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ORIGINAL PAPER

$La(OTf)_3$-catalyzed one-pot synthesis of *meso*-substituted porphyrinic thiazolidinones

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Abstract An improved synthetic procedure is developed for the regioselective nitration of a phenyl group of *meso*-tetraphenylporphyrin by using $NaNO_2$ in a mixture of trichloroacetic acid and AcOH. The *meso*-(4-nitrophenyl)porphyrins are successfully reduced to corresponding *meso*-(4-aminophenyl)porphyrins by $SnCl_2$ under acidic conditions. In addition, an efficient one-pot methodology for synthesizing a series of novel *meso*-substituted porphyrinic thiazolidinone conjugates is developed by reacting *meso*-(4-aminophenyl)porphyrins with various aromatic aldehydes and mercaptoacetic acid in refluxing toluene using $La(OTf)_3$ as a catalyst. The products obtained are characterized on the basis of their spectral data. Preliminary photophysical properties of the newly synthesized compounds are reported.

Keywords Porphyrins · Photosensitizer · Photodynamic therapy · Regioselective nitration

Introduction

The peripheral functionalization of easily available *meso*-tetraarylporphyrins has received significant attention owing to their potential use as phototherapeutic agents in photodynamic therapy [1–3]. Porphyrins and their metal analogues play a very significant role in essential biological processes such as photosynthesis [4, 5]. Moreover, well-designed porphyrin analogues can act as catalysts [6], chemical sensors [7], organic photoelectrical devices [8], molecular wires [9], fluorescence switches [10, 11], and agents for molecular recognition [12]. The unusual electronic and redox properties of porphyrins can be modified by attaching various functionalities to the periphery or incorporating metal ions in the cavity of the macrocycle. At present, the development of synthetic strategies to functionalize porphyrins at the periphery is an exciting area of research because it provides a variety of highly conjugated materials including picenoporphyrin architectures [13–17].

In the past decades, several unsymmetrical porphyrins attached to bioactive functionalities have been prepared by reported methodologies [18–21] and screened for various biological activities, but the medicinally important thiazolidinone [22–26] moiety has not yet been linked to the porphyrin macrocycle. The most frequently used synthetic strategy for the production of 1,3-thiazolidin-4-one compounds involves reaction of aldehydes or ketones with amines and mercapto acids either in a one-pot or two-step process. Recently, a reaction of imines and mercapto acids was efficiently catalyzed by using Lewis acid to obtain 1,3-thiazolidinones in good yields [27, 28]. A thorough literature survey revealed that metal triflates have stronger Lewis acidity than the corresponding metal halides because of the electron-withdrawing nature of the trifluoromethanesulfonyl group [29–31]. Among these, lanthanide triflates are known to act as stronger Lewis acids because of their hard character and activate carbonyl compounds even in aqueous media as a result of their strong affinity towards carbonyl oxygen atoms [32, 33]. Moreover, they were recovered quantitatively after completion of the reactions and could be recycled. Hence, in the course of our efforts to develop a one-pot synthetic approach to prepare *meso*-substituted porphyrinic thiazolidinone conjugates, $La(OTf)_3$ was chosen as a Lewis acid catalyst. In this paper we describe an improved procedure for regioselective

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nitration of the *para* position of a *meso*-phenyl group at the porphyrin periphery which leads to the synthesis of 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin in high yield. On reduction under standard $SnCl_2$/HCl conditions, *meso*-(4-nitrophenyl)porphyrins afford the corresponding *meso*-(4-aminophenyl)porphyrins. These molecules have been used as precursors for the synthesis of a new series of porphyrins bearing the biologically important thiazolidinone ring system on the *meso*-phenyl groups by using $La(OTf)_3$-catalyzed one-pot methodology in moderate to good yields. Such new products may be useful as precursors for the development of new materials as well as potential candidates for biological evaluations.

Results and discussion

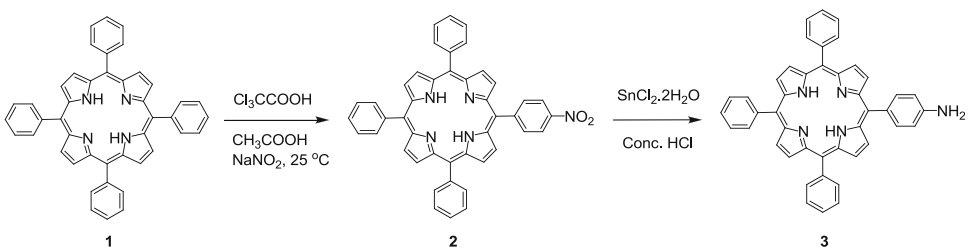
The current synthetic procedures to obtain 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin (**2**) involve the electrophilic nitration of a *meso*-phenyl group of 5,10,15,20-tetraphenylporphyrin (TPP, **1**). In the first method, Kruper et al. [34] obtained mono-nitroporphyrin (**2**) in moderate yield (~56%) after the treatment of TPP with fuming nitric acid in chloroform. Under these reaction conditions, the formation of di- and trinitroporphyrins along with degradation of the macrocycle was also observed. Although slightly improved yields (~74%) of the desired product **2** were obtained by using a combination of HNO_3, H_2SO_4, or acetic acid, complete nitration usually affords a mixture of nitration products [35]. Later, Smith et al. [36] reported another route to nitro-substituted porphyrins through regioselective *meso*-phenyl nitration of TPP by using sodium nitrite in trifluoroacetic acid and rationalized that the milder reaction conditions lead to better yields (80–90%) of the *meso*-substituted mono-nitroporphyrin (**2**). Recently, we have developed an alternative and economical synthetic procedure for the preparation of 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin (**2**) via regioselective *meso*-phenyl nitration of TPP at the *para* position using sodium nitrite in a mixture of trichloroacetic acid and acetic acid at ambient temperature. Under these reaction conditions, mono-nitroporphyrin (**2**) was obtained in 95% yield in 1.5 h at room temperature (Scheme 1).

