Electronic Supplementary Information (ESI)

For

Design and synthesis of two novel functional metal-organic microcapsules, an investigation on ligand expansion effects on metal-organic microcapsules' properties

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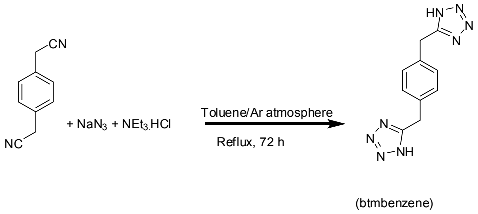
Contents **Page Number**

1. Characterization

Perkin–Elmer 597 and Nicolet 510P spectrophotometers were utilized to record FT-IR spectra. The elemental analysis was carried out with a Heraeus CHN-O- rapid analyzer. The thermal stability was determined with a PL-STA 1500 device between 35 and 800 ˚C in a static atmosphere of nitrogen. A Hitachi H-9500 device was used to capture transmission electron microscopy (TEM) images. NMR spectra were recorded on a BRUKER DRX500 AVANCE spectrometer. PL spectra were determined applying a spectrofluorimeter produced by cary eclipseFL0912M014. X-ray powder diffraction (XRD) analyses were accomplished utilizing a X'pert diffractometer constructed by Philips with monochromatized CuKa radiation. The morphology of prepared samples were investigated with scanning electron microscope (SEM) (Philips XL 30) with a gold coating.

2. Synthesis details and characterization of the btmbenzene ligand



Scheme S1 Synthesis route for btmbenzene ligand

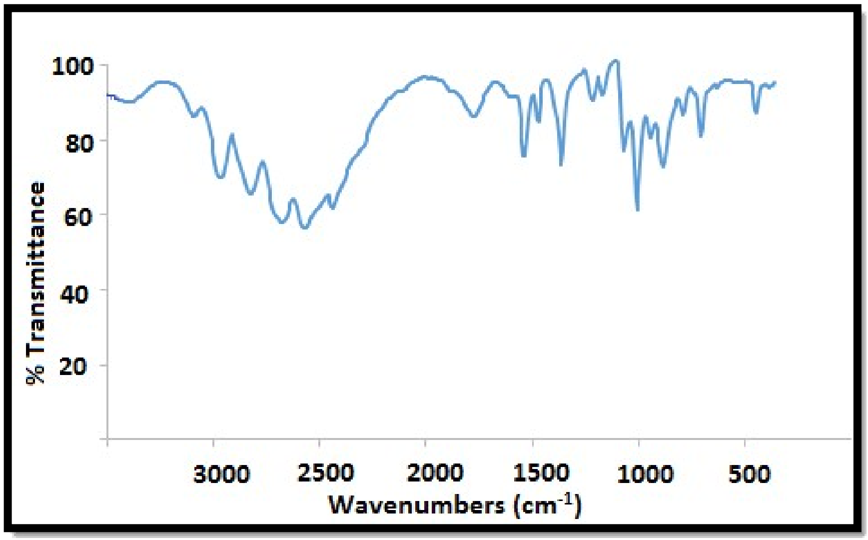
Synthesis of btmbenzene. Toluene (50 ml) was poured into a 100 ml round-bottom flask including 2,2'-(1,4-phenylene)diacetonitrile (2.4 mmol), sodium azide (15 mmol) and triethylamine hydrochloride (15 mmol). The reaction mixture was refluxed for three days which led to formation of a pale-brown solid on the wall of the flask. The precipitation was separated and dissolved in NaOH (30 mL, 1 M) under stirring. Afterward, HCl (1 M) was added to the solution until achieving a solution with the pH of 1 and the tetrazole precipitated completely. The obtained precipitation was separated by filtration and dried at RT yielding a pale-yellow powder (yield: 96%).

^{1}H NMR (d -DMSO): 7.25 (s, 4H), 4.27 (s, 4H)

^{13}C NMR: 134.9, 129.2, 28.69.

Anal. Calcd. for btmbenzene: C, 49.57; H, 4.13; N, 46.28. Found: C, 49.12; H, 4.04; N, 46.2.

Fig. S1 IR spectrum of btmbenzene



IR (cm^{-1}) selected bands: 487 (w), 746 (w), 831 (w), 925 (m), 986 (w), 1049 (m), 1108 (w), 1209 (w), 1259 (w), 1404 (m), 1515 (w), 1578 (w), 1816 (w), 2477 (m), 2613 (s), 2715 (s), 2865 (m), 3005 (m), 3128 (w) and 3439 (w).

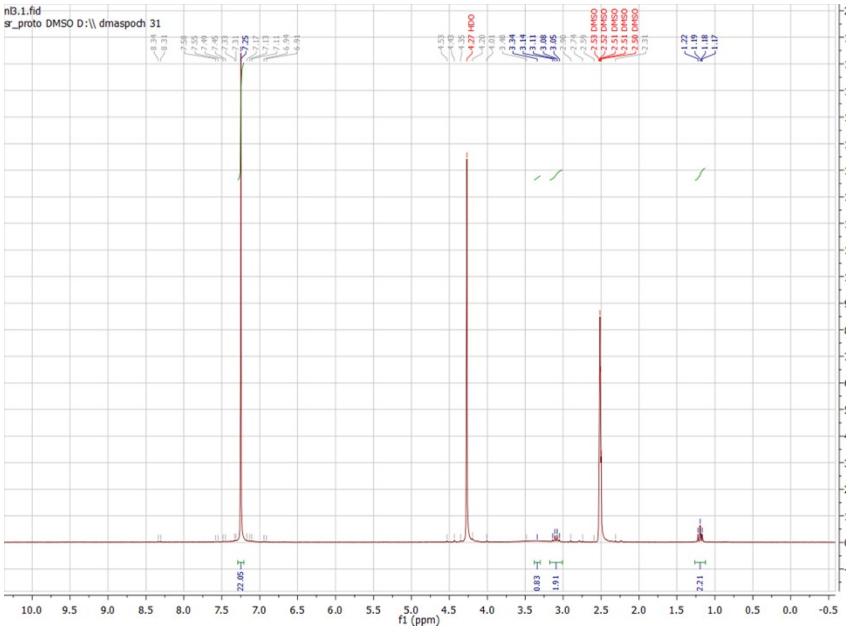


Fig. S2 ^{1}H NMR spectrum of the ligand, btmbenzene, (the peak in 2.5 ppm, is for solvent DMSO)

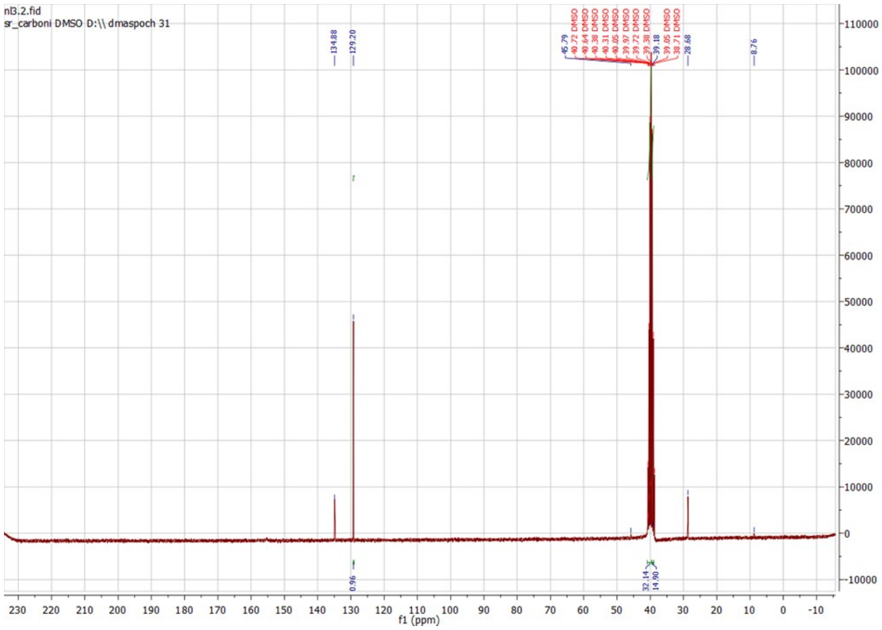
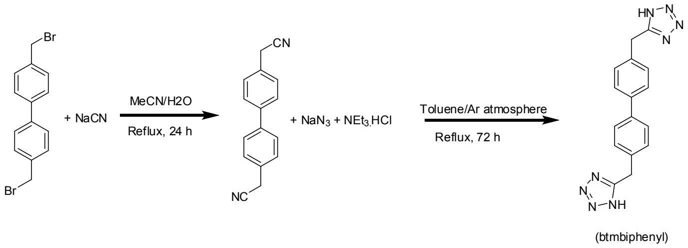


Fig. S3 ^{13}C NMR spectrum of the ligand, btmbenzene.

