

ENANTIODIFFERENTIATION OF ODOUR PERCEPTION OF α -AMBRINOLS

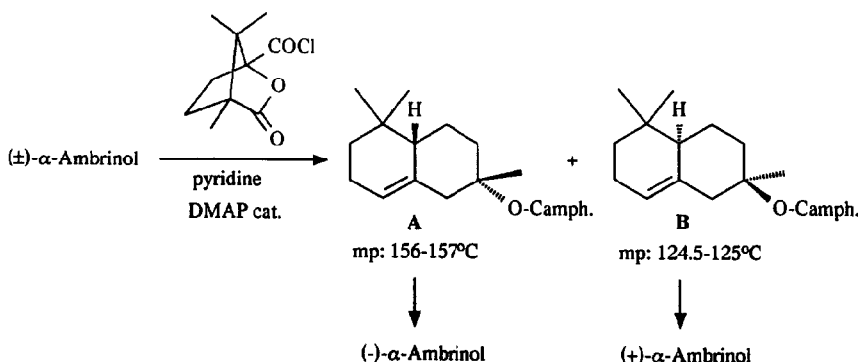
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Abstract Racemic α -ambrinol has been resolved by fractional crystallization of the diastereomeric mixture of its 1S(-) camphanic acid esters and subsequent reduction of the chemically pure diastereoisomers with lithium aluminium hydride.

(-)- α -Ambrinol, one of the characteristic components of ambergris, has been described twice in the literature [1]. It was made from (+)-ambrein several years ago [1]. There is no reference to the other enantiomer. The purpose of our work was to test the pure enantiomers for olfactory disparity.

Chemically pure racemic α -ambrinol [2] was esterified with (-)-camphanoylchloride in excess pyridine and dichloromethane in presence of a catalytic amount of 4-dimethylaminopyridine (DMAP) [3]. The crude product was fractionally recrystallized to constant melting points from pentane-diethyl ether mixtures under consistent control of the diastereomeric purity by HPLC (on Partisil 5.5 microns with 1.5 % dioxane in n-heptane). Using this procedure we obtained diastereoisomer A (mp: 156-157°C/[α]_D: -60.5 with c=1.1 in CHCl₃) and diastereoisomer B (mp: 124.5-125°C/[α]_D: +55 with c=1.4 in CHCl₃), both in more than 99.5 % chemical as well as diastereomeric purity.



Reduction of A with lithium aluminium hydride in diethyl ether gave, after column chromatography on silicagel and consequent short path distillation in vacuo, pure (-)- α -ambrinol of more than 99.5 % e.e. (determined by GLC on a 26 m glass capillary coated with β -cyclodextrin M and hydrogen as carrier gas; determined by HPLC on β -cyclodextrin 5 microns with 35 % acetonitrile/ 65 % water as eluent).

The identical procedure applied on diastereoisomer B furnished (+)- α -ambrinol exhibiting the same e.e.

The measured optical rotations $[\alpha]_D^{20}$ in chloroform were -125.98 with $c=1.14$ and +125.35 with $c=1.08$. We could observe a tremendous odour difference between the two enantiomers. While the "unnatural" (+)- α -ambrinol exhibits a strongly dry earthy, musty tonality which reminds perfumery experts immediately of geosmine [4] [5], the natural (-)- α -ambrinol shows its animal, indol- or skatol-like naphthalenic odour properties which seem to dominate the odour impression of the racemate [6].

Notes and References

- [1] a) E.Jegou et al., *Nouveau Journal de Chimie*, vol. 1, 529 (1977)
b) G.Ohloff et al., *Helv.Chim.Acta* 60, 2763 (1977).
- [2] Several syntheses of racemic α -ambrinol are described in literature e.g. O.Takazawa et al., *Chemistry Letters* 1257 (1980).
We used our own procedure vide EP-patent application No. 406572 and purified the crude product by column chromatography on silicagel.
- [3] H.Gerlach, *Helv.Chim.Acta* 61, 2773 (1978).
H.G.Capraro et al., *ibidum* 63, 1347 (1980).
- [4] J.A.Maga, *Food Reviews International* 3, 269 (1987).
- [5] R.Kaiser, C.Nussbaumer, *Helv.Chim.Acta* 73, 133 (1990).
- [6] The odour thresholds of the two enantiomers differ only by a factor of 1.5 to 2.