THIONIUM ION-ACTIVATED PINACOL REARRANGEMENTS. GENERALITY AND SCOPE‡

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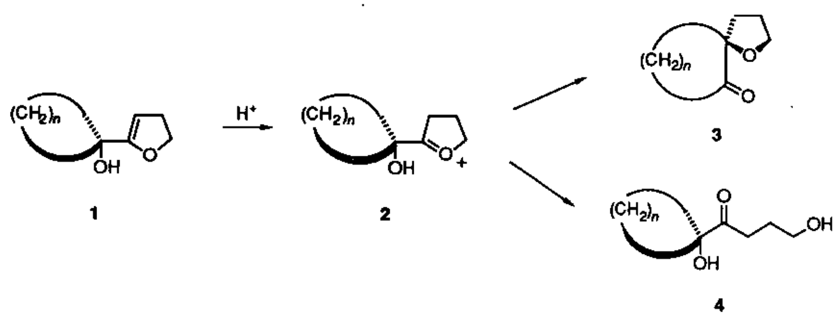
Abstract - The acid-catalyzed rearrangement of tertiary allylic alcohols produced by the addition of 5-lithio-2,3-dihydrothiophene to cyclic ketones of various ring size has been probed.

The overwhelming kinetic preference exhibited by alcohols of general formula **1** for oxonium ion generation under acidic conditions has recently been recognized.[2] Although allylic cation intervention is not observed, pinacolic ring expansion to give spirocyclic ketones such as **3** does not materialize universally. When n = 3 or 4, ring strain release is controlling and high yields (> 95%) of **3** are



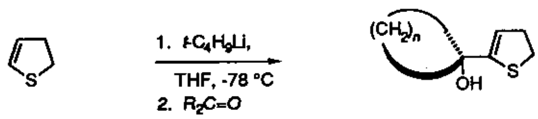
realized.[2,3] Adamantanone[2] and adducts of bicyclic ketones[4] behave similarly. The absence of this driving force permits slower hydrolysis to become competitive with generation of **4**. For example, in the

‡This paper is dedicated to Professor Alan Katritzky on the occasion of his 65th birthday.

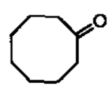
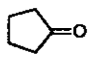
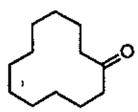
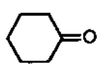
cyclooctyl example (n = 7), 31% of **4** is formed after exposure to Dowex-50x in CH_2Cl_2 at rt for 24 h.[5] Interestingly, the propensity for Wagner-Meerwein migration returns at n = 11, as reflected in the formation of significantly more **3** (66%) than **4** (6%) after only 2 h at 20 °C.[5]

These observations suggest that oxonium ions may perhaps be too stabilized to drive bond migration in those systems where ring strain increases. Evidence does exist that thionium ions are considerably less stable and more reactive.[6] Their utility in electrophilic aromatic substitution reactions has been clearly demonstrated.[7] For these reasons, we have now expanded upon our earlier studies to include the sulfur-containing carbinols **6**.

Exposure of 2,3-dihydrothiophene (**5**)[8] to tert-butyllithium in THF at -78 °C → 0 °C resulted in smooth formation of the 5-lithio derivative as expected.[9] The results of its condensation with several cyclic ketones are compiled in the Table. In the case of cyclopentanone, use was made of anhydrous $CeCl_3$ to deter adventitious enolization.[10]

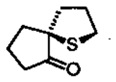


5 **6**

Ketone	Yield of 6	Ketone	Yield of 6
	Not isolated (see text)		72%
	65%[a]		52%
	75%		

[a] Anhydrous $CeCl_3$ (1 mol equiv) added to curb enolization.

Carbinol **6** (n = 3) was directly slurried with Dowex-50x resin in CH_2Cl_2 at 20 °C. After 2 days, the resin was filtered off and the product purified chromatographically. Only **7** was formed (89% isolated).[11] The rearrangement of **6** (n = 4) to **8** (29%) was likewise much slower than its oxygen counterpart (CH_2Cl_2, reflux, 1.5 days). This kinetic regardation was still more obvious when the higher homologues (n = 5, 7,



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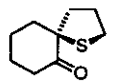

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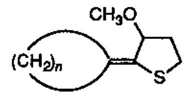
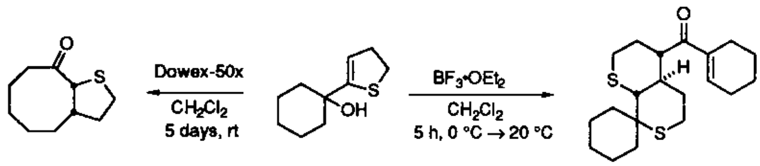


