Pergamon
Tetrahedron Letters 42 (2001) 5155–5157
TETRAHEDRON LETTERS

Diastereoselectivity during 2-pyridone photo-[4+4] cycloaddition. The tribenzylsilyl protecting group

Scott McN. Sieburth,* Christina B. Madsen-Duggan and Fangning Zhang

Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY 11794-3400, USA

Received 7 May 2001; revised 3 June 2001; accepted 4 June 2001

Abstract—The use of a silyloxy group as a stereocontrol element on the most distant carbon of a pyrindinone during intermolecular [4+4] photocycloaddition was tested using silyl groups varying in size (*tert*-butyldimethylsilyl<triisopropylsilyl<tribenzylsilyl). The ratio of the diastereomeric products was proportional to the size of the silyl group, with the largest, tribenzylsilyl, giving the best ratio of 10:1. The expected stereochemistry was confirmed by X-ray crystallography. © 2001 Elsevier Science Ltd. All rights reserved.

Cycloaddition reactions are highly valued as synthetic methods, in part because of their generally high selectivities. The [4+4] photodimerization of 2-pyridones is a higher-order cycloaddition that occurs with a very high regioselectivity (exclusively head-to-head) and good relative stereoselectivity (*trans*-**2** dominating over *cis*-**3**).[1] In addition, we have found that stereoselectivity engendered by a chiral center near a pyridone can be substantial. For intramolecular photocycloaddition of tethered pyridones **1**, the stereogenic center on the tether controls formation of the nearest chiral center, yielding only the *anti* relationship of the silyloxy group and the adjacent carbonyl in **2** and **3**.[2] In this paper we describe the use of a silyloxy group to control the face selectivity for the intermolecular photocycloaddition of **4**, with a stereogenic center remote from the newly forming chiral carbons (Fig. 1).

In comparison to **1**, the silyloxy group in **4** is remote from the centers of reactivity and the developing stereogenic centers, and is located on the flexible flap of a cyclopentene ring with the potential to adopt a conformation that would minimize its steric impact and thereby lower its stereochemical influence. Silyl groups are also known for their attenuated steric bulk.[3] The '*A*' value for a trimethylsilyl group is significantly

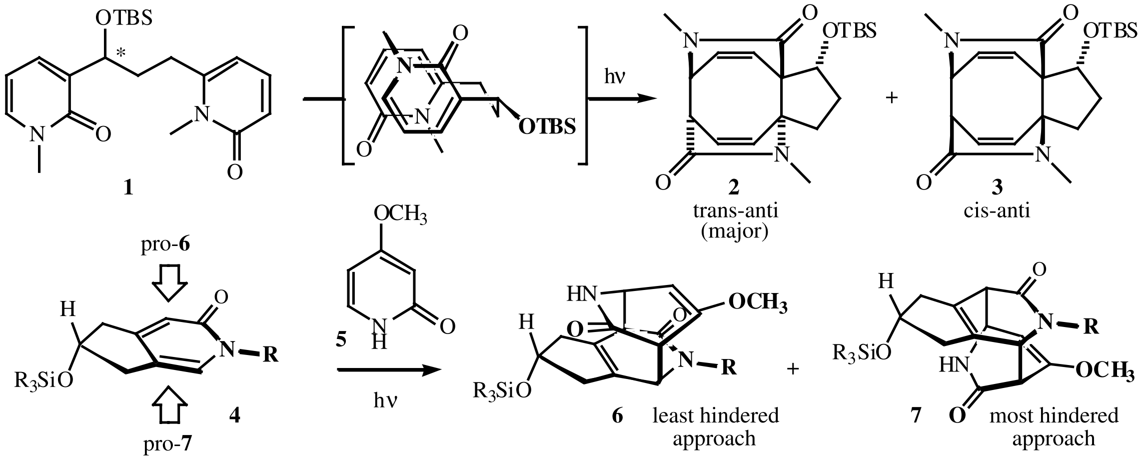


Figure 1. A tether substituent in **1** exerts a strong stereochemical influence. The remote stereocenter in **4** has the potential to act similarly.

---

* Corresponding author.

0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(01)00953-4

smaller than a *tert*-butyl group even though it has a substantially larger volume.[4] Nevertheless, Eliel and Satici found that for silyl ethers of cyclohexanols, increased sterics led to a greater preference for an *axial* conformation.[5] Should this prove to be the case for **9**, such a conformation would enhance the desired steric effect.

The starting pyrindinone **9** was prepared using Vollhardt's cobalt-catalyzed cycloaddition of isocyanates with 1,6-diynes. The requisite diynes **8** were synthesized in two steps from propargyl bromide and ethyl formate, employing the aluminum-mediated method of Sondheimer[6] to minimize allene formation, followed by *O*-silylation with the necessary chlorosilane or silyl triflate. The cross cyclization of the diyne **8** and phenethylisocyanate to give **9** initially gave a mixture with **10**, a product formed by trimerization of **8**, presumably as a mixture of diastereomers. Formation of byproduct **10** could be minimized by very slow addition of the diyne to the irradiated catalyst and isocyanate in refluxing xylene (Fig. 2).

