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Polymers with quadruple hydrogen-bonding end groups: controlling molecular weight using a small molecule photoswitch†

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The molecular weight and topology of polymer chains is typically defined during their synthesis, after which these parameters remain fixed. This limitation has motivated efforts to develop reversibly reconfigurable polymers, which offer opportunities for advanced applications and/or efficient reprocessing. Herein, we report the preparation of a library of poly(methyl acrylate) (PMA) homopolymers and a poly(methyl methacrylate) (PMMA) homopolymer bearing pendant hydrogen bonding motifs (HBMs) which have the potential to generate reconfigurable materials. This approach includes the synthesis of alkyne-functional HBMs which were successfully coupled to an azide-functionalised RAFT agent *via* alkyne/azide "click" chemistry. The resulting ureidopyrimidinone (UPy) and amidonaphthyridine (NAP) RAFT agents could successfully be used to prepare PMA, but the attempt using the diamidonaphthyridine (DAN) RAFT agent was unsuccessful. In this example, a post-polymerisation technique was demonstrated as a viable alternative (in this case with a PMMA homopolymer). To demonstrate proof-of-concept that this can be achieved using a supramolecular approach: a small molecule photoswitch comprising ditopic azobenzene linked ureidopyrimidinone (UPy) was shown to effect reconfiguration of polymer molecular weight of DAN-functionalised PMMA under visible/UV light irradiation. In the *cis* (*Z*) photostationary state, intramolecular UPy·UPy homodimerization within the photoswitch was preferred, whereas in the *trans* (*E*) configuration, the need for UPy to satisfy its hydrogen-bonding requirements resulted in intermolecular DAN·UPy heterodimerization with the DAN motif of poly(methyl-methacrylate) resulting in a doubling of its molecular weight as observed by ^{1}H DOSY NMR spectroscopy.

Introduction

Supramolecular polymers have had significant impact in materials research,[1,2] spanning a range of applications[3] that include: self-healing,[4,5] adhesives,[6–8] biomaterials,[9,10] actuating and memory materials.[11–13] Hydrogen-bond assembled polymers[14] have proven attractive given the availability of a range of hydrogen-bonding motifs (HBMs);[14,15] when hydrogen-bond donor and acceptor groups are combined to give patterns, this leads to sequence selective recognition modules with a range of dimerization affinities[14] that directly influence macromolecular behaviour.[16–18] In solution, polymers assembled through main chain hydrogen-bonds require high affinity HBMs,[19] whereas weaker affinities can be accommodated where hydrogen-bonds between side chains are used for assembly[20–22] or hydrogen-bonds are used for crosslinking. A specific category amongst the former class, are those which involve assembly *via* a single HBM at the chain end of the polymer and which have been used to prepare *e.g.* diblock copolymers[23] which phase separate.[24] Indeed, the topology of a polymer plays a key role in determining its shape, which in turn must be considered for different applications, however, polymer topology is usually static once synthesis is complete and has motivated efforts to generate reconfigurable polymers.[25] Thus, the ability to readily reconfigure polymers assembled through HBMs at the chains ends would be desirable, but is not yet readily achievable. Amongst available stimuli *e.g.* temperature, pH, redox control and light, light is attractive.[26–29] Indeed, a number of light responsive hydrogen-bond assembled supramolecular "condensation" and side-chain functionalized polymers have been described.[30–36] We

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recently reported on the photoswitchable hydrogen-bond mediated assembly of ditopic azobenzene linked HBMs;[37] the *cis* (*Z*) and *trans* (*E*) photostationary states were shown to be biased toward cyclic or extended conformations leading to different supramolecular assemblies based on the concentration dependent ring-chain equilibrium and varying hydrogen-bond dimerization affinity of the HBMs.

