value for **2**. Given that our theoretical calculations predict **2** to be an energy minimum, but a less stable minimum than **1**, and that Szeimies has been able to trap **2** as well as other bridged bicyclobutenes, it appears that the unbridged bicyclobutene **1** is likely to exist and might be observable in a low-temperature matrix.

Acknowledgment. This work was supported in part by the National Science Foundation (Grant no. CHE-8605951). We also thank the National Science Foundation for providing supercomputer time for this project.

Photoinduced Lactonization. A Useful but Mechanistically Complex Single Electron Transfer Process

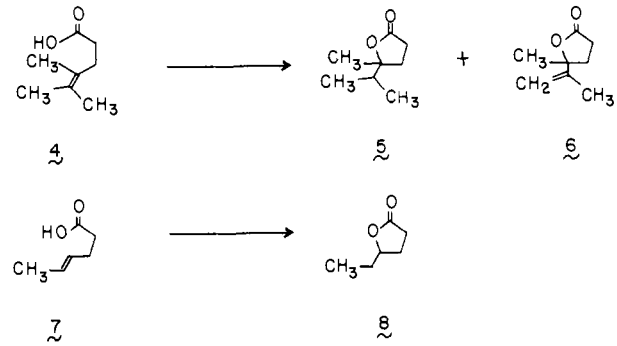
Paul G. Gassman* and Kyle J. Bottorff

Department of Chemistry, University of Minnesota Minneapolis, Minnesota 55455

Received August 6, 1987

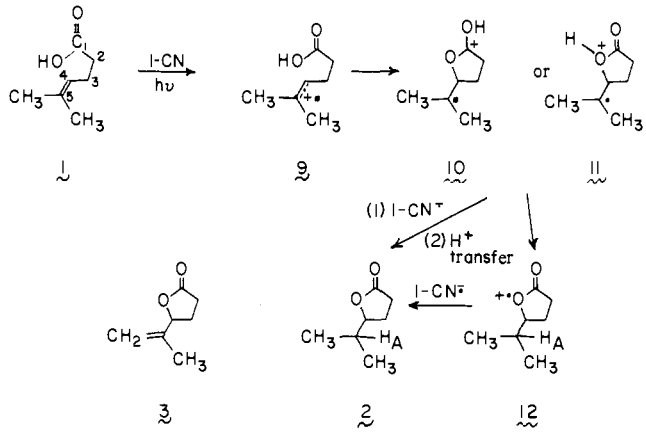
A wide variety of biologically active natural products contain the five-membered lactone moiety. Often, these lactones are the products of the anti-Markovnikov intramolecular addition of a carboxylic acid to a carbon–carbon double bond. Synthetically, this type of lactonization can be difficult to achieve. We now report that this transformation can be accomplished in acceptable yields through a mechanistically complex single electron transfer photoprocess.

In general, any organic molecule with an $E_{1/2}$ for oxidation of 2.2 V or less (vs SCE) should be susceptible to oxidation via a photosensitized single electron transfer process.[1,2] The resulting cation radical should be highly reactive and, under the proper conditions, should collapse either intermolecularly or intramolecularly with available nucleophiles.[3] This concept is nicely demonstrated by the photoinduced cyclization of γ,δ-unsaturated carboxylic acids to γ-lactones.[4] In a typical procedure, a Pyrex vessel containing a 65:35 acetonitrile/water solution (240 mL), 4.27 g of **1**,[5,6] 2.57 g (0.5 equiv) of 1-cyanonaphthalene (1-CN), and 2.55 g (0.5 equiv) of biphenyl (BP) was irradiated for 8 h in a Rayonet reactor fitted with 16 3000-Å lamps. The reaction mixture was steam distilled, and the steam distillate, after workup, yielded 43% of **2** and 5% of **3**.[7,8] When this reaction was carried out for 145 min in 55:45 acetonitrile/water, GLC analysis indicated the presence of 51% of **2** and 10% of **3**. This mixture was readily converted to **2** through catalytic reduction over 5% palladium on carbon. Utilizing the same general procedure, **4**[5] gave



69% of **5**[9a] and 10% of **6**[6,10] after 85 min, and **7**[5] gave 36% of **8**[9b] after 800 min. As these examples demonstrate, the photolactonization reaction shows a propensity for five-membered ring formation, even when this results in an anti-Markovnikov addition as in the conversion of **1** into **2**.

