



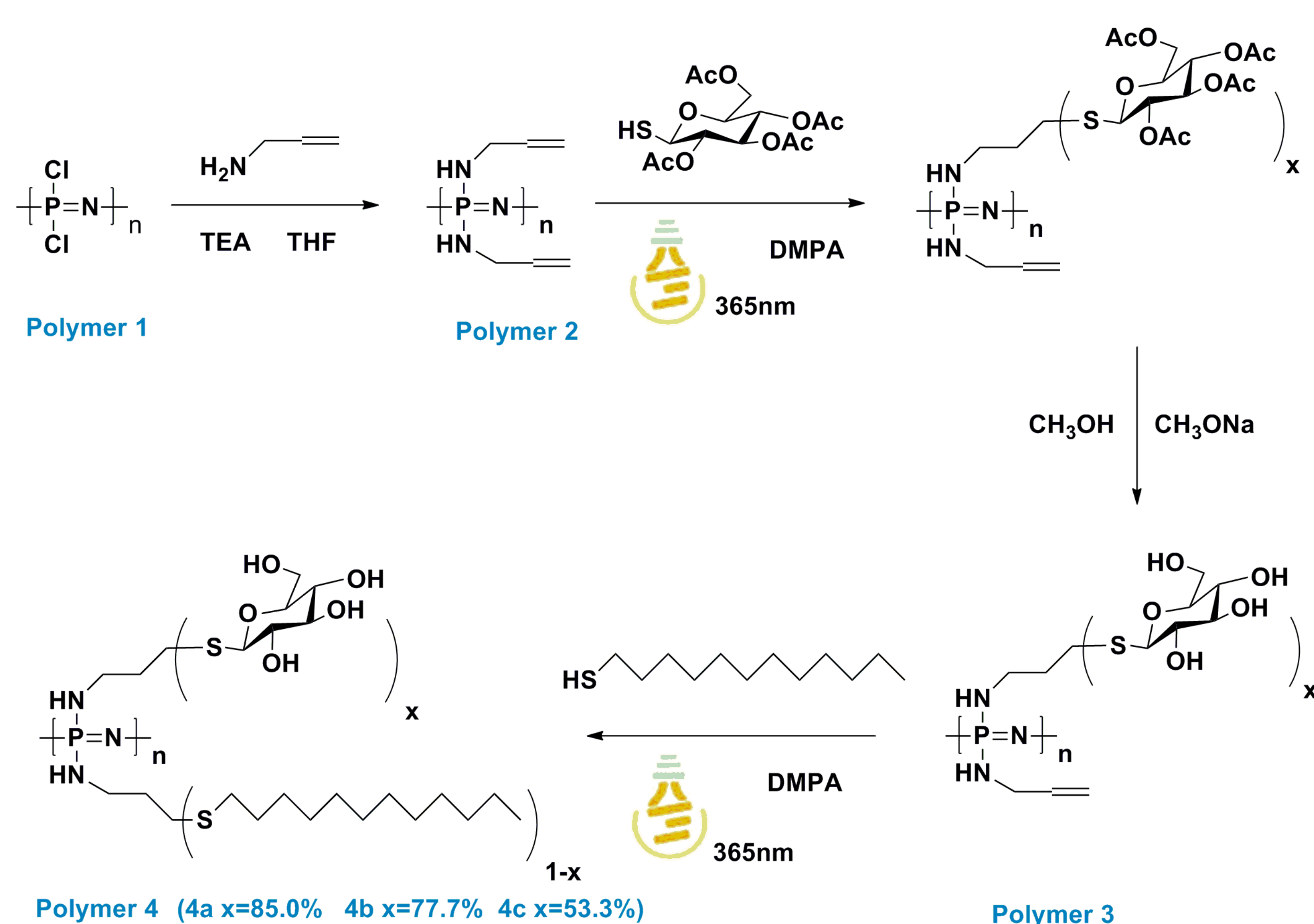
Synthesis and Self-assembly of Amphiphilic Polyphosphazene with Controllable Composition via Two Step Thiol-ene Click Reaction

