Semiconductor quantum dots (QDs) have attracted tremendous attention in the field of photocatalysis, owing to their superior optoelectronic properties for photocatalytic reactions, including high absorption coefficients and long photogenerated carrier lifetimes. Herein, by choosing 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile as a model substrate, we demonstrate that the stereoselective (> 99 %) C–C oxidative coupling reaction can be realized with a high product yield (99 %) using zwitterionic ligand capped CsPbBr₃ perovskite QDs under visible light illumination. The reaction can be generalized to different starting materials with various substituents on the phenyl ring and varied functional moieties, producing stereoselective di-isomers. A radical mediated reaction pathway has been proposed. Our study provides a new way of stereoselective C–C oxidative coupling via a photocatalytic means using specially designed perovskite QDs.

**Introduction**

Semiconductor quantum dot (QD) nanocrystals (NCs) have been exploited in diverse practical applications including solar energy harvesting,[1] biological imaging and labeling,[2] light-emitting diodes,[3] and next-generation displays,[4] owing to their superior optical and optoelectronic properties.[5] Recently, QDs have shown great promise as efficient photocatalysts for organic reactions such as oxidation,[6] high photo- and chemical stabilities,[5b,c] large absorption coefficient,[7] and redox reactions,[8] taking advantages of their unique optoelectronic properties for photocatalytic reactions, including high absorption coefficients and long photogenerated carrier lifetimes. Herein, by choosing 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile as a model substrate, we demonstrate that the stereoselective (> 99 %) C–C oxidative coupling reaction can be realized with a high product yield (99 %) using zwitterionic ligand capped CsPbBr₃ perovskite QDs under visible light illumination. The reaction can be generalized to different starting materials with various substituents on the phenyl ring and varied functional moieties, producing stereoselective di-isomers. A radical mediated reaction pathway has been proposed. Our study provides a new way of stereoselective C–C oxidative coupling via a photocatalytic means using specially designed perovskite QDs.

**Stereoselective C–C Oxidative Coupling Reactions Photocatalyzed by Zwitterionic Ligand Capped CsPbBr₃ Perovskite Quantum Dots**

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*Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202007520.*
accessible using other oxidants or catalysts,[21] can be used as intermediates to form indenes with significant pharmaceutical potentials.[22] Our study suggests that colloidal perovskite QDs with proper surface modifications are promising photocatalysts in chemical transformations and organic syntheses.

Results and Discussion

To explore and compare different QDs as photocatalysts for the C–C oxidative coupling of α-aryl ketonitriles, we synthesized eight types of QDs with different compositions and capping ligands (Table 1; Supporting Information, Figures S1–S3). In particular, zwitterionic ligand (that is, 3-(N,N-dimethylethylhexadecylammonio)propanesulfonate, DMOA-PS) capped colloidal CsPbBr3 perovskite QDs were synthesized modifying a previously reported method (Figure 1).[23] The prepared CsPbBr3 perovskite QDs show a cubic shape and a high morphological uniformity with an average edge length of 10.6 ± 1.2 nm (Figure 1a). High-resolution transmission electron microscopy (HR-TEM) measurement shows orthogonal atomic lattice fringes with a clear visualization of the (200) plane ($d$-spacing of 2.9 Å) and the (110) plane ($d$-spacing of 4.2 Å; Figure 1b), indicating a high crystallinity of the sample. The cubic perovskite crystal phase was confirmed by the powder X-ray diffraction (XRD) measurement with all the Bragg diffraction peak positions matching with the standard (space group: $Pm\bar{3}m$) (Figure 1d). The obtained zwitterionic ligand-capped CsPbBr3 (ZW-CsPbBr3) perovskite QDs exhibit a PL peak centered at 515 nm with a full width at half maximum of 78 meV (ca. 17 nm), similar to that

