A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: An Ultra-Robust and Crystalline Redeemable Hydrogen-Bonded Organic Framework for Synergistic Chemo-Photodynamic Therapy

Authors: Rong Cao, Tian-Fu Liu, Qi Yin, Zhao Peng, Rong-Jian Sa, Guang-Cun Chen, and Jian Lü

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201800354
Angew. Chem. 10.1002/ange.201800354

Link to VoR: http://dx.doi.org/10.1002/anie.201800354
http://dx.doi.org/10.1002/ange.201800354

WILEY-VCH

10.1002/anie.201800354

COMMUNICATION

WILEY-VCH

An Ultra-Robust and Crystalline Redeemable Hydrogen-Bonded Organic Framework for Synergistic Chemo-Photodynamic Therapy

Qi Yin,[a] Zhao Peng,[b] Rong-Jian Sa,[a] Guang-Cun Chen,[b] Jian Lü,[c] Tian-Fu Liu,*[a] and Rong Cao*[a]

ABSTRACT: The low structural stability of hydrogen-bonded organic frameworks (HOFs) is a thorny issue retarding the development of HOFs field. Herein, we proposed a rational design approach for construction of stable HOF. The resultant HOF (PFC-1) exhibits high surface area of 2,122 m²/g and excellent chemical stability of being intact in concentrated HCl for at least 117 days. Moreover, we demonstrated a new methodology of acid-assisted crystalline redemption to readily cure the thermal damage to PFC-1. With periodic integration of photoactive pyrene in the robust framework, PFC-1 can efficiently encapsulate Doxorubicin (Doxo) for synergistic chemo-photodynamic therapy, showing comparable therapeutic efficacy with the commercial Doxo yet considerably lower cytotoxicity. This work demonstrates the notorious stability issue of HOFs can be properly addressed through rational design strategy, paving a way for developing robust HOFs and offering promising application perspectives.

Hydrogen bonding plays critical roles in biological systems for both structure and functionality,[1] which has inspired chemists to use of hydrogen bonds to construct hydrogen-bonded organic frameworks (HOFs, also called SOFs, abbreviation of supramolecular organic frameworks).[2] As with other periodic frameworks for example metal-organic frameworks,[3] zeolite-imidazolate frameworks (ZIFs),[4] and covalent organic frameworks (COFs),[5] HOFs possess the merits of high surface area, predictable structure and tailored pore size/shape.[6] Beyond that, the hydrogen bonding endows HOFs unique traits such as mild synthetic conditions,[7] solution processability,[8] and easy regeneration.[9] More strikingly, HOF materials exhibit considerable biocompatibility and low toxicity attributed to their metal-free nature, representing an excellent candidate for drug delivery and biological application. Despite many obvious advantages, the field of HOFs is still in its early stage especially when compared with the impressive success of MOFs, ZIFs and COFs counterparts. The main limitation lies in the structural stability of HOFs. A long-standing challenge is the hydrogen bonds are too weak to stabilize the HOF structure, and the frameworks usually collapse upon solvent removal. The low stability issue severely compromises the intrinsic merits of HOFs and encumbers their wide applications.

Despite the efforts of several decades, a very few HOFs have been reported with permanent porosity in solid state and even fewer HOFs can survive harsh conditions.[2,9-10] Moreover, strategies to improve the stability of HOF materials are obscure and the relevant investigation is rather rare. Learning the lessons from previous HOFs studies,[6-11] we envision that several approaches can be employed to construct HOFs with enhanced stability. The first one is to "create multiple hydrogen bonds". HOFs are constructed by the hydrogen bonds between organic building blocks. Therefore, more numerous intermolecular hydrogen bonds will strengthen the entire structure. In this sense, multi-topic organic ligands which can generate more hydrogen bonds would be promising candidates for constructing stable HOFs. The second approach relies on "taking advantage of π-π interactions".[12] While the hydrogen bonding has employed as an important intermolecular forces for construction of periodic frameworks, the contribution of π-π interaction is usually overlooked. Looking carefully into the crystal structures of SOF-7[10c] and HOF-TCBP[9], which are stable after heating or aqueous treatments, one can observe that π-π interactions are widespread throughout the entire structure. This phenomenon has also been observed in some COF materials.[13] Therefore, choice of planar organic building blocks with large π-conjugate system would favor a structure with extensive and strong π-π interactions, and thus a stable framework. Last but not least, "avoiding the residual hydrogen donors/acceptors after self-assembly" represents another approach. It is well known that the unsaturated metal centers are more reactive and labile than saturated ones.[14] Similarly, the organic building blocks with unpaired hydrogen donor or acceptor groups are reactive to involve the intermolecular interactions with solvent molecules, which would introduce extra stress and tension upon solvent removal, and thus destroying the integrity of frameworks.

