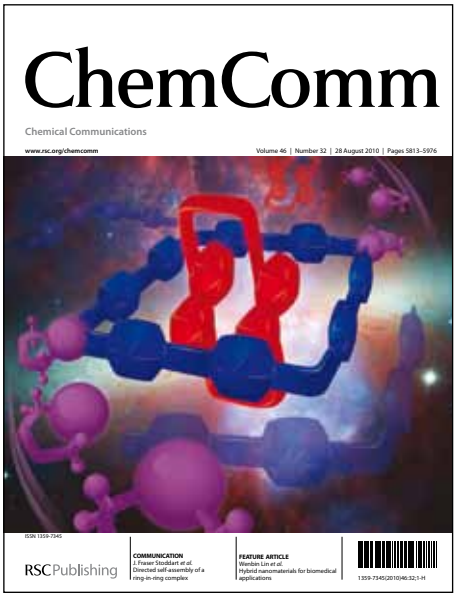
ChemComm

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the RSC Publishing peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, which is prior to technical editing, formatting and proof reading. This free service from RSC Publishing allows authors to make their results available to the community, in citable form, before publication of the edited article. This *Accepted Manuscript* will be replaced by the edited and formatted *Advance Article* as soon as this is available.

To cite this manuscript please use its permanent Digital Object Identifier (DOI®), which is identical for all formats of publication.

More information about *Accepted Manuscripts* can be found in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics contained in the manuscript submitted by the author(s) which may alter content, and that the standard **Terms & Conditions** and the **ethical guidelines** that apply to the journal are still applicable. In no event shall the RSC be held responsible for any errors or omissions in these *Accepted Manuscript* manuscripts or any consequences arising from the use of any information contained in them.

View Online

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Narcissistic self-sorting of hydrogen-bonded dimeric capsules formed through self-assembly of flexible tripodal receptors in polar solvents

Ashutosh S. Singh and Shih-Sheng Sun*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

Purely hydrogen-bonded dimeric capsule formation through self-sorting of three different tripodal receptors having similar size and bearing the same functionality have been reported through dynamic self-assembly in polar solvents.

Controlled formation of discrete compartments with different domains in response to external stimuli by artificial receptors is of paramount significance to mimic biological phenomenon[1] and also to develop system chemistry[2]. Weak intermolecular interactions provide primary tools to achieve the self-sorting process through dynamic self-assembly with good feasibilty and high fidelity.[3] Several elegent examples of H-bonded compartmentalization by self-sorting process have been reported in literature by Böhmer,[4] Isaacs,[3a] Rebek,[5] Schalley,[4b] Sijbesma,[6] and others.[7] However, formation of purely hydrogen-bonded discrete compartments by the self-sorting process in a polar solvent is highly demanded yet a challenging task due to the unfavorable competition from solvation interactions.

Both urea[4,8] and amide[5,9] moieties have been explored in non-polar solvents for the formation of a hydrogen-bonded discrete entity through self-sorting phenomenon. In polar solvents, these two moieties have been explored either with the formation of gel[10] or recently with the formation of micelles.[6] To the best of our knowledge, simple amide functionality based discerete compartmentalization (or capsule formation) in a mixture of competitive components through self-sorting process is not known.

Herein, we report the first example of hydrogen-bonded discrete compartmentalization of three flexible acyclic tripodal receptors having similar size and shape incorporating simple amide moieties on each branch with different substituents at *para* positions of the *N*-terminal aromatic rings (Fig. 1) in polar solvents. Previously, we have shown solvent polarity dependent molecular capsule formation by receptor **1** through dynamic self-assembly where the *nitro* group at *ortho* position of *N*-terminal aromatic ring is mandatory for the self-assembled molecular capsule formation.[11]

Institute of Chemistry, Academia Sinica, 115 Nankang, Taipei, Taiwan, Republic of China Fax: +011-886-2-27831237; Tel: +011-886-2-27898596; E-mail:sssun@chem.sinica.edu.tw

† Electronic Supplementary Information (ESI) available: experimental procedure, characterization data and titration spectra. See DOI: 10.1039/b000000x/

