

THE EFFECT OF CHROMOPHORE TRANSPOSITION ON THE
STEREOCHEMICAL OUTCOME OF THE INTRAMOLECULAR DIOXENONE
PHOTOCYCLOADDITION REACTION

Jeffrey D. Winkler*¹, Cheryl L. Muller², John P. Hey, Ronald J. Ogilvie and
Nizar Haddad

Searle Chemical Laboratories, Department of Chemistry, The University of Chicago,
Chicago, IL 60637

Philip J. Squatrito³

Department of Chemistry, Texas A & M University, College Station, TX 77843

Paul G. Williard⁴

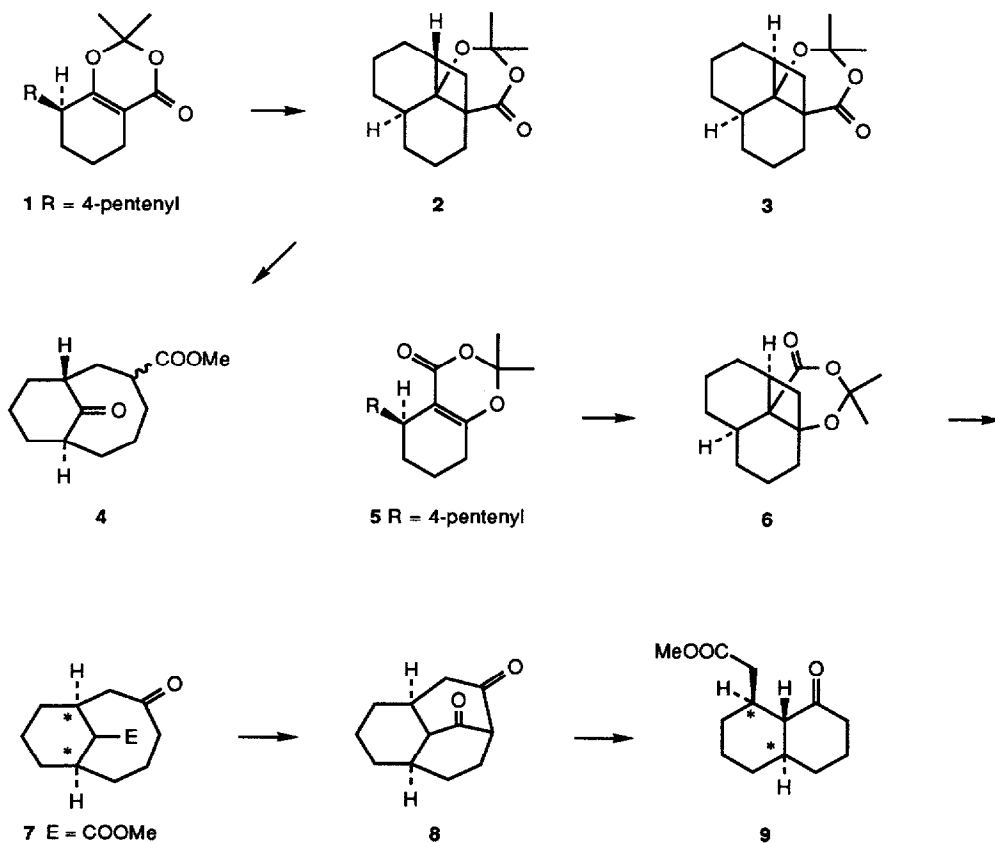
Department of Chemistry, Brown University, Providence, Rhode Island 02912

Abstract. *Transposition of the chromophore leads to complete reversal of previously observed stereoselectivities in the intramolecular dioxenone photocycloaddition. A proposal to explain this change in stereoselectivity is presented, and the facile transannular reaction of the photoaddition/fragmentation product derived from the transposed photosubstrate 5 is described.*

