Manuscript version: Author’s Accepted Manuscript
The version presented in WRAP is the author’s accepted manuscript and may differ from the published version or Version of Record.

Persistent WRAP URL:
http://wrap.warwick.ac.uk/159877

How to cite:
Please refer to published version for the most recent bibliographic citation information. If a published version is known of, the repository item page linked to above, will contain details on accessing it.

Copyright and reuse:
The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions.

Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher’s statement:
Please refer to the repository item page, publisher’s statement section, for further information.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk.
Title: Flower-like colloidal particles through precipitation polymerization of redox responsive liquid crystals

Authors: Xiaohong Liu, Mohammad-Amin Moradi, Tom Bus, Michael G. Debije, Stefan A. F. Bon, Johan P.A. Heuts, and Albert P. H. J. Schenning

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Angew. Chem. Int. Ed. 10.1002/anie.202111521

Link to VoR: https://doi.org/10.1002/anie.202111521
Flower-like colloidal particles through precipitation polymerization of redox responsive liquid crystals

Xiaohong Liu,[a,b] Mohammad-Amin Moradi,[b,c] Tom Bus,[a,b] Michael G. Debije,[a] Stefan A. F. Bon,[d] Johan P.A. Heuts,[b,e]* and Albert P.H.J. Schenning[a,b]*

Abstract: We report on the synthesis of monodisperse, flower-like, liquid crystalline (LC) polymer particles by precipitation polymerization of an LC monomer mixture consisting of benzoic acid-functionalized acrylates and disulfide-functionalized diacrylates. Introduction of a minor amount of disulfide-functionalized diacrylates (≤ 10 wt%) induced the formation of flower-like shapes. The shape of the particles can be tuned from flower-like to spherical by elevating the polymerization temperature. The solvent environment also has a pronounced effect on the particle size. Time-resolved TEM reveals that the final particle morphology was formed in the early stages of the polymerization and that subsequent polymerization resulted in continued particle growth without affecting the morphology. Finally, the degradation of the particles under reducing conditions was much faster for flower-like particles than for spherical particles, likely a result of their higher surface-to-volume ratio. As an important factor in biological cell interactions and uptake, [19,20]

Despite the plethora of available anisotropic colloids, it remains challenging to fabricate non-spherical polymer particle colloids. One approach is to physically deform spherical thermoplastic polymer particles by stretching above their glass transition temperature, [21–23] or via template-guided 2D[24,25] and 3D[26] partial film formation. Templated or confined geometric synthetic routes, such as photolithography,[27,28] particle replication in non-wetting templates (PRINT),[29] and droplet-based microfluidic routes,[30,31] can also bring results. Although these methods allow for direct control of morphology, they face difficulties as the dimension of the particles decreases to submicron range; in addition, the low productivity and stringent preparation conditions remain challenging.

Bottom-up, template-free synthetic routes, though impressive, still commonly result in rounded morphologies, such as dumbbells,[32,33] patchy,[34] and raspberry-type armored particles,[35] or more exotic “octopus ocellatus” particles.[36] Even polymerization-induced self-assembly (PISA) techniques usually lead to rounded spherical, cylindrical or vesicular shapes.[37] To obtain suprastructures with angular shapes, crystallization is often employed. Indeed living-crystallization driven self-assembly,[38] allows for this angular complexity in particle geometry. Alternatively, by using a liquid crystalline monomer, colloidal suprastructures obtained through PISA by radical polymerization showed a more angular appearance, characteristic of crystallinity.[39]

In the 1960s, highly crystalline polyimide powders of intricate morphology were prepared through imidization of polyamide-acids.[40,41] An illustrative example of this were 1-5 µm average diameter polyimide particles with sheaf or coral-like morphologies.[42] Synthesis of conjugated polymers under hetero-phase conditions produce crystalline cylindrical-shaped

