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A Glass Forming Module for Organic Molecules: Making Tetraphenylporphyrin Lose its Crystallinity

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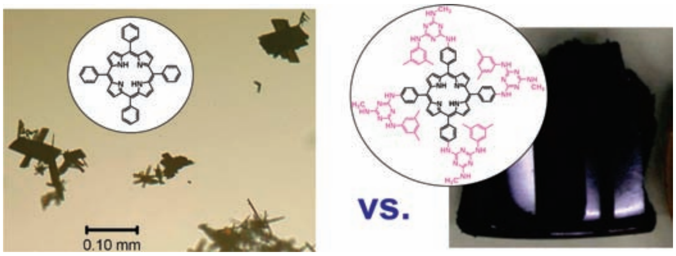
ABSTRACT



Formation of stable glassy phases can be induced through rational design in compounds which otherwise readily crystallize, such as tetraphenylporphyrin, by simple functionalization with moieties known to promote glass formation such as mexylaminotriazine units.

Understanding how molecular structure influences the physical properties of bulk materials is key to unlocking the design of more efficient materials. However, current knowledge does not allow one to reliably predict the properties of materials solely from structure since most properties do not depend solely on the structure of individual molecules but also on how molecules interact with each other in bulk. For these reasons, functional groups which can be strategically introduced on any relevant core compound to modulate their physical properties are extremely valuable, especially when an otherwise inaccessible state of matter can be induced.[1] Such “magic recipes” have been developed to promote the formation of porous crystals,[2] liquid crystals,[3] and glasses[4] with some degree of accuracy.[5]

Recent advances in the design of glass-forming small molecules, called molecular glasses or amorphous molecular materials, in the last 20 years have resulted in the development of compounds with improved properties,[4,6] especially in the context of the two principal issues traditionally enountered with small glass-forming molecules: (1) glassy phases only being accessible upon extremely fast cooling or other special processing techniques and (2) the propensity of small molecules in the glassy phase to revert to their more stable crystalline forms when heated or upon prolonged standing at ambient temperature.[7] Some guidelines have been established for molecular glass design, including nonplanar-

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(1) Michinobu, T.; Nakanishi, T.; Hill, J. P.; Funahashi, M.; Ariga, K. *J. Am. Chem. Soc.* **2006**, *128*, 10384–10385.

(2) (a) Tranchemontagne, D. J.; Mendoza-Cortes, J. L.; O’Keeffe, M.; Yaghi, O. M. *Chem. Soc. Rev.* **2009**, *38*, 1257–1283. (b) Wuest, J. D. *Chem. Commun.* **2005**, 5830. (c) Hosseini, M. W. *Acc. Chem. Res.* **2005**, *38*, 313–323.

(3) 3,4-Dialkoxyphenyl or 3,4,5-trialkoxyphenyl groups with long alkyl chains have been known to induce liquid crystalline behavior since the late 1980s. Meier, H.; Prass, E.; Zerban, G.; Kosteyn, F. *Z. Naturforsch. B: J. Chem. Sci.* **1988**, *43*, 889–896.

(4) For reviews on molecular glasses, see: (a) Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1–25. (b) Yu, L. *Adv. Drug Delivery Rev.* **2001**, *48*, 27–42. (c) Strohriegl, P.; Grazulevicius, J. V. *Adv. Mater.* **2002**, *14*, 1439–1452. (d) Shirota, Y. *J. Mater. Chem.* **2005**, *15*, 75–93. (e) Grazulevicius, J. V. *Polym. Adv. Technol.* **2006**, *17*, 694–696.

(5) (a) Wilson, M. R. *Chem. Soc. Rev.* **2007**, *36*, 1881–1888. (b) Neumann, M. A.; Leusen, F. J. J.; Kendrick, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 2427–2430.

(6) For examples of recent reports, see: (a) Nakano, H.; Takahashi, T.; Tanino, T.; Shirota, Y. *Dyes Pigments* **2010**, *84*, 102–107. (b) Paspirgelyte, R.; Grazulevicius, J. V.; Grigalevicius, S.; Jankauskas, V. *Synth. Met.* **2009**, *159*, 1014–1018. (c) Chien, C.-H.; Kung, L.-R.; Wu, C.-H.; Shu, C.-F.; Chang, S.-Y.; Chi, Y. *J. Mater. Chem.* **2008**, *18*, 3461–3466.

