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COMMUNICATION

Enyne [4+4] Photocycloaddition with Polycyclic Aromatics†‡

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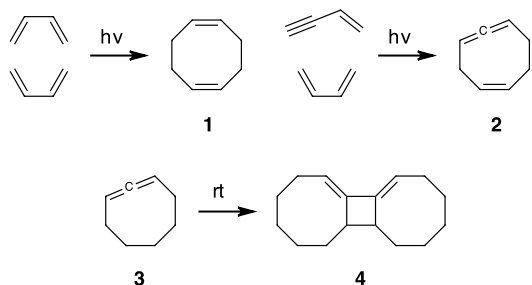
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Polycyclic aromatics undergo [4+4] photocycloaddition to give substituted cyclooctadiene products. We have examined the [4+4] photoreactivity of these aromatics with enynes using a recently developed substitution pattern that undergoes a 1,3-hydrogen migration, forming a single cycloadduct. Several substrates yield stable, isomerized [4+4] adducts.

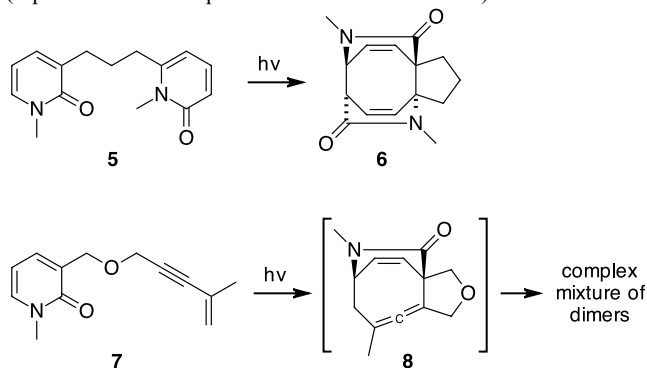
Higher-order cycloaddition reactions are powerful approaches for construction of molecular complexity.^{1,2} Photo-[4+4] dimerization of 1,3-dienes is, in principle, a direct way to access 1,5-cyclooctadienes **1**, with up to four stereogenic centers, but the yield of this reaction is less than 1%, Scheme 1.³ Similarly, an enyne might undergo a [4+4] cycloaddition with a 1,3-diene to yield 1,2,5-cyclooctatriene **2**. The product **2**, unlike **1**, is rare because of its strain.⁴ This strain is nicely illustrated by 1,2-cyclooctadiene **3**, which undergoes a thermal [2+2] cycloaddition producing dimer **4**.⁵



Scheme 1. Cycloaddition of dienes and enynes can yield medium rings. Cycloocta-1,2-dienes are unstable.

The use of 2-pyridones as [4+4] photocycloaddition partners has proven to be a general and efficient method for constructing densely functionalized 1,5-cyclooctadiene structures like **6**, Scheme 2.⁶ Pyridones undergo [4+4] photocycloaddition not only with themselves, but with furan, naphthalene and 1,3-dienes.⁷ We have

recently added 1,3-enynes to this list.^{8,9} The photocycloaddition of the tethered pyridone–enyne **7** efficiently yields adduct **8** but this compound is very short lived. The isolated products are derived from dimerization of **8**, structures analogous to the parent 1,2-cyclooctadiene dimer **4**. This dimerization occurs with both of the allene double bonds, with more than twenty products possible (representative examples have been characterized).⁹

