Pergamon

Tetrahedron Letters, Vol. 37, No. 15, pp. 2553-2556, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00328-0

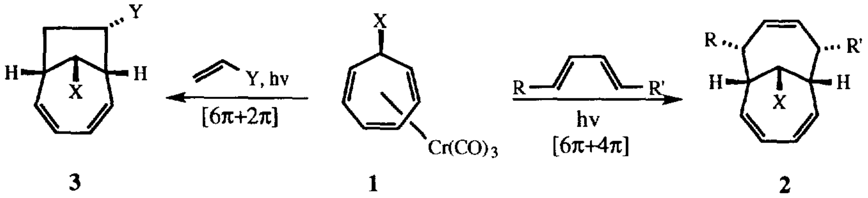
Studies on Electrocyclization in Bicyclo[4.4.1]undeca-2,4-diene and Bicyclo[4.2.1]nona-2,4-diene Systems

James H. Rigby,* Valérie de Sainte Claire and Mary Jane Heeg‡

Department of Chemistry, Wayne State University, Detroit, Michigan 48202-3489 USA

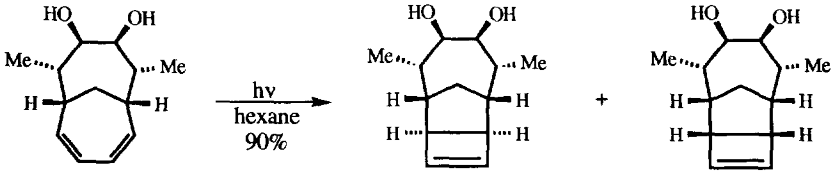
Summary: Photoinduced electrocyclization of substituted bicyclo[4.4.1]undecadienes and bicyclo[4.2.1]nonadienes, derived from chromium(0)-promoted [6π+4π] and [6π+2π] cycloadditions, respectively, afforded polycyclic products possessing substantial stereochemical information.

Metal-promoted higher-order cycloaddition can provide access to structurally elaborate polycyclic systems that exhibit considerable functionality and stereochemical information.[1] The synthetic utility of these adducts would be augmented if selective post-cycloaddition manipulation of extant functionality could be achieved.[2]



Scheme I

The 1,3-diene unit present in both [6+4] and [6+2] adducts provides a number of opportunities for subsequent conversion into other useful sub-structures. In this paper we report a study on the photochemical electrocyclization of these systems to cyclobutene products.[3]



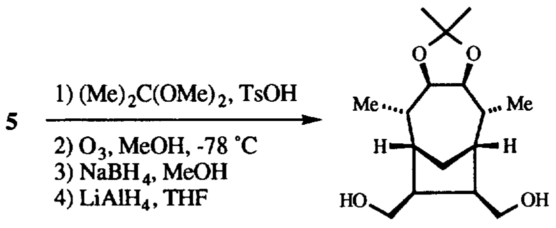
4 5 (74%) 6 (16%)

Irradiation (quartz) of bicyclo[4.4.1]undecadiene **4**,[4] derived from **2** (R, R' = Me, X = H) by dihydroxylation (OsO_4, Et_3NO, t-BuOH, H_2O, 22%), afforded a 4.6:1 mixture of exo-cyclobutene **5**[4,5] and endo-**6**,[4] respectively in 90% yield.[6] Protection of the cis-diol in **5** as the acetonide followed by reductive ozonolysis[7] afforded the stereochemically-rich diol-acetal **7**[4] in 30% overall yield. It is

---

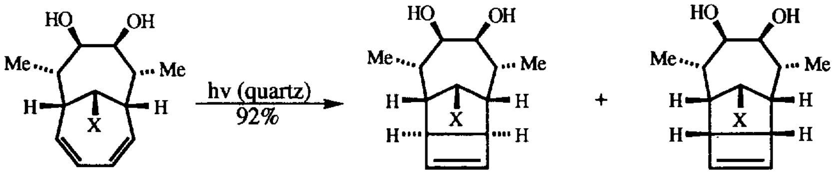
‡ Author to whom inquiries regarding x-ray determination should be addressed.

noteworthy that compound **7** exhibits relative stereogenicity that is complementary to that produced in Cr(0)-mediated [6π+2π] cycloadditions.[8]



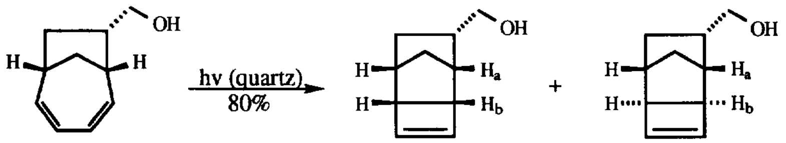
7 (30%)

Additional stereochemical information can be incorporated into the tricyclic product by employing a 7-substituted cycloheptatriene complex in the initial cycloaddition step. Thus electrocyclization of the diene moiety in the readily available methoxy-substituted substrate **8**,[4] derived from **2** (X = OMe, R, R' = Me), provided a 6:1 mixture of exo-**9**[4] and endo-**10**[4] in 92% combined yield. It is interesting that a non-hydrogen substituent facing the diene on the one-carbon bridge appears to exert only a minor influence on the stereochemical outcome of the cyclization step. The stereochemistry of **9** and **10** was determined by comparing relevant coupling constants with those in **5** and **6**.



