Pergamon

Tetrahedron Letters, Vol. 37, No. 23, pp. 3939-3942, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00747-2

The Photochemistry of 3-Nitro-2-cyclohexenone[1]

Tracy M. Quevillon and Alan C. Weedon*

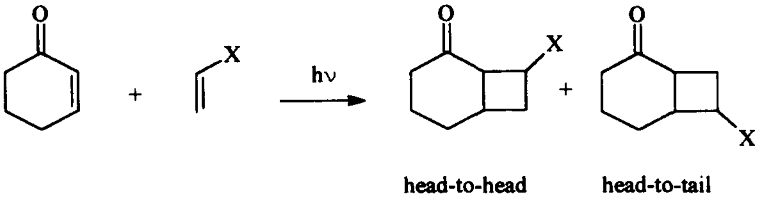
The Photochemistry Unit, Department of Chemistry
The University of Western Ontario
London, Ontario, N6A 5B7, Canada

Key Words: enone, nitro group, photochemistry, cycloaddition, alkene, regiochemistry.

Abstract: *3-Nitro-2-cyclohexenone appears to be unreactive when irradiated with ultra-violet light; no rearrangement of the nitro group to a nitrite ester or dimerization of the enone to cyclobutane adducts was observed. Cyclobutane containing photoadducts are also not formed when the electron poor alkenes, acrylonitrile or methyl acrylate are present. However, cyclobutane adducts are produced with more electron rich alkenes. The cycloadducts from reaction with cyclopentene can be reduced with zinc and acid to give a cyclo-octanedione identical with the product of de Mayo reaction of cyclohexane-1,3-dione with cyclopentene. Photoadducts are also formed with 2-methylpropene; treatment of these with AIBN followed by hydrogenation yields products identical with those produced by hydrogenation of the photoadducts formed from ultra-violet light irradiation of 2-cyclohexenone with 2-methylpropene. The presence of the nitro group on the cyclohexenone increases the proportion of the head-to-head regioisomers from 13% of the adduct mixture to 63%.*

The intermolecular photochemical cycloaddition reaction of alkenes with cyclic enones to give cyclobutane adducts has frequently been used for the synthesis of new compounds and natural products.[2] Despite 30 years of study the mechanism continues to be the subject of some controversy; however, it is generally accepted that the reaction occurs from the enone triplet excited state, which reacts with the alkene partner to form a triplet 1,4-biradical intermediate that partitions between closure to product and fragmentation to ground state starting materials[3]. The synthetic utility of the reaction can be limited by the formation of mixtures of head-to-head and head-to-tail regioisomers when an unsymmetrical alkene is used (Scheme 1).[2,3] Attempts have been made to control the reaction regiochemistry by placing removable directing groups on the enone. For example, a trimethylsilyl group at the 2-position of 2-cyclopentenone has been found to increase the proportion of the head-to-tail isomer in the photocycloaddition reaction with 2-acetoxypropene;[4] the silyl group can be removed from the adducts by treatment with fluoride ion. Electron withdrawing substituents such as cyano and carbomethoxy groups have also been placed on the enone and their effect on the reaction regiochemistry examined.[5] It seemed to us that a nitro group might also perturb the regiochemistry of the enone photocycloaddition reaction, as well as offering the advantage that it could be removed or manipulated following cycloaddition. We report here the preliminary results of an investigation of the photochemistry of 3-nitro-2-cyclohexenone, **1**.[6]