Since HOFs are capable of being designed at molecular level, the strategies mentioned above can be implemented through judiciously tailoring the organic building blocks. Therefore, in our attempts to target a robust HOF, we chose 1,3,6,8-tetrakis (p-benzoic acid) pyrene (H4TBAPy) as a building block which is a planar molecule with very large π-conjugated system and four carboxylate acid groups.[15] As expected, the resultant HOF, named PFC-1 (PFC = Porous materials from FJIRSM, CAS), exhibits high surface area of 2,122 m²/g and excellent chemical stability of being intact in concentrated HCl (12 M) for at least 117 days. Strikingly, the thermal damage to PFC-1 can be readily remedied by acid-assisted crystalline redemption (AACR), a methodology here we observed for the first time in HOF materials. PFC-1 meets the prerequisites of a drug carrier including large pore size, high chemical stability, biocompatibility and low cytotoxicity.[16] Meanwhile, periodic integration of pyrene, an efficient photosensitizer to generate singlet oxygen ($^1O_2$), makes PFC-1 a promising material for photodynamic therapy (PDT). [17] The concurrence of permanent void space and photoactive moiety in structure inspired us to investigate the synergistic chemo-photodynamic therapy of PFC-1. Herein, we demonstrated that the size of PFC-1 can be precisely tuned from micron-scale to nano-scale, and doxorubicin (Doxo) was successfully encapsulated in Nano-PFC-1 with a high uptake of 26.5 *wt*%. In vitro PDT studies on Hela cell (human cervical cancer) shows Doxo@Nano-PFC-1 exhibits synergetic chem-photodynamic therapy with the merits of considerable biocompatibility, low cytotoxicity and high therapeutic efficacy.

In crystal structure of PFC-1, each H_4TBAPy molecule interacts with four neighboring ones through eight O–H···O hydrogen bonds to extend into a two-dimensional (2D) layer. The O–H···O distance and angle are 2.597 Å and 176.0°, respectively, falling into strong hydrogen bond range according to literature 2.49 to 3.15 Å.[1a] Each 2D square layers (sql) interacts with adjacent layers through face-to-face π-π stacking interactions (interlayer distance 3.338 Å), stacking as AA mode along 100 direction to form a one-dimensional square channels of 18 × 23 Å (Figure 1). The activated PFC-1 adsorbs significant amounts of N_2 (606.7 cm^3/g) with displaying type-I isotherm typical of a microporous material (Figure 2b). Fitting the Brunauer-Emmett-Teller (BET) equation to the N_2 isotherms in the region of $10^{-3} < p/p_o < 0.03$ (chosen based on the Rouquerol plot in Figure S11 in SI) gave a surface area of 2,122 m^2/g,[18] which is the second highest record among the previously reported HOF materials (Table S2).

[a] Q. Yin, Dr. R. J. Sa, Prof. T. F. Liu, and Prof. R. Cao
State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences
Fujian Fuzhou 350002, P. R. China
E-mail: *rcao@fjirsm.ac.cn, *tfliu@fjirsm.ac.cn

[b] Dr. P. Zhao, Dr. G. C. Chen
Suzhou Institute of Nano-Tech and Nano-Bionics (SINANO), Chinese Academy of Science
Jiangsu Suzhou 215123, P. R. China

[c] Prof. J. Lü
College of Resources and Environment, Fujian Agriculture and Forestry University,
Fuzhou 350002, P.R. China

Supporting information for this article is given via a link at the end of the document.

