

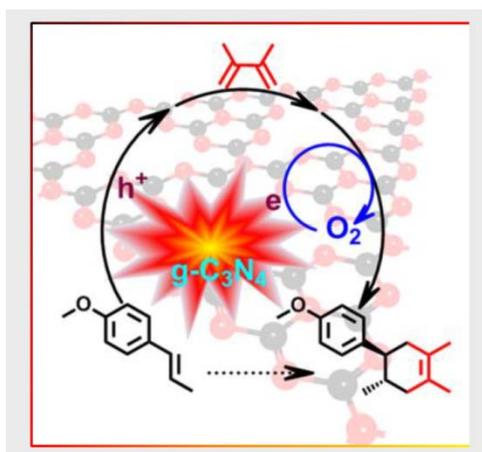


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Visible Light Irradiated Graphitic Carbon Nitride ($g\text{-C}_3\text{N}_4$) Photocatalyzed Cation Radical Diels-Alder Reactions with Dioxygen as Sustainable Mediator for Photoinduced Electrons

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Photocatalytic Diels-Alder (D-A) reaction with electron rich olefins is realized by graphitic carbon nitride ($g\text{-C}_3\text{N}_4$) under visible light irradiation, with an apparent quantum yield of 47 % for the model reaction. Dioxygen plays a critical role as electron mediator. The cycloaddition process is validated to be the combination of direct [4 + 2] cycloaddition and [2 + 2] cycloaddition followed by photocatalytic rearrangement of the vinylcyclobutane intermediate.

Visible Light Irradiated Graphitic Carbon Nitride (g-C₃N₄) Photocatalyzed Cation Radical Diels-Alder Reactions with Dioxygen as Sustainable Mediator for Photoinduced Electrons

Yubao Zhao* and Markus Antonietti

Abstract: Photocatalytic Diels-Alder (D-A) reaction with electron rich olefins is realized by graphitic carbon nitride (g-C₃N₄) under visible light irradiation and aerobic condition. This heterogeneous photo-redox reaction system is highly efficient, and apparent quantum yield reaches a remarkable value of 47 % for the model reaction. Dioxygen plays a critical role as electron mediator, which is distinct from the previous reports in the homogeneous Ru(II) complex photo-redox system. Moreover, the reaction intermediate vinylcyclobutane is captured and monitored during the reaction, serving as a direct evidence for the proposed reaction mechanism. The cycloaddition process is thereby determined to be the combination of direct [4 + 2] cycloaddition and [2 + 2] cycloaddition followed by photocatalytic rearrangement of the vinylcyclobutane intermediate.

Photo-redox catalysis, which could potentially employ the renewable solar energy to realize diverse chemicals conversions, has been resurged in the recent decade, not only because of the current global energy and environmental crisis, but also due to the attractive novel reaction mechanisms enriching the potentialities in organic synthesis.^[1] Visible light accounts for 44% (versus 3% for UV light) of the solar spectrum, setting the motivation for the development of the visible light driven photocatalytic systems for synthesis of value-added or complex molecules.^[2] Additionally, UV light harms many sensitive molecules, and visible light photocatalysis promises wider applicability for realizing increasingly ambitious photo-redox reactions.^[2a]

Diels-Alder (D-A) reactions are an exceptionally versatile tool in organic synthesis for C-C bond formation.^[3] According to the Frontier Molecular Orbital (FMO) theory, the reactions between electron-rich dienes and electron-poor dienophiles are dominated by HOMO_(diene) - LUMO_(dienophile) interactions and are facile thermal reactions. If electron density of dienes and dienophiles do not favor such an interaction, harsh reaction conditions are required, or some orbital energy tuning methodologies can be employed with restrictions.^[3c] Fortunately, it was found that oxidation to the cation radical of the dienophile drives a significantly enhanced reaction rate of the D-A cycloaddition. One-electron chemical oxidation (commonly by aminium salts) or photoinduced electron transfer to a photosensitizer (such as 9,10-dicyanoanthracene) is required for

initiating the radical chain reactions.^[4] Recently, novel photo-redox systems for D-A reaction were developed, and the cation radical D-A reactions with electron-rich dienophiles were described, realized by homogeneous photo-redox systems catalyzed by Ru(II) complexes under visible light and Cr (III) complexes under UV light irradiation.^[5] Interestingly, the reaction mechanism in Cr (III) complex system is distinct from that in Ru(II) photo-redox system. The radical chain propagation is dominating in the Ru(II) system, while the dioxygen mediated photocatalytic process is favorable in Cr(III) complex system.^[5a,c] From the perspectives of both basic science and practical applications, a heterogeneous photo-redox system with a low cost visible light-driven photocatalyst is highly desirable. g-C₃N₄, with band gap of 2.7 eV and valence band level of 1.4 V vs. NHE at pH = 7,^[6] is a promising candidate to achieve the goal of cation radical D-A reaction with electron rich dienophiles employing visible light as energy input.