Mechanistically, the conversion of **1** into **2** might be viewed as occurring through the transfer of an electron from **1** ($E_{1/2}^{ox}$ vs SCE = 1.80 V) to excited state 1-CN ($E_{1/2}^{red}$ vs SCE = 1.83 V) to yield the cation radical **9**. Cyclization would be expected



to yield the distonic cation radicals **10** or **11**.[11,12] The fate of **10**/**11** was surprisingly complex (vide post). It was immediately obvious that *at least* two paths from **10**/**11** to **2** must exist. The presence

(1) For earlier studies of photoinduced electron transfer reactions from our laboratory, see: Gassman, P. G.; Olson, K. D.; Walter, L.; Yamaguchi, R. *J. Am. Chem. Soc.* **1981**, *103*, 4977. Gassman, P. G.; Olson, K. D. *J. Am. Chem. Soc.* **1982**, *104*, 3740. Gassman, P. G.; Olson, K. D. *Tetrahedon Lett.* **1983**, *24*, 19. Roth, H. D.; Schilling, M. L. M.; Gassman, P. G.; Smith, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 2711. Gassman, P. G.; Hay, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 4075. Gassman, P. G.; Hay, B. A. *J. Am. Chem. Soc.* **1986**, *108*, 4227.

(2) For leading references, see: Mattes, S. L.; Farid, S. *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker, Inc.: New York, 1983; Vol. 6, p 233. Pac, C.; Miyauchi, Y.; Ishitani, O.; Ihama, M.; Yasada, M.; Sakurai, H. *J. Org. Chem.* **1984**, *49*, 26. Davidson, R. S. *Molecular Association*; Foster, R., Ed.; Academic Press: New York, 1975; p 215.

(3) Maroulis, A. J.; Arnold, D. R. *J. Chem. Soc., Chem. Commun.* **1979**, 351. Mattes, S. L.; Farid, S. *J. Am. Chem. Soc.* **1983**, *105*, 1386. Lewis, F. D.; DeVoe, R. J. *Tetrahedron* **1982**, *38*, 1069.

(4) For other non-lactonization examples of intramolecular photoinduced nucleophilic cyclizations, see: Foote, C. S.; Jiang, Z. Q. *Tetrahedron Lett.* **1983**, *24*, 461. Kropp, P. J.; Krauss, H. J. *J. Am. Chem. Soc.* **1969**, *91*, 7466.

(5) The syntheses of **1**, **4**, and **7** were achieved through exchange reactions between the appropriate allyl alcohol and triethyl orthoacetate, followed by Claisen rearrangements. Saponification of the resulting esters gave the desired unsaturated carboxylic acids. The reactions employed were similar to those described in the literature: Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. Blosick, G. J., Ph.D. Thesis, The Ohio State University, 1974; *Diss. Abstr.* **1974**, *35*, 726-B.

(6) Satisfactory elemental analyses and/or exact mass molecular weights were obtained on all new compounds. All compounds reported had ^{1}H NMR, ^{13}C NMR, and IR spectra consistent with the assigned structures.

(7) The spectral data for **2** and **3** matched those previously reported in the literature: Timmer, R.; tar Heide, R.; de Valois, P. J.; Wabben, H. J. *J. Agric. Food Chem.* **1975**, *23*, 53. Naya, Y.; Kotake, M. *Nippon Kagaku Zasshi* **1968**, *89*, 1113.

(8) In the course of this photocyclization, approximately 70% of the 1-CN was consumed. The biphenyl was recovered quantitatively.

(9) (a) Edwards, J. T.; Cooke, E.; Paradellis, T. C. *Can. J. Chem.* **1981**, *59*, 597. (b) Henkanen, E.; Pippuri, A.; Pyysalo, H.; Enquist, J. *Finn. Chem. Lett.* **1975**, *129*.

(10) Catalytic reduction of the mixture of **5** and **6** over 5% Pd/C gave a 73% yield of **5** from **4**.

(11) Yates, B. F.; Bouma, W. J.; Radom, L. *Tetrahedron* **1986**, *42*, 6225. Radom, L.; Bouma, W. J.; Nobes, R. H.; Yates, B. F. *Pure Appl. Chem.* **1984**, *56*, 1831. Golding, B. T.; Radom, L. *J. Am. Chem. Soc.* **1976**, *98*, 6331. See, also: Crow, F. W.; Gross, M. L.; Bursey, M. M. *Org. Mass Spectrom.* **1981**, *16*, 309. Terlouw, J. K.; Heerma, W.; Dijkstra, G. *Org. Mass Spectrom.* **1981**, *16*, 326. For the simplest case, $[CH_3CH_2OH]^{\bullet+}$ is calculated to be 43 kcal/mol less stable than its distonic counterpart $[CH_2CH_2OH_2]^{\bullet+}$.

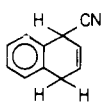
(12) Attack of the carbonyl oxygen on the initially generated cation radical would produce **10**. The relative stabilities of **10**, **11**, and **12** are unknown.