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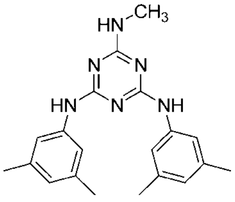
ity, irregular shapes, and conformational ambiguity, and have proved efficient in generating relatively stable glassy materials.[4] Since it is essential to easily access the amorphous state and keep the bulk material amorphous for practical applications involving amorphous materials, the development of more efficient molecular glasses has allowed the use some such compounds in opto-electronic devices including OLEDs with relatively high device lifetimes.[8]

However, the current “state of the art” in glass design is still facing challenges. While an appreciable number of glass-forming compounds that do not recrystallize on heating during T_g measurement have been reported,[9] even stable molecular glasses reported so far eventually crystallize when heated above T_g for extended periods of time. In other fields using different families of glass-forming compounds, in particular amorphous drug formulation, crystallization still constitutes a serious problem for several systems.[10] Furthermore, despite recent advances, it is still currently impossible to predict glass-forming ability and longevity solely from molecular structure; even the most advanced strategies still require some degree of screening to find compounds with the desired glass-forming properties.[11]

For compounds which would be of interest in the amorphous state but cannot intrinsically form glassy phases, strategies to induce glass formation by altering their molecular structure are highly desirable, and while this concept has been demonstrated on compounds such as azobenzene[12] and spiropyran photochromic dyes,[13] there currently exists no ubiquitous glass-inducing moiety that can be introduced efficiently through a straightforward and high-yielding procedure. It must also be noted that care must be taken to modify the preferred physical state of the compound without altering significantly its relevant properties (electronic, opto-electronic, biological, etc.).

Recently, we have developed a series of 4,6-bis(mexylamino)-1,3,5-triazines which can readily form extremely stable glassy phases.[14] Hydrogen bonding has been shown to contribute to the exceptional stability of their glassy phases by producing small aggregates and by limiting molecular reorganization.[15] 2-Methylamino-4,6-bis(mexylamino)-1,3,5-triazine **1**, one of the most stable glass-forming organic compounds developed in our group, has been shown to withstand heating above its T_g for 3 weeks and shearing at rates up to 60000 rpm with no signs of crystallization.[16,17] The mexylaminotriazine unit thus represents a suitable candidate to graft on other compounds because of their formidable glass-forming ability and stability. Since one of the mexyl groups can be substituted with other aryl groups without loss of glassy behavior,[14] it can be assumed that these triazine units can be introduced onto multifunctional compounds through one aryl group to convey the exceptional glass-forming ability of the mexylaminotriazine moiety to the core unit.



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Herein, our strategy for generating molecular glasses was successfully applied to the rational design and synthesis of a mexylamino-substituted derivative of tetraphenylporphyrin (TPP), which is otherwise well-known to readily crystallize to generate a material intrinsically capable of spontaneously forming long-lived glassy phases.

To test this approach toward inducing glassy behavior in more complex molecules, tetraphenylporphyrin derivative **3** was synthesized in 54% yield from tetrakis(4-aminophenyl)porphyrin (**2**)[18] by sequential addition of the corresponding amines on cyanuric chloride in a one-pot procedure (Scheme 1).

Porphyrin **3** readily formed glassy films from solution upon removal of the solvent, and DSC of compound **3** has revealed that it indeed undergoes glass transition at 205 °C, with no crystallization observed upon heating (Figure S1, Supporting Information). In sharp contrast, parent tetraphenylporphyrin melts at 444 °C[19] and undergoes facile crystallization from the melt upon cooling or from solution. Optical micrographs of parent tetraphenylporphyrin and its glass-forming derivative **3** illustrate this difference in solid-state behavior (Figure 1). The amorphous nature of porphyrin **3** was further confirmed by lack of birefringence under polarized light.

To further test the resistance to crystallization of molecular glass **3**, an amorphous sample was submitted to DSC under

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(8) (a) Hancock, B. C.; Zografi, G. *J. Pharm. Sci.* **1997**, *86*, 1–12. (b) Hartel, R. W. *Crystallization in Foods*; Springer: Boston, MA, 2001. (c) Shirota, Y.; Kageyama, H. *Chem. Rev.* **2007**, *107*, 953–1010. (d) Bratton, D.; Ayothi, R.; Deng, H.; Cao, H. B.; Ober, C. K. *Chem. Mater.* **2007**, *19*, 3780–3786.

(9) Typically, a compound is considered to “not crystallize when heated” when no crystallization is observed by DSC during heating at 10 °C/min.

(10) (a) Gao, P. *Mol. Pharmaceutics* **2008**, *5*, 903–904. (b) Gunawan, L.; Johari, G. P.; Shanker, R. M. *Pharm. Res.* **2006**, *23*, 967.

(11) However, T_g can be approximated for compounds of known families by computational methods: (a) Xu, J.; Chen, B. *J. Mol. Model.* **2005**, *12*, 24–33. (b) Yu, X.-L.; Yi, B.; Wang, X.-Y. *J. Theor. Comp. Chem.* **2008**, *7*, 953–963.

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(13) Nagahama, D.; Nakano, H.; Shirota, Y. *J. Photopolym. Sci. Technol.* **2008**, *21*, 755–757.

