Pergamon

PII: S0040-4039(96)00697-1

Tetrahedron Letters, Vol. 37, No. 21, pp. 3695-3696, 1996
Copyright © 1996 Published by Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

Synthesis of Nor-Norambracetal

Frédéric Chauvet, Ivan Coste-Manière, Paul Martres, Patricia Perfetti, Bernard Waegell* and Jean-Pierre Zahra*.

Laboratoire de Stéréochimie associé au CNRS LASCO, Faculté des Sciences de
Saint-Jérôme, case 532, 13397 Marseille Cédex 20, France.

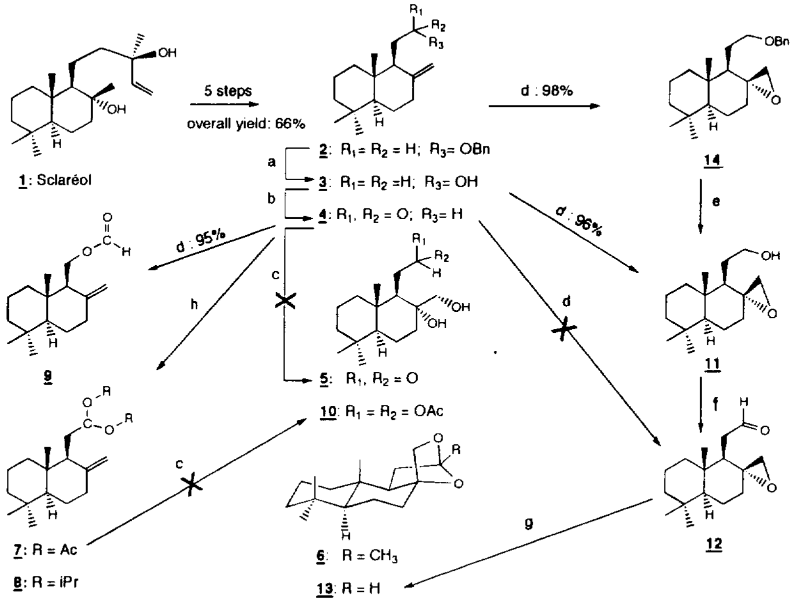
Key Words : Nor-norambracetal, Ambergris fragrances, Sclareol.

Abstract : *We describe the synthesis of nor-norambracetal* **13** *from sclareol* **1**, *using γ-homobicyclo-farnesylic alcohol* **3** *as a key intermediate.*

Fragrance properties are most probably related with the environment of polar groups which play an important role in the fixation process on the receptor[1]. As fragrance tests on nor ambracetal **6**[2], had shown that this derivative had a strong but fugacious ambergris fragrance, it was of interest to have an access to nor-norambracetal **13**, the synthesis of which is reported in the present paper. We had initially thought that we could have an easy access to this target molecule by catalytic osmylation[3] of γ-homofarnesylic aldehyde **4**[4], which we had previously used as key intermediate in the synthesis of norambracetal **6**. Unfortunately this reaction yields degradation products instead of the expected glycol **5** which could have been cyclised into the corresponding bicyclic acetal **13**. Neither was successfull the osmylation of **7** where the aldehyde carbonyl had been protected as an hydrate diacetate, or acylal which can be formed without isomerisation of the double bond[5]. Epoxidation of the double bond of aldehyde **4** did not yield the expected epoxide **12** which could have been cyclised into nor-norambracetal **13**[6], but rather formiate **9** resulting from a Bayer Villiger reaction[7]. Epoxidation with *m* CPBA of the isopropyl acetal **8**[8], obtained from **4**, did not succeed either.

The successfull synthetic pathway used as starting material γ-homofarnesylic alcohol **3** obtained by deprotection of benzilic ether **2** by sodium in ammonia[9]. This alcohol was transformed into epoxyalcohol **11** by *m* CPBA at -78°C[10]. A similar epoxidation[11] could be achieved on protected alcohol **2** to yield **14** which was hydrogenolyzed into **11**. Acid hydrolysis with PPTS in methylene chloride[12] of the epoxy aldehyde **12** obtained from the later product by PDC oxidation[13], gave nor-norambracetal **13**[14]. The overall yield of this synthesis (9 steps from sclareol) ranges around 33,2%. Fragrance tests are under progress.