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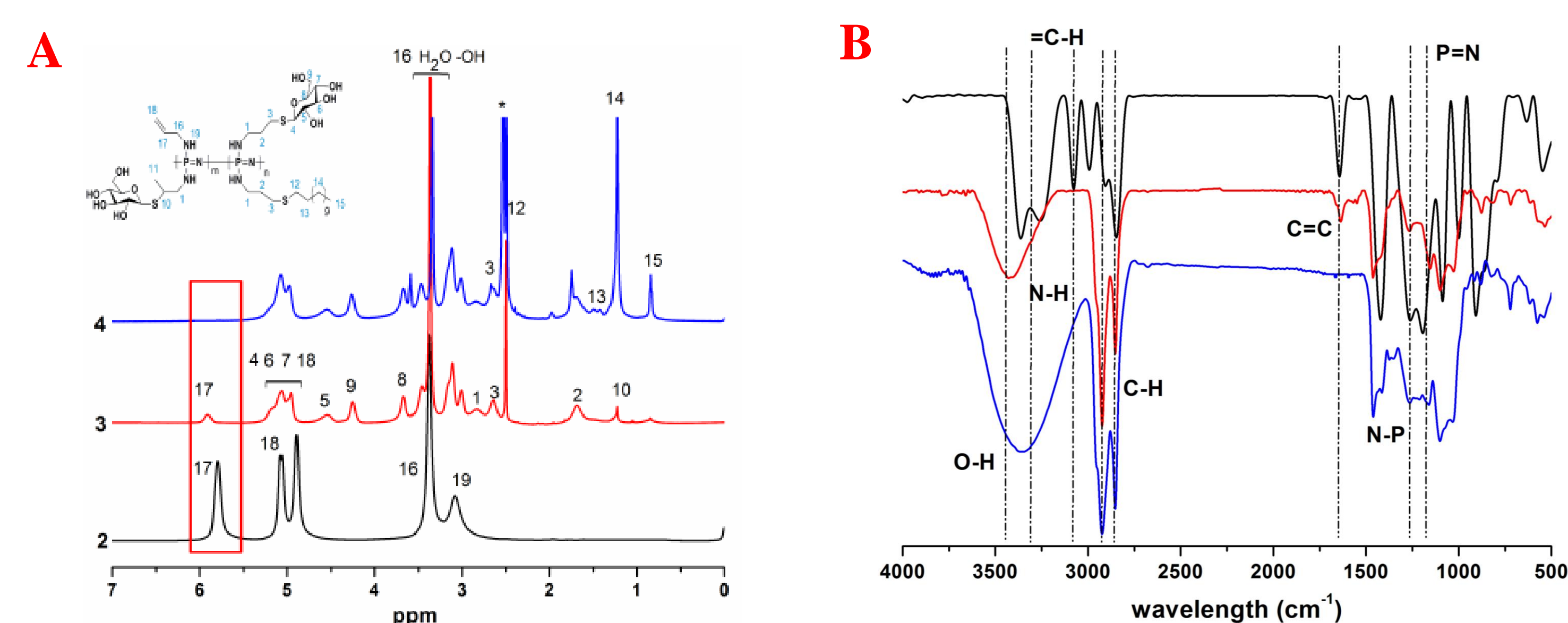


Sequential thiol-ene click reaction is reported for amphiphilic glycosylated polyphosphazene. Poly[bis(allylamino)phosphazene] (PBAAP) was used as precursor to go through UV irradiation with 2,3,4,6-tetra-O-acetyl-1-thiol- β -D-glucopyranose (SH-GlcAc₄) and 1-dodecanethiol in sequence. Variation of the reaction conditions, including click reaction time and the dose of photoinitiator, led to different hydrophilic/hydrophobic ratios. As a result, glycosylated polyphosphazenes were synthesized with 53.3%, 77.7% and 85.0% of glucose moieties. The different residual composition could give rise to different self-assembly behaviors. Micelles of amphiphilic polyphosphazenes were formed in aqueous solution and the CMC value (0.79×10^{-3} to 4.00×10^{-3} mg/ml) as well as mean diameter (170–220 nm) varied along with the hydrophilic glucose moiety/hydrophobic dodecyl moiety ratio.

