

Muscopyridines

Alkaloids that complete the animalistic character of musk.

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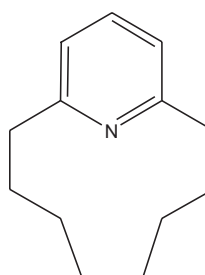
Natural muscone, traditionally harvested from the Asian musk deer (pictured, at right), is (R)-3-methylcyclopentadecanone (**F-1**). Found in nature with a small amount of muscopyridine, which completes the animalistic character of musk, muscone supplies a pyridinic, urinaceous undertone.¹ In samples where muscopyridine was found, the muscone detected was most likely derived from male musk deer.² However, muscopyridine was also identified in civet.³

Muscopyridine is an unusual metapyridinophane, which was originally isolated by Prelog et al. from the ether extract of 2 kg of crude musk by exhaustive extraction with an aqueous solution of tartaric acid and 10% HCl. The filtered aqueous solutions were made alkali with KOH and extracted with ether. Distilling off the ether leaves a residue and oil. Distillation of the oil yields 0.75 g of muscopyridine (~0.04% of the crude musk).⁴ Convergent total synthesis of muscopyridine has been achieved in its enantiomerically natural form by ring closing metathesis strategy, enabling the determination of its absolute stereochemistry more than 50 years after its isolation by Prelog.⁵

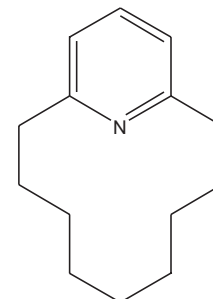
The presence of muscopyridine in natural musk established a method for differentiating natural and artificial musk. GC/MS was used to detect the extract of musk, and several characteristic components were qualitatively differentiated simultaneously. The results showed that two characteristic components—muscopyridine and 3-methylcyclotridecanone—could be used to



F-2. 2,6-Nonamethylene pyridine and 2,6-decamethylene pyridine

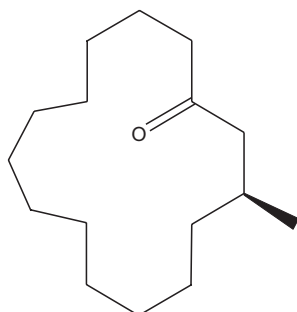


2,6-Nonamethylene pyridine



2,6-Decamethylene pyridine

F-1. (-)-(R)-3-Methylcyclopentadecanone

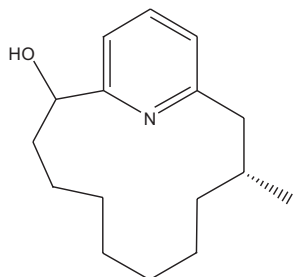


(R)-(-)-3-methylcyclopentadecanone
(Muscone)

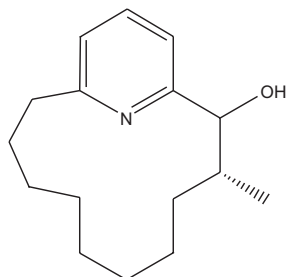
Physical Data of Muscopyridine¹¹

Molecular weight	231.4
Molecular formula	C ₁₆ H ₂₅ N
Refractive index n_D^{25}	1.5206
Density D ²⁵	0.9669
Optical rotation	+13.3°
Log P _{o/w}	5.86
Boiling point	138-143°C (2.2 mmHg)