The intramolecular dioxenone photocycloaddition reaction⁵ provides unique approaches to the synthesis of compounds with "inside-outside" or *trans* intrabridgehead stereochemistry.⁶ For example, irradiation of **1** leads to the exclusive formation of **2**, which is ca. 6 kcal/mol less stable than the *cis* isomer, **3**.⁷ Acid-catalyzed fragmentation of photoadduct **2** then gives the "inside-outside" bicycloalkanone, **4**.^{6e} To explore the effect of the orientation of the dioxenone⁸ on the unusual stereochemical outcome of the photocycloaddition of **1**, we have now examined the irradiation of **5**, in which the chromophore of the original photosubstrate **1** has been transposed. We report herein that irradiation of **5** leads to strikingly different stereochemical results from those observed with **1**, and that subsequent reaction of the photoadduct derived from **5** underscores the propensity of the bicyclo[5.3.1]undecane skeleton towards transannular reaction.⁹

Irradiation of **5**¹⁰ [12 mM in acetone/acetonitrile (1:9), medium-pressure Hg lamp, Pyrex filter] leads to the exclusive formation of the *cis*-fused photoadduct **6** in 88% yield, the stereochemistry of which was determined by X-ray analysis.¹¹ Acid-catalyzed fragmentation of **6** (10 mol % *p*-toluenesulfonic acid in 90 % aqueous methanol, reflux, 3 h) did not give the expected photoaddition/fragmentation product, **7**, in analogy with the formation of **4** from **2**, but instead gives the isomeric ketoester **9**, in 85% yield, the structure and stereochemistry of which were also determined by X-ray analysis.¹² We envisioned that the rearrangement of ketoester **7** to **9** might proceed *via* the intermediacy of diketone **8**, the product of transannular acylation of **7**. Diketone **8**¹³ could in fact be isolated under carefully controlled reaction conditions (5

mol % p-toluenesulfonic acid in 95% aqueous methanol, 12 h, 25°C) in 61% yield, and subsequently converted to **9** in 78% yield under the conditions described above for the transformation of **6** to **9**. The *cis* relative stereochemical relationship between the two starred hydrogens in **9** then follows from the *cis* intrabridgehead stereochemistry (starred hydrogens) of **7**.



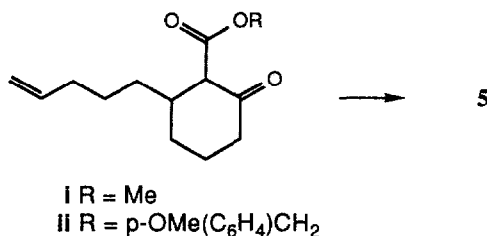
In contrast to the results obtained on photocycloaddition of **1**, the exclusive formation of the more stable *cis*-fused product **6** on irradiation of **5** is consistent with the reversibility of the step in the photocycloaddition mechanism in which the relative stereochemistry of the photoadduct is established. The relative rates of spin inversion¹⁴ of the intermediate triplet diradicals, or simply the difference in strain energy between the *cis*- and *trans*-fused photoadducts, could then be responsible for the exclusive formation of the *cis*-fused photoproduct, **6**. Experiments designed to test this proposal are currently underway in our laboratory.

