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Synthesis of Natural Compounds with Antifungal Activity

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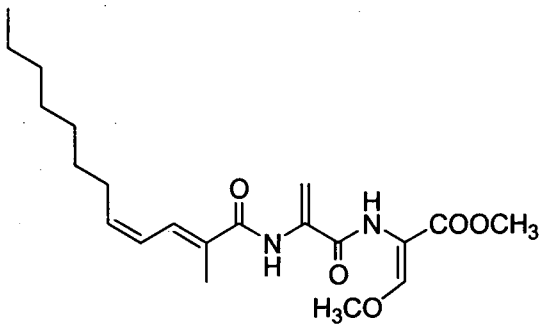
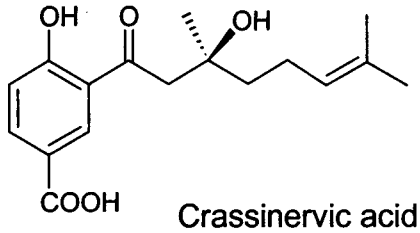
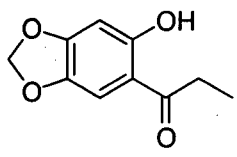
Over the last decades, natural products have played a major role in the discovery of new active ingredients, both in the pharmaceutical and the crop protection industry. Notwithstanding the growth of the impact of parallel or combinatorial synthetic methods on modern drug discovery, natural products or their derivatives still account for a major portion of today's portfolio of active ingredients. In the crop protection area, only very few natural products are directly used as active ingredients due to several reasons: the compound needs to be readily available on a large scale, to be sufficiently stable under field conditions, and to be biologically selective and compatible with a variety of crops. However, natural products exert a much stronger influence on modern crop protection research by serving as lead structures for the discovery of new active ingredients, often featuring novel modes of action, the most successful example being the strobilurin story. This success shows the potential advantages of collaborations between academic research groups and industry. Today and in future, such collaborations might become even more important since most crop protection companies have stopped their in-house natural product research, mainly due to overall low success rates and high cost.[1]



Cyrmenin B1



Crassinervic acid



Kakuol

The need to develop new fungicides has been a major driving force for applied phytopathological and mycological research efforts in the past, and this is likely to remain the

case in future as fungal plant pathogens continue to develop resistance against existing fungicides at great speed, and also because new disease situations continually arise. One increasingly stringent requirement for new fungicides is their biodegradability in natural situations. This is likely to be met most readily by substances derived from natural products.[2]

Natural substances with fungicidal activity are found in plants, fungi and marine organisms. The total synthesis of natural lead substances and the synthesis of derivatives will be illustrated in the case of three natural products recently studied in our laboratories, e.g. Cyrmenin B1,[3] crassinervic acid[4] and kakuol.[5]

References

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3. N. Chakor et al. *J. Org. Chem.* **2009**, *74*, 844-849.
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