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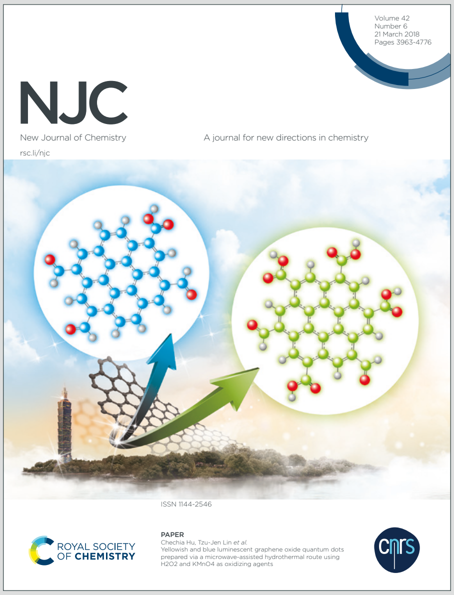

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PAPER
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Yellowish and blue luminescent graphene oxide quantum dots prepared via a microwave-assisted hydrothermal route using H2O2 and KMnO4 as oxidizing agents

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COMMUNICATION

Visible light induced radical cascade cyclization of ortho-cyanoarylacrylamides with phosphine oxides for the preparation of phosphorylated quinoline-2,4(1*H*,3*H*)-dione

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Visible light induced cascade cyclization of ortho-cyanoarylacrylamides with phosphine oxides for the preparation of phosphorylated quinoline-2,4(1*H*,3*H*)-dione. Products with moderate to good yields were efficiently isolated. Radical mechanism was proposed for this transformation.

Quinoline-2,4-dione scaffolds are central core in a large number of natural products, pharmaceuticals and agrochemicals.[1-5] Additionally, they are also intermediates for the synthesis of bioactive and novel heterocyclic compounds.[6, 7] As a consequence, the development of efficient and novel protocols for their construction has aroused great interest over the past decades.[8-11] Among these reported synthetic methods, the radical cascade cyclization reactions were proved to be the most effective methods. For example, the copper-catalyzed cascade addition/cyclization for the synthesis of phosphonylated,[12] carbonylated,[13] methylated,[14] trifluoromethylated and sulfonated[15] quinoline-2,4(1H,3H)-diones was described by Li group. The difluorinated quinoline-2,4-diones were efficiently prepared by Shi group[16] and Lu group.[17] However, new versatile and practical methods for the synthesis of various substituted quinoline-2,4(1*H*,3*H*)-diones are still desirable.

Visible light has proved to be highly economical and eco-friendly energy source.[18-22] Organic transformations induced by visible light have obtained much progress in recent years.[23-28] Among these reactions, radical cascaded cyclization reactions for the synthesis of various substituted heterocyclic products induced by visible light have received much attention. At present, visible light induced cyclization reactions for the preparation of azepane cores,[29] 2-amino-1,4-naphthoquinone derivatives,[30] trifluoromethylated dihydroisoquinolinones,[31] phosphoryl-substituted dihydroisoquinolones,[32] spiro[4,5]trienones,[33] sulfur-containing compounds[34] and so on[35-38] have been reported. In line with our interests in radical chemistry,[39-43] herein, visible light induced radical cascade cyclization of ortho-cyanoarylacrylamides with phosphine oxides for the preparation of phosphorylated quinoline-2,4(1H,3H)-dione was efficiently realized.

In order to find the optimized reaction conditions, the reaction of N-(2-cyanophenyl)-N-methylmethacrylamide and diphenylphosphine oxide was chosen as a model reaction for this investigation. To our delight, the desired product was isolated in 29% yield using CHCl$_3$ as solvent, 4CzIPN as photocatalyst and LPO (Dilauroyl peroxide) as oxidation (table 1, entry 1). The use of THF as solvent led to 84% yield (table 1, entry 2). The reactions which conducted in dioxane or DCE generated the corresponding products in 71-76% yields (table 1, entries 3-4). Solvents containing halogen and ether solvents may be favorable for the reaction. Poor yields of the products were obtained when the reaction was performed in DMF, DMSO, toluene. Most of the substrates were unreacted and only trace of unknown side products was detected in these reactions (table 1, entries 5-7). Photocatalyst also play an important role in this reaction. To our disappointment, no desired products was isolated when Eosin Y, [Acr+-Mes]ClO^{4-}, Ru(bpy)$_3$Cl$_2$, tetrabromofluorescein or Eosin B was subjected to this reaction (entries 8-12). Subsequently, we examined the effect of oxidant on this reaction. Encouraged by this result, we investigated the effect of different oxidants for this reaction. It revealed that BPO (dibenzoyl peroxide) could delivered the desired in moderate yield (table 1, entry 16). Low yields of the products were isolated when DCP (dicumyl peroxide), TBHP (t-butylhydroperoxide), TBPB (tert-butyl peroxybenzoate) or DTBP (di-tert-butyl peroxide) was used as oxidant (table 1, entries 14-15, 17-18). No reaction could proceed in the presence of PIDA (table 1, entry 13). Visible light, photocatalyst nitrogen protection and oxidant was crucial for this reaction, because no desired product was isolated when the reaction was performed in the absence of any of them (table 1, entries 22-25)

