RECENT PROGRESS IN ALKALOID SYNTHESIS

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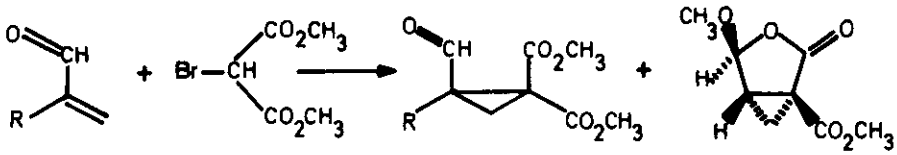
The stereoselective condensation of cyclopropane-aldehydes (chart I) to tryptamine is reported and the configuration of the corresponding reaction products is discussed (chart II). As may be expected these cyclopropane-intermediates undergo a number of easy ring opening reactions. While proton catalyzed processes proceed via formation of the most stable cation (chart III) completely nucleophilic ring opening takes place at the least substituted center (chart IV). In connection with proton catalysis an unexpected stereospecificity is disclosed which indicates a concerted reaction mechanism (chart V). Nucleophilic ring opening products formed with cyano-acetates proved to be useful intermediates for the preparation of vincamine and vincamine-derivatives . The configurational stability of stereoisomers in this series is discussed as well as a few quite unexpected reactions of the intermediates (chart VI). Having easy access to eburnamonine new and quite efficient techniques to convert this alkaloid into vincamine will be presented (chart VII).
In connection with synthetic access to a number of alkaloids with an exocyclic trisubstituted double bond the stereoselectivity of the methylene-lactam rearrangement was investigated (chart VIII, chart IX) and it will be shown that by forcing the molecule into the unfavourable conformation with an axial substituent next to the exocyclic double bond the naturally occurring E-configuration is secured with excellent stereoselectivity (chart X). This compound proves to be a very useful intermediate for a highly stereoselective total synthesis of geissoschizine as well as an attractive starting material for other alkaloids containing trisubstituted double bonds of a given configuration. Various ring opening processes are discussed which completely retain the double bond configuration and provide easy access to compounds of the anthirine- and akagerine-type (chart XI, chart XII).
In the last part of the lecture the biogenetic relationship between the alkaloids histrionicotoxine and gephyrotoxine from Histrionicus dendrobatis will be discussed

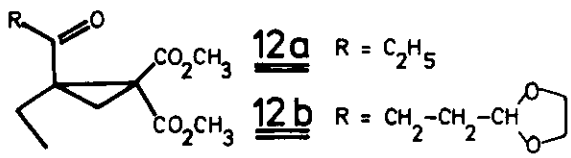
(chart XIII). A synthetic strategy taking advantage of this concept will be presented (chart XIV) as well as a few step synthesis of an attractive intermediate. The stereoselectivity of spirocyclisations turns out to be very high and to lead into the epi-series (chart XV). As this product easily can be dehydrogenated it additionally gives rise to perhydro-histrionicotoxin itself (chart XVI). Taking this result into consideration and at the same time simplifying several steps a very efficient approach to his type of alkaloid will be discussed (chart XVII, chart XVIII).