3. Synthesis details and characterization of btmbiphenyl ligand



Scheme S2 Synthesis route for btmbiphenyl ligand

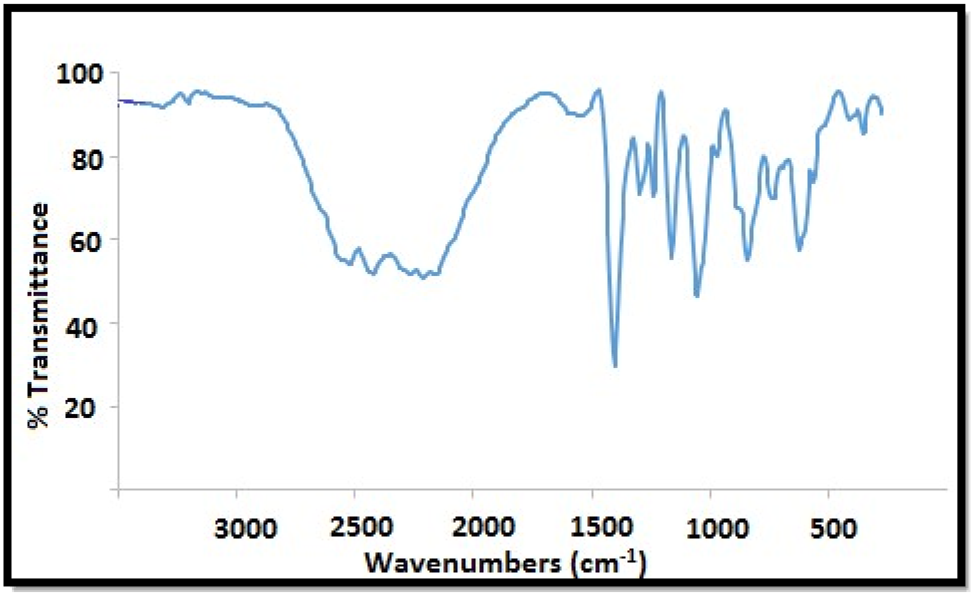
Acetonitrile (50 mL) was added to a 100 mL round-bottom flask including 4,4'-bis(bromomethyl)biphenyl (1.5 mmol) and the mixture was stirred to dissolve the precursor. In next step, a solution of sodium cyanide (3.2 mmol) in H_2O (5 mL) was added to the mixture dropwise. The mixture was stirred for 1 h and then refluxed for 24 h. Afterward, the solvent was removed by evaporation and H_2O (50 mL) was added to the solid and was stirred for 30 min. Then, the yellow solid was separated by filtration. The filtrate was dried at RT to yield a yellow powder. In next step, toluene (50 ml) was poured into a 100 ml round-bottom flask including 2,2'-(biphenyl-4,4'-diyl)diacetonitrile (2.4 mmol) sodium azide (15 mmol) and triethylamine hydrochloride (15 mmol). The reaction mixture was refluxed for three days which led to formation of a pale-yellow solid on the wall of the flask. The work-up procedure was similar to the btmbenzene preparation (yield: 88%).

^{1}H NMR (d -DMSO): 7.5 (q, 8H), 4.34 (s, 4H)

^{13}C NMR: 155.42, 138.64, 135.36, 129.48, 127.16, 28.71.

Anal. Calcd. for btmbiphenyl: C, 52.57; H, 6.56; N.40.85. Found: C, 52.41; H, 6.43; N, 40.73.

Fig. S4 IR spectrum of btmbiphenyl



IR (cm^{-1}) selected bands: 490 (w), 557 (w), 731 (w), 801 (m), 925 (w), 1048 (m), 1290 (m), 1413 (m), 1501 (w), 1567 (w), 1689 (s), 1842 (w), 2612 (m), 2855 (m) and 2965 (m).

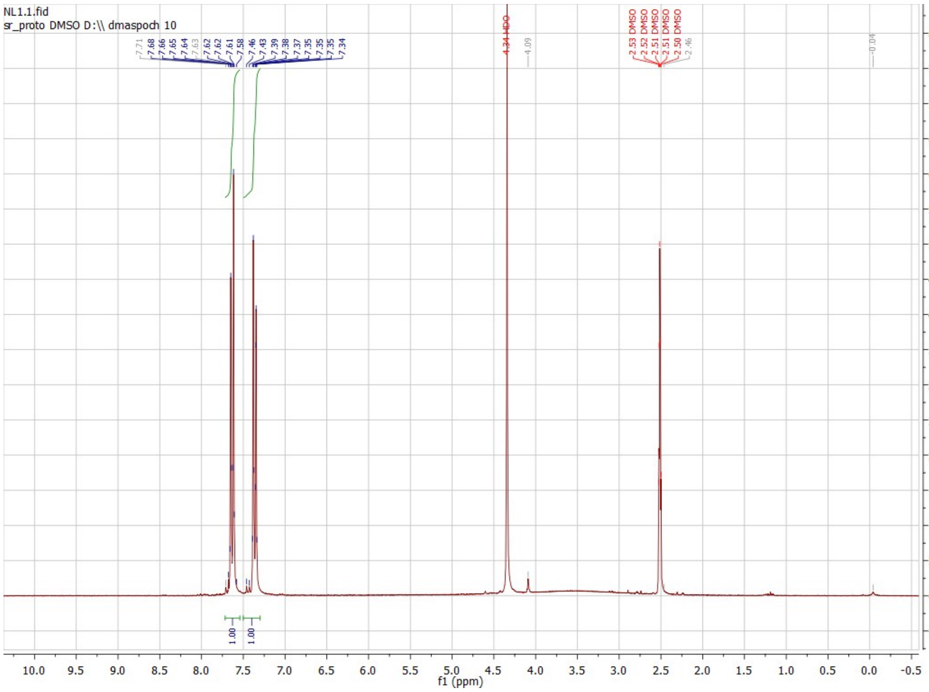


Fig. S5 ^{1}H NMR spectrum of the ligand, btmbiphenyl, (the peak in 2.5 ppm, is for solvent DMSO)

