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The Photochemical Cycloaddition Reaction of 2-Cyclohexenone with Alkenes: Trapping of Triplet 1,4-Biradical Intermediates with Hydrogen Selenide[1]

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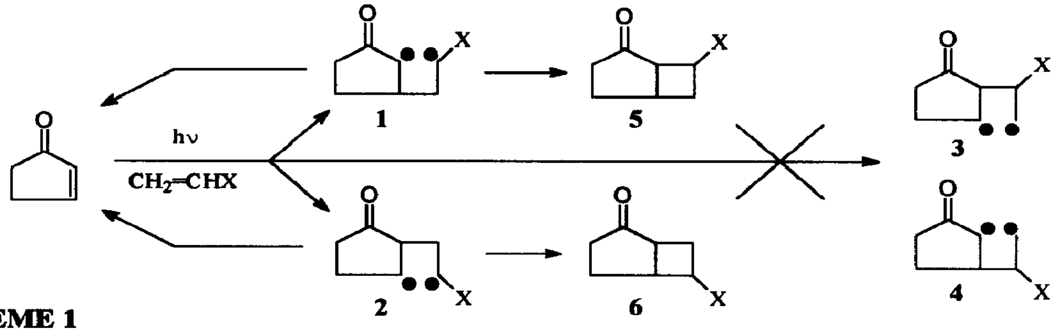
Key Words: enone, photochemistry, cycloaddition, alkene, triplet 1,4-biradicals, hydrogen selenide, trapping, regiochemistry.

Abstract: *The triplet 1,4-biradical intermediates formed in the photochemical cycloaddition reaction between 2-cyclohexenone and the alkenes cyclopentene and ethoxyethene have been trapped quantitatively with hydrogen selenide. The structures of the biradicals reveal that they are formed by bonding of both the 2-position and the 3-position of the enone to one terminus of the alkene; in the case of ethoxyethene it is exclusively the less substituted terminus of the alkene that becomes bonded to the enone in the biradical intermediates. The yields of the trapped biradicals indicate that the regiochemistry of the photocycloaddition reaction is determined by the manner in which the biradicals partition between fragmentation to give ground state starting materials and closure to give product, and not by their relative rates of formation. The results suggest that the mechanistic factors governing the photocycloaddition chemistry of cyclohexenone are similar to those controlling the photochemistry of cyclopentenones.*

The photochemical cycloaddition reaction of alkenes with cyclic enones is an important synthetic reaction[2] whose mechanism has been the subject of some controversy. For many years the regiochemical outcome of the reaction was rationalised by the intermediacy of oriented exciplexes formed between the triplet excited state of the enone and the ground state alkene. However, new evidence suggests that exciplexes may not be involved[3] and that the regiochemistry can be explained in terms of the properties of triplet 1,4-biradical intermediates,[4,5] as was suggested some years ago by Bauslaugh.[6] We have recently reported direct evidence that the photocycloaddition reaction of 2-cyclopentenones with some substituted ethenes proceeds predominantly *via* the triplet 1,4-biradicals **1** and **2** shown in Scheme 1.[4,5] These are formed by bonding of both the 2-position and the 3-position of the enone to the less substituted end of the alkene. In general, the primary radical containing biradicals **3** and **4** are either not formed in detectable amounts, or are present as minor components; the only exceptions to this rule observed to date are when methyl acrylate[7] or allene[8] is used as the alkene partner. We have also shown that the regiochemical outcome of the reaction (i.e., the proportions of the head-to-head and head-to-tail products **5** and **6**) is determined by the extent to which each of the isomeric biradical