Chart I



5a R = H
5b R = C_2H_5

11



12a R = C_2H_5
12b R = CH_2-CH_2-CH

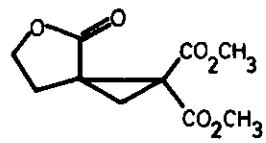


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Chart II

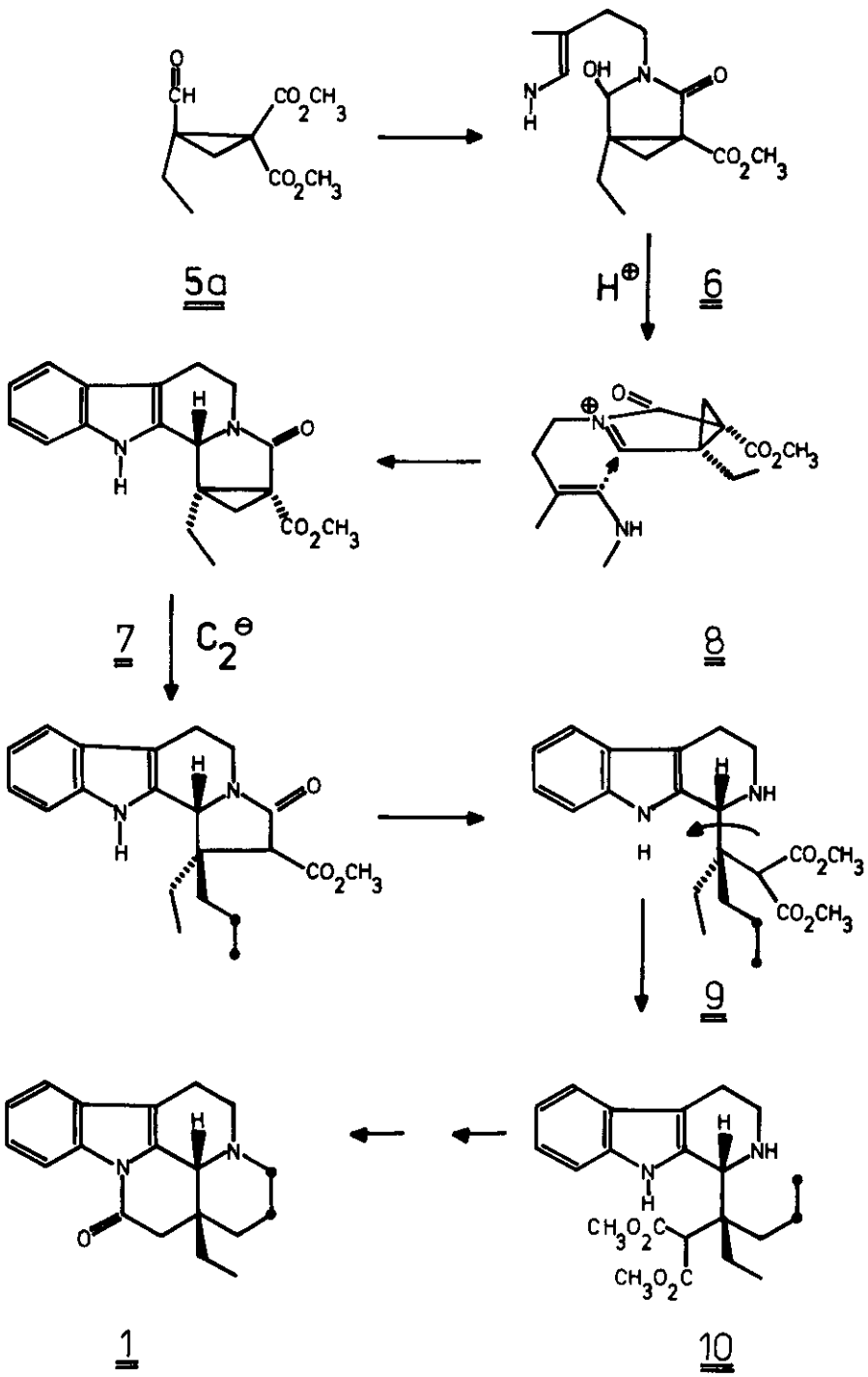


Chart III

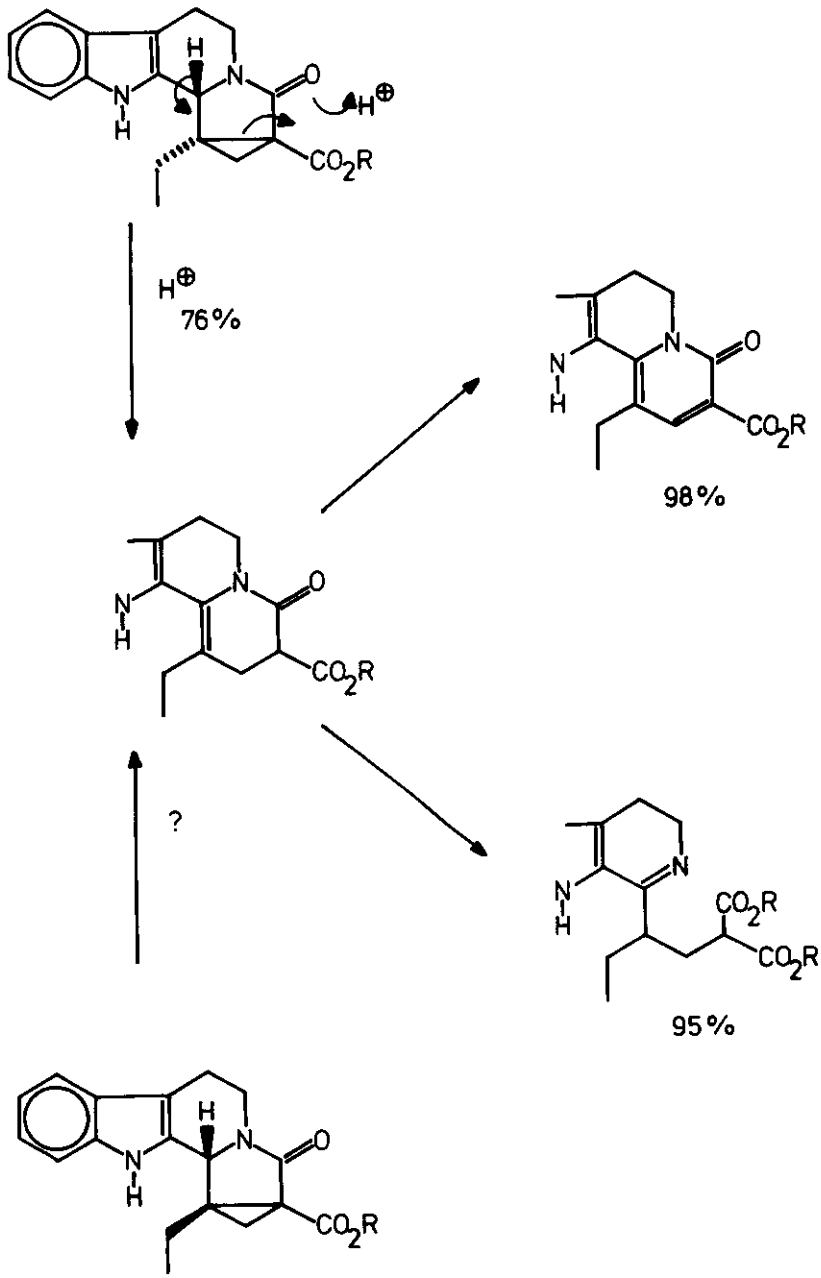


Chart IV

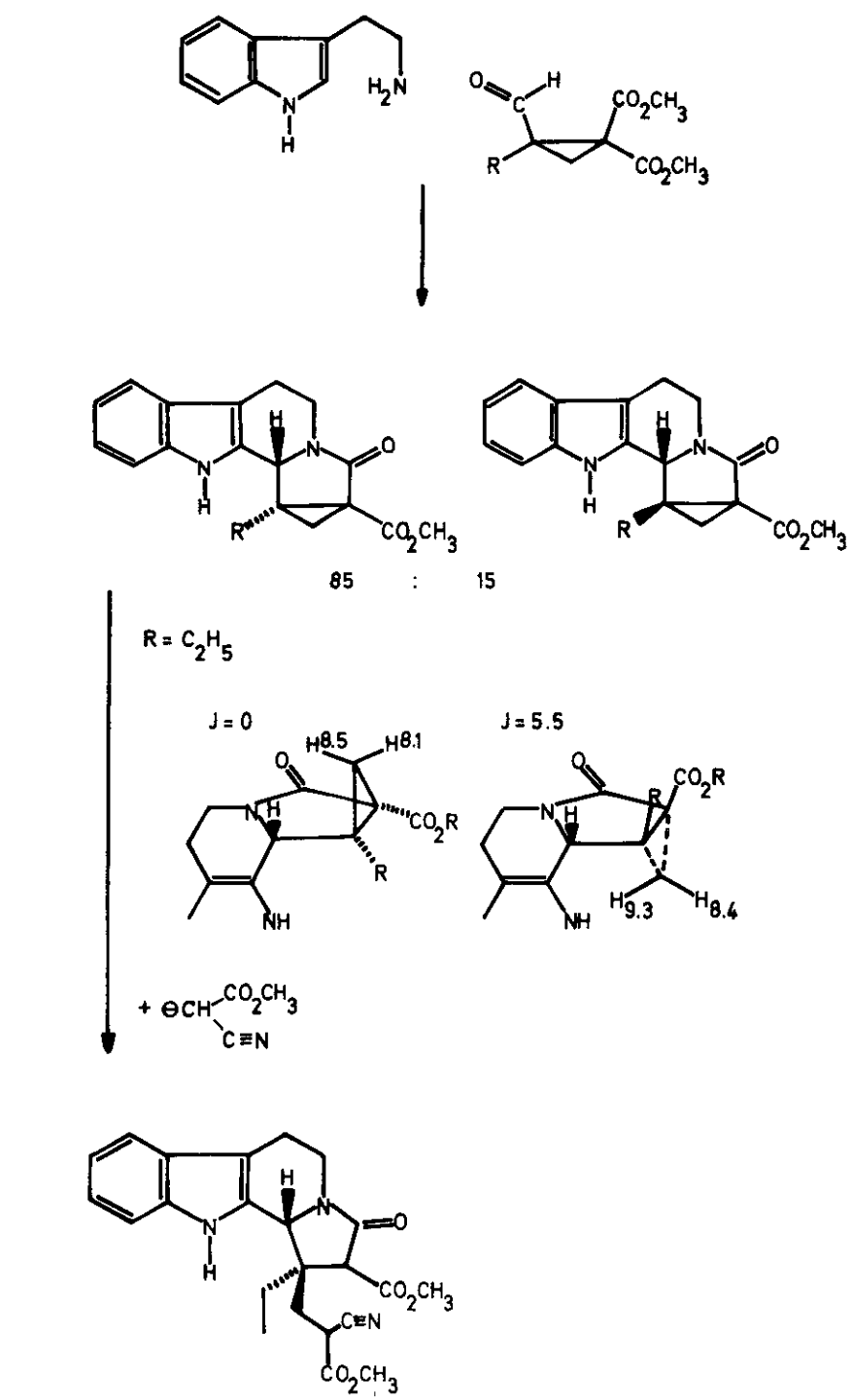

H2N
N
H
O
C
H
CO2CH3
R
CO2CH3
85 : 15
R = C2H5
J = 0
H8.5
H8.1