Cross [4+4] photocycloaddition of **9** with 4-methoxy-2-pyridone **5** was carried out using the standard conditions devised earlier: a 1:7 molar ratio of **9**:**5** in methanol with a total (pyrindinone+pyridone) concentration of 0.5 M.[7,8] This reaction relies on the photostability of 4-alkoxy-2-pyridones toward dimerization,[9,10] and the discovery that they can, nonetheless, undergo [4+4] photocycloaddition with other pyridones.[7,11]

In each case, two major photoproducts were formed that differed only in the stereochemistry of the silyloxy group, with one of the two isomers dominating. In contrast to the high stereoselectivity found for **1** (Fig. 1) for which only *anti*-products were observed,[2] the *tert*-butyldimethylsilyl (TBS) group of **9a** had little influ-

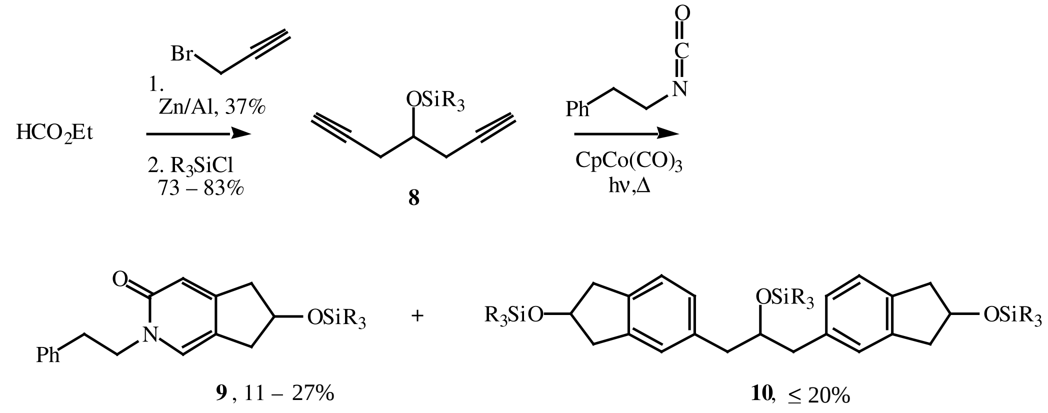
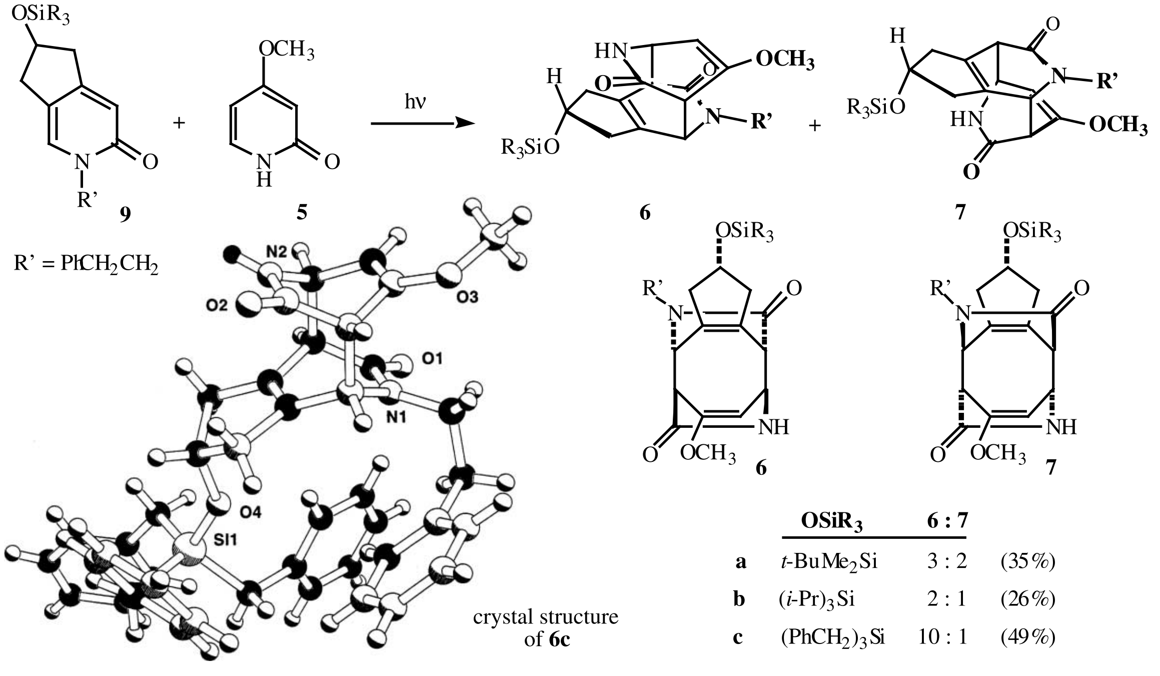


Figure 2. Synthesis of pyrindinone **9**.