Introduction

Shape-anisotropic colloids are of great interest across a wide range of scientific disciplines and application areas. When we look at particles dispersed in a liquid, their geometry may impact individual particle motions[1–4] and interaction with other objects,[5] with shape entropy influencing assembly behavior in crowded environments.[6,7] Surface roughness alters the hydrodynamics and rheological behavior of particle dispersions.[8] Shape-anisotropy affects particle interaction with light,[9] leading to advances in plasmonic nanosensors,[10] opacifiers,[11] and switchable, full-color reflective dispersions.[12] The shape and surface roughness[13] of colloidal particles alters their wetting characteristics, with applications in fluid repellent coatings,[14–16] and Pickering emulsions.[17,18] Particle geometry is also emerging...
particles, also with sharp edges.\textsuperscript{[43]} This concept of preparing polymers which phase separate from and precipitate out of solution into particles which then crystallize is intriguing, especially when providing a route to angular shapes, especially if control of the particle size distribution can be achieved. Whereas precipitation polymerization often shows a lack of control over particle formation and growth, when the conditions are right it is possible to prepare monodisperse particles, as for example in the free radical precipitation polymerization of divinylbenzene in acetonitrile.\textsuperscript{[44]}

Previously, we reported on the preparation of spherical polymer particles via precipitation polymerization of a smectic LC monomer mixture consisting of a crosslinker and benzoic acid hydrogen-bonded dimers.\textsuperscript{[45]} In this paper, we report the preparation of monodisperse, ‘flower-like’ particles via precipitation polymerization of a liquid crystalline (LC) monomer mixture. The monomer mixture consists of the same benzoic acid-functionalized acrylates as used before but the crosslinker is replace by a redox responsive disulfide-functionalized diacylate. It is found that the introduction of a minor fraction of the disulfide-functionalized diacylates (≤ 10 wt%) induces the formation of a flower-like morphology. The shape of these particles can be tuned from flower-like to spherical simply by elevating the polymerization temperature, while the solvent itself mainly influences the particle size. The flower-like morphology already forms during the early stages of the polymerization, after which particle growth occurs. Degradation of the particles by breaking the disulfide groups under reducing conditions is dramatically accelerated in the flower-like particles, attributed to their high surface-to-volume ratio.

Results and Discussion

Monomer 1 (Figure 1a) was synthesized by esterification of the disulfide core and benzoic acid-functionalized acrylates (see the supporting information (SI) for details).\textsuperscript{[46]} The LC monomer mixture was then prepared by mixing monomers 1 and 2 (Figure 1a) in a 10/90 weight ratio. Differential scanning calorimetry (DSC) shows an exothermal peak at around 92 °C, corresponding to the LC-to-isotropic transition, with a peak at approximately 50 °C, corresponding to the LC-to-crystalline transition (Figure S5). The monomers and thermal initiator were dissolved in a solvent, polymerized overnight, and washed with ethanol to yield the final particles (for experimental details, see the SI). Initial studies were conducted in phenyl acetate at 65 °C based on our earlier results using a similar LC monomer mixture containing a different cross-linker, \textit{vide supra}.\textsuperscript{[46]} The resulting polymer particles were flower-like, with ‘petal’ moieties on the surfaces (Figure 1b and 1c). The average diameter of the particles was ~750 nm, with a coefficient of variation (CV) of 7.2% and an average circularity of 0.59. 3D Tomography was used to investigate the particle morphology, in more detail (Figure 1d) confirming the flaky moieties throughout the particles. The glass transition temperature ($T_g$) of the LC polymer particles was determined by DSC and found to be around 82 °C (Figure S6). The flower-like polymer particles do not change their shape when heated above $T_g$ at 105 °C overnight (Figure S7), confirming the permanent shape of the particles.

The concentration of cross-linking monomer 1 was varied to investigate its impact on the final shape of the particles. As shown in Figure 2a, without monomer 1, fairly spherical particles with rough surfaces were obtained. Flower-like particles were obtained when 5% or 10% of monomer 1 was used (Figures 1 and 2b). Further increasing the weight ratio of monomer 1 to above 20% resulted in particles with nearly spherical shapes, and no particles were formed at all when pure monomer 1 was used. Meanwhile, the diameter of the particles increased from 500 nm to 1.3 μm with increasing monomer 1. It is concluded that the introduction of a minor amount of monomer 1 (≤ 10 wt%) can induce the flower-like shape, while further increasing the amount of monomer 1 led to spherical particles, probably because the rapid cross-linking prevented the rearrangement of the polymer chains or monomer 1 disrupted the molecular order. The monomer composition of

![Figure 1](image1.png)

**Figure 1.** (a) LC monomer mixture used to prepare LC polymer particles (weight ratio 1:2 = 10:90). (b) SEM images (scale bar = 2 μm (larger image) and 200 nm (inset)) and (c) TEM image (scale bar = 500 nm) of the flower-like particles prepared in phenyl acetate at 65 °C. (d) 3D tomography of the flower-like particles.

