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Photocatalytic dis-assembly of tertiary amine-based dendrimers to monomers and its application to 'catch and release' of a dye in aqueous solution

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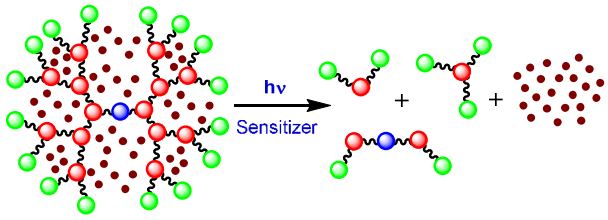
Graphical Abstract



Covalent bond dis-assembly of tertiary amine based dendrimers and their application to 'catch' and 'release'of a water-insoluble dye are reported.

Cite this: DOI: 10.1039/c0xx00000x

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Communication

Photocatalytic dis-assembly of tertiary amine-based dendrimers to monomers and its application to 'catch and release' of a dye in aqueous solution

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Photocatalytic dis-assembly of tertiary amine-based poly(propyl ether imine) dendrimers, in the presence of either 9,10-anthraquinone or riboflavin tetra-acetate and O_2 (g) leads to di- and tripropanolamine monomers. An application is shown by solubilisation of a water-insoluble sudan I in aq. dendrimer solution ('catch'), followed by its 'release' upon dis-assembly of the dendrimer.

Introduction

Covalent assembly of monomer building blocks with complete branching constitutes the general class of dendritic structures.[1] Dendrimers find manifold applications due to their molecular and supramolecular properties that are distinctly different from that of other types of macromolecular structures.[2-4] Dendrimer synthesis was intensively investigated over last three decades, but their covalent bond dis-assembly into smaller fragments is explored much less. In order to initiate the dis-assembly of dendrimers into smaller structural units, a chemical or photochemical reaction occurring at the core or periphery is typically used.[5, 6] A one-step dis-assembly involving ortho- and/or para-quinine methide rearrangement was used in the case of dendrimers with aryl-moieties.[7-10] A recent report describes the H_2O_2-mediated cleavage of a PAMAM dendrimer, through a cascade of oxidation and elimination reactions.[11] However, despite potential interesting applications,[12,13] the development of methods to dis-assemble the covalent bonds of aliphatic dendrimers remained largely unexplored. We describe herein the photochemical dis-assembly of aliphatic tertiary amine-based poly(propyl ether imine) (PETIM) dendrimers.[14, 15]

Results and discussion

PETIM dendrimers contain tertiary amines as the branching unit, ether as the linker functionality and n-propyl spacer connecting the branch units with the linker. Tertiary amines are efficient electron donors as a result of their low ionization potential of ~0.76 eV *vs* SCE.[16] In a photochemical reaction, tertiary amines donate an electron to an acceptor, the acceptor being generally a photoactive dye molecule. Mechanistic studies of Santamaria[17] and Catalina[18] on the photochemical oxidation of trialkyl amines, such as, triethyl amine, show that sensitizers, such as, 9,10-anthraquinone, either in the singlet or triplet state, abstract an electron initially from a tertiary amine to generate an amine radical cation ($E_{(AQ/AQ^{\bullet-})}$ = -1.11 V). Deprotonation of the radical cation, followed by electron loss, generates an iminium ion, which subsequently undergoes hydrolysis to afford the corresponding secondary amine. Aliphatic dendrimers having multiple tertiary amine sites may encounter a similar possibility and, in such an event, the photochemical method shall provide a facile and benign route to dis-assemble a dendritic structure to smaller fragments. With this premise, we undertook studies of photochemical cleavage of PETIM dendrimers.

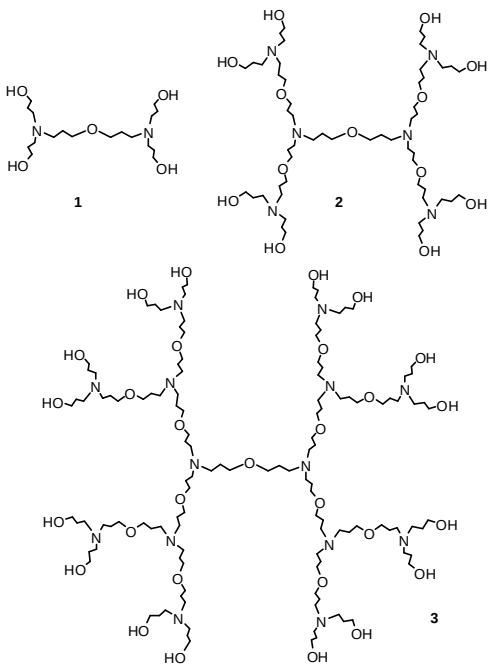


Figure 1. Structures of the first, second and third generation PETIM dendrimers.

