Tetrahedron Letters, Vol. 34, No. 9, pp. 1463-1466, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Synthesis of Substituted Hexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecanes. A Novel Method for Bridging Across the 8,11-Positions of Pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione and Related Diketones

Alan P. Marchand* and Dayananda Rajapaksa
Department of Chemistry, University of North Texas, Denton, Texas 76203-0068

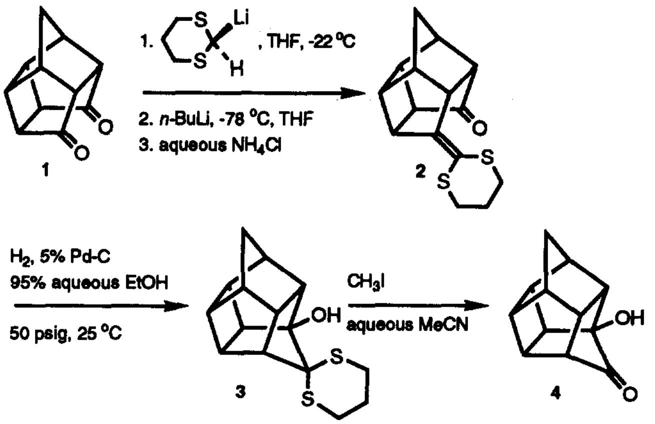
Abstract: Reaction of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione mono(ketene dithioacetal), **2**, with hydrogen at 50 psig over palladized charcoal catalyst results in reductive cyclization, thereby affording the corresponding bridged dithioketal, **3**. The results of similar reactions with other cage and noncage 1,4-dione systems point to the need for spatial proximity between reacting centers in order to achieve ring formation via this process.

Introduction: As part of a continuing program that involves the synthesis and chemistry of novel polycyclic "cage" systems,[1] we have investigated new methods for introducing a methylene (or substituted methylene) bridge across the 8,11-positions of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione (PCU-8,11-dione, **1**).[2] This approach has provided a new synthesis of 1,3-bishomopentaprismane,[3] and it has also been used to generate intermediates in a novel synthesis of homopentaprismane-8-carboxylic acid.[4] Recent interest in the chemistry of dithioacetals[5] and of ketene dithioacetals[6] prompts us to report a new method for introducing a "masked carbonyl" bridge across the 8,11-positions of **1** with cocomitant formation of a substituted hexacyclo-[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane.

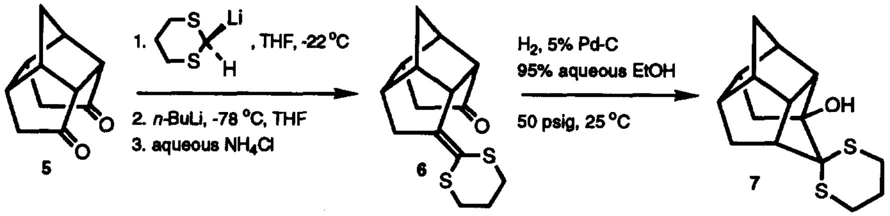
Results: Reaction of **1** with 2-lithio-1,3-dithiane[7] (1 equivalent) at -22 °C for 15 minutes followed by treatment with *n*-BuLi (1 equivalent) resulted in the formation of the corresponding mono(ketene dithioacetal), **2**, in 70% yield (Scheme 1). Subsequent hydrogenation of **2** over 5% Pd-C catalyst at 50 psig in a Parr hydrogenation apparatus at room temperature directly afforded the corresponding bridged dithioketal, **3**, in essentially quantitative yield. The structure of **3** was established via analysis of its proton and ^{13}C NMR spectra and by the fact that hydrolysis of the dithioketal moiety in **3** afforded 3-hydroxyhexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecan-4-one (**4**), which has been prepared previously in our laboratory.[4]

To our knowledge, the unusual course of hydrogenation of the C=C double bond in **2** that results in the introduction of a functionalized methylene bridge across the 8,11-positions in **2** is unprecedented.[5,6] In an effort to explore the potential applicability of this procedure to other systems which contain ketone C=O groups in close mutual proximity, a similar reaction sequence was applied to tetracyclic diketone **5**[8] (Scheme 2). Conversion of **5** to the corresponding mono(ketene dithioacetal), **6**, proceeded smoothly in *ca.* 60% yield. Catalytic hydrogenation of **6** proceeded slowly (36 h at room temperature) to afford the corresponding bridged thioketal, **7**, in essentially quantitative yield.