The same synthetic strategy was applied to prepare *meso*-tetrakis(4-nitrophenyl)porphyrins by increasing the amount of $NaNO_2$, but it is extremely difficult to incorporate four nitro substituents into the *meso*-phenyl groups. Instead, *meso*-tetrakis(4-nitrophenyl)porphyrin was synthesized according to a literature procedure [37] in 20% yield by condensation of pyrrole and 4-nitrobenzaldehyde under acidic conditions. Usual reduction of the nitro group [34, 37] with $SnCl_2$/conc. HCl was applied to mono- and tetrakis(4-nitrophenyl)porphyrins to produce the corresponding 5-(4-aminophenyl)-10,15,20-triphenylporphyrin (**3**) and *meso*-tetrakis(4-aminophenyl)porphyrin (**6**) in 95 and 50% yields, respectively. The resulting *meso*-substituted aminoporphyrins **3** and **6** were purified by column chromatography on activated neutral aluminum oxide using $CHCl_3$ as an eluent and characterized spectroscopically. An efficient and novel one-pot methodology was developed for the synthesis of the target compounds **4a**–**4j** via the reaction of 5-(4-aminophenyl)-10,15,20-triphenylporphyrin (**3**) with aromatic aldehydes and mercaptoacetic acid in toluene containing $La(OTf)_3$ as a catalyst at reflux temperature (Scheme 2).

A possible mechanistic pathway of the reaction is shown in Scheme 3. The reaction likely proceeds through initial formation of an iminoporphyrin intermediate, which on activation [38] by $La(OTf)_3$ reacts with a sulfur nucleophile to form a zwitterionic intermediate **5**. This probably undergoes a proton shift from the electron deficient sulfur to the negatively charged nitrogen and thus regenerates the catalyst. The resulting intermediate cyclizes intramolecularly to produce a gem-diol. On irreversible dehydration in refluxing toluene, the gem-diol affords the desired product (**4**).

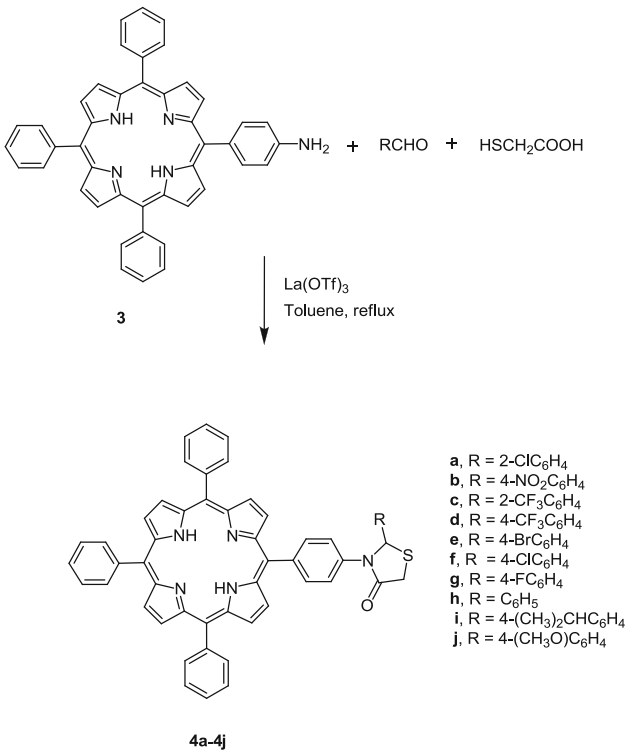
The completion of the reaction was monitored by TLC and compounds **4a**–**4j** were purified over a neutral alumina column using 1% MeOH in chloroform. Under optimized conditions, the reaction proceeds smoothly with aromatic aldehydes containing electron-withdrawing substituents on the phenyl ring (R = F, Cl, Br, NO_2, and CF_3) and afforded porphyrins **4a**–**4g** in high yields (79–96%). In contrast, the reaction of porphyrin (**3**) with less reactive aldehydes having electron-donating substituents on the aromatic ring (R = methoxy and isopropyl) was found to be sluggish and provided compounds **4j** and **4i** in poor to moderate yields