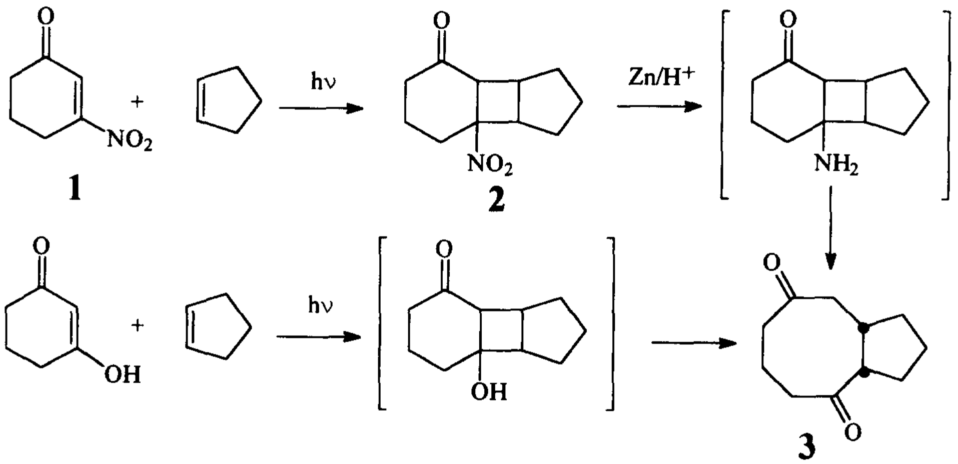
SCHEME 1



Nitroarenes readily undergo a photochemical rearrangement to give the nitrite ester of a phenol.[7] To determine if this was a significant pathway for nitroenone **1** a 0.1M benzene solution was irradiated.[8] No reaction occurred, even on extended photolysis; in addition, no photodimerization of the nitroenone was observed. This contrasts with the photochemistry of 2-cyclohexenone, where a mixture of cyclobutane dimers are formed under these conditions.[9] This pattern of reactivity was also observed when the electron deficient alkenes acrylonitrile and methyl acrylate were present. No reaction was observed upon irradiation of 0.1M solutions of **1** in benzene containing 1M of either of the alkenes, whereas cyclohexenone reacts with these alkenes to yield 2+2 cycloadducts under similar conditions.[10]

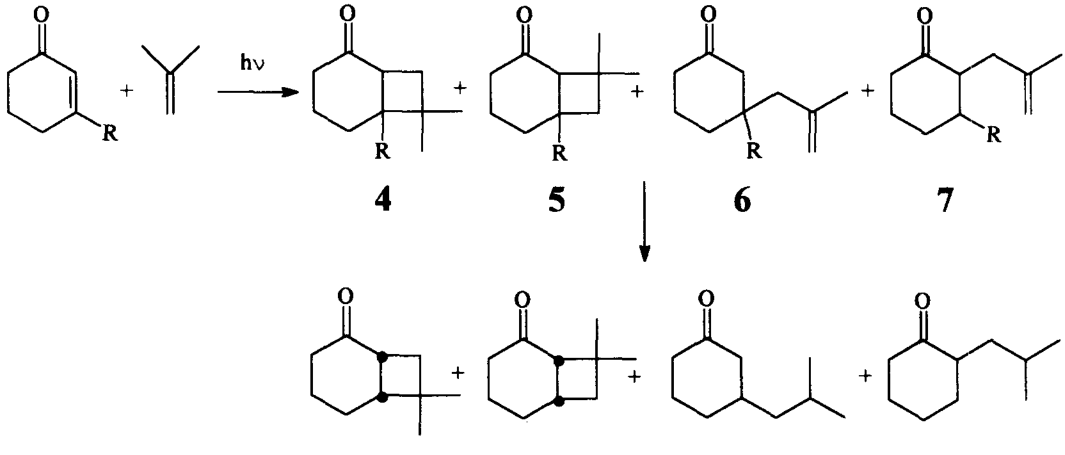
Cycloadducts were however obtained when more electron rich alkenes were used. Ultra-violet light irradiation of a benzene solution of **1** (0.1M) containing cyclopentene (1M) gave a mixture of three products in a ratio of 92:5:3. Analysis of the mixture by GC-MS indicated that the three compounds possessed masses and fragmentation patterns consistent with their being stereoisomers of the expected cyclobutane adducts **2** (Scheme 2). The major product was obtained in 58% yield following isolation and purification by chromatography over silica gel, and the structure was confirmed by ^{1}H- and ^{13}C-NMR spectroscopy. The identity of the major product was further verified by reduction with zinc and HCl; this proceeded in 95% yield to give the known cyclo-octanedione **3**. The structure of **3** was confirmed by comparison with an authentic sample produced by the photocycloaddition reaction between cyclopentene and the enol of cyclohexane-1,3-dione.[11] This result demonstrates that not only can nitroenone **1** undergo 2+2 photocycloaddition with a suitable alkene, but also that it can be used as a masked 1,3-diketone for the preparation of de Mayo reaction adducts with suitable alkenes.[12]

