PHOTOINITIATED INTRAMOLECULAR YLIDE-ALKENE CYCLOADDITION REACTIONS

James P. Dittami*, Xiao-Yi Nie, Christopher J. Buntel and Steven Rigatti Department of Chemistry Worcester Polytechnic Institute Worcester, Massachusetts 01609

<u>Abstract</u>: The intramolecular olefin addition reactions of phototransient species were investigated. Photolysis of aryl vinyl sulfides which incorporate the ethyl butenoate functional group provide ene-like products and or (3+2) adducts. Product formation is governed by both structural features and reaction conditions.

We recently reported a novel intramolecular olefin addition reaction which occurs during photolysis of aryl vinyl sulfides and aryl vinyl ethers.^{1,2} Herein we detail some of our more recent studies in this area and report on an unusual substrate dependent cycloaddition reaction.

In our previous work we examined photocyclizations of systems which incorporated a simple unsubstituted olefin in the side chain. The results of these studies are exemplified by the photocyclization of aryl vinyl sulfide 1. Thus, pyrex filtered irradiation of a solution of the aryl vinyl sulfide 1 (10^{-3} M, toluene) at temperatures ranging from 25 to -70 °C provided the dihydrothiophene 2 in 78 to 100% yield.² Conversely, irradiation of a solution of 1 at 110 °C (10^{-3} M, toluene) provided the intramolecular addition product 3 in 78 % isolated yield. Control experiments were conducted which demonstrated that both light and heat are required to effect the transformation $1 \rightarrow 3$. The photolyses of several similar systems were examined over a range of temperatures. In every case, the ratio of intramolecular addition products to photocyclized untrapped products (e.g. 3: 2) increased with increasing temperature. Furthermore the optimum temperature for formation of the intramolecular addition products (such as 3) was found to be substrate dependent. In this report we examine the effect of an electron withdrawing substituent in the side chain.



The preparation of 10 illustrates the general method which was used in the synthesis of photoprecursors. This procedure is adaptable for the preparation of several different photoprecursors for the present and future studies via the key intermediates 7 and 9. The yields shown are typical for each step.³



Incorporation of the butenoate side chain markedly influences the facility and outcome of the intramolecular addition reaction. Thus, pyrex filtered irradiation of a solution of 10 in toluene $(4.7 \times 10^{-3} \text{ M})$ at room temperature provided 11 as the major product (84 % isolated yield). Indeed, formation of intramolecular addition product 11 can even observed at -70 °C (60 % isolated yield).⁴ These results contrast those obtained for the low temperature photolysis of 1 (-70 °C, toluene) where formation of 2 was observed to the exclusion of any intramolecular addition product 3. In general, the incorporation of the butenoate function in all systems which we have examined leads to reduction in reaction temperatures and increased yields relative to the corresponding unsubstituted butenyl systems.

Two additional products were isolated from the room temperature photolysis of 10. Formation of 12 is consistent with a six-electron cyclization from 10 to provide a thiocarbonyl ylide intermediate which undergoes an intramolecular hydrogen shift.⁵ Formation of 13 on the other hand could arise via intramolecular dipolar cycloaddition to an intermediate thiocarbonyl ylide. The observation of 13 in the reaction mixture is significant since it represents the first reported example of an intramolecular dipolar cycloaddition during the heteroatom directed photoarylation reaction.⁶ A temperature profile for the photolysis of 10 is given in Table I. It is of interest to note that the ratio of intramolecular addition products 11 and 13 to photocyclized untrapped product 12 increases with increasing temperature.^{7,8}



Labelling experiments were conducted to determine the origin of the hydrogen abstraction which is required for the formation of 3 and 11. These experiments demonstrate that hydrogen abstraction does not involve the solvent. Thus, photolysis of a solution of 1 in toluene- d_8 (12 x 10⁻³ M, 110 °C) provided 3 which did not show any detectable deuterium incorporation. Likewise, irradiation of a solution of 10 in toluene- d_8 (2.4 x 10⁻³ M, 25 °C) provided 11 which was also free of deuterium.⁹ These data support a mechanism for formation of 3 and 11 which involves intramolecular hydrogen abstraction. Possible pathways to 3 and 11 could involve intermediates such as 2a, 12a, 14 or 15. Control experiments, however, eliminate 2 as a possible intermediate. Thus, on resubjection to the photolysis conditions used in formation of 3, compound 2 remains unchanged.¹