Scheme 1

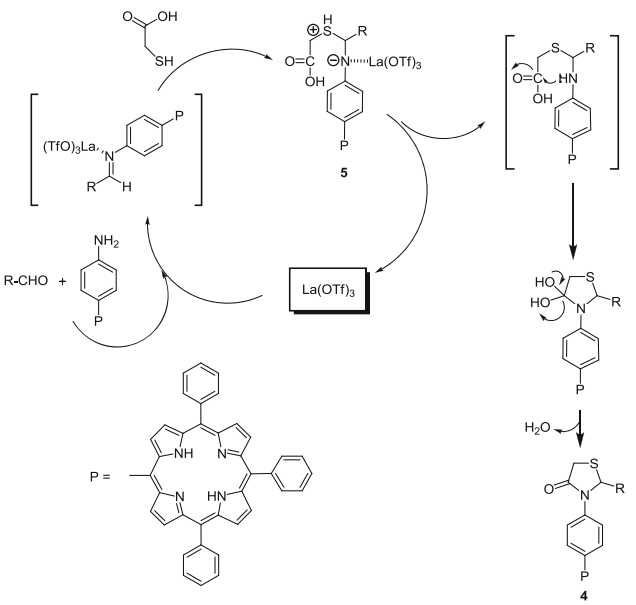


(40–60%). Further, this reaction was also attempted in the absence of $La(OTf)_3$ under the same reaction conditions but it generated an inseparable mixture of products along with unreacted starting material. To demonstrate the versatility of this one-pot methodology for making novel *meso*-substituted porphyrinic thiazolidinone derivatives, the reaction of *meso*-tetrakis(4-aminophenyl)porphyrin (**6**) was carried out similarly with 4-fluorobenzaldehyde and mercaptoacetic acid in the presence of a catalytic amount of $La(OTf)_3$ at 120 °C in toluene. The desired porphyrin **7** was obtained as a reddish-purple solid in 45% yield (Scheme 4).

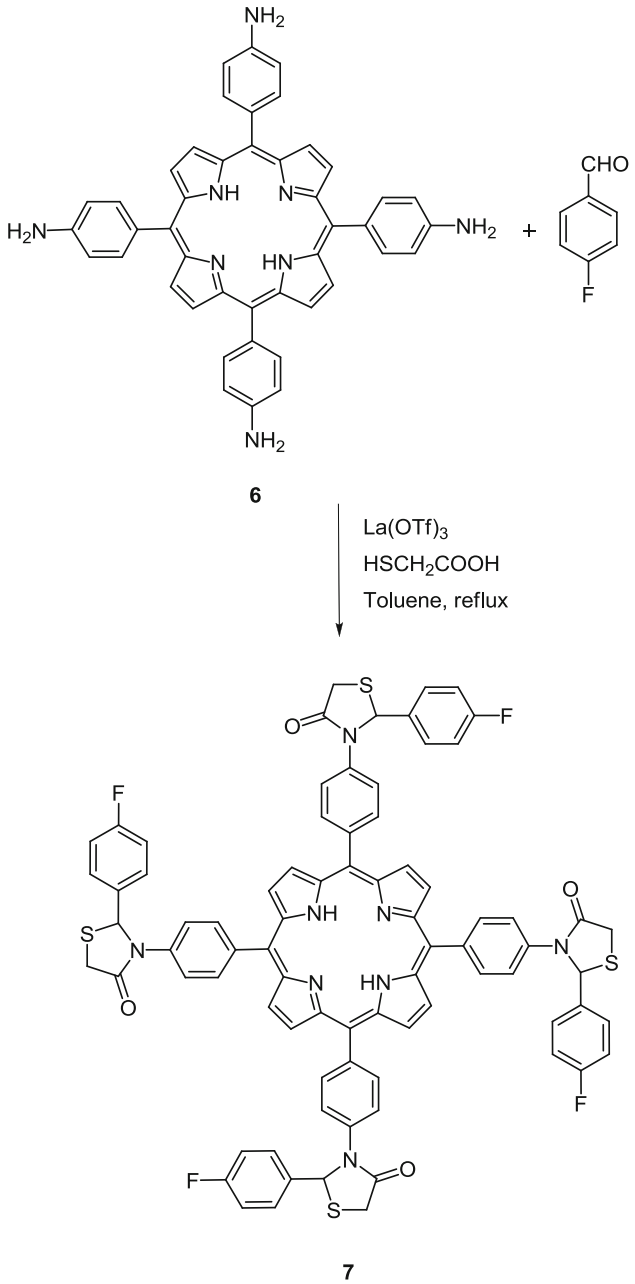
The new porphyrins **4a**–**4j** and **7** were characterized by NMR, UV–vis, IR, and mass spectrometry and spectral data were in full agreement with the proposed structures. The infrared absorption spectra of novel porphyrinic thiazolidinones **4a**–**4j** and **7** exhibited a characteristic strong



Scheme 2



Scheme 3



Scheme 4

absorption band at 1,677–1,699 cm^{-1} due to stretching of the C=O bond. In addition, from the ^1H NMR spectra in $CDCl_3$ the internal NH protons of porphyrins **4a**–**4j** and **7** appeared as one singlet around $\delta = -2.8$ ppm and characteristic signals for β-pyrrolic protons were present as a singlet, doublet, or multiplet at $\delta = 8.6$–8.9 ppm. The presence of a thiazolidinone moiety in the products **4a**–**4j** and **7** was also confirmed by ^1H NMR spectroscopy. In all cases, the spectra showed a characteristic singlet at approximately 6.2 ppm for one proton corresponding to N–CH–S with additional doublets at 3.9 and 4.1 ppm due to the coupling between two geminal protons of the SCH_2CO group of the thiazolidinone ring.