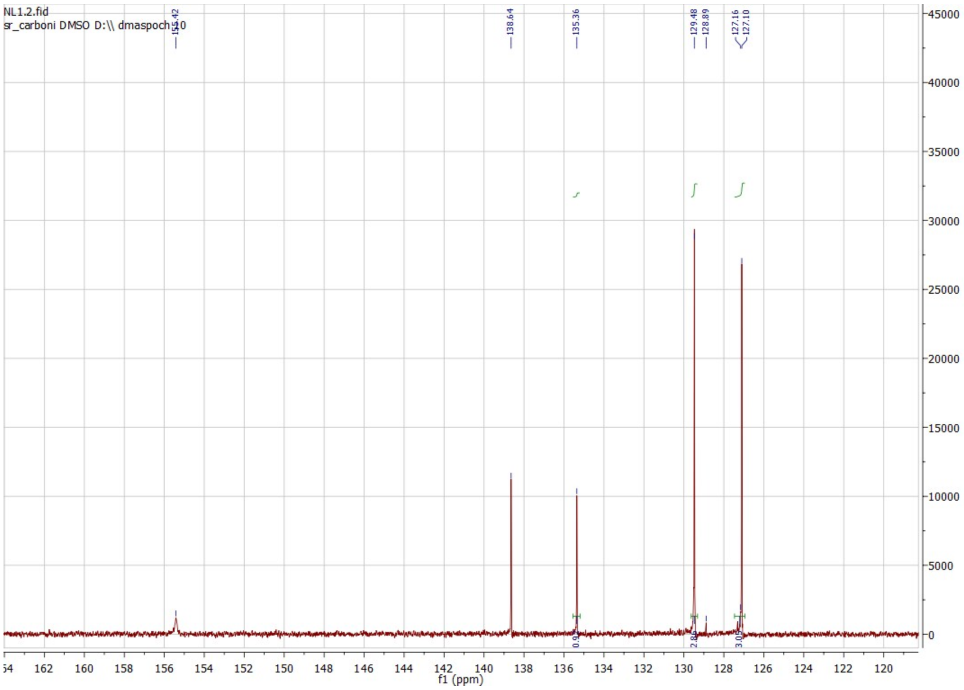


Fig. S6 ^{13}C NMR spectrum of the ligand, btmbiphenyl.

4. Preparation of spherical capsules, Zn(btmbenzene)-1

A solution of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) in methanol (2.5 mL) was added to btmbenzene (0.5 mmol) in DMF (12.5 mL) and stirred for 2 min. The mixture was transferred to a Teflon-lined stainless steel autoclave and heated to 120 ^oC for 12 h. The mixture was centrifuged and the separated product was washed with DMF several times. IR for Zn(btmbenzene)-1 (KBr pellet, cm^{-1}): 695 (w), 773 (m), 1104 (m), 1292 (w), 1431 (m),1486 (m), 1657 (s), 2931 (m) and 3422 (m). Anal. Calcd. for Zn(btmbenzene)-1: C, 39.3 H, 2.61; N, 36.67. Found: C, 39.2; H, 2.5; N, 36.43.

5. Preparation of Zn(btmbenzene)-2

To synthesize Zn(btmbenzene)-2 particles, methanolic solution (2.5 mL) of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) was added to btmbenzene (0.5 mmol) in DMF (12.5 mL) under vigorous stirring. After 1 h the colloidal mixture was centrifuged and the small particles were washed with DMF through centrifugation-redispersion cycles. IR for Zn(btmbenzene)-2 (KBr pellet, cm^{-1}): 620 (w), 827 (w), 1106 (m), 1150 (w), 1 (m), 1387 (m), 1654 (s), 2401 (m) and 3445 (m). Anal. Calcd. for Zn(btmbenzene)-2: C, 39.3 H, 2.61; N, 36.67. Found: C, 39.1; H, 2.35; N, 36.58.

6. Preparation of Zn(btmbenzene)-3

Aqueous solution (9 mL) of $Zn(NO_3)_2.6H_2O$ (0.044 M) was mixed with btmbenzene (0.2 M) in DMF and poured into a 50 mL flask and refluxed for 72 h at 140 ^oC. The rod-like product was isolated by centrifuge and washed with DMF several times. IR for Zn(btmbenzene)-3 (KBr pellet, cm^{-1}): 427 (s), 687 (w), 777 (w), 1106 (w), 1423 (m), 1654 (s), 2349 (w), 2935 (w), 3428 (m). Anal. Calcd. for Zn(btmbenzene)-3: C, 39.3 H, 2.61; N, 36.67. Found: C, 39.2; H, 2.56; N, 36.62.

7. Preparation of Zn(btmbenzene)-4

A solution of $Zn(NO_3)_2.6H_2O$ in distilled water (9 mL) with concentration of 0.044 M was poured into a beaker containing a solution of btmbenzene (0.2 M) in DMF (1 mL) and stirred for 15 min. The mixture was sealed in a Teflon-lined stainless steel autoclave and heated to 140 ^oC for 12 h. The flower-like structures were separated by centrifuge and washed with DMF several times. IR for Zn(btmbenzene)-4 (KBr pellet, cm^{-1}): 575 (w), 791 (w), 922 (w), 1089 (w), 1183 (w), 1279 (w), 1413 (s), 1491 (m), 1566 (s), 1647 (m), 2350 (w), 2942 (w), 3037 (w) and 3436 (m). Anal. Calcd. for Zn(btmbenzene)-4: C, 39.3 H, 2.61; N, 36.67. Found: C, 39.16; H, 2.48; N, 36.4.

8. Preparation of Zn(btmbiphenyl)-1

A solution of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) in methanol (2.5 mL) was added to btmbiphenyl (0.5 mmol) in DMF (12.5 mL) and stirred for 2 min. Afterward, the mixture was poured into a Teflon-lined stainless steel autoclave and heated to 120 ^oC for 12 h. The spherical capsules were separated by centrifuge and washed with DMF several times. IR for Zn(btmbiphenyl)-1 (KBr pellet, cm^{-1}): 699 (w), 786 (m), 1008 (w), 1060 (w), 1103 (w), 1166 (w), 1257 (w), 1430 (s), 1491 (s), 1604 (m), 1655(m), 2922 (w), 3027 (w) and 3418 (w). Anal. Calcd. for Zn(btmbiphenyl)-1: C, 50.35; H, 3.14; N, 29.36. Found: C, 50.2; H, 3.1; N, 29.2.

9. Preparation of Zn(btmbiphenyl)-2

A solution of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) in methanol (2.5 mL) was added to a 50 mL round-bottom flask including btmbiphenyl (0.5 mmol) in DMF (12.5 mL) under stirring gradually. After 1 h the colloidal mixture was centrifuged and the small particles were washed with DMF through centrifugation-redispersion cycles. IR for Zn(btmbiphenyl)-2 (KBr pellet, cm^{-1}): 700 (w), 764 (w), 819 (w), 919 (w), 1092 (w), 1185 (w), 1294 (m), 1374 (s), 1667(s), 2362 (w), 2963 (m), 3430 (m). Anal. Calcd. for Zn(btmbiphenyl)-2: C, 50.35; H, 3.14; N, 29.36. Found: C, 50.29; H, 2.96; N, 29.28.

10. Preparation of Zn(btmbiphenyl)-3

An aqueous solution (9 mL) of $Zn(NO_3)_2.6H_2O$ (0.044 M) was added to btmbiphenyl (0.2 M) in DMF and poured into a 50 mL flask and refluxed for 72 h at 140 ^oC. The rod-like structures were separated by centrifuge and washed with DMF several times. IR for Zn(btmbiphenyl)-3 (KBr pellet, cm^{-1}): 581 (w), 698 (w), 762 (w), 1103 (w), 1182 (w), 1257 (w), 1433 (m), 1487 (m), 1656 (s), 2360 (w), 2930 (w), 3428 (m). Anal. Calcd. for Zn(btmbiphenyl)-3: C, 50.35; H, 3.14; N, 29.36. Found: C, 50.14; H, 3; N, 29.16.

11. Synthesis details of dye and drug encapsulation in Zn(btmbenzene)-1

A methanolic solution (2.5 mL) of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) was added to a solution of Rhodamine B (0.08 mmol) and btmbenzene ligand (0.5 mmol) in DMF (12.5 mL). Next, the mixture stirred for 2 min. Afterward the mixture transferred to a Teflon-lined stainless steel autoclave and heated to 120 ^oC for 12 h. The spherical capsules were separated by centrifuge and washed with DMF several times. 5-FU@Zn(btmbenzene)-1 capsules were prepared following the same procedure.