![Figure 2](image2.png)

**Figure 2.** SEM images of particles prepared with monomer 1 and 2 in weight ratios (a) 0/100, (b) 5/95, (c) 20/80, and (d) 50/50 in phenyl acetate at 65 °C. Scale bar = 2 μm in all large images and 200 nm in all insets.
measurements. The first and second order peaks correspond in the isotropic state the polymer chains might align resulting in a layer spacing of 3.2 nm. 

Figure 5. MAXS patterns of particles prepared at 65 °C (a), 90 °C (b), and 105 °C (c). (d) MAXS 1D profile derived from (a) to (c). The first order and second order peaks were found to decrease with increasing polymerization temperature, indicating that the order was decreased at elevated temperatures (Figure 5). Although the thermotropic LC mixture is in the isotropic state the polymer chains might align resulting in the layered structure in the different shaped particles. 

The evolutions of the morphologies of the particles were investigated by time-resolved TEM. A small volume of the polymerization mixture was withdrawn from the flask every hour and washed with ethanol to remove the unreacted monomers for time-resolved TEM. As shown in Figure 6a to 6e, the particles prepared at 65 °C showed flower-like morphologies from the outset (1-hour polymerization) which continued to grow in size as the polymerization progressed. The initial diameter was approximately 300 nm, increasing to 750 nm overnight. Both spherical and ellipsoidal shapes were initially observed in the 90 °C polymerization, eventually leading to formation of disk-shaped particles (Figure 6f to 6j). For polymerizations carried out at 105 °C, only spherical particles were observed throughout the entire polymerization process (Figure 6k to 6o). In all cases, the increases in particle size are accompanied by an increase in monomer conversion (see SI for details). In summary, the shape of the LC particles is already formed at the initial stage of the polymerization, and subsequent polymerization only results in the growth of the particles with no change in morphology.

Based on these results, we postulate the formation of the flower-like morphology was the combined result of liquid crystalline molecular order and limited chain mobility. The liquid crystalline molecular order is reduced and the chain mobility is increased at elevated temperatures, and resulting in the rounded morphology of the particles.
As the disulfide bonds in the cross-linker are sensitive to a reductive environment, particles prepared in phenyl acetate at 65 °C and 105 °C were subjected to degradation experiments. LC particles were first dispersed in 10 mM KOH solution to prepare a 0.1 mg/mL particle suspension, and then 2-mercaptoethanol was added so that its concentration was 1 mM. A rapid decrease in hydrodynamic diameter from 1.59 μm to 0.1 μm indicated the rapid degradation of the flower-like particles into soluble linear polymers, whereas no apparent change in hydrodynamic diameter was observed for the spherical particles (Figure 7). Such a discrepancy can be attributed to the difference in surface-to-volume ratio, even though these particle samples have the same chemical composition and comparable size.

Rhodamine B was used as a tracer dye to demonstrate that the flower-like particles can be used a redox-responsive delivery system. The empty particles were first introduced to an aqueous solution of Rhodamine B for an hour (Figure 7c). After centrifugation of the suspension, the dye was mainly localized in the particle fraction. After redispersion of the loaded particles, 2-mercaptoethanol was added. After 15 min the solution was centrifuged again: there was no evidence of remaining particles, suggesting complete degradation of the particles (vide supra), indicating that the flower-like particles can be used as redox-responsive carrier systems (see Figure S10).

**Figure 6.** Time-resolved TEM images of the particles prepared in phenyl acetate at different polymerization temperatures and times (scale bar = 500 nm).

**Figure 7.** (a) Time-resolved hydrodynamic diameter of the degradation process monitored with DLS. (b) Images of the particle suspension before and after degradation of flower-like particles (left, polymerized in phenyl acetate at 65 °C) and spherical particles (right, polymerized in phenyl acetate at 105 °C). (c) Images of (left) the initial Rhodamine B solution (5 μg/mL), (middle) the dispersion after centrifugation (the sedimented particles are circled in yellow), and (right) the dispersion after degradation and centrifugation.

