Tetrahedron Letters,Vol.27,No.22,pp 2519-2522,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

TOTAL SYNTHESIS OF (+)-ELDANOLIDE FROM *D*-RIBONOLACTONE

R. M. Ortuño, R. Mercé and J. Font*

Departament de Química (Divisió de Química Orgànica), Facultat de Ciències
Universitat Autònoma de Barcelona, Bellaterra (Barcelona), Spain.

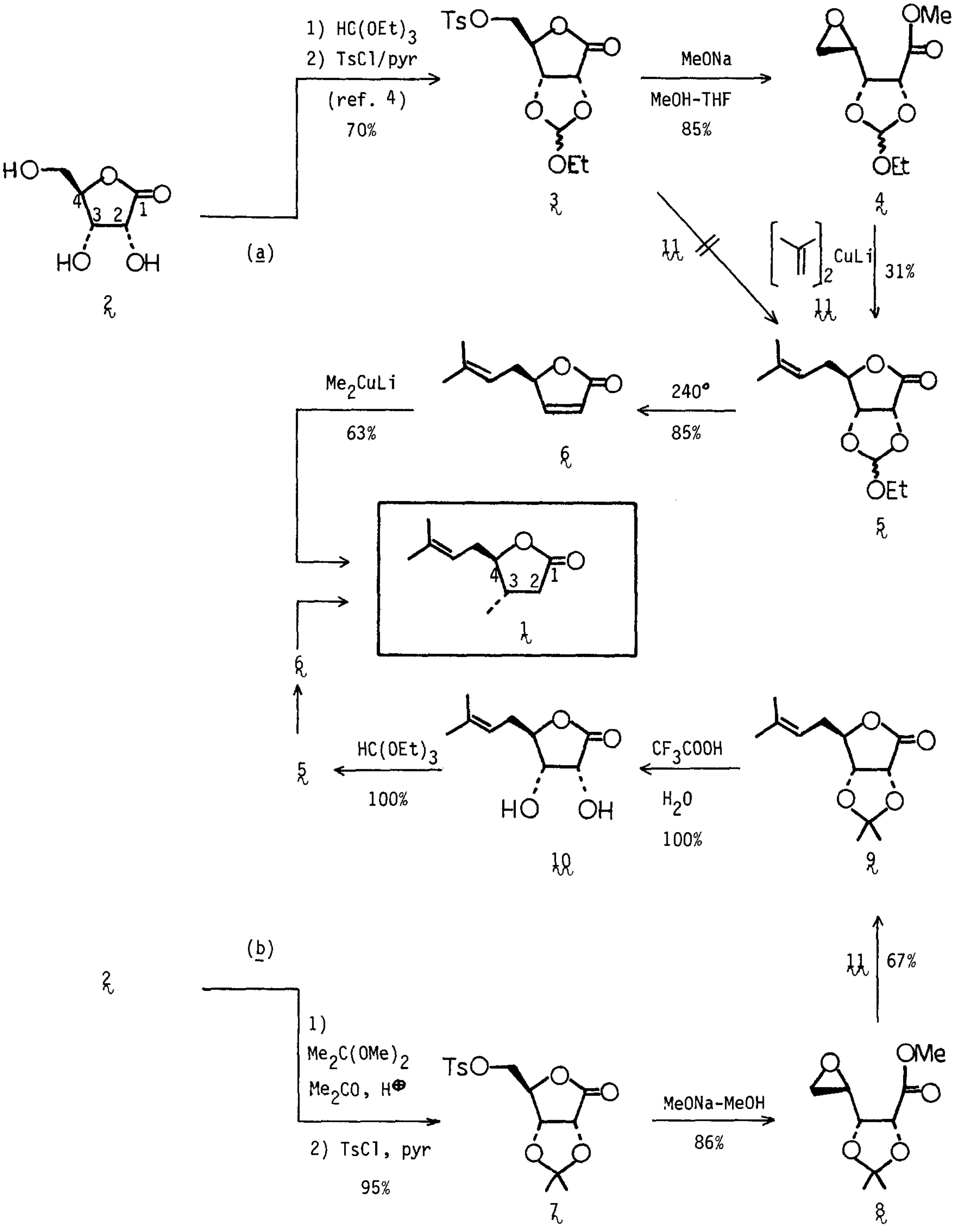
Abstract.- A new and useful synthesis of (+)-Eldanolide is reported, *D*-ribonolactone being used as a chiral starting product.

