Tetrahedron Letters,Vol.26,No.33,pp 3899-3902,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain ©1985 Pergamon Press Ltd.

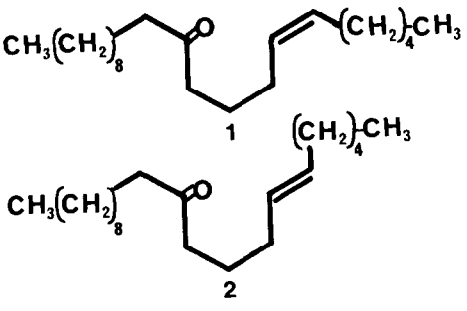
NOVEL SYNTHESES OF THE SEX PHEROMONE OF THE DOUGLAS-FIR TUSSOCK MOTH (ORGYIA PSEUDOTSUGATA) AND SOLENOPSIN A, A CONSTITUENT OF FIRE ANT VENOM.

Bradford P. Mundy* and Michael Bjorklund
Department of Chemistry, Montana State University
Bozeman, Montana 59715

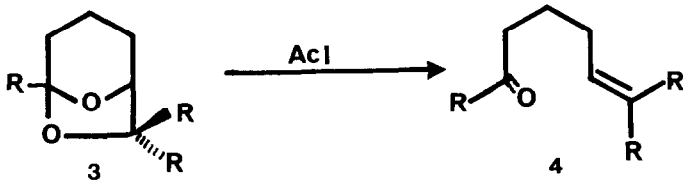
ABSTRACT: Use of a novel bicyclic ketal fragmentation protocol provides a simple entry into the sex pheromone of the tussock moth, as well as into the fire ant venom constituent, Solenopsin A.

SYNTHESIS OF THE PHEROMONE OF THE TUSSOCK MOTH

The Douglas fir tussock moth (**Orgyia pseudotsugata**) is a pernicious defoliator of the fir trees of the Northwestern United States. The active pheromone constituent has been identified as (Z)-6-heneicosen-11-one[1], (**1**); however, in field tests the (E)-isomer, (**2**), has been found to have equivalent bioactivity[1]. In a separate bioassay[2] othes have found that a 60:40 (E)/(Z) mixture of the 6-heneicosene-11-ones was considerably more active as a pheromone than pure material isolated from female tussock moths.



As part of a continuing program involved with the synthesis and utility of members of the 6,8-dioxabicyclo[3.2.1]-octane series[3], (**3**), we have recently demonstrated a novel fragmentation procedure for the synthesis of δ,ε - unsaturated ketones[4] (**Eq. 1**). We now report the application of this methodology to a synthesis of a (Z)/(E) mixture of 6-heneicosen-11-one.



(1)

The preparation of the requisite bicyclic ketal was achieved by a modification[5] of the Cohen synthesis of brevicomin[6]. The dimer of acrolein, (**5**) was treated with three equivalents of n-pentyl magnesium bromide to yield **6** (78%). Alkylation of the enol ether carbon was achieved by the method of Boeckman[5], where slightly greater than two equivalents of tert-butyllithium were added to **6**, followed by an equivalent of decyliodide. The reaction product, (**7**), was taken to a 70: 30 mixture of exo/endo **8** without purification. Fragmentation of **8** with acetyliodide, prepared in situ, gave an (E)/(Z) [78/22] mixture of 6-heneicosen-11-ones. The synthesis of the pheromone is presented in Figure 1.

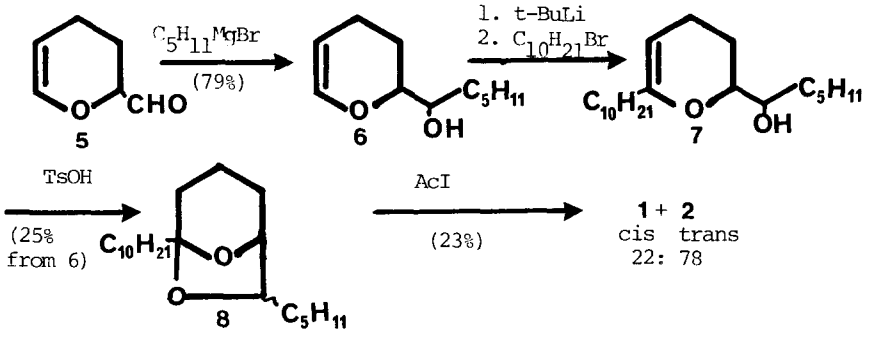
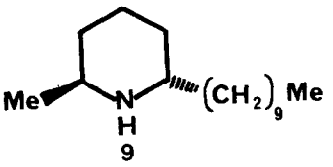


Figure 1. The Synthesis of the Tussock Moth Pheromone

SYNTHESIS OF THE VENOM CONSTITUENT OF THE FIRE ANT

The fire ant, Solenopsis saevissima, derives its name from the painful effects of the venom delivered in its bite. Of more practical interest is the known hemolytic, insecticidal and antibiotic activity of the venom.[7] There have been determined to be a number of trans-2-methyl-6-alkyl or alkyny piperidines serving as constituents of the venom; in this report we describe a synthesis of one of these- Solenopsin A, (**9**)[7].



Our approach to the synthesis is characterized by (1) a new methodology that should find application to a variety of 2,6-disubstituted piperidines, and (2) a natural selection for the

trans-substitution pattern. Retrosynthetic analysis demonstrates the salient features of our approach (**Figure 2**).

