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Light triggered switchable ionic liquid aqueous two-phase systems

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ABSTRACT: Aqueous two-phase systems (ATPSs) consist of two immiscible aqueous phases where the mole fraction of water in both upper and bottom phases is higher than 0.8. ATPS has been widely used in many different fields since its discovery in 1896. However, easy control of phase transition is highly desired in many cases, which is still a challenge. Herein, we report the first work for the reversible switching of transition between two-phase ATPSs and single phase solution by light irradiation. It was found that azobenzene-based ionic liquids and inorganic salts in water systems could be reversibly switched between two-phase ATPS and homogeneous solution at ambient conditions by alternatively UV and visible light irradiation. Mechanism studies reveal that cationic isomerization of the azobenzene-based ionic liquids and size change of their micelles by UV and visible light irradiation is the main driving force for such reversible phase transition of ATPSs. This unique phase behavior has bridged the gap between ATPSs and chemical reactions, which is useful to create new chemistry in ATPSs. As an example of applications, highly efficient and selective aza-Michael reactions were performed in this novel kind of switchable ATPSs, which was well integrated with heterogeneous product

separation, and the phase components could be easily reused. This work opens a new way to conduct reactions efficiently with easy separation process.

KEY WORDS: *Aqueous two-phase system, Ionic liquid, Light switching, Reversible phase behavior, Aza-Michael reaction.*

INTRODUCTION

Aqueous two-phase systems (ATPSs) are usually formed as a result of mutual incompatibility of two polymers (such as PEG and dextran) or one polymer and one salt (such as PEG-K₃PO₄) in water above a certain concentration. Both upper and lower phases of ATPSs mainly consist of water with mole fraction greater than 0.8. The ATPSs were discovered by Beijerinck in 1896,¹ and applied to the extraction of biomaterials by Albertsson in 1958 for the first time.² These pioneering works eventually led to the wide application of ATPSs in the separation and purification of biomolecules, such as proteins^{3, 4}, amino acids⁵, antibodies⁶, bioparticle^{7, 8} and DNA,⁹ nano-materials^{10, 11} and rare earth metals.¹² Due to the advantages of ATPSs such as short processing time, relative reliability in scale-up, low energy consumption and a biocompatible environment¹³, the large-scale purification of enzymes had been successfully performed by Kroner et al¹⁴ more than 40 years ago.

Inspired by the great success of ATPSs in extraction and separation, various efforts have been made to expand their application to chemical reactions, where reversible switching between ATPSs (two phases) and a homogeneous solution without affecting the integrity of the biphasic system is a challenge. In this context, chemical reactions may be performed in homogeneous solution with high efficiency, while product separation takes place in heterogeneous phase together with the recycling of solvent and catalyst. So that, the limit of two-phase characteristics of ATPSs would be broken through, and they can work as a switchable microreactor with functions of reaction, separation and recycling. Stimuli responses triggered by pH, CO₂ and visible light are possible strategies to switch the ATPSs.¹⁵⁻¹⁸ However, none of such strategies have been successfully applied in chemical reactions due to the introduction of acid, base, amine and other compounds which may affect the chemical reactions occurred in these systems. Also, light triggered reversible switching of transition between two-phase ATPSs and single phase solution without additives has not been reported up to date.

In the last two decades, ionic liquids (ILs) have been widely used in chemical reactions,^{19, 20} separation science,^{21, 22} biomass processing,²³ gas capture,^{24, 25} material preparation²⁶⁻²⁹ and

energy production,³⁰⁻³² because of their tunable physical and chemical properties with a judicious design of the structures of cations and anions.³³⁻³⁷ More interestingly, hydrophilic ILs can be used as a phase component to form ATPSs.³⁸⁻⁴¹ The various structures of ILs bring great opportunities for the tuning of microscopic structures and physico-chemical properties of ATPSs,⁴²⁻⁴⁶ and this also provides the possibility for the fabrication of stimulus-responsive ATPSs. In addition, light is easy to obtain with reliability and stability, and its signal can be delivered remotely and precisely in space and time, and switched rapidly in a clean and non-invasive manner.^{47, 48} Thus, combination of ILs with light may create new chemistry in ATPSs.