(3*S*,4*R*)-(+)-Eldanolide, **1**, is a sex attractant pheromone, isolated from the male wing glands of the African sugar cane borer *Eldana Saccharina* (Wlk)[1]. The structure and absolute configuration assignment and a total synthesis of this natural product have been reported by Vigneron and Larchevêque *et al*.[2] Other syntheses of Eldanolide in enantiomerically pure and racemic forms have also been published by other authors, as a consequence of a general interest on this target molecule[3].

We describe herein a new and convenient synthetic pathway to (+)-Eldanolide, **1**, using D-ribonolactone, **2**, as a chiral starting product.

D-Ribonolactone, **2**, has been proved to be a useful precursor in the preparation of many interesting chiral compounds, such as ranunculin[4], some pheromones[5], litsenolides[6] and (-)-blastmycinone[7]. In our synthetic strategy chirality at C-4 of **2** is transferred to C-4 of the target **1**, through the sequences (*a* and *b*) depicted in the Scheme. In these convergent routes, the butenolide **6** is a common key precursor, that leads to **1** by a stereospecific Michael addition of Me_2CuLi. Indeed, conjugate additions of nucleophiles to γ-substituted α,β-butenolides are reported to occur in a higly stereocontrolled manner, giving *trans*-3,4-disubstituted butyrolactones[8]. In this sense, chirality at C-4 of **2** is also responsible for the asymmetry induced at C-3 when a Michael addition is performed on butenolide **6**.

Preparation of **1** according to sequence *a* involves conversion of *D*-ribonolactone, **2**, into the known tosylate orthoester **3**[4], that yielded by treatment with MeONa at 0° the new epoxide **4**, b.p. 89°/0.5 torr[9]. Compound **4** is the intermediate to obtain the butenolide **6**, since opening of the oxirane ring by nucleophilic attack of a cuprate and subsequent lactonization could lead to


2
(a)
1) HC(OEt)$_3$
2) TsCl/pyr
(ref. 4)
70%
3
MeONa
MeOH-THF
85%
4
11
[isobutenyl]$_2$CuLi
31%
5
240°
85%
6
Me$_2$CuLi
63%
1
6
5
HC(OEt)$_3$
100%
10
CF$_3$COOH
H$_2$O
100%
9
11
67%
(b)
2
1) Me$_2$C(OMe)$_2$
Me$_2$CO, H$^⊕$
2) TsCl, pyr
95%
7
MeONa-MeOH
86%
8
TsO
OMe
OEt
HO
OH

Scheme

the isopentenyl side-chain formation, while pyrolysis of the orthoester would allow the creation of the conjugate C-C double bond of **6**. Thus, reaction of epoxide **4** with lithium diisobutenyl cuprate[10], **11**, afforded **5**, b.p.120°/1torr, that, by heating at 240°, gave (*R*)-(-)-7-methyl-2,6-octadiene-4-olide[2], **6**, $\{\alpha\}_D^{20}$ = -132.8° (c=1.56, MeOH), in 85 % yield. Finally, addition of Me_2CuLi led to (+)-Eldanolide, **1**, as a liquid, b.p. 120°/12 torr, $\{\alpha\}_D^{20}$ = +50.7° (c=2.8, MeOH), in 63 % yield. (Lit.[2] $\{\alpha\}_D^{20}$ = +51.5° (c=1.15, MeOH).

Yields of the transformations performed in this synthetic sequence are quite good, except in step **4** → **5**. We have already verified in our laboratory that reactions of tosylate **3** with lithium dialkylcuprates give only poor yields, probably due to steric hindrance effects, and this is the reason we carried out the reaction on epoxide **4** instead of on tosylate **3**. Moreover, we have reported in an earlier publication[5] that the orthoester function is not compatible with the reaction conditions involved in this kind of transformation, and leads to the formation of undesired by-products and polymeric material resulting in low yields.