12. Synthesis details of Fe_3O_4 nanoparticles encapsulation in Zn(btmbenzene)-2

A certain quantity of Fe_3O_4 nanoparticles (0.04 mmol) was added to a solution of btmbenzene ligand (1 mmol) in DMF (25 mL) and dispersed by sonication. Afterward, a methanolic solution (5 mL) of $Zn(NO_3)_2.6H_2O$ (1 mmol) was added to the mixture dropwise. Finally, Fe_3O_4@ Zn(btmbenzene)-2 capsules were formed. Theses capsules were separated by centrifuge and washed with DMF through centrifugation-redispersion cycles.

13. Synthesis details of dye and drug encapsulation in Zn(btmbiphenyl)-1

A methanolic solution (2.5 mL) of $Zn(NO_3)_2.6H_2O$ (0.5 mmol) was added to a solution of Rhodamine B (0.08 mmol) and btmbiphenyl ligand (0.5 mmol) in DMF (12.5 mL) and the mixture stirred for 2 min. Next, the mixture poured into a Teflon-lined stainless steel autoclave and heated to 120 ^oC for 12 h. The spherical capsules of RhB@Zn(btmbiphenyl)-1 were separated by centrifuge and washed with DMF several times. 5-FU@Zn(btmbiphenyl)-1 capsules were synthesized according to the same procedure.

14. Preparation of zinc oxide hollow sphere

Zn(btmbenzene)-1 and Zn(btmbiphenyl)-1 capsules separately were put in a furnace and calcinated at 450 ^oC in the air. After 3 h heating at the furnace, the produced ZnO was cooled to room temperature. Moreover, the same experiments were performed at 550 ^oC for both Zn(btmbenzene)-1 and Zn(btmbiphenyl)-1 capsules.

15. Zn(btmbenzene)-2 transformation to Zn(btmbenzene)-1

0.05 g of the Zn(btmbenzene)-2 powder was added to 2.5 mL methanol and 12.5 mL DMF and sealed in a Teflon-lined stainless steel autoclave and heated at 120 ^oC for 12 h. The mixture was cooled to room temperature and centrifuged. The product was washed with DMF several times and dried at room temperature.

16. Zn(btmbenzene)-2 transformation to cubic-like structures

0.05 g of the Zn(btmbenzene)-2 powder was added to 9 mL H_2O and 1 mL DMF and sealed in a Teflon-lined stainless steel autoclave and heated 140 ^oC for 24 h. The mixture was cooled to room temperature and centrifuged. The product was washed with distilled H_2O several times and dried at room temperature.

17. Zn(btmbiphenyl)-2 transformation to Zn(btmbiphenyl)-1

0.05 g of the Zn(btmbiphenyl)-2 powder was added to 2.5 mL methanol and 12.5 mL DMF and sealed in a Teflon-lined stainless steel autoclave and heated at 120 ^oC for 12 h. The mixture was cooled to room temperature and centrifuged. The product was washed with DMF several times and dried at room temperature.

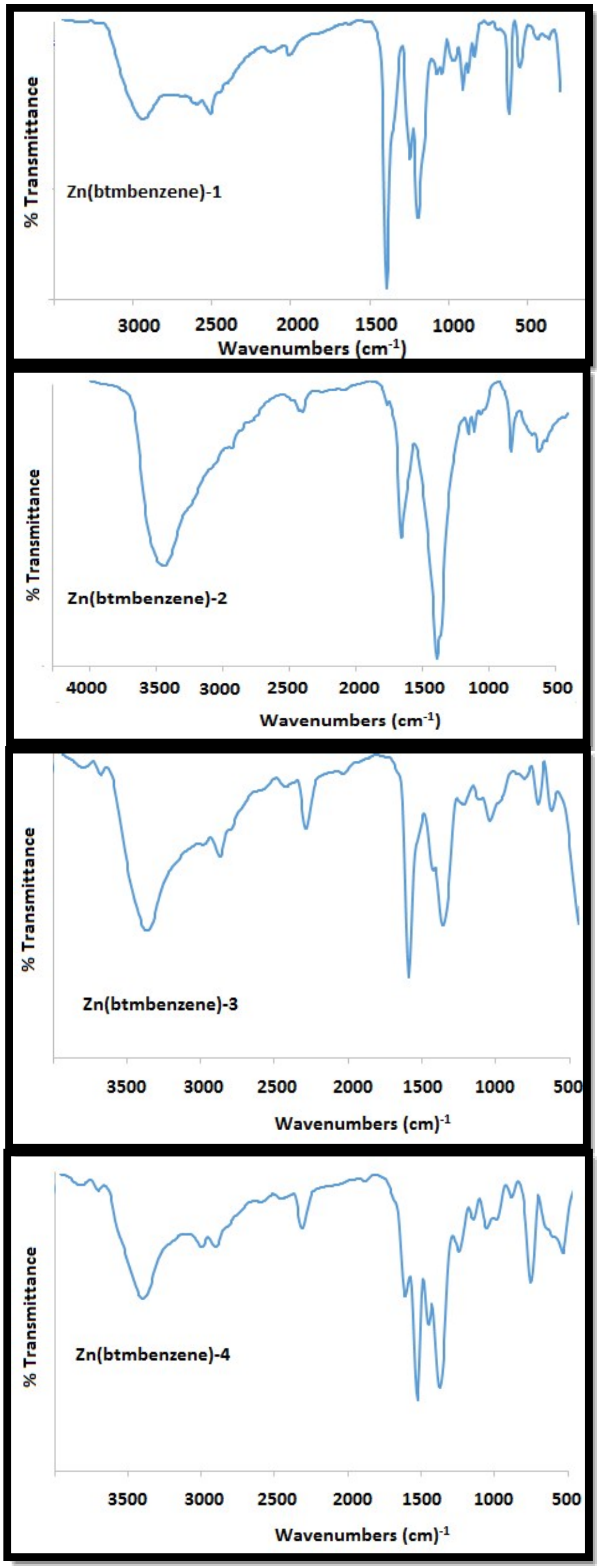


Fig. S7 IR spectra of Zn(btmbenzene)-1, Zn(btmbenzene)-2, Zn(btmbenzene)-3 and Zn(btmbenzene)-4