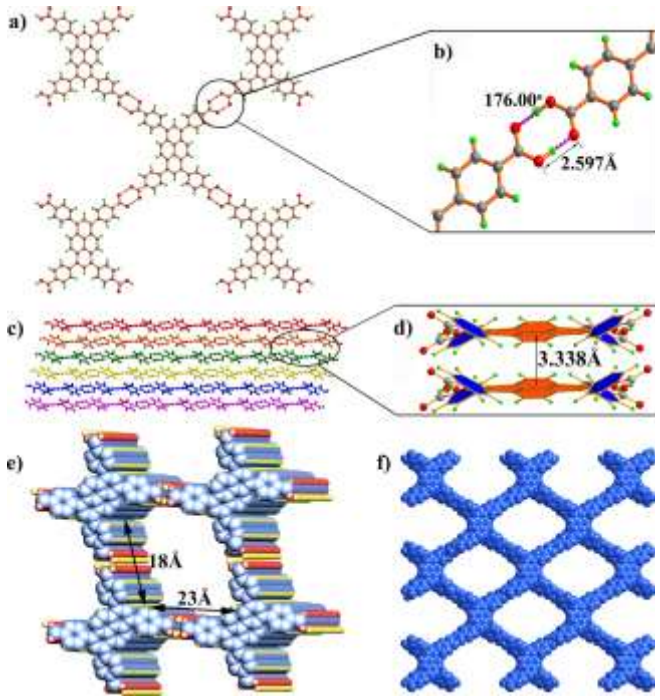

Figure 1. Crystal structure of PFC-1. a) View of the structure and the connection of adjacent building blocks. b) Hydrogen bonds Length and Angle. c) The stacking of 2D layers. d) Face-to-face π-π interactions. e) One-dimensional (1D) channels. f) Representation of the porous framework.

Previous study shows that as the π system enlarges from benzene to pentacene, the interaction energy of π-π stacking significantly increases from -1.563 to -14.908 kcal/mol.[19] In PFC-1, the large π-conjugated pyrene were further stacking in AA arrangement along *a*-axis, and thus the augment of energy would be more significant. To illustrate the increment, the π-π interaction energies of PFC-1 dimer and trimer were calculated at the level of M06-2X/6-31G (d, p). As shown in Table 1, the energy dramatically increases from -20.351 kcal/mol for PFC-1 dimer to -40.607 kcal/mol for PFC-1 trimer. These values are much higher than hydrogen bonding energy of -18.986 kcal/mol, demonstrating a vital role of π-π stacking for the structural stability. Consequently, PFC-1 exhibits high chemical stability in acidic condition as shown in Figure. 2a and 2b, wherein the crystallinity and porosity of PFC-1 maintain intact upon boiling in water for 10 days or with methanol, acetone, and deionized water for 117 days. More strikingly, even being soaked in 0.1 M and concentrated HCl (12 M) aqueous solutions for 117 days, PFC-1 well maintained the crystallinity and only showed negligible disparity on N_2 uptake. Such structural robustness has been unprecedented in HOF materials.

Table 1. Interaction energies (ΔE) and inter monomer distances (R) of optimized moieties.

System	ΔE (kcal/mol)	R (Å) [a]
Isolated pyrene dimer	-8.807	3.419
PFC-1 dimer	-20.351	3.748
PFC-1 trimer	-40.607	3.356
H-bonding of PFC-1 dimer	-18.986	

[a] *R* is the central benzene ring distance between monomers.

The outstanding thermal stability of PFC-1 was confirmed by thermogravimetric analysis (TGA) and various temperature powder X-ray diffraction (VT-PXRD) patterns, which showed that the frameworks maintain crystallinity till 250 °C (Figure S2, S4). The N_2 isotherms indicated that the gas uptakes of PFC-1 were not detracted after being heated at 90 °C and 120 °C for 6 hours. Further increase of the temperature to 150 °C and 210 °C caused a N_2 uptake decrease to 415 and 218 cm^3/g, respectively. When immersing the impaired samples in concentrated HCl aqueous solutions for 12 hours, surprisingly, the gas uptake rose to 581 cm^3/g which is nearly identical to the pristine sample