11a, $n = 5$
b, $n = 7$
c, $n = 11$



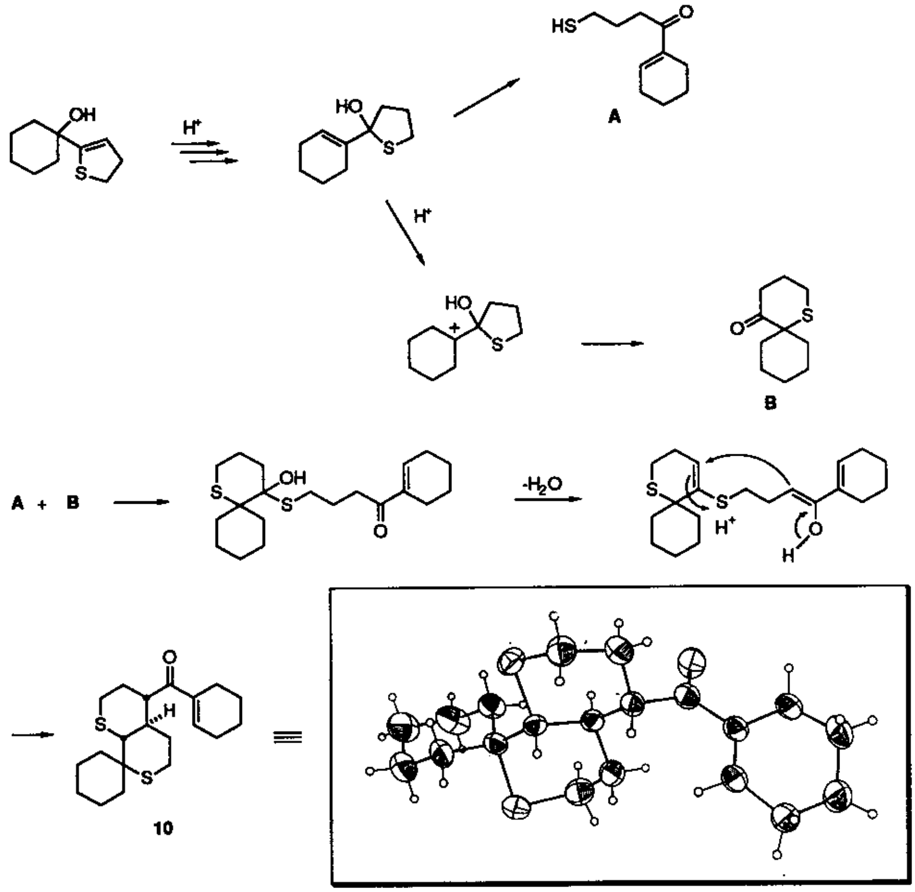
9 6 ($n = 5$) 10

11) were analogously processed. After 5 days at 20 °C, these carbinols could be recovered intact to the extent of 70-80%. Since several very minor products were seen to develop during this treatment (TLC analysis), the most prevalent among these was pursued in the cyclohexyl series and identified as **9** (4% isolated) on the strength of nOe experiments. When recourse was made to a more powerful Lewis-acidic catalyst (BF_3•OEt_2), a different reaction occured leading to **10** (24%), a colorless crystalline solid whose structural assignment was corroborated by X-ray diffraction. A reasonable mechanistic rationalization of the formation of **10** (Scheme I) rests on the need to invoke early intervention of the allylic cation, a process not heretofore observed in the oxygen analogs.

Added insight into this phenomenon was gained by allowing the three higher molecular weight alcohols **6** to stir overnight with methanol-premoistened Dowex-50x in CH_2Cl_2 at room temperature. Subsequent chromatography on silica gel led to the isolation of **11a** (58%), **11b** (46%), and **11c** (94%). In the first of these experiments, the O-methyl ether of the starting alcohol was also produced (12%).

Several interesting points of comparison can now be made: (a) the substitution of S for O as in **1** and **6** does not provide added driving force to pinacol ring expansion and in fact is a more substantive deterrent to the Wagner-Meerwein shift; (b) the presence of the sulfur atom renders these systems more prone to ionization of the tertiary hydroxyl substituent with resultant product-forming consequences; and (c) a thermodynamically favorable exit step such as that available to **6** (n = 3, 4) continues to be recognized, causing thionium ion intervention to be of kinetic significance in these examples. Such

Scheme I



factors need to be accorded proper consideration when this methodology is to be applied to structurally more complex systems.

ACKNOWLEDGMENT

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REFERENCES AND NOTES

1. (a) "Diplomandin" on leave from the Universität Münster, Münster, Germany. (b) Procter and Gamble Graduate Fellow, 1993.
2. L. A. Paquette, D. E. Lawhorn, and C. A. Teleha, Heterocycles 1990, **30**, 765.
3. (a) J. T. Negri, R. D. Rogers, and L. A. Paquette, J. Am. Chem. Soc. 1991, **113**, 5073. (b) L. A. Paquette, J. T. Negri, and R. D. Rogers, J. Org. Chem. 1992, **57**, 3947.
4. L. A. Paquette, J. F. P. Andrews, C. Vanucci, D. E. Lawhorn, J. T. Negri, and R. D. Rogers, J. Org. Chem. 1992, **57**, 3956.
5. U. Dullweber, unpublished results.
6. B. M. Trost and G. K. Mikhail, J. Am. Chem. Soc. 1987, **109**, 4124.
7. (a) B. M. Trost and T. Sato, J. Am. Chem. Soc. 1985, **107**, 719. (b) B. M. Trost and E. Murayama, Tetrahedron Lett. 1982, **23**, 1047.
8. G. Sosnovsky, Tetrahedron 1962, **18**, 15, 903.
9. (a) K. Oshima, K. Shimoji, H. Takahashi, H. Yamamoto, and H. Nozaki, J. Am. Chem. Soc. 1973, **95**, 2694. (b) R. C. Cookson and P. J. Parsons, J. Chem. Soc., Chem. Commun. 1976, 990. (c) I. Vlattas, L. Della Vecchia, and A. O. Lee, J. Am. Chem Soc. 1976, **98**, 2008. (d) B. Harirchian and P. J. Magnus, J. Chem. Soc., Chem. Commun. 1977, 522. (e) R. R. Schmidt and B. Schmid, Tetrahedron Lett., 1977, 3583.
10. (a) T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiya, J. Am. Chem. Soc. 1989, **111**, 4392. (b) L. A. Paquette, W. He, and R. D. Rogers, J. Org. Chem. 1989, **54**, 2291 and relevant references cited in these papers.
11. All new compounds reported herein have been fully characterized by ir , high-field ^{1}H and ^{13}C nmr , and high-resolution mass spectrometry and/or combustion analysis.

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