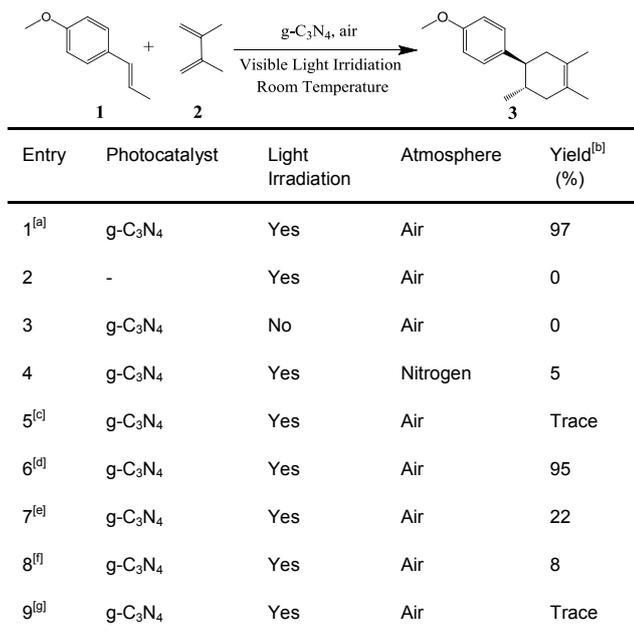
Herein, we report a highly efficient visible light driven heterogeneous photo-redox system for D-A reaction on g-C₃N₄. It exhibits high apparent quantum yield and broad substrate scope. Moreover, two critical points in the reaction mechanism are validated: 1) dioxygen serves as an active mediator for photo-induced conduction band electrons; 2) vinylcyclobutane is determined to be an intermediate in the reaction.

Using 0.5 mmol trans-anethole (**1**) and 1.5 mmol 2,3-dimethyl butadiene (**2**) as the substrates, the photocatalytic D-A reaction was successfully realized on g-C₃N₄ with 97 % yield of cycloadduct (**3**) after 1 hour visible light irradiation. A series of control reactions and optimization experiments were conducted to figure out the roles of each part in this photocatalytic system (Table 1). Visible light irradiation and g-C₃N₄ are the requisites for the system as energy source and photocatalyst, respectively (Table 1, entries 2 and 3). Flushing the system with nitrogen lowers the yield to only 5 %; and the addition of 14 mol % of benzoquinone, which is an efficient (superoxide) radical scavenger,^[7] the reaction is inhibited to trace amount of conversion (Table 1, entries 4 and 5). Aerobic condition is obviously necessary to this system, and the detailed contribution of dioxygen to this reaction system is discussed later in the reaction mechanism. This efficient cycloaddition reaction was further scaled up to 1 mL trans-anethole, and a remarkable yield of 95 % was achieved within 2.5 h visible light irradiation, indicating the applicability of this methodology (Table 1, entry 6). The photocatalyst possesses good stability, showing a high yield of 94% at the 5th cycle.

Table 1. Control and optimization experiments of the photocatalytic cation radical [4 + 2] cycloaddition of trans-anethole with 2,3-dimethyl-1,3-butadiene.

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[a] Standard reaction conditions: 0.5 mmol **1**, 1.5 mmol **2**, 25 mg g-C₃N₄, 30 mg MgSO₄, 5 mL CH₃NO₂ was added in a photoreactor with 15 mL volume, followed by 1 hour visible light irradiation. [b] Yield is based on the ¹H-NMR analysis with an internal standard. [c] 37 μmol Benzoquinone was added in the reaction mixture for capturing the superoxide radical. [d] Gram scale reaction: 1 mL (6.7 mmol) of **1**, 2.3 mL **2**, 100 mg MgSO₄, and 200 mg g-C₃N₄ was added in a flask with 40 mL CH₃NO₂, followed by 2.5 h visible light irradiation. [e] CH₃CN as solvent. [f] CH₂Cl₂ as solvent. [g] Cyclohexane as solvent.