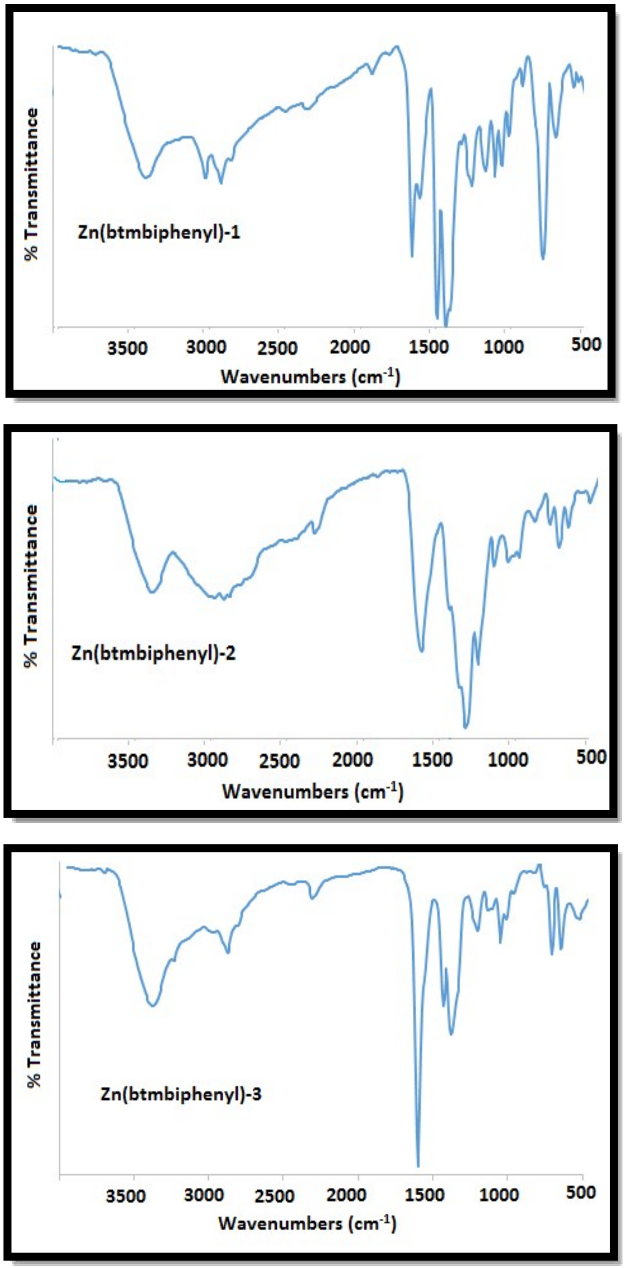


Fig. S8 IR spectra of Zn(btmbiphenyl)-1, Zn(btmbiphenyl)-2 and Zn(btmbiphenyl)-3

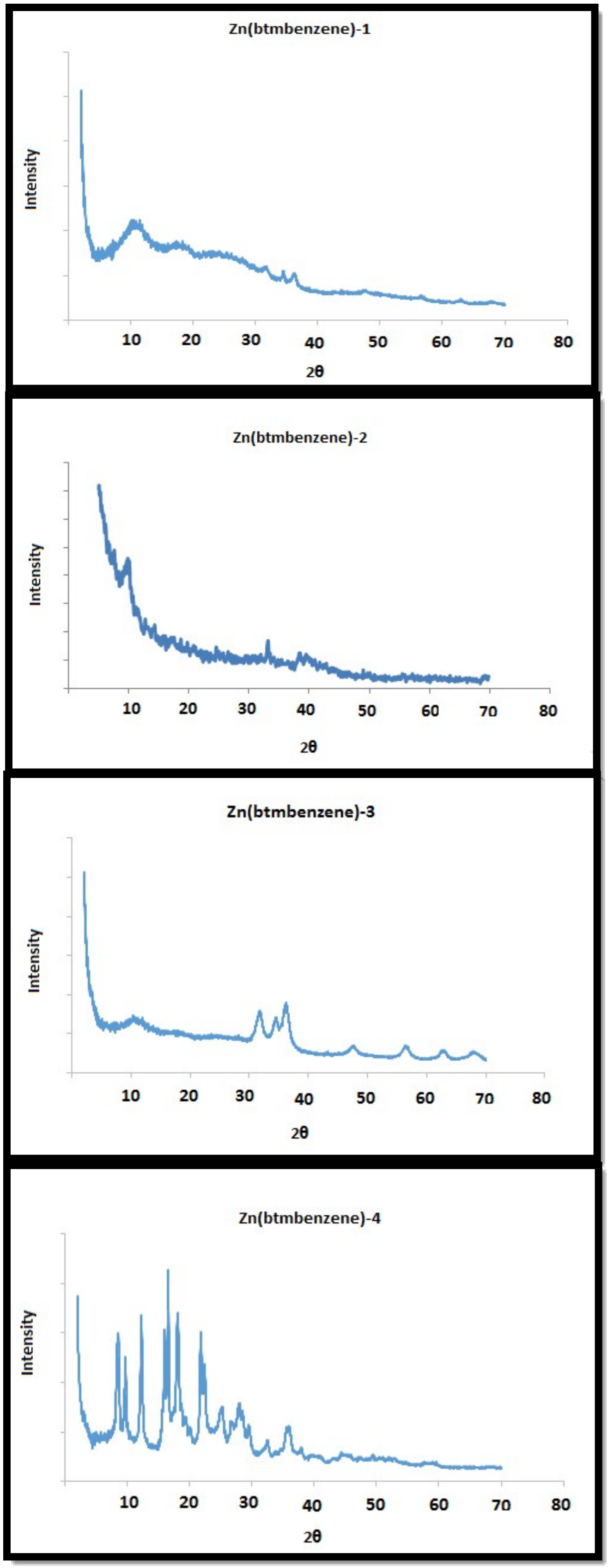


Fig. S9 PXRD patterns of of Zn(btmbenzene)-1, Zn(btmbenzene)-2, Zn(btmbenzene)-3 and Zn(btmbenzene)-4

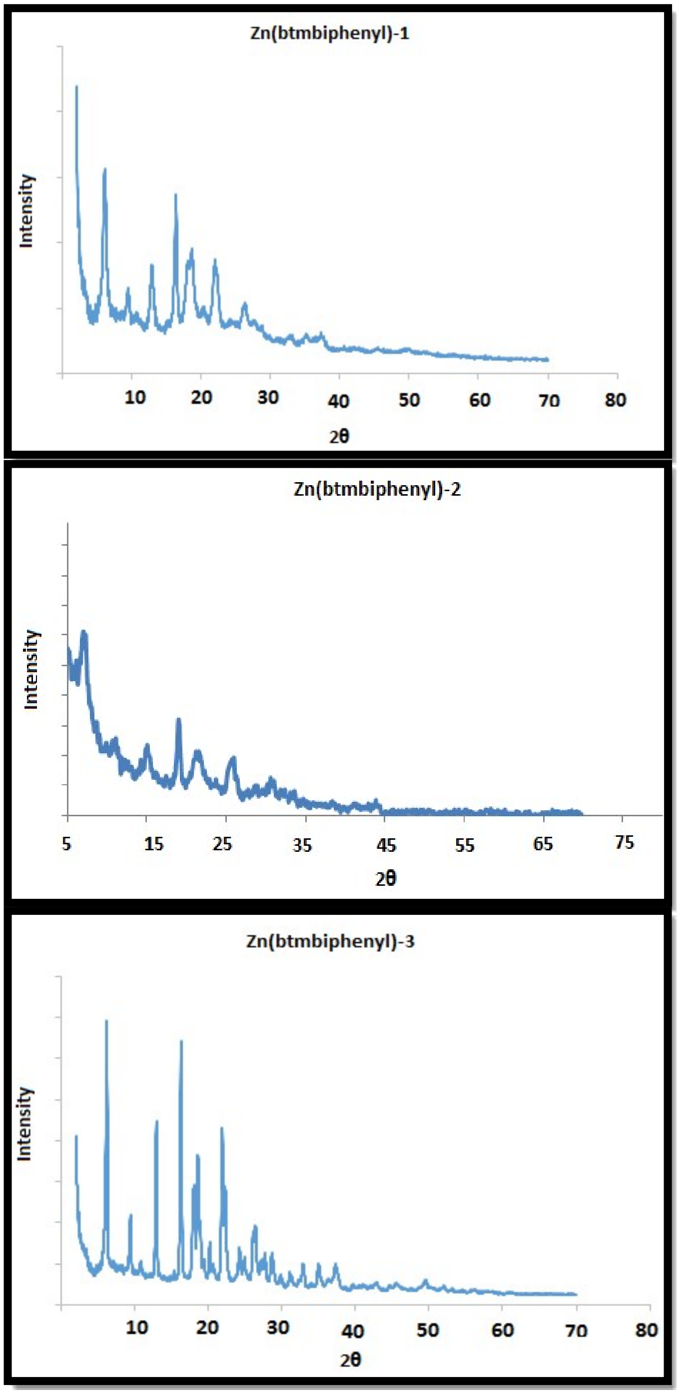


Fig. S10 PXRD patterns of Zn(btmbiphenyl)-1, Zn(btmbiphenyl)-2 and Zn(btmbiphenyl)-3