The UV–vis spectra of **4a**–**4j** exhibit an intense Soret band and four weak Q bands. In comparison to *meso*-5-(4-aminophenyl)-10,15,20-triphenylporphyrin (**3**, 420 nm), the Soret bands of the newly prepared compounds **4a**–**4j** are slightly blue shifted (by 1–4 nm). This tendency toward blue shifting is also observed for Q bands (Table 1). Similarly, the electronic absorption spectrum of porphyrin **7** shows a strong Soret band with a maximum absorption at 421 nm. This band is slightly blue shifted (by 6 nm) compared to 427 nm for *meso*-tetrakis(4-aminophenyl)porphyrin (**6**) but slightly red shifted by 1 and 4 nm in comparison to 420 nm for **3** and 417 nm for porphyrin **4g**, respectively (Fig. 1).

The absorptions of all the newly synthesized porphyrinic thiazolidinones (Table 1) indicate that the introduction of a thiazolidinone moiety onto the *meso*-phenyl substituent of TPP did not greatly change the energy of the singlet excited state (S_1). Finally, the order of shift in Soret band absorption for these compounds is as follows:

$$\lambda_{\mathbf{6}} > \lambda_{\mathbf{7}} > \lambda_{\mathbf{3}} > \lambda_{\mathbf{4a}} = \lambda_{\mathbf{4d}} > \lambda_{\mathbf{4c}} = \lambda_{\mathbf{4e}} = \lambda_{\mathbf{4f}} = \lambda_{\mathbf{4i}} > \lambda_{\mathbf{4g}} = \lambda_{\mathbf{4b}} = \lambda_{\mathbf{4j}} > \lambda_{\mathbf{4h}}$$

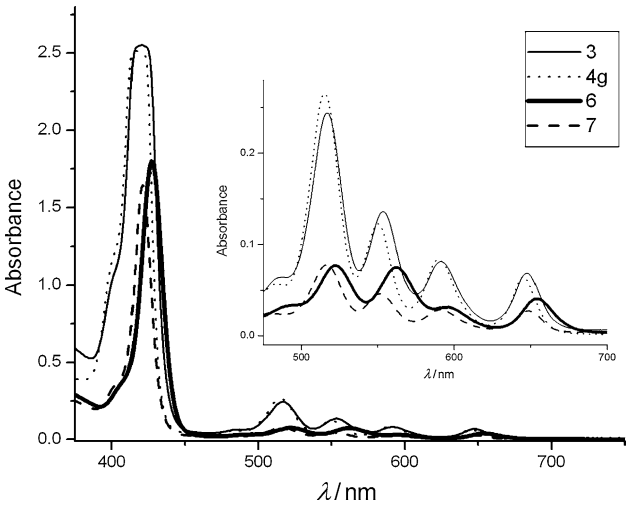


Fig. 1 UV–vis absorption spectra for porphyrins **3**, **4g**, **6**, and **7** in $CHCl_3$ at 25 °C

The fluorescence emission spectra of the free base porphyrins **3**, **4g**, **6**, and **7** excited at 420 nm are shown in Fig. 2. The order of fluorescence intensity of porphyrins was **6** > **3** > **7** > **4g**. From Fig. 2 it can be seen that the newly prepared free base porphyrin **4g** displayed two emission peaks at ~647 and 705 nm.

Comparing **3** and **4g**, the fluorescence intensity increases in the case of compound **3** as a result of the presence of an electron-donating amino group, which resulted in an increment in the average electron density of the porphyrin conjugated system. In contrast, the presence of a cyclic amide group in porphyrinic thiazolidinone analogue **4g** leads to lower fluorescence intensity with slight blue shift (~3 nm) in the emission band possibly as a result of a decrease in the average electron density of the macrocycle as compared to starting compound **3**. A similar trend was

Table 1 Electronic absorption and emission data for porphyrins **3**, **6**, **4a**–**4j**, and **7**

Compd.	Absorption[a] λ_{max}/nm ($\varepsilon/10^3$ mol^{-1} dm^3 cm^{-1})	Fluorescence[a,b] λ_{em}/nm
3	420 (488.6), 516 (32.5), 554 (17.6), 591 (10.2), 647 (8.7)	650, 710
6	427 (359.9), 523 (15.3), 562 (14.9), 596 (6.2), 655 (8.1)	660
4a	419 (484.2), 515 (30.8), 551 (15.5), 590 (10.9), 645 (11.1)	648, 705
4b	417 (498.5), 515 (45.4), 550 (21.5), 590 (14.5), 645 (10.5)	647, 707
4c	418 (490.2), 515 (32.8), 551 (15.7), 590 (10.8), 646 (8.0)	648, 709
4d	419 (490.2), 515 (32.4), 550 (16.5), 590 (11.0), 645 (8.1)	648, 706
4e	418 (495.5), 515 (39.1), 550 (18.6), 590 (13.1), 645 (9.6)	647, 708
4f	418 (473.9), 515 (26.1), 550 (12.1), 590 (8.6), 645 (6.1)	646, 707
4g	417 (502.3), 515 (53.1), 550 (24.4), 590 (16.7), 645 (12.9)	647, 705
4h	416 (501.9), 515 (55.2), 551 (25.2), 590 (11.5), 645 (12.3)	647, 707
4i	418 (498.4), 515 (43.8), 551 (21.5), 590 (15.0), 645 (8.0)	647, 706
4j	417 (518.0), 515 (82.3), 551 (41.0), 590 (28.2), 646 (21.0)	648, 707
7	421 (328.9), 516 (15.5), 552 (9.2), 691 (5.7), 649 (5.5)	650, 707