In lieu of the polar CH₃NO₂, some less polar solvents were tested in this system. A dramatic slowing down of the reaction rate is observed: 21 % and 8 % yields for reactions in CH₃CN and CH₂Cl₂, respectively. The reaction in the non-polar cyclohexane gives no conversion (Table 1, entries 7, 8, and 9). The dependence of the photocatalytic performance on the polarity of the solvent strongly demonstrates that the D-A reaction in this system occurs *via* a pathway involving cation radical.^[8]

To further study the effect of visible light irradiation on the reaction, an experiment with alternating light and dark phases was conducted. As shown in Figure 1a, the initial 5 min irradiation leads to 37% yield. The reaction stops immediately when the light is blocked, and it restarts in the following light irradiation interval, reflecting the possibility of temporal control of the reaction. After total 35 min light irradiation segments, the reaction with 0.5 mmol **1** reaches complete conversion. To quantitatively describe the efficiency of this photocatalytic reaction system, the apparent quantum yield (AQY) was measured. The AQY of the reactions with 5, 10, and 15 min visible light irradiation is 47.6 ± 3.0 %, 43.9 ± 1.4 %, and 38.9 ± 1.4 %, respectively, demonstrating the remarkable photo-conversion efficiency of this photocatalytic system (Figure 1b).

By GC-MS and NMR analysis, the intermediate in the photocatalytic D-A cycloaddition reaction is identified to be the vinylcyclobutane derivative, which originates from the photocatalytic [2 + 2] cycloaddition of **1** and **2**.^[5b, 8, 10] The variation of vinylcyclobutane intermediate concentration and the product amount during the photocatalytic reaction is shown in Figure 1c. After a transient raise, the concentration of the

vinylcyclobutane intermediate reaches a peak, and then, gradually decreases to zero; while for **3**, the concentration keeps increasing until the dienophile is completely converted. These curves are characteristic for a consecutive reaction with vinylcyclobutane as the intermediate and **3** as the final product. Due to the appropriate photocatalytic activity of g-C₃N₄ towards the conversion of **1** to vinylcyclobutane (reaction rate constant, k_1) and vinylcyclobutane to **3** (reaction rate constant, k_2), the balance of k_1 and k_2 engenders the temporary building up of the vinylcyclobutane intermediate, providing important hint to a valid reaction mechanism.

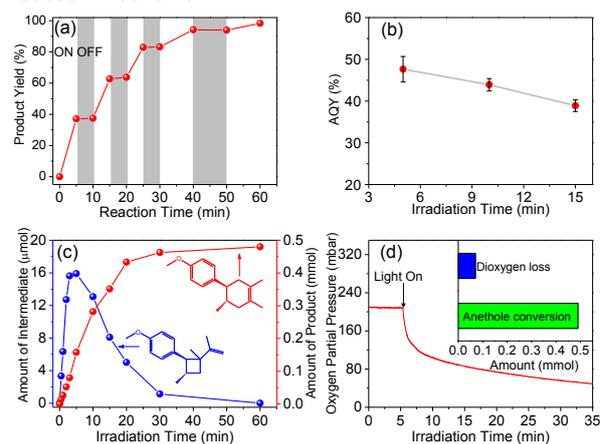


Figure 1. (a) The yield of **3** in the reaction with alternating light irradiation and dark intervals. (b) Apparent quantum yield (AQY) of the reaction. (c) The variation of the amount of D-A cycloadduct (**3**) and vinylcyclobutane intermediate during the reaction. (d) Oxygen partial pressure of the headspace (10 mL) in the photoreactor.

As mentioned above, the presence of dioxygen is a prerequisite to the effectiveness of this photo-redox system. As such, a quantitative analysis of the dioxygen variation during the reaction could lead to a fresh insight into the role of dioxygen as well as the reaction mechanism. The dioxygen concentration of the head space in the photo-reactor was thereby monitored by an oxygen sensor throughout the photocatalytic reaction process.^[9] As shown in Figure 1d, the dioxygen partial pressure drops rapidly in the initial 5 min, and decreases gently in the following 25 min, until the end of the reaction. The inset in Figure 1d shows that the dioxygen loss is only 14 (mol) % of the trans-anethole conversion. Meanwhile, the excess diene **2** undergoes oxidative cleavage of the C=C bond to produce 3-Methyl-3-buten-2-one, which accounts for 70 (mol) % of the dioxygen loss. Accordingly, less than 0.05 equiv. of dioxygen services the D-A reaction cycle, converting 1 equiv. of the trans-anethole into D-A cycloadduct. The dioxygen loss data herein is suggesting two possible facts: 1) dioxygen could be regenerated during the reaction (working as mediator for photoinduced electrons); or 2) radical chain propagation dominates the reaction. However, the latter is less significant than the former according to the experimental result that the absence of dioxygen leads to minimal reactivity of the system. Additionally, ESR (electron spin resonance) spectra show the characteristic peaks of the DMPO-O₂⁻ (DMPO, 5,5-Dimethyl-1-pyrroline N-oxide), demonstrating

the formation of the superoxide radical under visible light irradiation (Figure S3).

