

form, and no chromatographic purification was necessary. Furthermore, this reaction scheme shows a general route for the synthesis of various kinds of N-substituted Glorin.

Acknowledgement. We wish to thank Ministry of Education for a grant of financial support for this work.

References and Notes

1. E. Schiffmann, B.A. Corcoran, and S.M. Wahl, *Proc. Natl. Acad. Sci. USA*, **72**, 1059 (1975).
2. O. Shimomura, H.L.B. Suthers, and J.T. Bonner, *ibid.*, **79**, 7376 (1982).
3. O. Shimomura, H.L.B. Suthers, and J.T. Bonner, *FEBS Letters*, **155**, 155 (1983).
4. N-Propionyl-L-glutamic acid- α -ethyl- γ -benzyl ester was prepared from L-glutamic acid. Treatment of the diester with HF give N-propionyl-L-glutamic acid α -ethyl ester, which was coupled with **5** yielding **1**. The final

product was purified by column chromatography on Sephadex LH-20 using acetonitrile/water, 9:1 (vol/vol) as the eluent.

5. M. Bergmann and L. Zervas, *Ber.*, **65**, 1192 (1932).
6. E. Klieger, E. Schroder, H. Gibian, *Liebigs Ann. Chem.*, **640**, 157 (1961).
7. K. Golankiewicz, M. Wiewioroski, *Acta. Biochim. Pol.*, **10**, 433 (1964).
8. K. Golankiewicz, M. Dezor, M. Wiewiorowski, *ibid.*, **13**, 1 (1966).
9. G.W. Anderson, J.E. Zimmerman, F.W. Collahan, *J. Am. Chem. Soc.*, **89**, 5012 (1967).
10. The compound, **6** was purified by crystallization in EtOAc. MP 124–126°C; TLC, Rf 0.21, silica gel (CHCl₃, 95% EtOH = 15:1); $[\alpha]_D^{25} = +52.6$ (c = 0.5, CHCl₃); Anal. calcd. for C₂₀H₂₆N₃O₆: C 59.40, H 6.48, N 10.39; found: C 59.38, H 6.63, N 10.03.

A Biogenetic-Type Synthesis of Rose Furan

Eun Lee*, Yong Pyo Hong, Junghun Suh, and Sae-Hee Chang

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151. Received October 20, 1986

Rose furan(**1**) was isolated from Bulgarian rose oil in 1968 and the structure was assigned and confirmed by synthesis by G. Büchi and coworkers¹. Since then it has been isolated from other natural sources².

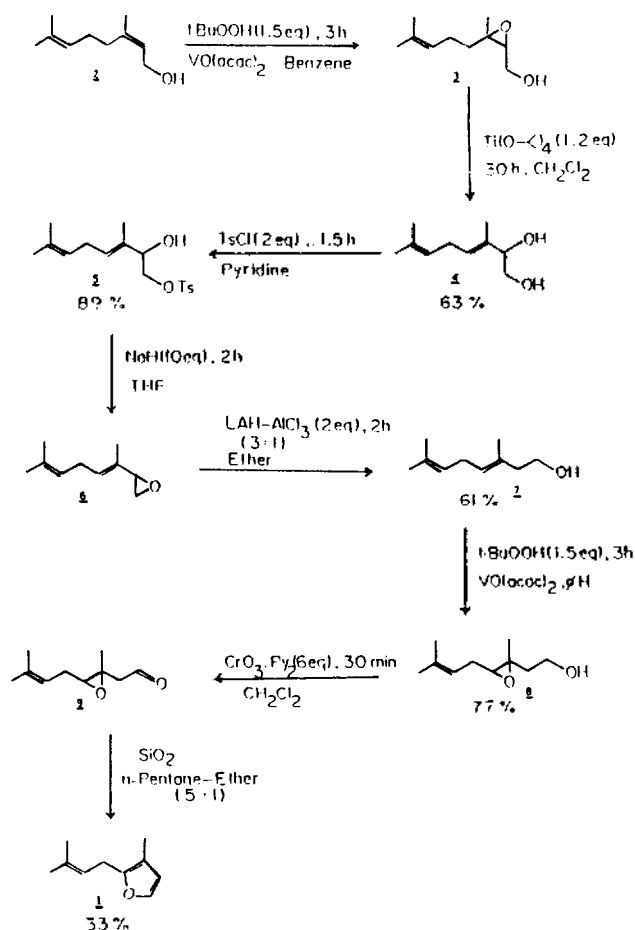
Following the first synthesis by Büchi¹, many successful schemes were published. In a number of syntheses³⁻⁸, pre-formed furan precursors were used and different strategies for introduction of the prenyl group were investigated. Other synthetic routes involve primarily oxidative furan ring formation of acyclic intermediates⁹⁻¹¹.