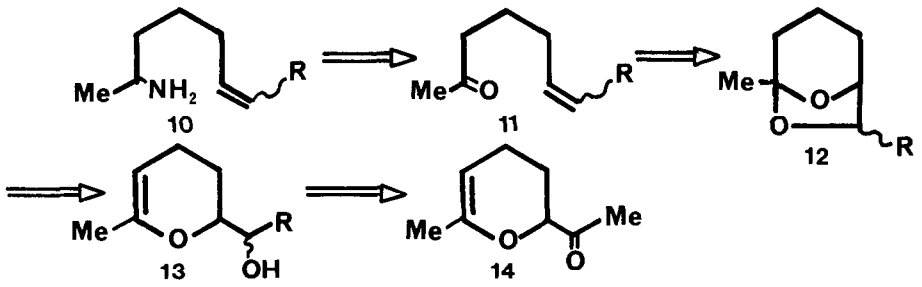


Figure 2. Retrosynthetic Analysis

The amino-mercuration reaction of **10** has been previously reported[8] as an approach to **9**; thus, a new synthesis of **10** would constitute a formal synthesis. We thus focused our attention on a new approach to **10**. As a consequence of our finding of a unique ketal fragmentation protocol[4] to accomplish conversions such as **12** → **11**, our synthesis was directed towards the preparation of **12** (**Figure 3**).

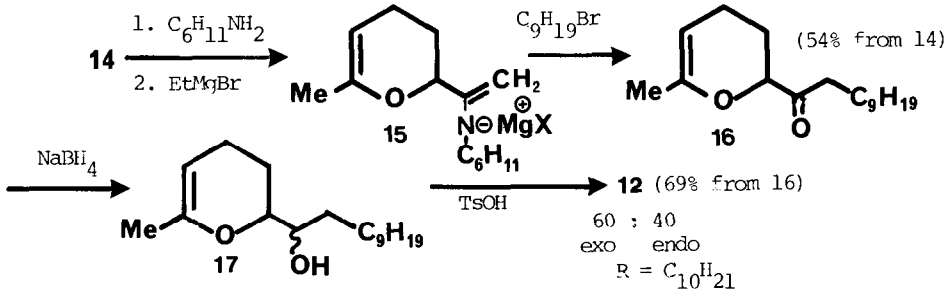


Figure 3. A Synthesis of the Bicyclic Ketal

Using the imine-alkylation procedure developed by Stork[9], and as utilized in our synthesis of a mouse pheromone[10], the dimer of methyl vinyl ketone, (**14**), was converted to **16**. Borohydride reduction of the ketone, followed by acid-catalyzed cyclization yielded an **exo/endo** mixture of **12** (60/ 40). Fragmentation of **12** gave 28% of a predominantly trans alkene. This is the only example encountered so far where the ketal ratios are not closely mirrored by the alkene ratios. We have some preliminary data that might suggest that bulky C-7 substituents may result in kinetic differences in the fragmentations; however, more work needs to be done.

The unsaturated amine, (**10**), was prepared according to the sequence provided by **Figure 4**. Treatment of **11** with two equivalents of hydroxylamine hydrochloride and sodium acetate gave **18**.

To our surprise, the expected routine reduction of **18** to **10** gave us problems. Under a variety of conditions we could not affect a clean conversion. Using the procedure of Ipaktschi[11], MoO_3 and $NaBH_4$, we were finally able to carry out the reduction in 81% yield. An additional 10% of the reaction mixture was the cyclized product, (**9**). We were able to quantitatively convert **10** to **9** by treatment with mercuric acetate followed by basic $NaBH_4$. Moriyama[8] had also demonstrated that the cyclization of an alkene mixture seemed to enrich the **trans** isomer.

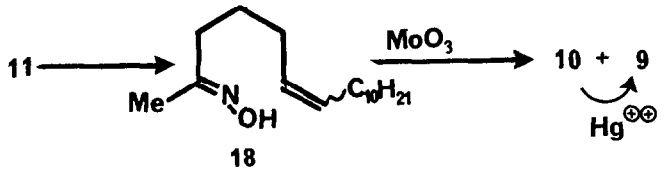


Figure 4. Preparation of the Unsaturated Amine

ACKNOWLEDGMENTS:

Support from the Montana Agricultural Station, and the EPSCOR program of NSF (ISP-801149), We acknowledge the contributions of the NSF and the Murdock Foundation towards acquisition of the instruments used in this study.

REFERENCES AND NOTES:

1. L.M. Smith, R.G. Smith, T.M. Loehr, G.D. Daves,Jr., G.E. Daterman and R.H. Wohleb, J. Org. Chem., (1978), **43**, 2361 and earlier references.

2. G.E. Daterman, L.J. Peterson, R.G. Robbins, L.L. Sower, G.D. Daves,Jr., and R.G. Smith, Environ. Entomol., (1976), **5**, 1187.

3. See, for example: Y. Kim and B.P. Mundy, J. Org. Chem., (1982), **47**, 3556.

4. Preceeding paper in this Journal.

5. R.K. Boeckman, Jr. and K.J. Bruza, Tetrahedron, (1981), **37**, 3997.

6. T. Cohen and M. Bhupathy, Tetrahedron Letters, (1983), 4163.

7. a. G.A. Adrouny, V.J. Derbes and R.C. Jung, Science, (1959), **130**, 449.

b. M.S. Blum, J.R. Walker, P.S. Callahan and A.F. Novak, Science, (1958), **128**, 306.

8. Y. Moriyama, D. Doan-Huynh, C. Monneret and Q. Khuong-Huu, Tetrahedron Letters, (1977), 825.

9. G. Stork and S.R. Dowd, J. Amer. Chem. Soc., (1963), **85**, 2178.

10. B.P. Mundy and W.G. Bornmann, J. Org. Chem., (1984),**49**, 5264

11. J. Ipaktschi, Chem. Ber., (1984), **117**, 856.

(Received in USA 20 February 1985)