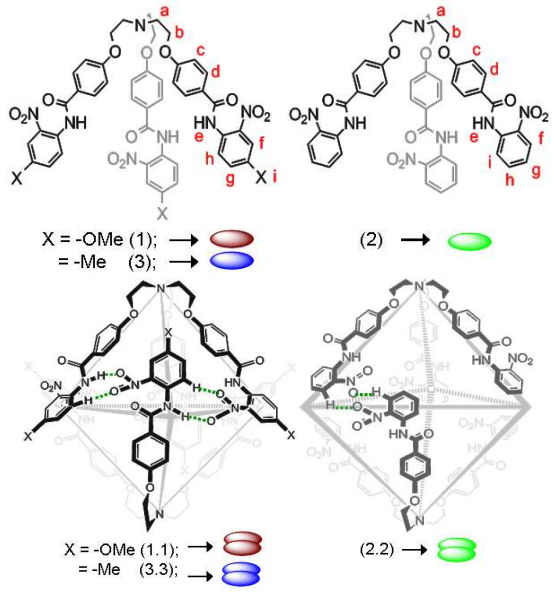


Fig 1. A schematic representation of receptors employed for studies (top) and the topographical representation of binding patterns (bottom) in their corresponding self-assembled capsules.

To explore the effect of substituents on *N*-terminal aromatic ring, receptors **2** and **3** have been synthesized in a similar way as reported previously[11] and their identities were confirmed by high-resolution electrospray ionization mass spectrometry (HRESIMS) and NMR spectra (see supporting information).

The ^{1}H NMR titration spectra of receptor **3** in a DMSO-d_6 solution with gradual addition of $CDCl_3$ showed a similar pattern of peak shifting as observed previously[11] with receptor **1**, indicative of the formation of homo-dimeric capsule (**3.3**). However, a different binding mode was observed for the formation of homodimer (**2.2**). The ^{1}H NMR titration spectra of receptor **2** in a DMSO-d_6 solution with gradual addition of $CDCl_3$ showed a downfield shift of the *meta* C-H protons of *N*-terminal aromatic rings (proton *f* of receptor **2**, see Supplementary Information Fig. S16-S18). In receptor **2**, a nitro group at *ortho* position of the *N*-terminal aromatic ring makes the *meta* position (*ortho* position with respect to the nitro group) electron deficient and thus protons *f* in receptor **2** participate in the intermolecular hydrogen bonds. However, electron donating groups at *para* position for receptors **1** and **3** render the *ortho* positions with respect to the amide groups of

the *N*-terminal aromatic ring the most electron deficient and thus protons *h* of receptors **1** and **3** are most susceptible to the intermolecular hydrogen bonding interactions to form the self-assembled homodimeric capsules (**1.1** and **3.3**). The self-assembled homodimeric capsules were also observed by gradual addition of either acetone-d_6 or CD_3NO_2 into DMSO-d_6 solutions of receptors **1**, **2** and **3**, as confirmed by their corresponding titration spectra and positive mode HRESI mass spectra (Fig. S14-S15, S17-S18, and S20-S21). No solvent molecules were identified encapsulated in these self-assembled homodimeric capsules as evidenced by HRESI mass spectra. Evaporation of the volatile solvent from solution mixture brought the spectrum back to the original one recorded in DMSO-d_6, which demonstrates the reversibilty of capsule formation. These experiments suggested individual dimeric capsule formation in their respective polar solvents although their binding patterns along the seam of capsule are different, which depends upon the electronic nature of *N*-terminal aromatic ring (see Fig. 1 and Fig. S30).

