Intermolecular [2+2] Photocycloaddition of β-Nitrostyrenes to Olefins upon Irradiation with Visible Light

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Dedicated to Victor Snieckus, a dear colleague and friend, on the occasion of his 80th birthday

Abstract
The title compounds were found to undergo a [2+2] photocycloaddition with olefins at λ = 419 nm in CH₂Cl₂ as the solvent. The resulting cyclobutanes were isolated in yields of 32–87% (11 examples) and showed a defined relative configuration at C1/C4 in the major diastereoisomer (nitro and aryl trans). The analysis of side products and triplet sensitization experiments support a mechanistic scenario in which a 1,4-diradical is formed as a key intermediate.

Key words
cycloaddition, cyclobutanes, diastereoselectivity, nitro compounds, photochemistry, stereoselective synthesis, umpolung, visible light

Although [2+2] photocycloaddition chemistry originates historically from experiments performed with visible light, the advent of artificial UV light sources led – starting in the middle of the 20th century – to the almost exclusive use of short-wavelength (λ = 250–380 nm) irradiation in all areas of photochemistry. Interest in reactions that were promoted by long-wavelength (λ > 380 nm) irradiation was spurred in the 1970s and in the 1980s by the desire to find suitable energy storage systems mainly based on the [2+2] photocycloaddition of norbornadienes to quadricyclenes. Aromatic carbonyl compounds and transition-metal salts were found to act as triplet sensitizers in this transformation allowing the reaction to occur with visible light. More recently, triplet energy sensitization has been employed for enantioselective [2+2] photocycloaddition reactions that are promoted by visible light in the presence of an appropriate sensitizer. In the context of our work on the activation of chromophors by Lewis or Brønsted acids, we became interested in the photochemistry of nitrostyrenes. The compound class seemed amenable to undergo direct intermolecular [2+2] photocycloaddition reaction upon excitation with visible light and we report in this communication on our preliminary results on this topic.

Already in the 19th century, the [2+2] photodimerization of trans-β-nitrostyrene was observed to occur upon exposure to sunlight. However, reactions with olefins in the spirit of an intermolecular [2+2] photocycloaddition have remained rare and were performed exclusively with short-wavelength light. Chapman et al. mentioned in a review on the photochemistry of unsaturated nitro compounds the reaction with olefins but did not provide any experimental details.

Later, Majima et al. employed the reaction of trans-β-nitrostyrene (1) and indene (2a) to form cyclobutane 3a (Scheme 1). A high-pressure mercury lamp was employed as the light source in this transformation. In more recent work, pyrex-filtered irradiation was used to study the reaction of nitrostyrenes with silyl enol ethers.

Inspection of the UV-Vis spectrum of trans-β-nitrostyrene in CH₂Cl₂ (Figure 1) reveals a strong absorption centered at λ = 312 nm (ε = 16500 M⁻¹ cm⁻¹). This band has been previously assigned to an allowed ππ*-transition with significant charge-transfer character. At high concentration it is evident that the absorption continues into the visible region of the electromagnetic spectrum in line with the fact that trans-β-nitrostyrene (1) is a yellow-colored solid.
Further experiments were undertaken to identify a less problematic solvent but benzene and to optimize the reaction conditions at \( \lambda = 419 \) nm. While toluene was found less suited to substitute benzene, dichloromethane turned out to be an excellent solvent. A larger excess of the olefin led to higher product yields and the concentration was lowered to 20 mM in order to allow for small-scale reactions with more precious, not commercially available nitrostyrenes (vide infra). At optimized conditions the \([2+2]\) photocycloaddition products \(3a/3a'\) were obtained in a yield of 87% after 24 hours of irradiation at \( \lambda = 419 \) nm. A variety of other olefins was employed in the reaction, and the results are summarized in Scheme 2.

It should be noted that the reactions were not always complete and that in some cases substantial amounts (up to 22%) of starting material were recovered, mostly as \(cis-\) nitrostyrene. Yields refer to isolated products, however, and are not corrected for conversion. With olefins \(2b, d, f, g\), the fact that the polarity of the excited state is opposite to the ground state polarity (photochemical umpolung) becomes particularly apparent. C–C bond formation occurs formally between two – in the ground state – electrophilic centers (C1–C2) and between two nucleophilic centers (C3–C4). The reactions with olefins \(2b–d\) led to a mixture of diastereoisomers the relative configuration of which could be in most cases elucidated by NOESY experiments (see Supporting Information for further details). Cyclobutanes \(3e–g\) were obtained as single products. For the reaction of the electron rich olefin \(2b\), it was checked that there was no reaction in the absence of irradiation.22

Contrary to unsaturated hydrocarbons \(2e\) and \(2g\), cyclopentene \(2h\) did not react with a sufficient rate at \( \lambda = 419 \) nm. The \([2+2]\) photocycloaddition could, however, be successively conducted if nitrostyrene \(1\) was irradiated in a
solution of cyclopentene at $\lambda = 350$ nm (Scheme 3). The products were found to be a mixture of diastereoisomers in which product 3h with the nitro group in exo position to the cyclopentyl ring prevailed (d.r. = 87:13).