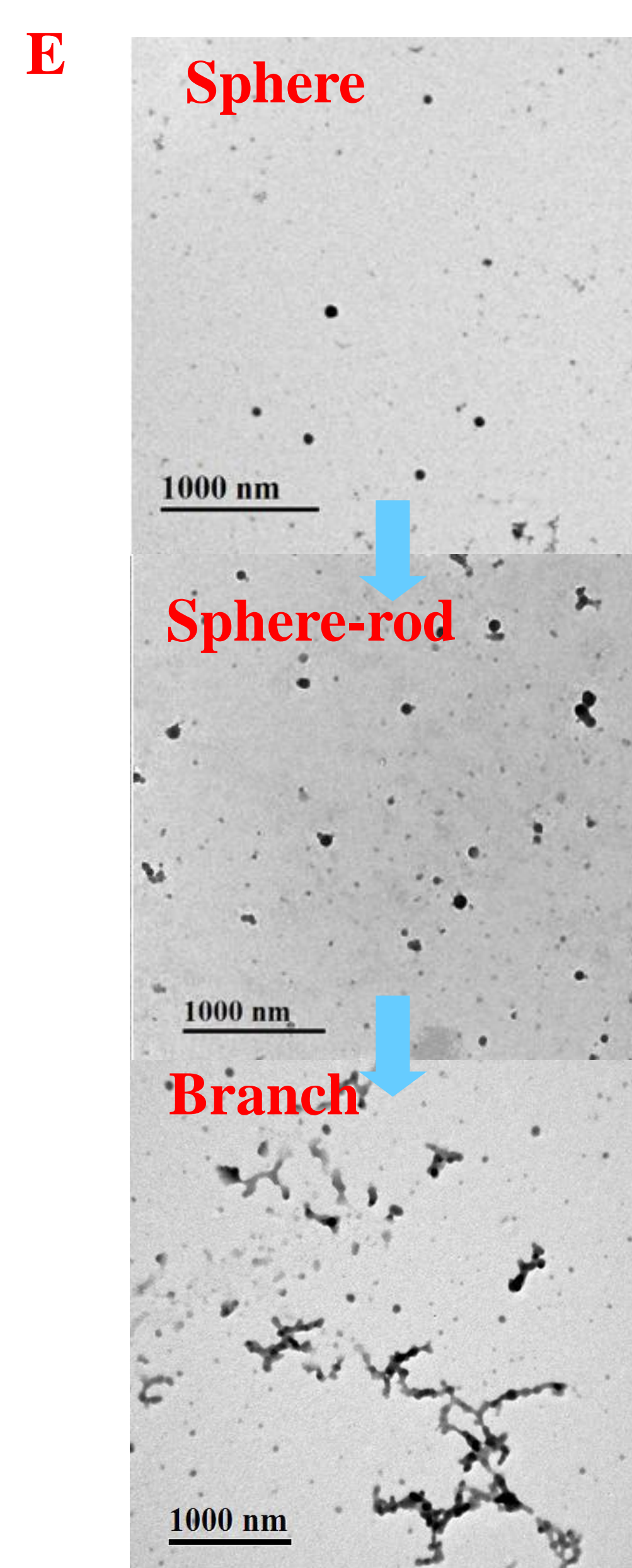
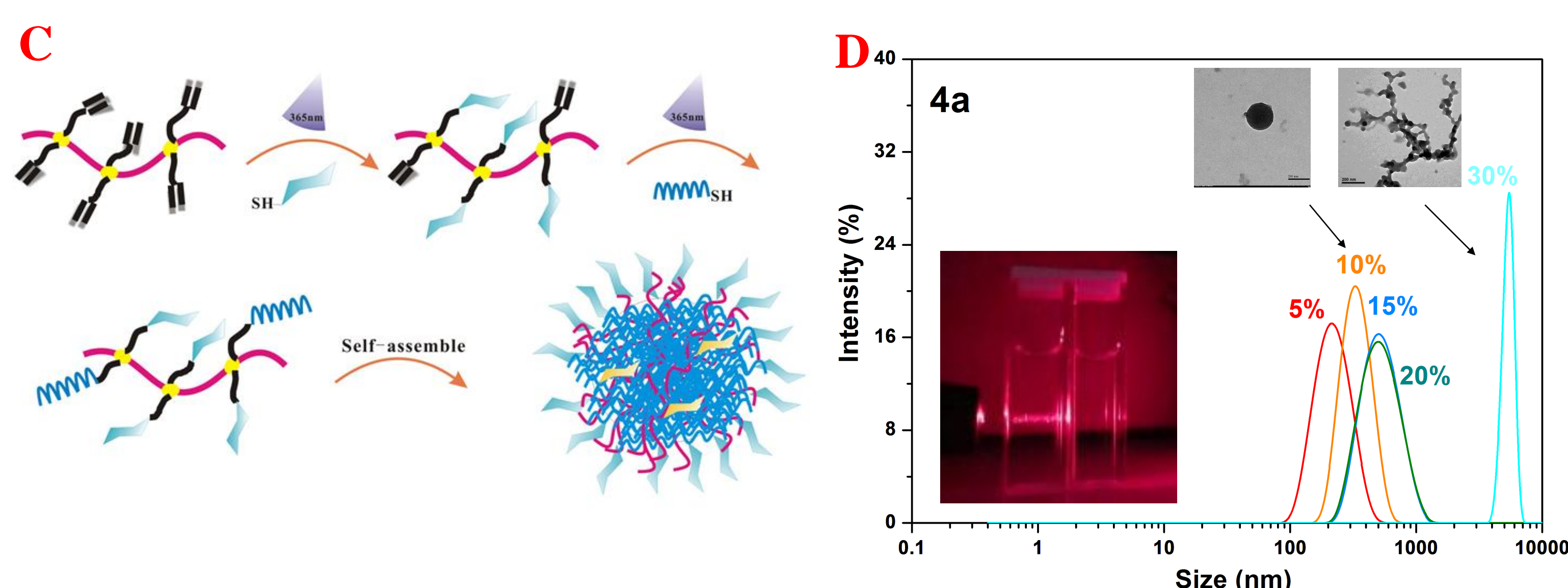


