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SYNTHESIS OF (±)-ANASTREPHIN AND (±)-EPIANASTREPHIN

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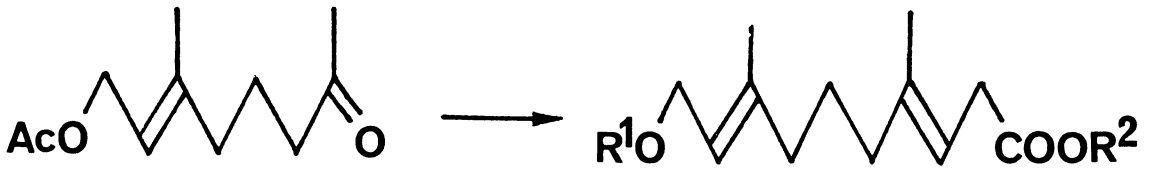
(±)-Anastrephin and (±)-epianastrephin, sex and aggregation pheromenes of Caribbean and Mexican fruit flies, were synthesized by acid-catalyzed cyclization of 10-hydroxy-4,8-dimethyldeca-(3E,8E)-3,8-dienoic acid in 67% yield as a 1:1 mixture.

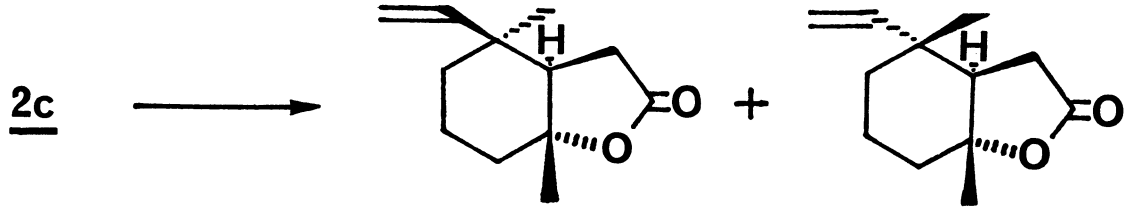
Anastrephin 3 and epianastrephin 4 have recently been isolated as sex and aggregation pheromones of Caribbean and Mexican fruit flies, Anastrepha suspensa (Loew) and Anastrepha ludens (Loew).[1] The syntheses of these compounds reported by Battiste and co-workers were based on the cyclization of the corresponding trans-γ-hydroxy acids.[2] We have already reported that concerted cyclization of polyene carboxylic acid is one of the most convenient methods for the synthesis of trans-γ-lactone fused to cyclohexane ring.[3] Here we report a facile synthesis of 3 and 4 by the cyclization of 10-hydroxy-4,8-dimethyldeca-(3E,8E)-3,8-dienoic acid 2c.

8-Acetoxy-6-methyl-(E)-6-octene-2-one 1 was quantitatively obtained by acetylation of the corresponding hydroxy ketone[4] (Ac_2O/py, rt, 5 h). Wittig reaction of 1 and 2-carboxyethyltriphenylphosphonium chloride afforded a ca. 6:4



1

2a : R^1=Ac, R^2= H ,
2b : R^1=Ac, R^2=Me,
2c : R^1= H , R^2= H ,



3 4

mixture of 10-acetoxy-4,8-dimethyldeca-(3E,8E)-3,8-dienoic acid 2a and its (3Z)-isomer in 65% yield (2NaH/1:1 DMSO-THF, 30 °C, 10 h).[5] The mixture was esterified by diazomethane, and 2b and the geometrical isomer were separated by repeated silica gel column chromatography (hexane:AcOEt=9:1).[6] Acetoxy ester 2b was hydrolyzed to 2c without conversion of the olefin geometry (10% KOH/MeOH, rt, 2 h).

Cyclization was carried out by dropwise addition of boron trifluoride etherate (3 equiv.) to 1% dichloromethane solution of 2c at 10 °C followed by stirring at this temperature for 10 min. The usual work-up of the reaction mixture afforded a 1:1 mixture of 3 and 4 in 67% yield. The lactones, 3 and 4, were easily separated by silica gel column chromatography (hexane:AcOEt=9:1), and all the spectral data of 3 and 4 were identical with the authentic data of anastrephin and epianastrephin respectively.[1]

In this work the concerted lactonization was again revealed to be an effective and versatile method for the synthesis of trans-fused γ-lactone. Furthermore, since some species of insect have been known to secrete several compounds which have the same 3,7-dimethyldecane skeleton as 2c,[7] it seems probable that also in vivo, 3 and 4 would be formed from 2c by a cyclization reaction similar to that mentioned above.

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References

1) M. A. Battiste, L. Strekowski, D. P. Vanderbilt, M. Visnick, and R. W. King, Tetrahedron Lett., 24, 2611 (1983); J. B. Stokes, E. C. Uebel, J. D. Warthen, Jr., M. Jacobson, J. L. Flippen-Anderson, R. Gilardi, L. M. Spishakoff, and K. R. Wilzer, J. Agric. Food Chem., 31, 1162 (1983).

2) L. Strekowski and M. A. Battiste, Tetrahedron Lett., 22, 279 (1981); L. Strekowski, M. Visnick, and M. A. Battiste, Synthesis, 1983, 493.

3) A. Saito, H. Matsushita, Y. Tsujino, T. Kisaki, K. Kato, and M. Noguchi, Chem. Lett., 1978, 1065; A. Saito, H. Matsushita, Y. Tsujino, and H. Kaneko, ibid., 1981, 757; A. Saito, H. Matsushita, and H. Kaneko, ibid., 1983, 729.

4) Y. Fujita, T. Ohnishi, and T. Nishida, J. Chem. Soc., Chem. Commun., 1978, 972.

5) H. S. Corey, Jr., J. R. D. McCormick, and W. E. Swensen, J. Am. Chem. Soc., 86, 1884 (1964).

6) The spectral data of 2b are as follows; IR(neat) ν=1740, 1670 cm^{-1}; MS m/e 208 (M^+-CH_3COOH); ^1H NMR($CDCl_3$) δ=1.45-2.16(6H,m), 1.63(3H,s), 1.70(3H,s), 2.06(3H, s), 3.06(2H,d,6Hz), 3.69(3H,s), 4.59(2H,d,7Hz), 5.34(2H,broad); ^{13}C NMR($CDCl_3$) δ=16.3, 16.4, 21.1, 25.6, 33.5, 39.0(two carbons), 51.7, 61.4, 116.0, 118.5, 138.9, 142.2, 171.1, 172.8.

7) H. H. Shorey and J. J. McKelvey, Jr., "Chemical Control of Insect Behavior," Wiley-Interscience, New York(1977), p. 262; J. W. Wong, V. Verigin, A. C. Oehlschlager, J. H. Borden, H. D. Pierce, Jr., A. M. Pierce, and L. Chong, J. Chem. Ecol., 9, 451 (1983).

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