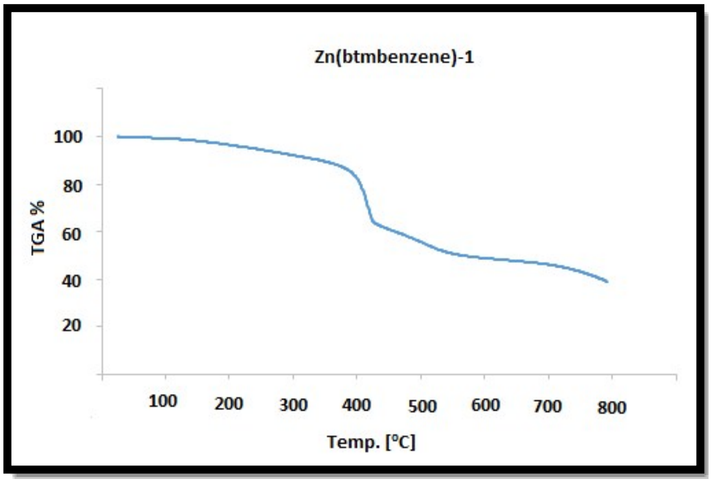


Fig. S11 TGA curve of Zn(btmbenzene)-1

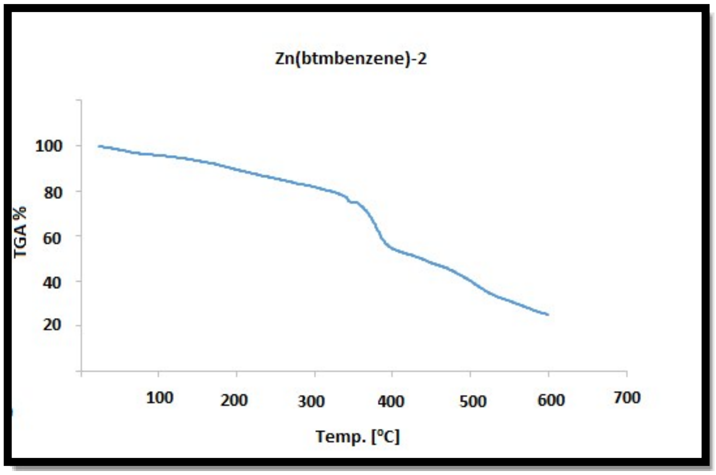


Fig. S12 TGA curve of Zn(btmbenzene)-2

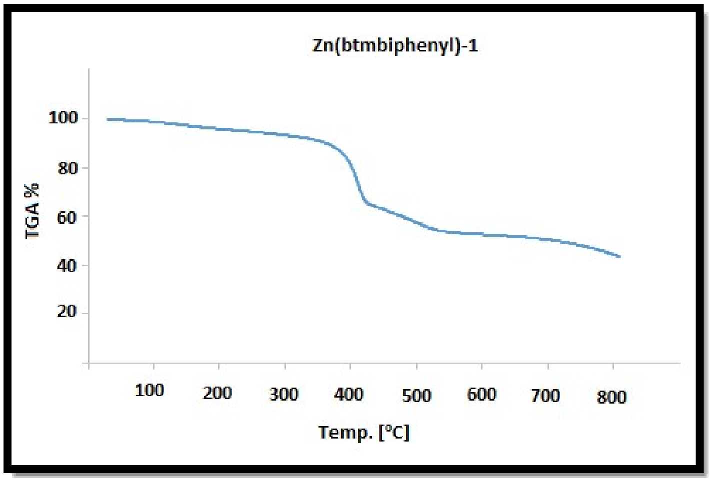


Fig. S13 TGA curve of Zn(btmbiphenyl)-1

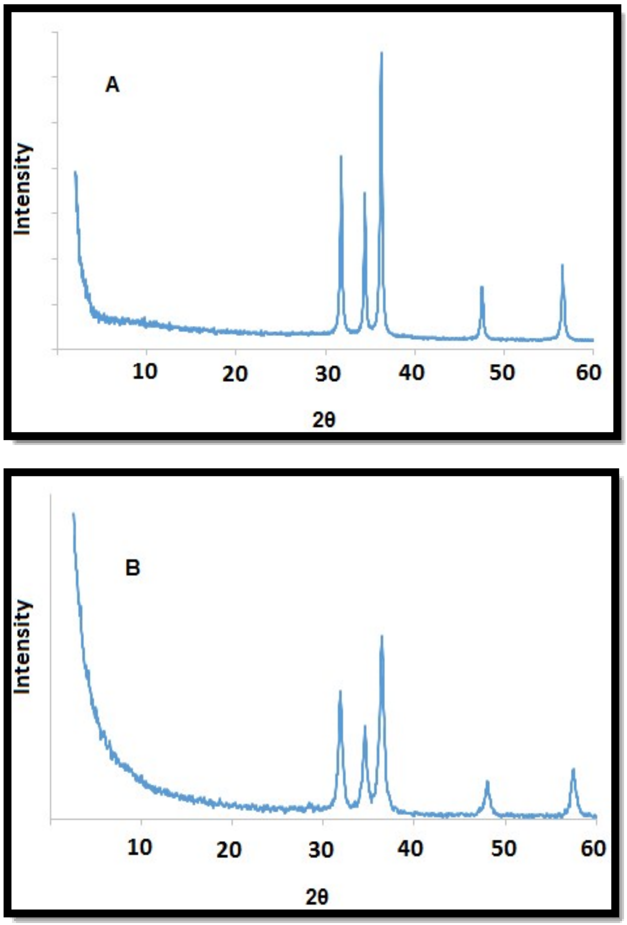


Fig. S14 PXRD patterns of crystalline ZnO prepared after calcination of (A) Zn(btmbenzene)-1, (B) Zn(btmbiphenyl)-1.

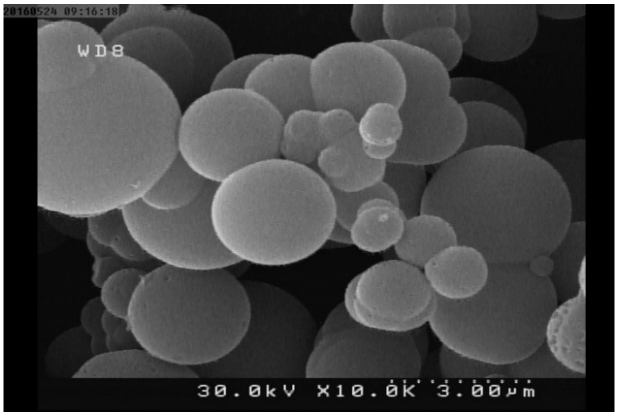


Fig. S15 FE-SEM image of the sphere particles Zn(btmbenzene)-1, obtained from Zn(btmbenzene)-2 to Zn(btmbenzene)-1 transformation.

