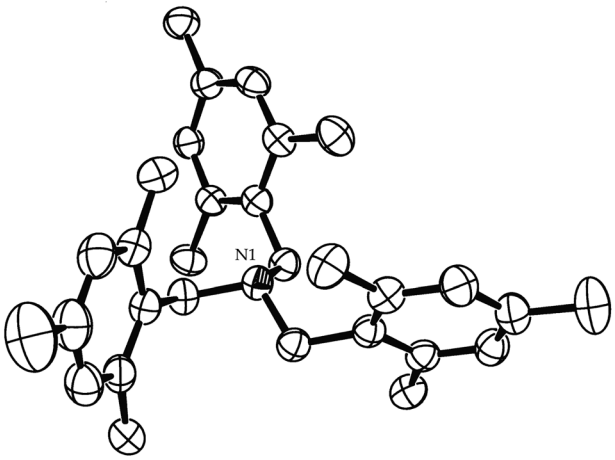


Fig. 1 ORTEP plot for **2** with 50% thermal ellipsoids. Hydrogen atoms are omitted for clarity.

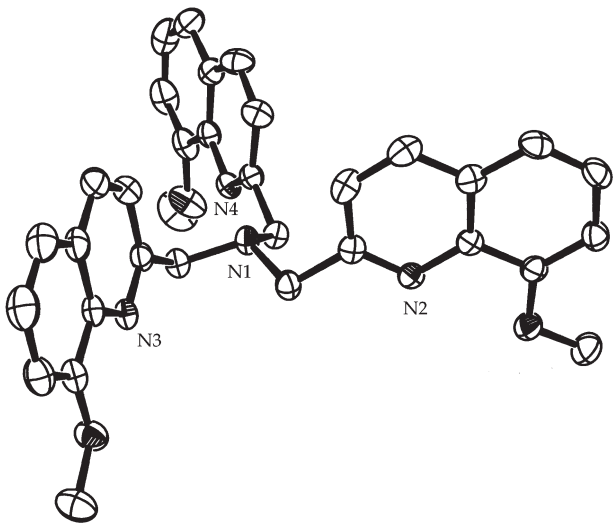


Fig. 2 ORTEP plot for 8-MeOTQA·0.5CH_2Cl_2 (**4**·0.5CH_2Cl_2) with 50% thermal ellipsoids. Solvents and hydrogen atoms are omitted for clarity.

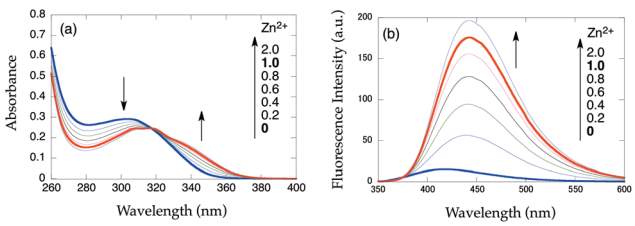


Fig. 3 (a) Absorption and (b) fluorescence spectra of 34 μM 8-MeOTQA (**4**) in DMF–H_2O (1 : 1) at 25 °C in the presence of various concentration of Zn^{2+} ranging from 0 to 68 μM (λ_{ex} = 335 nm).

Titration curves (Fig. S1†) and a clear isosbestic point at 317 nm observed in the absorbance spectra indicate the 1 : 1 binding stoichiometry for 8-MeOTQA with Zn^{2+}. Although the 8-hydroxy/alkoxy substituted quinolines with di(2-pyridylmethyl)amine (DPA) group have been extensively studied as fluorescent Zn^{2+} or Cd^{2+} probes,[39–44] no C_3-symmetric TQA derivatives utilizing 8-hydroxy/alkoxyquinoline have been reported. The dissociation constant (K_d) for $[Zn(8\text{-MeOTQA})]^{2+}$ was estimated to be (5.5 ± 2.4) × 10^{-7} M. Fluorescence enhancement is significant for Zn^{2+} (I_{Zn}/I_0 = 16, ϕ_{Zn} (fluorescence quantum yield of Zn^{2+} complex) = 0.51). These binding and fluorescence properties of 8-MeOTQA lower the limit of detection (LOD) of Zn^{2+} as low as 3.4 nM (Fig. S2†). The working pH window of 8-MeOTQA for Zn^{2+} detection is rather narrow (pH = 4–8, Fig. S3†) due to the moderate binding affinity of tetradentate nitrogen ligand, but this range covers physiological pH for cell studies.