In this manuscript we synthesise a series of poly(methyl acrylate) and poly(methyl methacrylate) (PMA and PMMA) homopolymers, end-functionalised with HBMs using alkyne/azide "click" chemistry. This was facilitated using a commercially available azide functional RAFT agent, combined with alkyne functionalized HBMs reported in our previous work.[37] To develop a photoresponsive reconfigurable polymer, PMMA bearing a single terminal DAN HBM[38] was mixed with a ditopic azobenzene linked ureidopyrimidine (UPy) HBM.[39] By switching between *E* and *Z* photostationary states using visible light at a concentration below the supramolecular polymerization regime of the ring-chain equilibria for the ditopic azobenzene linked UPy HBM, we show that the molecular weight of the polymer bearing a single terminal diamidonapthyridine (DAN) HBM can be reversibly doubled through multiple cycles of photoswitching.
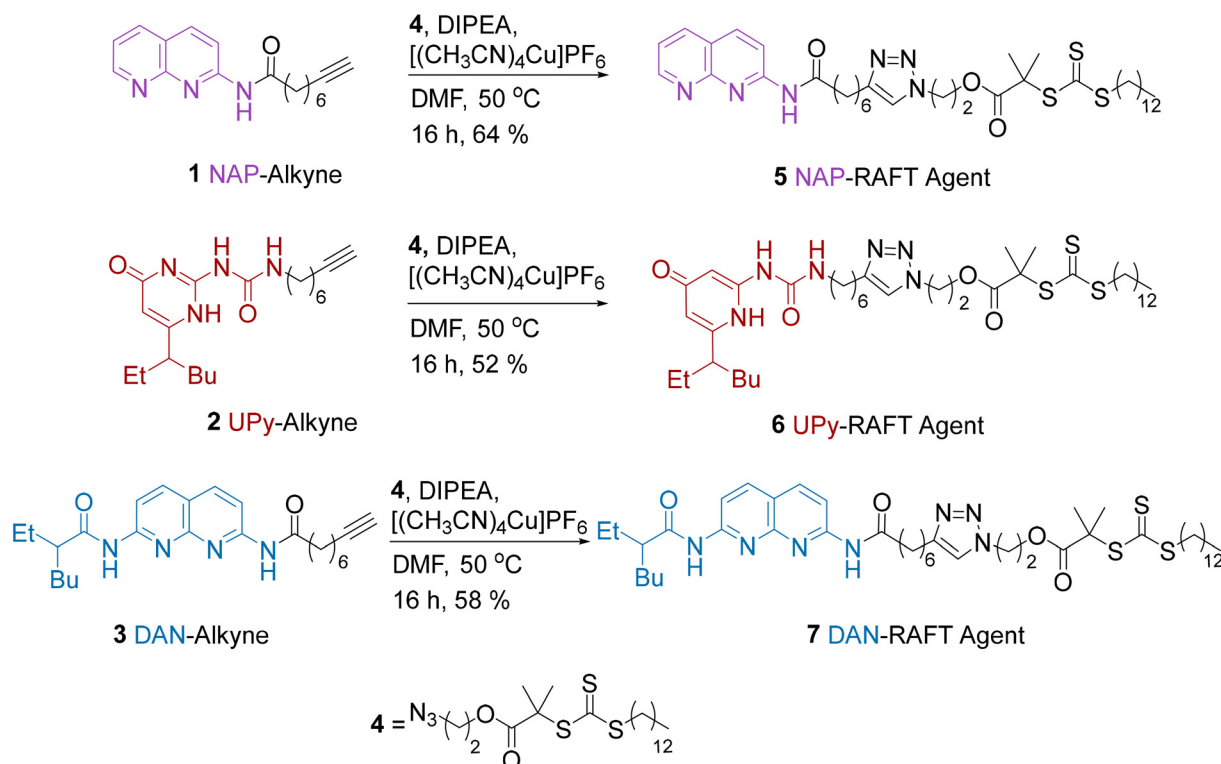
Results and discussion