Molecular structures of PETIM dendrimers used in the present study are shown in Figure 1. In the initial stage, first generation dendrimer **1** was investigated. A solution of **1** in aq. CH_3CN (1:1) was irradiated using a low-pressure 400 W mercury-vapor lamp, in the presence of a catalytic amount of 9,10-anthraquinone (10 mol%) and continuous purging of O_2 (g). Changes to the

reaction mixture were monitored by ^{1}H NMR spectroscopy. Figure 2 shows a compilation of the spectra of **1**, recorded at varying time intervals of the photochemical reaction. The spectra of **1** changed over ~ 9 h during photolysis, and then remained constant. The resonances of intact **1** appear at 1.73, 2.60, 3.47 and 3.63 ppm, corresponding to the CH_2 moieties.[14, 15] After photolysis, the relative intensities of the CH_2 protons of **1** decreased and new signals appeared. The formation of a number of products having slightly different chemical environment was inferred from the spectra. Analysis of the products was facilitated further by treatment of the reaction mixture with Ac_2O/pyridine, followed by purification of the reaction mixture (SiO_2, $CHCl_3$/MeOH 9:1). The major products formed during the course of the reaction were identified, as given in Scheme 1.

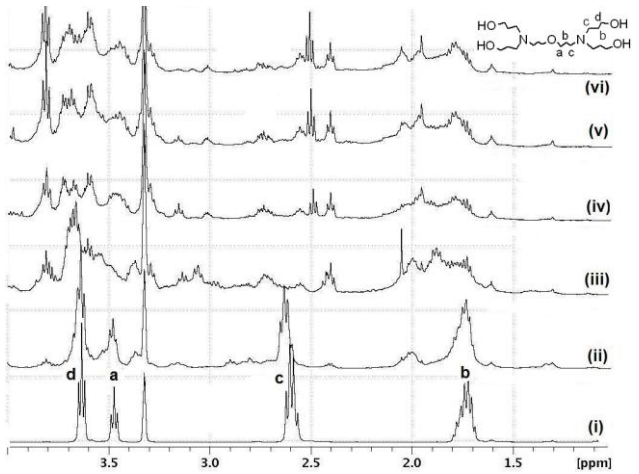
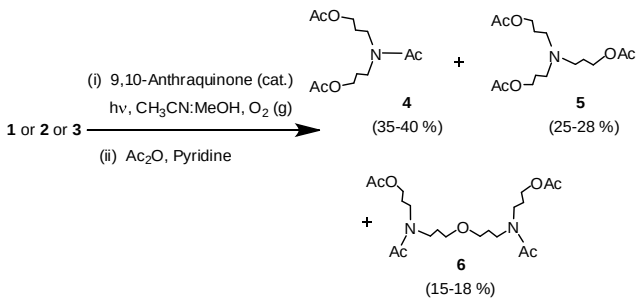


Figure 2. ^{1}H NMR spectra (i) – (vi) obtained after subjecting **1** to photolysis at 0, 3, 6, 9, 12, 15 h, respectively.

Scheme 1



The structure of **4**-**6** were determined by NMR spectroscopy. The methylene protons adjacent to tertiary amine and acetate groups in **4** appeared between δ 3.34-3.28 and 4.01-3.99 ppm. The internal methylene protons were observed at δ 1.86-1.80 ppm. The acetyl group signals were observed at δ 2.02, 2.00 and 1.98 ppm. In the ^{13}C NMR spectrum, -*C*OCH$_3$ resonated at 170.9, 170.7 and 170.2 ppm. The methylene carbon resonance signals adjacent to nitrogen and acetate group appeared at δ 45.7, 42.7 and 62.1, 61.3 ppm, respectively, whereas the internal methylene carbon signal appeared at 27.9 and 26.8 ppm, and OCO*C*H$_3$ appeared at 21.3, 20.8 and 20.7 ppm. The mass spectrometric analysis of **4** further confirmed the identity.

