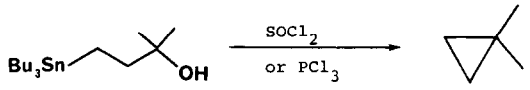
Tetrahedron Letters,Vol.25,No.46,pp 5255-5258,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF FUSED CYCLOPROPANES FROM γ-STANNYL ALCOHOLS

John F. Kadow and Carl R. Johnson*
Department of Chemistry, Wayne State University
Detroit, MI 48202

Summary--Fused cyclopropanes including 3-carene and isosequicarene have been prepared by treatment of γ-stannyl alcohols with thionyl chloride.

In 1970 Davis and co-workers reported that γ-trialkylstannyl alcohols undergo 1,3-eliminations to produce cyclopropanes upon treatment with thionyl chloride or phosphorus trichloride (eq 1).[1]



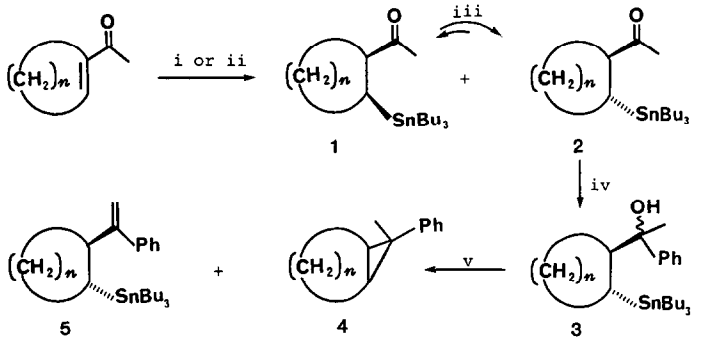
(1)

In a subsequent study by the Davis group it was established that the reaction proceeds with inversion at both centers.[2] From a synthetic point of view the method lay dormant until 1982 when Ueno and co-workers reported on the utilization of 3-(tributylstannyl)propanal as a cyclopropane building block; addition of various organometallics to the carbonyl group of this reagent followed by treatment with thionyl chloride resulted in fair to excellent yields of substituted cyclopropanes.[3,4] During the course of our study Fleming and Urch reported the "rediscovery" of this cyclopropanation method.[5] They found that cyclopropanes were formed when tertiary and benzyl alcohols bearing a γ-trialkylstannyl group were treated with $BF_3.2AcOH$; the tendency for the reaction to occur with inversion at both carbon centers was reaffirmed. Fleming and Urch summarized two general failures of their cyclopropane syntheses as follows: "One limit is that simple secondary alcohols with a γ-stannyl group decompose without noticeable cyclopropane formation. The other is more serious: we have failed to make the reaction work in such a way as to fuse a gem dimethylcyclopropane onto a five- six-, or seven-membered ring." The results of Ueno and co-workers had already established that that thionyl chloride/pyridine was an adequate reagent for the conversion of secondary alcohols bearing a γ-stannyl group to the corresponding cyclopropanes. In this communication we describe our results which expand the synthetic applicability of this chemistry and demonstrate that the limitations of the Fleming procedure can be readily circumvented by use of thionyl chloride as orginally promulgated by Davis.

The preparation of *trans*-1-acetyl-2-tributylstannylcycloalkanes (2) was acheived by the conjugate addition of either Bu_3SnLi[6] or $[Bu_3SnCuSPh]Li$[7] to the corresponding 1-acetylcycloalkene followed by

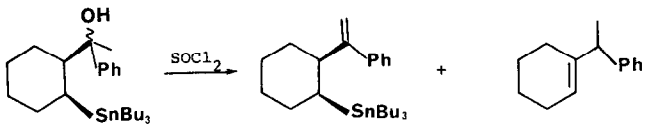
equilibration with KOtBu/tBuOH and purification by medium pressure liquid chromatography over silica gel (hexane/ethyl acetate).[8] Addition of phenyllithium to 2 provided the corresponding tertiary alcohols 3 as mixtures of diastereomers. Treatment of alcohols 3 either as mixtures or as purified diastereomers with thionyl chloride/pyridine at 0°C resulted in the fused ring cyclopropanes 4 (only diastereomer)[9] along with the by-products 5 (Scheme 1). The lack of stereospecificity as a result of ionization at the tertiary benzylic center was not unexpected; the cyclopropane products obtained are those with the smaller substituent group "endo".

Scheme 1



a n = 3 27% 65% i Bu_3SnLi ii $[Bu_3SnCuSPh]Li$
b n = 4 ca. 55% ca. 30% iii KOtBu/tBuOH iv $_2$PhLi
c n = 5 33% 47% v $SOCl_2$/Pyridine, 0°C

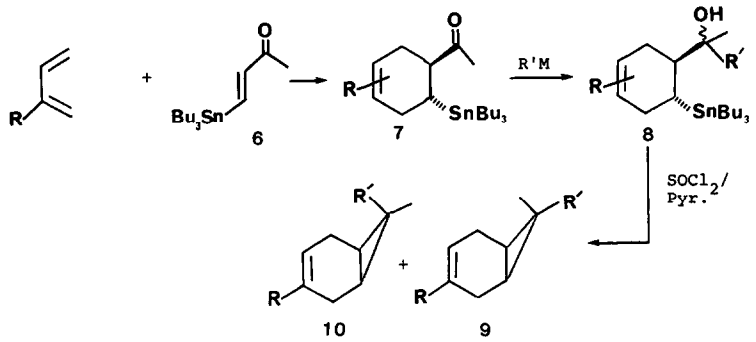
Treatment of the six-membered cis diastereomeric alcohols, prepared from 1 (n = 4), with thionyl chloride resulted exclusively in olefinic elimination products (eq 2).