In this report, we wish to describe a new biogenetic-type synthesis of rose furan(**1**) from nerol(**2**), one of its probable biogenetic progenitors.

2,3-Epoxynerol(**3**) was prepared by epoxidation of nerol(**2**) with t-butyl hydroperoxide in benzene in the presence of vanadyl acetylacetonate as reported by Sharpless and coworkers¹². The reaction was complete in 3 hours at room temperature and the product **3** was isolated in almost quantitative yield.

The reaction of 2,3-epoxynerol(**3**) with titanium isopropoxide in dichloromethane at room temperature for 30 hours yielded the enediol **4** in 63% overall yield from nerol(**2**).¹³ In the nmr spectrum, a new vinylic proton (H-4) signal appeared at δ 5.36 as a broad triplet and C-5 bisallylic methylene protons gave rise to another broad triplet at δ 2.67.

Partial esterification of **4** with p-toluenesulfonyl chloride in pyridine produced the monotosylate **5** in 89% yield which was cleanly cyclized to yield the epoxide **6** upon treatment with excess sodium hydride in THF for 2 hours. Reaction with methanolic sodium bicarbonate for 36 hours resulted in the formation of several byproducts. In the nmr spectrum of **6**, the characteristic triplet at δ 3.35 was assigned to H-2.



Surprisingly, diisobutylaluminum hydride reduction of **6** in THF¹⁴ was unsuccessful in sharp contrast to the similar reaction results in the dendrolasin synthesis¹⁵. Instead, an alternative procedure employing aluminum chloride-lithium aluminum hydride (1:3)¹⁶ worked quite well producing the desired homoallylic alcohol **7** in 61% yield from **5**. The active reducing agent appears to be aluminum hydride (AlH₃) produced in situ. Two methylene triplets appeared in the nmr spectrum at δ 3.52 and 2.18 confirming the structural assignment.

The standard Sharpless epoxidation of the homoallylic alcohol **7** gave rise to the epoxyalcohol **8** in 77% yield. One of the vinylic proton signals disappeared in the nmr spectrum and a new triplet at δ 2.92 was assigned to the H-4 signal.

Oxidation of the epoxyalcohol **8** was accomplished by a careful reaction with chromium trioxide-pyridine complex in dichloromethane¹⁷ for 30 minutes yielding relatively clean epoxyaldehyde **9**. The unstable epoxyaldehyde **9** was converted to rose furan(**1**) by passing through a silica gel column with pentane-ether (5:1) as the eluting solvent. The overall yield from **8** was 33%. The nmr spectrum displayed typical furan peaks at δ 7.19 and 6.13.

The facile conversion of the epoxyaldehyde **9** to the furan **1** under mild conditions suggests a possible biogenetic routes for **1**.

Acknowledgements. This research was supported by a grant (1983) of the Ministry of Education.