The Zn^{2+}-induced absorbance and fluorescence spectral changes of 6-MeOTQA (**3**) and 6,8-DiMeOTQA (**5**) are shown in Fig. 4a–d and S4a–d.† Other compounds, 5,6,7-TriMeOTQA (**6**) and 8-MeSTQA (**7**), are not included because they exhibited fluorescence quenching upon addition of Zn^{2+} (see next section). Considering that 6-MeOTQA exhibits much weaker fluorescence intensity upon addition of Zn^{2+} (Fig. 4b, ϕ_{Zn} = 0.027) in comparison to 8-MeOTQA (ϕ_{Zn} = 0.51), the position of methoxy substitution on TQA is critical (Fig. S5†). Introduction of two methoxy groups at 6- and 8-position of TQA (6,8-DiMeOTQA, **5**) induced slight long-wavelength shift of fluorescence maximum with moderate enhancement in intensity (Fig. 4d). Comparison of the fluorescence quantum yields of zinc complexes of 8-MeOTQA and 6,8-DiMeOTQA (ϕ_{Zn} = 0.15) reveals that the introduction of 6-methoxy substituents to 8-MeOTQA reduces the fluorescence intensity of Zn^{2+} complex. Because the Zn^{2+}-induced absorbance changes are almost identical for both compounds (Fig. 3a and 4c), the extent of electronic perturbation of quinoline ring upon Zn^{2+} binding is similar. No clear explanation can be given for this result at the present stage and further measurements as well as theoretical calculations would be necessary to elucidate the quenching effect in 6-methoxy substituent of 6,8-DiMeOTQA.

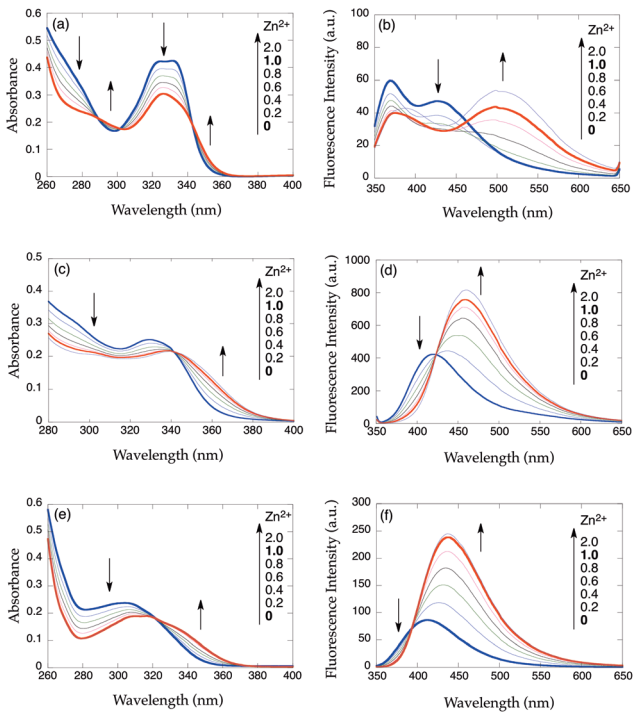
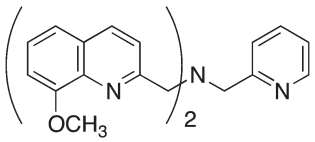


Fig. 4 (a, c, e) Absorption and (b, d, f) fluorescence spectra of 34 μM (a, b) 6-MeOTQA (**3**), (c, d) 6,8-DiMeOTQA (**5**) and (e, f) 8-MeOBQPA (**8**) in DMF–H_2O (1 : 1) at 25 °C in the presence of various concentration of Zn^{2+} ranging from 0 to 68 μM (λ_{ex} = 332 nm for 6-MeOTQA; 347 nm for 6,8-DiMeOTQA; 335 nm for 8-MeOBQPA).