In this work, a class of novel ATPSs has been prepared from azobenzene-based ionic liquid (IL) surfactant and inorganic salt in water for the first time. Notably, these ATPSs are responsive to UV and visible light. They become completely miscible upon UV light irradiation, then return to two-phase ATPSs by further visible light irradiation (see Figure 1). Thus, the reversible transition between two-phase ATPSs and homogeneous solution can be switched by alternatively UV and visible light irradiation. It is shown that the light switchable liquid-liquid phase transition of ATPSs is attributed to the light control on the isomerization of cations of the ILs and the size of their micelles in the systems. This unique light-responsive phase behavior provides a useful platform for the integration of homogeneous reaction and heterogeneous separation by using ATPSs as reaction medium. As an example, a highly efficient and selective aza-Michael reaction has been performed in homogeneous solutions at room temperature, and coupled with heterogeneous product separation and recycling of the phase components.

Figure 1. Schematic diagram of the switchable liquid-liquid phase transition of ATPSs.

EXPERIMENTAL SECTION

Materials. K_2CO_3 (99%), K_3PO_4 (99%), K_2HPO_4 (99%), KOH (99%), octanol (99%), ethyl acetate (99%), benzylamine (99%), methyl acrylate (99%), ethyl acrylate (99%), 4-methoxybenzylamine (98%), 4-chlorobenzylamine (99%), 3-methylbenzylamine (99%), 2-

methylbenzylamine (98%) and 3-chlorobenzylamine (98%) were purchased from Shanghai Adamas-beta Ltd and used as received. Deionized water was used throughout in this study.

Measurements of binodal curves. Binodal curves of the azobenzene-based ILs + inorganic salts + water systems were determined by the cloud point titration method according to the procedures described in literature.^{49,50} Briefly, a known concentration of aqueous azobenzene-based IL solution was added in a test tube at 25.0 °C, and a salt solution of known mass fraction was then added dropwise until the mixture became turbid, then a known mass of water was added to make the mixture clear again. This procedure was repeated to obtain sufficient data for the building of a liquid-liquid equilibrium binodal curve.

Droplet size measurements. The droplet size and size distribution of the aggregates were determined by dynamic light scattering (DLS) technique using a Malvern Zetasizer Nano-ZS 90 light scattering instrument. The scattering angle was 90°, light of $\lambda = 633$ nm from a solid-state He-Ne laser was used as the incident beam. In order to avoid the influence of possible dust in the sample on the experimental results, all samples were filtered by a 0.45 μm filter, and placed overnight before the measurements to ensure them in a thermodynamic equilibrium state.

Small-angle X-ray scattering (SAXS) measurements. SAXS experiments were performed on an Anton Paar SAXS Space scattering instrument equipped with a Kratky block-collimation system at 25.0 °C. The samples were placed in a quartz capillary. The X-ray was generated using a generator with Cu target and the wavelength was 0.1542 nm.

Cryogenic transmission electron microscopy (Cryo-TEM) measurements. A FEI Talos L120C Cryo-TEM was used to observe the morphology of aggregates. Before the measurements, the samples were prepared using a custom-built chamber. A 5 μL of solution sample was dropped on a copper mesh, after a thin liquid film was formed on the copper mesh, the sample was quickly inserted into the liquid nitrogen for cooling, and then the cooled sample was transferred into the equipment for observation and recording. The acceleration voltage of TEM was 200 kV, and the operating temperature was kept at about -175 °C.

Aza-Michael reaction in ATPSs. Taking the reaction of benzylamine and methyl acrylate in $[\text{C}_4\text{AzoC}_2\text{mim}][\text{Br}] + \text{K}_2\text{CO}_3 + \text{H}_2\text{O}$ ATPS as an example, 0.05 g of $[\text{C}_4\text{AzoC}_2\text{mim}][\text{Br}]$ was dissolved in 3.0 mL of water under stirring, then 3.00 g of K_2CO_3 was added to form an ATPS. Then, 32 mg (0.3 mmol) of benzylamine and 65 mg (0.75 mmol) of methyl acrylate were added dropwise in the system. After the addition was completed, the mixture was irradiated by a LED light source for 1 h at 25.0 °C under stirring. The reaction was carried out in a homogeneous solution, and monitored by thin layer chromatography (TLC). After the reaction was completed, the mixture was irradiated by visible light for 4 h until the two-phase ATPS was reformed. At

this stage, the product was partitioned in the top phase, while the salt was in the bottom phase. Then, the top phase was extracted with ethyl acetate, [C₄AzoC₂mim]Br and product was separated by decantation. Removing ethyl acetate by rotary evaporation, the product was obtained. The [C₄AzoC₂mim]Br and bottom aqueous salt phase could then be used in the next cycle. Once new substrates were added in the ATPS, the same reaction occurred again.

