

Synthesis of Ambergris-fragrances and (+)-Ambreine

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Ambergris, a precious animal perfume obtained as an intestinal concret ion in the sperm whale, is composed principally of non-volatile material: 30-40% of epicoprosterol and 25-45% of ambrein (**1**) – a tricyclic triterpene alcohol. Autoxidative decomposition of ambreine (**1**) resulted in volatile odoriferous constituents as follows: C₁₁- γ -cyclohomogeranial, C₁₃-dihydro- γ -ionone (**2**), C₁₄- γ -coronal (**5**), C₁₆-ambrox (**3**) and C₁₇-dehydroambra oxide (**4**).

First, the absolute stereochemistry of dihydro- γ -ionone (**2**) was confirmed by synthesis of (+)-(S)-**2** from (-)-(S)- α -cyclogeranic acid (**6**). Cyclization of farnesyl acetate with chlorosulfonic acid gave (\pm)-drimane-8,11-diol 11-acetate, which was resolved by lipase catalyzed hydrolysis to give (+)-drimane-8,11-diol (**7**). A series of one carbon elongation reactions of (+)-**7** gave (-)-ambrox (**3**). Wittig reaction of (+)-ambreinolal, prepared from (+)-**7**, with 1-methoxycarbonyl ethylidene triphenylphosphorane, followed by DIBAL reduction, chlorination and then the reaction with sodium tolylsulfinate, gave the allylic sulfone (**8**). Enantiomerically pure (+)-ambreine (**1**) was synthesized by the coupling of the C₂₀-bicyclic building block (**8**) and (+)- γ -cyclogeranyl bromide (**9**). (+)- γ -Coronal (**5**) was synthesized by the coupling of (+)-**9** with ethyl 3-tributylstannyl-2-methylene propanoate by Baldwin's method, followed by DIBAL reduction and MnO₂ oxidation.

