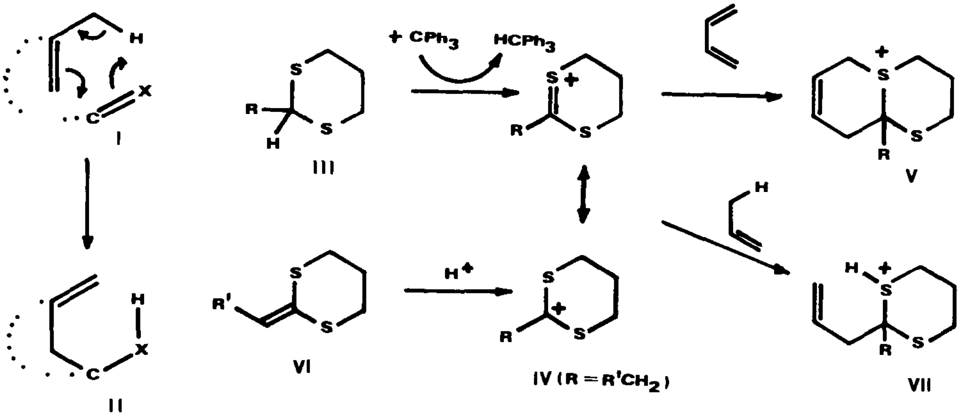
Tetrahedron Letters No. 51, pp 4547 - 4550, 1975. Pergamon Press. Printed in Great Brita

DITHIANE CHEMISTRY I UTILIZATION OF THE DITHIAN-2-YLIDENE FUNCTION FOR INITIATING CATIONIC CYCLIZATIONS

Niels H. Andersen*, Yasusi Yamamoto‡, and Alan D. Denniston
Department of Chemistry, University of Washington, Seattle, WA 98195

(Received in USA 30 September 1975, received in UK for publication 13 November 1975)

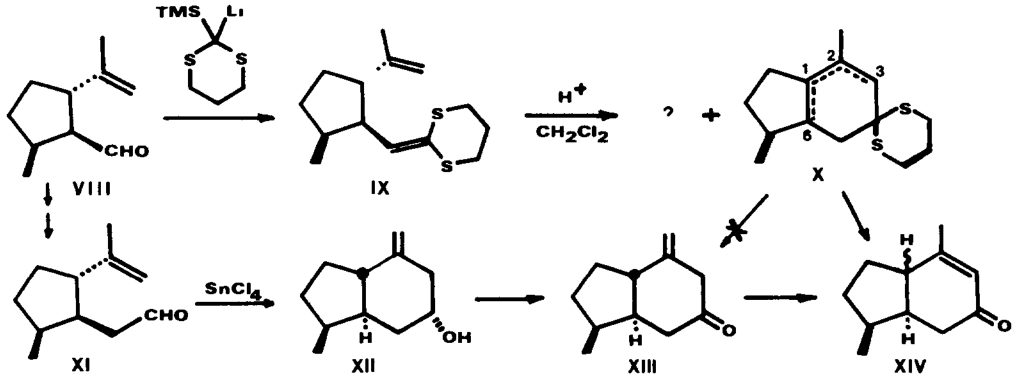
For some time we have been exploring the ene reaction of olefinic aldehydes as a method for producing carbocycles in total synthesis (e g. XI → XII, vide infra).[1,2,3] We were intrigued by the possibility that this was only one example of a more general process (I → II), which, with various X groups, could offer an extension in cyclization methodology. In the case of X = S, the sequence III → IV → V reported by Corey[4] indicated dienophilic (if not enophilic) character for dithianium cations (IV). Our attempts to extend this chemistry to other dithianes (III R = Me, phenyl, t-Bu) suggest that trityl cation generation of ion IV is of preparative value only for dithiane itself (III, R = H) For this reason we employ the protonation of ylidene dithianes (VI) as an entry to this chemistry. We can now report successful cyclizations proceeding by a cationic, not ene, mechanism.



---

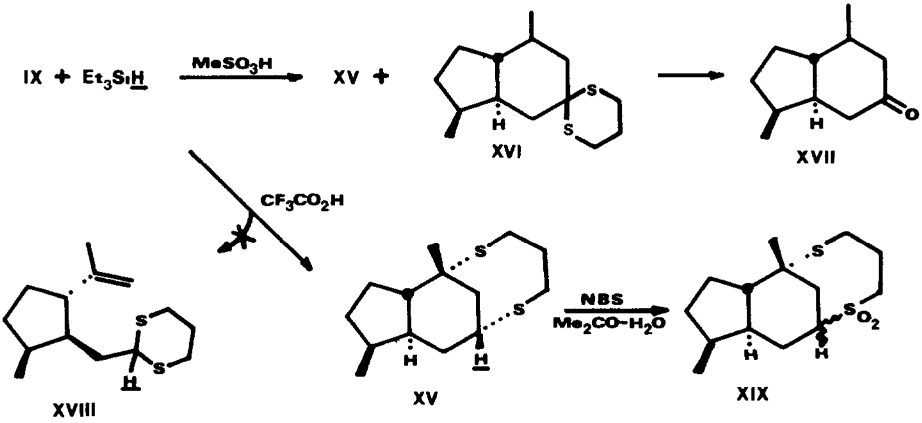
[*] Alfred P. Sloan Foundation Fellow, 1972-1974, Camille and Henry Dreyfus Teacher-Scholar, 1974-1979.