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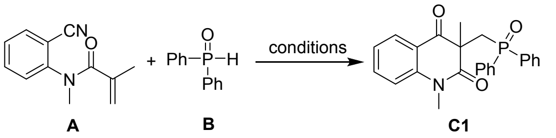
Table 1. Optimization Studies [a]

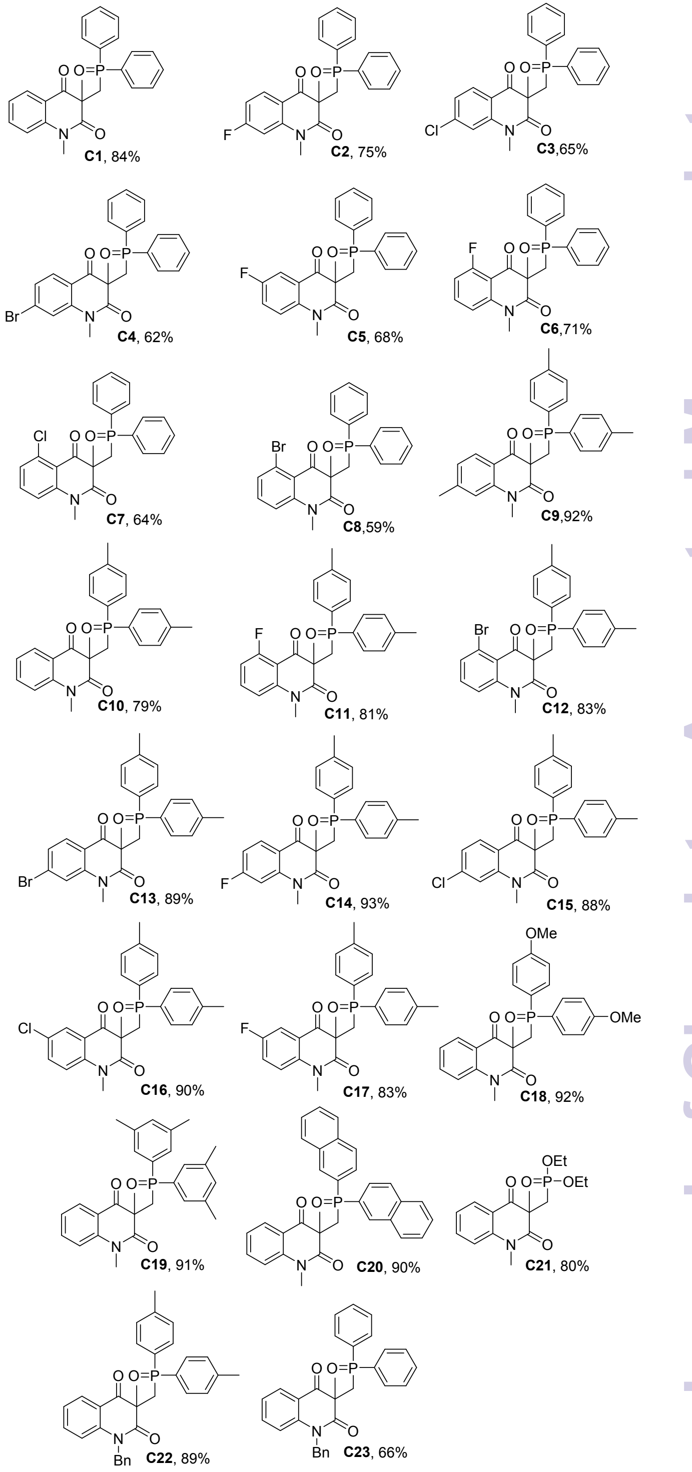


Entry	Potocatalyst	Oxidant	Solvent	Yield[b](%)
1	4CzIPN	LPO	$CHCl_3$	29
2	4CzIPN	LPO	THF	84
3	4CzIPN	LPO	Dioxane	71
4	4CzIPN	LPO	DCE	76
5	4CzIPN	LPO	DMF	Trace
6	4CzIPN	LPO	DMSO	Trace
7	4CzIPN	LPO	Toluene	Trace
8	Eosin Y	LPO	THF	N.D.
9	$[Acr^+\text{-}Mes]ClO_4^-$	LPO	THF	N.D.
10	$Ru(bpy)_3Cl_2$	LPO	THF	N.D.
11	Tetrabromofluorescein	LPO	THF	N.D.
12	Eosin B	LPO	THF	N.D.
13	4CzIPN	PIDA	THF	N.D.
14	4CzIPN	DCP	THF	11
15	4CzIPN	TBHP	THF	13
16	4CzIPN	BPO	THF	74
17	4CzIPN	TBPB	THF	38
18	4CzIPN	DTBP	THF	23
22[c]	4CzIPN	LPO	THF	N.D.
23	4CzIPN	-	THF	*trac*e
24	-	LPO	THF	N.D.
25[d]	4CzIPN	LPO	THF	N.D.