SCHEME 2

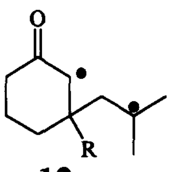


In order to probe the regiochemistry of addition of an unsymmetrical alkene, the photoaddition of **1** with 2-methylpropene was investigated. The photoaddition of 2-methylpropene to 2-cyclohexenone has been reported previously[10,13] and yields a mixture of cyclobutane adducts **4** and **5** and "ene" products **6** and **7** (Scheme 3, R=H). The latter arise from intramolecular disproportionation of intermediate triplet 1,4-biradicals. When the reaction with nitroenone **1** was carried out in benzene six products were obtained in a total yield of 73%. The number of products and the appearance of their mass spectra obtained by GC-MS of the crude reaction mixture suggested that cycloadducts and ene products were also formed in the reaction between **1** and 2-methylpropene. To confirm this, and also to simplify the structural assignment, the products were treated with tributyltin hydride and azobisisobutyronitrile in refluxing benzene. This has been reported to convert alkylnitro compounds to the parent alkane.[14] The six products in the irradiation mixture were converted to four new compounds and these were produced in the ratio 18:45:29:8 and a total yield of 95%. However, analysis by GC-MS revealed that the products were not the expected adducts 4-7 (R=H) since they possessed molecular weights of 150 instead of 152 expected for replacement of the nitro group by hydrogen. It was concluded that the photoadducts had undergone elimination of nitrous acid rather than the expected reduction. This was confirmed by hydrogenation of the products which yielded a mixture of **8**-**11** in the ratio 29:18:45:8, respectively. These were identified by comparison with the same compounds produced by hydrogenation of the photoadducts obtained from irradiation of 2-methylpropene with 2-cyclohexenone. The ratio of **8**-**11** produced in this case was 65:8:7:21, respectively.[15] Since **10** and **11** arise from intramolecular disproportionation of the biradicals **12** and **13**, which are the precursors of the head-to-head and head-to-tail cycloadducts, respectively, the ratio **9**+**10**:**8**+**11** can be takene to reflect the overall head-to-head:head-to-tail ratio for each cycloaddition. For the reaction of 2-methylpropene with **1** this is 63:37, while for the reaction with 2-cyclohexenone this is 13:87. Therefore the presence of the nitro group on the cyclohexenone ring increases the proportion of the head-to-head regioisomers.

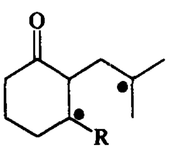
SCHEME 3



We have recently shown that the regiochemistry of the intermolecular photocycloaddition reaction between the cyclic enones cyclopentenone and cyclohexenone and a variety of alkenes is governed by the extent to which each of the isomeric triplet 1,4-biradical intermediates partition between reaction to product and reversion to ground state alkene and enone, rather than by the relative rates of formation of the biradical intermediates.[16] We have also shown that, with the exception of the electron poor alkene methyl acrylate, the biradicals are formed by attachment of the less substituted end of the alkene to the enone.[16,17] In addition, we have shown that the alkene becomes attached to both the 2-position and the 3-position of the enone, and to approximately equal extents.[16-18] For the photocycloaddition of 2-methylpropene to 2-cyclohexenone, and also to nitroenone **1**, the structures of the triplet 1,4-biradicals that are likely to be important intermediates are therefore **12** and **13**. A major difference between the pairs of biradicals from each enone is that in the head-to-tail adduct precursor **13** the radical site at the enone 3-position is delocalized when R=NO_2 and localized, probably in an sp^3 orbital, when R=H. This may account for the perturbation of the regiochemistry of the photoaddition reaction by the nitro group since the delocalized radical site may be less able to take part in bonding or disproportionation processes; this



12



13

could favour fragmentation to starting materials and so decrease the proportion of head-to-tail product. Steric interactions of the nitro substituent with the isobutyl side chain in **13** could also be of importance and would have the same result.

We have also found that 3-nitro-2-cyclohexenone, **1**, produces photoadducts when irradiated in the presence of the alkenes ethoxyethene and vinyl acetate; the results of these reactions will be described in the full paper.