8-MeOBQPA (**8**)

Chart 1

In order to evaluate the 8-methoxy substituent effect in C_3-symmetric structure of TQA, the mono pyridine analog of 8-MeOTQA, bis(8-methoxy-2-quinolylmethyl)(2-pyridylmethyl)-amine (8-MeOBQPA (**8**), Chart 1) was investigated (Fig. 4e,f and S4e,f†). The Zn^{2+}-induced fluorescence enhancement was significantly weak (ϕ_{Zn} = 0.095, I_{Zn}/I_0 = 3.5) compared with 8-MeOTQA (Fig. S5†). The significant contribution of C_3-symmetric location of 8-methoxyquinoline in 8-MeOTQA-Zn complex leading to strong fluorescence is revealed by X-ray crystallography (see below).

Fluorescence metal ion specificity of 3–8

Fig. 5 and S6† show the metal ion selectivity of all quinoline compounds (**3–8**). Here also, the 8-MeOTQA (**4**) exhibits the most attractive property. Fluorescence enhancement of 8-MeOTQA is significant for Zn^{2+} (I_{Zn}/I_0 = 16), whereas Cd^{2+}-induced fluorescent response was small (I_{Cd}/I_{Zn} = 16%). The pre-incubation of 8-MeOTQA in the presence of 1 equiv. of Co^{2+}, Ag^+, Cd^{2+} and Hg^{2+} prevented the fluorescence detection of Zn^{2+}. On the other hand, the fluorescence of 8-MeOTQA-Zn complex was quenched by the addition of 1 equiv. of Ag^+ and Hg^{2+}. It should be noted that the Cu^{2+}-induced fluorescence quenching of 8-MeOTQA-Zn complex was very small in both measurements.

Interestingly, tris(5,6,7-trimethoxy-2-quinolylmethyl)amine-(5,6,7-TriMeOTQA, **6**) exhibited a Cd^{2+} preference (Fig. 5d and S6d†). The Cd^{2+} titration of 5,6,7-TriMeOTQA is shown in Fig. S7.† As mentioned above, introduction of more than two methoxy groups induces long-wavelength shift of fluorescence maximum (λ_{em}) upon Zn^{2+}/Cd^{2+} binding. These features, including metal preference change toward Cd^{2+}, are in good agreement with the methoxy substitution effect on