	OSiR$_3$	6 : 7	
a	*t*-BuMe$_2$Si	3 : 2	(35%)
b	(*i*-Pr)$_3$Si	2 : 1	(26%)
c	(PhCH$_2$)$_3$Si	10 : 1	(49%)

Figure 3. Photocycloaddition of pyrindinones **9a**–**c** with **5** yields primarily **6**. Crystal structure of tribenzylsilylether product **6c**.

ence, giving only a 1.5:1 ratio of products. Use of the larger triisopropylsilyl (TIPS, **9b**) group gave little improvement, yielding products in a ratio of 2:1.

In considering other protecting groups that would present a greater steric advantage, we found that tribenzylchlorosilane was one of the few commercially available reagents with β-branching, often a prime factor in relevant steric bulk.[12] Use of this silyl ether (TBnS, **9c**) gave a substantial improvement in the stereochemical outcome, with a product ratio of 10:1.

The expected diastereomeric result of this photoreaction was confirmed by X-ray crystallography of the major TBnS product **6c** (Fig. 3).[13] While this does not necessarily represent the minimum energy conformation of the tribenzylsilyloxy group, the structure is consistent with Eliel's finding that bulky silyl ethers prefer an *axial* conformation.[5] The large size of this unit and its potential as a blocking reagent approach is readily apparent.

Although the tribenzylsilyl group has been known for nearly a century,[14] we are aware of only two prior uses to control stereochemistry. Both examples are part of the pioneering studies of E. J. Corey in the design and use of silicon-protecting groups.[15,16] The stereoselectivities reported here reinforce and complement these earlier findings. In particular, the tribenzylsilyl group is useful where steric influence is important and the more typically used TIPS group is insufficiently bulky.

Acknowledgements

This work was supported by grants from the National Institutes of Health. The authors would like to thank Jun Xiao, Jianfeng Jiang and Professor Joseph Lauher for assistance with the X-ray crystallography.

References

1. Sieburth, S. McN. In *Advances in Cycloaddition*; Harmata, M., Ed. The Inter- and Intramolecular [4+4] Photocycloaddition of 2-Pyridones and Its Application to Natural Product Synthesis.; JAI: Greenwich, CT, 1999; Vol. 5, pp. 85–118.
2. Sieburth, S. McN.; Hiel, G.; Lin, C.-H.; Kuan, D. P. *J. Org. Chem.* **1994**, *59*, 80–87.
3. Hwu, J. R.; Wang, N. *Chem. Rev.* **1989**, *89*, 1599–1615.
4. Kitching, W.; Olszowy, H. A.; Drew, G. M.; Adcock, W. *J. Org. Chem.* **1982**, *47*, 5153–5156.
5. Eliel, E. L.; Satici, H. *J. Org. Chem.* **1994**, *59*, 688–689.
6. Sondheimer, F.; Amirl, Y.; Gaoni, Y. *J. Am. Chem. Soc.* **1962**, *84*, 2270–2274.
7. Sieburth, S. McN.; Lin, C.-H. *Tetrahedron Lett.* **1996**, *37*, 1141–1144.
8. Sieburth, S. McN.; Lin, C.-H.; Rucando, D. *J. Org. Chem.* **1999**, *64*, 950–953.
9. De Selms, R. C.; Schleigh, W. R. *Tetrahedron Lett.* **1972**, 3563–3566.
10. Fujii, H.; Shiba, K.; Kaneko, C. *J. Chem. Soc., Chem. Commun.* **1980**, 537–538.
11. Sieburth, S. McN.; Chen, J.; Ravindran, K.; Chen, J.-l. *J. Am. Chem. Soc.* **1996**, *118*, 10803–10810.
12. Isaacs, N. S. *Physical Organic Chemistry*, 2nd ed.; Wiley: New York, 1995.
13. Compound **6c** crystallizes in the monoclinic space group $P2_1/c$ with $a=11.6918(1)$, $b=30.906(4)$, $c=10.248(1)$ Å, $\beta=101.248$ (3)°, $V=3631.8$ (5) Å^3, and $Z=4$. Final least-squares refinement using 1315 unique reflections with $I>3\sigma(I)$ gave R $(R_w)=0.063$ (0.059).
14. Martin, G.; Kipping, F. S. *J. Chem. Soc.* **1909**, *95*, 302–314.
15. Corey, E. J.; Ensley, H. E. *J. Org. Chem.* **1973**, *38*, 3187–3189.
16. Corey, E. J.; Nicolaou, K. C.; Toru, T. *J. Am. Chem. Soc.* **1975**, *97*, 2287–2288.