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References

- 1 Recipient of the American Cyanamid Young Faculty Award (1989-1992) and a National Institutes of Health Research Career Development Award (1988-1993). Fellow of the Alfred P. Sloan Foundation (1987-1989).
- 2 Fellow of the National Institutes of Health Predoctoral Training Program (GM07183).
- 3 Author to whom correspondence regarding the X-ray structure of **6** should be addressed.
- 4 Author to whom correspondence regarding the X-ray structure of **9** should be addressed.
- 5 Winkler, J. Hey, J.; Hannon, F.; Williard, P. *Heterocycles* **1987**, *25*, 55.
- 6 For a recent review, see Alder, R. *Acc. Chem. Res.* **1983**, *16*, 321. For other syntheses of inside-outside bicycloalkanes, see a) Winkler, J.; Hey, J.; Williard, P. *Tetrahedron Lett.* **1988**, 4691; b) Winkler, J.; Henegar, K.; Williard, P. *J. Am. Chem. Soc.* **1987**, *109*, 2850; c) Funk, R.; Olmstead, T.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298; d) Winkler, J. Hey, J.; Darling, S. *Tetrahedron Lett.* **1986**, 5959; e) Winkler, J.; Hey, J.; Williard, P. *J. Am. Chem. Soc.* **1986**, *108*, 6425; f) McMurry, J.; Hodge, C. *J. Am. Chem. Soc.* **1984**, *106*, 6450; g) Gassman, P. G.; Hoyer, R. *J. Am. Chem. Soc.* **1981**, *103*, 215, 2496, 2498; h) Haines, A.; Harntiang, P. *J. Chem. Soc., Perkin I* 1979, 2577; i) Gassman, P.; Thummel, R. *J. Am. Chem. Soc.* **1972**, *94*, 7183; j) Park, C.; Simmons, J. *J. Am. Chem. Soc.* **1972**, *94*, 7184.
- 7 Calculated using the Gajewski/Gilbert modification of the Allinger MM2 program (#395, Quantum Chemistry Program Exchange, Indiana University), which is commercially available through Serena Software, Bloomington, IN.
- 8 For a discussion of the geometry and charge distribution for the dioxenone excited state, see Seebach, D.; Zimmermann, J.; Gysd, U.; Ziegler, R.; Ha, T. *J. Am. Chem. Soc.* **1988**, *110*, 4763.

- 9 For another example of facile transannular reaction in a bicyclo[5.3.1]undecane, see Winkler, J.; Sridar, V.; Rubo, L.; Hey, J.; Haddad, N. *J. Org. Chem.*, **1989**, *54*, 3004.
- 10 The requisite photosubstrate **5** was prepared by conjugate addition of di-(4-pentenyl)copper magnesium bromide to cyclohexenone, followed by trapping of the resulting enolate with methyl cyanoformate [Mander, L.; Sethi, S. *Tetrahedron Lett.* **1983**, 5425] to give **i**. Exchange of **i** with p-methoxybenzyl alcohol provided the p-methoxybenzyl ketoester **ii** in 56 % overall yield from cyclohexenone. Carboxylation with methyl cyanoformate followed by exchange with p-methoxybenzyl alcohol proved more convenient than our previously described procedure using p-methoxybenzyl cyanoformate [Henegar, K.; Winkler, J. *Tetrahedron Lett.* **1987**, 1051]. Treatment of **ii** with trifluoroacetic anhydride and trifluoroacetic acid in acetone led to the formation of the photosubstrate, **5**, in 69% yield.



- 11 Photoadduct **6** crystallized in the monoclinic space group P2₁/c. The unit cell parameters were determined to be $a = 8.14$ (2) Å, $b = 11.587$ (3) Å, $c = 14.299$ (4) Å, and $\beta = 96.56$ (6)^o; $R = 0.058$, $R_w = 0.080$.
- 12 Ketoester **9** crystallized in the monoclinic space group P2₁/n. The unit cell parameters were determined to be $a = 9.426$ (3) Å, $b = 12.293$ (3) Å, $c = 16.979$ (3) Å, and $\beta = 98.08$ (2)^o; $R = 0.063$, $R_w = 0.076$.
- 13 Spectral data for diketone **9**: ¹H-NMR (C₆D₆): 3.27 (br s, 1H), 2.23 (br t, $J = 4.5$ Hz, 1H), 2.15 (H_a, $J = 19$, 8.4 Hz, 1H), 2.03 (H_b, $J = 19$, 8.4 Hz, 1H), 1.75 (m, 2H), 1.55 (m, 2H), 0.95-1.2 (m, 7H), 0.8 (m, 1H). ¹³C-NMR: 211.5, 210.1, 65.1(*), 52.4(*), 44.6, 38.6(*), 33.5, 29.5, 28.9, 28.2(*), 25.2, 14.8. The four tertiary carbons (*) were assigned by APT. IR (CDCl₃): 1709, 1730 cm⁻¹.
- 14 For a discussion of the geometry dependence of spin orbit coupling, see Caldwell, R.; Carlacci, L.; Doubleday, C.; Furlani, T.; King, H.; McIver, J. *J. Am. Chem. Soc.* **1988**, *110*, 6907.

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