CO2R
J = 5.5
H9.3
H8.4
+ ⊖CH
CO2CH3
C≡N
C≡N
CO2CH3

Chart V

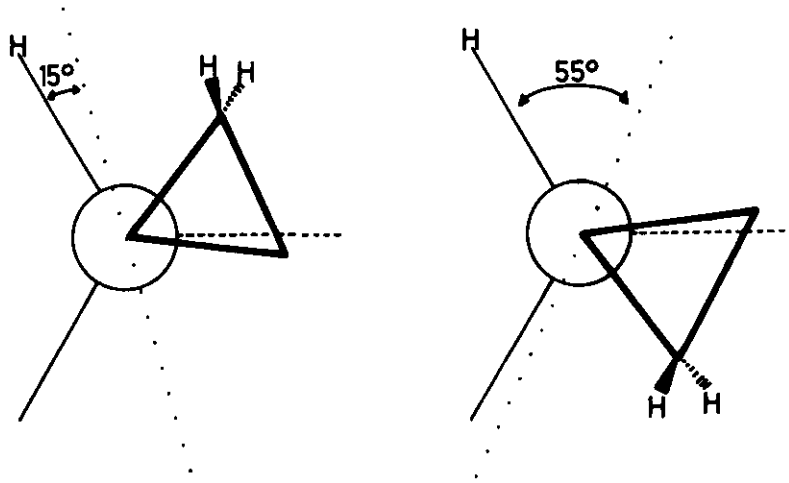


Chart VI

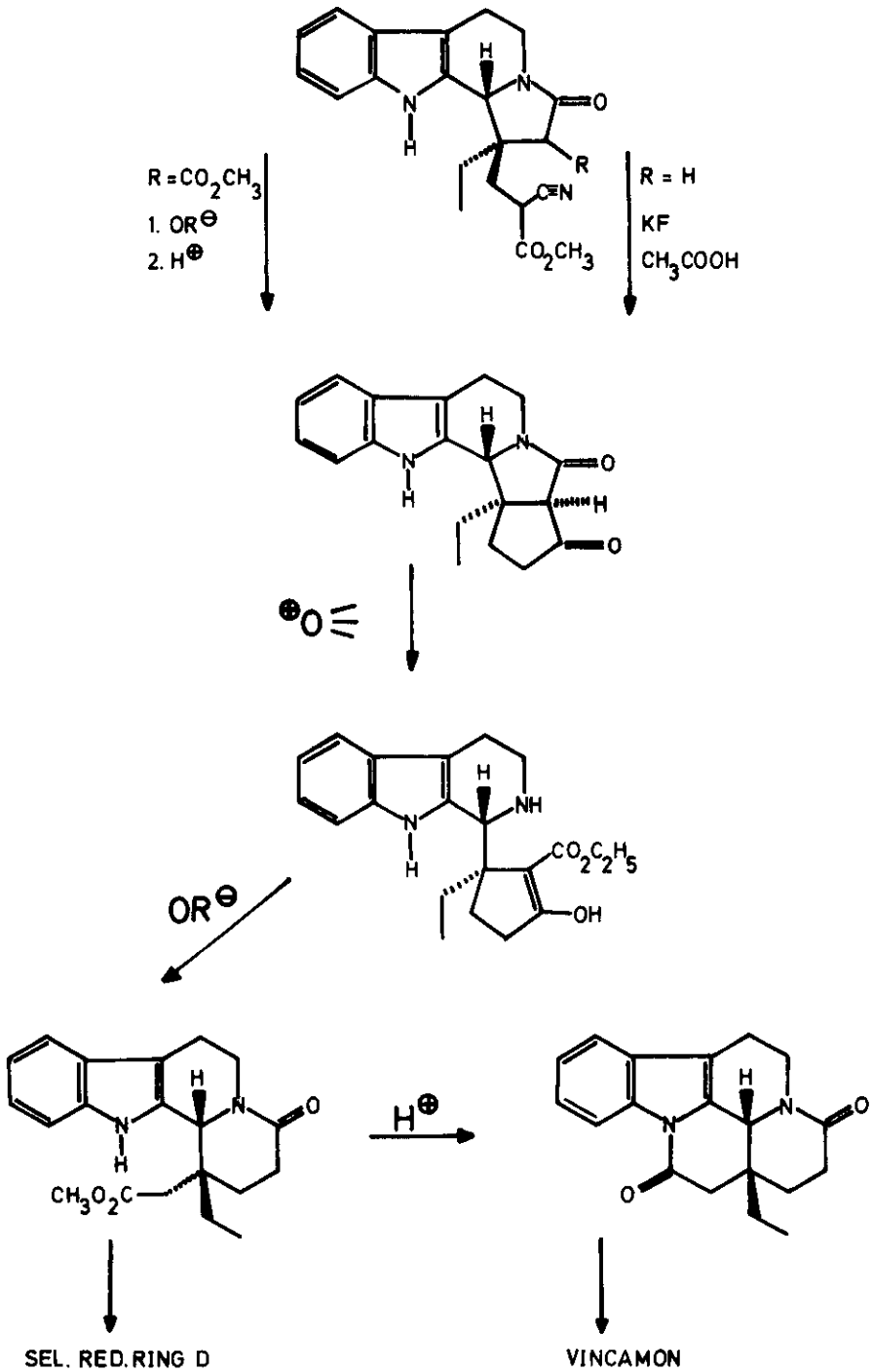
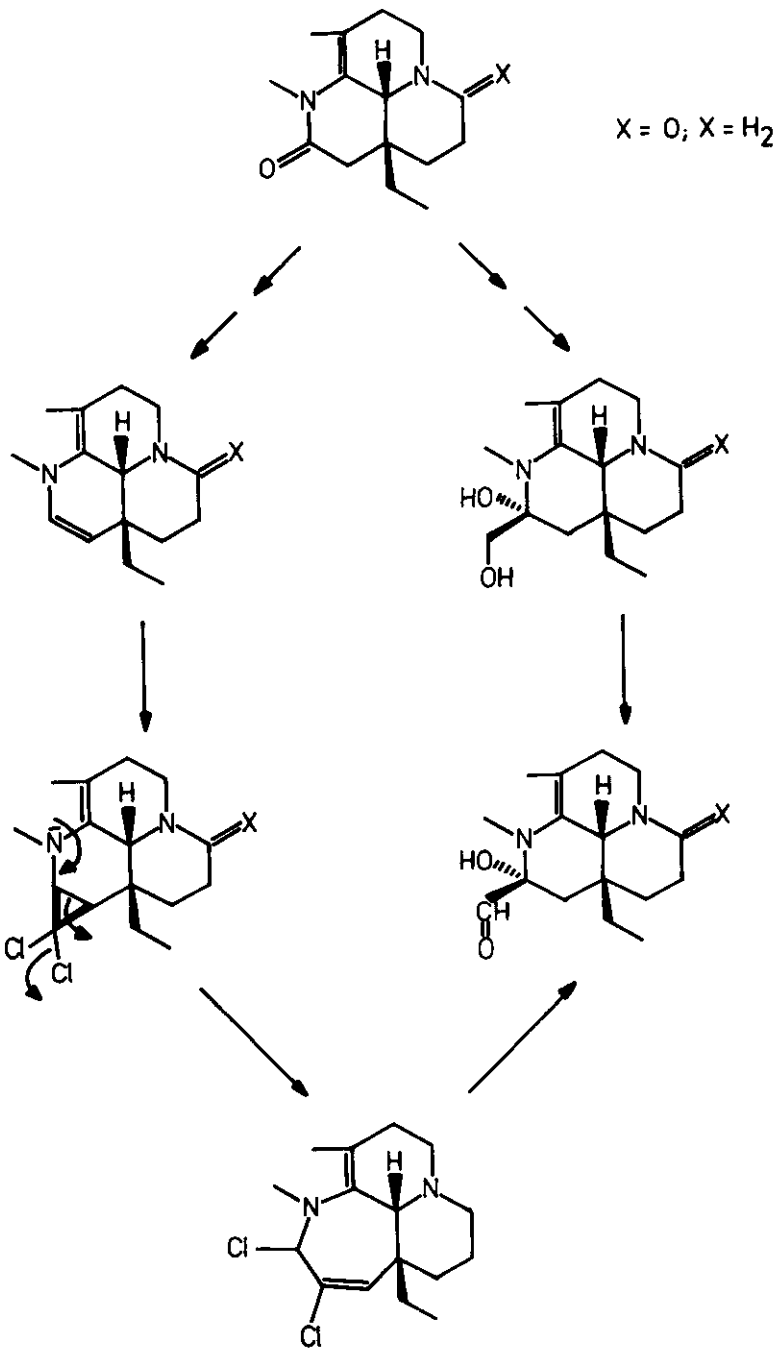