8, X = OMe **9** (79%) **10** (13%)

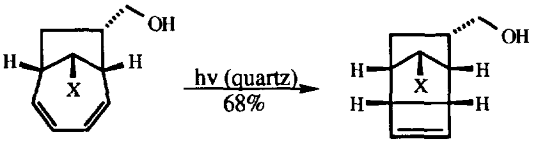
Adducts conveniently available from Cr(0)-promoted [6+2] cycloadditions are also amenable to diene electrocyclization. In a typical example, irradiation of bicyclic alcohol **11**, obtained by $LiAlH_4$ reduction of adduct **3** (Y = CO_2Et, X = H), afforded an 80% yield of a mixture of two products in a 2:1



11 **12** (53%) **13** (27%)

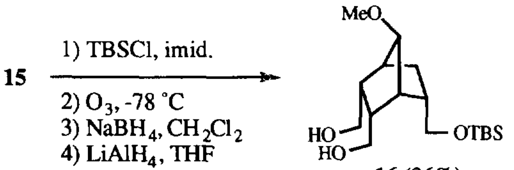
ratio. The major product proved to be the corresponding endo isomer, a result that is qualitatively consistent with precedent in related ring systems.[3] It is noteworthy that efforts to reverse the stereochemical course of this reaction using various sensitizers failed.[3d]

The stereochemistry of **12** and **13** was determined by noting the relevant coupling constants. Thus, for compound **12** an observed J_{ab} = 5 Hz was consistent with a calculated (MM2) dihedral angle of 36°, and for isomer **13**, a J_{ab} = 0 Hz was in reasonable agreement with the calculated angle of 70°.



14, X = OMe **15**, X = OMe

In contrast to the above results, electrocyclization of a bicyclo[4.2.1]nonadiene with a methoxy substituent positioned over the diene moiety afforded only the endo product **15**. In this case the substituent provided sufficient steric hindrance to completely suppress the alternative cyclization pathway. This observation can be contrasted with the results in the corresponding bicyclo[4.4.1]undecadiene system (vide supra). Straightforward cleavage of the cyclobutene moiety in **15** provided the highly substituted bicyclo[2.2.1]heptane product, **16** in good overall yield.



16 (36%)

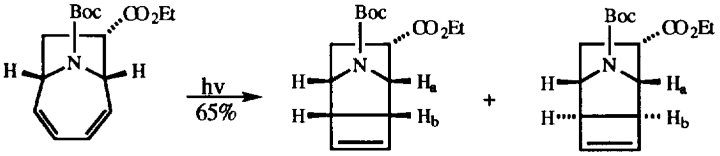
Since appropriately disposed substituents on the one-carbon bridge were observed to control the stereochemical course of diene electrocyclization in bicyclo[4.2.1]nonadiene substrates, we wondered what role substituents at other locations in the molecule would play. To address this issue, a range of groups were positioned on the endo surface of the two-carbon bridge and photocyclizations were performed. The results are collected in Table I. The remarkably large influence of the isomenthyl ester substituent was particularly noteworthy and may be due to factors other than steric hindrance. Work to sort out this issue is currently underway.

Table I. The Influence of Substituents on the Stereochemistry of Electrocyclization.

Substrate	Exo-product	Endo-product	Yield (%)
11	1	2	80%
3, Y = CH_2OTBS	1	1.6	85%
3, Y = $C(CH_3)_2OH$	1.1	1	51%
3, Y = CO_2R^*	1	0	80%

R* = (+)-isomenthyl, X = H in all substrates.

Finally, heterocyclic substrates are also effectively converted into tricyclic products under standard photocyclization conditions. Irradiation of the azepine derived adduct **17**[8] afforded two isomeric cyclobutenes paralleling the results with compound **11**.



17 **18** (46%) **19** (19%)

In summary, electrocyclization of the diene moiety in higher-order cycloadducts affords structurally elaborate, stereochemically-rich products. The utility of some of these products in natural product synthesis will be reported in due time.

Acknowledgment: The authors wish to thank the National Institutes of Health (GM-30771) for their financial support of this research, and VSC thanks Wayne State University for a Rumble graduate fellowship.

References

1. Rigby, J. H. *Acc. Chem. Res.* **1993**, *26*, 579.
2. For an example in another ring system, see: Lautens, M.; Kumanovic, S *J. Am. Chem. Soc.* **1995**, *117*, 1954 and references cited therein.
3. For related electrocyclizations, see: a) Mukai, T.; Akasaki, Y.; Hagiwara, T. *J. Am. Chem. Soc.* **1972**, *94*, 675. b) Jefford, C. W.; Delay, F. *Ibid.* **1972**, *94*, 4794. c) Hahn, R. C.; Johnson, R. P. *Ibid.* **1975**, *97*, 212. d) Jefford, C. W.; Delay, F. *Ibid.* **1975**, *97*, 2272.
4. This compound exhibited spectral (^{1}H NMR, ^{13}C NMR, IR) and analytical (HRMS and/or combustion analysis) data consistent with the assigned structure.
5. The structure of this compound was established by single crystal x-ray analysis of the corresponding diacetate derivative.
6. *General procedure for electrocyclization of dienes:* The diene was dissolved in a small amount of an appropriate solvent (hexanes, ether or dichloromethane) and introduced along with 320 mL of hexanes into a dry photochemical reaction vessel equipped with a quartz glass immersion well. Argon was bubbled vigorously through the solution for 15 min., and then the reaction mixture was irradiated (Canrad-Hanovia 450 W medium pressure mercury vapor lamp) for 15 min. The solvent was removed *in vacuo* and the residue chromatographed with the appropriate eluent.
7. Zhai, D.; Zhai, W.; Williams, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 2501.
8. Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Henshilwood, J. A.; Short, K. M.; Sugathapala, P. M. *Tetrahedron* **1993**, *49*, 5495.

(*Received in USA* 22 *January* 1996; *accepted* 12 *February* 1996)