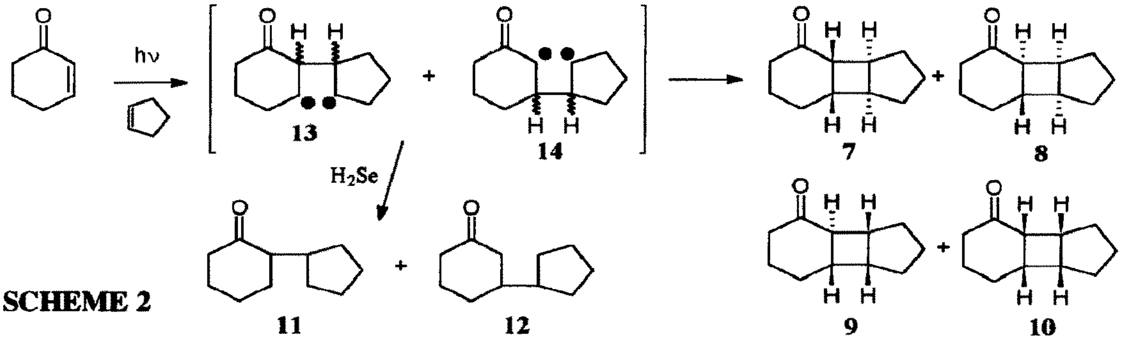


SCHEME 1

intermediates partitions between fragmentation (to give back ground state 2-cyclopentenone and alkene) and closure to cyclobutane adducts, and not by their relative rates of formation as has long been assumed. These conclusions have been reached using three methods to probe the relative yields, structures and properties of the triplet 1,4-biradical intermediates. These are: (1) independent generation of the biradicals and monitoring of their decay pathways;[9] (2) interception of the biradical intermediates using radical rearrangement reactions;[10] (3) trapping of the biradicals using hydrogen selenide as a hydrogen atom donor.[4,5,7,8]

All of our work reported to date has focused on the photocycloaddition chemistry of 2-cyclopentenones. However, 2-cyclohexenones also form cyclobutane adducts when irradiated with ultra-violet light in the presence of alkenes, and from a synthetic standpoint the photocycloaddition chemistry of the larger ring enone is of equal importance to that of 2-cyclopentenone;[2] furthermore, the greater flexibility of the cyclohexenone ring might be expected to perturb the properties of the enone triplet excited state and the triplet 1,4-biradical intermediates produced by its interaction with alkenes. For these reasons we have now probed the structures of the biradical intermediates formed in the photochemical reaction of 2-cyclohexenone with the alkenes cyclopentene and ethoxyethene. Reported here are the preliminary results of this study in which we have used hydrogen selenide to trap the biradical intermediates.

The products of the photocycloaddition reaction of cyclopentene with 2-cyclohexenone in acetonitrile have recently been characterised by Schuster and coworkers.[11] We repeated this reaction in order to determine the product ratio when toluene is used as the reaction solvent; ultra-violet light irradiation[12] of a toluene solution of 2-cyclohexenone (0.2M) containing cyclopentene (2.0M) yielded the four racemic cyclobutane adducts **7-10** in the ratio 68 : 5 : 26 : 1, respectively (Scheme 2). When the irradiation was performed under the same conditions but in the presence of hydrogen selenide[13] (*circa* 0.3M) cycloadduct formation was completely suppressed and the only photochemically generated products were 2-cyclopentylcyclohexanone, **11**, and 3-cyclopentylcyclohexanone, **12**. Products **11** and **12** were obtained in a ratio of 17 : 33 and correspond to reduction of the biradical intermediates **13** and **14** by hydrogen selenide. The structures of **11** and **12** were confirmed by comparison with authentic samples prepared by unambiguous routes.[14]