| Table 1: Optimization of reaction conditions.¶ |

<table>
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<th>Entry</th>
<th>Catalyst[¶]</th>
<th>Ligand of catalyst</th>
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<th>Size distribution [nm][°]</th>
<th>$E_{\text{g}}$ [eV][¶]</th>
<th>$t$ [h][¶]</th>
<th>dl/(dl + meso) [%]</th>
<th>Yield [%][¶]</th>
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[a] Reaction conditions: 1a (0.05 mmol) in THF (0.2 mL) was added to a QD toluene solution (3.2 mL). [b] The optical density (OD) of absorbance was 7.7 at 440 nm for all the catalysts used. For CsPbBr3 QDs, the amount was 1.3 × 10−3 mol·%. [c] 0.6 mg (the calculated equivalent amount of ligands used in Entry 8). [d] Diameter for spherical QDs and edge length for cubic QDs. [e] Bandgap energy determined by Tauc plot fitting (Supporting Information, Figure S3). [f] Reaction completion time. [g] Reaction was not complete and stopped after 70 h. [h] High-performance liquid chromatography (HPLC) determined reaction yields (Supporting Information, Figure S4). [i] Light triggered dimerization induced by small spectral overlap between the absorption of 1a and the LED light (Supporting Information, Figure S5). No reaction occurred under dark. [j] A mixture of dl and meso isomers (dl/meso = 15:1; yield, 95%) was detected when photocatalyzed by molecular photocatalyst [Ru(bpy)3][PF6]2 (2 mol·%) after 50 h (see the Supporting Information). [k] The reaction was run under the conditions in Entry 8 for 5 min, then the QDs were precipitated by addition of methanol. The supernatant was washed using methanol for another three times and the solvent was evaporated to 3.4 mL, then the resulting solution was irradiated for another 0.2 h, in which process no detectable increased amount of product was produced.
of oleate/oleylamine-capped CsPbBr$_3$ (OA/OAm-CsPbBr$_3$) perovskite QDs (Figure 1c).

With different QDs in hand, we started with 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile (1a) as a model substrate to investigate the feasibility of photocatalytic coupling reactions using the QDs as photocatalysts. With twoelectron-donating methoxy groups on the phenyl ring, 1a has been reported to convert to benzo[b]furan via oxidative intramolecular cyclization$^{[24]}$ or to a dimer via oxidative intermolecular C–C coupling.$^{[21,22]}$ When 1a was treated with CdSe QDs passivated with surface ligands of trioctylphosphine (TOP), octadecylphosphonic acid (ODPA), trioctylphosphine oxide (TOPO), 99% of the dimer (2a) product with negligible amount of benzo[b]furan was obtained after 44 h of irradiation using a blue LED light source (435–445 nm) (Table 1, Entry 1). When replacing with OA-CdSe QDs, the reaction time was shortened to 15 h, which can be attributed to the increased permeability of the ligand shell (OA compared to a combination of TOP, TOPO and ODPA) and the increased redox potential due to a smaller size (2.9 nm vs. 5.2 nm, Table 1, Entry 2; Supporting Information, Figure S3). CdSe–CdS core–shell QDs exhibited less photocatalytic reactivity, which can be explained by a strong confinement of photo-generated holes to the CdSe core region, limiting their accessibility to the particle surface for the subsequent oxidative coupling reaction (Table 1, Entry 3).$^{[25]}$ In contrast, CdS QDs accelerated the reaction to complete in 10 h at the expense of lowering 2a product yield to 89% (Table 1, Entry 4). We further tested using CdS-CdSe core–shell QDs with a reverse Type-I band gap alignment, in which the photo-generated carriers (both electron and hole) can migrate to the expense of lowering 2a.