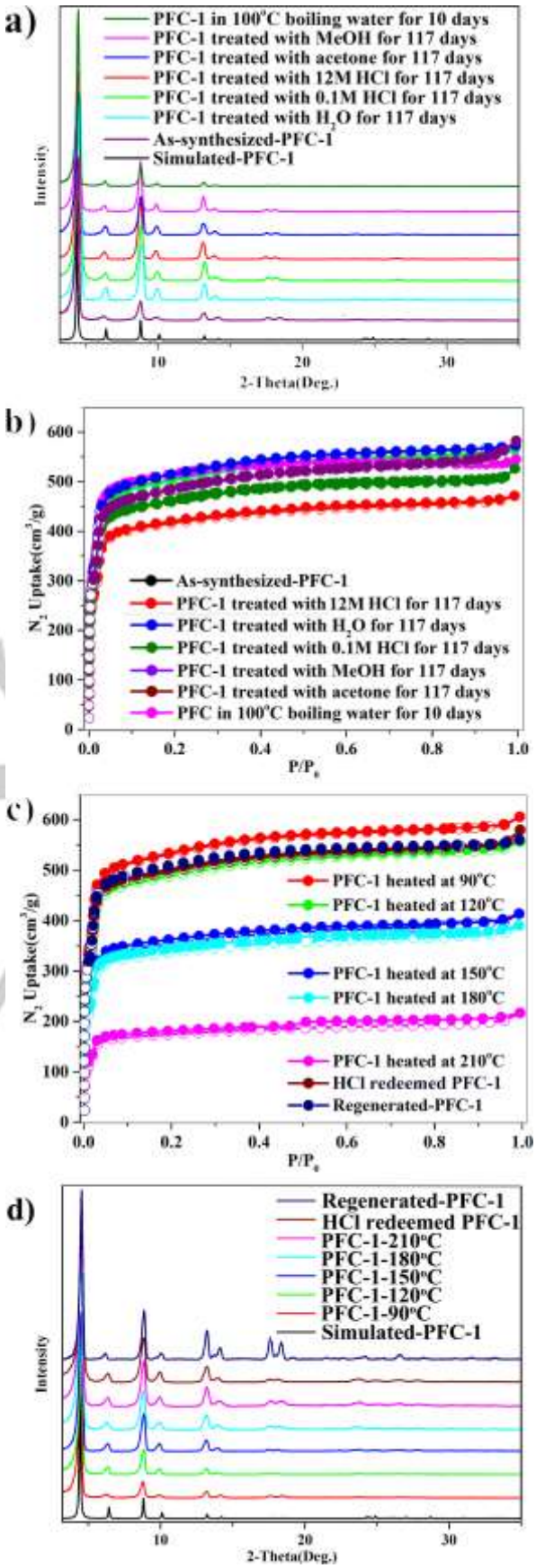

Figure 2. Structural stability of PFC-1. a) PXRD patterns and b) N_2 adsorption isotherms (77 K) of as-synthesized PFC-1 and samples treated with different solutions. c) N_2 adsorption isotherms (77 K) and d) PXRD of PFC-1 heated at different temperature for 6 hours, the HCl-redeemed and Regenerated PFC-1.

(Figure 2c). This finding demonstrated that the acidic solution recovery route, which we call "AACR", can reverse the thermal impairment to PFC-1. We speculate that high temperature might destroy hydrogen bonds and induce the deprotonation of carboxylic acid, while addition of proton causes re-association of hydrogen bonds and thus recovers the porosity of frameworks. To confirm this speculation, deuterium chloride was used instead of HCl for the redemption of PFC-1. If indeed the dissociation/re-association of hydrogen bonds occur during the heating and AACR process, addition of deuterium will inevitably generate the O–D···O bonds in the redeemed sample. Since ^{2}D has a faster chemical exchange rate than ^{1}H, substitution of COOH with COOD would give rise to a sharper peak for the carboxylic acid in ^{1}H-NMR (exchange broadening).[20] As expected, the full width at half maximum (FWHM) at 13.12 ppm for pristine PFC-1 is 1.25 Hz, while that for the DCl-redeemed PFC-1 dramatically decrease to 4.06 Hz (width is inversely proportional to frequency), suggesting the hydrogen bond re-association mechanism for AACR (Figure S21). Therefore, the AACR reported here represents for the first time a strategy to readily cure the thermal damage to HOFs. Besides the ability to redeem the thermal damage, PFC-1 has the virtue of facile regeneration. Highly crystalline PFC-1 can be easily regenerated through dissolving the used samples in DMF and recrystallizing in methanol. The reprocessed sample exhibits as high N_2 uptakes (561 cm^3/g) and BET surface area (2103 m^2/g) as the pristine material (Figure 2c, 2d).

Chemotherapy nowadays is still the most common treatment for cancer. It, however, has intrinsic limitations including terrible side effects, poor pharmacokinetics and undesirable bio-distribution, which encourages the development of combination therapies such as chemo-photodynamic therapy.[16c] With periodic integration of photoactive pyrene moiety in framework, PFC-1 is expected to generate $^{1}O_2$ upon irradiation for PDT. Meanwhile, the inherent porosity, chemical stability and metal-free components make PFC-1 an ideal candidate for drug carrier. As a proof of concept, Doxorubicin (Doxo), a well-known commercial drug for cancer, was chosen to incorporate into photoactive PFC-1 for synergetic chemo-photodynamic therapy.