[a] Absorption and emission data were measured using $CHCl_3$ solutions of porphyrins at 298 K

[b] Excitation wavelength for emission data is 420 nm

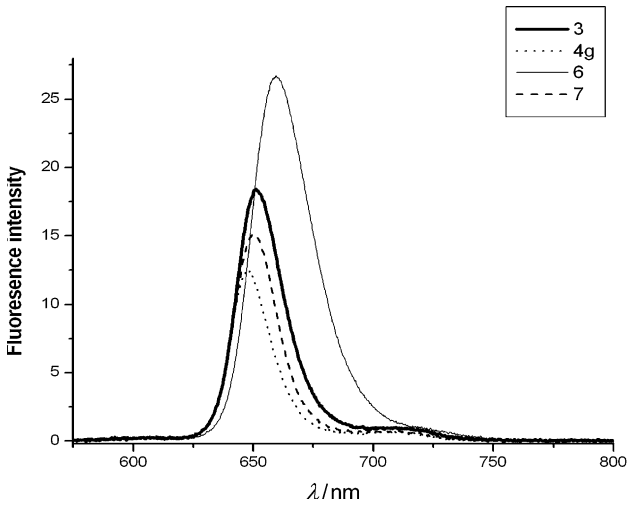


Fig. 2 Emission spectra of porphyrins **3**, **4g**, **6**, and **7** in $CHCl_3$ (5×10^{-6} mol/dm^3) at 25 °C

observed in the difference of fluorescence intensities of compounds **6** and **7**.

In summary, we have demonstrated a mild, economical, and alternative procedure for electrophilic nitration of a phenyl group of TPP by using $NaNO_2$ in a trichloroacetic acid and AcOH mixture. This approach incorporates the nitro substituent regiospecifically at the *para* position of a phenyl group in TPP at 25 °C. The nitroporphyrins are easily reduced to corresponding aminoporphyrins which are used as precursors for the synthesis of novel *meso*-substituted porphyrinic thiazolidinone conjugates through $La(OTf)_3$-catalyzed domino reactions. This methodology provides an efficient approach for the construction of various porphyrinic thiazolidinone systems which may be considered as potential candidates for biological evaluations.

Experimental

All reactions were performed under a nitrogen atmosphere. Pyrrole, aromatic aldehydes, mercaptoacetic acid, and $La(OTf)_3$ were purchased from Aldrich and used without further purification. Solvents were purchased from Merck and dried according to literature procedures. 5-(4-Aminophenyl)-10,15,20-triphenylporphyrin (**3**), *meso*-tetrakis(4-nitrophenyl)porphyrin, and *meso*-tetrakis(4-aminophenyl)porphyrin (**6**) were prepared by following the reported procedures [34, 37]. Thin-layer chromatography (TLC) was performed using silica gel 60 F254 (precoated aluminum sheets) from Merck. Reactions were monitored by TLC and products were purified by column chromatography using activated neutral aluminum oxide (Brokmann grade I-II, Merck). ^{1}H NMR spectra were obtained in $CDCl_3$ using a Bruker 300 MHz NMR spectrometer. Chemical shifts are expressed in parts per million (ppm) relative to tetramethylsilane (TMS, 0 ppm) as an internal standard. Coupling constants J are reported in hertz (Hz). ^{13}C NMR spectra were recorded on Bruker 300 or Jeol 400 MHz NMR spectrometer. Infrared spectra were recorded on a Perkin Elmer IR spectrometer and absorption maxima are given in cm^{-1}. Elemental analysis was performed on an Elementar Analysensysteme GmbH VarioEL V3.00. Mass spectra were recorded on an ESI–MS (micromass LCT, waters) mass spectrometer. A Varian Cary 100 Bio UV–vis spectrophotometer was used for UV measurements. The fluorescence spectra were obtained by using a Shimadzu RF-5301PC spectrofluorophotometer.

5-(4-Nitrophenyl)-10,15,20-triphenylporphyrin (**2**)
To a solution of 6 g trichloroacetic acid (36.7 mmol) in 4 cm^3 acetic acid was added 0.1 g TPP (0.163 mmol) followed by 20 mg $NaNO_2$ (0.29 mmol) at 25 °C. The reaction mixture was stirred at room temperature for 1.5 h. After completion of the reaction, the mixture was poured into 200 cm^3 of water and extracted with chloroform. The organic layers were combined and washed with saturated aqueous $NaHCO_3$ solution followed by water. The chloroform layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. The crude product was washed with methanol and further purified by column chromatography on neutral alumina using chloroform as an eluent to afford pure product in 95% yield. The spectroscopic data were in agreement with those reported in the literature [34].

