Tetrahedron Letters, Vol.32, No.9, pp 1129-1132, 1991
Printed in Great Britain

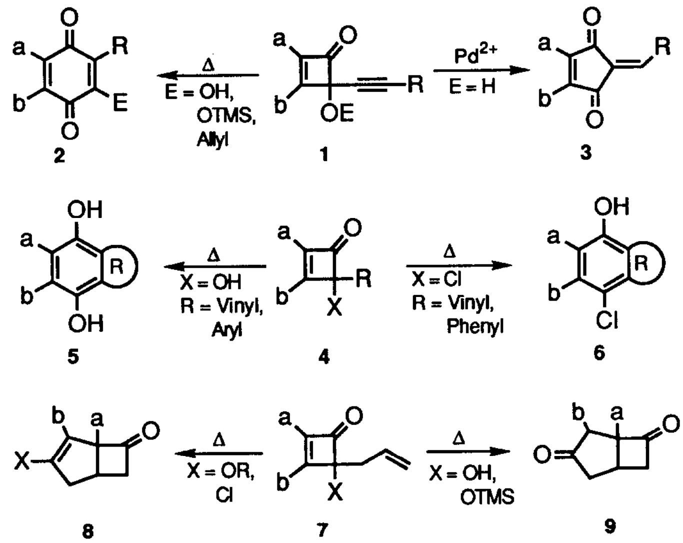
0040-4039/91 $3.00 + .00
Pergamon Press plc

Synthesis of Substituted Cyclobutenediones from 3-Ethenyl-4-methoxycyclobutene-1,2-dione

Simon Xu, Benjamin R. Yerxa, Robert W. Sullivan and Harold W. Moore
Department of Chemistry
University of California
Irvine, CA 92717

Abstract: *The synthesis of 3-ethenyl-4-methoxycyclobutene-1,2-dione from dimethylsquarate is described. This compound was observed to undergo facile 1,6-addition of both carbon and non-carbon nucleophiles to the 3-alkenyl group. Thus, it serves as a versatile starting material for the synthesis of a variety of substituted cyclobutenediones which are convenient starting materials to a variety of other ring systems.*

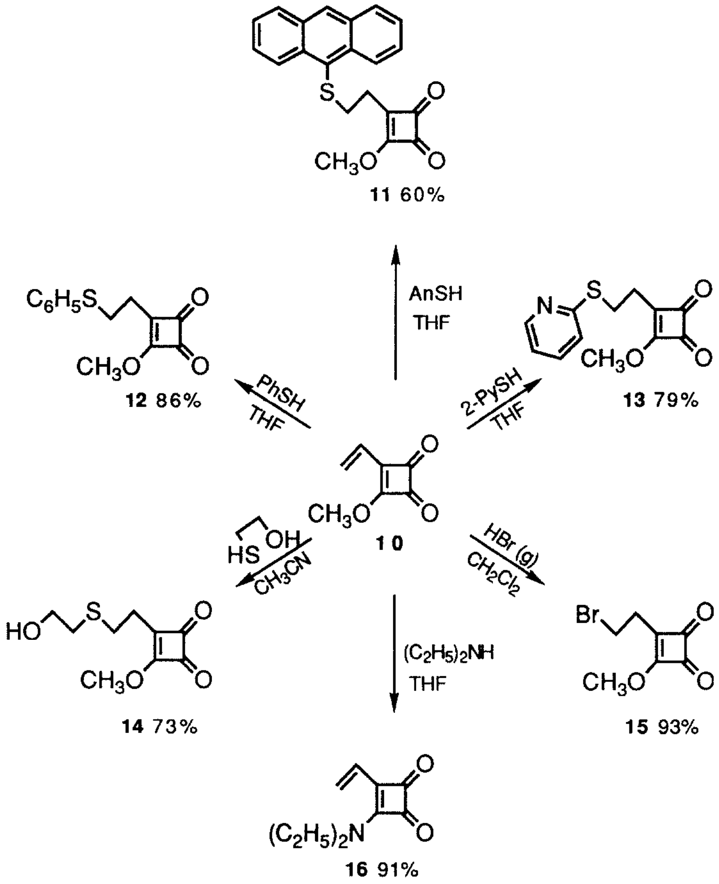
Scheme-1



Introduction

Reported here are the synthesis of 3-ethenyl-4-methoxycyclobutenedione, **10**, and the use of this compound as a starting material for other substituted cyclobutenediones. This is of interest since cyclobutenediones are proving to be useful precursors to highly functionalized aromatic compounds, quinones, 2-alkylidene-1,3-cyclopentenediones and bicyclo[3.2.0]heptenones.[1-16] For example, 4-alkynylcyclobutenones **1** rearrange to quinones **2** upon thermolysis or to 5-alkylidene-2-cyclopentene-1,3-diones **3**