It was anticipated that the most efficient route for the preparation of PMA end-functionalised with HBMs was *via* either a pre-polymerisation functionalisation or post-polymerisation functionalisation. The pre-polymerisation approach, by employing HBM-functional RAFT agents was initially preferred on the basis that all chains bear the HBM. Although this would be possible with the post-polymerization approach, there is the potential for incomplete reaction, which is likely to be exacerbated by the steric hindrance of the long polymer chains.
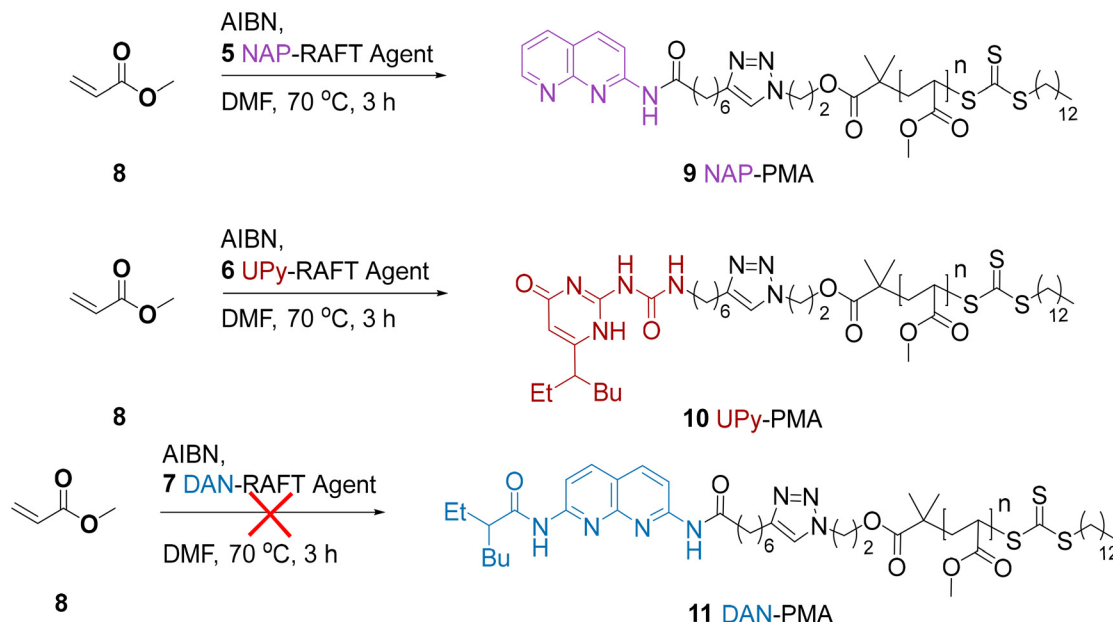
For the pre-polymerisation strategy, we identified a series of alkyne-functional HBMs from our previous work which could be reacted with an azide-functionalized RAFT agent *via* an alkyne/azide click reaction (Scheme 1). This resulted in a series of CTAs where alkynes **1**, **2** and **3** were linked to azide functionalised RAFT agent **4** by a triazole ring. Using this approach amidonaphthyridine (NAP)-RAFT agent **5**, UPy-RAFT agent **6** and DAN-RAFT agent **7** were all successfully synthesised in reasonable yields. The ability of **5**–**6** to serve as chain transfer agents was then assessed for the RAFT polymerization of MA (Scheme 2).

GPC and ^{1}H NMR analysis conducted on the resulting products (Table 1 and Fig. 1) indicated that the NAP-RAFT agent **5** produced reasonably low dispersity polymer **9** ($Đ$ = 1.19) but monomer conversion was only 31% after three hours. This suggested that the addition of the NAP HBM had an adverse impact on polymerisation. More promising was the UPy-RAFT agent **6**, which afforded reasonably low dispersity polymers ($Đ$ = 1.18) alongside a much more respectable monomer conversion of 84%. However, the resulting UPy functionalized

Scheme 1 Click chemistry syntheses of NAP-RAFT agent **5**, UPy-RAFT agent **6** and DAN-RAFT agent **7**.

Scheme 2 RAFT polymerisations of MA **8** using NAP–RAFT agent **5**, UPy–RAFT agent **6**, and DAN–RAFT agent **7**.

Table 1 Data from polymerisations of MA **8** using RAFT agents **5**, **6** and **7**. GPC was obtained in DMF eluent, M_n and $Đ$ were calculated based on a series of near-monodispersie poly(methyl methacrylate) standards