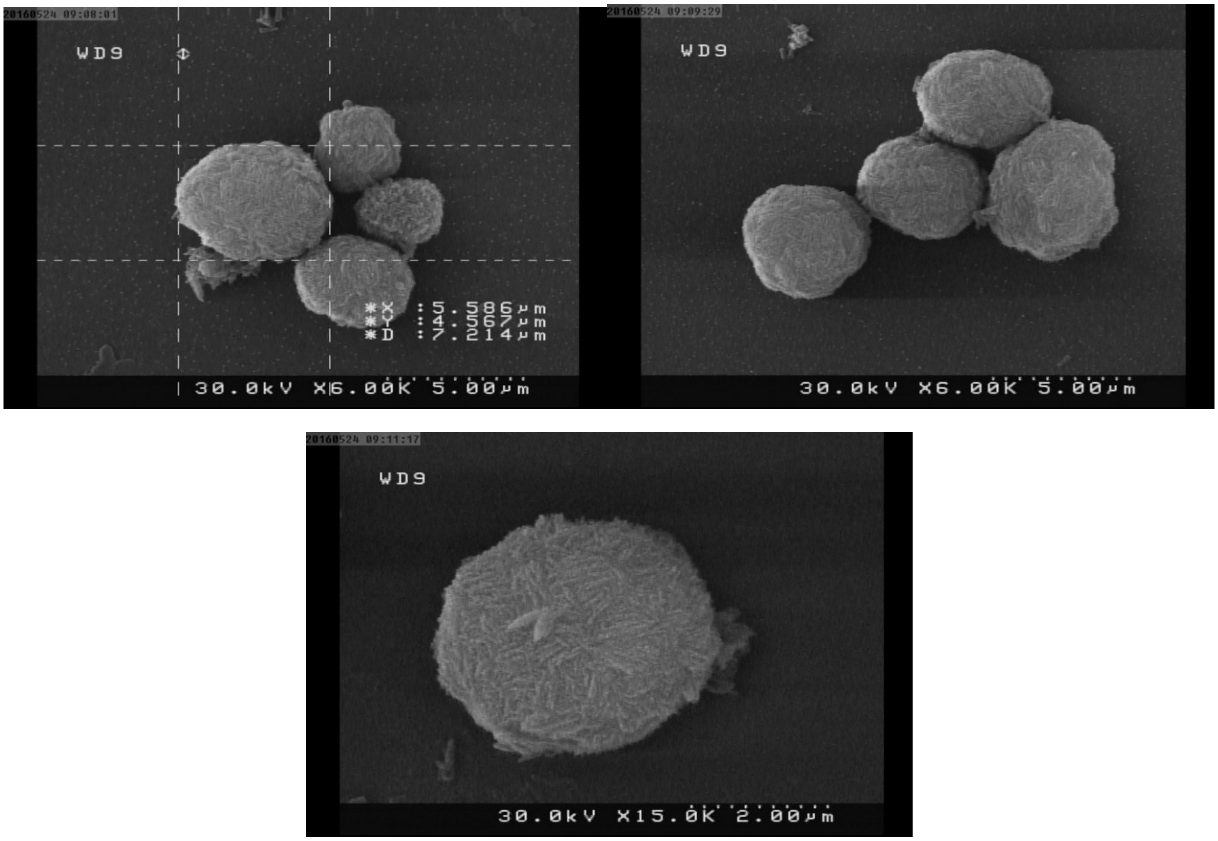


Fig. S16 FE-SEM images of the sphere particles Zn(btmbiphenyl)-1, obtained from Zn(btmbiphenyl)-2 to Zn(btmbiphenyl)-1 transformation.

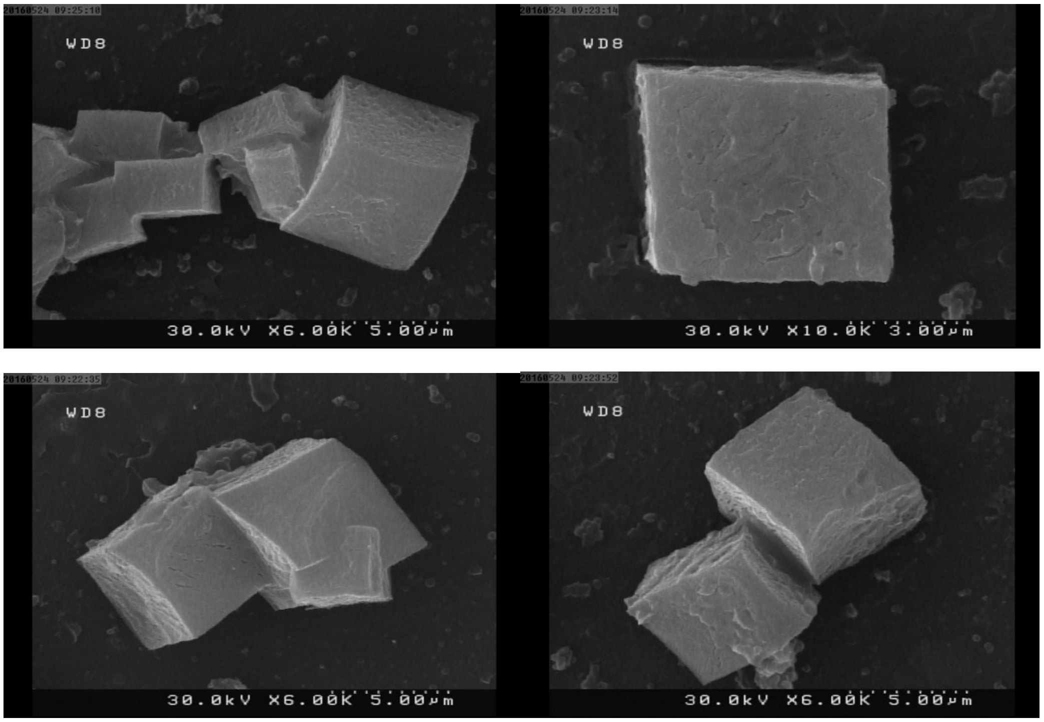


Fig. S17 FE-SEM images of the cubic particles, obtained from Zn(btmbenzene)-2 transformation.

18. 5-fluorouracil standard solution for loading estimation:

Standard 5-fluorouracil (5-FU) solutions in deionized water (1.5–20 mg/L) at pH of 5 was prepared and analyzed on UV-vis spectrophotometer at 260 nm. The absorbance of the solutions can be seen in Table S1. Figure S17 shows a standard plot for 5-fluorouracil standard solutions.

Table S1. Absorbance values for 1.5–20 mg/L 5-FU containing deionized water solutions

mg/L	UV-vis absorbance
1.5	0.14
3	0.32
6	0.63
10	1.01
20	2.04

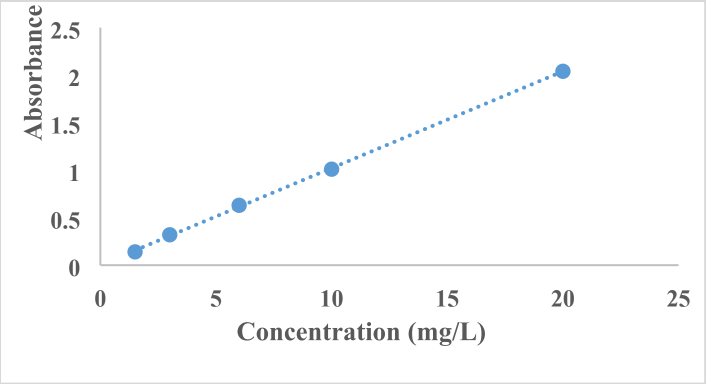


Fig. S18 Standard plot of 5-FU in deionized water solution.

Calculation of 5-FU loaded quantity:

3 mg of both 5-FU@Zn(btmbenzene)-1 and 5-FU@Zn(btmbiphenyl)-1 was separately dispersed in 5 mL deionized water at pH of 5 and stirred for 72 h. Afterward two mixtures were centrifuged and absorbency of supernatant solutions (Solution A and B, respectively) was determined at 260 nm utilizing UV-vis spectrophotometer which was 1.26 for solution A and 1.5 for solution B.

5-FU in Solution A and B = (Absorbance value – intercept of standard plot) / (slope of standard plot)

19. Rhodamine B (RhB) standard solution for loading estimation:

Standard Rhodamine B (RhB) solutions in deionized water (1–8 mg/L) at pH of 5 was prepared and analyzed on UV-vis spectrophotometer at 560 nm. The absorbance of the solutions can be seen in Table S2. Figure S18 shows a standard plot for Rhodamine B standard solutions.