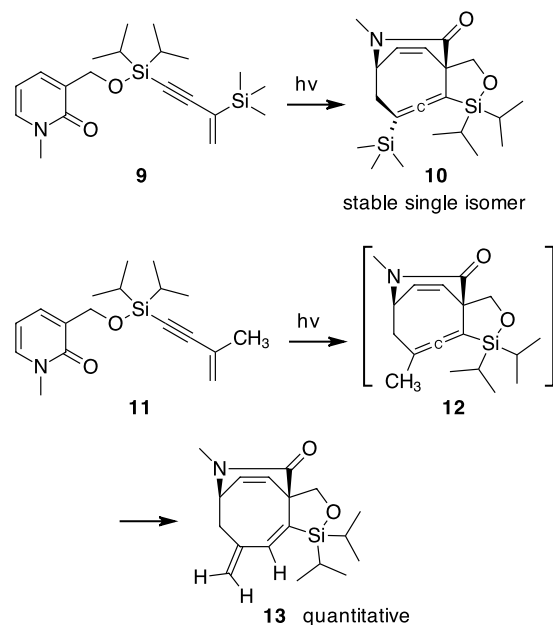


Scheme 2. Photocycloaddition of pyridones with themselves and with enynes are efficient reactions but the latter yields unstable products.

In more recent studies we have explored approaches to stabilize and/or trap the reactive allene photoproducts **8**. Johnson demonstrated that a *tert*-butyl group attached to allene **3** results in a stable structure⁵ and we therefore have explored analogs of **8** designed to slow or prevent dimerization. This strategy led to the cycloadduct **10** with silanes on both ends of the allene, Scheme 3. Structure **10** appears to be indefinitely stable when stored cold, however, it remains unstable to chromatography.¹⁰ For photosubstrate **11**, with diisopropylsilyl and methyl groups on the enyne, a rearrangement path to stability was discovered. Photocycloaddition of **11** presumably leads to cyclooctatriene **12**. This allene is not observed, because it undergoes a rapid 1,3-

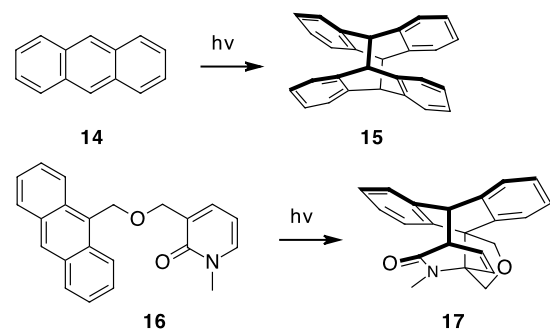
hydrogen shift producing 1,3-diene **13** quantitatively. While still sensitive, this product can be readily isolated in 67% yield.¹⁰

After identifying this combination of methyl and diisopropylsilyl groups in **11** as an ideal enyne [4+4] participant that quantitatively yields a single product, we have explored the participation of this enyne unit with other unsaturated structures known to participate in [4+4] photocycloadditions, and report the results of those studies herein.



Scheme 3. Steric hindrance leads to stabilization of cyclooctatriene products.

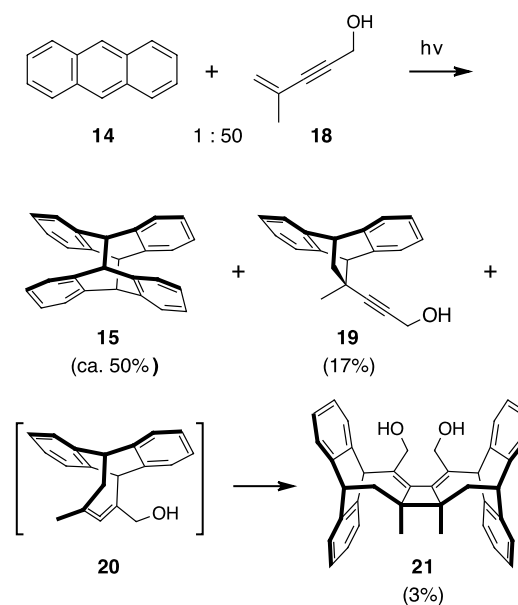
The first organic photoreaction, reported in 1867, was [4+4] photocycloaddition of anthracene **14** dimerizing to **15**, Scheme 4.¹¹ Both inter- and intramolecular photodimerization of anthracenes have been extensively studied.¹²⁻¹⁴ With these as precedence and inspiration, enyne-anthracene photocycloaddition was studied with inter- and intramolecular examples (Schemes 5 and 6, respectively). As a preamble to those studies we have investigated the photoreactivity of anthracene with 2-pyridones using **16** as a substrate, Scheme 4. Irradiation of this substrate with a medium-pressure mercury lamp for one hour gave quantitative conversion to adduct **17**.