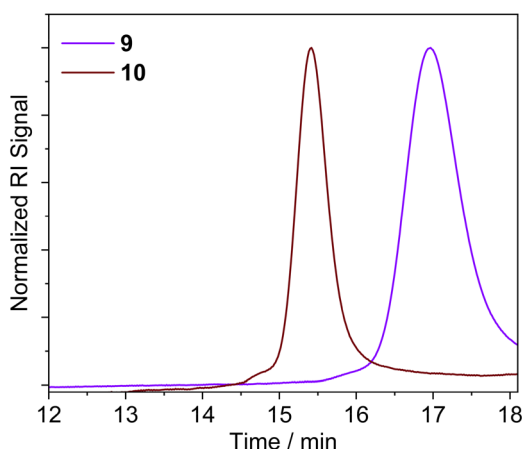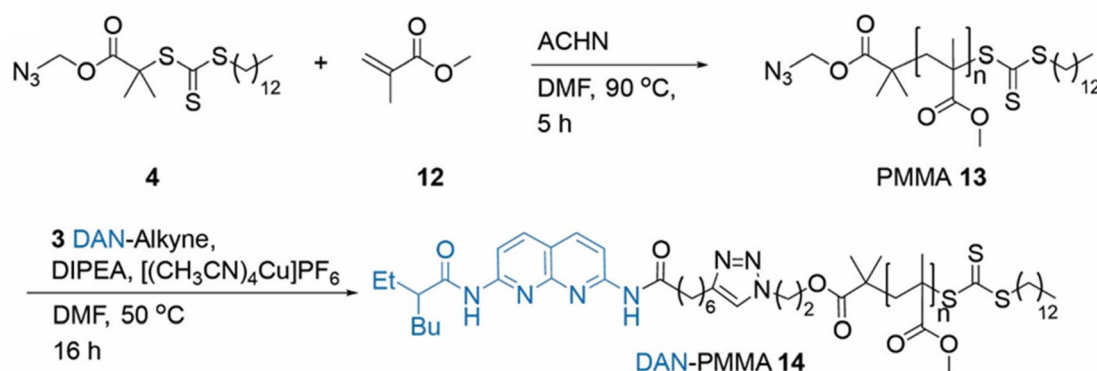| Raft agent	% MA conver.	DP	M_n (NMR) (g mol^{-1})	M_n (GPC) (g mol^{-1})	$Đ_{(GPC)}$
5	31	24	2800	3700	1.19
6	84	148	13 500	18 200	1.18
7	—	3	1100	—	—

Fig. 1 GPC traces of NAP–PMA **9**; and UPy–PMA **10** obtained in DMF.

polymer **10**, was considered less desirable for reconfiguring, given the self-dimerization of the UPy motif. Unfortunately, the DAN–RAFT agent **7** failed to control the MA polymerization, with negligible conversion indicated by NMR.

Given our objective to switch molecular weight using a small molecule, it was desirable to have a polymer functionalized with an HBM, such as DAN, that does not self-associate. Hence, we instead evaluated the use of post-polymerisation functionalization. Furthermore, we also moved to methyl methacrylate (MMA) instead of MA owing to the latter polymers being challenging to purify due to their low T_g. In principle, the behaviour of PMMA and PMA in solution should be similar enough to allow for proof-of-concept reconfiguration experiments to be explored.

The polymerization of MMA was conducted in DMF in the presence of the azide functionalised RAFT agent **4**. The azide group was maintained in the resulting PMMA **13**, allowing for an azide click reaction to be performed using the DAN-alkyne **3** (Scheme 3). Due to RAFT agent **4** being less suited for polymerisation of MMA, the polymers synthesised had a higher dispersity than those obtained with MA (Table 2 and Fig. 1); the trithiocarbonate RAFT was not ideal for controlling the polymerization of methacrylate monomers, resulting in a larger molar mass dispersity of 1.52 compared to values <1.20 recorded for the acrylate monomers. After functionalization with DAN, GPC (Fig. 2) indicated that the M_n increased from 24 600 g mol^{-1} for **13** to 31 200 g mol^{-1} for **14** On first appearance, this increase seems large for a simple end-group functionalization, but it is unsurprising given the additional purification performed after functionalisation involved a size exclusion column which would have also resulted in the removal of some of the shorter polymer chains in the sample (which also resulted in subtle reduction in molar mass dispersity). Analyses by NMR were more challenging; whilst conversion and some structural data could be obtained it was not possible to perform end group analysis

Scheme 3 Synthesis of PMMA **13** using azide RAFT agent **4** and post-polymerisation azide click reaction producing DAN–PMMA **14**.