References

1. G. Büchi, E. sz. Kovats, P. Enggist, G. Uhde, *J. Org. Chem.* **33**, 1227 (1968).
2. (a) R. Kaiser, D. Lamparsky, *Helv. Chim. Acta.* **59**, 1797 (1976); (b) G.S.R. Subba Rao, K. Srinvasa Rao, B. Ravindranath, *Tetrahedron Lett.* 1019 (1976).
3. A. Takeda, K. Shinhama, S. Tsuboi, *Bull. Chem. Soc. Japan.* **50**, 1903 (1977).
4. N. Dinh Ly, M. Schlosser, *Helv. Chim. Acta.* **60**, 2085 (1977).
5. A.J. Birch, J. Slobbe, *Tetrahedron Lett.* 2079 (1976).
6. D.R. Gedge, G. Pattenden, *Tetrahedron Lett.* 4443 (1977).
7. O.P. Vig, A.K. Vig, V.K. Handa, S.D. Sharma, *J. Ind. Chem. Soc.*, **51**, 900 (1974).
8. R.C. Cookson, K.H. Schulte-Elte, A. Hauser, *Ger. Offen.* 2,827,383 (Jan. 11, 1979).
9. K.H. Schulte-Elte, Swiss Pat. 603,614 (Oct. 6, 1975).
10. I.M. Zaks, A.M. Moiseenkov, *Izv. Akad. Nauk SSSR. Khim.* **11**, 2614 (1982).
11. M. Tada, K. Chiba, T. Hashizume, *Agric. Biol. Chem.* **46(3)**, 819 (1982).
12. (a) R.C. Michaelson, K.B. Sharpless, *J. Amr. Chem. Soc.* **95**, 6136 (1973); (b) S. Tanaka, H. Yamamoto, H. Nozaki, J.D. Cutting, R.C. Michaelson, K.B. Sharpless, *J. Amr. Chem. Soc.* **96**, 5254 (1974).
13. D.J. Morgans, K.B. Sharpless, and S.G. Traynor, *J. Amr. Chem. Soc.* **103**, 462 (1981).
14. R.A. Lenox, J.A. Katzenellenbogen, *J. Amr. Chem. Soc.* **95**, 957 (1973).
15. E. Lee, Y.H. Paik, S.K. Park, *Tetrahedron Lett.* **23**, 2671 (1982).
16. (a) E.L. Eliel, D.W. Delmote, *J. Amr. Chem. Soc.* **78**, 3226 (1956). (b) M.N. Rerick, E.L. Eliel, *J. Amr. Chem. Soc.* **84**, 2356 (1962).
17. R. Ratcliffe, R. Rodehorst, *J. Org. Chem.* **35**, 4000 (1970).

Chiral Guaiazulenes from Limonene*

Eun Lee and Jong In Hong

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151. Received October 20, 1986

Limonene is one of the cheapest chiral starting material in the natural product synthesis. Both (R)-(+)- and (S)-(-)-limonene are readily available and one synthetic sequence can be applied to the synthesis of both optical isomers of a target molecule. This report concerns with a synthesis of a chiral guaiazulenic intermediate from (R)-(+)-limonene, in which the original chiral center is preserved at the hydroazulene ring junction.

(R)-(+)-Limonene is known to produce chiral 1-formyl-5-isopropenyl-2-methyl-1-cyclopentene when it is subjected to selective epoxidation, hydrolysis to the diol, cleavage by periodate, and intramolecular condensation with piperidine and acetic acid¹. If the ketone **6** is used as the starting material in the same sequence of reactions, one would obtain the

ketoaldehyde **10**, which should serve as an ideal substrate for aldol condensation to form hydroazulene derivatives.

The ene reaction of (R)-(+)-limonene with methyl vinyl ketone in the presence of aluminum chloride at room temperature was reported to afford the ketone **6**², but we could not obtain the product of useful purity under the conditions reported. Various other Lewis acid catalysts were tested and zinc bromide³ was found to provide a small yield (<10%) of the ketone **6** in acceptable purity. Since other direct routes employing metalated (R)-(+)-limonene⁴ did not turn out to be practical, a conventional reaction sequence from (+)-limonen-10-ol(**1**)⁵ was devised.

Thus (+)-limonen-10-ol(**1**) was subjected to orthoester Claisen rearrangement to provide the ethyl ester **2**, which was reduced to the alcohol **3**. The corresponding tosylate **4** was converted to the homologous nitrile **5**, which afforded the ketone **6** upon treatment with methylolithium. (Scheme 1) The overall yield of **6** was 55% from **1**.

* Dedicated to Professor Sae-Hee Chang on the occasion of his both birthday.