Scheme 4. Anthracene undergoes a quantitative [4+4] cycloaddition with 2-pyridone.

The intermolecular photoreaction of enynes and anthracene **14** was first tested with 4-methyl-4-penten-2-yn-1-ol **18**. Irradiation of mixture of **14** with 50 equivalents of enyne **18** in benzene at ambient temperature for 2 h gave dimerization of anthracene (**15**) as the major reaction path, isolated in 50% yield. An apparent [4+2] adduct **19** was isolated in 17% yield. Compound **21** was isolated in 3% yield. Product **21** results from [4+4] cycloaddition of the enyne with anthracene and the initially formed **20** undergoes a thermal [2+2] dimerization. The [4+2] adduct **19** could result from a thermal Diels-Alder reaction, however the short duration and low temperature of this reaction makes photo-[4+2] reaction a more likely pathway.¹⁵

Dimer **21** is a symmetric product (NMR, twenty ¹³C signals) with the cyclobutane formed from the methyl-substituted end of the allene. This identification is based, in part, on the chemical shift of the methyl group singlet for **21** that is consistent with its attachment to an aliphatic carbon rather than an alkene (1.89 ppm).⁸ While depicted as the cis isomer, the trans substituted cyclobutane isomer cannot be ruled out.

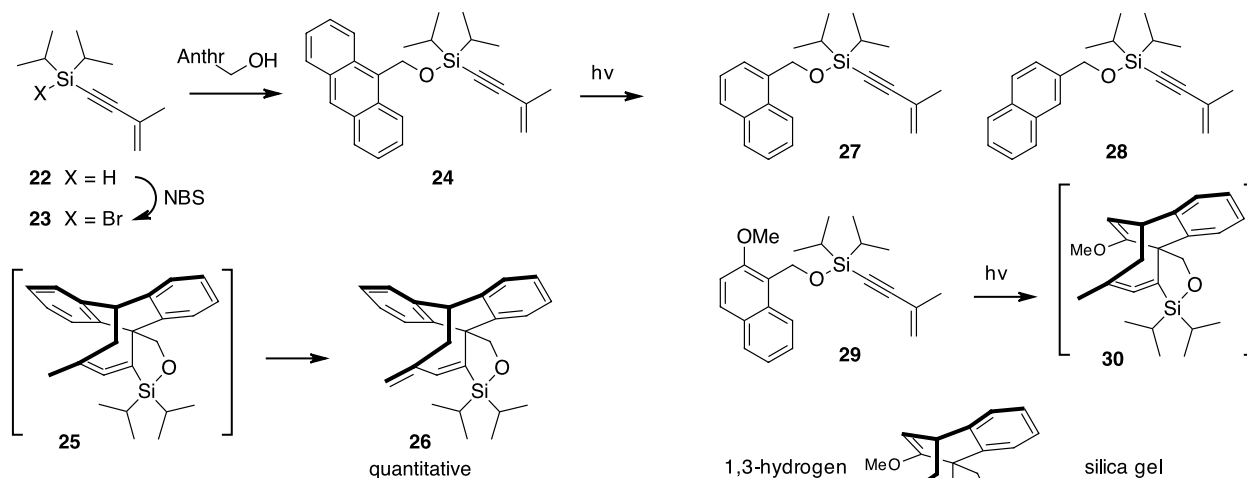


Scheme 5. Intermolecular anthracene-enyne photoreaction yields a small amount of [4+4] cross adduct as the dimer.

In contrast to the intermolecular reaction in which a [4+4] product was formed in low yield, the intramolecular reaction with the diisopropylsilyl ether gave a quantitative yield of the [4+4] adduct. Preparation of photosubstrate silyl ether **24** from 9-hydroxymethylantracene began with oxidative bromination of silane **22** using NBS, to give **23**, Scheme 6. Bromosilane **23**, without isolation, was mixed with the alcohol and triethylamine to yield ether **24**.