[‡] Visiting Scientist supported by Shin-Etsu Chemical Industries Co., Ltd



To facilitate product identification initial experiments were performed on ketene thioacetal IX[6] (The sequence VIII → XI → XII → XIII → XIV has already been reported).[3,5] Treatment with 10-20 mole % CF_3CO_2H or CH_3SO_3H[8] at 0° gave complete reaction in 5-10 min affording a complicated mixture of substances of which 20-65% can be represented by structure X. Dithiane hydrolysis under a variety of conditions[9] afforded mixtures of conjugated and non-conjugated ketones, but little or no XIII. The presence of XIV initially, and in greater quantity after treatment with methanolic KOH, was established by gc and spectral comparisons with authentic material. Overall yields of XIV approach 50% using CH_3SO_3H for cyclization but in all cases the initial cyclization products include unknown (not dithianes) sulfur containing compounds.

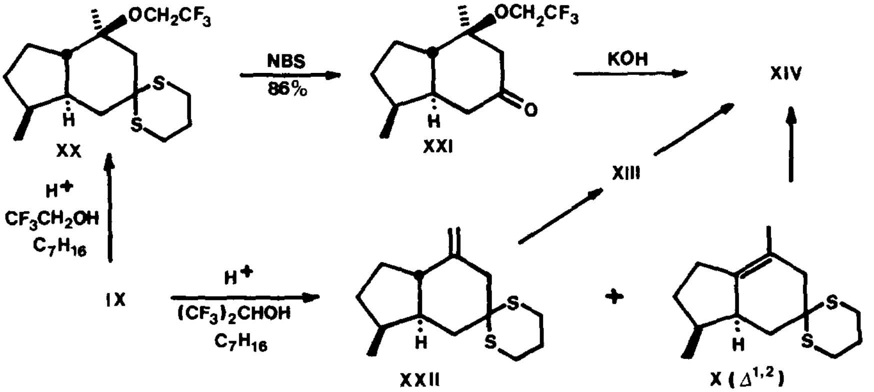
In order to reduce the complexity of the product mixture we varied the quenching agents employed (KOAc, K_2CO_3, Et_3SiH), eventually finding that cyclization competes favorably with a potential two stage reduction[10] (which would have led to XVIII) even when excess Et_3SiH was present throughout.



Using 1 equiv. of CH_3SO_3H and 1.5 equiv of Et_3SiH we obtained in addition to ca. 20% of X and 26% of a crystalline compound (XV), ca 15% of a saturated dithiane (XVI). The structure of XVI is based on hydrolysis (NBS, Me_2CO-H_2O)[9c] to a cyclohexanone, XVII[11a] [ir (film) 1715 cm^{-1}, δ_{CDCl_3} 0.89 and 0.98 ppm (2 Me d, 6.5 Hz)], recognized by gc as a hydrogenation product of XIII.

Using an equivalent of CF_3CO_2H in the presence of excess Et_3SiH afforded only XVI (ca. 15%) and a 77% yield of crystalline material (XV).[11b] mp 127.5-128.5° (from hexane), δ_{CDCl_3} 3.59 (1H, ∿ quint, 3.3), 2.4-3.2 (4H, m, $S\underline{CH_2}$), 1.33 (3H, Me s), and 0.80 ppm (3H, Me d, 6.5 Hz). Compound XV could not be converted to a ketone under any conditions,[9] the NBS conditions afforded a mixture of sulfoxides and sulfones from which a monosulfone[11b] (XIX?) could be isolated in 27% yield mp 183-184°, ir (film) 1290 and 1130 cm^{-1}, δ_{CDCl_3} 3.92 (1H, A of ABXY, J_{AB} = 16, $J_{X,Y}$ = 4, 10.5), 2.95-3.45 (2H, m), 2.6-2.95 (2H, m), 1.39 (Me, s), and 0.80 ppm (Me, d, 6.5 Hz). The assignments in the case of XV and XIX follow largely from nmr data.[16] In any case, the experiments establish that the sulfur groups migrate (1,3- or multiple 1,2-shifts) and explain the non-dithiane products observed in the original acid-catalyzed cyclization experiments.

In polyolefin cyclizations and double bond isomerizations,[12] we had found heterogeneous systems such as octane/HCO_2H and octane/H^+-CF_3CH_2OH useful for obtaining kinetic deprotonation products without further rearrangement. The results obtained using such media are shown below.