The ^{1}H NMR spectrum of **5** showed resonances at 4.05 (J = 6.5 Hz), 2.42 (J = 6.8 Hz), and 1.70 (J = 6.7 Hz) ppm, corresponding to the OCH_2, NCH_2 and internal methylene groups, respectively. In the ^{13}C NMR spectrum, signals at 62.6, 50.2 and 26.4 correspond to the OCH_2, NCH_2, and interior CH_2 carbons, respectively. The mass spectrum showed an m/z signal at 318.1915, corresponding to the [M+H] ion of **5**.

Similarly, in the ^{1}H NMR spectrum of **6**, the methylene proton resonance signals attached to the acetate group were seen as a multiplet at δ 4.07 ppm. The methylene protons adjacent to the nitrogen overlay with the signal of the ether linked CH_2 protons appeared between δ 3.40-3.34 ppm. The methyl proton resonance signal of the acetate groups were observed between 2.02 and 1.98 ppm. The internal methylene signals were observed at δ 1.89 and 1.82 ppm. The structure of **6** was confirmed further by mass spectrometric analysis, which showed a signal at 439.2419, corresponding to the [M+Na] ion.

The photochemical cleavage of **1** led to a C-N cleavage, in addition to a C-O cleavage, as confirmed by the formation of the above products. The C-O cleavage is presumed to occur through a β-elimination of the alkoxy aldehyde, which results upon hydrolysis of the iminium ion.

Further, the amount of dye to mediate the photochemical reaction was reduced gradually down to 0.1 mol %. From these attempts, 0.5 mol% of the sensitizer *per* one tertiary amine moiety in the dendrimer scaffold was found optimal to mediate the photochemical cleavage. In the absence of oxygen, the reaction required stoichiometric amount of the sensitizer and reaction times of more than 48 h. Further, in the absence of sensitizer and light, the reaction did not proceed.

Upon standardizing the reaction, the method was extended for the photochemical cleavage of second and third generation dendrimers, namely, **2** and **3** (Scheme 1). The reaction was conducted under similar conditions as that of the reaction with **1**, and the products of the reaction were analysed, after acetylation. Products formed from dendrimers **2** and **3** were identical to the products **4**-**6**, obtained from the photochemical cleavage of **1**, although in varying yields.

Further the cleavage of the dendrimer by riboflavin tetra-acetate (RFT), a sensitizer derived from vitamin B2, was undertaken. The redox potential of riboflavin tetra-acetate [$E_{(RFT/RFT^{\cdot-})}$ = -1.18 V (Ag/AgCl)],[19] closely matches that of the redox potential of 9,10-anthraquinone. Riboflavin is a proficient photosensitizer for the oxidation of functionalities, such as, benzyl alcohols, benzyl amines, methylbenzenes, styrene, phenyl acetic acid, benzyl methyl ethers, sulphides and glucose.[20-22] Further, amino acids, proteins, lipids and nucleic acids undergo photodegradation, in the presence of riboflavin.[23-27] In the photooxidation, riboflavin tetra-acetate first abstracts an electron from the substrate, followed by a hydrogen transfer and a second electron transfer. The reduced form of flavin is regenerated in the presence of dioxygen or air with production of H_2O_2.[22]

The photochemical cleavage of the PETIM dendrimer **1** was performed by using riboflavin tetra-acetate (0.5 mol % *per* tertiary amine group in the dendrimer) as the sensitizer, in the presence of O_2 for 8-15 h, and subsequently treated with Ac_2O/pyridine. Products, obtained upon purification, were found to match essentially **4**-**6**, obtained by using 9,10-anthraquinone in

differing yields. It is thus concluded that the end products of the photochemical cleavage result from both C-N and C-O cleavages, when riboflavin tetra-acetate was used as the sensitizer. Similarly the cleavage of second and third generation dendrimers, **2** and **3** was performed and the yields of **4**-**6** were in the range as that obtained in the photocleavage mediated by 9,10-anthraquinone.

Thus a photochemical cleavage of a tertiary amine-based aliphatic dendrimer was established. The photochemical instability of tertiary amines is the key step for all studied photodegradation reactions.