Chart VII



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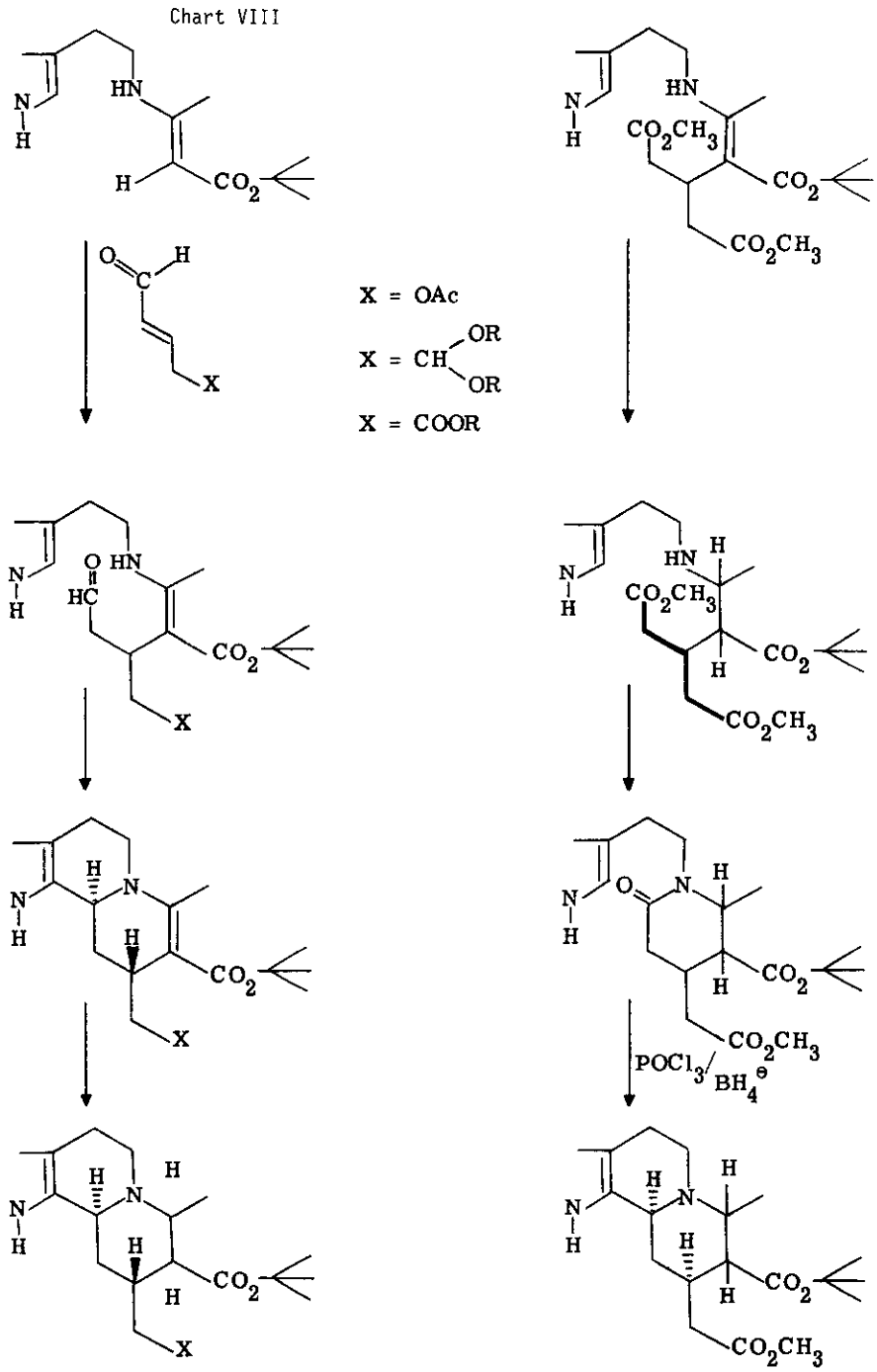
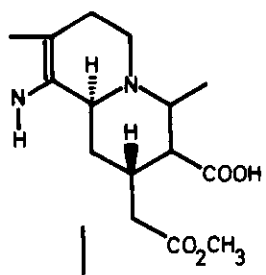
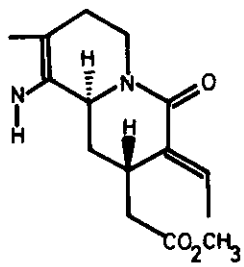
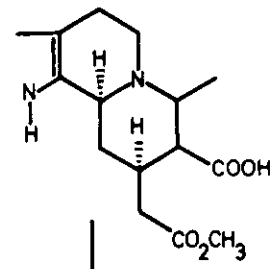


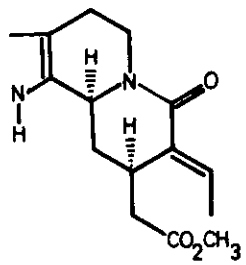
Chart IX



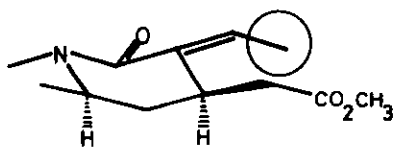


HAUPTPRODUKT
RASCH





HAUPTPRODUKT
LANGSAM
HOHE TEMPERATUR



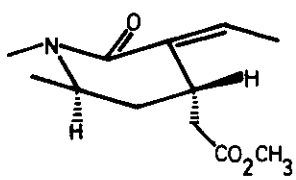
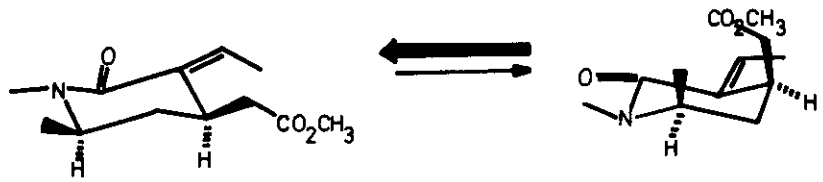
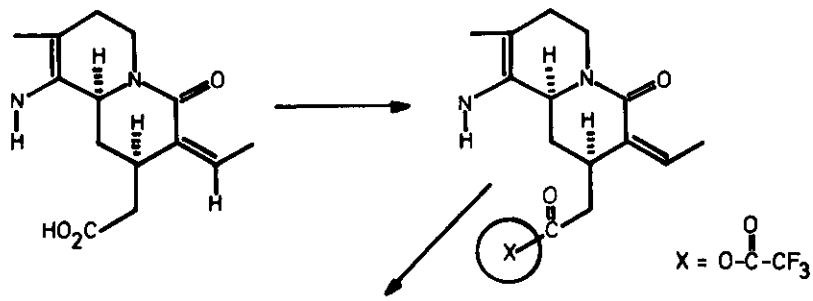
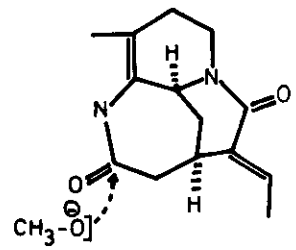


Chart X







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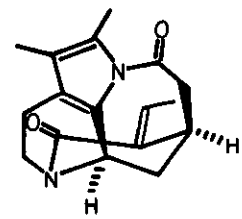

