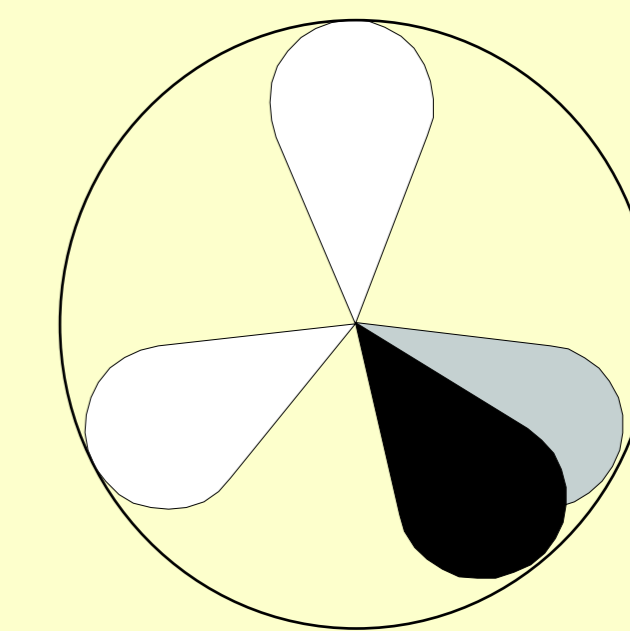


Synthesis of musk macrocyclic compounds



Piotr Wawrzyniak

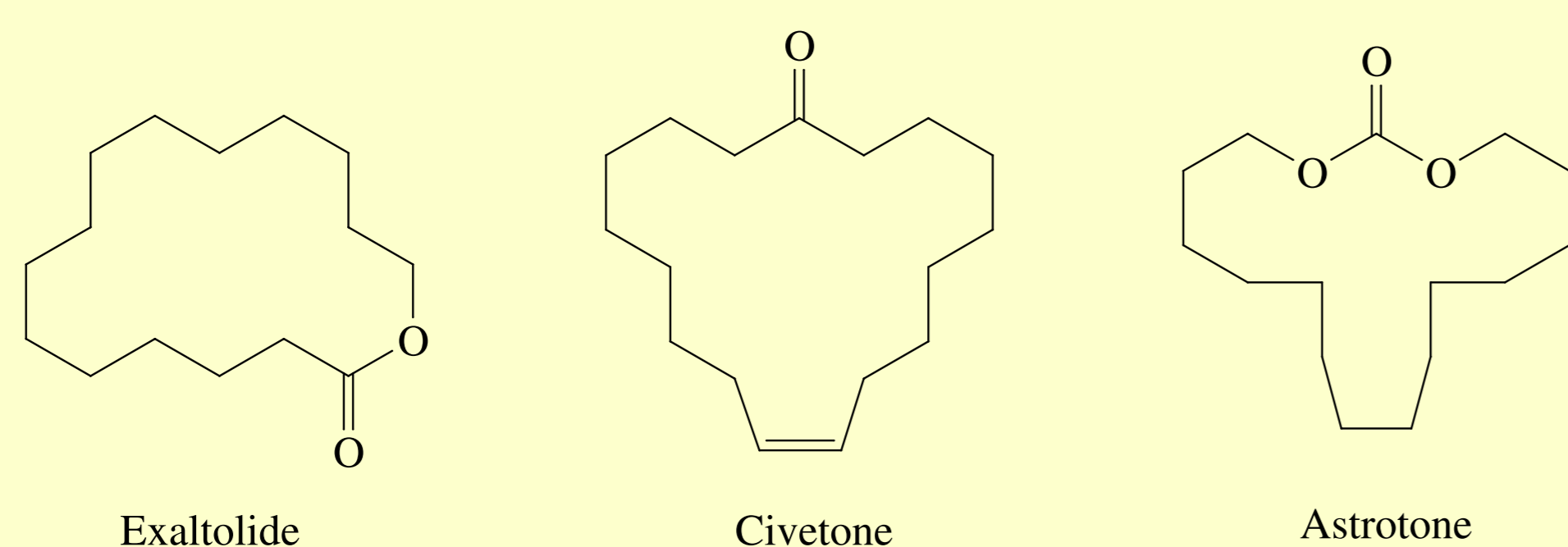
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1 Introduction