We conclude that the placement of a nitro group at the 3-position of cyclohexenone does not inhibit the formation of photoadducts as long as electron rich alkenes are used, and that the nitro group does perturb the regiochemistry of the reaction. Furthermore, the presence of the nitro group suppresses the formation of enone dimers completely; for cyclohexenone itself this can be an important side reaction unless high concentrations of alkene are used. Finally, 3-nitro-2-cyclohexenone can be used as a masked enolised 1,3-diketone to produce cycloadducts that can be converted to normal de Mayo reaction products by zinc reduction of the nitro group.

REFERENCES

1. Contribution Number 522 from the Photochemistry Unit, The University of Western Ontario. Financial support from the Natural Sciences and Engineering Research Council of Canada (NSERC) is gratefully acknowledged.
2. Weedon, A.C. in *Synthetic Organic Photochemistry,* Horspool, W.M. (ed.), Plenum, New York, 1984, pp 61-144.
3. Schuster, D.I. *Chem. Rev.* **1993**, *93*, 3.
4. Swenton, J.S.; Fritzen, E.L. *Tetrahedron Lett.* 1979, 1951
5. Cantrell, T.S. *Tetrahedron* **1971**, 27, 1227; Agosta, W.C.; Lowrance, W.W. *J. Org. Chem.* **1970**, *35*, 3851.
6. For the preparation of 3-nitro-2-cyclohexenone see: Garbisch, E.W. *J. Org. Chem.* **1965**, *30*, 2109; Vankar, Y.D.; Bawa, A. *Synthetic Commun.* **1985**, *15*, 1253.
7. For a recent review of the photochemical reactivity of the nitro group see Döpp D. in *CRC Handbook of Organic Photochemistry and Photobiology,* Horspool, W.M.; Song, P.-S. (eds), CRC Press, Boca Raton, 1994, Chapter 81, pp 1019-1062.
8. Irradiations were conducted using Pyrex and water filtered light from a medium pressure mercury lamp.
9. Lam, E.Y.Y.; Valentine, D.; Hammond, G.S. *J. Am. Chem. Soc.* **1967**, *89*, 4944; Wagner, P.J.; Bucheck, D.J. *J. Am. Chem. Soc.* **1969**, *91*, 5090.
10. Corey, E.J.; Bass, J.D.; LeMahieu, R.; Mitra, R.B. *J. Am. Chem. Soc.* **1964**, *86*, 5570.
11. Challand, B.D.; Hikino, H.; Kornis, G.; Lange, G.; de Mayo, P. *J. Org. Chem.* **1969**, *34*, 794.
12. For a recent review of the de Mayo reaction see Weedon, A.C. in *CRC Handbook of Organic Photochemistry and Photobiology,* Horspool, W.M.; Song, P.-S. (eds) CRC Press, Boca Raton, 1994, Chapter 54, pp 670-684.
13. Wexler, A.J.; Hyatt, J.A.; Reynolds, P.W.; Cottrell; C. Swenton, J.S. *J. Am. Chem. Soc.* **1978**, *100*, 512.
14. Ono, N.; Miyaki, H.; Tamura, R.; Kaji, A. *Tetrahedron Lett.* **1981**, *22*, 1705; Tanner, D.D.; Blackburn, E.V.; Diaz, G.E. *J. Am. Chem. Soc.* **1981**, *103*, 1557.
15. In the photocycloaddition reaction between 2-cyclohexenone and 2-methylpropene compound **4**, R=H, is formed as a mixture of *cis* and *trans* fused adducts; the *trans* fused isomer was epimerized to the more stable *cis* fused isomer **8** when the mixture was hydrogenated.
16. Hastings, D.J.; Weedon, A.C. *J. Am. Chem. Soc.* **1991**, *113*, 8525.
17. Andrew, D.; Hastings, D.J.; Weedon, A.C. *J. Am. Chem. Soc.* **1994**, *116*, 10870.
18. Maradyn, D.J.; Weedon, A.C. *Tetrahedron Lett.* **1994**, *35*, 8107; Andrew, D.; Weedon, A.C. *J. Am. Chem. Soc.* **1995**, *117*, 5647.

(*Received in USA* 21 *March* 1996; *accepted* 11 *April* 1996)