Chart XI

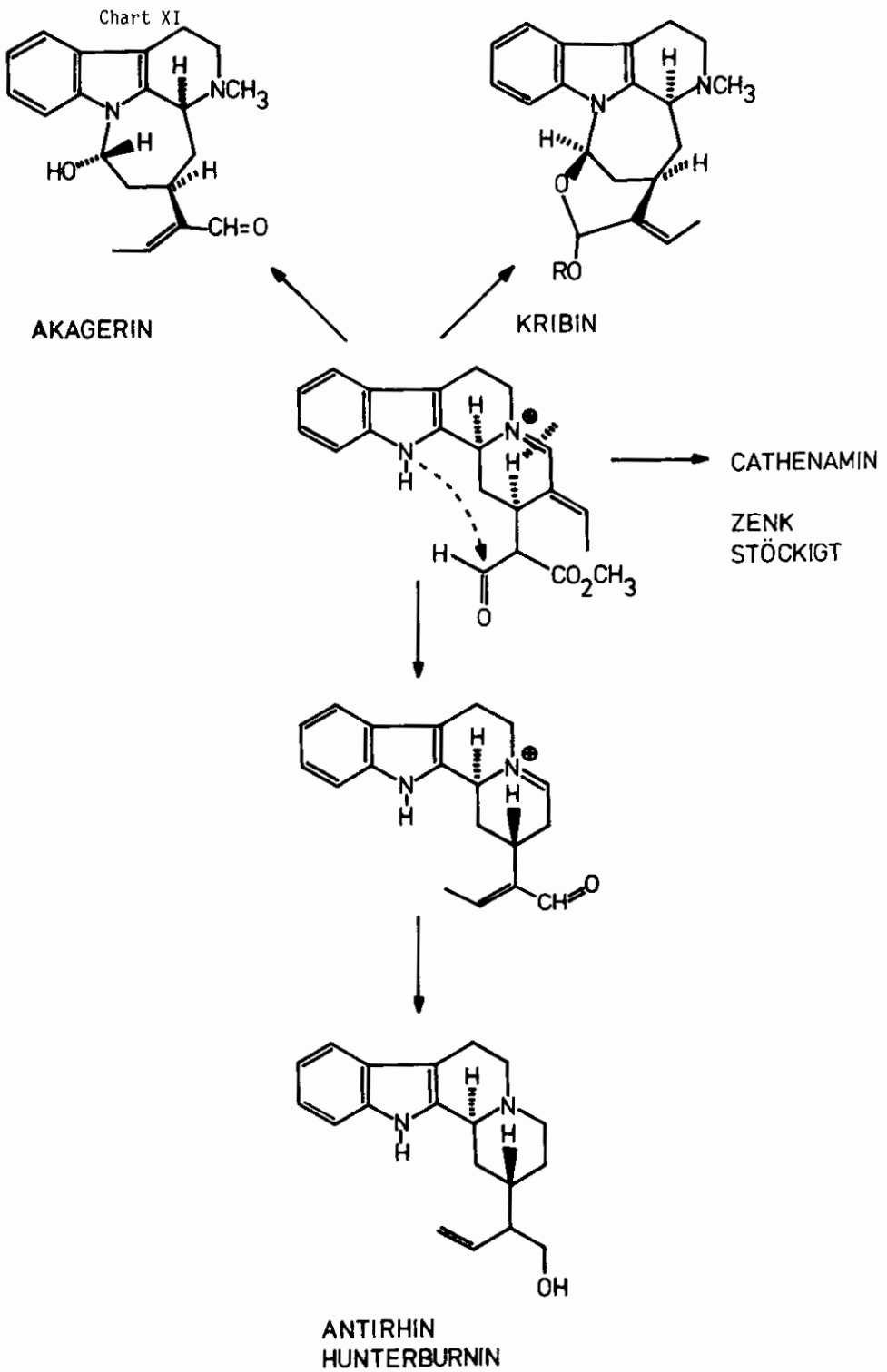
AKAGERIN
KRIBIN
CATHENAMIN
ZENK
STÖCKIGT
ANTIRHIN
HUNTERBURNIN

Chart XII

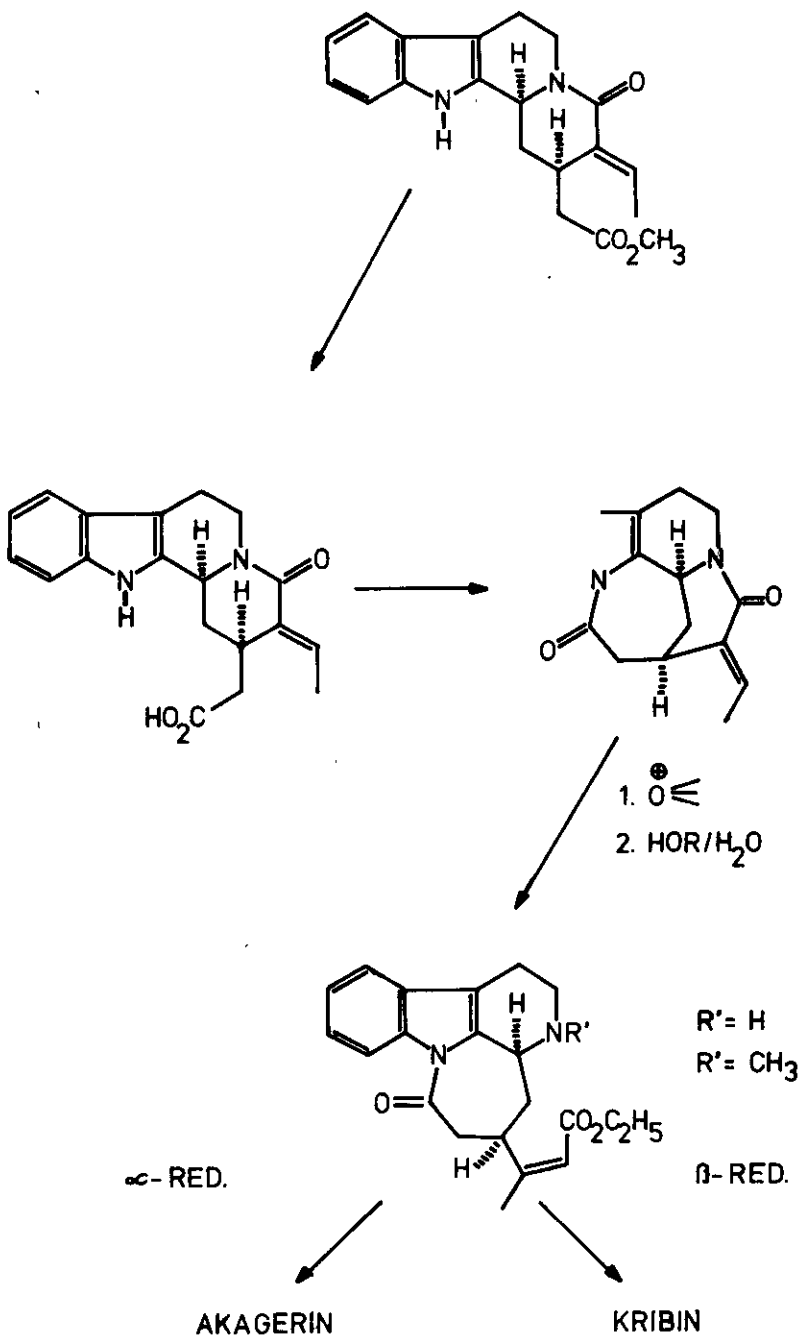

Chart XIII