0002-7863/87/1509-7547$01.50/0

of **3** suggested a deprotonation–disproportionation of **10**/**11**. When **1**, with completely deuteriated methyl groups was used, approximately 22% of H_A in **2** was replaced by deuterium. This was consistent with the ratio of **3**:**2** being 2:10.

In order to determine what percentage of **2** was formed directly from **10**/**11** either by hydrogen atom transfer to produce **12** followed by back electron transfer from the 1-CN anion radical or by back electron transfer followed by proton transfer, an acetonitrile solution of **1-*O*-*d*** and 1-CN was irradiated. Only 34% of H_A was replaced by deuterium. These results demanded the incursion of additional mechanistic paths in order to account for the source of the other 44% of the hydrogen at H_A.

In order to establish the nature of any additional mechanisms, the non-lactone portion of the reaction mixture was carefully analyzed. This allowed the isolation of 1,4-dihydro-1-cyanonaphthalene, **13**. The reduction of 1-CN to **13** could be ra-



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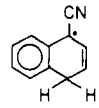

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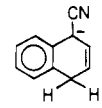

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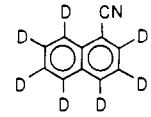

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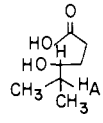
tionalized by a variety of paths, but either proton transfer or hydrogen atom transfer to the 1-CN radical anion seems most rational. This should yield **14** or **15**, respectively. Subsequent hydrogen atom transfer to **14** or proton transfer to **15** would yield **13**. Since **14** should be a significant hydrogen atom source, it would serve as a hydrogen atom carrier which would disproportionate with **10**/**11** (or their deprotonated analogues) to produce **2**. In order to test this theory, we prepared **16** from naphthalene-d_8 and used it as a photosensitizer. Two entirely different deuterium labeling experiments showed that ca. 11% of H_A of **2** was replaced by deuterium from **16**. These experiments implicate **14** as a significant reaction intermediate[15] and left the source of 33% of H_A undetermined.

A major change in the workup procedure provided part of the answer to the remaining source of H_A. Omission of the steam distillation step coupled with extraction of any free carboxylic acid and careful neutralization gave 12% of **17** and 2% of **18**.[16] Both



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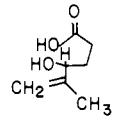

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17 and **18** resulted from the addition of water to the initially formed cation radical **9**. These compounds were readily converted into **2** and **3** under the normal reaction workup conditions,[16] providing an additional source of H_A in **2**. When an acetonitrile–deuterium oxide solution of **1-*O*-*d*** and 1-CN was irradiated and worked up under the standard conditions, 60% of H_A of **2** was replaced by deuterium. This implies that substantial amounts of **17** and **18** were converted into **2** and **3**, respectively.

Addition of the 60% deuterium at H_A, obtained from the combination of **1-*O*-*d*** with deuterium oxide, to the 22% deuterium at H_A, obtained from disproportionation with the labeled methyl groups, and 11% deuterium at H_A, obtained from exchange with **16**, accounts for the source of 93% H_A on **2**.[17] This demonstrates that at least four reaction paths are involved in the synthetically useful SET-photoconversion of γ,δ-unsaturated acids into γ-lactones.

Acknowledgment. We are indebted to the National Science Foundation for a grant which supported this investigation.

(13) Irradiation of a solution of **1** and 1-CN in acetonitrile-d_3 gave no replacement of H_A by deuterium. The use of biphenyl-d_{10} as a cosensitizer showed that none of the biphenyl deuteriums replaced H_A by deuterium.

(14) Deuterium analyses were carried out by a combination of ^2H NMR, ^{13}C NMR, and GC-CI-MS.

(15) Irradiation of an acetonitrile–deuterium oxide solution of **1-*O*-*d***, 1-CN, and biphenyl followed by isolation and spectral analysis of the 1,4-dihydro-1-cyanonaphthalene showed the 1-position of **13** to be 98% deuteriated while the 4-position was 58% deuteriated. ^2H NMR showed that only the 1- and 4-positions contained deuterium. Isolation of the 1-CN followed by spectral analysis showed that approximately 10% of the 1-CN had incorporated deuterium at C-4. Because of the possible involvement of isotope effects and the added role which 1-CN may have played in the transfer of hydrogen from either the methyls of **1** or the acidic hydrogen of **1**, the 11% transfer of a deuterium to C-5, when **16** was used, represents a minimal value for the involvement of **14** and/or **13**.

(16) Control experiments demonstrated that **2** and **3** were not converted into **17** and **18**, respectively, during the base extraction. In addition, steam distillation resulted in the complete conversion of **17** and **18** to **2** and **3**, respectively.

(17) Deuterium labeling experiments demonstrated that the hydrogens at C-2, C-3, and C-4 were not transferred to C-5 in the formation of **2**.