Table 2 Monomer conversion (recorded by ^{1}H NMR) and Mn and Đ (recorded by DMF GPC) for polymerisation of PMMA **13** and post-polymerisation functionalised DAN–PMMA **14**

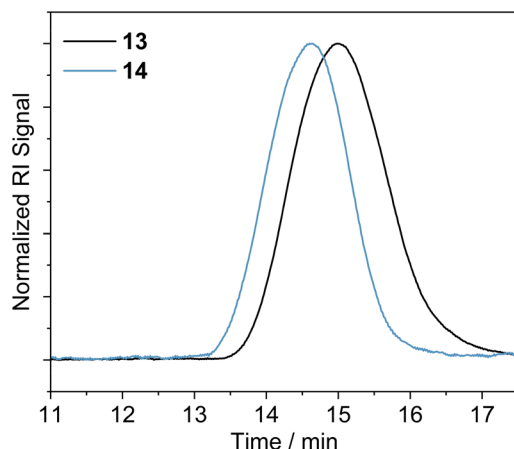| Polmyer	% MMA conver.	M_n (GPC) (g mol^{-1})	$Đ_{(GPC)}$
13	99	24 600	1.52
14	—	31 200	1.32

Fig. 2 GPC traces of PMMA **13** (pre-functionalisation); and DAN–PMMA **14** (post-functionalisation) obtained in DMF.

due to overlapping RAFT agent and polymer proton resonances (see ESI for further details†). Nevertheless, it was deemed sufficiently modified to continue proof-of-concept studies.

To develop a photoresponsive reconfigurable polymer system, DAN-PMMA polymer **14** was mixed with supramolecular synthon **15** (Fig. 3a) comprising ditopic azobenzene linked UPy species where the UPy is capable of forming quadruply hydrogen-bonded UPy·UPy homodimers through self-association or DAN·UPy heterodimers.[37] We hypoth-