Irradiation of **24** using a Pyrex-filtered medium pressure mercury lamp for one hour cleanly converted **24** to the cycloaddition product **26**. Analogous to our findings for cycloaddition with 2-pyridone, isomerization by 1,3-hydrogen shift was too fast to observe; compound **26** formed cleanly and was the only product formed.

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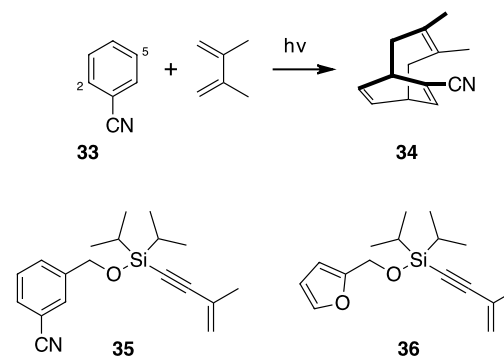
Scheme 6. Anthracene undergoes a rapid and quantitative cycloaddition–isomerization reaction with the methyl enyne.

A somewhat more complex reaction sequence is observed with the lower homolog naphthalene. Silyl ethers of both 1- and 2-naphthyl methanols **27** and **28** were prepared analogously to **24**, Scheme 7. Irradiation of these substrates with a Pyrex-filtered medium-pressure mercury lamp did not result in productive photochemistry, nor did irradiation with Vycor-filtered light. When the 2-methoxy analog **29** was irradiated, however, a rapid photoreaction again was observed, quantitatively forming the cycloaddition – rearrangement product **31**. Purification of this product by chromatography over silica gel did not yield **31** but instead gave the corresponding ketone **32**.

The very facile hydrolysis of enol ether **31** is well precedented in the literature of naphthalene photodimerization reactions, and reflects the strain inherent in these [4+4] photoproducts.¹⁶

Scheme 7. Methoxy-substituted naphthalene **29** undergoes a rapid and quantitative cycloaddition–isomerization reaction with the tethered enyne. Chromatography results in enol ether hydrolysis.

Following successful cycloadditions of the silicon-tethered enyne with anthracene and naphthalene, we turned our attention to the next lower homologue. Benzene has a rich photochemistry literature, with three primary modes of addition with alkenes and alkynes, so called ortho, meta and para cycloadditions.¹⁷ Among these, meta cycloaddition has been most widely studied. In reactions with 1,3-dienes only benzonitrile has been reported to yield [4+4] "para" photoadduct **34**, Scheme 8. Photocycloaddition with 2,3-dimethyl-1,3-butadiene and with furan leads to adducts attached at the positions 2 and 5 of the benzonitrile.^{18,19} Coupling enyne **23** with the corresponding alcohols gave **35** and **36**. Irradiation of these using a Rayonette photoreactor equipped with 254 nm lights, and with a medium-pressure mercury lamp – both Pyrex and Vycor filtered – failed to yield any cycloaddition products.



Scheme 8. Benzonitrile undergoes [4+4] (a k a "para") cycloaddition with 1,3-dienes but neither **35** nor **36** photoadd to tethered enynes.

In the work described here we have studied the use of enynes as [4+4] photocycloaddition participants with reactants other than 2-pyridones, our original vehicle. Comparing anthracene reactions with those of 2-pyridones, dimerization of the [4+4] products is a dominant path when the products are relatively unhindered. Intermolecular reactions form [4+4] adducts in low yield. Intramolecular reactions, in contrast, efficiently form [4+4] adducts between the enyne and the aromatic. When the [4+4] adducts of enynes are formed, dimerization of the resulting allenes is rapid unless steric shielding of the allene is substantial. A diisopropylsilyl group can provide enough shielding to allow for competing strain-relief paths to compete with the dimerization. In these examples, a 1,3-hydrogen migration leads to a single 1,3-diene product. This has allowed us to identify anthracene and naphthalenes as substrates for enyne [4+4] photocycloaddition chemistry, opening up new avenues for application of this cycloaddition process.

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Notes and references

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† Dedicated to Professor Max Malacria on the occasion of his 65th birthday.

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