Molecular dynamics simulation. The atom charges were reassigned by fitting the electrostatic potential surface (EPS) of isolated ions, and the structures of the isolated ions were optimized at B3LYP/6-311+g(d,p) level by using the Gaussian 09 package.⁵¹ Considering the effect of charge transfer and polarizability, the charges were uniformly scaled by 0.8 as in a previous study.⁵² For all the simulations, the temperature was kept constant at 25 °C using the Nosé–Hoover thermostat with a coupling constant of 0.2 ps. The pressure was maintained constant at 1 bar using a Parrinello–Rahman barostat with a coupling constant of 1 ps. The bond lengths were constrained using the LINCS algorithm, and an integration time step of 2 fs was used for all the simulations. Electrostatic interactions were evaluated using the particle mesh Ewald method⁵³ with a real space cutoff of 1.2 nm and a grid spacing of 0.16 nm. Lennard-Jones interactions were truncated at 1.2 nm. The simulations containing 24 ion pairs of [C₄AzoC₂mim]Br with 40000 water molecules (1.48 wt%) were performed to study the aggregation of the ILs in net water and aqueous K₂CO₃. Furthermore, 1500 K₂CO₃ molecules (28.77 wt%) were added in the simulation system to obtain the different aggregation structures influenced by *trans*- and *cis*-isomer of [C₄AzoC₂mim]Br. The final configurations of the aggregated cations of [C₄AzoC₂mim]Br after 200 ns simulation (equilibrium state) were shown in Figure S1. Radial distribution functions (RDFs) for the cation-cation (terminal alkyl chain - terminal alkyl chain) and cation-anion (C2-H of the imidazole head group-Br⁻) were computed to analyze the interactions in the aggregates. Intermolecular energies in such systems were included in Table S1.

RESULTS AND DISCUSSION

Light switchable transition between two-phase system and homogeneous solution of ATPSs. The azobenzene-based ILs were synthesized by using the procedures described in our previous work,⁵⁴ and their chemical structures (Figure 2) were confirmed by ¹H NMR (Supporting Information). Then, binodal curves of each azobenzene-based IL surfactant + inorganic salt (K₂CO₃, K₃PO₄, K₂HPO₄ or KOH) + water system were determined before and after UV irradiation by the cloud point titration method according to the procedures described in literature,^{49,50} and the results were shown in Figure 3 and Figure S2-S3. The binodal data for

the ATPSs were given in Tables S2-S9 (Supporting Information). As a selected example, Figure 3(a) showed the binodal curves of $[\text{C}_4\text{AzoC}_2\text{mim}]\text{Br} + \text{K}_2\text{CO}_3 + \text{water}$ ATPS. It is clear that after UV irradiation, the binodal curve of the system shifts toward high salt concentration, which is further away from the origin, indicating that the miscible region is significantly extended upon UV irradiation.⁵⁵ On the other hand, with further visible light irradiation, the binodal curve of the system shifts almost back to the position before UV irradiation. Within any phase composition between the two binodal curves in Figure 3(a) and 3(b), ATPS can be formed under environmental conditions. Therefore, reversible regulation of liquid-liquid phase transition can be achieved by alternatively UV and visible light irradiation in this composition region. The other ATPSs formed by IL ($[\text{C}_2\text{AzoC}_4\text{mim}]\text{Br}$, $[\text{C}_4\text{AzoC}_4\text{mim}]\text{Br}$, $[\text{C}_4\text{AzoC}_2\text{TMA}]\text{Br}$ or $[\text{C}_4\text{AzoC}_2\text{DMEA}]\text{Br}$) + inorganic salt (K_2CO_3 , K_3PO_4 , K_2HPO_4 or KOH) + water have the similar light switchable liquid-liquid phase transition (Figure S2-S3). As far as the effect of salt types is concerned, it can be explained by the Gibbs hydration free energy (ΔG_{hyd}) of the anions,⁵⁶ and more hydrophilic anions have a larger immiscible region because of the stronger interactions between the anion and water than those between water molecules.⁴²

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Figure 2. Chemical structures of the azobenzene-based ILs.

