form, and no chromatographic purification was necessary. Furthermore, this reaction scheme showes 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 coulumn 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 ($CHCl_3$, 95% EtOH = 15:1); $[\alpha]_D^{18} = +52.6$ (c = 0.5, $CHCl_3$); Anal. calcd. for $C_{20}H_{26}N_3O_6$: C 59.40, H6.48, N10.39; 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 coworkers[1]. Since then it has been isolated from other natural sources[2].

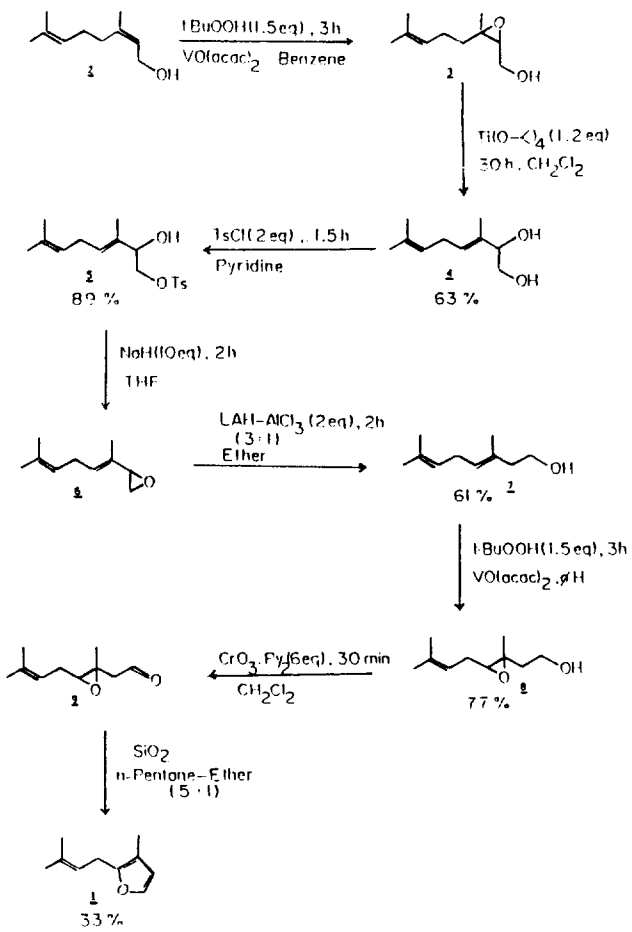
Following the first synthesis by Büchi[1], many successful schemes were published. In a number of syntheses[3-8], preformed furan precursors were used and different strategies for intorduction of the prenyl group were investigated. Other synthetic routes involve primarily oxidative furan ring formation of acyclic intermediates[9-11].

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 coworkers[12]. 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 THF[14] was unsuccessful in sharp contrast to the similar reaction results in the dendrolasin synthesis[15]. 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 (AlH_3) 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 dichloromethane[17] 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 acid[1]. 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 bromide[3] was found to provide a small yield(<10%) of the ketone **6** in acceptable purity. Since other direct routes employing metalated (R)-(+)-limonene[4] did not turn out to be practical, a conventional reaction sequence from (+)-limonen-10-ol(**1**)[4] 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 methyllithium. (Scheme 1) The overall yield of **6** was 55% from **1**.

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