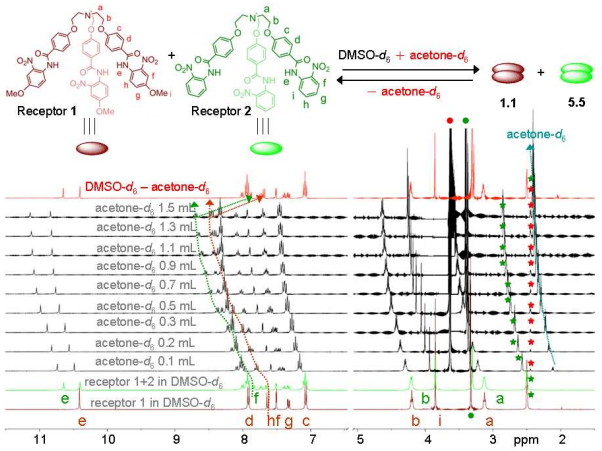


Fig. 2 Two-component self-sorting: ^{1}H NMR (400 MHz, 30 ºC) titration spectra of receptors **1** and **2** in a 1:1 ratio (6.25 mM each) in a DMSO-d_6 solution upon addition of varying amount of acetone-d_6. After partial evaporation of acetone-d_6, the resulting spectra (in red color) merged to the original one recorded in DMSO-d_6. Star marks in green and red colors in spectra represent peaks for DMSO-d_6 solvent and from internal reference in TMS, respectively. Circle marks in green and red colors represent the residual water peaks from deuterated solvents.

Inspired from these results, we envisaged the possiblity of co-existence of both types of capsules in the same mixture solution with a self-sorting behavior. The ^{1}H NMR spectra of an equimolar mixture solution (6.25 mM) of receptors **1** and **2** as well as an equimolar mixture solution (6.25 mM) of receptors **2** and **3** in DMSO-d_6 displayed well resolved peaks for amide N-Hs and aromatic protons (see Fig. 2 and Fig. S31-S32). A similar observation was noted for an equimolar mixture solution of receptors **1** and **3** (Fig. S33). Upon titration of the DMSO-d_6 mixture solution of receptors **1** and **2** with $CDCl_3$ (Fig. S34), the peaks for amide N-H protons and aromatic proton *h* of receptor **1** and proton *f* of receptor **2**, respectively, responsible for hydrogen bonding along the seam of capsules **1.1** and **2.2**, shifted downfield in a similar way to their individual solutions (see Fig. S13 and S16) without appearance of any new peak. After partial evaporation of $CDCl_3$, the corresponding peak of resulting spectra (shown in red color, Fig. S34) alomost merged to the parent spectra, indicative of reversibility of capsule formation. The similar observation noted upon titration of equimolar mixture solution of receptors **1** and **2** in DMSO-d_6 with gradual increasing amount of acetone-d_6 (Fig. 2). After partial evaporation of acetone-d_6, peaks of the resulting spectrum merged to the original one. Similar observations noted in titration spectra of other two-component systems (receptors **1** with **3** and receptors **2** with **3**, see Fig. S35-S38).

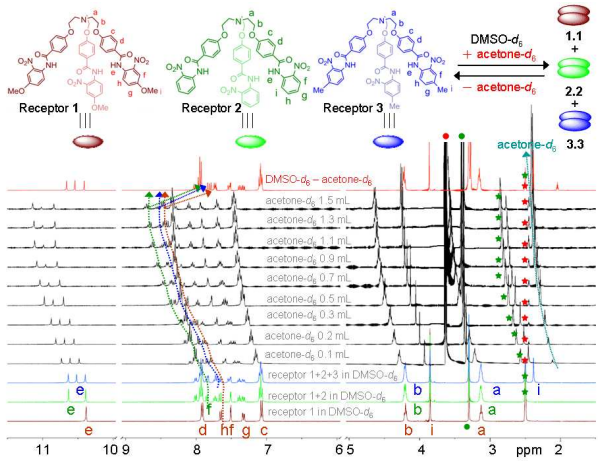


Fig. 3 Three-component self-sorting: ^{1}H NMR (400 MHz, 30 ºC) titration spectra of receptors **1, 2** and **3** (in a 1:1:1 ratio, 6.25 mM each) in a DMSO-d_6 solution upon addition of varying amount of acetone-d_6. After partial evaporation of acetone-d_6, the resulting spectra (in red color) merged to the original one recorded in DMSO-d_6. The color marks are defined the same as those shown in Fig. 2.

The present studies were further elaborated for the three-component system. An equimolar mixture of all the three receptors **1**, **2**, and **3** in DMSO-d_6 also showed well resolved peaks for amide N-H and aromatic protons (Fig. 3 and Fig. S39). Upon titration of DMSO-d_6 solution containing a mixture of the three receptors **1**, **2** and **3** with gradual increasing amount of $CDCl_3$, a similar pattern of peak shifting for amide N-Hs as well as for aromatic protons without appearance for any new peaks observed (Fig. 3, top). After partial evaporation of $CDCl_3$, the resulting spectrum essentially superimposed to the original one, indicative of the reversible conversion of respective capsules in the mixture solution. The smililar observations were also noted for titrations carried out in polar solvents like acetone-d_6 (Fig. 2, bottom).