Figure 3. The binodal curves of IL+ K₂CO₃ + H₂O systems before and after UV irradiation: (a), IL = [C₄AzoC₂mim]Br; (b), IL = [C₄AzoC₄mim]Br.

In order to understand the effect of UV and visible light irradiation on the miscible-immiscible transition of ATPSs from a macroscopic level, we determined the partition coefficients of the ILs between n-octanol and water phases before and after UV irradiation, and the results were shown in Table 1. It can be seen that the partition coefficients of them significantly reduced after UV irradiation, which indicates that their hydrophilicity is greatly increased in this case. It is known that azobenzene structure can be changed from *trans*-isomer into *cis*-isomer (Figure S4) under UV light irradiation and the opposite process appears under visible light irradiation in water.⁵⁴ Therefore, the data in Table 1 suggest that the *cis*-isomer is more hydrophilic than *trans*-isomer, and has a stronger ability to be miscible with water and aqueous salt solutions. As a result, UV irradiation results in the dissolution of a phase separation system, but visible light irradiation leads to the phase separation of a completely miscible solution. Moreover, the partition coefficients could be used to rationalize the effect of the chemical structure of the ILs on the miscible regions shown in Figure S3. It is clearly noted that for the IL with a more hydrophilic property, the miscible region of the systems become wider, indicating that more hydrophilic IL is harder to form an ATPS under the same conditions.

Table 1. Partition coefficients (*K*) of the azobenzene-based ILs between n-octanol and water phases before and after UV irradiation at 25.0 °C

IL	<i>K</i> ^a	
	before UV (<i>trans</i> -isomer)	after UV (<i>cis</i> -isomer)
[C ₄ AzoC ₂ mim]Br	66.8	1.58
[C ₂ AzoC ₄ mim]Br	39.7	4.48
[C ₄ AzoC ₄ mim]Br	117	21.6

[C ₄ AzoC ₂ DMEA]Br	55.7	1.02
[C ₄ AzoC ₂ TMA]Br	39.8	0.69

^aThe maximum absorption wavelength ($\lambda_{\max}$) and the initial concentrations of the azobenzene-based ILs were listed in Table S10.

Mechanism of the light switchable phase behavior of ATPSs. To gain a deeper insight into the light-switchable liquid-liquid phase transition of the ATPSs, we investigated the self-assembly of the azobenzene-based ILs in water and in aqueous salt solutions by conductivity titration, dynamic light scattering (DLS), small-angle X-ray scattering (SAXS), cryogenic transmission electron microscopy (Cryo-TEM) and molecular dynamics (MD) simulation. It was found from conductivity titration that before and after UV irradiation, the critical aggregate concentrations (CAC) of *trans*-[C₄AzoC₂mim]Br and *cis*-[C₄AzoC₂mim]Br in water were 1.9×10^{-3} and 9.1×10^{-3} mol/kg, respectively, indicating that UV irradiation has obvious effect on the self-assembly of [C₄AzoC₂mim]Br (Figure S5). As a selected example, the results for [C₄AzoC₂mim]Br + K₂CO₃ + water system were given in Figure 4 and Tables S11-S12. As shown in Figure 4(a), at a given concentration of 1.48 wt%, [C₄AzoC₂mim]Br could form aggregates in neat water, and the size was about 4.6 nm. By adding K₂CO₃ into water with salt content from 4.7 to 25.6 wt%, the size of the aggregates was increased from 5.4 nm to 37 nm. Further increase of the concentration of K₂CO₃ to 30.7 wt%, a sharp increase in the size of the aggregates (67 nm) was observed, which is very close to the concentration at which two-phase ATPSs was formed. This result indicates that the self-assembly of [C₄AzoC₂mim]Br in aqueous salt solution becomes stronger with increasing concentration of K₂CO₃.

Figure 4. (a), Number-average size distribution of aggregate of [C₄AzoC₂mim]Br (1.48 wt%) in aqueous K₂CO₃ solutions observed by DLS as a function of salt concentration; (b), Number-average size distribution of aggregate of [C₄AzoC₂mim]Br (1.48 wt %) in 30.7 wt% of K₂CO₃

aqueous solution observed by DLS after UV irradiation for different time.