Scheme-2



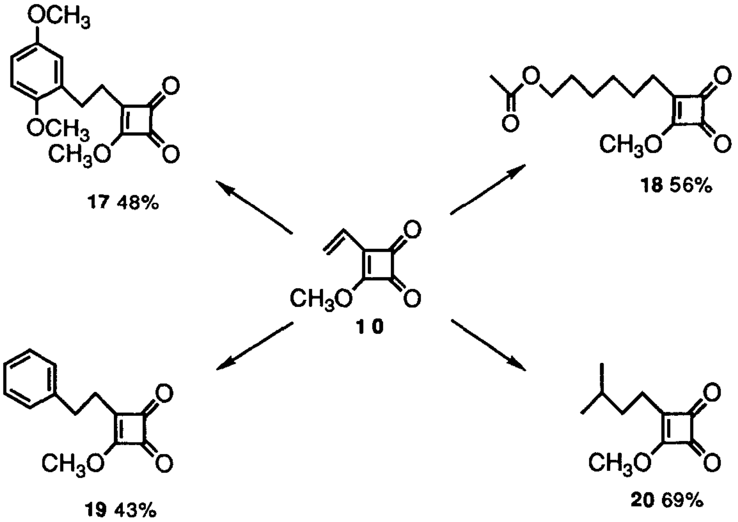
when subjected to catalytic Pd^{2+} (Scheme-1). Analogously, thermolyses of 4-aryl(or vinyl)-4-hydroxycyclobutenones **4** (X=OH) lead to hydroquinones **5**, 4-chlorocyclobutenones **4** (X = Cl) give *p*-chlorophenols **6**, and 4-allylcyclobutenones **7** result in bicyclo[3.2.0]heptenones **8** or bicyclo[3.2.0]heptanedione **9** depending on the substitution pattern of the starting cyclobutenones (Scheme-1).

The general synthesis of substituted cyclobutenediones outlined here involves the facile 1,6-additions of carbon- and noncarbon-nucleophiles to the ethenyl group of **10**. This method is complimentary to others appearing during the last few years.[17-22] Among these are improved syntheses of substituted cyclobutenediones from dialkoxycyclobutenediones, cross-coupling reactions employing tri-n-butylstannyl substituted cyclobutenediones and cyclobutenedione monoketals, and the palladium catalyzed cross-coupling of halocyclobutenediones with organostannanes.

Results and Discussion

3-Ethenyl-4-methoxycyclobutene-1,2-dione **10** was prepared by addition of vinyllithium to dimethyl squarate followed by quenching of the resulting alkoxide with trifluoroacetic anhydride.[18,23] Outlined in Scheme-2 are examples involving the 1,6-addition of non-carbon nucleophiles to this reagent. Specifically, treatment of **10** with 9-mercaptoanthracene, thiophenol or 2-mercaptopyridine in tetrahydrofuran at ambient temperature resulted in the diones **11**,**12**, and **13**, respectively. For the more nucleophilic thiol, 2-mercaptoethanol, acetonitrile was employed as the solvent to reduce the formation of bis-addition thus giving **14** in 73% isolated yield. Interestingly, when **10** was treated with a nitrogen nucleophile, diethylamine, the product obtained was 3-ethenyl-4-(N,N-diethylamino)-3-cyclobuten-1,2-dione **16** rather than the 1,6-addition product. Finally, treatment of **10** with gaseous hydrogen bromide resulted in an excellent yield of the dione **15**.

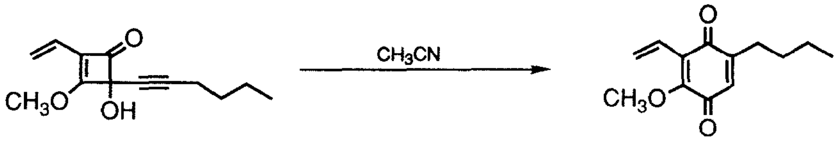
Scheme-3



Carbon nucleophiles (cuprates or zinc cuprates) also undergo 1,6-addition to **10**. For example, zinc alkyl cuprates (generated from the alkyl iodides) add in the presence of TMSCl to give moderate yields of the corresponding adducts **18** (56%) and **20** (69%) (Scheme-3)[24] . Similarly, the appropriate aryl cuprates (generated from the aryl bromides) lead to the cyclobutenediones **17** (48%) and **19** (43%).