F-3. Hydromuscopiridine A and B



Hydroxymuscopiridine A



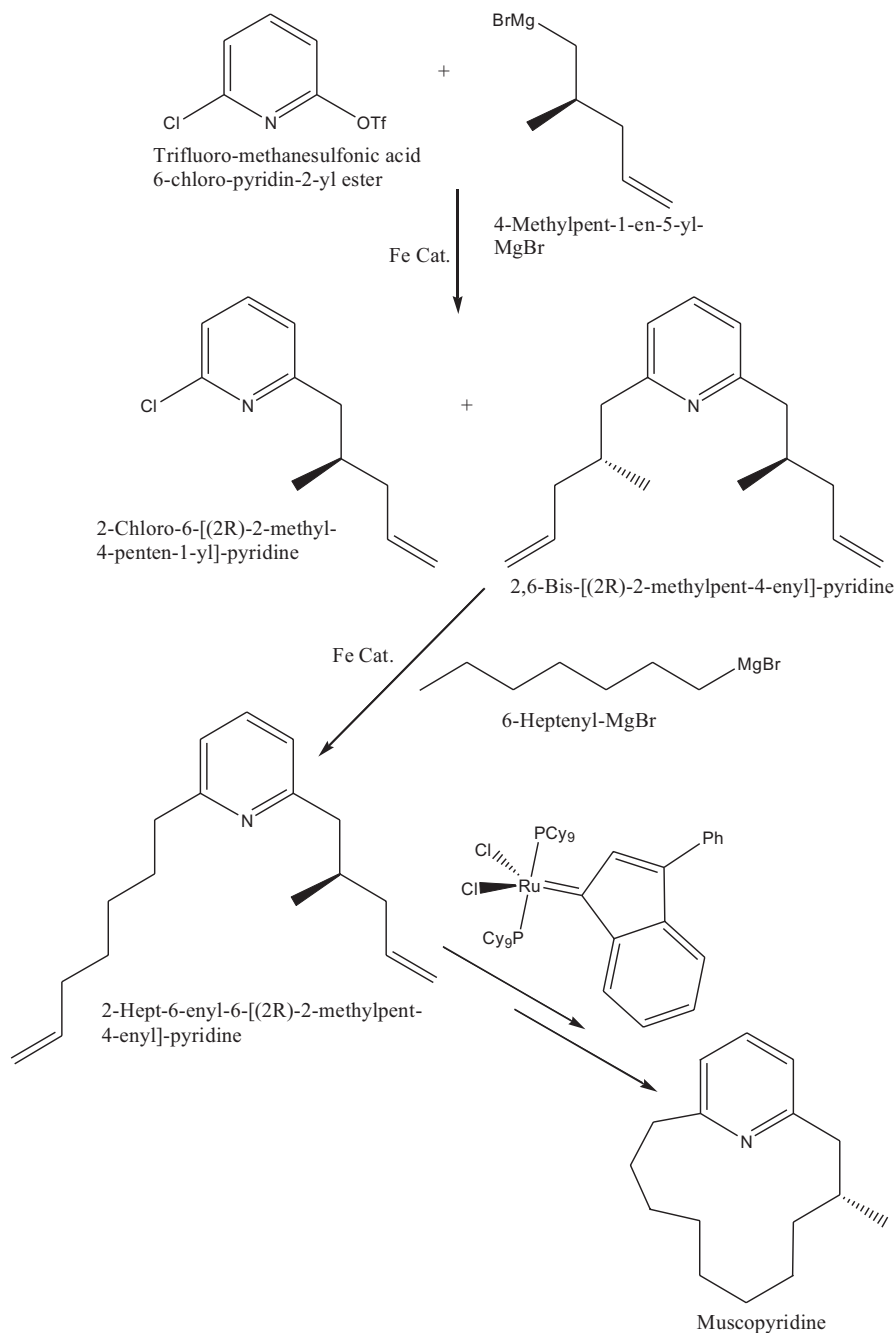
Hydroxymuscopiridine B

differentiate natural and artificial musk. This method has the advantages of simple operation, less consumption of samples and reliable qualitative results.⁶

Additional odoriferous lower homologues were isolated from musk grains and identified by Mookherjee and Ledig, for example: 2,6-nonamethylpyridine [56912-80-2] (**F-2**); 14-azabicyclo[8.3.1]-tetradeca-1(14),10,12-triene and 2,6-decamethylenepyridine [56929-81-8] (**F-2**); and methyl 15-azabicyclo-[9.3.1]-pentadeca-1(15),11,13-triene.⁷

A basic fraction of musk extract used in Chinese medicine was chromatographed on a silica gel column using chloroform containing increasing amounts of methanol. The fraction, after the separation of muscopyridine, was subjected to TLC on

F-4. Muscopyridine synthesis



alumina plates to produce hydroxymuscovopyridine A [89368-39-8] (**F-3**); 16-azabicyclo[10.3.1]hexadeca-1(16),12,14-trien-2-ol, 10-methyl-; and hydroxymuscovopyridine B [89368-40-1] (**F-3**). 16-Azabicyclo[10.3.1]hexadeca-1(16),12,14-trien-2-ol, 3-methyl- is described as a colorless oil with a special odor.⁸ According to Arcadi Boix-Camps, who spoke with this author in April 2013, muscovopyridine derivatives present in musk are more responsible for the real musk odor than molecules like muscone.⁹ Muscovopyridine was synthesized (**F-4**) by Furstner and Leitner, starting from trifluoromethanesulfonic acid 6-chloropyridin-2-yl ester and 4-methylpent-1-en-5-yl. The first starting material was prepared from 6-chloro-1*H*-pyridin-2-one; the Grignard reagent was produced from (S)-(+)-3-bromo-2-methyl-1-propanol.¹⁰

References

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