HETEROCYCLES, Vol. 76, No. 1, 2008, pp. 129 - 132. © The Japan Institute of Heterocyclic Chemistry
Received, 7th November, 2007, Accepted, 20th December, 2007, Published online, 21st December, 2007. COM-07-S(N)2

PHOTODIMERIZATION OF PYRIDO[2,1-*a*]ISOINDOL-6(4*H*)-ONE‡

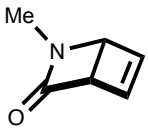
Leo A. Paquette,* Robert D. Dura, and Judith C. Gallucci

Evans Chemical Laboratories, The Ohio State University, Columbus, OH 43210, USA; e-mail: paquette.1@osu.edu

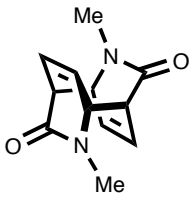
Abstract - When subjected to acetone-sensitized irradiation, the title compound undergoes near-quantitative self-coupling to give an uncommon [4+2] dimer, whose reaction with several oxidants demonstrated the enamide double bond of the photoproduct to be the more reactive.

INTRODUCTION

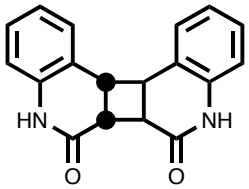
The excited state chemistry of heterocyclic systems containing an enamide chromophore has established that a select number of reaction pathways may be adopted depending upon the core structure, degree and type of substitution, ring size, and reaction conditions. As a result, such photochemical processes continue to serve as a convenient source of structurally appealing end-products. Representative examples include the conversion of *N*-methyl-2-pyridone to **1** under dilute conditions[1] and to **2** in saturated aqueous environments.[3] No such transformations are exhibited by carbostyryl, which experiences regio- and stereo-controlled [2+2] dimerization to give **3** instead.[3] This pathway is comparable to that preferred by the well- known uracil and thymine examples.[4] A second carbonyl group can effect a quite different series of events as illustrated by the conversion of 1,3-dimethyl-5,5-diphenylpyridine-(1*H*,5*H*)-2,6-dione to **4**.[5]



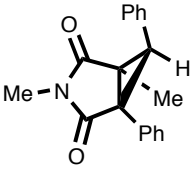
1



2



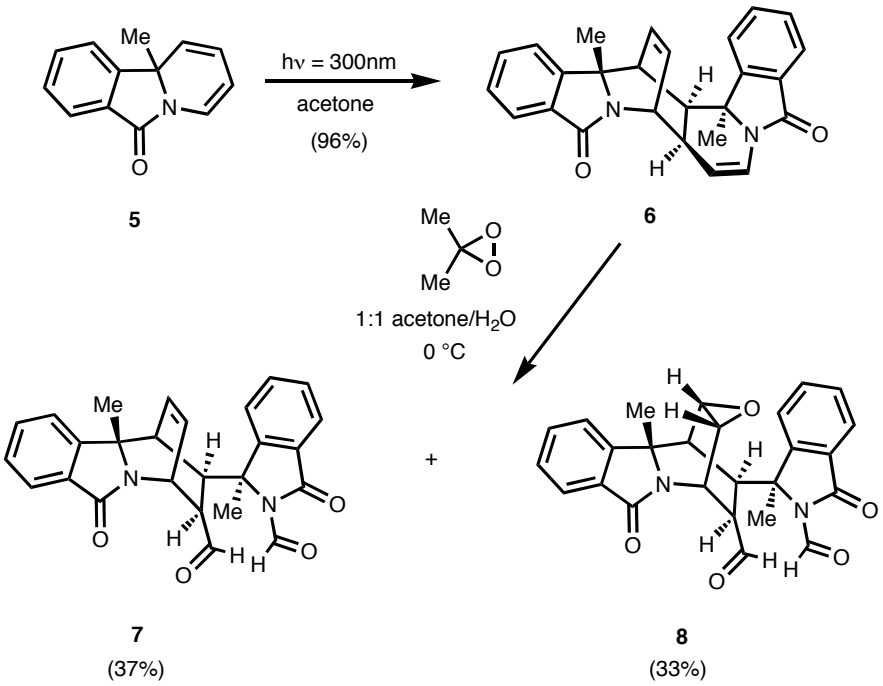
3



4

‡Submitted in celebration of the 70th birthday of Ryoji Noyori whose leadership role in the chemical sciences is legendary.