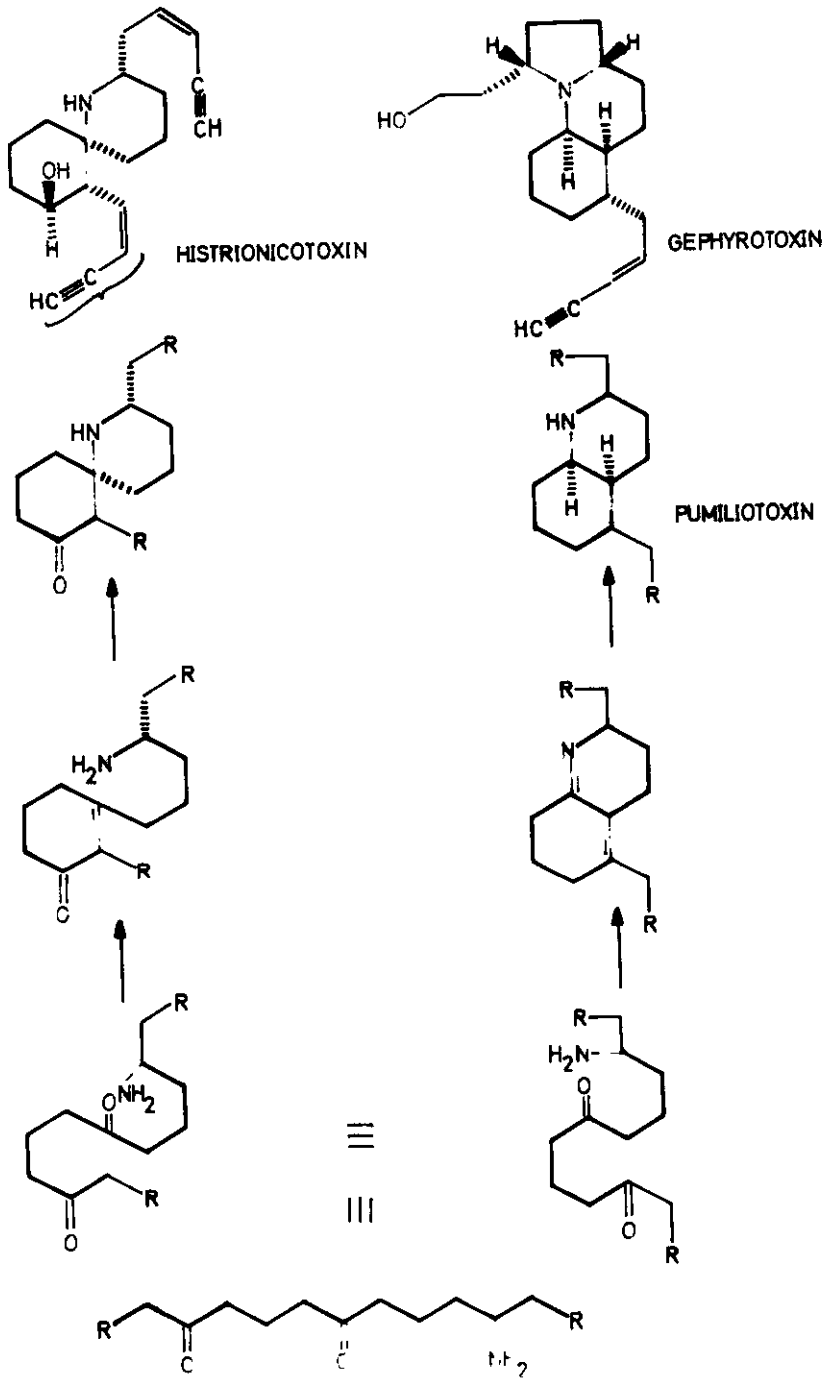

Chart XIV

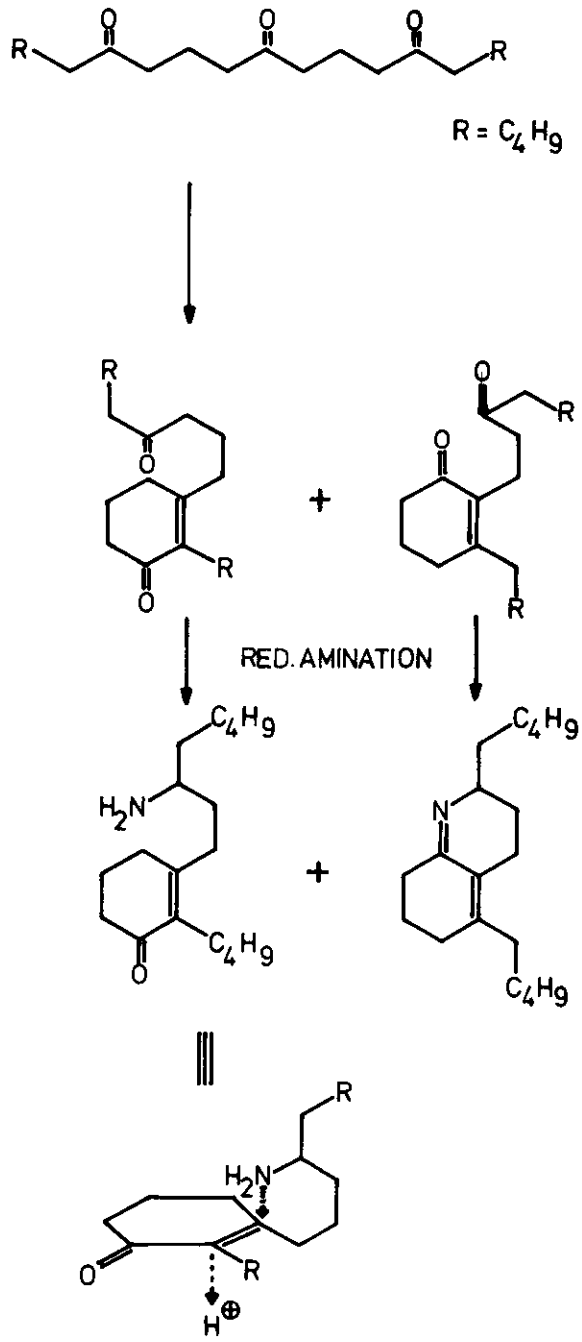

Chart XV

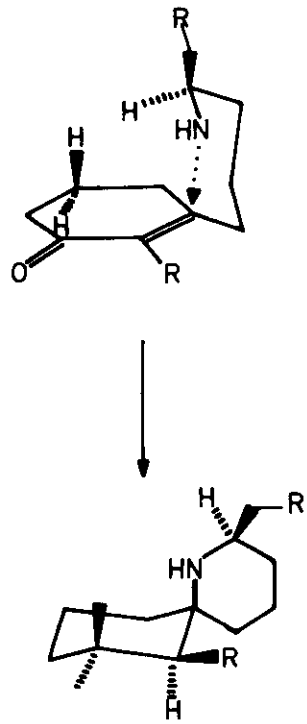

Chart XVI

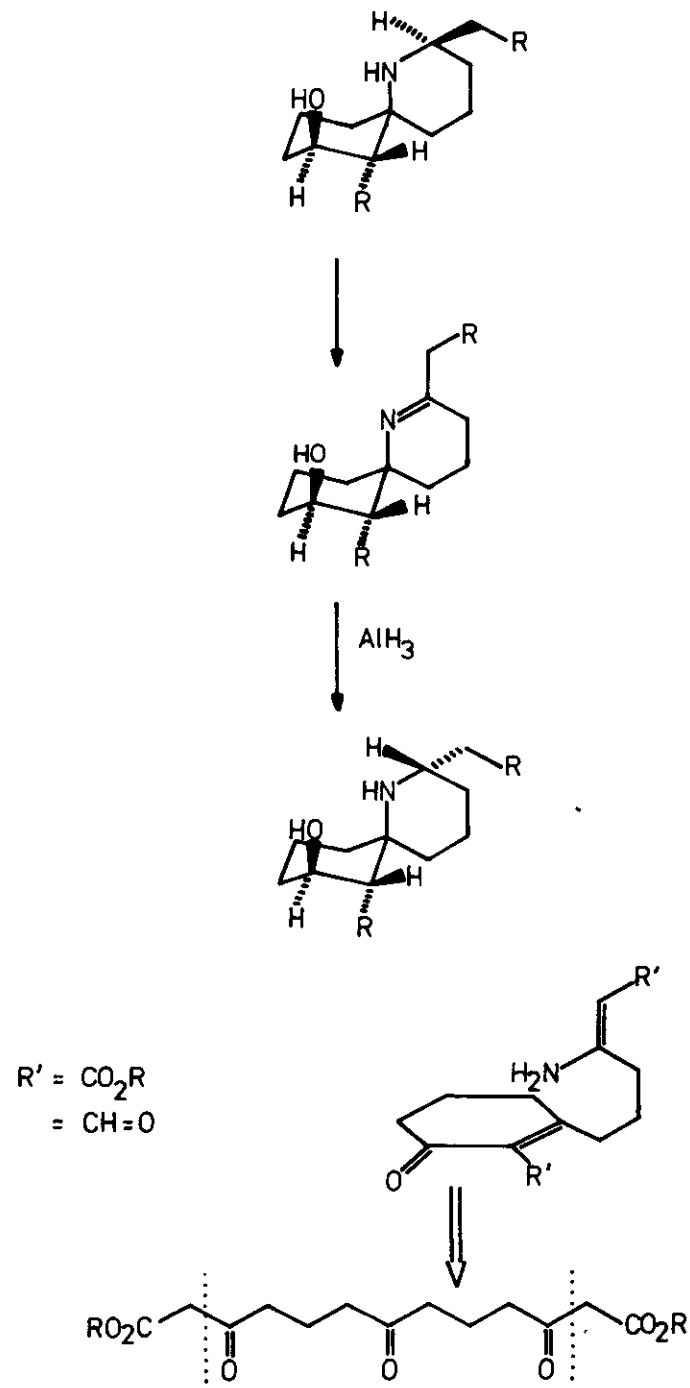
