

PII: S0040-4039(96)00697-1

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. Copyright © 1996 Published by Elsevier Science Ltd

Fragrance properties are most probably related with the environment of polar groups which play an important role in the fixation process on the receptor¹. 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 osmylation³ 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 bond⁵. 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 reaction⁷. 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 ammonia⁹. This alcohol was transformed into epoxyalcohol 11 by *m* CPBA at -78°C¹⁰. A similar epoxidation¹¹ could be achieved on protected alcohol 2 to yield 14 which was hydrogenolyzed into 11. Acid hydrolysis with PPTS in methylene chloride¹² of the epoxy aldehyde 12 obtained from the later product by PDC oxidation¹³, gave nor-norambracetal 13¹⁴. 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 NH₃, Et₂O, - 45°C, 30mn, rdt = 93%; b) PCC, 25°C, CH₂Cl₂, 75mn, rdt=90%; c) OsO₄ cat[(CH₃)₃NO, 2 H₂O], tBuOH, H₂O, pyr reflux, 6hrs; d) m CPBA, NaHCO₃, CH₂Cl₂ -78°C, overnight; e) Pd/C 10%, H₂, THF, RT, 1hr, rdt=98%; f) 1,5 PDC, molecular sieves 4A, ACOH, CH₂Cl₂, 30 mn, rdt=72%; g) PPTS, CH₂Cl₂, Δ, 2hrs, rdt=92%; h) IPrOH, PPTS, molecular sieves 4A, RT, 3hrs give <u>8</u>, rdt=63%, for <u>7</u> 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 C6H5 CN/H2O2; Payne, G.B. Tetrahedron Lett. 1962, 18, 763-765; ii) Ethylchloroformiate/H2O2; 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 Locwenthal, 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, ¹H, ¹³C NMR spectroscopy, and centesimal analysis or Mass Spectroscopy.

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