*General procedure for the synthesis of porphyrinic thiazolidinones **4a–4j***

A mixture of 50 mg 5-(4-aminophenyl)-10,15,20-triphenylporphyrin (0.079 mmol), 9 mg La $(OTf)_3$ (0.016 mmol), aromatic aldehyde (0.12 mmol), and 0.025 cm^3 mercaptoacetic acid (0.30 mmol) in 10 cm^3 toluene was refluxed (12 h for **4a–4h**, 16 h for **4i**, and 20 h for **4j**). After completion of the reaction, the solvent was evaporated under reduced pressure and the sticky solid was treated with 30 cm^3 10% $NaHCO_3$ solution, and the product was extracted with chloroform (2×30 cm^3). The organic layer was washed with water (2×30 cm^3), dried over anhydrous sodium sulfate, and evaporated. The residue was washed with 10 cm^3 methanol and the crude product was chromatographed through neutral alumina using 1% MeOH in chloroform as an eluent. The products were characterized spectroscopically.

2-(2-Chlorophenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4a**, $C_{53}H_{36}ClN_5OS$)
Yield 80%; IR (film): $\bar{\nu}$ = 1,694, 1,597, 1,473, 1,441, 1,370, 1,261, 966, 801, 750 cm^{-1}; ^{1}H NMR (300 MHz,

$CDCl_3$): $\delta = -2.90$ (s, 2H, internal NH), 3.91 (d, $J = 15.9$ Hz, 1H, SCH_2CO), 4.03 (d, $J = 15.9$ Hz, 1H, SCH_2CO), 6.78 (s, 1H, CH), 7.37–7.26 (m, 2H, ArH), 7.43 (d, $J = 8.1$ Hz, 1H, ArH), 7.54 (d, $J = 6.9$ Hz, 1H, ArH), 7.71–7.69 (m, 11H, *meso*-ArH), 8.07 (d, $J = 8.1$ Hz, 2H, *meso*-ArH), 8.13 (d, $J = 5.7$ Hz, 6H, *meso*-ArH), 8.64 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.76 (s, 6H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.16$, 64.53, 118.09, 120.19, 120.83, 121.89, 126.68, 127.74, 128.35, 129.87, 130.65, 134.53, 134.99, 137.03, 138.02, 140.79, 142.06, 170.69 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{36}ClN_5OS$ 825.2329, found 825.2318.

2-(4-Nitrophenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4b**, $C_{53}H_{36}N_6O_3S$)

Yield 85%; IR (KBr): $\bar{\nu} = 1{,}702$, 1,525, 1,473, 1,348, 966, 802, 734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 3.99 (d, $J = 14.1$ Hz, 1H, SCH_2CO), 4.09 (d, $J = 14.1$ Hz, 1H, SCH_2CO), 6.35 (s, 1H, CH), 7.50 (d, $J = 8.4$ Hz, 2H, ArH), 7.60 (d, $J = 8.7$ Hz, 2H, *meso*-ArH), 7.80–7.72 (m, 9H, *meso*-ArH), 8.09 (d, $J = 8.4$ Hz, 2H, *meso*-ArH), 8.21–8.17 (m, 6H, *meso*-ArH), 8.28 (d, $J = 8.4$ Hz, 2H, ArH), 8.62 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.81 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.84 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.53$, 64.24, 118.16, 120.38, 120.53, 122.84, 124.48, 126.71, 127.76, 131.17, 134.50, 135.35, 136.63, 141.08, 141.90, 146.92, 148.21, 170.89 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{36}N_6O_3S$ 836.2570, found 836.2566.

2-(2-Trifluoromethylphenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one
(**4c**, $C_{54}H_{36}F_3N_5OS$)

Yield 79%; IR (KBr): $\bar{\nu} = 1{,}698$, 1,597, 1,473, 1,347, 1,312, 1,163, 1,119, 1,035, 965, 800, 730 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 4.05 (d, $J = 15.9$ Hz, 2H, SCH_2CO), 4.17 (d, $J = 16.2$ Hz, 1H, SCH_2CO), 6.87 (s, 1H, CH), 7.51 (dd, $J = 7.8$, 7.5 Hz, 1H, ArH), 7.65 (d, $J = 8.4$ Hz, 2H, *meso*-ArH), 7.75–7.70 (m, 11H, ArH, *meso*-ArH), 7.86 (d, $J = 7.8$ Hz, 1H, ArH), 8.12 (d, $J = 8.4$ Hz, 2H, *meso*-ArH), 8.66 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.27–8.17 (m, 6H, *meso*-ArH), 8.80 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.83 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.21$, 60.59, 118.60, 120.19, 120.43, 121.85, 126.67, 127.49, 127.73, 128.82, 132.90, 134.51, 134.99, 137.05, 139.15, 140.65, 142.06, 171.46 ppm; HRMS (ESI): $[M + H]^+$ calcd for $C_{54}H_{37}F_3N_5OS$ 860.2671, found 860.2680.