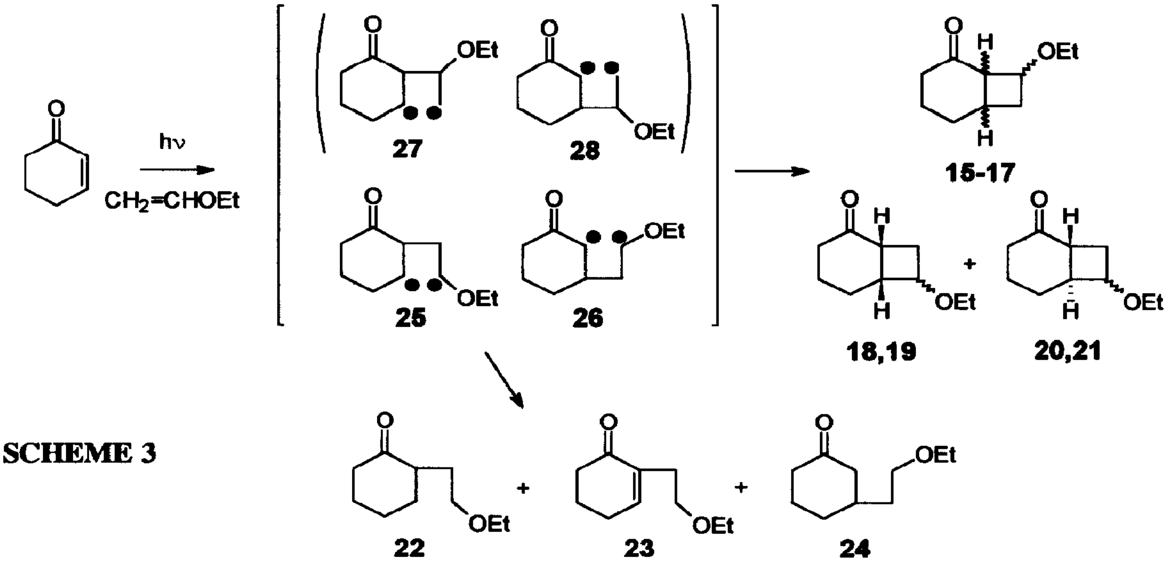


SCHEME 2

The absence of cycloadducts **7-10** in the reaction mixture obtained when hydrogen selenide was present confirms that trapping of the triplet 1,4-biradicals is quantitative and that none are undergoing competitive closure to product or fragmentation to starting material. Therefore, the relative yields of **11** and **12** reflect the relative yields (and hence the relative rates of formation) of the mixtures of stereoisomers of the biradicals **13** and **14**. The observation of both **11** and **12** indicates that in this reaction biradical formation occurs by bonding of both the 2-position and the 3-position of the enone to a terminus of the alkene. This result is qualitatively very similar to that obtained for the reaction of cyclopentenone with cyclopentene where the biradicals analogous to **13** and **14** were formed in the ratio 9 : 8.2.[4]

Ultra-violet light irradiation of a toluene solution of 2-cyclohexenone with ethoxyethene gave the seven racemic cycloadducts **15-21** in the ratio 7 : 2 : 10 : 23 : 28 : 7 : 23, respectively (Scheme 3). The first three adducts (**15-17**) were identified as diastereomers resulting from head-to-head addition of the alkene to the enone.

Normally, cyclohexenone cycloadducts possessing a *cis*-fused cyclobutane ring are stable to acid or base, while the *trans*-fused isomers are epimerised to the more stable *cis*-fused isomer on acid or base treatment. Thus cycloadduct **17** (obtained in 10% relative yield) was unchanged by acid or base and so possesses a *cis*-fused cyclobutane ring; however, the stereochemistry of the cyclohexane-cyclobutane ring junction was not determined for cycloadducts **15** and **16** because of their apparent instability under acidic or basic conditions. Cycloadduct **21** (obtained in a 23% relative yield) possesses a *trans*-fused cyclobutane ring and was epimerised in the presence of alumina (neutral, activity I) to cycloadduct **18**; similarly, cycloadduct **20** (obtained in a relative yield of 7%) was epimerised under the same conditions to give **19**. The stereochemistry of the ethoxy group relative to the ring fusion hydrogens was not determined for any of the adducts. Cycloadduct **18** was isolated by column chromatography of the epimerised cycloadduct mixture and its structure characterised by ms and nmr spectroscopy. Cycloadducts **15**, **17** and **19** were identified by converting a crude cycloadduct mixture to the corresponding lactones by Baeyer-Villiger oxidation and then separating the individual lactones by column chromatography. The structures of the separated lactones were assigned by ms and nmr spectroscopy. By these means it was possible to determine that the regioisomeric ratio of head-to-head to head-to-tail cycloadducts was 19 : 81.