With these points in mind, we designed the alternative sequence *b*. *D*-Ribonolactone, 2, was converted into the tosylate acetonide **7**[11], that led to epoxide **8**, $\{\alpha\}_D^{20}$ = -14.5° (c=2.4, CH_2Cl_2) in 86 % yield. Reaction of **8** with lithium diisobutenyl cuprate, **11**, afforded **9**, $\{\alpha\}_D^{20}$= -34.1° (c=1.7, CH_2Cl_2), in 67 % yield; **9** was quantitatively hydrolyzed[12] to the diol **10**, m.p. 103-104°, $\{\alpha\}_D^{20}$ = +33.5° (c=1.0), MeOH), and orthoesterification of **10** led to **5**, converging with the former route. The longer synthetic route *b* is more convenient because of the improved yield in the epoxide opening step (**8** *vs* **4**) with cuprate **11**. On the other hand, both additional transformations -acetonide formation and hydrolysis- were achieved almost quantitatively. The overall yield in (+)-Eldanolide, **1**, obtained through sequence *b* is 30 % from *D*-ribonolactone, being the best yield reported till now, starting from a commercially available compound.

Studies on syntheses of other interesting products, using *D*-ribonolactone derivatives as chiral precursors, are in progress[13].

Acknowledgements.- Financial support from "Comisión Asesora de Investigación Científica y Técnica" (project 2013/83 is gratefully acknowledged.

Notes and References

1. G. Kunesch, P. Zagatti, J. Y. Lallemand, A. Debal and J. P. Vigneron, *Tetrahehedron Lett.* **22**, 5271 (1981).
2. J. P. Vigneron, R. Méric, M. Larchevêque, A. Debal, G. Kunesch, P. Zagatti and M. Gallois, *Tetrahedron Lett.* **23**, 5051 (1982); J. P. Vigneron, R. Méric, M. Larchevêque, A. Debal, J. Y. Lallemand, G. Kunesch, P. Zagatti and M. Gallois, *Tetrahedron*, **40**, 3521 (1984).
3. (a) Y. Yokoyama and M. Yunokihara, *Chem. Lett.* **1983**, 1245; (b) T. K. Chakraborty and S. Chandrasekaran, Tetrahedron Lett. **25**, 2891 (1984); (c) H. G. Davies, S. M. Roberts, B. J. Wakefield and J. A. Winders, *J. Chem. Soc., Chem. Commun.* **1985**, 1166; (d) K. Suzuki, T. Ohkuma and G. Tsuchihashi, *Tetrahedron Lett.* **26**, 861 (1985).
4. P. Camps, J. Cardellach, J. Font, R. M. Ortuño and O. Ponsatí, *Tetrahedron*, **38**, 2395, (1982).
5. J. Cardellach, J. Font and R. M. Ortuño, *J. Heterocycl. Chem.* **21**, 327 (1984).
6. S. Chen and M. Joullié, *J. Org. Chem.* **49**, 2168 (1984).
7. J. Cardellach, J. Font and R. M. Ortuño, *Tetrahedron Lett.* **26**, 2815 (1985).
8. J. P. Vigneron, R. Méric and M. Dhaenens, *Tetrahedron Lett.* **1980**, 2057.
9. Compounds **3**, **4** and **5** were obtained as a diastereoisomeric mixture of orthoesters and were not separated. Therefore, optical rotation values are not given. All new products, **4**, **5**, **8**, **9** and **10**, gave correct elemental analysis and spectroscopical behaviour as expected.
10. M. Nilsson and R. Wahren, *Journal of Organometal. Chem.* **1969**, 515.
11. L. Hough, J. K. N. Jones and D. L. Mitchell, *Can. J. Chem.* **36**, 1720 (1958).
12. C. Papageorgiu and C. Benezra, *Tetrahedron Lett.* **25**, 6041 (1984).
13. Part of this work was presented at the 4th European Symposium on Organic Chemistry, ESOC IV, held in Aix-en-Provence, France, on September 1985.

(Received in UK 11 April 1986)