The use of hydrophobic cavities in PETIM dendrimers to solubilize water insoluble drugs, such as, ketoprofen, was previously reported.[28] In order to verify the solubilisation of a hydrophobic guest molecule by the dendrimer, followed by release of the guest as a result of covalent bond dis-assembly of the dendrimer, dye sudan I (aq. solubility: 0.051 μM)[29] was chosen. A solution of hydroxyl terminated dendrimers (1 mM) in water was stirred with sudan I (2 mg) for 24 h at room temperature. The solution was then filtered (0.2 μ) and the concentration of solubilized sudan I was identified by recording its absorbance at 479 nm (ε = 16300 $M^{-1}cm^{-1}$).[30] The amount of sudan I solubilized were found to be 4.6 μg, 8.8 μg and 17.7 μg for the first (**1**), second (**2**) and third (**3**) generation dendrimers, respectively. The above solubilities represent 90, 172 and 350 fold increase for first, second and third generation dendrimer containing aq. solutions, respectively, in comparison to the solubility of sudan I in water. The corresponding dendrimer-to-dye molar stoichiometries were: 0.03, 0.05 and 0.1, respectively. Solubilization was confirmed by HPLC (silica column) of the dye extracted from the dendrimer solution with EtOAc, using hexane-EtOAc (60:40, v/v) as eluent. The retention time of a peak corresponding to the dye was validated by the pure dye recorded at identical condition and ^{1}H NMR analysis.

In the subsequent 'release' of the dye, the dendrimer-dye complex and added RFTA (0.5 mol% *per* tertiary amine site) was irradiated for a defined period of time. The reaction mixture was then extracted with EtOAc, concentrated and the extract was analyzed by HPLC. The amount of sudan I released was identified by comparing the area of the peak (see Supporting Information) in each case, before and after the photochemical cleavage. The recovered amount of sudan I was 70±2%, 67±3%, and 62±5% for the first, second and third generation dendrimer, respectively.

In a control experiment, a solution of sudan I in EtOH (56.6 μM) was irradiated for 8 h, in order to verify its photochemical stability. From UV-Vis spectra, as well as, the HPLC profile, the dye was found to be stable under the experimental condition. Similarly, the photochemical stability of the dye in the presence of RFTA was also confirmed upon irradiation of the dye-RFTA containing EtOH solution. In another experiment, solubility of the dye in a preformed fragmented third generation dendrimer-containing aq. solution (0.05 μM) was assessed, by following the protocol as that used for solubilisation of the dye in dendrimer-containing aq. solution. A solubility of 1.08 μM was identified, thus confirming the significantly enhanced solubilities of the dye in intact dendrimer containing aq. solutions (*vide infra*), through dendrimer-mediated solubilisation. The partial loss of the dye in the 'release' experiment might be due to the reaction of the dye with cation-radicals of the fragmented dendrimer.

Conclusion

In conclusion, aliphatic tertiary amine-based PETIM dendrimers undergo a photocatalytic cleavage by using anthraquinone or riboflavin-tetraacetate as the photocatalyst. Upon irradiation in the presence of catalytic amounts of the sensitizer and O_2 (g), the dendrimers underwent photocleavage to monomer fragments. The photocleavage of the dendrimer was then used in a 'catch' and 'release' experiment of the water-insoluble sudan I dye. Intact dendrimer containing aqueous solutions solubilized the dye approximately two orders of magnitude higher ('catch'). Upon photocleavage of the dendrimer, the dye was recovered ('release') to a large extent. The photochemical cleavage methodology reported herein expands the scope of dis-assembly of a covalently constituted fully aliphatic dendrimer and their use as a host to solubilize water-insoluble guest and its subsequent release as a result of photolytic fragmentation.

Experimental Section

Materials

Commercially available reagent grade chemicals were used as received. The reactions were followed by TLC (SiO_2 or neutral Al_2O_3), with detection by staining with I_2. Column chromatography was performed on silica gel (100-200 mesh). IR spectra were recorded as thin films. ^{1}H and ^{13}C NMR spectra were recorded on an instrument, operating at 400 and 100 MHz, respectively. HR-MS analysis was performed on an electro-spray ionization mass spectrometer. Chemical shift values are reported in ppm relative to TMS and the following notations were used to describe the multiplicity: s (singlet), app. quintet (apparent quintet), m (multiplet).