Scheme 1



Scheme 2

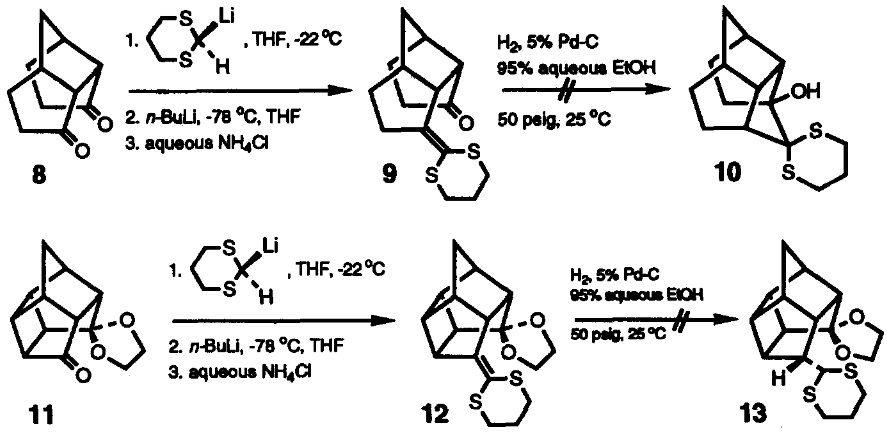


This same reaction sequence was applied to *cis,cisoid,cis*-tricyclo[6.3.0.$0^{2,6}$]undecane-3,11-dione (**8**).[9] Whereas **8** could be converted into the corresponding mono(ketene dithioacetal), **9**, hydrogenation of **9** over palladized charcoal failed to produce **10**; only unreacted **9** could be recovered from this reaction. Similarly disappointing results were obtained when we attempted to hydrogenate mono(ketene dithioacetal) **12** over palladized charcoal. As was the case for the corresponding attempted catalytic hydrogenzation of **9**, only unreacted starting material could be obtained (Scheme 3).

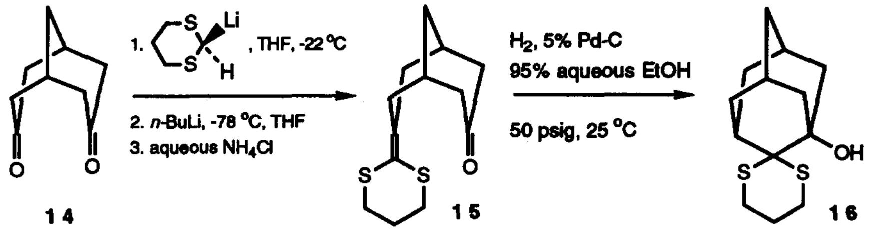
Next, a somewhat more flexible system, bicyclo[3.3.1]nonane-3,7-dione (**14**) was converted into the corresponding mono(ketene dithioacetal), **15**. Subsequent hydrogenation of **15** over palladized charcoal resulted in reduction of the C=C bond with concomitant cyclization, thereby producing the corresponding bridged thioketal (i.e., **16**, a substituted adamantane) in 77% yield (Scheme 4).

At this juncture, we deemed it desirable to attempt to utilize this reaction sequence as a means to perform ring closure in an acyclic system. To this end, hexane-2,5-dione was converted into the corresponding mono(ke-