H
R
HN
HO
H
H
R
R
N
HO
H
H
R
AlH3
H
R
HN
HO
H
H
R
R'
R' = CO2R
= CH=O
H2N
O
R'
RO2C
O
O
O
CO2R

Chart XVII

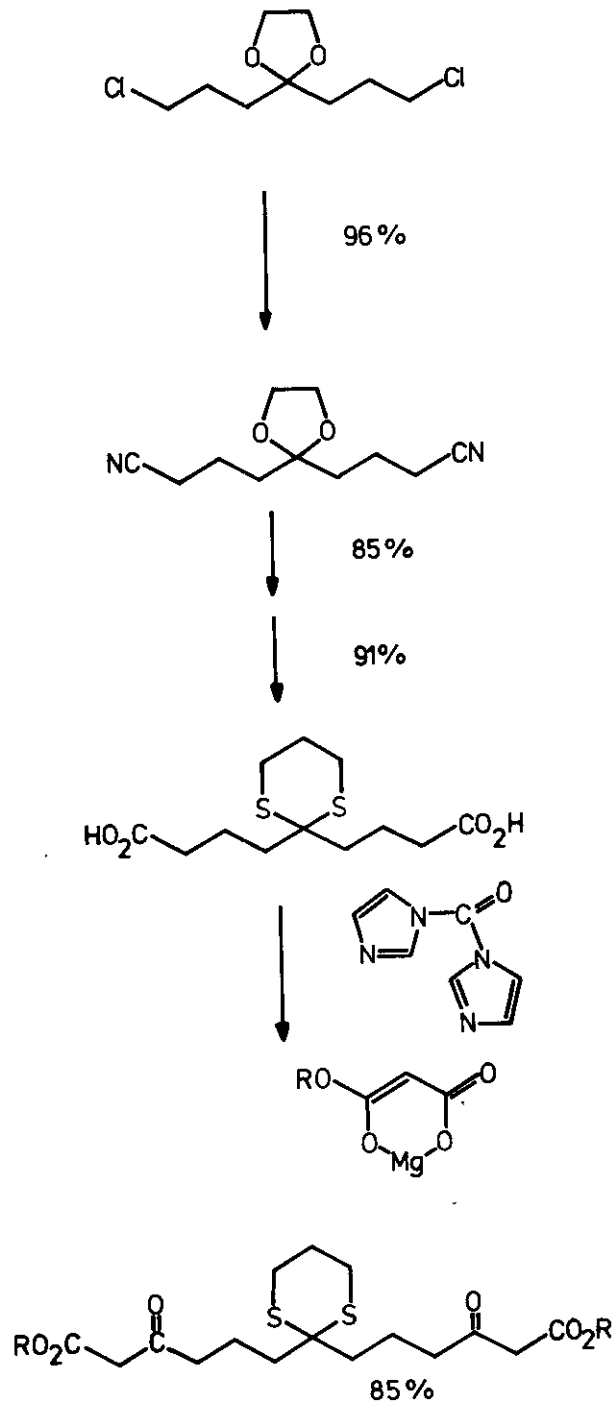

Chart XVIII