Design of a Double-Stranded DNA Cleaving Agent with Two Polyamine Metal-Binding Arms: $Ru(DIP)_2Macro^{n+}$

Lena A. Basile and Jacqueline K. Barton*

Department of Chemistry, Columbia University
New York, New York 10027

Received August 3, 1987

There is considerable interest in the design of small molecules which react at specific sites along the DNA strand as reactive models for protein–nucleic acid interactions, in developing new probes of DNA structure, as an aid to drug design, and as tools in molecular biology.[1] In our laboratory, a family of chiral metal complexes have been developed which are DNA conformation-specific cleaving molecules, and these may be targeted along the helical strand with site specificity to examine local variations in DNA secondary structure.[2] We report here the synthesis[3,4] and

(1) (a) Dervan, P. B. *Science* (*Washington, D.C.*) **1986**, *232*, 464. (b) Spassky, A.; Sigman, D. S. *Biochemistry* **1985**, *24*, 8050. (c) Sugiyama, H.; Kilkuskie, R. E.; Hecht, S. M.; van der Marel, G. A.; van Boom, J. H. *J. Am. Chem. Soc.* **1985**, *107*, 7765. (d) Hertzberg, R. P.; Dervan, P. B. *J. Am. Chem. Soc.* **1982**, *104*, 313. (e) Fleisher, M. B.; Waterman, K. C.; Turro, N. J.; Barton, J. K. *Inorg. Chem.* **1986**, *25*, 3549. (f) Youngquist, R. S.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 2565.

(2) (a) Barton, J. K. *Science* (*Washington, D.C.*) **1986**, *233*, 727. (b) Mei, H. Y.; Barton, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 7414.

(3) The Macro ligand is first synthesized by the reaction of 4,7-diphenyl-1,10-phenanthroline (DIP), disodium salt (GFS), with $SOCl_2$ in dimethylformamide at ~80 °C for 3–4 h. The resultant disulfonyl chloride, which is amber in color, is then reacted in situ with excess tren to form a disulfonamide (Macro ligand). After purification by gel chromatography (Sephadex G-10), Macro is then heated at ~60 °C with $Ru(DIP)_2Cl_2$ in 30% acetonitrile/70% H_2O for 1 h, which gives a color change from purple to yellow-orange, indicative of coordination of a third phenanthroline ligand to the metal center. Purification by gel chromatography (Sephadex G-15) yields a deeply colored yellow-orange, hygroscopic compound, $Ru(DIP)_2Macro^{n+}$. The racemic complex is then recrystallized from ethanol to remove excess salt. $Ru(DIP)_2Cl_2$ is synthesized in an analogous manner to $Ru(bipy)_2Cl_2$. See: Sullivan, B. P.; Salmon, D. J.; Meyer, T. J. *Inorg. Chem.* **1978**, *17*, 3334.

(4) UV-vis: ϵ (275 nm) = 1×10^5 M^{-1} cm^{-1}; ϵ (340 nm) = 6×10^4 M^{-1} cm^{-1}; ϵ (440 nm) = 2×10^4 M^{-1} cm^{-1}. Infrared: S=O stretch at 1170 and 1305 cm^{-1}; aliphatic C–N vibrations at 1095, 1130, 1140, and 1205; overtones at 1980 cm^{-1}; aromatic C–C stretches at 1450 and 1395 cm^{-1}; and characteristic bands at 610 and 480 cm^{-1}. ^1H NMR (in D_2O): methylene protons at δ 2.25, 2.30, 2.45, 2.65 ppm, and aromatic protons centered at δ 7.9. Integration of the methylene/aromatic regions varies substantially with solvent and acquisition parameters, consistent with the different correlations times and relaxation rates of the two distinct components of the molecule. FAB mass spectrum: 1514 ($Ru(DIP)_2Macro^{2+}$); 1492 ($Ru(DIP)_2Macro^+ - CH_2CH_2NH_2 + Na$; 1469 ($Ru(DIP)_2Macro^+ - CH_2CH_2NH_2$); 1410 ($Ru(DIP)_2Macro^{2+} - CH_2NH_2 - CH_2NH_2 - CH_2CH_2NH_2$); 1298 ($Ru(DIP)_2Macro^+ - NHCH_2CH_2N(CH_2CH_2NH_2)_2 - CH_2CH_2NH_2 - CH_2CH_2NH_2 + H_2O$); 1223 ($Ru(DIP)_2Macro^+ - NHCH_2CH_2N(CH_2CH_2NH_2)_2 - NHCH_2CH_2N(CH_2CH_2NH_2)_2$); 1181 ($Ru(DIP)Macro^+$); 1079 ($Ru(DIP)Macro^{3+} - CH_2NH_2 - CH_2NH_2 - CH_2CH_2NH_2$).

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