esized that as a consequence of preferential intramolecular cyclization (as shown previously),[37] Z-**15** would show limited interaction with DAN-PMMA **14**, but that upon photoisomerization to give E-**15**, intermolecular dimerization would be suppressed in favour of chain extension permitting interaction between DAN-PMMA **14** and E-**15**. Such a change would be anticipated to result in a change in molecular weight of the polymer, effectively doubling the size of each chain *via* central hydrogen bonded linkages. This size change would result in a reduction in diffusion coefficient in the solution, meaning DOSY NMR would provide an ideal tool to assess this behaviour. We previously established a critical concentration of ~24 mM for the ring chain equilibrium for **15** in chloroform. Therefore to limit supramolecular polymer formation by **15**, samples of DAN-PMMA **14** and **15** prepared at lower concentrations (8 mM and 4 mM respectively). At a concentration of 4 mM, DOSY measurements on **15**, indicate it adopts a cyclic monomer in the E form and tends towards a cyclic dimer in the Z form as previously published.[37] Samples were first exposed to green light (530 nm) for 10 minutes to maximize the concentration of Z isomer (photostationary state, 530 nm = 71 : 29 Z : E), then DOSY NMR was performed (Fig. 3c). This process was repeated after exposure to blue light (405 nm) for 10 minutes to maximize the concentration of E isomer (photostationary state at 405 nM = 23 : 73, Z : E, Fig. 3b). A reduction in diffusion coefficient was observed after blue light irradiation, to confirm this behaviour was reversible, irradiation was performed using each wavelength again, and DOSY spectra recorded. The data obtained showed good evidence of a reversible change in diffusion coefficient upon irradiation (Fig. 3c and d). When converted to molecular weight it became clear that the species approximately doubles in size after blue light irradiation (Fig. 3d). Using the diffusion co-efficient and the Stokes Einstein relationship we estimated a hydrodynamic radius (r_s) for the assembly of DAN-PMMA **14** in the presence of Z-**15** ~34 nm and (E-**15**) ~43 nm.
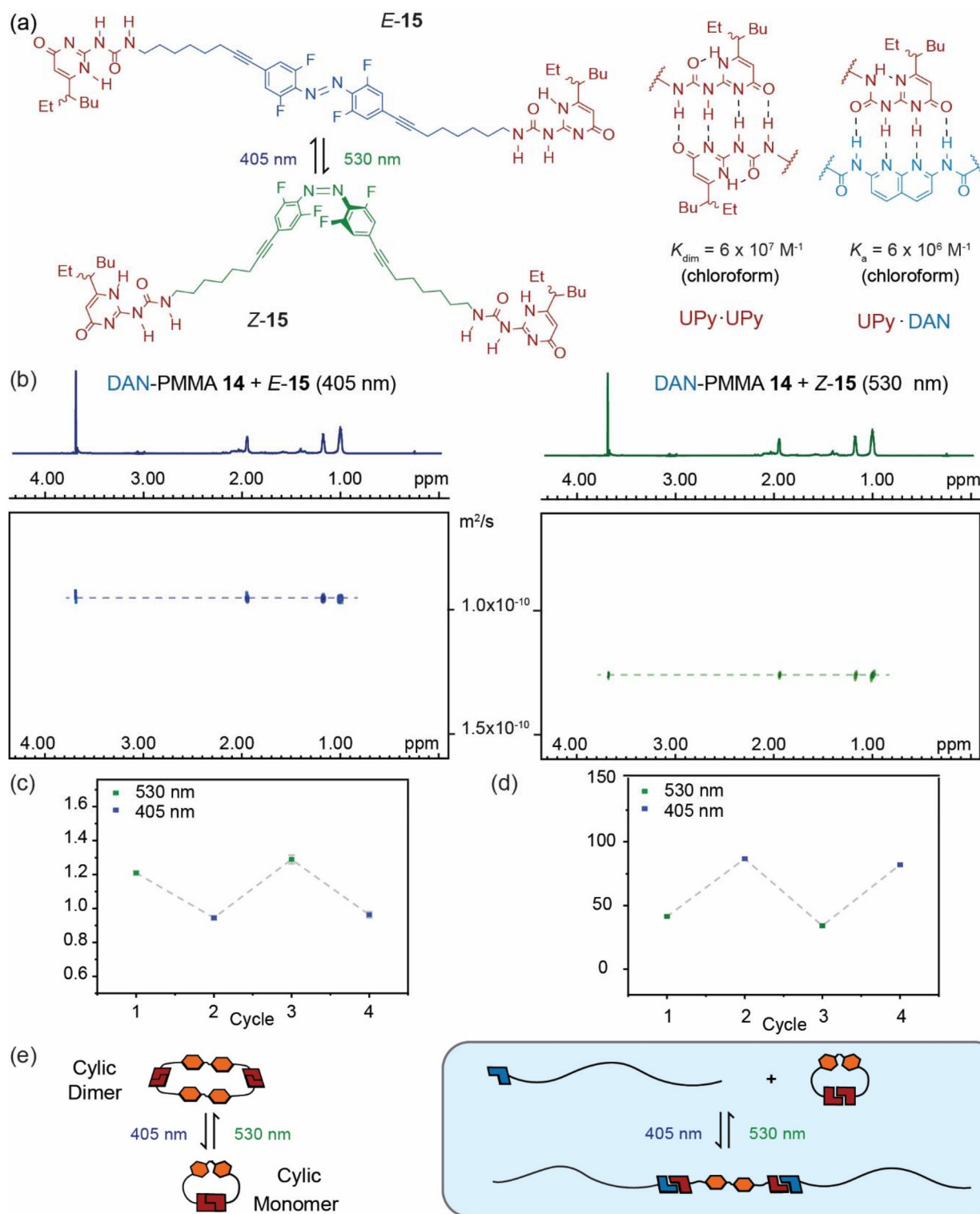
Fig. 3 Controlling polymer weight using a hydrogen-bonding photoswitch: (a) structure of *E*- and *Z*-**15** alongside structures and affinities of UPy·UPy homodimer and UPy·DAN heterodimer (b) DOSY spectra for DAN-PMMA **14** and **15** after irradiation at 405 nm (blue) and 530 nm (green); (c) diffusion coefficient of DAN-PMMA **14** and **15** after 2 cycles of green and blue light irradiation; (d) molecular weight of DAN-PMMA **14** and UPy·UPy foldamer **15** after 2 cycles of green and blue light irradiation; (e) schematic illustrating reversible rearrangement of **15** in the absence and presence of DAN-PMMA **14** in response to blue and green light.