**Conclusion**

In this paper, we report the facile synthesis of monodisperse flower-like particles via one-step precipitation polymerization of liquid crystalline monomers. By adding ≤ 10 wt% of cross-linker 1 to the monomer mixture, a flower-like morphology was induced. Particle sizes and the number of "petals" in the "flower" were found to mainly depend on the solvent used as reaction medium, whereas the morphology of the particles can be tuned from flower-like to disk-shape and further to spherical by elevating the polymerization temperature. A gradual decrease in the molecular order in particles prepared at higher polymerization temperature may contribute to the formation of rounded particles. It was found that the morphology of the particles was formed at the early stage of polymerization, while continued polymerization resulted in the growth of particle size without significantly changing the morphology. Finally, the flower-like particles were degraded much more rapidly than their spherical counterparts in reductive environments, attributed to their significantly higher surface-to-volume ratio.

Our work introduces a facile and scalable preparation of non-spherical organic particles of a narrow size distribution and may lead to potential applications ranging from superhydrophobic coatings to redox responsive carrier systems.

**Acknowledgements**

The authors thank Jie Liu, Dr. Xianwen Lou, and Dr. Johan Lub for the MS measurement and discussion, and Sean Lugger for the X-ray measurements. We are grateful for the financial support by the Netherlands Organization for Scientific Research (TOP-PUNT 718.016.003)

**Keywords:** liquid crystal • flower-like particles • precipitation polymerization • keyword 4 • keyword 5

[1] F. Perrin, J. Phys. Radium 1934, 5, 497–511.
[2] F. Perrin, J. Phys. Radium 1936, 7, 1–11.
[3] Y. Han, A. M. Alsayed, M. Nobili, J. Zhang, T. C. Lubensky, A. G. Yodh, Science 2006, 314, 626–630.
[4] Y. C. Saraswat, F. Ibis, L. Rossi, L. Sassó, H. B. Eral, P. Fanzio, J. Colloid Interface Sci. 2020, 564, 43–51.
[5] L. Onsager, Ann. N. Y. Acad. Sci. 1949, 5, 627–659.
[6] M. Adams, Z. Dogic, S. L. Keller, S. Fraden, Nature 1998, 393, 349–352.
[7] G. van Anders, D. Klotza, N. K. Ahmed, M. Engel, S. C. Glotzer, Proc. Natl. Acad. Sci. 2014, 111, E4812–E4821.
[8] L. C. Hsiao, S. Pradeep, Curr. Opin. Colloid Interface Sci. 2019, 43, 94–112.
[9] G. Mie, Ann. Phys. 1908, 330, 377–445.
[10] L. Rodríguez-Lorenzo, R. de la Rica, R. Álvarez-Puebla, L. M. Liz-Marzán, M. M. Stevens, Nat. Mater. 2012, 11, 604–607.
[11] G. Jacucci, B. W. Longbottom, C. C. Parkins, S. A. F. Bon, S. Vignolini, J. Mater. Chem. C 2021, 9, 2695–2700.
[12] Q. He, K. H. Ku, H. Vijayamohan, B. J. Kim, T. M. Swager, J. Am. Chem. Soc. 2020, 142, 10424–10430.
[13] M. Hu, C.-P. Hsu, L. Isa, Langmuir 2020, 36, 11171–11182.
[14] W. Jiang, C. M. Grozea, Z. Shi, G. Liu, ACS Appl. Mater. Interfaces 2014, 6, 2629–2638.
RESEARCH ARTICLE

[15] D. Xu, M. Wang, X. Ge, M. Hon-Wah Lam, X. Ge, J. Mater. Chem. 2012, 22, 5764–5791.

[16] A. M. Telford, B. S. Hawkett, C. Such, C. Neto, Chem. Mater. 2013, 25, 3472–3479.

[17] M. Zanini, C. Marschelke, S. E. Anachkov, E. Marini, A. Syntyska, L. Isa, Nat. Commun. 2017, 8, 15701.

[18] T. M. Ruhland, A. H. Gröschel, N. Ballard, T. S. Skelhon, A. Walther, A. H. E. Müller, A. F. Bon, Langmuir 2013, 29, 1388–1394.