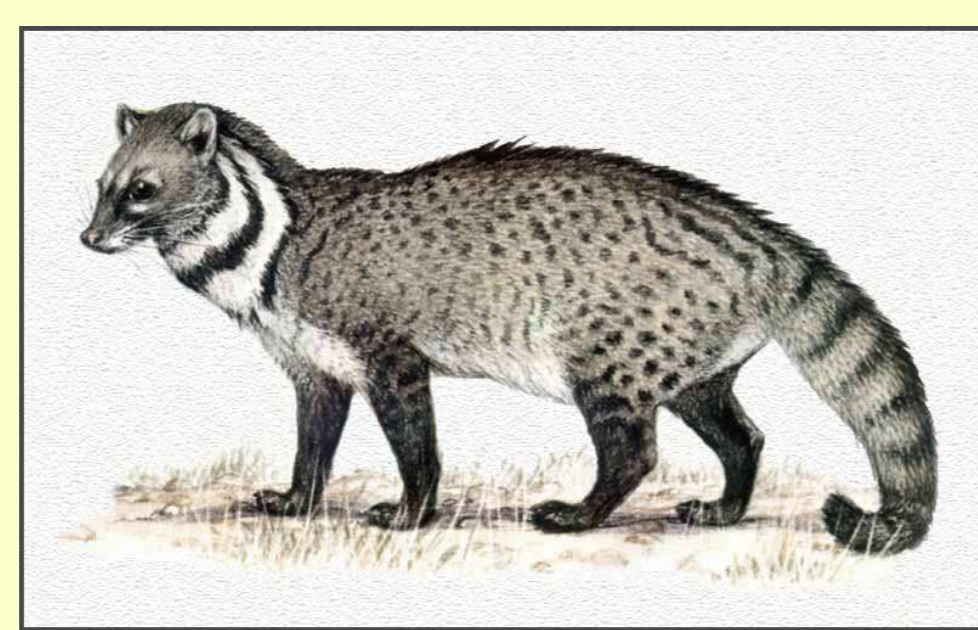
The musk has been recognised from ancient times as one of the most attractive scents. It was a component of all aromatic compositions. The large ring cyclic carbonates such as Astrotone are valuable synthetic musks. Natural macrocyclic musks, especially Muscone and Civetone are attractive ingredients in many perfumes.



The natural sources of musk has been limited and products from them receive very high prices. Natural musk is mainly originated from animals (*Viverra Civeta* and *Moschus Moschiferus*), whose death is sometimes prerequisite for the harvesting of musk scent.



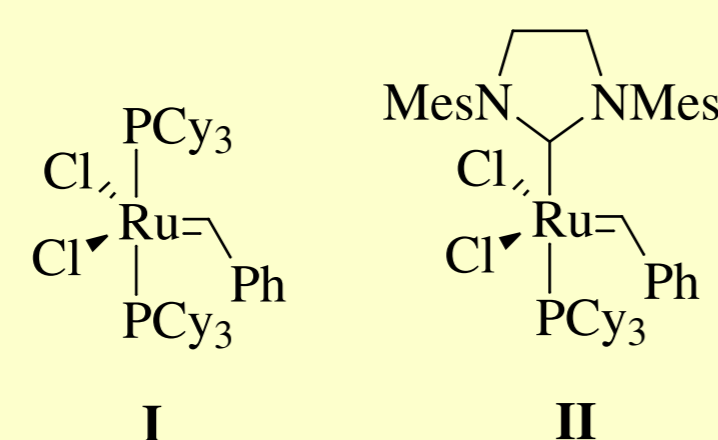
Moschus Moschiferus



Viverra Civeta

On the other hand, the use of easier accessible synthetic nitro- and polycyclic musks was reduced in recent years because of their health and environment damaging properties. Hence, there is a need for the development of new natural-like biodegradable non-toxic odorants. Olefin metathesis is an efficient carbon-carbon bond forming method that can be applied in the synthesis of various carbo- and heterocycles. The ring-closing metathesis (RCM) approach was used by Wiegers et al., who prepared a series of macrocyclic carbonates **1** ($m, n = 1 - 8$) using ill-defined $WCl_6/SnMe_4$ catalyst.