To unravel the catalytic role of the CsPbBr$_3$ perovskite QDs play in the C–C coupling reaction, a kinetic study was carried out and the reaction order was examined by monitoring the concentration evolution of product 2a using high performance liquid chromatography (HPLC). The concentration of 2a increased linearly as a function of the reaction time with a rate constant ($k$) of 1.17 × 10$^{-5}$ M s$^{-1}$ (3.33 × 10$^{-6}$ Ms$^{-1}$ for OA/OAm-CsPbBr$_3$ QDs), and then remained nearly constant (7.4 × 10$^{-3}$ M) upon consumption of 1a substrates (Figure 2; Supporting Information, Figures S4, S13). This result suggests a zero-order reaction with respect to the reactant, 1a, signifying the catalytic nature of the coupling reaction. Importantly, in contrast to resulting in a mixture of dl- and meso-isomers ($\text{dl/mol}=5:3$, Table 1) for the reactions without QD catalysts, all the QDs photocatalyzed reactions studied here showed a stereoselectivity of dl-isomer over meso-isomer (>99%, Table 1; Supporting Information). Such a high stereoselectivity cannot be obtained with any conventional oxidants$^{[21b]}$ or catalytic metal complex.$^{[21a]}

To further expand the scope of the photocatalytic reaction, various o-aryl ketonitriles with different R$^1$ and R$^2$ groups as substrates were examined under the optimized reaction conditions using ZW-CsPbBr$_3$ perovskite QDs as catalysts, and the results are summarized in Figure 3. Since the dimerization reactions studied in our system are likely through a radical mediated reaction pathway, different EDGs and conjugated π systems, both of which can stabilize free radical intermediates,$^{[26]}$ were chosen as R$^1$ substituents on the benzene ring of substrates. In particular, the substrates bearing EDGs (that is, 3,4-dimethoxy, 3,4-methylenedioxy, and 4-methoxy) at the para-position of the benzene ring could produce the corresponding dimers efficiently (reaction yield > 90% within 30 mins, Figure 3, 2a–c; Supporting Information, Figures S14, S15). Whereas, no desired products were produced when the EDGs (that is, methoxy group) were

![Figure 2. Concentration evolution of product 2a (a) and reaction rate constant (b) as a function of reaction time under optimized reaction conditions.](image-url)
placed at the ortho- or meta-positions (Figure 3, 2d, e). The less electron-donating effect from the methoxy group at meta-position leads to an increased oxidation potential required for the dimerization, resulting in the product yield staying at a negligible level (Figure 3, 2d). Although the methoxy group at the ortho-position provides a stronger electron-donating effect, the steric hindrance induced by close proximity between the ortho-methoxy group and the benzylic position (reaction site) reasonably explains the failure of the dimerization reaction (Figure 3, 2e). While retaining the para-methoxy group, and adding a meta-bromo group as an electron-withdrawing substituent, the reduced effect in electron donating of the substrate cause a slower dimerization reaction (reaction completion time of 2.5 h) with a lowered reaction yield of 85% mixed dimers (dl/meso = 80:20; Figure 3, 2f). To further demonstrate the requisite of strong electron donating effect in the dimerization reaction, the substrates either with a weaker EDG (that is, methyl group) on the para-position or without any functional groups on the aromatic ring were tested and brought no desired dimer products as expected (Figure 3, 2g, h). Alternative to the addition of EDGs, expansion of the conjugated π-system of the substrate can also stabilize free radical intermediates through electron delocalization effect.[20] Evidently, replacing the benzene ring with a naphthyl group on the substrate delivered desired dimer products (dl/meso = 67:33) with a yield of 85% in a 4-h reaction time (Figure 3, 2l). Besides varying R$^1$ substituents, we further expand the reaction scope by altering the R$^2$ substituent from methyl group to aryl (Figure 3, 2j) or methoxy group (Figure 3, 2k, l). In all cases, the dimerization reaction occurred to generate the corresponding products with reasonable reaction yields (≥ 50%), Figure 3, 2j-l). The dl- and meso-isomers were distinguished using nuclear magnetic resonance (NMR) spectroscopy, in which meso-isomers exhibit a broad single peak at a chemical shift of around 2.35 ppm (a sharp peak for dl-isomer at around 2.45 ppm) for COMe group (see NMR spectra in the Supporting Information). [21] The assignments were confirmed by variable temperature NMR and heteronuclear single quantum coherence spectroscopy (HSQC) measurements using 2c as an example (see discussion in the Supporting Information, Figures S14, S15).