The combination of all the above experimental facts strongly suggest that dioxygen plays a critical role of electron mediator ($O_2/O_2^{\cdot-}$, -1.42 vs. Fc^+/Fc in CH_3CN),^[10] accepting the photoinduced conduction band electrons and transporting them to the cationic adduct intermediates to neutralize the charge and close the photocatalytic cycle.

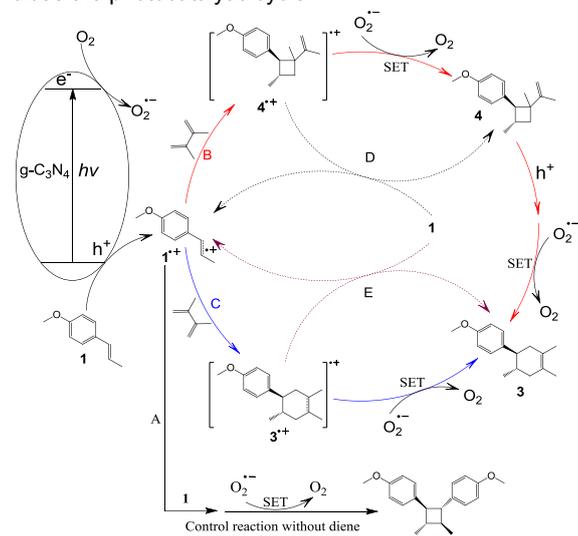


Figure 2. Proposed mechanism of the photocatalytic [4+2] cycloaddition of **1** and **2** on $g-C_3N_4$ under visible light irradiation. SET, single electron transfer.

According to the above solid analysis, a detailed reaction mechanism is proposed (Figure 2). Visible light irradiation drives charge separation in $g-C_3N_4$, producing oxidative valence band holes and reductive conduction band electrons.^[6b,c] The conduction band electrons reduce the dioxygen and produce superoxide radicals. The valence band hole oxidize **1** to the corresponding cation radical 1^+ ($1/1^+$, 1.0 V vs. Fc^+/Fc in CH_3NO_2).^[5e] If there is no diene available (Pathway A), this cation radical will react with another molecular **1** to produce a [2 + 2] cycloadduct (**5**), being consistent with the solvent polarity dependence feature of the system.^[11b,12]

Via pathway B, 1^+ reacts with **2** to produce the vinylcyclobutane cation radical, which then extracts electron from superoxide radical and converts to molecular **4**. As analyzed above, **4** is an intermediate, and will continue a photocatalytic cation radical sigmatropic shift to the final [4 + 2] cycloadduct **3**. This kind of rearrangement was also independently observed in Cr(III) complex photo-redox system, under thermal conditions, as well as in the cation radical reaction initiated by PET or aminium salt.^[5b,13] In addition, pathway C describes the direct [4 + 2] cycloaddition of 1^+ and **2**, producing a cycloadduct cation radical 3^+ . After a further one electron transfer from the superoxide radical to 3^+ , the final cycloaddition product **3** is produced.

Pathways D and E describe the possible radical chain propagation, in which the cycloadduct cation radicals (3^+ and 4^+) extract electrons from olefin **1**, producing neutral molecules and regenerating 1^+ . Although these reactions are

thermodynamically feasible,^[5] according to the previous discussion, the chain propagation pathways are not very persistent, as indicated by the inactivity of the system without dioxygen.