To further characterize the aggregates, SAXS measurements were performed for [C₄AzoC₂mim]Br in aqueous K₂CO₃ with different concentrations. The data were desmeared with the beam length by the SAXS quant software, and the model-fitting was carried out with the SASfit software. Several models like micelles (sphere, ellipsoid and cylinder) and vesicles (single wall and double walls) were tried and only spherical micelle model⁵⁷ gave the best fittings as shown in Figure 5(a) and 5(b). These results indicate that the aggregates of [C₄AzoC₂mim]Br in the investigated systems are spherical micelles. The structure factor $S(q)$ of the micelles could be calculated with the Percus-Yevick approximation for the closure relation.⁵⁸

$$S(q)=1/(1+24 \eta_{\text{HS}}G(qR_{\text{HS}})/qR_{\text{HS}}) \quad (1)$$

where η_{HS} is the hard sphere volume fraction, q is length of the scattering vector, and R_{HS} is the radius of hard sphere. The detailed expression of the function $G(qR_{\text{HS}})$ in equation (1) can be found in the literature.⁵⁸ The value of the hard sphere radius R_{HS} was set to be the radius of a corresponding spherical micelle. The diameter of micelles obtained from SAXS was listed in Tables S11-S12. It was found from Table S11 that the size of sphere micelles of [C₄AzoC₂mim]Br increased from 4.9 nm to 68 nm with increasing K₂CO₃ concentrations in the systems. In addition, the diameter values are in good agreement with the aggregate size of [C₄AzoC₂mim]Br at given concentrations of K₂CO₃ determined by DLS. This result indicates that the aggregates observed by DLS are actually the micelles. Such spherical morphology and salt concentration dependence of the micelles size were confirmed by direct observation with Cryo-TEM images (Figure 5(c), 5(d) and 5(e)).

Figure 5. (a), Spherical micelle model fitting of SAXS data for [C₄AzoC₂mim]Br in different concentrations of K₂CO₃ aqueous solutions before UV irradiation; (b), Spherical micelle model fitting of SAXS data for [C₄AzoC₂mim]Br in 30.7 wt% of K₂CO₃ aqueous solution after UV irradiation; (c)-(e), Cryo-TEM images for the aggregates of [C₄AzoC₂mim]Br in aqueous K₂CO₃ solution before (c, d) and after (e) UV irradiation; the concentration of K₂CO₃ for (c) and (d, e) is, respectively, 4.7 wt% and 30.7 wt%. The concentration of [C₄AzoC₂mim]Br is 1.48 wt% in all cases.

Next, we investigated the possible change in microstructure and size of the micelles by UV and visible light irradiation. It is interesting to note from Figure 4(b) that the micelles size of [C₄AzoC₂mim]Br in aqueous 30.7 wt% K₂CO₃ solution was obviously decreased by UV light irradiation, and the micelle size went back from 67 nm to 4.7 nm after 30 min UV irradiation, which is very close to the size distribution (4.6 nm) of [C₄AzoC₂mim]Br micelles in neat water (Figure 4(a)). Similar size and morphology was observed by Cryo-TEM (Figure 5(e)), but no change in micelles structure was revealed by SAXS (Figure 5(b)). On the contrary, if this final solution was further irradiated by visible light for 2 h, the size of [C₄AzoC₂mim]Br micelles in aqueous solution containing 30.7 wt% of K₂CO₃ could return to 67 nm without change in micelles structure. These results are in line with the fact mentioned above that the cation of the *cis*-isomer is more hydrophilic than that of the *trans*-isomer, and is not beneficial to the growth of micelles in aqueous solution. In addition, comparison of Figure 4(a) and 4(b) suggests that

in apparent terms, the role of UV irradiation in the control of micelles size of the ILs is equivalent to the decrease of salt concentration. In other words, K_2CO_3 has a “salting out” effect, while the UV irradiation has a “salting in” effect on the azobenzene-based ILs. However, visible light behaves like a salt, and also has a “salting out” effect on the investigated ILs. Therefore, by using UV and visible light irradiation, we can switch the miscible - immiscible transition of the ATPSs on demand.