Acknowledgments : We thank the Givaudan-Roure Company (Grasse), MRT and Région PACA for financial support.



a) Na NH$_3$, Et$_2$O, - 45°C, 30mn, rdt = 93%; b) PCC, 25°C, CH$_2$Cl$_2$, 75mn, rdt=90% ; c) OsO$_4$ cat[(CH$_3$)$_3$NO, 2 H$_2$O] , tBuOH, H$_2$O, pyr reflux, 6hrs ; d) m CPBA, NaHCO$_3$, CH$_2$Cl$_2$ -78°C, overnight ; e) Pd/C 10%, H$_2$, THF, RT, 1hr, rdt=98%; f) 1,5 PDC, molecular sieves 4A, AcOH,CH$_2$Cl$_2$, 30 mn,rdt=72%;g) PPTS,CH$_2$Cl$_2$,Δ, 2hrs, rdt=92%;h) iPrOH, PPTS, molecular sieves 4A,RT, 3hrs give **8**, rdt=63%, for **7** ref. 5a, rdt 80%.

REFERENCES

1 - a) Ohloff, G. ; Winter, B. ; Fehr, C. p.289-291 in "*Perfumes : Art, Sciences and Technology*" Müller, P.M. ; Camparsky D. Elsevier Sc. Publ. London **1991**. b) Winter, B. *Pure and Appl.Chem.*, **1990**, *62*, 1377-1380 and references mentioned therein.

2 - Martres, P. ; Perfetti, P. ; Zahra, J.P. ; Waegell, B. *Tetrahedron Lett.*, **1993**, *34*, 3127-3128.

3 - Ray, R. ; Matteson, D.S. ; *Tetrahedron Lett.*, **1980**, *21*, 449-450.

4 - Ohloff, G. ; Giersdr, W. *Croatica Chem.Acta* , **1985**, *58*, 491-509.

5 - a) Kochhar, K.S. ; Bal, B.S. ; Desphande, R.P. ; Rajadhyaksha, S.N. ; Pinnick, H.W. *J.Org.Chem.*, **1983**,*48*, 1765-1767. b) All classical protection techniques of the aldehyde carbonyl as a dioxolanne failed in the sense that they were at the origin of the double bond isomerisation : i) ethylene glycol, benzene, TsOH ; ii) percolation on amberlyst 15 and molecular sieves in THF ; iii) TsOH, benzene.

6 - Hanzlik, R.P. ; Leittwetter, M. *J.Org.chem.*, **1978**, *43*, 438-440.

7 - Other epoxidation procedures known to avoid the Bayer Villiger reaction turned out to be unsuccessfull, or to give low yields (<4%) of epoxide ; i) Payne that is C_6H_5 CN/H_2O_2 ; Payne, G.B. *Tetrahedron Lett.* **1962**, *18*, 763-765 ; ii) Ethylchloroformiate/H_2O_2 ; Bach, R.D. ; Klein, M.W. ; Ryntz, R.A. ; Holubka, W. *J.Org.Chem.* **1979**, *44*, 2569-2571 ; iii) Hexacarbonyl molybdum/tBuOOH ; Rouchaud, J. *J.Ind.Chim.Belg.* **1972**, *37*, 741-755.

8 - Loewenthal, H.J.E. in "*Protective Groups in Organic Chemistry*", McOmie, J.F.W., Ed., Plenum Press, London and New York, **1973**, 327-328.

9 - Reist, E.J. ; Bartuska, V.J. ; Goodman, L. *J.Org.Chem.*, **1964**, *29*, 3725-3726.

10 - Mori, K. ; Tamura, H. *Liebigs Ann.Chem.* **1990**, 361-368.

11 - Corey, E.J. ; Venkateswarlu A. *J.Amer.Chem.Soc.*, **1972**, *94*, 6190-6191.

12 - Costa, M do Ceu ; Tavares, R. ; Motherwell, W.B. ; Curto, M.J.M. *Tetrahedron Lett.*, **1994**, *47*, 8839-8842.

13 - Czernecki, S. ; Georgoulis, C. ; Stevens, C.L. ; Vijayakumaran, K. *Tetrahedron Lett.*, **1985**, *26*,1699-1702.

14 - All compounds reported here have been caracterized by IR, ^{1}H, ^{13}C NMR spectroscopy, and centesimal analysis or Mass Spectroscopy.

(*Received in France* 8 *March* 1996; *accepted* 9 *April* 1996)