[a]Reaction conditions: A (0.1mmol), B (0.1mmol), PC (5 mol%), oxidant (2.0 equiv), solvent (2 ml) for 24 h under N_2. PC = photocatalyst, 4CzIPN=1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene, LPO = dilauroyl peroxide, N.D. = not detected. [b] Isolated yield. [c] dark. [d] Under Air.

Under the optimized reaction conditions, the scope of a variety of ortho-cyanoarylacrylamides and phosphine oxides was investigated. Ortho-cyanoarylacrylamides possessing various electron-withdrawing groups such as F, Cl, Br on the phenyl ring show good performance and afforded the corresponding products in 59-84% yields (C1-C8). Products bearing these groups are favorable for their further modification. Additionally, ortho-cyanoarylacrylamides modified by electron-donating methyl group was also effective for this reaction, providing the product with 92% yield (C9). Next, the effect of substituents on phenyl group of phosphine oxides was also examined. To our delight, phenyl ring containing methyl, methoxyl and dimethyl group all suitable for this reaction. The substrates were successfully converted to the desired products with good to excellent yields (C10-C19). It is worthwhile to note that products whit high yields were isolated when di(naphthalen-2-yl)phosphine oxide and diethyl phosphonate were examined (C20-C21). For the substituent on nitrogen of ortho-cyanoarylacrylamides, benzyl group was also applicable for the reaction, give the desired product with 66-88% yields (C22-C23)

Table 2. Reaction Scopes [a,b]



[a] Reaction conditions: ortho-cyanoarylacrylamides (0.1mmol), phosphine oxides (0.1mmol), 4CzIPN (5 mol%), LPO (2.0equiv), white LEDs (10 W) for 24 h under N_2.

In order to gain some insight to the mechanism of this transformation, some control experiments were conducted. No

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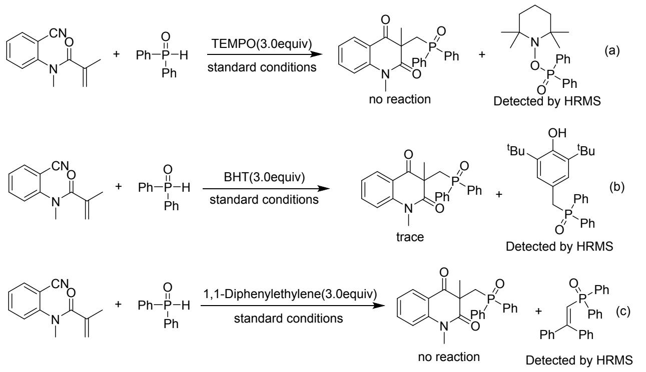
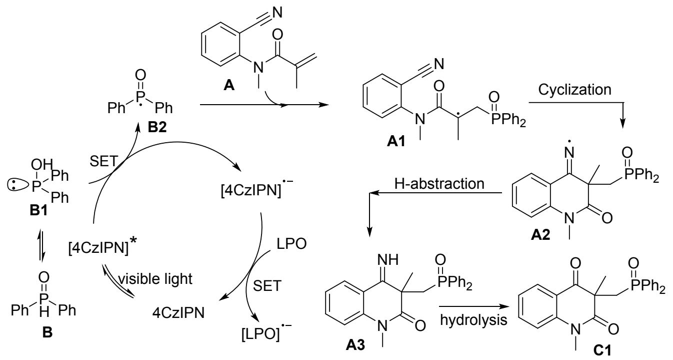
target product was isolated when radical scavenger 2,2,6,6-tetramethyl-1piperidinyloxy (TEMPO), butylated hydroxytoluene (BHT) or 1,1-Diphenylethylene(3.0equiv) was added in the model reaction (Scheme 1). These results indicated that a radical process was involved in this reaction.



Scheme 1. Control experiments.

Based on the above mentioned results and previous reports,[44-47] a plausible reaction mechanism was described for this reaction (Scheme 2). Initially, the ground state of 4CzIPN is converted into the excited state 4CzIPN* under the irradiation of visible light. Then the SET reaction between tri-coordinated isomer B1 of diphenylphosphine oxide and the excited 4CzIPN* occurred to give phosphoryl radical B2 and the radical anion $4CzIPN^{\cdot-}$. Then carbon-centered radical was formed via the addition reaction of phosphoryl radical B2 and carbon-carbon double bond of A, which was followed by cyclization to deliver intermediate A2. Next, imine intermediate A3 was generated from A2 via H abstraction. Finally, hydrolysis of imine intermediate A3 by water delivered the desired product C1.



Scheme 2. Proposed reaction mechanism.

In conclusion, we have developed a simple and practical protocol for the efficient synthesis of a series of phosphorylated quinoline-2,4(1H,3H)-dione. In the presence of visible light, products with moderate to high yields were obtained. Further studies on the reaction mechanism and expansion of the scope of the reaction to other complicated molecules are currently underway in our laboratory.

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Conflicts of interest

"There are no conflicts to declare".

Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.
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