SCHEME 3

When the reaction was repeated in the presence of hydrogen selenide compounds **22-24** were the only photochemical products and they were formed in the ratio 42 : 13 : 45, respectively. Cycloadducts **15-21** were not detected in the reaction mixture. By analogy with other hydrogen selenide trapping reactions,[4,5,7,8] compounds **22** and **24** are derived from hydrogen selenide reduction of biradicals **25** and **26**, respectively. Compound **23** is produced by partial reduction of biradical **25** followed by disproportionation of the radical produced with hydrogen selenyl radical. The structure of **23** was assigned from its mass spectrum and from the fact that it was converted to **22** by catalytic hydrogenation. Compound **22** was isolated from the reaction mixture by column chromatography and its structure assigned from its mass spectrum (efficient McLafferty Type II rearrangement) and nmr spectra. The identity of compound **24** was determined by comparison with an authentic sample synthesized by an independent route.[15]

The absence of products resulting from trapping of the triplet 1,4-biradicals **27** and **28** suggests that these are not intermediates in the reaction, or that if they are then they revert rapidly and exclusively to the ground state enone and alkene and play no part in cycloadduct formation. The structures of the trapped products **22-24** indicate that the triplet 1,4-biradical intermediates responsible for the formation of products in the absence of hydrogen selenide are produced by bonding of both the 2-position and the 3-position of the enone to the less substituted end of the alkene. Furthermore, the ratio of the relative yields of the products (**22** + **23**) to **24** (and hence the ratio **25** : **26**) is 55 : 45 while the head-to-head : head-to-tail ratio found for the cycloadducts **15-21** is 19 : 81; this means that the proportion of biradical **25** that closes to give cyclobutane product is greater than the proportion of biradical **26** undergoing closure. Consequently, the reaction regiochemistry is determined by manner in which each of the biradicals partition between starting materials and product, and not by their relative rates of formation. This is very similar to the situation found for the addition of ethoxyethene to 2-cyclopentenone, where the only product-forming radical intermediates were the analogous lower homologues corresponding to **25** and **26**; these were formed in a 1 : 1 ratio while the head-to-head : head-to-tail ratio was approximately 1 : 3.

Based upon the results described here, we conclude that the factors governing the regiochemistry of the photochemical cycloaddition of alkenes to cyclic enones are similar for both 2-cyclopentenones and 2-cyclohexenones, and that the conclusions drawn from our work with cyclopentenones[4,5,7-10] can be applied with reasonable confidence to cyclohexenones.

ACKNOWLEDGEMENTS

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12. Irradiations were performed at room temperature using Pyrex and water filtered light from a medium pressure mercury lamp.
13. Hydrogen selenide gas was prepared as required by the addition of water to aluminum selenide in the absence of oxygen. The gas evolved was dissolved in the toluene solution to be irradiated. ***CAUTION:*** **ALUMINUM SELENIDE REACTS RAPIDLY WITH WATER TO GENERATE HYDROGEN SELENIDE GAS WHICH IS EXTREMELY TOXIC AND SHOULD BE HANDLED WITH UTMOST CARE.**
14. Compound **11** was prepared by the method of Mousseron, M.; Mousseron-Cadet, M. *Bull. Soc. Chim. France*, **1956**, 1220. Compound **12** was prepared by conjugate addition of cyclopentyl magnesium chloride to 2-cyclohexenone mediated by zinc chloride.
15. Compound **24** was prepared from 2-(3'-ethylenedioxycyclohexyl)ethanol (Etheridge, S.J. *J. Org. Chem.*, **1966**, *31*, 1990) by Williamson ether synthesis using ethyl bromide, followed by deprotection of the ketone with 10% perchloric acid.

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