Tetrahedron Letters, Vol 32, No 33, pp 4107-4110, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .0
Pergamon Press plc

The Origin of the Regioselectivity in the 2+2 Photochemical Cyclo-Addition Reactions of N-Benzoylindole with Alkenes: Trapping of 1,4-Biradical Intermediates with Hydrogen Selenide[1]

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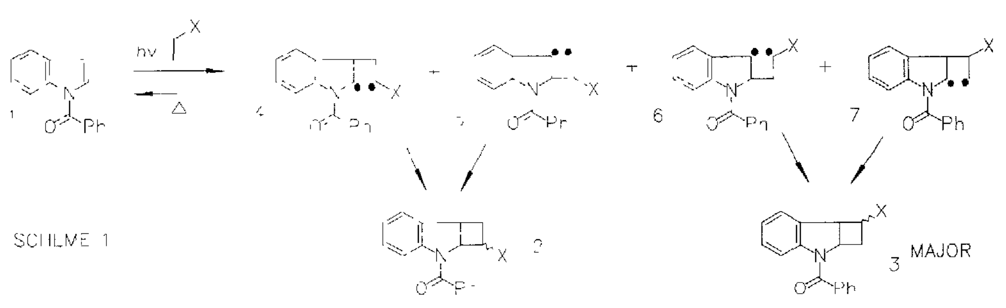
Key Words: *N-benzoylindole; photochemical cycloaddition, 1,4-biradicals, trapping.*

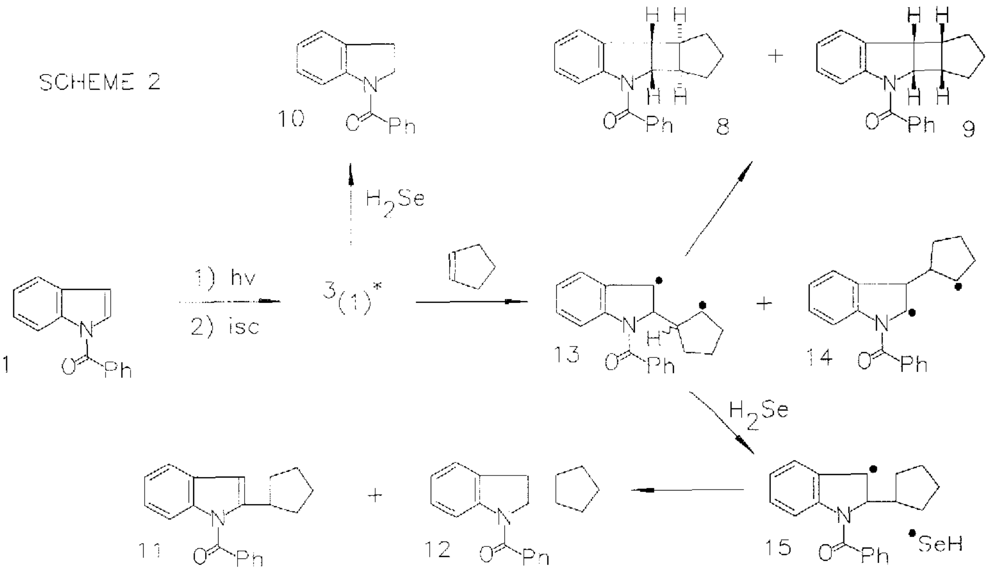
Abstract: *The 1,4-biradical species previously proposed as intermediates in the formation of cyclobutane adducts in the photochemical cycloaddition reaction between N-benzoylindole and alkenes have been trapped with hydrogen selenide. The structures of the trapped biradicals are consistent with the proposal that the first bond formed between the triplet excited state of the indole derivative and the alkenes is from the indole 2-position to that terminus of the alkene which is less able to stabilise a radical centre. This allows prediction of the reaction regiochemistry*

Ultra-violet light irradiation of N-benzoylindole, **1**, in the presence of mono-substituted alkenes results in the formation of cyclobutane adducts of potential synthetic utility.[2,3] The reaction is regioselective but not stereoselective, so that stereoisomers of adduct **3** are formed while **2** is either not observed or comprises a minor proportion of the products. We have shown that the lowest singlet excited state of many N-benzoylindole derivatives exhibits unusual fluorescence[4] but is not involved in this cycloaddition reaction. Rather, adduct formation proceeds from the triplet excited state[5] in competition with photo-Fries rearrangement of the N-benzoyl group.[6] Kinetic evidence[5] and the finding[7] that both *cis* and *trans* alkenes yield the similar mixtures of stereoisomeric adducts have led us to propose[5] that the triplet excited state of the N-benzoylindole reacts non-concertedly with the alkene to produce one or more triplet 1,4-biradical intermediates **4-7**, as shown in Scheme 1. The evidence suggests that following spin inversion these 1,4-biradicals either ring close to give the isolated adducts or fragment back to the ground state starting materials. We have shown that this partitioning



