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PYROCINE SYNTHESIS - A NEW APPROACH TO CHRYSANTHEMIC ESTER

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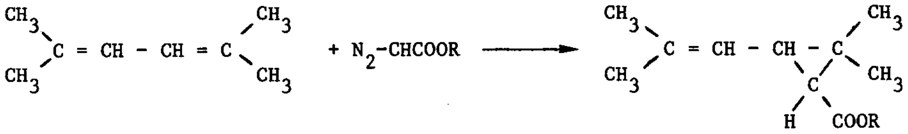
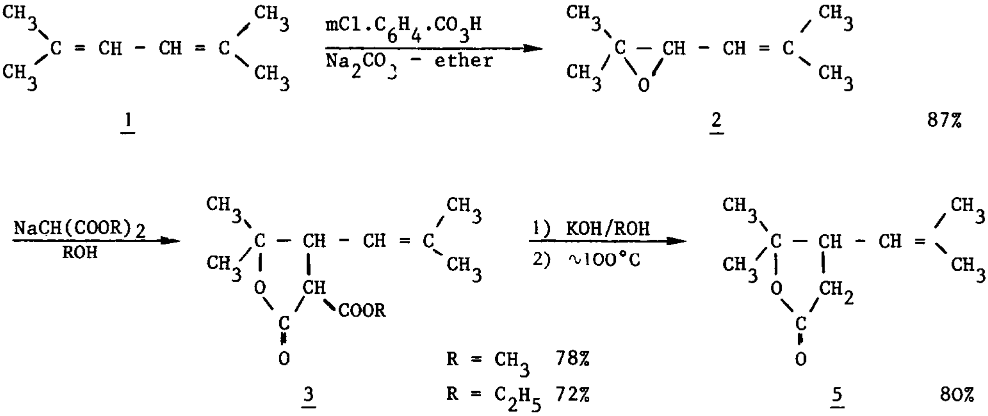
Several strategies have been published for chrysanthemic acid synthesis [1]; among these is the one starting from 2,5-dimethyl 2,4-hexadiene 1 and diazoacetate [2] which is used at industrial scale [3]. This is a cheap route but highly dangerous especially on large scale (Scheme I).

SCHEME I



We present here a new route to chrysanthemic acid which starts from 2,5-dimethyl 2,4-hexadiène 1 [4] already used for the industrial synthesis mentionned above and which overcomes the dangerous step.

2,5-dimethyl 2,4-hexadiene 1 is efficiently transformed to the corresponding mono epoxide 2 (m $Cl-C_6H_4-CO_3H$-ether powdered Na_2CO_3 : 2 hrs at room temperature)[5] which is readily opened by sodio-diethyl or dimethyl malonate in ethanol or methanol [6] (3 hrs reflux) producing the lactone 3 in 72 and 78% yield respectively.
Hydrolysis of 3 by 1 eq. of KOH in alcohol (3hrs at room temperature) produces the acid lactone 4 from which pyrocine 5 is quantitatively prepared (by gentle heating of the molten compound)



1

2 87%

3

R = CH_3 78%

R = C_2H_5 72%

5 80%

As the high yield transformation of pyrocine 5 to trans chrysanthemic acid was already described by several authors [7], the synthesis of pyrocine described here is a formal chrysanthemic acid synthesis.

This simple synthesis needs some comments .
Reverse activations have been used in diazoacetate and sodio malonate approaches; the two carbon unit introduced being electrophilic in the first one and nucleophilic in our approach. The prime project was to transform in one step the highly functionalized lactone 3 to chrysanthemic ester. However, the different reaction conditions used have met little if no success [8]. The work directed towards this goal is in progress in our laboratory.

References

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8. These conditions include :

   a) the same reaction conditions as described for pyrocine-chrysanthemic ester transformation, cfr ref.7

   b) thermolysis at 180° or flash thermolysis at 600°C.