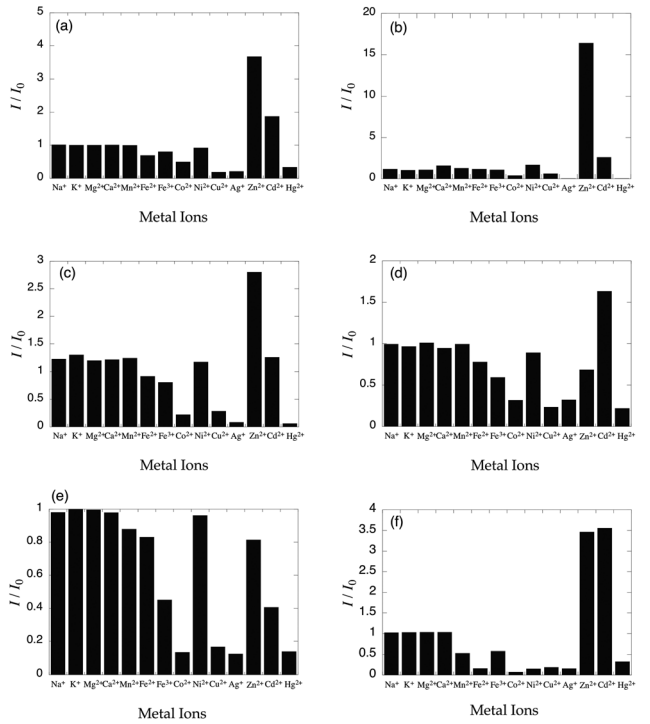


Fig. 5 The relative fluorescence intensity of (a) 6-MeOTQA (**3**) at 509 nm, (b) 8-MeOTQA (**4**) at 442 nm, (c) 6,8-DiMeOTQA (**5**) at 457 nm, (d) 5,6,7-TriMeOTQA (**6**) at 494 nm, (e) 8-MeSTQA (**7**) at 441 nm and (f) 8-MeOBQPA (**8**) at 437 nm in the presence of 1 equiv. of metal ions in DMF–H_2O (1 : 1) at 25 °C. I_0 is the emission intensity of free ligand.

TQEN (tetrakis(2-quinolylmethyl)ethylenediamine).[45] The moderate (52 nm) long-wavelength shift of λ_{em} for trimethoxy compound **6** upon Cd^{2+} binding may give some clues to design ratiometric probes. The long-wavelength emission of metal-bound species is probably due to the formation of intramolecular excimer formation between adjacent quinoline rings.[46,47] Thus, the Cd^{2+}-specific fluorescence spectral change of **6** is indicative for the excimer formation with seven or higher coordinate structure for the metal-bound species. Fig. S8† demonstrates the ratiometric descriptions of 6,8-DiMeOTQA (**5**) and 5,6,7-TriMeOTQA (**6**) upon metal binding, but more sensitive and specific compound is necessary for clear discrimination of the target metal.

Importantly, 8-MeOBQPA exhibits Cd^{2+}-induced fluorescence enhancement in similar extent with Zn^{2+} (Fig. 5f and S6f†). The Cd^{2+} titration of 8-MeOBQPA is shown in Fig. S9.† Thus, the three 8-methoxy substituents in 8-MeOTQA play crucial role in fluorescence intensity of Zn^{2+} complex and Zn/Cd selectivity. The detail of this point is discussed in the following section.

As summarized in Table 2, 8-MeOTQA exhibits superior sensitivity for zinc detection (I_{Zn}/I_0), Zn^{2+} specificity over other metal ions (I_{Cd}/I_{Zn}) and the extremely high fluorescence quantum yield upon binding Zn^{2+} (ϕ_{Zn}) among the present compound library. The structure–property relationship for 8-hydroxy- or 8-alkoxyquinoline derivatives including

Table 2 Fluorescent properties for TQA derivatives[a]

Ligand	λ_{ex}	λ_{em}	I_{Zn}/I_0	I_{Cd}/I_{Zn} (%)	ϕ_{Zn}
TQA	317	445	18	47(22[b])	—
6-MeOTQA (**3**)	332	405,509	3.7	51	0.027
8-MeOTQA (**4**)	335	442	16	16	0.51
6,8-DiMeOTQA (**5**)	347	457	2.8	45	0.15
5,6,7-TriMeOTQA (**6**)	332	494	0.7	240	0.033[c]
8-MeSTQA (**7**)	332	441	0.8	50	—
8-MeOBQPA (**8**)	335	437	3.5	103	0.095

[a] In DMF–H_2O (1 : 1). [b] In methanol–water (1 : 1).[33] [c] ϕ_{Cd}.

previously reported compounds (Chart S1†) is demonstrated in Table S5,† in which 8-MeOTQA still exhibits the total superiority on the basis of I_{Zn}/I_0, I_{Cd}/I_{Zn} and ϕ_{Zn}.

X-ray crystallography of Zn^{2+} and Cd^{2+} complexes of 4, 3 and 8

The steric effect of the C_3-symmetric methoxy group of 8-MeOTQA (**4**) that likely enhances fluorescence quantum yield of the Zn^{2+} complex was revealed by the X-ray crystallography (Fig. 6). The tetradentate ligands such as TQA and TPA usually form trigonal bipyramidal, octahedral or higher coordinate metal complexes with additional solvents or counter anions bound to the metal centre. As shown in Fig. 6 and Table 3, such solvent/counterion coordination is blocked by weak interaction of the methoxy oxygen atoms of 8-MeOTQA ($Zn–O_{methoxy}$ = 2.47–2.59 Å), which strengthens the coordination of quinoline nitrogen atoms ($Zn–N_{quinoline}$ = 2.04–2.07 Å) to similar values with those for tripodal pyridine (TPA) and isoquinoline (isoTQA) ligands with a solvent-bound, five-coordinate Zn^{2+} center ($Zn–N_{isoquinoline}$ = 2.05–2.08 Å).[18,48] The short $Zn–N_{quinoline}$ distances for 8-hydroxy- and 8-alkoxy-2-aminomethylquinoline systems have also been reported.[39,41,49,50]