The reactant selected for the present study was the readily available pyrido[2,1-*a*]isoindolone **5**.[6] The significant structural modification resident in **5** is the positioning of the lactam carbonyl external to the dihydropyridine ring. The extended conjugation inherent to **5** [λmax (isooctane) 333 (ε 5,865) and 233 (ε 21,975)] was expected to allow comparison of this constitutional relationship to those enumerated above. When the direct irradiation of hexane solutions of **5** through quartz at various wavelengths proved unrewarding, recourse was made instead to acetone sensitization (300 nm, Rayonet reactor). Under these conditions, a colorless gum was produced (96% yield), the spectral properties of which revealed it to be a dimer lacking symmetry (Scheme 1). Its 500 MHz ^{1}H NMR spectrum in $CDCl_3$ confirmed several key elements of its structure, including most notably the presence of one and not two enamide functionalities. HMQC studies confirmed the pairwise distribution of both sets of olefinic protons/carbons. Particularly informative as well were COSY measurements that proved diagnostic of the fact that the two vinyl systems were neither proximal to each other nor styrenyl in nature.



Scheme 1

Our quest of a crystalline substance with which to corroborate these quite unusual structural features and also overlay configurational parameters led us to examine the oxidation of **6**[7] with excess dimethyldioxirane. The expectation was that a diepoxide would be produced. This proved not to be the case. Instead, the diformyl compounds **7**[8] and **8**[9] were generated in approximately equal amounts. The identity of these highly functionalized entities was ultimately revealed by solid-state X-ray analysis (Figures 1 and 2, respectively). These proofs of structure likewise confirmed the propensity of the enamide double bond for uncommon oxidative cleavage in the presence of the dioxirane. In contrast, the

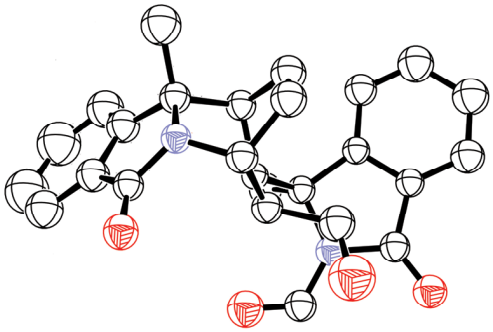


Figure 1. Ortep diagram of **7**.

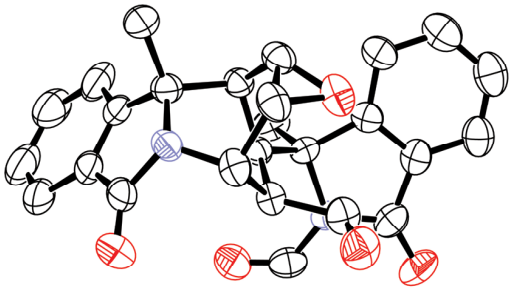
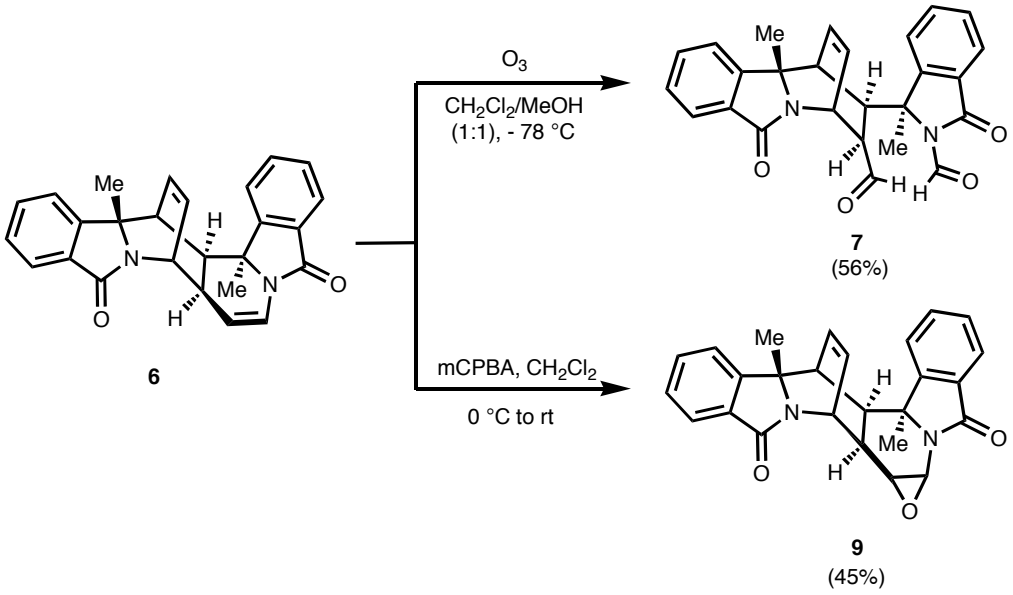


Figure 2. Ortep diagram of **8**.

site of unsaturation in the [3.2.1] bicyclic framework is subject to stererocontroled introduction of an epoxide oxygen atom. The more elevated reactivity of the heteroatom-substituted π-bond toward the dioxirane reagent was also seen to be operational during ozonolysis in CH_2Cl_2/CH_3OH (1:1) at -78 °C. Treatment of **6** in this manner provided **7** as the only characterizable product (Scheme 2).