Moreover, the GROMACS package⁵⁹ and visual molecular dynamics (VMD)⁶⁰ were also used to study the structure of micelles. For this purpose, all atom force field (OPLS-AA) was employed in the simulations, and the parameter of C-N=N-C torsion potential was derived from the literature.⁶¹ Interestingly, the small micelles in neat water, large micelles in aqueous K_2CO_3 solution, and spherical morphology of micelles of the *trans*-isomer of $[C_4AzoC_2mim]Br$ were qualitatively reproduced (Figure S1), where spherical micelles were formed by cations comprising hydrophobic tail groups as core and hydrated head groups as corona. Because the azobenzene group of the cations was located in the core of the micelles, the size of micelles was sensitive to light irradiation. Additionally, analysis of the radial distribution functions (RDFs) for the cation-cation and cation-anion of $[C_4AzoC_2mim]Br$ in neat water and in aqueous K_2CO_3 (28.77 wt%) solution reveals that addition of salt significantly enhanced alkyl-alkyl interaction of *trans*-isomer of cations (Figure 6(a)), which led to the growth of micelles of the ILs in aqueous solutions. However, presence of K_2CO_3 remarkably reduced the binding of anion (Br^-) with imidazolium head groups on the surface of micelles formed by *trans*-isomer of the cations (Figure 6(b)) due to the much stronger interaction between the imidazolium head groups and CO_3^{2-} . The calculated intermolecular energy data (Table S1) support these deductions. Overall, the above results show that the self-assembly/disassembly of the azobenzene-based ILs plays an important role in the reversible switching of transition between two-phase ATPSs and single phase solution. The formation of large sized micelles of azobenzene-based ILs in water enhances the inhomogeneity of the system and finally induces the phase separation of the systems.⁶²⁻⁶⁴ Conversely, UV light irradiation results in the small sized micelles, which is beneficial for the formation of homogenous solution. Nevertheless, the disassembly of the large micelles reduces the inhomogeneity of the system, and the ATPS changes into a single phase solution.

Figure 6. Radial distribution functions for terminal alkyl tails of the *trans*-isomer and *cis*-isomer of the cation (a) as well as for cations and anions of [C₄AzoC₂mim]Br (b) in water and in 28.77 wt% K₂CO₃ aqueous solution.

Light switchable ATPSs for homogeneous reaction and heterogeneous separation. Aza-Michael reaction is an important kind of atomic economic reaction.⁶⁵ In modern organic synthesis, aza-Michael reaction is a powerful tool for building C-N bonds, and its products, such as β -amino carbonyl derivatives, are valuable building blocks for the synthesis of various nitrogen-containing biologically active compounds.⁶⁶ However, aza-Michael reaction is usually performed in volatile organic solvents, such as methanol and tetrahydrofuran, due to the poor solubility of reactants in water. Besides possible environmental pollution, the separation of the products is also a common problem.⁶⁵ Furthermore, it is often difficult to produce double addition products from such reactions although they are more valuable chemicals.⁶⁷

Here, as a proof of concept, our light switchable ATPSs were used as reaction medium for the aza-Michael reaction of benzylamine and methyl acrylate⁶⁷ to address these problems by demonstrating the integration of homogeneous reaction, heterogeneous separation, and recycle of the phase components of the ATPS. The formation of IL micelles in the system solubilized organic reactants, therefore, our systems could be used as homogeneous reaction media for aza-Michael reactions. As shown in Figure 7, after UV irradiation, the benzylamine and methyl acrylate reacted in the homogenous IL+ salt + water solution at 25.0 °C, then using visible light to irradiate the system after the reaction, the two-phase ATPS was reformed again under stirring. The product was partitioned in the top phase, then the top phase was extracted with ethyl acetate, and [C₄AzoC₂mim]Br and product were separated by decantation. Removing ethyl acetate by rotary evaporation, the product was obtained, while [C₄AzoC₂mim]Br and the bottom aqueous salt phase could be reused in the next cycle. Upon addition of another batch of

substrates to the ATPSs, the same reaction occurred without significantly affecting the yield of product.

Figure 7. (a), Reaction between benzylamine and methyl acrylate in $[\text{C}_4\text{AzoC}_2\text{mim}]\text{Br} + \text{K}_2\text{CO}_3 + \text{water}$ ATPS; (b), The reaction and separation procedures for the aza-Michael reaction of benzylamine and methyl acrylate. 0.05g of $[\text{C}_4\text{AzoC}_2\text{mim}]\text{Br}$, 0.3g of K_2CO_3 and 2.0g of H_2O were used for the formation of ATPS.