In contrast, the metal centre of 6-MeOTQA-Zn complex adopts pseudo hexacoordinate geometry with strongly bound solvent (DMF) and weakly bound counterion (perchlorate) molecules (Fig. 7; $Zn–O_{DMF}$ = 1.98 Å, $Zn–O_{perchlorate}$ = 2.76 Å).

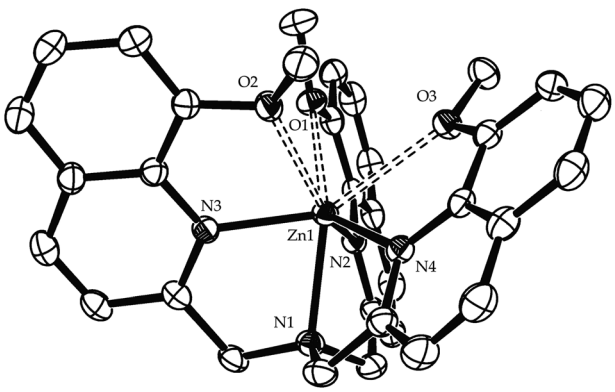


Fig. 6 ORTEP plot for cationic portion of $[Zn(8\text{-MeOTQA})](ClO_4)_2$ with 50% thermal ellipsoids. Counter anions and hydrogen atoms are omitted for clarity.

Table 3 Selected bond distances (Å) for $[Zn(8\text{-MeOTQA})](ClO_4)_2$, $[Cd(8\text{-MeOTQA})](ClO_4)_2$, $[Zn(6\text{-MeOTQA})(DMF)(ClO_4)]ClO_4$, $[Zn(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2$ and $[Cd(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2$

	$[Zn(8\text{-MeOTQA})](ClO_4)_2$	$[Cd(8\text{-MeOTQA})](ClO_4)_2$	$[Zn(6\text{-MeOTQA})(DMF)(ClO_4)]ClO_4$	$[Zn(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2$	$[Cd(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2$
M–N1(aliphatic)	2.2429(14)	2.435(3)	2.123(4)	2.199[a]	2.435(3)
M–N2(quinoline)	2.0684(16)	2.272(3)	2.189(3)	2.049[a]	2.280(3)
M–N3(quinoline)	2.0633(14)	2.276(3)	2.067(3)	2.175[a]	2.279(3)
M–N4(quinoline)	2.0429(16)	2.251(3)	2.149(4)	—	—
M–N4(pyridine)	—	—	—	2.127[a]	2.310(3)
M–O1(methoxy)	2.4883(14)	2.481(2)	—	2.567[a]	2.500(2)
M–O2(methoxy)	2.4665(13)	2.519(2)	—	2.777[a]	2.584(2)
M–O3(methoxy)	2.5915(11)	2.525(2)	—	—	
M–O(solvent)	—	—	1.978(3)	2.074[a]	2.337(2)
M–O(perchlorate)	—	—	2.755(4)	—	—
Mean M–N(quinoline)	2.058	2.266	2.135	2.112	2.280
Mean M–O(methoxy)	2.515	2.508	—	2.672	2.542

[a] Mean value for two crystallographically independent molecules.