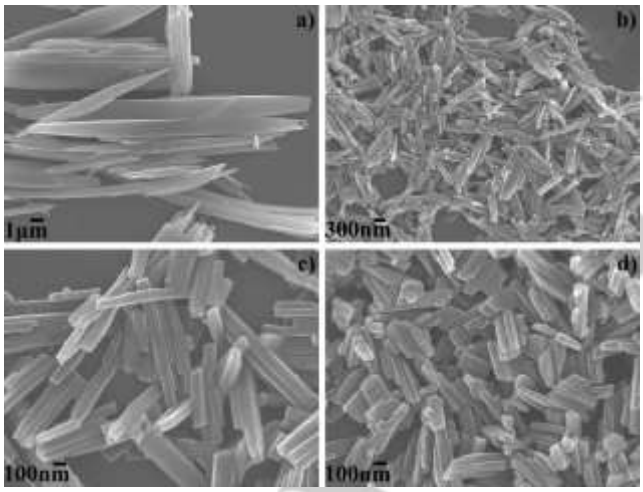

Figure 3 Scanning electron microscopy (SEM) images of PFC-1 with different particle size.

We first set out to prepare nano-sized PFC-1 for applying in biological system. Through adjusting solvent polarity and synthetic condition, the HOFs materials can be prepared with controlled particle sizes with the minimum size about 100 nm × 300 nm (denoted as Nano-PFC-1 hereafter) (Figure 3d). The N_2 adsorption of Nano-PFC-1 preserved the type-I isotherm with a relative lower BET surface area of 1,144 m^2/g and an obvious up-tail appeared at high P/P_o, which are probably caused by the stacking of the nanoparticles (Figure 4a).[21] Doxo loading capacity of bulky PFC-1 was 16.6 *wt*% in aqueous solution (denoted as Doxo@PFC-1 hereafter). The acidic environment (with 0.001 mmol/mL HCl in Doxo solution) and the scaled-down particle size result in an optimized loading capacity of 26.5 *wt*% (denoted as Doxo@Nano-PFC-1 hereafter) (Figure 4b, Figure S12-S14). The successful incorporation of Doxo in PFC-1 and Nano-PFC-1 was confirmed by solid state UV-Vis absorbance and ^{1}H-NMR spectroscopy (Figure S16, S20). Remarkably, the crystallinity and morphology of PFC-1 and Nano-PFC-1 were well preserved throughout the loading process, which were revealed in PXRD (Figure 4c, S6) and SEM imaging (Figure S17-S18). The robustness of PFC-1 promises its application in chemo-photodynamic therapy.

The singlet oxygen generation (SOG) was monitored by chemical trapping of $^{1}O_2$ with 9,10-Diphenylanthracene (DPA). As shown in Figure 4d, irradiation of the DPA solution for 60 minutes with visible light gave negligible decrease of absorbance at λ = 355 nm. With the addition of PFC-1 (bulky sample) into DPA solution, the UV-Vis absorption of DPA evidently decreased along with time, indicating efficient generation of singlet oxygen. A higher decreasing rate was observed for Nano-PFC-1, which demonstrates the superiority of nanomaterials for SOG. Moreover, the incorporation of Doxo does not detract the SOG efficacy, indicating the possibly synergistic effect of chemo-photodynamic therapy.

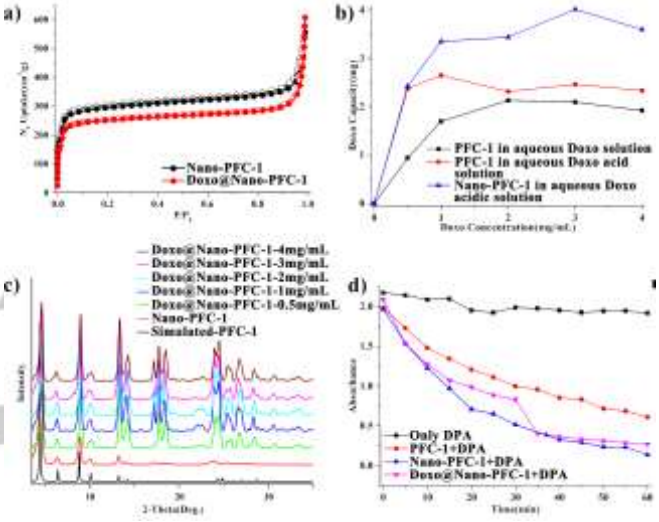

Figure 4 a) N_2 isotherms of Nano-PFC-1 (black) and Doxo@Nano-PFC-1 (red) at 77 K, b) Doxo loading capacity of bulky PFC-1 and nano-PFC-1 under different conditions, c) PXRD of Doxo@Nano-PFC-1, d) Time-dependent UV-Vis absorbance of DPA only (black), in the presence of PFC-1 (blue), Nano-PFC-1 (pink), and Doxo@PFC-1 (red).