Reaction using CF_3CH_2OH[13] (per mmole IX.6 ml C_7H_{16}, 10 mg CH_3SO_3H, 0.30 ml CF_3CH_2OH, 15 min, 0°) to 80% completion gave ether XX[14] (69%)[11a] ir (film) 1290, 1160, 1125 cm^{-1}, δ_{CDCl_3} 3.80 (2H, q, 9), 1.38 (Me s), and 0.85 ppm (Me d, 6 Hz) - together with small amounts of XXII and X. Prolonged reaction gave complex mixtures. The structure of ether XX is based on the spectral data and hydrolysis to ketone XXI[11a]. ir (film) 1720 cm^{-1}, δ_{CDCl_3} 3.8 (q), 2.52 (2H, s, H-3), 1.13 (Me s), and 0.90 ppm (Me d, 7 Hz).[15] The rest of the sequence is shown in the flow scheme. Using a 30 min reaction time and no intermediate purifications, the yield of enone XIV is 70%.

With $(CF_3)_2CHOH$ the reaction proceeds more slowly, but at 40-60% reaction the product is a 1·1 mixture of the exocyclic (XXII) and $\Delta^{1,2}$ olefin isomers: no solvent capture is observed.

The use of the dithian-2-ylidene function to initiate cyclizations using electrophiles other than proton is now under study, as are application of these methods to natural product total synthesis.

Acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

REFERENCES AND NOTES

1. J. A. Marshall and N. H. Andersen, *Tetrahedron Letters*, 1219 (1967), J. A. Marshall, N. H. Andersen, and P. C. Johnson, *J. Amer. Chem. Soc.*, **89**, 2748 (1967), J. A. Marshall, N. H. Andersen, and J. W. Schlicher, *J. Org. Chem.*, **35**, 858 (1970).

2 The reaction can also be viewed as an intramolecular Prins reaction proceeding by a concerted rather than cationic mechanism.

3. N. H. Andersen, H. S. Uh, S E. Smith, and P.G M. Wuts, *J.C.S. Chem. Comm.*, 956 (1972).

4. E. J. Corey and S. W. Walinsky, *J. Amer. Chem. Soc.*, **94**, 8932 (1972)

5 For details see the Ph.D. thesis of H. S. Uh (U.W. 1973) a full manuscript is in preparation.

6. Compound IX (89% yield) was prepared from photocitral-A and 2-trimethylsilyldithian-2-yllithium.[7]

7. F A. Carey and A S. Court, *J. Org Chem.*, **37**, 1926, 4474 (1972); D. Seebach, B. -Th. Grobel, A. K. Beck, M. Braun, and K. H. Geiss, *Angew. Chem. Internat. Ed* , **11**, 443 (1972), P. F Jones, M. F. Lappert, and A. C. Szary, *J.C.S. Perkin I*, 2272 (1973)

8. Weaker acids such as HOAc gave recovered starting material. With CCl_3CO_2H cyclization was slow and the products included materials with a C-2-O_2CCCl_3 grouping.

9. a) FSO_3Me-NaOH: T. -L. Ho and C. M. Wong, *Synthesis*, 561 (1972), b) Chloramine-T· W Huurdeman and H. Wynberg, *Synthetic Commun.*, **2**, 7 (1972), c) $HgCl_2$, $CaCO_3$, or NCS,$AgNO_3$, or aq. NBS· E. J. Corey and B. W. Erickson, *J. Org. Chem* , **36**, 3553 (1971); d) $(NH_4)_2Ce(NO_3)_6$· T. -L Ho, H. C. Ho, and C. M. Wong, *J.C S. Chem. Comm.*, 791 (1972).

10 F A. Carey and J. R. Neergaard, *J. Org. Chem* , **36**, 2731 (1971).

11. a) In addition to spectral data, the formula is supported by high resolution exact mass measurements for the parent peak ($\pm$.003 amu) and b) by combustion analysis (C,H,S, $\pm$0.2%)

12. Largely unpublished results, see however. N. H. Andersen and D. D Syrdal, *Tetrahedron Letters*, 899 (1972), 2455 (1972), N. H. Andersen, S. E. Smith, and Y. Ohta, *J.C.S. Chem. Comm.*, 447 (1973).

13. Replacing CF_3CH_2OH with MeOH gave no reaction. Apparently $MeOH_2^+$ is not sufficiently acidic (compare $CF_3CH_2OH_2^+$)

14 Solvent capture of the cationic intermediate was not expected in media of such low nucleophilicity, see D. J. Raber, *Tetrahedron Letters*, 667 (1974).

15. The axial-Me assignment is suggested by the δ-changes on introducing the carbonyl group.

16. The δ 1.3-1.4 methyl singlet indicates the location of one sulfur and the δ 3.59 quintet of XV indicates the location and stereochemistry of the other sulfur group. The single downfield hydrogen resonance of the monosulfone appears to correspond to the axial-like hydrogen of the methylene α to the sulfone oxygen rather than to hydrogen corresponding to the downfield signal of the disulfide (XV), the latter is assigned as part of the δ 2.95-3.45 multiplet. The alternative structure with the other sulfur in the oxidized form cannot be excluded