Scheme 2

A contributing factor to this chemoselectivity may well be the elevated degree of electron density in the enamide component. This simplistic view of the prevailing electronic distribution in **6** holds predictive value, as recourse to oxidation with *m*-chloroperbenzoic acid in CH_2Cl_2 was met with conversion to **9**.

The effort outlined herein has documented an efficient example of light-induced [4+2] cycloaddition proceeding via the triplet state of an isoindoline. The resulting installation of two new C-C bonds proceeds with endo selectivity and projects the two chemically distinctive olefinic sites in **6** into a very specific polycyclic arrangement. The dense confluence of polar functionality residing in this photodimer

is further enhanced following oxidation by dimethyldioxirane, ozone, or a peracid. All three reagents preferentially target the enamide sector, with formation either of a diformyl derivative as in **7** or an epoxide as in **9**. Thus, the prospect of using an isoindolone framework as a matrix for elaborating attractive new synthetic building blocks is an attractive one.

ACKNOWLEDGMENT

We thank The Ohio State University for financial support.

REFERENCES AND NOTES

1. E. J. Corey and J. Streith, *J. Am. Chem. Soc.*, 1964, **86**, 950.
2. (a) G. Slomp, F. A. MacKellar, and L. A. Paquette, *J. Am. Chem. Soc.*, 1961, **83**, 4472. (b) W. A. Ayer, R. Hayatsu, P. deMayo, S. T. Reid, and J. B. Stothers, *Tetrahedron Lett.*, 1961, 648. (c) L. A. Paquette and G. Slomp, *J. Am. Chem. Soc.*, 1963, **85**, 765. (d) E. C. Taylor and R. O. Kan, *J. Am. Chem. Soc.*, 1963, **85**, 776. (e) R. C. De Selms and W. R. Schleigh, *Tetrahedron Lett.*, 1972, 3563.
3. (a) O. Buchart, *Acta Chem. Scand.*, 1964, **18**, 1389. (b) G. G. Spence, E. C. Taylor, and O. Buchart, *Chem. Rev.*, 1970, **70**, 231.
4. A. A. Demola and J. P. Mittal, *Science (New York, NY)*, 1966, **154**, 1560.
5. H. E. Zimmerman and O. D. Mitkia, *J. Org. Chem*., 2007, **72**, 6091.
6. R. D. Dura, I. Modolo, and L. A. Paquette, *Heterocycles*, 2007, **74**, 145.
7. For **6**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.67-7.64 (m, 2H), 7.54-7.49 (m, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.5 Hz, 1H), 6.35-6.32 (m, 1H), 5.91 (t, *J* = 7.5 Hz, 1H), 5.25 (dd, *J* = 8.0, 3.5 Hz, 1H), 4.90-4.87 (m, 1H), 3.20-3.17 (m, 1H), 2.52 (d, *J* = 6.5 Hz, 1H), 1.80 (d, *J* = 8.5 Hz, 1H), 1.18 (s, 3H), 1.17 (s, 3H).
8. For **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.24 (d, *J* = 5.5 Hz, 1H), 7.89 (dd, *J* = 17.0, 7.5 Hz, 1H), 7.73-7.66 (m, 2H), 7.59-7.54 (m, 4H), 7.44 (d, *J* = 7.5 Hz, 1H), 6.80 (t, *J* = 7.0 Hz, 1H), 6.44 (td, *J* = 6.5, 1.0 Hz, 1H), 4.83-4.80 (m, 1H), 3.64 (d, *J* = 6.0 Hz, 1H), 3.17-3.13 (m, 1H), 3.01 (d, *J* = 9.5 Hz, 1H), 1.60 (s, 3H), 1.48 (s, 3H).
9. For **8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.87 (s, 1H), 7.94 (dd, *J* = 11.5, 7.5 Hz, 2H), 7.76 (t, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 5.22 (t, *J* = 4.5 Hz, 1H), 3.91 (t, *J* = 5.0 Hz, 1H), 3.57 (t, *J* = 4.5 Hz, 1H), 3.29 (d, *J* = 5.0 Hz, 1H), 2.80 (d, *J* = 11.0 Hz, 1H), 2.59 (dd, *J* = 10.5, 4.5 Hz, 1H), 1.73 (s, 3H), 1.52 (s, 3H).