¹H NMR (Fig. A) confirmed the exact structure of PBAAP. Two main peaks corresponding to vinyl protons at 4.97–5.17 ppm ($-\text{CH}=\text{CH}_2$) and 5.85–5.92 ppm ($-\text{CH}=\text{CH}_2$) were present in the ¹H NMR spectrum. FTIR spectra (Fig. B) showed that the C=C bonds appeared at 1640 cm^{-1} .

After the click reaction between PBAAP and SH-GlcAc₄, new multiplets appeared in the ¹H NMR spectrum at 5.13–3.67 (protons of glucosyl ring). The FTIR spectra illustrated successful introduction of a hydroxyl group by means of the absorption at 3400 cm^{-1} . The ultimate poly(β -D-glucose-co-1-dodecyl)phosphazene, P-85.0%, P-77.7% and P-53.3% (4a-4c), was obtained after the second step of the thiol-ene reaction. The peak for vinyl protons vanished.



Depending on the extent of glucosylation, 4a-4c possessed varying solubility in water. Samples of 4a-4c were first dissolved in DMF with the concentration 0.1 mg/mL and then water was gradually added (25 $\mu\text{L}/\text{min}$). As presented by Fig. D, global micelles were formed and the mean diameter ranged from 100–200 nm at low water content (WC). Continuous water addition to high WC could result in hyperbranched or micronetwork structure.



Water Content (%wt)	4a (0.1mg/ml)	4b (0.1mg/ml)	4c (0.1mg/ml)
1			Sphere
5	Sphere	Sphere	Branch
10	Sphere	Sphere	Branch
15	Sphere	Sphere	Branch
20	Sphere	Sphere+Rod	
30	Branch		

Furthermore, with regard to hydroxyl group of glucose moieties, surface of sphere micelles could adhere to each other through formation of hydrogen bond. With a view to lower surface energy as well as surface area, sphere micelle went through morphological transition from sphere to branched structure (Fig. E). On the other hand, the different ratio of glucose/1-dodecyl could affect the transition speed (Fig. F).

Conclusion:

Amphiphilic polyphosphazene was successfully synthesized via a two step thiol-ene reaction, which involved the original PBAAP and the corresponding mercaptan reagents. As a result, amphiphilic polyphosphazenes P-85.0%, P-77.7% and P-53.3% and P-37.1% were prepared and the relative ratio of glucose versus dodecyl group greatly affected the self-assembly behavior of the polyphosphazenes above. These self-assembled amphiphilic polyphosphazenes have potential uses in hydrophilic modification, protein adsorption, and drug loading.

References:

- [1] X Huang, XJ Huang, ZK Xu. "Click chemistry" as a facile approach to the synthesis of polyphosphazene glycopolymers. *Macromol. Chem. Phys.* 2011, 212: 272-277.
- [2] YC Qian, C Chen, XJ Huang, ZK Xu. Glycosylation of polyphosphazene nanofibrous membranes by click chemistry for protein recognition. *Macromol. Chem. Phys.* 2013, 214: 1852-1858.

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