[19] A. E. Nel, L. Mätzler, D. Velegol, T. Xia, E. M. V Hoek, P. Somasundaran, F. Klaessig, V. Castranova, M. Thompson, Nat. Mater. 2009, 8, 543–557.

[20] K. Zhang, H. Fang, Z. Chen, J. S. A. Taylor, K. L. Wooley, Bioconjug. Chem. 2008, 19, 1880–1887.

[21] M. Nagy, A. Keller, Polym. Commun. 1989, 30, 130–132.

[22] J. A. Champion, Y. K. Katare, S. Mitragotri, Proc. Natl. Acad. Sci. U. S. A. 2007, 104, 11901–11904.

[23] C. C. Ho, A. Keller, J. A. Odell, R. H. Otterwill, Colloid Polym. Sci. 1993, 271, 469–479.

[24] L. Zheng, P. Huang, L. Zhang, D. Guo, Q. Yan, Part. Part. Syst. Charact. 2016, 33, 842–850.

[25] L. M. Ramirez, S. T. Milner, C. E. Snyder, R. H. Colby, D. Velegol, Langmuir 2010, 26, 7644–7649.

[26] B. W. Longbottom, B. Somuncuoglu, J. J. Punter, S. Longbottom, S. A. F. Bon, Soft Matter 2017, 13, 4285–4293.

[27] D. C. Pregibon, M. Toner, P. S. Doyle, Science 2007, 315, 1393–1396.

[28] S. Badaire, C. Cottin-Bizonne, A. D. Stroock, Langmuir 2008, 24, 11451–11463.

[29] T. J. Merkel, K. P. Herlihy, J. Nunes, R. M. Orgel, J. P. Rolland, J. M. DeSimone, Langmuir 2010, 26, 13086–13096.

[30] S. Xu, Z. Nie, M. Seo, P. Lewis, E. Kumacheva, H. A. Stone, P. Garstecki, D. B. Weibel, I. Gillin, G. M. Whitesides, Angew. Chemie Int. Ed. 2005, 44, 724–728.

[31] Z. Nie, S. Xu, M. Seo, P. C. Lewis, E. Kumacheva, J. Am. Chem. Soc. 2005, 127, 8058–8063.

[32] H. R. Sheu, M. S. El-Aasser, J. W. Vanderhoff, J. Polym. Sci. Part A Polym. Chem. 1990, 28, 629–651.

[33] J.-G. Park, J. D. Forster, E. R. Dufrénoy, J. Am. Chem. Soc. 2010, 132, 5960–5961.

[34] A. Lotierzo, B. W. Longbottom, W. H. Lee, S. A. F. Bon, ACS Nano 2019, 13, 399–407.

[35] C. Barhet, A. J. Hickey, D. B. Cairns, S. P. Armes, Adv. Mater. 1999, 11, 408–410.

[36] M. Okubo, K. Kanalda, T. Matsumoto, Colloid Polym. Sci. 1987, 265, 876–881.

[37] F. D’Agosto, J. Rieger, M. Lansalot, Angew. Chemie Int. Ed. 2020, 59, 8368–8392.

[38] L. MacFarlane, C. Zhao, J. Cal, H. Qiu, I. Manners, Chem. Sci. 2021, 12, 4661–4662.

[39] S. Guan, C. Zhang, W. Wen, T. Qu, X. Zheng, Y. Zhao, A. Chen, ACS Macro Lett. 2018, 7, 358–363.

[40] E. A. Laszlo, Aromatic Polyimide Particles from Polycyclic Diamines, 1965, U.S. Patent No. 3,179,631.

[41] E. A. Laszlo, Aromatic Polyimides from Meta-Phenylene Diamine and Para-Phenylene Diamine, 1965, U.S. Patent No. 3,179,633.

[42] Y. Nagata, Y. Ohnishi, T. Kajiyama, Polym. J. 1996, 26, 980–985.
Flower-like particles of a liquid crystalline monomer mixture prepared by precipitation polymerization are reported. The respective influences of monomer composition, polymerization temperature, and solvent on the particle shape are investigated. The shape formed in the early stage of polymerization remain unchanged. The flower-like particles are degraded much more rapidly than the spherical particles due to their higher surface-to-volume ratio.