The affinity for self-recognition (*narcissistic self-sorting*)[3b,12] between the individual receptor components is remarkable. The titration spectra showed no appearance of any new peak and the patterns of peak shifting were similar to that of an equimolar mixture in both $CDCl_3$ (Fig. 4 and S41) and acetone-d_6 (Fig. S40-S41) even with increasing one component to five-fold excess. Furthermore, after partial evaporation of $CDCl_3$ or acetone-d_6, the resulting spectra merged to that of original ones, showing hydrogen-bonded self-assembled capsule formation through *narcissistic self-sorting* process with high fidelity in a polar solvent.

In conclusion, in contrast to the basic molecular recognition codes (size and shape) generally reported for self-sorting

process,[3b] we have disclosed unique examples of *narcissistic self-sorting* by highly flexible acyclic tripods possessing similar size and shape with the same functionality appended on each branch. Both receptors **1** and **3** having electron donating groups on *N*-terminal aromatic rings and the same binding motifs for seaming along the curvature for self-assembled capsule formation, The degree of electron donating ability (intrinsic information coded in the molecule) of these receptors that results in different binding modes of the cooperative hydrogen bonding interactions in the subsequent capsule formation can be expressed with high fidelity in polar solvents. Hence, it is viable to achieve the selective recognition and separation of guest molecules through the present approach and the related research is currently underway for detail studies.

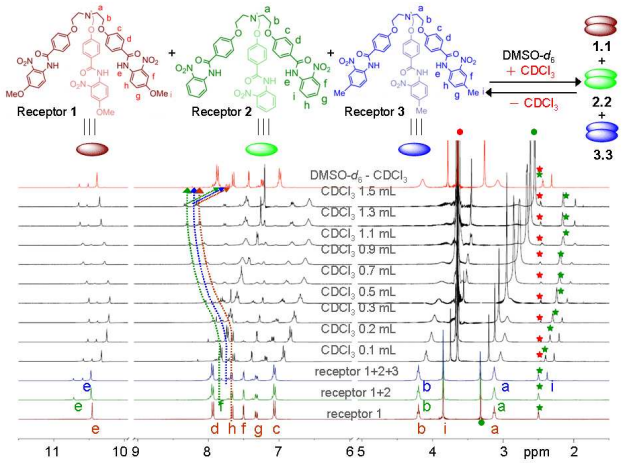


Fig. 4 Three-component self-sorting: ^{1}H NMR (400 MHz, 30 ºC) titration spectra of receptors **1,** (31.3 mM) **2** (6.25 mM) and **3** (6.25 mM) in a DMSO-d_6 solution upon addition of varying amount of $CDCl_3$. After partial evaporation of $CDCl_3$, the resulting spectrum (in red color) merged to that of original one recorded in DMSO-d_6. The color marks are defined the same as those shown in Fig. 2.

We are grateful to the National Council of Taiwan (Grant No 100-2628-M-001-002-MY3) and Academia Sinica for support of this research. A.S.S. thanks the postdoctoral fellowship sponsored by the National Science Council of Taiwan (Grant No 100-2811-M-001-090). Mass spectrometry analyses were performed by Mass Spectrometry facility of the Institute of Chemistry, Academia Sinica.

Notes and references

1 M. Edidin, *Nat. Rev. Mol. Cell. Biol.* 2003, **3**, 414-418.

2 (a) J.-M. Lehn, *Chem. Eur. J.* 2000, **6**, 2097-2102; (b) M. Kindermann, I. Stahl, M. Reimold, W. M. Pankau and von Kiedrowski, *Angew. Chem. Int. Ed.* 2005, **44**, 6750-6755; (c) R. F. Ludlow and S. Otto, *Chem. Soc. Rev.* 2007, **37**, 101-108; (d) V. E. Campbell, X. De Hatten, N. Delsuc, B. Kauffmann, I. Huc and J. R. Nitschke, *Nature Chem.* 2010, **2**, 864-867.