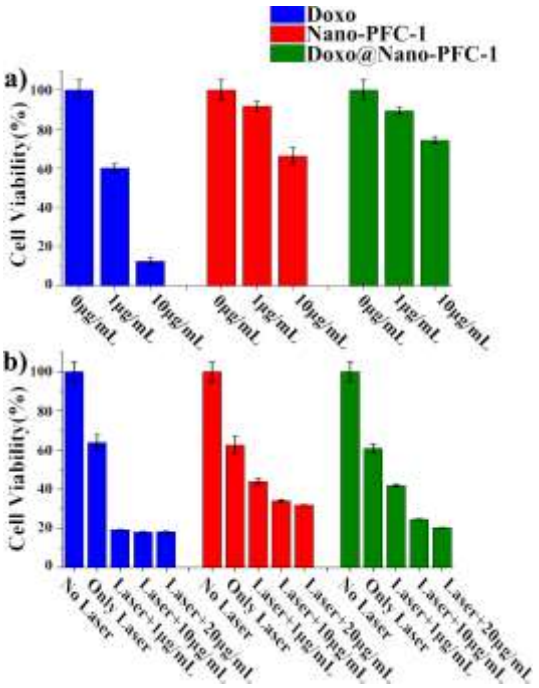

Figure 5. In vitro a) cytotoxicity and b) PDT efficacy of Doxo (blue), Nano-PFC-1 (red), and Doxo@Nano-PFC-1 (green) at various concentrations in Hela cells.

Doxo, Nano-PFC-1 and Doxo@Nano-PFC-1 were incubated with Hela cells to investigate the cooperative therapeutic effects in vitro. As shown in Figure S24, the resulting cells exhibited blue fluorescence from HOFs and red fluorescence from Doxo, indicating efficient internalization of materials. Figure 5a shows that the cell viability drop to 10% for the Doxo group at the concentration of 10 μg/mL. Compared with Doxo drug group alone, Nano-PFC-1 and Doxo@Nano-PFC-1 show much lower cytotoxicity, demonstrating their outstanding biocompatibility. Under the exposure of 400 nm light for 30 minutes, Doxo@Nano-PFC-1 causes the fraction of surviving cell dropped to *ca.* 20.4%, delivering higher therapeutic efficacy than Nano-PFC-1 (31.9% cell survival) and comparable efficacy as commercial Doxo drug (18.3% cell survival) (Figure 5b). These results indicate that PFC-1 would be a promising delivery system for combinational therapy with the advantages of low toxicity and high efficacy.

In summary, an ultra-robust hydrogen-bonded organic framework PFC-1 has been synthesized. The high chemical stability of PFC-1 was attributed to the introduction of multiple hydrogen bonding, the strong π-π interactions and the avoidance of unpaired hydrogen donors/acceptors. We believe that these design principles pave a way for developing robust HOF materials. Moreover, the acid-assistant crystalline redemption discovered in this work offers an inexpensive and facile method to recover the depressed surface area and porosity of HOFs. As a proof of concept, we demonstrated that the photoactive PFC-1 is an excellent drug carrier for synergetic chemo-photodynamic therapy with the merit of low cytotoxicity and high efficacy, representing the first example of HOF materials for multiple therapeutics for cancer.

Acknowledgements

R. C. thanks the National Natural Science Foundation of China (NSFC, Grant 21520102001, 21521061, 21331006, 9162214), Key Research Program of Frontier Science, CAS (QYZDJ-SSW-SLH045). T.-F. L thanks “Strategic Priority Research Program” of the Chinese Academy of Sciences (Grant No. XDB20000000) and NSFC (Grant 21441008). The authors also thank Suzhou NIR-Optics Technology Co. Ltd. for its instrumental and technical supports on the fluorescence imaging and photo-dynamic therapy.

Keywords: Hydrogen-Bonded Organic Frameworks • Structural Stability • π-Stacking Interactions • Singlet Oxygen Generation • Chemo-Photodynamic Therapy.