Consistent with our earlier studies, the intramolecular addition reaction is less favorable for systems which incorporate a phenyl group as the aromatic component. Thus low temperature photolysis of a solution of phenyl vinyl sulfide 16 (2.29 x 10^{-3} M, -70 °C) provides predominantly ring closed product 17 with less than 8 % of the intramolecular addition product 18. As can be seen from Table II, an increase in the reaction temperature for the photolysis provides increased yields of intramolecular addition products. The temperature required for the conversion of $16 \rightarrow 18$ is significantly higher than that observed for the conversion $10 \rightarrow 11$ This difference may reflect the difference in resonance stabilization afforded the intermediate thiocarbonyl ylide derived from 10 and 16. With 10 aromatic character is retained in the intermediate ylide whereas aromaticity is lost in the intermediate derived from 16.



We are currently examining the temperature and wavelength dependence for these reaction in an effort to further elucidate the mechanism for these interesting reactions.

Acknowledgement is made to WPI-RDC, NIH (GM 37939-01) and Pfizer Central Research for their generous support.

References and Notes

1. Dittami, J.P; Ramanathan, H; Breining, S. Tet. Lett 1989 30 795.

2. Dittami, J.P.; Nie, Xiao-Yi Syn. Commun. 1990 20 (4) 541.

3. All products gave spectral data (¹H NMR, IR, MS) which were consistent with the assigned structures. Satisfactory combustion analyses or high resolution mass spec data were obtained for all new products.

4. Photochemical experiments were conducted using a 450-watt Canrad-Hanovia medium pressure quartz mercury-vapor lamp. The lamp was placed in a water-cooled pyrex immersion well. Reaction solutions were saturated with argon prior to irradiation. For high and low temperature runs a vacuum-jacketed quartz immersion well was employed with a pyrex sleeve filter. The immersion well was placed in a large scale (~200 mL) reactor. Heating was carried out with a silicon oil bath and cooling was achieved with a Neslab ULT-80DD low-temperature circulating bath. For details see reference 2.

5. For reviews see Schultz, A.G. Acc. Chem. Res. 1983 16 210; Schultz, A.G.; Motyka, L. in Organic Photochemistry, A. Padwa, Ed., Marcel Dekker, New York, 1983, V. 6, p. 1.

6. a) For a review of intramolecular dipolar cycloaddition reactions see: Padwa, A. in *New Synthetic Methods* Verlag Chemie: New York, 1979, V. 5 pp. 25-69 b) For a recent review of 1,3-dipolar cycloaddition chemistry see 1,3-Dipolar Cycloaddition Chemistry, Padwa, A., Ed., Wiley Interscience: New York 1984 V.1-2 c) Advances in Cycloaddition V. 1, Curran, D.P. Ed., Jai Press, Inc.: Greenwich, CT 1988 d) For an example of an <u>intermolecular</u> dipolar cycloaddition to an ylide intermediate during the heteroatom directed photoarylation reaction see Schultz, A.G.; Detar, M.B. J. Am. Chem. Soc. 1976 98 3564.

7. The stereochemical assignment for 13 is based on the following. The stereochemical relationship at centers C-1, C-2, C-3 and C-6 is inferred from concerted conrotatory ring closure in the photochemical step to give a trans ring fusion (see references 5 and 6d) followed by syn addition of the side chain to the thiocarbonyl ylide intermediate. Further support for the stereochemical assignment is gained by comparison of chemical shift data for hydrogens at C-1, C-4 and C-5 with data reported by M.P. Cava and N.M. Pollack for similar sulfur bridged systems; J. Am. Chem. Soc. 1967 89 3639. Thus hydrogens syn to the sulfur are deshielded relative to systems where the hydrogens are anti to the sulfur bridge. The anti relationship of the C-4 H and C-5 H is assigned on the basis of the relatively small coupling observed (~4 Hz, dihedral angle ~121°). A larger coupling constant (~11 Hz) would be predicted for the system where these hydrogens are cis (dihedral angle ~15°).