3 (a) A. Wu and L. Isaacs, *J. Am. Chem. Soc.* 2003, **125**, 4831-4835; (b) M. M. Safont-Sempere, G. Fernández and F. Würthner, *Chem. Rev.* 2011, **111**, 5784-5814 and references therein.

4 (a) D. Braekers, C. Peters, A. Bogdan, Y. Rudzevich, V. Böhmer and J. F. Desreux, *J. Org. Chem.* 2008, **73**, 701-706; (b) Y. Rudzevich, V. Rudzevich, F. Klautzsch, C. A. Schalley and V. Böhmer, *Angew. Chem. Int. Ed.* 2009, **48**, 3867-3871.

5 (a) D. Ajami, M. P. Schramm, A. Volonterio and J. Rebek, Jr. *Angew. Chem. Int. Ed.* 2007, **46**, 242-244; (b) D. Ajami, J.-L. Hou, T. J. Dale, E. Barrett and J. Rebek, Jr. *Proc. Natl. Acad. Sci. USA* 2009, **106**, 10430-10434.

6 (e) A. Pal, S. Karthikeyan and R. P. Sijbesma, *J. Am. Chem. Soc.* 2010, **132**, 7842-7843; (f) A. Pal, P. Besenius and R. P. Sijbesma, *J. Am. Chem. Soc.* 2011, **133**, 12987-12989.

7 (a) D. L. Caulder and K. N. Raymond, *Angew. Chem. Int. Ed.* 1997, **36**, 1440-1442; (b) Y. G. Ma, S. V. Kolotuchin and S. C. Zimmerman, *J. Am. Chem. Soc.* 2002, **124**, 13757-13769; (c) A. D. Shaller, W. Wang, H. Y. Gan and A. D. Q. Li, *Angew. Chem. Int. Ed.* 2008, **47**, 7705-; (d) B. H. Northrop, Y. R. Zheng, K. W. Chi and P. J. Stang, *Acc. Chem. Res.* 2009, **42**, 1554-1563.

8 M. Chas, G. Gil-Ramírez, E. C. Escudero-Adán, J. Benet-Buchholz and P. Ballester, *Org. Lett.* 2010, **12**, 1740-1743.

9 (a) A. Wu, A. Chakraborty, J. C. Fettinger, R. A. Flowers II and L. Isaacs, *Angew. Chem. Int. Ed.* 2002, **41**, 4028-4031; (b) S. Ghosh, A. Wu, J. C. Fettinger, P. Y. Zavalij and L. Isaacs, *J. Org. Chem.* 2008, **73**, 5915-5925; (c) A. Matsuzawa, A. Nojiri, N. Kumagai and M. Shibasaki, *Chem. Eur. J.* 2010, **16**, 5036-5042.

10 (a) A. Brizard, M. Stuart, K. van Bommel, A. Friggeri, M. de Jong and J. Van Esch, *Angew. Chem. Int. Ed.* 2008, **47**, 2063-2066; (b) J. R. Moffat and D. K. Smith, *Chem. Commun.* 2009, 316-318; (c) A. Das, M. R. Molla, A. Banerjee, A. Paul and S. Ghosh, *Chem. Eur. J.* 2011, **17**, 6061-6066.

11 (a) A. S. Singh, B.-Y. Chen, Y.-S. Wen, C. Tsai and S.-S. Sun, *Org. Lett.* 2009, **11**, 1867-1870; (b) A. S. Singh and S.-S. Sun, *Chem. Commun.* 2011, **47**, 8563-8565; (c) A. S. Singh and S.-S. Sun, *J. Org. Chem.* 2012, **77**, 1880-1890.

12 (a) R. Kramer, J.-M. Lehn and A. Marquis-Rigault, *Proc. Natl. Acad. Sci. U.S.A.* 1993, **90**, 5394-5398; (b) L. Avram and Y. Cohen, *J. Am. Chem. Soc.* 2004, **126**, 11556-11563; (c) E. S. Barrett, T. J. Dale and J. Rebek, Jr., *J. Am. Chem. Soc.* 2008, **130**, 2344-2350.