(2)

Compound 6[10] has been found to be an excellent dienophile; it readily participates in Diels-Alder reactions with maintainance of trans stereochemistry of the stannyl and carbonyl moiety. The utilization of 6 in the synthesis of bicyclo[4.1.0]heptenes is illustrated in Scheme 2. Addition of methyllithium (83%) to 7 (R = Me) followed by treatment with thionyl chloride resulted in 3-carene (9, R = R' = Me) (82%). Addition

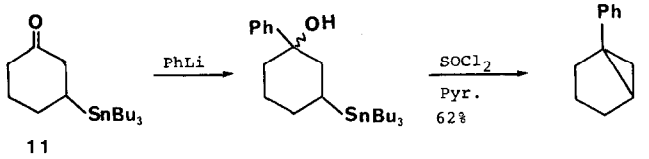
Scheme 2



of 4-methyl-3-butenylmagnesium bromide to 7 (R = Me) resulted in a mixture 8 (R = Me, R' = $CH_2CH_2CH{=}CMe_2$) which could be separated by silica gel chromatography into pairs of compounds (structural isomers as a result of the positions of the ring methyl). Treatment of pair A (obtained in 16% yield) with thionyl chloride provided isosequicarene (9, R = Me, R' = $CH_2CH_2CH{=}CMe_2$) in 66% yield. Pair B (obtained in 30% yield) gave the isomer 10 (R = Me, R' = $CH_2CH_2CH{=}CMe_2$) of isosesquicarene in 78% yield. This non-stereocontrolled three reaction sequence to l-isosesquicarene from 6 can be compared to the recent twenty-step stereocontrolled synthesis of the compound from tropone by Uyehara, Yamada, and Kato.[11] Reduction of 7 (R = Ph) with sodium borohydride gave a mixture of secondary alcohols 8 (R = Ph, R' = H) (72%) which were directly treated with thionyl chloride to provide a mixture of 9 and 10 (R = Ph, R' = H) (74%).

In saturated six-membered rings the cyclopropane fusion step most likely occurs from a conformation with the carbon bearing the leaving group and the stannyl group occupying axial positions; such conformations are highly congested. This steric congestion is considerably relieved by the introduction of a double bond in the ring. These factors may account for the much higher yields of fused cyclopropanes obtained in Scheme 2 compared to that obtained according to Scheme 1.

The synthesis of a bicyclo[3.1.0]hexane derivative is illustrated in eq 3. Compound 11 was obtained by the addition of Bu_3SnLi to 2-cyclohexenone.



11 (3)

Acknowledgement. This work was supported by grant CHE-83 06594 from the National Science Foundation with additional financial assistance by the Pharmaceuticals Division of CIBA-GEIGY Corporation.

References and Notes

1. D. D. Davis, R. L. Chambers, H. T. Johnson, *J. Organomet. Chem.*, 25, C13 (1970).

2. D. D. Davis, H. T. Johnson, *J. Am. Chem. Soc.*, 96, 7576 (1974).

3. Y. Ueno, M. Ohta, M. Okawara, *Tetrahedron Lett.*, 23, 2577 (1982).

4. Homoallylstannes are also known to give cyclopropanes upon treatment with electrophiles. D. J. Peterson, M. D. Robbins, J. R. Hansen, *J. Organomet. Chem.*, 73, 237 (1974); D. J. Peterson, M. D. Robbins, *Tetrahedron Lett.*, 18, 4045 (1977); ref. 3.

5. I. Fleming, C. J. Urch, *Tetrahedron Lett.*, 24, 4591 (1983)

6. W. C. Still, *J. Am. Chem. Soc.*, 100, 1481 (1978); 99, 4836 (1977).

7. E. Piers, H. E. Morton, *Chem. Commun.*, 1033 (1978)

8. A superior method to obtain 2b is by reduction of the Diels-Alder adduct of 6 and butadiene.

9. The stereochemical assignments of cyclopropanes 4a,b, and c are based on ^{13}C NMR compression shifts of the endo methyl. Compound 4a and its *endo*-phenyl diastereomer were prepared by independent means. The compound with the phenyl group endo exhibits characteristic diamagnetic shifts in the ^{1}H NMR due to ring currents.

10. An efficient preparation of compound 6 and a survey of its chemistry will be subjects of a future publication by the authors. In Diels-Alder reactions of 6 with unsymmetrical dienes, regio isomers are formed with one isomer predominating. The proportion of major isomer was dramatically increased in one case in the presence of a Lewis acid.

11. T. Uyehara, J.-i. Yamada, T. Kato, *Tetrahedron Lett.*, 24, 4445 (1983).

12. Satisfactory microanalysis and/or high resolution mass spectra have been obtained on all new compounds herein described.

(Received in USA 25 July 1984)