It is interesting to compare the data with the Ru(II) and Cr(III) complex systems. The Ru(II) complex system without air only loses 50 % photocatalytic efficiency.^[5a] In the Cr(III) systems, the absence of air causes $\sim 90\%$ of activity loss, and the presence of the 10 mol% superoxide radical scavenger (benzoquinone) lead to 60 % yield loss (from 88 % to 34 % yield).^[5e] In the present $g-C_3N_4$ photocatalytic system, substitution of air by nitrogen causes $> 95\%$ activity loss, and the addition of the superoxide radical scavenger leads to completely inactivity. The D-A reactions in the photo-redox systems proceed via multiple pathways. The radical chain propagation is dominating in the Ru(II) complex system; and the dioxygen mediated pathway accounts for higher percentage in the Cr(III) complex systems. In the heterogeneous $g-C_3N_4$ system, the dioxygen mediated pathway make a main contribution to the reaction.

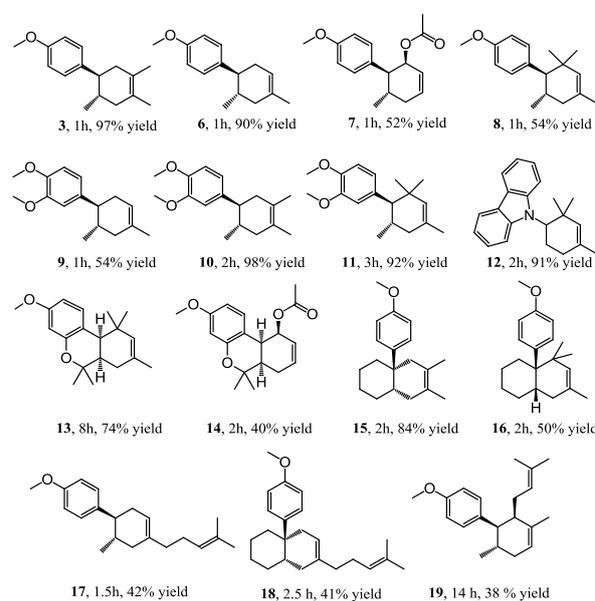


Chart 1. The scope of the $g-C_3N_4$ photocatalyzed cation radical Diels-Alder reactions under visible light irradiation.

$g-C_3N_4$ photocatalyzed system exhibits broad substrate scope. A series of dienes and dienophiles are successfully converted to their respective D-A cycloaddition products with high yield and excellent stereoselectivity (Chart 1). With **1** as the dienophile, isoprene shows slightly lower activity than **2** in the cycloaddition reaction, giving 90 % yield (**6**) after 1 h visible light irradiation. With 1-acetoxy-1,3-butadiene and 2,4-dimethyl-1,3-pentadiene, the reactions produce **7** and **8** with 52 % and 54 % yield, respectively. With more electron-rich 1,2-dimethoxy-4-propenylbenzene as the dienophile, cycloaddition reactions with a series of dienes give **9**, **10**, and **11** with 54 %, 98 % and 92% yield, respectively. The N-Vinylcarbazole (enamine) is capable of being dienophile in the cycloaddition reaction in this system, resulting **12** with 91 % yield in 2 h photocatalytic reaction.

Dienophiles with cyclohexene unit, such as precocene I and 1-(4-methoxyphenyl)-1-cyclohexene, are also active in this system (**13**, **14**, **15**, and **16**). Dienes with longer carbon chain are suitable for this reaction as well, although with relatively lower yield (**17**, **18**, and **19**). The reaction involving cyclohexadiene gives no D-A product, repeatedly indicating the cationic radical reaction mechanism, rather than the triplex D-A reaction.^[8,14]

In summary, we have developed a heterogeneous photocatalytic system with low cost, metal-free g-C₃N₄ sheets for visible light harvesting and conversion. D-A reactions with electron-rich dienophiles could be efficiently realized, and the apparent quantum yield reaches a remarkable value of 47%. Dioxygen plays a critical role as an active electron mediator (0.05 equiv. O₂ for 1 equiv. of olefin) in this photo-redox system; and the reaction is overwhelmingly dominated by dioxygen mediated reaction pathway. In addition, the reaction intermediate of vinylcyclobutane is captured and monitored during the reaction, serving as a direct evidence for the proposed reaction mechanism. The cycloaddition process is thereby presumably a combination of direct [4 + 2] cycloaddition and a [2 + 2] cycloaddition followed by photocatalytic rearrangement of the vinylcyclobutane. There are some unique advantages from this system, such as the heterogeneous metal-free photocatalyst being low cost and environmental benign, visible light being the energy input, and the aerobic reaction condition, which endow this protocol with significance in potential heterogeneous photocatalytic synthetic utility.

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Keywords: Photocatalysis • Graphitic Carbon Nitride • Visible Light Irradiation • Electron Mediator • Diels-Alder Reaction

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