(14) (a) Lebel, O.; Maris, T.; Perron, M.-È.; Demers, E.; Wuest, J. D. *J. Am. Chem. Soc.* **2006**, *128*, 10372–10373. (b) Wuest, J. D.; Lebel, O. *Tetrahedron* **2009**, *65*, 7393–7402.

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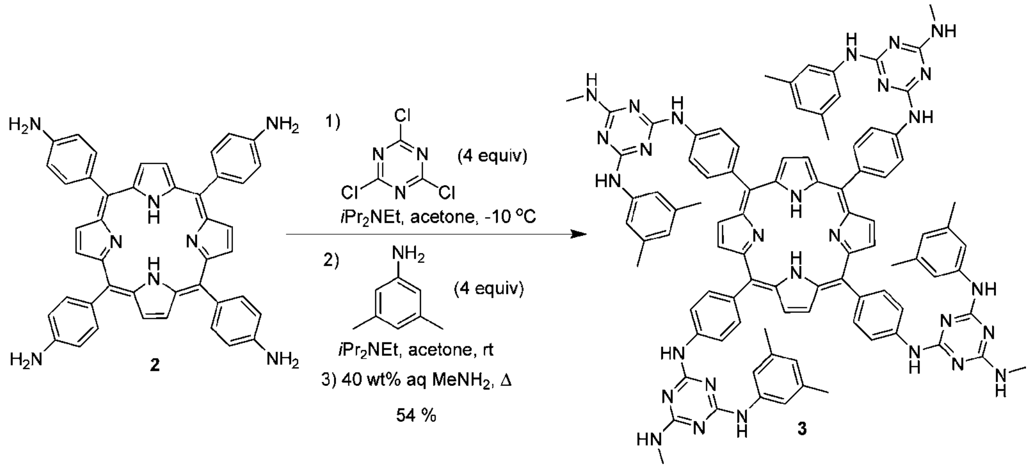
(16) Plante, A.; Mauran, D.; Carvalho, S. P.; Pagé, J. Y. S. D.; Pellerin, C.; Lebel, O. *J. Phys. Chem. B* **2009**, *113*, 14884–14891.

(17) The *N*-ethylamino derivative is even more thermally stable; no crystallization was detected even after 18 months of continuous heating at 120 °C (approximate $T_g + 40$ °C).

(18) Yuasa, M.; Oyaizu, K.; Yamaguchi, A.; Kuwakado, M. *J. Am. Chem. Soc.* **2004**, *126*, 11128–11129.

(19) Bergstresser, T. R.; Paulaitis, M. E. *ACS Symp. Ser.* **1987**, *329*, 138–148.

Scheme 1. Synthesis of Molecular Glass **3**



isothermal heating at 225, 250, and 275 °C for periods of time ranging from 36 to 72 h (Figure S2, Supporting Information), and in each case no crystallization was observed (Figures S3 and S4, Supporting Information).[20] Compound **3** thus shows exceptional resistance toward crystallization, even at temperatures above T_g, in a way similar to that for the related molecular glass **1**.

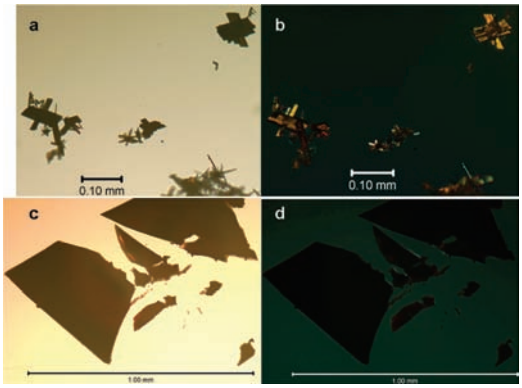


Figure 1. Optical micrographs of tetraphenylporphyrin, under (a) normal and (b) polarized light and of glass-forming porphyrin **3** under (c) normal and (d) polarized light.

The absorption spectrum of glass **3** was recorded in both THF solution and as a solid film and compared to the spectra of both TPP and tetraamino derivative **2**.[21] The absorption peaks are listed in Table 1, and the spectra are reported in Figure S5(Supporting Information). There is a good agreement with previously reported values for TPP and compound **2**, and molecular glass **3** was found to exhibit a spectrum similar to that of porphyrins **1** and **2** in the visible range,[22] with the Soret band and all Q bands red-shifted compared to parent TPP. However, unlike tetraamine **2**, all four Q bands are clearly visible for glass **3**, and the bathochromic shift observed for the Q bands is less pronounced than for compound **2** as a consequence of the presence of the electron-deficient triazine rings which decrease the electron density of the amino groups.