8. Spectral data for Photoproducts 11 and 13 is as follows: 11: ¹H NMR (200 MHz, CDCl₃): δ 7.95 (d, 1H, J = 8.39 Hz), 7.82 (d, 1H, J = 7.85 Hz), 7.7 (d, 1H, J = 8.61 Hz), 7.47 (t, 1H, J = 6.88 Hz), 7.37 (t, 1H, J = 6.86 Hz) 7.20 (d, 1H, J = 8.57 Hz), 4.13 (q, 2H, J = 7.13 Hz), 3.20-2.70 (m, 4H), 2.47-2.37 (m, 2H), 2.18-1.34 (m, 7H), 1.23 (t, 3H, J = 7.13 Hz); ¹³C NMR (50.3 MHz, CDCl₃): δ 208.07 (C=O), 172.66 (C=O), 137.45 (4°), 136.96 (4°), 132.68 (4°), 129.53 (C-H: double intensity), 129.27 (4°), 126.49 (C-H), 124.16 (C-H), 122.24 (C-H), 119.66 (C-H), 75.07 (4°), 68.53 (4°), 60.15 (CH₂), 42.78 (C-H), 40.34 (CH₂), 36.30 (CH₂: double intensity), 35.88 (CH₂), 29.79 (CH₂), 19.45 (CH₂), 14.10 (CH₃): IR (film): 3030, 2930, 2850, 1720, 1690 cm⁻¹; GC/MS (70 eV); m/e 380 (M⁺); UV (CH₃CN) $\lambda_{max}(\varepsilon)$: 219.5 (26888), 256 (35703). 13: ¹H NMR (200 MHz, CDCl₃); δ 7.23-6.95 (m, 4H), 6.38 (d, 1H, J = 9.84 Hz), 5.78 (d, 1H, J = 9.86 Hz), 4.15 (dq, 2H, J = 7.2 Hz, J = 2.16 Hz) 4.07 (s, 1H), 3.23 (d, 1H, J = 6.02 Hz), 3.05 (m, 1H), 2.70-1.75 (m, 10H), 1.25 (t, 3H, J = 7.2 Hz); ¹³C NMR (50.3 MHz, CDCl₃); δ 207.74 (4°), 171.14 (4°), 136.59 (4°), 130.99 (4°), 128.49 (C-H), 127.95 (C-H), 127.81 (C-H), 126.84 (C-H), 126.35 (C-H), 122.70 (C-H), 71.81 (4°), 66.38 (4°), 62.58 (C-H), 60.76 (CH₂), 60.20 (4°), 59.69 (C-H), 40.50 (CH₂), 40.10 (CH₂), 38.37 (CH₂), 31.27 (CH₂), 29.75 (CH₂), 24.28 (CH₂), 14.42 (CH₃): IR (film) 2880, 1730, 1710 cm⁻¹; GC/MS (70 eV); m/e 380 (M⁺); UV (CH₃OH) $\lambda_{max}(\varepsilon)$: 224.6 (45518); m.p. 156-157 °C.

9. Analyses of products from the deuterium labelling studies were carried out with a Hewlett Packard GC-MS system consisting of a Hewlett Packard 5890A Gas Chromatograph, a 12.5 meter x 0.2 mm capillary column (p.n. 896-4-15A) crosslinked with dimethyl silicone, and a Hewlett Packard 5970B Mass Selective Detector with 70 eV electron energy. All products were compared with products obtained in control experiments (toluene- d_8 vs toluene- h_8).

(Received in USA 28 March 1990; 3 May 1990)