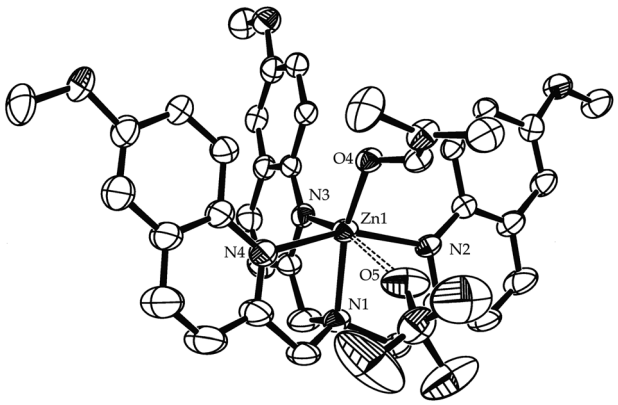


Fig. 7 ORTEP plot for cationic portion of $[Zn(6\text{-MeOTQA})(DMF)(ClO_4)]ClO_4{\cdot}0.5H_2O$ with 50% thermal ellipsoids. Counter anions, solvents and hydrogen atoms are omitted for clarity.

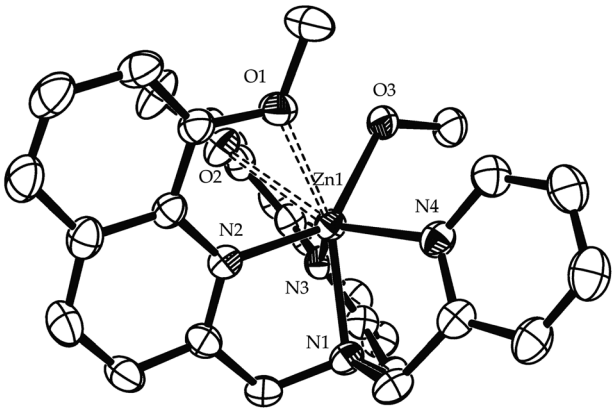


Fig. 8 ORTEP plot for cationic portion of $[Zn(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2{\cdot}0.5H_2O$ with 50% thermal ellipsoids. Counter anions, solvents and hydrogen atoms are omitted for clarity.

As a result, $[Zn(6\text{-MeOTQA})(DMF)(ClO_4)]^+$ exhibits long Zn^{2+}–quinoline nitrogen coordination distances ($Zn–N_{quinoline}$ = 2.07–2.19 Å), which are comparable with those for $[Zn(TQA)(H_2O)(ClO_4)]^+$ complex ($Zn–N_{quinoline}$ = 2.11–2.16 Å).[33] Since the solvent- or counterion-bound species were not obtained for 8-MeOTQA in the similar co-solvent system used for 6-MeOTQA-Zn complex ($CHCl_3$–MeOH–DMF = 0.2/1.0/0.2) resulting in the formation of $[Zn(8\text{-MeOTQA})](ClO_4)_2$, the position of methoxy substituent plays crucial role for determination of the coordination geometry of zinc complex.

Similar result was obtained for Zn^{2+} complex with 8-MeOBQPA (Fig. 8). The resulting pseudo heptacoordinate geometry of $[Zn(8\text{-MeOBQPA})(CH_3OH)]^{2+}$ includes a strongly bound solvent (methanol) molecule ($Zn–O_{methanol}$ = 2.07 Å), which weakens quinoline coordination and fluorescence intensity (mean $Zn–N_{quinoline}$ = 2.11 Å, ϕ_{Zn} = 0.095). For the 8-MeOTQA complex, the steric bulk and weak metal coordination of three 8-methoxy substituents effectively kick out the solvent/counterion coordination, leading to the short $Zn–N_{quinoline}$ distance and high fluorescence intensity of the Zn^{2+} complex. Thus, C_3-symmetric structure of 8-MeOTQA is extremely important for high fluorescence intensity of Zn^{2+} complex and Zn/Cd selectivity.