It is known that α-aryl ketonitriles can be converted to either dimers or benzo[ b]furans under oxidative conditions.[22-24] Specifically, intermediate radicals of 1a-1 or 1a-2 need to be generated through dissociating either C–H$^+$ or C–H$^-$ bond, respectively for the subsequent formation of dimer (from 1a-1) or benzo[ b]furan (from 1a-2). However, in our reaction system, only dimer products were collected for all the substrates inspected (Figure 3). To understand the underlining mechanism, the bond dissociation energies for C–H$^+$ and C–H$^-$ bonds were calculated using density functional theory (DFT) calculations (see the Supporting Information). A 62% smaller bond dissociation energy of 71 kcal mol$^{-1}$ was obtained for the C–H$^+$ bond than that of the C–H$^-$ bond (dissociation energy of 115 kcal mol$^{-1}$), indicating 1a-1 radical is the energetically favored product (Figure 4a). The DFT calculation result is in good agreement with the sole observation of dimer products (Table 1). To further confirm the presence of the tertiary carbon radical (1a-1) formed from C–H$^+$ bond cleavage, electron paramagnetic resonance (EPR) spectroscopy measurements were carried out using 5,5-dimethyl-pyrroline N-oxide (DMPO) as a radical scavenger.[13] Under the optimized reaction conditions, however
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energy calculation and EPR results agree well with the experimentally observed exclusive dimerization reaction, strongly supporting the proposed free-radical-based reaction pathway.

Our photocatalytic reaction results and mechanistic studies clearly delineated a proposed reaction mechanism as shown in Figure 5. During the reaction, after absorbing an excitation photon, one electron will be excited to the conduction band (CB) of the CsPbBr\(_3\) perovskite QD and then consumed by reacting with a surrounded O\(_2\) molecule to form superoxide radical (O\(_2^•−\)). Meanwhile, the hole left in the valence band (VB) oxidizes the substrate molecule (such as 1a) to form radical intermediates \(1a\)-1, \(1a\)-1, \(1a\)-1, \(1a\)-1. Given the Pb-rich surface nature of the CsPbBr\(_3\) perovskite QDs (Supporting Information, Figure S17), the reactants and resultant free radical intermediates can dynamically attach to surface Pb\(^{2+}\) ions through donating a lone pair of electrons of the oxygen atom in the carbonyl group, acting as a L-type ligand, which was supported by the broadening and shifting of the CH and COCH\(_3\) peaks of the substrate in the NMR spectra (Supporting Information, Figure S18).\(^{[18,27]}\) Consequently, dimer products can be formed by the C–C bond formation between two neighboring radicals. Depending on the relative configuration of the two radicals on the QD surfaces, either \(dl\)- or \(meso\)-isomers can be obtained (Figure 5). However, less steric hinderance between the aryl groups of the radicals in the \(trans\)-arrangement makes the \(dl\)-isomer a kinetically favored reaction product (Figure 5). The same \(dl\)-configuration is also a thermodynamically favored geometry because of the attractive interaction between the \(gauche\) cyano groups upon molecular structural relaxation after detaching from the QD surfaces.\(^{[28]}\) Furthermore, the reactions using the substrates with relatively large substituent groups delivered pure \(dl\)-isomers (Figure 3, 2a, b, j), strongly supporting our hypothesis of steric hinderance induced stereoselectivity. To confirm that the photogenerated hole, rather than the in situ formed superoxide species (O\(_2^•−\)), is

![Figure 4](image-url)