SCHEME 1

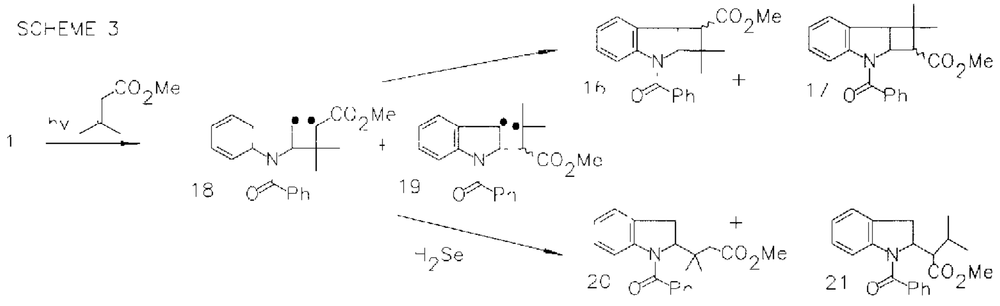
results in reaction inefficiency which varies depending upon the structure of the alkene.[5,7] On the basis of the structures of the products formed by u.v. irradiation of N-benzoylindole in the presence of vinylcyclopropane we have also proposed[8] that the first bond formed between the indole derivative and the alkene is to the 2-position of the indole ring and that the resultant biradical has a lifetime of the order of 100 ns. This implies that biradicals of the type **4** and **7** are not intermediates leading to adducts. If the site of initial bonding is indeed the 2-position of the indole, then the observed regioselectivity of the photochemical cycloaddition with mono-substituted alkenes suggests that the biradical intermediates formed are those in which the indole 2-position is bonded to that end of the alkene less able to support a radical centre. This implies that biradical **6** is the dominant intermediate in the formation of **3** from **1**. In order to confirm these proposals we have attempted to trap the intermediate biradical species. The results and their consequences are described here.



The estimated lifetime of the intermediate 1,4-biradicals indicates that complete trapping requires a species capable of reacting with a carbon centred radical with a rate constant of the order of at least 10^8 $M^{-1}s^{-1}$. This is faster than most radical addition or abstraction reactions[9]; however, it has recently been shown[10] that hydrogen selenide can act as a hydrogen donor and reduce radical centres sufficiently rapidly for the application envisaged here. As we have shown previously,[5,7] irradiation[11] of benzene solutions of **1** in the presence of cyclopentene yields similar quantities of the stereoisomeric adducts **8** and **9**; however we have now found that if sufficient[12] hydrogen selenide (TOXIC[13]) is present in the solution then cycloadduct formation is *completely* suppressed and instead three new products are formed. These were identified as N-benzoylindoline, **10**, N-benzoyl-2-cyclopentylindole, **11**, and N-benzoyl-2-cyclopentylindoline, **12**, respectively.[14] Compound **10** is assumed to arise from direct photoreduction of the triplet excited state of **1** by the hydrogen selenide as shown in Scheme 2. Products **11** and **12** are presumably formed by hydrogen atom abstraction by biradical **13** to give radical **15** which either disproportionates with hydrogen selenyl radical to give **11** or abstracts a second hydrogen atom to give **12**. The absence of adducts or products derived from trapping of biradical **14** suggests that this is either not formed or that it reverts to starting materials extremely rapidly and does not proceed to adducts **8** or **9**.

These results verify our previous proposal that the biradical intermediates leading to products in the photocycloaddition chemistry of **1** are produced by bonding of one terminus of the alkene to the 2-position of the indole derivative. It therefore follows that the observed regioselectivity of the reaction (e.g. preferential formation of **3** over **2**) may result from preferential formation of the biradical intermediates resulting from bonding of the indole 2-position to that end of the alkene least able to support a radical centre. This conclusion could be tested by using H_2Se to trap the biradicals formed during the irradiation of **1** in the presence of methyl acrylate. Unfortunately, while adduct formation is regioselective in the absence of H_2Se (**3**, $X=CO_2Me$, is the major product[3]), we were unable to trap completely all of the biradical intermediates when the reaction was performed in the presence of H_2Se. Thus the trapped biradicals, which were shown to be present by g.c.-ms., were contaminated with, and inseparable from the adducts **2** and **3**. It was, however, possible to trap completely the biradical intermediates formed during the irradiation of **1** in the presence of methyl 3-methyl-2-butenoate. In the absence of H_2Se, stereoisomers of the adducts **16** and **17** were obtained in a 1:1 regioisomeric ratio[14] Thus with this alkene a mixture of regioisomers is obtained because both ends of the alkene can stabilise a radical centre so that biradicals **18** and **19** are both formed. This was confirmed when the irradiation was carried out with H_2Se present; the products were the indoline **20** and a single diastereomer of **21**, in a 1:1 ratio.[14]

SCHEME 3



Based upon these results it can be concluded that the regiochemistry of photochemical cycloaddition of alkenes to N-acylindoles is indeed governed by the preferential formation of biradical intermediates resulting from attachment of the indole 2-position to that end of the alkene least able to support a radical centre. We are currently examining a series of poly-substituted alkenes in order to determine the generality of this conclusion.

ACKNOWLEDGEMENTS

This work was made possible by financial assistance provided by the Natural Sciences and Engineering Research Council (NSERC) of Canada.

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11. Irradiations were performed using Pyrex and water filtered light from a medium pressure mercury lamp. Concentrations of **1** and alkene were *circa* 0 2M and 5M, respectively.
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13 Hydrogen selenide was prepared under nitrogen gas as required; F. Feher in Handbook of Inorganic Chemistry, G. Brauer (Ed.), Academic press, New York, 1963, Vol. 1, p418. HYDROGEN SELENIDE IS AN EXCEEDINGLY TOXIC GAS AND SHOULD BE USED WITH THE UTMOST CARE.
14. Products were separated and purified by chromatography. Their structures were assigned on the basis of the appearance of their ^1H-nmr and ^{13}C-nmr spectra, and their mass spectra.

(Received in USA 13 May 1991)