Conclusions

In this work, we successfully synthesised a range of RAFT agents by reacting alkyne functionalised NAP, UPy and DAN precursors with an azide functional RAFT agent by alkyne/azide click chemistry. The resulting NAP and UPy RAFT agents were successfully used for the RAFT polymerisation of methyl acrylate, yielding low molar mass dispersity polymers. However, neither reached 100% conversion, with the NAP only reaching 31%. Despite this, each polymer was successfully purified, resulting in polymers with terminal NAP and UPy functionalities (9 and 10). On the contrary, the attempt to polymerise MA with the DAN functionalised RAFT agent was unsuccessful, with no conversion obtained. However, in this case polymers bearing terminal HBMs could be obtained by post polymerization addition of the DAN to poly(methyl-methacrylate) to give 14.

We then demonstrated that a DAN-terminated poly(methyl-methacrylate) 14 could undergo a reversible change in molecular weight upon photoisomerization of Z-15 to E-15. This was due to the ability of Z-15 to readily cyclize through homodimerization of its UPy motif and the preference for E-15 to satisfy the hydrogen-bonding requirements of its UPy through intermolecular heterodimerization with the DAN motif of 14. Such behaviour represents a first step in being able to reversibly reconfigure polymer architecture and subsequent assembly; for instance, our future studies will be geared towards photoswitchable reconfigurations that lead to diblock formation and subsequent phase separation.

Author contributions

N. J. W. and A. J. W. conceived and designed the research program, E. M. H and Y. J. designed studies and performed the research. The manuscript was written by A. J. W. and edited into its final form by N. J. W. and A. J. W. with contributions from all authors.

Data availability

All relevant data are included in the ESI.†

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

References

1 T. Aida, E. W. Meijer and S. I. Stupp, *Science*, 2012, **335**, 813–817.

2 L. Yang, X. Tan, Z. Wang and X. Zhang, *Chem. Rev.*, 2015, **115**, 7196–7239.

3 L. R. Hart, J. L. Harries, B. W. Greenland, H. M. Colquhoun and W. Hayes, *ACS Appl. Mater. Interfaces*, 2015, **7**, 8906–8914.

4 Y. Chen and Z. Guan, *Chem. Commun.*, 2014, **50**, 10868–10870.

5 Y. Yang and M. W. Urban, *Chem. Soc. Rev.*, 2013, **42**, 7446–7467.

6 S. Chen, Z. Li, Y. Wu, N. Mahmood, F. Lortie, J. Bernard, W. H. Binder and J. Zhu, *Angew. Chem., Int. Ed.*, 2022, **61**, e202203876.

7 Y. Ahn, Y. Jang, N. Selvapalam, G. Yun and K. Kim, *Angew. Chem., Int. Ed.*, 2013, **52**, 3140–3144.

8 C. A. Anderson, A. R. Jones, E. M. Briggs, E. J. Novitsky, D. W. Kuykendall, N. R. Sottos and S. C. Zimmerman, *J. Am. Chem. Soc.*, 2013, **135**, 7288–7295.

9 Y. Liu, L. Wang, L. Zhao, Y. Zhang, Z.-T. Li and F. Huang, *Chem. Soc. Rev.*, 2024, **53**, 1592–1623.

10 O. J. G. M. Goor, S. I. S. Hendrikse, P. Y. W. Dankers and E. W. Meijer, *Chem. Soc. Rev.*, 2017, **46**, 6621–6637.

11 A. Goujon, G. Mariani, T. Lang, E. Moulin, M. Rawiso, E. Buhler and N. Giuseppone, *J. Am. Chem. Soc.*, 2017, **139**, 4923–4928.

12 T. Liu, S. Zou, C. Hang, J. Li, X. Di, X. Li, Q. Wu, F. Wang and P. Sun, *Polym. Chem.*, 2020, **11**, 1906–1918.

13 C. Li, A. Iscen, H. Sai, K. Sato, N. A. Sather, S. M. Chin, Z. Álvarez, L. C. Palmer, G. C. Schatz and S. I. Stupp, *Nat. Mater.*, 2020, **19**, 900–909.

14 A. J. Wilson, *Soft Matter*, 2007, **3**, 409–425.

15 H. M. Coubrough, S. C. C. van der Lubbe, K. Hetherington, A. Minard, C. Pask, M. J. Howard, C. Fonseca Guerra and A. J. Wilson, *Chem. – Eur. J.*, 2019, **25**, 785–795.