Procedure for cleavage the hydroxyl terminated dendrimer

4-**6**. Either 9,10-anthraquinone (1.4 mg, 6.73 μmol for **1**, 1.5 mg, 7.2 μmol for **2** and **3**) or RFTA (3.7 mg, 6.8 μmol for **1**, 3.9 mg, 7.2 μmol for **2** and **3**) was added to a solution of **1**[14, 15] (0.25 g, 0.68 mmol) or **2** (0.25 g, 0.24 mmol) or **3** (0.25 g, 0.10 mmol) in CH_3CN/MeOH (1:1) (15 mL) in a quartz tube. The reaction mixture was irradiated by a 400 W low pressure Hg lamp for 15 h, while purging with O_2 (g). The reaction mixture was then evaporated *in vacuo* and the crude product was dissolved in pyridine (5 mL), Ac_2O (0.5 mL, 5.3 mmol) was added, stirred for 6 h, evaporated *in vacuo*, purified by column chromatography (SiO_2) (100-200 mesh), using $CHCl_3$/MeOH gradient elution, to afford compounds **4**-**6**, as oils.

4: R_f = 0.6 ($CHCl_3$:MeOH = 9.5:0.5); IR (neat) ν 2925, 2360, 2341, 1737, 1638, 1365, 1234, 1042; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.01 (app. quint, 4H, OCH_2), 3.29 (m, 4H, NCH_2), 2.02 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 1.83 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.7, 170.2, 62.1, 61.3, 45.7, 42.7, 27.9, 26.8, 21.3, 20.8, 20.7; HRMS: calcd. for $C_{12}H_{21}NO_5Na$: 282.1317; found 282.1312.

5: R_f = 0.5 ($CHCl_3$:MeOH = 9.5:0.5); IR (neat) ν 2950, 2360, 2341, 1738, 1365, 1238, 1042; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.05 (t, J = 6.5 Hz, 6H, OCH_2), 2.42 (t, J = 6.8 Hz, 6H, NCH_2),

2.00 (s, 9H, 3 x CH_3), 1.70 (t, J = 6.7 Hz, 6H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9 (CO), 62.6 (OCH_2), 50.2 (NCH_2), 26.4 (CH_2), 20.8 (CH_3); HRMS: calcd. for $C_{15}H_{27}NO_6H$: 318.1917; found 318.1915.

6: R_f = 0.3 ($CHCl_3$:MeOH = 9.5:0.5); IR (neat) ν 2932, 1738, 1627, 1367, 1241, 1047; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (app. quint, 4H, OCH_2), 3.40-3.34 (m, 12H, NCH_2 and OCH_2), 2.07, 2.05, 2.03 (s, 12H, 4 × CH_3), 1.89-1.85 (m, 4H, CH_2), 1.82-1.77 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 170.0, 169.9, 169.7 (CO), 68.15 (OCH_2), 67.14 (OCH_2), 61.1 (OCH_2), 61.0 (OCH_2), 49.8 (NCH_2), 45.5 (NCH_2), 42.5 (NCH_2), 27.5 (CH_2), 26.4 (CH_2), 26.0 (CH_2), 20.9 (CH_3), 20.8 (CH_3); HRMS: calcd. for $C_{20}H_{36}N_2O_7Na$: 439.2420; found 439.2419.

Solubilization of sudan I dye:

Sudan I (2 mg) was added to an aq. solution of hydroxy-terminated dendrimer solution (1 mM) (6 mL) and stirred for 24 h. The solution was filtered (0.2 μ) and analysed by UV-Vis spectroscopy (479 nm). The filtrate was then extracted with EtOAc, the organic portion concentrated *in vacuo* and dried. The resulting residue was re-dissolved in EtOAc and analyzed by HPLC (silica, 250×10.00 mm), using hexane-EtOAc (60:40, v/v) as eluent and UV-Vis spectroscopic detection at 479 nm.

'Release' of sudan I upon fragmentation of the dendrimer:

A dendrimer solution containing solubilized dye was added with RFTA, subjected to photolysis for 15 h, as described previously. The reaction mixture was extracted with EtOAc, the organic portion concentrated *in vacuo* and dried. The resulting residue was re-dissolved in EtOAc and analyzed by HPLC method as described above. Percentage value of the recovered dye is the average of triplicate experiments.

Acknowledgment

We are grateful to Department of Science and Technology, New Delhi, for a financial support. We thank INDIGO program supported by German Academic Exchange (DAAD) for a travel support.