Scheme 3



Scheme 4

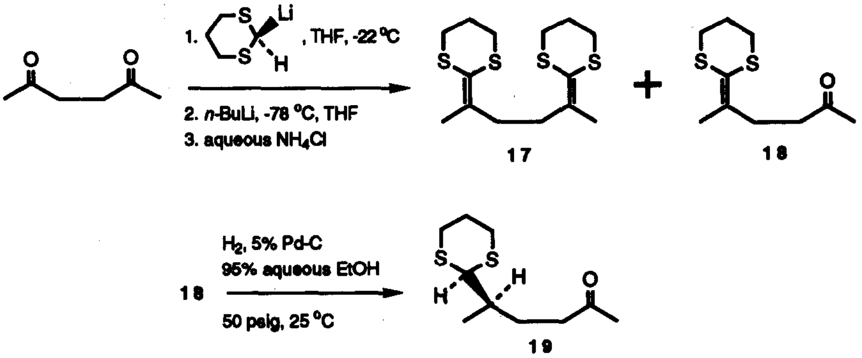


tene dithioacetal), **18**. Subsequent hydrogenation of **18** over palladized charcoal resulted in reduction of the C=C bond *without* concomitant ring closure, thereby affording **19** (Scheme 5). This result demonstrates the requirement of close mutual spatial proximity between the ketene dithioacetal moiety and the distant reacting C=O group in order for ring closure to occur.

Discussion. It seems reasonable to suggest that this reductive cyclization process proceeds via a discrete intermediate which either is trapped by the distant C=O group (thereby affording cyclized product) or is reduced further to afford the corresponding (noncyclic) saturated ketone. The foregoing results point to the need for spatial proximity between reacting centers in order to achieve ring formation via this process.

In order to better understand the effect of proximity between reacting centers on the course of the reduction process, a series of model compounds was chosen in which the dithioketene acetal moieties in **2**, **6**, **9**, and **15** were replaced by exocyclic methylene groups. The structure of each of these model enones was optimized by application of molecular mechanics methods (MM2)[10]. Then, a new series of structures was generated by reacting each enone in turn with atomic hydrogen, and the structure of each of the resulting radicals was optimized by using MM2 methods. The distance between reacting centers, *r*, in each of the radicals then could be estimated.[11a]

Scheme 5



The value of *r* obtained for the model enone derived from **9** turned out to be the largest of the four model systems studied. This result suggests that, among the four reductive cyclization processes which have been modeled, the least compelling "proximity effect" should be operative for the attempted reductive cyclization of **9** to **10**, a prediction which is consistent with experimental observations.

Our results appear to be consistent with the operation of a stepwise process for the reductive cyclizations which have been studied herein. Experiments designed to clarify the nature of the intermediate(s) in these reactions are underway at present.[11b]

Acknowledgment. We thank the Robert A. Welch Foundation (Grant B-963) and the Office of Naval Research (Grant N00014-92-J-1362) for financial support of this study.

References and Footnotes

1. See: Marchand, A. P. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P.; Ed.; JAI; Greenwich, CT; 1989; Vol. 1, pp. 357-399 and references cited therein.

2. Marchand, A. P.; Allen, R. W. *J. Org. Chem.* **1974**, *39*, 1596.

3. Marchand, A. P.; Wu, A.-h. *J. Org. Chem.* **1986**, *51*, 1897.

4. Marchand, A. P.; Deshpande, M. N. *J. Org. Chem.* **1989**, *54*, 3226.

5. Luh, T.-Y. *Acc Chem. Res.* **1991**, *23*, 257.

6. (a) Kolb, M. *Synthesis*, **1990**, 171. (b) Junjappa, H., Ila, H.; Asokan, C. V. *Tetrahedron*, **1990**, *46*, 1423. (c) Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* **1989**, *22*, 152.

7. Corey, E. J.; Seebach, D. *Org. Synth.* **1970**, *50*, 72.

8. Wenkert, E.; Yoder, J. E. *J. Org. Chem.* **1970**, *35*, 2986.

9. Mehta, G.; Srikrishna, A.; Reddy, A. V.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543.

10. Allinger, N. L.; Yuh, Y. H.; Li, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551.

11. (a) Details of these calculations will be presented in the full paper. (b) Satisfactory C,H microanalytical and/or high-resolution mass spectral data has been obtained for all new compounds reported herein. In addition, all new compounds have been characterized via analysis of their IR spectra and ^{1}H and ^{13}C NMR spectra.

(Received in USA 1 December 1992; accepted 22 December 1992)