16 H. M. Coubrough, M. Reynolds, J. A. Goodchild, S. D. A. Connell, J. Mattsson and A. J. Wilson, *Polym. Chem.*, 2020, **11**, 3593–3604.

17 A. Gooch, N. S. Murphy, N. H. Thomson and A. J. Wilson, *Macromolecules*, 2013, **46**, 9634–9641.

18 T. Park and S. C. Zimmerman, *J. Am. Chem. Soc.*, 2006, **128**, 14236–14237.

19 L. Brunsveld, B. J. B. Folmer, E. W. Meijer and R. P. Sijbesma, *Chem. Rev.*, 2001, **101**, 4071–4098.

20 J. M. Pollino and M. Weck, *Chem. Soc. Rev.*, 2005, **34**, 193–207.

21 R. J. Thibault, P. J. Hotchkiss, M. Gray and V. M. Rotello, *J. Am. Chem. Soc.*, 2003, **125**, 11249–11252.

22 R. McHale and R. K. O'Reilly, *Macromolecules*, 2012, **45**, 7665–7675.

23 K. E. Feldman, M. J. Kade, T. F. A. de Greef, E. W. Meijer, E. J. Kramer and C. J. Hawker, *Macromolecules*, 2008, **41**, 4694–4700.

24 K. E. Feldman, M. J. Kade, E. W. Meijer, C. J. Hawker and E. J. Kramer, *Macromolecules*, 2010, **43**, 5121–5127.

25 H. Sun, C. P. Kabb, Y. Dai, M. R. Hill, I. Ghiviriga, A. P. Bapat and B. S. Sumerlin, *Nat. Chem.*, 2017, **9**, 817–823.

26 F. Xu and B. L. Feringa, *Adv. Mater.*, 2023, **35**, 2204413.

27 B. J. Cafferty, R. R. Avirah, G. B. Schuster and N. V. Hud, *Chem. Sci.*, 2014, **5**, 4681–4686.

28 Y. Li, T. Park, J. K. Quansah and S. C. Zimmerman, *J. Am. Chem. Soc.*, 2011, **133**, 17118–17121.

29 D. Görl, B. Soberats, S. Herbst, V. Stepanenko and F. Würthner, *Chem. Sci.*, 2016, **7**, 6786–6790.

30 S.-L. Li, T. Xiao, W. Xia, X. Ding, Y. Yu, J. Jiang and L. Wang, *Chem. – Eur. J.*, 2011, **17**, 10716–10723.

31 J.-F. Xu, Y.-Z. Chen, D. Wu, L.-Z. Wu, C.-H. Tung and Q.-Z. Yang, *Angew. Chem., Int. Ed.*, 2013, **52**, 9738–9742.

32 T.-G. Zhan, M.-D. Lin, J. Wei, L.-J. Liu, M.-Y. Yun, L. Wu, S.-T. Zheng, H.-H. Yin, L.-C. Kong and K.-D. Zhang, *Polym. Chem.*, 2017, **8**, 7384–7389.

33 S. Tan, Y. Sha, T. Zhu, M. A. Rahman and C. Tang, *Polym. Chem.*, 2018, **9**, 5395–5401.

34 L. Wei, S.-T. Han, T.-T. Jin, T.-G. Zhan, L.-J. Liu, J. Cui and K.-D. Zhang, *Chem. Sci.*, 2021, **12**, 1762–1771.

35 S.-T. Han, H.-Y. Duan, L.-Y. Chen, T.-G. Zhan, L.-J. Liu, L.-C. Kong and K.-D. Zhang, *Chem. – Asian J.*, 2021, **16**, 3886–3889.

36 S.-T. Han, H.-Y. Duan, T.-G. Zhan, X.-B. Hu, L.-C. Kong and K.-D. Zhang, *Chin. Chem. Lett.*, 2023, **34**, 107639.

37 E. M. Hilton, M. A. Jinks, A. D. Burnett, N. J. Warren and A. J. Wilson, *Chem. – Eur. J.*, 2024, **30**, e202304033.

38 P. S. Corbin and S. C. Zimmerman, *J. Am. Chem. Soc.*, 1998, **120**, 9710–9711.

39 F. H. Beijer, R. P. Sijbesma, H. Kooijman, A. L. Spek and E. W. Meijer, *J. Am. Chem. Soc.*, 1998, **120**, 6761–6769.