However, this cyclisation required rather harsh reaction conditions and relatively high catalyst loading and resulted with low total conversions and isolated yields. To the best of our knowledge no investigations of the RCM of carbonates catalyzed by the modern, well-defined precatalysts I–II has been carried out.



2 Results and Discussion

Table 1 summarises representative ring-closing reactions mediated by the commercially available Grubbs' catalyst I.

The carbonates of unsaturated alcohols C6–C11 were treated with Grubbs first generation catalyst I under standard metathesis conditions (5 mol% of I, CH_2Cl_2 , 20–40 °C, $c = 0.01-0.02 M$). In result macrocyclic compounds of the ring sizes of 17–23 were received with good efficiencies.

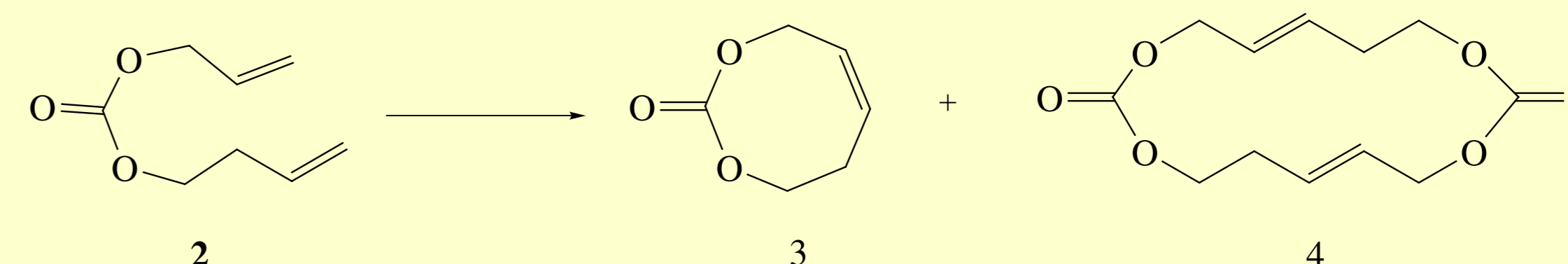
It was notice, that the longer coal chains in substrates were the more easily and with larger efficiencies it cycles to monomeric products. Received macrocyclic compounds smelled musk. Their scent was similar to the scent of synthetic musks applied in perfumes — Exaltolide and Civetone.

The easiness of cyclisation of carbonates including in it's structure the rest the allyl alcohol was also examined. It is known that some allylic substrates, such as ethers undergo a double bond isomerisation. Cyclic carbonates are precious monomers in receiving polycarbonates. The compounds with the sizes of the rings 7–15 has been prepared. The cyclisation of **2** gives only dimer **4**.

Table 1

Entry	Substrate	Product	Yield (%)
1			0
2			0
3	$n = 1, n = 2$		0
4	$m = 1, n = 3$		0
5	$m = 3, n = 8$		80
6	$m = 4, n = 4$		6
7	$m = 6, n = 6$		60
8	$m = 8, n = 8$		49
9	$m = 9, n = 9$		91

For the next homologues of carbonates the general tendency of creating dimers and oligomers has been noticed. Only C-15 ring came into with good efficiency as monomer. This last result shows that the allyl part in carbonates does not undergo isomerisation and carbonates can be applied as substrates in metathesis reactions. In summary, this study witnesses the efficiency of modern well-defined ruthenium catalysts for the formation of musk-odored macrocyclic carbonates of ring sizes 15–23. It also reveals that geometric factors are very important in this case and smaller ring carbonates are hardly accessible by RCM.



3 Acknowledgements

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