[1] a) T. Steiner, G. R. Desiraju, The weak hydrogen bond in structural chemistry and biology; OUP: *Oxford, 1999,pp 108-113*; b) A. Bitra, A. Biswas, R. Anand, *Biochemistry*, **2013**, *52*, 8106−8114.

[2] J. Lu, R. Cao, *Angew. Chem. Int. Ed.* **2016**, *55*, 9474-9480.

[3] a) H. Li, M. Eddaoudi, M. O'Keeffe, O. M. Yaghi, *Nature* **1999**, *402*, 276-279; b) S. L. James, *Chem. Soc. Rev.* **2003**, *32*, 276−288; c) H. C. Zhou, J. R. Long, O. M. Yaghi, *Chem. Rev.* **2012**, *112*, 673-674; d) J. Bae, J. W. Jung, H. Y. Park, C. H. Cho, J. Park, *Chem. Commun.* **2017**, *53*, 12100-12103. e) X.-D. Zhu, K. Zhang, Y. Wang, W.-W. Long, R.-J. Sa, T.-F. Liu, and J. Lü, *Inorg. Chem.* **2018**, *57*, 1060–1065.

[4] a) X. C. Huang, Y. Y. Lin, J. P. Zhang, X. M. Chen, *Angew. Chem. Int. Ed.* **2006**, *45*, 1557-1559; b) A. Phan, C. J. Doonan, F. J. Uribe-Romo, C. B. Knobler, M. O'Keeffe, O. M. Yaghi, *Acc. Chem. Res.* **2010**, *43*, 58-67.

[5] a) A. P. Cote, A. I. Benin, N. W. Ockwig, M. O'Keeffe, A. J. Matzger, O. M. Yaghi, *Science* **2005**, *310*, 1166-1170; b) X. Feng, X. Ding, D. Jiang, *Chem. Soc. Rev.* **2012**, *41*, 6010-6022; c) S. Y. Ding, W. Wang, *Chem. Soc. Rev.* **2013**, *42*, 548-568.

[6] a) M. Mastalerz, I. M. Oppel, *Angew. Chem. Int. Ed.* **2012**, *51*, 5252-5255; b) Z.-B. Han, Z.-Z. Xiao, M. Hao, D.-Q. Yuan, L. Liu, N. Wei, H.-M. Yao, M. Zhou, *Cryst. Growth Des.* **2015**, *15*, 531-533; c) I. Hisaki, S. Nakagawa, N. Ikenaka, Y. Imamura, M. Katouda, M. Tashiro, H. Tsuchida, T. Ogoshi, H. Sato, N. Tohnai, M. Miyata, *J. Am. Chem. Soc.* **2016**, *138*, 6617-6628.

[7] a) Y. He, S. Xiang, B. Chen, *J. Am. Chem. Soc.* **2011**, *133*, 14570-14573; b) P. Li, Y. He, Y. Zhao, L. Weng, H. Wang, R. Krishna, H. Wu, W. Zhou, M. O'Keeffe, Y. Han, B. Chen, *Angew. Chem. Int. Ed.* **2015**, *54*, 574-577; c) C. A. Zentner, H. W. Lai, J. T. Greenfield, R. A. Wiscons, M. Zeller, C. F. Campana, O. Talu, S. A. FitzGerald, J. L. Rowsell, *Chem. Commun.* **2015**, *51*, 11642-11645.

[8] H. Wang, B. Li, H. Wu, T. L. Hu, Z. Yao, W. Zhou, S. Xiang, B. Chen, *J. Am. Chem. Soc.* **2015**, *137*, 9963-9970.

[9] F. Hu, C. Liu, M. Wu, J. Pang, F. Jiang, D. Yuan, M. Hong, *Angew. Chem. Int. Ed.* **2017**, *56*, 2101-2104.

[10] a) S. Nandi, D. Chakraborty, R. Vaidhyanathan, *Chem. Commun.* **2016**, *52*, 7249-7252; b) W. Yang, A. Greenaway, X. Lin, R. Matsuda, A. J. Blake, C. Wilson, W. Lewis, P. Hubberstey, S. Kitagawa, N. R. Champness, M. Schroder, *J. Am. Chem. Soc.* **2010**, *132*, 14457-14469. c) J. Lu, C. Perez-Krap, M. Suyetin, N. H. Alsmail, Y. Yan, S. Yang, W. Lewis, E. Bichoutskaia, C. C. Tang, A. J. Blake, R. Cao, M. Schroder, *J. Am. Chem. Soc.* **2014**, *136*, 12828-12831; d) T. H. Chen, I. Popov, W. Kaveevivitchai, Y. C. Chuang, Y. S. Chen, O. Daugulis, A. J. Jacobson and O. Š. Miljanić, *Nat. Commum*, **2014**, 5, 5131.