The Cd^{2+} complex with 8-MeOTQA (Fig. 9) also exhibits short $Cd–N_{quinoline}$ distances (2.25–2.28 Å) in comparison to hexacoordinate $[Cd(TQA)(CH_3CN)(ClO_4)]^+$ complex ($Cd–N_{quinoline}$ = 2.32–2.37 Å).[25] For the $[Cd(8\text{-MeOTQA})]^{2+}$, the coordination of oxygen atoms at the 8-position is also significant and even in shorter distances than corresponding Zn^{2+} complex (Table 3) probably due to the insufficient coordination of quinoline nitrogen to the Cd centre. The observed $Cd–N_{quinoline}$ distances are similar values to those for $[Cd(8\text{-MeOBQPA})(CH_3OH)]^{2+}$ (2.28 Å, Fig. 10), which exhibits pseudo heptacoordinate geometry including a solvent molecule strongly bound to the Cd centre ($Cd–O_{methanol}$ = 2.34 Å). It is of also significant interest that 8-MeOTQA-Cd^{2+} and 8-MeOBQPA-Cd^{2+} complexes

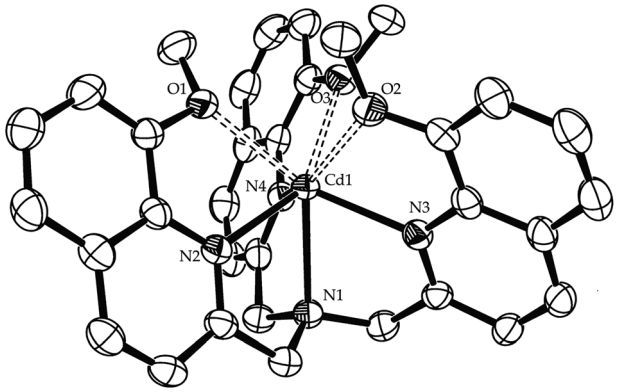


Fig. 9 ORTEP plot for cationic portion of $[Cd(8\text{-MeOTQA})](ClO_4)_2$ with 50% thermal ellipsoids. Counter anions and hydrogen atoms are omitted for clarity.

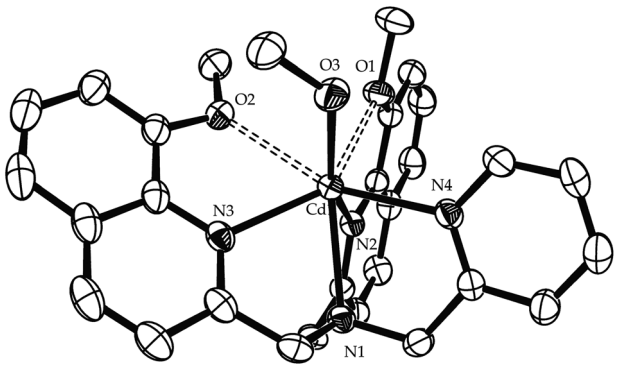


Fig. 10 ORTEP plot for cationic portion of $[Cd(8\text{-MeOBQPA})(CH_3OH)](ClO_4)_2{\cdot}CH_3OH$ with 50% thermal ellipsoids. Counter anions, solvents and hydrogen atoms are omitted for clarity.

exhibit similar fluorescence intensity (Fig. S10†). The poor Zn/Cd discrimination ability of 8-MeOBQPA is probably due to the flexibility of coordination environment upon metal binding. The above crystallographic analyses reveal that quinoline coordination to the Zn centre in the C_3-symmetric $[Zn(8\text{-MeOTQA})]^{2+}$ is extremely strong, leading to strong and specific Zn^{2+}-induced fluorescence enhancement concomitant with high Zn/Cd discrimination ability.

Conclusions

The present method utilizing acetaldehyde ammonia trimer (**1**) as an easy-handling nitrogen source provides highly efficient and convenient construction of a compound library of C_3-symmetric tribenzylamines. The screening of substituted TQA library revealed a synergistic effect of both steric and electronic roles of 8-methoxy substituents. The quasi-seven coordinate zinc center including three weak methoxy interactions significantly enhances the fluorescence intensity of $[Zn(8\text{-MeOTQA})]^{2+}$. Although intracellular Zn^{2+} detection with 8-MeOTQA needs to be tested, the present findings demonstrate a new approach to useful C_3-symmetric tertiary amine libraries and unexplored fluorescence properties of 8-methoxyquinolines.[51]

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