2-(4-Trifluoromethylphenyl)-3[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one
(**4d**, $C_{54}H_{36}F_3N_5OS$)

Yield 82%; IR (film): $\bar{\nu} = 1{,}699$, 1,508, 1,473, 1,324, 1,167, 1,129, 1,067, 966, 801, 732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -2.81$ (s, 2H, internal NH), 3.97 (d, $J = 15.6$ Hz, 1H, SCH_2CO), 4.17 (d, $J = 14.1$ Hz, 1H, SCH_2CO), 6.15 (s, 1H, CH), 7.38 (d, $J = 8.1$ Hz, 2H, ArH), 7.43 (d, $J = 7.8$ Hz, 2H, *meso*-ArH), 7.62 (d, $J = 8.1$ Hz, 2H, ArH), 7.75–7.72 (m, 9H, *meso*-ArH), 8.00 (d, $J = 8.4$ Hz, 2H, *meso*-ArH), 8.18–8.17 (m, 6H, *meso*-ArH), 8.58 (d, $J = 4.5$ Hz, 2H, β-pyrrolic H), 8.80 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.84 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.48$, 64.70, 118.40, 120.31, 120.55, 122.95, 126.01, 126.70, 127.28, 127.77, 131.05, 134.52, 134.93, 136.75, 140.71, 141.95, 143.43, 170.97 ppm; HRMS (ESI): $[M + H]^+$ calcd for $C_{54}H_{37}F_3N_5OS$ 860.2671, found 860.2670.

2-(4-Bromophenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4e**, $C_{53}H_{36}BrN_5OS$)

Yield 90%; IR (Nujol): $\bar{\nu} = 1{,}695$, 1,595, 1,462, 1,377, 1,072, 965, 800 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -2.82$ (s, 2H, internal NH), 4.01 (d, $J = 15.9$ Hz, 1H, SCH_2CO), 4.11(d, $J = 15.9$ Hz, 1H, SCH_2CO), 6.27 (s, 1H, CH), 7.34 (d, $J = 8.1$ Hz, 2H, *meso*-ArH), 7.49 (d, $J = 8.4$ Hz, 2H, ArH), 7.56 (d, $J = 8.4$ Hz, 2H, ArH), 7.78–7.72 (m, 9H, *meso*-ArH), 8.09 (d, $J = 8.1$ Hz, 2H, *meso*-ArH), 8.21–8.19 (m, 6H, *meso*-ArH), 8.65 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.83 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.84 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 33.57$, 64.97, 118.52, 120.28, 120.42, 123.04, 123.21, 126.70, 127.75, 128.72, 131.32, 132.16, 134.53, 134.95, 136.90, 138.45, 140.70, 142.01, 170.97 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{36}BrN_5OS$ 869.1824, found 869.1819.

2-(4-Chlorophenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4f**, $C_{53}H_{36}ClN_5OS$)

Yield 86%; IR (Nujol): $\bar{\nu} = 1{,}677$, 1,597, 1,463, 1,377, 966, 800 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = -2.82$ (s, 2H, internal NH), 4.03 (d, $J = 15.6$ Hz, 1H, SCH_2CO), 4.13 (d, $J = 15.3$ Hz, 1H, SCH_2CO), 6.34 (s, 1H, CH), 7.43 (s, 4H, ArH), 7.52 (d, $J = 8.1$ Hz, 2H, *meso*-ArH), 7.80–7.74 (m, 9H, *meso*-ArH), 8.10 (d, $J = 7.8$ Hz, 2H, *meso*-ArH), 8.20 (d, $J = 7.2$ Hz, 6H, *meso*-ArH), 8.65 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.82 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.83 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.63$, 65.07, 118.47, 120.30, 120.45, 123.31, 126.68, 127.74, 128.50, 129.36, 131.05, 134.52, 134.99, 137.00, 137.96, 140.74, 142.01, 171.01 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{36}ClN_5OS$ 825.2329, found 825.2335.

2-(4-Fluorophenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4g**, $C_{53}H_{36}FN_5OS$)

Yield 96%; IR (Nujol): $\bar{\nu} = 1{,}690$, 1,599, 1,506, 1,466, 1,377, 1,231, 1,176, 965, 802, 733 cm^{-1}; ^{1}H NMR

(300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 4.04 (d, $J = 15.9$ Hz, 1H, SCH_2CO), 4.13 (d, $J = 15.9$ Hz, 1H, SCH_2CO), 6.33 (s, 1H, CH), 7.16 (dd, $J = 8.7$, 8.4 Hz, 2H, ArH), 7.50–7.45 (m, 4H, *meso*-ArH, ArH), 7.80–7.72 (m, 9H, *meso*-ArH), 8.09 (d, $J = 8.4$ Hz, 2H, *meso*-ArH), 8.21–8.18 (m, 6H, *meso*-ArH), 8.64 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.81 (d, $J = 4.8$ Hz, 2H, β-pyrrolic H), 8.84 (s, 4H, β-pyrrolic H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 33.73$, 65.06, 115.87, 116.16, 118.62, 120.34, 120.45, 123.53, 126.77, 127.82, 129.14, 129.25, 131.41, 134.58, 134.96, 136.95, 140.75, 142.07, 170.98 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{36}FN_5OS$ 809.2625, found 809.2598.