[11] a) P. Li, Y. He, J. Guang, L. Weng, J. C. Zhao, S. Xiang, B. Chen, *J. Am. Chem. Soc.* **2014**, *136*, 547-549; b) Yasuhiro Aoyama, Masumi Asakawa, Y. Matsui, H. Ogoshi, *J. Am. Chem. Soc.* **1991**, *113*, 6233-6240; d) G. R. Desiraju, *Angew. Chem. Int. Ed.* **1995**, *34*, 2311-2327; c) K. D. Zhang, J. Tian, D. Hanifi, Y. Zhang, A. C. Sue, T. Y. Zhou, L. Zhang, X. Zhao, Y. Liu, Z. T. Li, *J. Am. Chem. Soc.* **2013**, *135*, 17913-17918; d) G. R. Desiraju, *J. Am. Chem. Soc.* **2013**, *135*, 9952-9967; e) R. S. Patil, D. Banerjee, C. Zhang, P. K. Thallapally, J. L. Atwood, *Angew. Chem. Int. Ed.* **2016**, *55*, 4523-4526.

[12] a) B. Kohl, F. Rominger, M. Mastalerz, *Org. Lett.* **2014**, *16*, 704-707; b) B. Kohl, M. V. Bohnwagner, F. Rominger, H. Wadepohl, A. Dreuw, M. Mastalerz, *Chem.Eur. J.* **2016**, *22*, 646-655.

[13] a) A. P. Cote, H. M. El-Kaderi, H. Furukawa, J. R. Hunt, O. M. Yaghi, *J. Am. Chem. Soc.* **2007**, *129*, 12914-12915; b) S. Wan, J. Guo, J. Kim, H. Ihee, D. Jiang, *Angew. Chem. Int. Ed.* **2009**, *48*, 5439-5442.

[14] R. H. Holm, P. Kennepohl, E. I. Solomon, *Chem. Rev.* **1996**, *96*, 2239-2314.

[15] a) K. C. Stylianou, R. Heck, S. Y. Chong, J. Bacsa, J. T. Jones, Y. Z. Khimyak, D. Bradshaw, M. J. Rosseinsky, *J. Am. Chem. Soc.* **2010**, *132*, 4119-4130; b) J. E. Mondloch, W. Bury, D. Fairen-Jimenez, S. Kwon, E. J. DeMarco, M. H. Weston, A. A. Sarjeant, S. T. Nguyen, P. C. Stair, R. Q. Snurr, O. K. Farha, J. T. Hupp, *J. Am. Chem. Soc.* **2013**, 135, 10294-10297.

[16] a) M. X. Wu, Y. W. Yang, *Adv. Mater.* **2017**, *29*; b) C. Song, Y. Zhang, C. Li, G. Chen, X. Kang, Q. Wang, *Adv. Funct. Mater.* **2016**, 26, 4192-4200; c) R. Ruiz-González, P. Milán, R. Bresolí-Obach, J. Stockert, A. Villanueva, M. Cañete, S. Nonell, *Cancers* **2017**, *9*, 18.

[17] a) J. Kagan, Organic Photochemistry: Principles and Applications, San Diego: Academic press, 1993; b) Y. Liu, C. T. Buru, A. J. Howarth, J. J. Mahle, J. H. Buchanan, J. B. DeCoste, J. T. Hupp, O. K. Farha, *J. Mater. Chem. A* **2016**, *4*, 13809-13813.

[18] K. S. Walton, R. Q. Snurr, *J. Am. Chem. Soc.* **2007**, *129*, 8552-8556.

[19] N. J. Silva, F. B. Machado, H. Lischka, A. J. Aquino, *Phys. Chem. Chem. Phys.* **2016**, *18*, 22300-22310.

[20] a) J. Kaplan, *J. Chem. Phys.* **1958**, *28*, 278-282; b) D. Lankhorst, J. Schriever, J. C. Leyte, *Chem. Phys.* **1983**, *77*, 319-340.

[21] J. Zhang, L. Sun, F. Xu, F. Li, H. Y. Zhou, Y. L. Liu, Z. Gabelica, C. Schick, *Chem. Commun.* **2012**, *48*, 759-761.