Some preliminary experiments were conducted with other aromatic nitroolefins 4 (Scheme 4). 2,3-Dimethyl-2-butene (2e) was employed as the reaction partner since its use avoids the formation of regio- or diastereomeric cyclobutane products. It was found that electron-rich aryl groups (para-tolyl, para-anisyl, 2-thiophenyl) in 2-position of the respective nitroethenes ($4a, 4b, 4d$) led in their [2+2] photocycloaddition to results similar to those of trans-$\beta$-nitrostyrene. Reaction times were short (2–4 h) and cyclobutanes 5a, 5b, and 5d were obtained in yields of 50–54%. The reaction with the para-cyano-substituted nitrostyrene 4c was less chemoselective and gave product 5c in a yield of only 32% after a longer reaction time (6 h). A side product could be isolated (vide infra).

If 2,3-dimethyl-2-butene was subjected to [2+2] photocycloaddition with cis-$\beta$-nitrostyrene instead of trans-$\beta$-nitrostyrene the reaction was slower. The reaction product was exclusively the trans-substituted cyclobutane 3e that was isolated in 43% yield. Irradiation of trans-$\beta$-nitrostyrene at $\lambda = 419$ nm in the absence of an olefin established an equilibrium between the cis and the trans diastereoisomer in a ratio of 86:14. This finding is in accord with the higher extinction coefficient of the trans diastereoisomer within the wavelength range of the light source. The absorption maximum of cis-$\beta$-nitrostyrene is centered at $\lambda = 309$ nm ($\epsilon = 5200$ M$^{-1}$ cm$^{-1}$) in CH$_2$Cl$_2$ solution.

Mechanistically, there is no indication for a reaction course which would deviate from the pathway of typical [2+2] photocycloaddition reactions. In this regard, it seems likely that olefin 2 adds to the excited substrate, for example, trans-$\beta$-nitrostyrene (1), most likely on the triplet hypersurface (Scheme 5). A 1,4-diradical 6 is formed as intermediate which collapses after intersystem crossing to product 3. Evidence for the postulated structure of diradical 6 is based on the constitution of the products and side products. Indeed, olefins such as 8 were isolated in a few instances and their formation is readily explained by a hydrogen abstraction in the intermediate 1,4-diradical. In the reaction of olefin 2e with styrene 4c, byproduct 8 was obtained in 5% yield and is putatively formed via intermediate 7.

Further support for the hypothesis that the reaction proceeds via a triplet intermediate was obtained from the reaction of styrene 1 and olefin 2e. In the absence of an additive the reaction was complete after 12 hours (Scheme 2), while a significant rate increase was noted upon addition of the triplet sensitizer 9H-thioxanthen-9-one (thioxanthone). No $\beta$-nitrostyrene was detected after three hours and product 3e was obtained in 47% yield (Scheme 6).

In summary, we have shown that nitro-substituted cyclobutanes can be accessed by a visible-light-induced [2+2] photocycloaddition of various 2-aryl-nitroethenes and olefins. The yields are moderate to good (32–87%) and can possibly be further improved by adjusting the wavelength and the reaction temperature. Given the straightforward reduc-
tion of nitro compounds to amines.\textsuperscript{11c,14,29} the method offers also access to various aminocyclobutanes. Mechanistically, upon encounter of the photoexcited nitro compound and the olefin, in addition, it might be worth to study whether other nitroethenes but nitrostyrenes are equally suited for [2+2] photocycloaddition reactions. Work along these lines is in progress in our laboratories and will be reported in due course.

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**Supporting Information**

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**References and Notes**


(13) In a later paper, the reaction of trans-β-nitrostyrene (1) and 2,3-dimethylbutadiene (2d) was reported to be performed at λ = 300 nm: Magner, J. T.; Selke, M.; Russell, A. A.; Chapman, O. L. J. Chem. Ed. 1996, 73, 854.


(21) **Representative Procedure**

29.8 mg of nitrostyrene (199 μmol, 1.00 equiv) and 10.0 equiv of olefin (2e (168 mg, 2.00 mmol) were dissolved in degassed, dry CH₂Cl₂ (c = 20 mM). The reaction solution was irradiated at...
λ = 419 nm in a Duran tube at r.t., and the reaction progress was monitored by TLC. When no further conversion was observed by TLC (t = 12 h), the reaction was stopped and all volatiles were removed. Purification by column chromatography (pentane/Et2O = 20:1) gave product 3e as a yellow oil (27.5 mg, 118 μmol, 59%). When performed on a mmol scale (150 mg 1), product 3e was obtained in 56% yield (132 mg).

1H NMR (500 MHz, CDCl3, 300 K): δ = 0.71 (s, 3 H, CH3-2), 1.15 (s, 3 H, CH3-3), 1.19 (s, 3 H, CH2-2), 1.24 (s, 3 H, CH3-3), 3.97 (d, J = 10.1 Hz, 1 H, H-1), 4.91 (d, J = 10.1 Hz, 1 H, H-4), 7.08–7.13 (m, 2 H, ortho-HAr), 7.23–7.28 (m, 1 H, meta-HAr), 7.30–7.37 (m, 2 H, para-HAr) ppm. 13C NMR (101 MHz, CDCl3, 300 K): δ = 19.5 (q, CH3-3), 21.5 (q, CH3-2), 22.8 (q, CH2-2), 24.3 (q, CH2-3), 39.3 (s, C-2), 44.9 (s, C-3), 49.4 (d, C-1), 84.9 (d, C-4), 127.0 (d, ortho-CAr-H), 127.1 (d, meta-CAr-H), 136.4 (s, CAr) ppm.


(27) The reaction time was 6 h. If the isomerization was performed starting from cis-β-nitrostyrene under otherwise identical conditions, the cis/trans ratio was 82:18.