Table 1. Principal Absorption Bands of TPP and Derivatives **2** and **3** in THF Solution and As Solid Films

	compd	Soret (nm)^a	Q^a (nm)			
THF	TPP	417 (22)	513 (1.7)	547 (0.70)	590 (0.45)	646 (0.30)
	2	430 (21)	523 (0.96)	566 (1.3)		661 (0.55)
	3	430 (23)	521 (1.1)	560 (1.3)	598 (0.43)	653 (0.52)
solid	TPP	417	515	550	591	642
	2	438	526	572		663
	3	432	522	561	598	653

^{a} ε (× 10^4 M^{-1} cm^{-1}) are indicated in parentheses for spectra in THF.

In the solid state, the absorption of porphyrin **3** was found to be significantly higher than for the two other compounds, possibly a consequence of the formation of a more uniform film. While the absorption bands of the film of tetraamine **2** were further red-shifted relative to THF solution, no significant changes were observed between the spectra of compound **3** in THF and in the solid state. This could be due to fewer contacts between porphyrin moieties due to the bulk of the mexylaminotriazine units, resulting in a molecular environment closer to that found in solution. The optical band gaps were calculated from the solid-state spectra and reported in Table 2.[23] There is a good agreement with the value for

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(20) Zhou, D.; Zhang, G. G. Z.; Law, D.; Grant, D. J. W.; Schmitt, E. A. *Mol. Pharmaceutics* **2008**, *5*, 927–936.

(21) (a) Fagadar-Cosma, E.; Enache, C.; Tudose, R.; Armeanu, I.; Mosoarca, E.; Vlascici, D.; Costisor, O. *Rev. Chim.* **2007**, *58*, 451–455. (b) Lan, M.; Zhao, H.; Yuan, H.; Jiang, C.; Zuo, S.; Jiang, Y. *Dyes Pigments* **2007**, *74*, 357–362.

(22) In addition, a rather large band attributable to aromatic rings is visible at 270 nm.

(23) The band gaps were calculated with $E = hc/\lambda_{max}$ where λ_{max} is the maximum of the highest wavelength Q-band.

Table 2. HOMO and LUMO Energies for TPP and Porphyrins **2** and **3** Calculated by DFT Calculations (B3LYP, 6-31G*)

compd	HOMO (eV)	LUMO (eV)	HOMO−LUMO gap (eV)[a]
TPP[b]	−4.94	−2.18	2.76 (1.93)
2	−4.44	−1.87	2.57 (1.87)
3	−4.56	−1.98	2.58 (1.90)

[a] Optical band gaps calculated from absorption data in the solid state are indicated in parentheses. [b] Values taken from ref 25.

TPP and values previously reported,[24] and as expected, the band gap for compound **2** is slightly lower than that of TPP, and the value for glass **3** is intermediate between the values for TPP and tetraamine **2**.

The geometries of derivatives **2** and **3** were optimized using DFT calculations with the B3LYP functional and the 6-31G* basis set for both compounds, and the calculated frontier orbitals (shown in Figure S6, Supporting Information) were compared to previously reported results for TPP (Table 2).[25] The HOMO and LUMO energies of both derivatives **2** and **3** were found to be higher than those of parent TPP, but the values for glass **3** are slightly lower than those for compound **2**. The HOMO−LUMO gaps were found to be significantly higher than the values obtained from the absorption spectra for all three compounds, but the trends observed are consistent with those measured experimentally, with the band gap for glass **3** being higher than for TPP but lower than that of tetraamine **2**.

While the electron density within the porphyrin ring system is slightly altered by the presence of the mexylaminotriazine units (Figure S7, Supporting Information), the presence of electron-deficient triazine rings buffers the strong electron-donating effect of the amino groups and their impact is further limited in this case by the nonplanarity of the TPP phenyl groups. For core moieties more sensitive to electronic effects of substituents, it should be possible to prevent such effects through the insertion of alkyl spacers between the core moiety and the mexylaminotriazine units.

In conclusion, we have demonstrated the usefulness of the mexylaminotriazine moiety as a general glass-inducing group which can be easily introduced on desired compounds using a simple procedure to increase their propensity to spontaneously form glassy phases with extremely high resistance to crystallization. This strategy to engineer stable molecular glasses was successfully applied to tetraphenylporphyrin, which is otherwise known to readily crystallize. The strategies developed herein are promising for promoting glass formation through rational design in other compounds used in applications where crystallization is undesirable.

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Supporting Information Available: Experimental procedures, ^{1}H and ^{13}C NMR spectra for molecular glass **3**, DSC thermograms of compound **3**, optical microscopy images and NMR spectra of compound **3** after isothermal heating, absorption spectra of TPP and derivatives **2** and **3**, and frontier orbitals, electrostatic potential maps, and input and output data for DFT calculations on TPP and derivatives **2** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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