**Figure 4.** Mechanism study of photo-induced oxidative coupling of 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile (1a). a) Bond dissociation energies of the C–H\(^+\) and C–H\(^−\) bonds of 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile (1a) calculated by DFT. b) Reaction schemes showing the generation of DMPO-superoxide and DMPO-substrate species upon addition of radical trapping agent DMPO. c) EPR spectrum of a toluene/THF solution mixture of CsPbBr\(_3\) QDs, DMPO and 2-(3,4-dimethoxyphenyl)-3-oxobutanenitrile (1a) after irradiation for 20 min.

with absence of substrate 1a (see the Supporting Information for details), a four-fold EPR signal with a hyperfine coupling constant of N atom (\(a_N\)) of 12.8 G and a coupling constant of H atom (\(a_H\)) of 8.3 G (g value: 2.010) was detected and assigned to DMPO-superoxide adduct after 5-second illumination using a LED light source (435–445 nm) (Supporting Information, Figure S16).\(^{[16]}\) A three-fold hyperfine splitting profile (\(a_N\): 13.1 G and g value: 2.009) was observed with further illumination for a total of 20 min, as a result of the ring-opening of the DMPO-superoxide adduct (Supporting Information, Figure S16).\(^{[16]}\) When substrate 1a was introduced to the reaction solution, an EPR signal with two sets of hyperfine splitting patterns were obtained (Figure 4c). Detailed EPR signal analysis showed the presence of two active species, that is, DMPO-superoxide (\(a_N\): 12.6 G, \(a_H\): 12.2 G; and g value: 2.012) and DMPO-substrate-1a-1 species (\(a_N\): 9.4 G; \(a_H\): 32.6 G; and g value: 2.010) (Figure 4b,c).\(^{[16]}\) For each of the species, EPR signal first split into a triplet from the interaction between the radical (1a-1) and N nucleus, and then further split into quartet (for DMPO-superoxide species) and sextet (for DMPO-substrate-1a-1 species) as results of the interaction with H nucleus (Figure 4c). The EPR results unambiguously proved the formation of substrate 1a-1 radicals in the reaction. Together, both the bond dissociation...
investigating a series of starting substrate materials with reactivity. Moreover, we expand the reaction scope by the QD catalysts as well as enhance their photocatalytic activity mediated reaction mechanism (Figure 5).

Conclusion

We show the first example of stereoselective C–C oxidative dimerization reaction photocatalyzed by ZW-CsPbBr₃ perovskite QDs under visible light illumination. High stereoselectivities (> 99%) of di-α isomers are demonstrated by dimerizing two α-aryl ketonitriles. We found that the zwitierionic ligand coverage is crucial to stabilize/recycle the QD catalysts as well as enhance their photocatalytic reactivity. Moreover, we expand the reaction scope by investigating a series of starting substrate materials with different substituents on the aryl ring and varied functional moieties. We show that EDGs on the para-position of the aryl ring or an extended conjugated π system is necessity for efficient dimerization reactions to occur. Furthermore, mechanistic studies reveal a free-radical mediated reaction pathway with the steric hindrance effect being largely responsible for the observed stereoselectivity. Our study shows that halide perovskite QDs with an optimized ligand passivation hold a great potential of acting as efficient photocatalysts in a range of organic transformations with improved product yield and high selectivity.

Acknowledgements

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Conflict of interest

The authors declare no conflict of interest.

Keywords: C–C coupling · CsPbBr₃ · perovskite QDs · photocatalysis · stereoselectivity


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Stereoselective C–C Oxidative Coupling Reactions Photocatalyzed by Zwitterionic Ligand Capped CsPbBr$_3$ Perovskite Quantum Dots

C–C oxidative dimerizations of α-aryl ketonitriles are realized by using zwitterionic ligand capped CsPbBr$_3$ perovskite QDs as catalysts under visible light illumination, via a radical mediated reaction pathway. High stereoselectivities of $dl$-isomers were obtained owing to less steric hindrance during the bond formation process. Our study sheds new lights on using lead-halide perovskite QDs as photocatalysts for stereoselective organic synthesis.