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

‡ Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

1. D. A. Tomalia, J. M. J. Fréchet, *J. Polym. Sci., Part A: Polym. Chem.* 2002, **40**, 2719.
2. J. Khandare, M. Calderon, N. M. Dagia, R. Haag, *Chem. Soc. Rev*. 2012, **41**, 2824.
3. Y. M. Chabre, R. Roy, *Chem. Soc. Rev*. 2013, **42**, 4657.
4. T. Kehat, K. Goren, M. Portnoy, *New J. Chem*. 2007, **31**, 1218.
5. S. Li, M. L. Szalai, R. M. Kevwitch, D. V. McGrath, *J. Am. Chem. Soc.* 2003, **125**, 10516.
6. R. M. Kevwitch, C. S. Shanahan, D. V. McGrath, *New J. Chem.* 2012, **36**, 492.
7. R. J. Amir, D. Shabat, *Chem. Commun*. 2004, **21**, 1614.
8. R. J. Amir, N. Pessah, M. Shamis, D. Shabat, *Angew. Chem. Int. Ed.* 2003, **42**, 4494.
9. F. M. H de Groot, C. Albrecht, R. Koekkoek, P. H. Beusker, H. W. Scheeren, *Angew. Chem. Int. Ed*. 2003, **42**, 4490.
10. S. Watanabe, M. Sato, S. Sakamoto, K. Yamaguchi, M. Iwamura, *J. Am. Chem. Soc.* 2000, **122**, 12588.
11. S.-Y. Lin, T.-H. Wu, Y.-C. Jao, C.-P. Liu, H.-Y Lin, L.-W. Lo, C.-S. Yang, *Chem. Eur. J*. 2011, **17**, 7158.
12. B. M. Rosen, C. J. Wilson, D. A. Wilson, M. Peterca, M. R. Imam, V. Percec, *Chem. Rev*. 2009, **109**, 6275.
13. R. Duncan, L. Izzo, *Adv. Drug Delivery Rev*. 2005, **57**, 2215.
14. T. R. Krishna, N. Jayaraman, *J. Org. Chem.* 2003, **68**, 9694.
15. G. Jayamurugan, N. Jayaraman, *Tetrahedron* 2006, **62**, 9582.
16. S. F. Nelsen, P. J. Hintz, *J. Am. Chem. Soc.* 1972, **94**, 7114.
17. J. Santamaria, *Pure Appl. Chem.*1995, **67**, 141.
18. F. Catalina, C. Peinado, M. Blanco, T. Corrales, N. S. Allen, *Polymer* 2001, **42**, 1825.
19. B. König, M. Pelka, H. Zieg, T. Ritter, H. Bouas-Laurent, R. Bonneau, J.-P. Desvergne, *J. Am. Chem. Soc*. 1999, **121**, 1681.
20. J. Dadova, E. Svobodova, M. Sikorski, B. König, R. Cibulka, *Chem. Cat. Chem.* 2012, **4**, 620.
21. U. Megerle, M. Wenninger, R. J. Kutta, R. Lechner, B. Dick, B. König, E. Riedle, *Phys. Chem. Chem. Phys.* 2011, **13**, 8869.
22. R. Lechner, S. Kümmel, B. König, *Photochem. Photobiol. Sci.* 2010, **9**, 1367.
23. C. K. Remucal, K. McNeil, *Environ. Sci. Technol*. 2011, **45**, 5230.
24. E. Choe, R. Huang, D. B. Min, *J. Food Sci.* 2005, **70**, R28.
25. D. R. Cardoso, S. H. Libardi, L. H. Skibsted, *Food Funct.* 2012, **3**, 487.
26. P. C. Joshi, T. C. Keane, *Biochem. Biophys. Res. Commun.* 2010, **400**, 729.
27. C. B. Martin, X. Shi, M.-L. Tsao, D. Karweik, J. Brooke, C. M. Hadad, M. S. Platz, *J. Phys. Chem. B* 2002, **106**, 10263.
28. S. Jain, A. Kaur, R. Puri, P. Utreja, A. Jain, M. Bhide, R. Ratnam, V. Singh, A. S. Patil, N. Jayaraman, G. Kaushik, S. Yadav, K. L. Khanduja, *Eur. J. Med. Chem.* 2010, **45**, 4997.
29. M. H. Abraham, M. Amin, A. M. Zissimos, *Phys. Chem. Chem. Phys.* 2002, **4**, 5748.
30. C. Kocher, C. Weder, P. Smith, *Adv. Funct. Mater*. 2003, **13**, 427.