In conclusion, the results presented here provide a versatile entry to substituted cyclobutenediones and thus to highly substituted quinones and related compounds as generally outlined in Scheme-1. It is noteworthy that the functionalization must take place on the vinylcyclobutendione **10** and not at a vinylquinone stage. As an illustration, the cyclobutenone **21** was converted the the vinylquinone **22** (27% from the dione **10**) in refluxing acetonitrile and this compound gave complex mixtures when subjected to representative reactions outlined above (Scheme-4).

Scheme-4



21 22

The structures of all of the new compounds described here are based upon characteristic spectral and analytical data.

Acknowledgement The authors thank the National Institutes of Health (GM-36312) for financial support of this work. We also thank Catherine A. Moore for technical assistance in obtaining High Resolution Mass Spectral data on the new compounds reported here.

References

1. Enhsen, A.; Karabelas, K.; Heerding, J. M.; Moore, H. W. *J. Org. Chem.* **1990**, *55*, 1177.
2. Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 989.
3. Foland, L. D.; Karlsson, J. O.; Perri, S. T.; Schwabe, R.; Xu, S. L.; Moore, H. W. *J. Am. Chem. Soc.* **1989**, *111*, 975.
4. Iyer, S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1987**, *109*, 2759
5. Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S.; Leeds, J. P. *Tetrahedron Symposium in Print* **1985**, *41*, 5839.
6. Xu, S.L.; Moore, H.W. *J. Org. Chem.* **1989**, *54*, 4024.
7. Liebeskind, L. S.; Iyer, S.; Jewell, C. F. *J. Org. Chem.* **1986**, *51*, 3065.
8. Liebeskind, L. S.; *Tetrahedron Symposium in Print* **1989**, *45*, 3053.
9. Moore, H. W.; Perri, S. T. *J. Org. Chem.* **1988**, *53*, 996.
10. Perri, S. T.; Moore, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 1897.
11. Selwood, D. L.; Jandu, K. S. *Heterocycles* **1988**, *27*, 1191.
12. Liebeskind, L. S.; Chidambaram, R. *J. Am. Chem. Soc.* **1987**, *109*, 7908.
13. Liebeskind, L. S.; Mitchell, D.; Foster, B. *J. Am. Chem. Soc.* **1987**, *109*, 7908.
14. Liebeskind, L. S.: Chidambaram, R.; Mitchell, D.; Foster, B. *Pure Appl. Chem.* **1988**, *60*, 27.
15. Liebeskind. L. S.; Foster, B. S. *J. Am. Chem. Soc.* **1990**, in press
16. Xu, S.L.; Moore, H.W. *J. Org. Chem.* **1989**, *54*, 6018.
17. The preparative chemistry of cyclobutenediones before 1978 has been reviewed in three comprehensive articles. However, of the numerous methods presented none stand out as sufficiently general to allow the preparation of diversely substituted derivatives. See: Schmidt, A. H.; Reid, W. *Synthesis* **1978**, 1; Knorr, H.; Ried, W. *Synthesis* **1978**, 649; Schmidt, A. H.; Ried, W. *Synthesis* **1978**, 869.
18. Reed, M. W.; Pollart, D. J.; Perri, S. T.; Foland, L. D.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 2477.
19. Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988**, *53*, 2482.
20. Liebeskind, L. S.; Fengl. R. W. *J. Org. Chem.* **1990**, *55*, 5359.
21. Liebeskind, L. S.; Wirtz, K. R. *J. Org. Chem.* **1990**, *55*, 5350
22. Liebeskind, L. S.; Wang, J. *Tetrahedron Letters* **1990**, 4293.
23. For generation of vinyllithium from tetravinyltin, see: Nugent, W.A.; Hobbs, F.W. *J. Org. Chem.* **1986**, *51*, 3376.
24. The use of such reagents has been elegantly demonstrated by P. Knochel and his co-workers. See: Berk, S. C.; Knochel, P.; Yeh, M. C. *J. Org. Chem.* **1988**, *53*, 5789; Yen, M.; Knochel, P. *Tetrahedron Lett.* **1988**, 2395; Knochel, P.; Jeong, N.; Chou, T.; Knochel, P. *J. Org. Chem.* **1990**, *55*, 4791; Knochel, P.; Yen, M.; Berk, S.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

(Received in USA 26 November 1990)