Table S2. Absorbance values for 1-8 mg/L RhB containing deionized water solutions.

mg/L	UV-vis absorbance
1	0.32
2	0.58
4	1.24
6	1.89
8	2.08

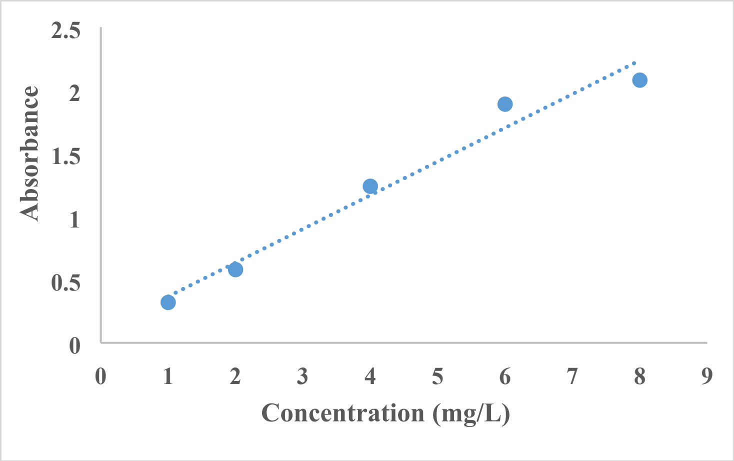


Fig. S19 Standard plot of RhB in deionized water solution.

Calculation of Rhodamine B loaded quantity:

3 mg of both RhB@Zn(btmbenzene)-1 and RhB@Zn(btmbiphenyl)-1 was separately dispersed in 5 mL deionized water at pH of 5 and stirred for 72 h. Next, mixtures were centrifuged and the 2 mL of supernatant solutions were diluted to 10 mL with deionized water (Solution A and B, respectively) and absorbency was determined at 554 nm utilizing UV-vis spectrophotometer which was 0.42 for solution A and 0.5 for solution B. RhB in two solutions were calculated according to the obtained equation.

To make sure that Rhodamine B is entrapped inside the capsules not in the surface, prepared samples of Zn(btmbenzene)-1 and Zn(btmbiphenyl)-1 spheres were dispersed in a solution of Rhodamine B and stirred for 24 h. After 24h, the samples were isolated and subsequently washed with DMF and methanol polar solvents via centrifugation-redispersion cycles. Then, Zn(btmbenzene)-1 and Zn(btmbiphenyl)-1 samples were dried and dispersed in deionized water at pH of 5 and stirred for 12 h. The mixtures were centrifuged and absorbency of the supernatants were determined at 554 nm utilizing UV-vis spectrophotometer. The UV-vis analyses did not show any peak at 554 nm.

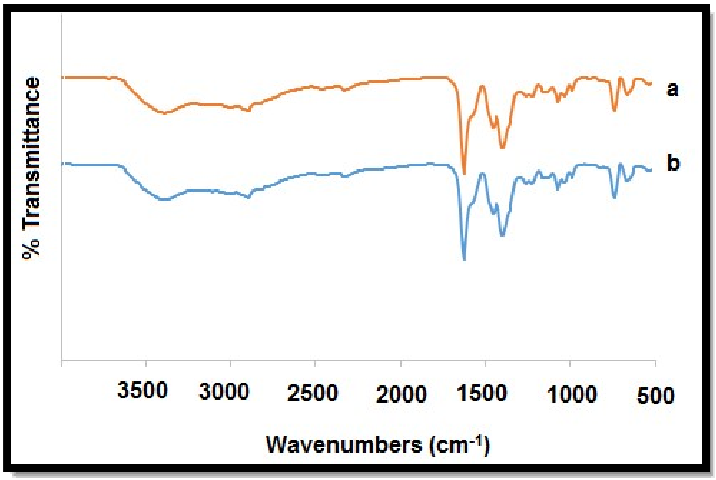


Fig. S20 FT-IR spectra of a) RhB@Zn(btmbenzene)-1, b) Zn(btmbenzene)-1.

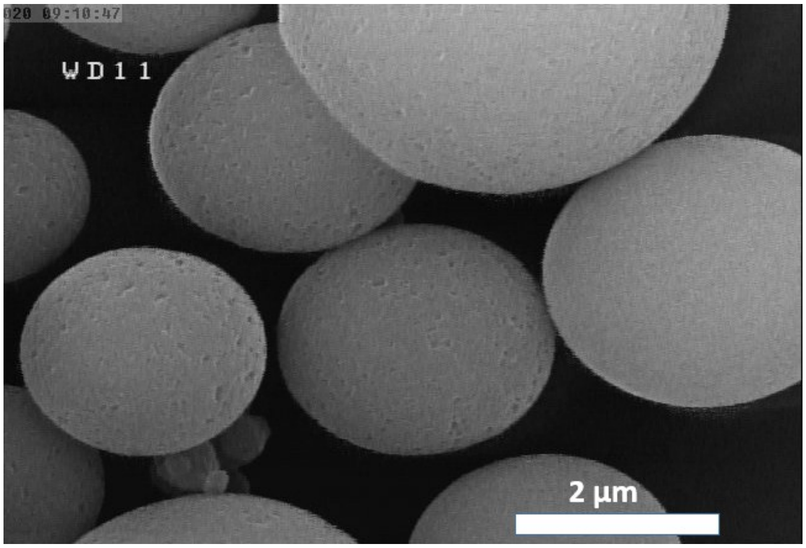


Fig. S21 FESEM image of RhB@Zn(btmbenzene)-1.

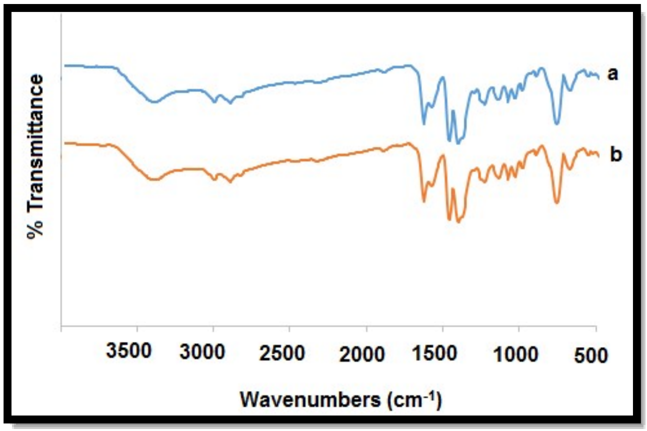


Fig. S22 FT-IR spectra of a) RhB@Zn(btmbiphenyl)-1, b) Zn(btmbiphenyl)-1.

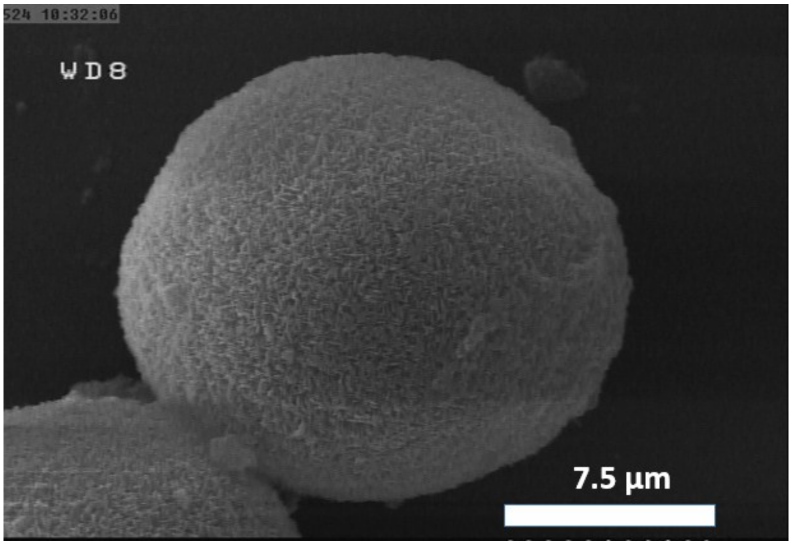


Fig. S23 FESEM image of RhB@Zn(btmbiphenyl)-1.