2-Phenyl-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4h**, $C_{53}H_{37}N_5OS$)
Yield 76%; IR (Nujol): $\bar{\nu} = 1{,}691$, 1,596, 1,462, 1,377, 1,175, 1,071, 966, 803 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 4.09 (d, $J = 16.8$ Hz, 2H, SCH_2CO), 6.39 (s, 1H, CH), 7.49 (s, 7H, *meso*-ArH, ArH), 7.75 (s, 9H, *meso*-ArH), 8.08 (s, 2H, *meso*-ArH), 8.20 (s, 6H, *meso*-ArH), 8.65 (s, 2H, β-pyrrolic H), 8.83 (s, 6H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.70$, 65.81, 118.70, 120.21, 120.33, 123.41, 126.67, 127.17, 127.72, 128.99, 129.11, 131.50, 134.51, 134.86, 137.20, 139.31, 140.53, 142.04, 171.19 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{53}H_{37}N_5OS$ 791.2791, found 791.2787.

2-(4-Isopropylphenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4i**, $C_{56}H_{43}N_5OS$)
Yield 60%; IR (film): $\bar{\nu} = 1{,}695$, 1,598, 1,465, 1,376, 1,174, 965, 802, 732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 1.28 (s, 6H, CH_3), 2.95 (brs, 1H, CH), 4.06 (d, $J = 16.5$ Hz, 2H, SCH_2CO), 6.33 (s, 1H, CH), 7.39 (s, 2H, ArH), 7.53 (s, 2H, ArH), 7.75 (s, 11H, *meso*-ArH), 8.07 (s, 2H, *meso*-ArH), 8.19 (s, 6H, *meso*-ArH), 8.65 (s, 2H, β-pyrrolic H), 8.83 (s, 6H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.78$, 33.86, 38.79, 65.73, 120.21, 120.51, 123.38, 126.33, 126.67, 127.08, 127.17, 127.70, 128.35, 131.07, 134.53, 134.90, 135.18, 135.27, 136.63, 140.42, 142.03, 171.29 ppm; HRMS (ESI): $[M]^+$ calcd for $C_{56}H_{43}N_5OS$ 833.3188, found 833.3202.

2-(4-Methoxyphenyl)-3-[4-(10,15,20-triphenylporphyrin-5-yl)phenyl]thiazolidin-4-one (**4j**, $C_{54}H_{39}N_5O_2S$)
Yield 40%; IR (film): $\bar{\nu} = 1{,}691$, 1,598, 1,511, 1,470, 1,350, 1,251, 1,175, 1,032, 966, 801,731 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = -2.83$ (s, 2H, internal NH), 3.84 (s, 3H, OCH_3), 4.04 (d, $J = 15.3$ Hz, 1H, SCH_2CO), 4.13 (d, $J = 16.2$ Hz, 1H, SCH_2CO), 6.35 (s, 1H, CH), 6.96 (d, $J = 8.1$ Hz, 2H, ArH), 7.44 (d, $J = 7.5$ Hz, 2H, ArH), 7.53 (d, $J = 7.2$ Hz, 2H, *meso*-ArH), 7.76 (s, 9H, *meso*-ArH), 8.10 (d, $J = 7.8$ Hz, 2H, *meso*-ArH), 8.21 (s, 6H, *meso*-ArH), 8.67 (s, 2H, β-pyrrolic H), 8.83 (s, 6H, β-pyrrolic H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 33.07$, 55.40, 64.72, 114.46, 118.53, 120.16, 121.11, 123.53, 126.68, 127.25, 127.74, 128.68, 131.12, 134.54, 134.96, 140.86, 142.06, 159.79, 171.17 ppm; HRMS (ESI): $[M + H]^+$ calcd for $C_{54}H_{40}N_5O_2S$ 822.2903, found 822.2915.

meso-Tetrakis[4-[2-(4-fluorophenyl)-4-oxothiazolidin-3-yl]phenyl]porphyrin (**7**, $C_{80}H_{54}F_4N_8O_4S_4$)
To a solution of 35 mg *meso*-tetrakis(4-aminophenyl)porphyrin (0.052 mmol) in 30 cm^3 toluene was added 6 mg $La(OTf)_3$ (0.01 mmol). To this mixture, 0.033 cm^3 4-fluorobenzaldehyde (0.32 mmol) was added followed by 0.063 cm^3 mercaptoacetic acid (0.94 mmol). The reaction mixture was heated at reflux temperature and the progress of the reaction was monitored by TLC. After 24 h, the solvent was evaporated under reduced pressure and the residue was treated with 30 cm^3 saturated aqueous $NaHCO_3$ solution. The product was extracted with 30 cm^3 ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure to afford the crude product. The compound was purified on a neutral alumina column by using 5% methanol in chloroform as eluent to produce pure compound **7** in 45% yield. IR (film): $\bar{\nu} = 1{,}682$, 1,601, 1,507, 1,367, 1,224, 1,155, 965, 842, 796, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = -2.99$ (s, 2H, internal NH), 4.08 (m, 8H, SCH_2CO), 6.40 (s, 4H, CH), 7.17 (s, 8H, ArH), 7.81 (s, 16H, *meso*-ArH, ArH), 8.05 (s, 8H, *meso*-ArH), 8.76 (s, 8H, β-pyrrolic H) ppm; HRMS (ESI): $[M]^+$ calcd for $C_{80}H_{54}F_4N_8O_4S_4$ 1,394.3087, found 1,394.3079.

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