Table 2. Isolated yields for the reactions of benzylamine derivatives and acrylate in $[\text{C}_4\text{AzoC}_2\text{mim}]\text{Br} + \text{K}_2\text{CO}_3 + \text{water}$ ATPS at 25.0 °C

entry	amine	acrylate	product	Yield
1.				99%
2.				98%
3.				98%
4.				97%
5.				96%
6.				95%
7.				90%
8.				90%

As a representative example, the products produced from the reaction of benzylamine and methyl acrylate were identified by ^1H NMR spectroscopy (Figure S6), and the yield of 98.6% was obtained under optimized conditions (see optimization experiments, Tables S13-S16). Interestingly, it was shown that only di-substituted product was obtained, which indicates that the selectivity of this reaction is very high. This is an important development for production of more valuable chemicals by aza-Michael reaction, because traditional methods usually resulted in mono-substituted products.⁶⁵⁻⁶⁷ Furthermore, it was found that the yields for the same reaction in the ATPSs with different compositions were all greater than 93.2% (Figure S7). Therefore, this reaction could be performed over a wide range of compositions. Then, the reaction was performed in other ATPSs investigated in this work, and it was shown that the isolated yield of the di-substituted product in $[\text{C}_2\text{AzoC}_4\text{mim}]\text{Br} + \text{K}_2\text{CO}_3 + \text{water}$ and $[\text{C}_4\text{AzoC}_2\text{mim}]\text{Br} + \text{K}_3\text{PO}_4 + \text{water}$ ATPSs was 94.0% and 94.1% (Table S14), respectively. To extend the substrate scope, several benzylamine derivatives were used to react with methyl acrylate or ethyl acrylate under the same conditions, and the products were confirmed by ^1H NMR spectroscopy (Figure S8-S15). As shown in Table 2, the isolated yields of the di-substituted products were 90-99%, indicating good versatility of the ATPS for aza-Michael reaction. In addition, the IL and aqueous salt phase were reused for five reaction cycles, no clear decrease in the isolated yield of the di-substituted product (98.6% to 97.4%, Figure S16) was observed. Compared with the procedures reported in literatures, the strategy described here is characterized by high efficiency, excellent selectivity, use of clean solvent, mild reaction conditions, simple production separation and recyclable reaction media.

CONCLUSIONS

In summary, we designed and prepared a novel class of light-responsive ATPSs. It was found that the ATPSs formed from azobenzene-based ILs, inorganic salts and water could be reversibly switched between two phases and homogeneous solution by alternatively UV and visible light irradiation. UV irradiation results in the configuration change of cation of the azobenzene-based ILs from *trans*-isomer to *cis*-isomer, which reduces hydrophobicity of the ILs, decreases the size of their micelles, and leads to the components dissolution of two-phase ATPS. Nevertheless, visible light irradiation plays the reverse roles, and promotes phase separation of a homogeneous solution. Because of the features of clean, non-invasive and remote control of light stimulus, this reversible and switchable light-responsive phase transition provides a useful platform for homogeneous reaction, heterogeneous separation and solvent/catalyst recycling by using ATPSs as reaction medium. As an example, these light

switchable ATPSs were used for the aza-Michael reaction of benzylamines and acrylate at room temperature where the use of volatile organic solvents was avoided, and the di-substituted product was selectively produced with excellent yield which could not be obtained by conventional procedures. In addition, highly efficient and selective reaction, simple product separation and phase components recycle were well integrated by using ATPSs as reaction media. We believe that the strategy developed here could be also used to integrate other kinds of chemical reactions, their product separation and solvent/catalyst recycle to fabricate greener and sustainable chemical processes.

ASSOCIATED CONTENT

Supporting Information:

The Supporting Information is available free of charge on the ACS Publications website at DOI: Intermolecular energies data, binodal data of the ATPSs, maximum absorption wavelength of the ILs, size of [C₄AzoC₂mim]Br micelles, optimization experiments of the aza-Michael reaction (Table S1-S16), snapshots of the final conformations, binodal curves of ATPSs, light-induced isomerization of IL, conductivity titration curves of [C₄AzoC₂MIM]Br, ¹H NMR spectrum of the products of aza-Michael reaction and the ILs (Figure S1-S21).

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

NOTES

There are no conflicts to declare.

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A novel class of light-switchable ATPSs were designed and prepared from azobenzene-based IL surfactants and inorganic salts in water for the integration of highly efficient and selective aza-Michael reaction, simple product separation and recycle of phase components.