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A STEREOSELECTIVE ROUTE TO TRISUBSTITUTED OLEFINES FROM β - LACTONES

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In connection with the studies on olefinic cyclisations in progress, it was found necessary to develop new routes for the formation of a trisubstituted trans double bond[1]. Thus it has been found that trisubstituted β - lactones[2] can be cleaved stereoselectively to olefines[3] by refluxing in collidine.

For the preparation of the model system, the β - keto ester I, ($R_1 = n - C_4H_9$)[4] was converted to the dialkyl β - keto ester II,[5] which was reduced with sodium borohydride in methanol to give the hydroxy ester III, ($R_1 = R_2 = n - C_4H_9$) in almost equal proportions. This mixture of diastereoisomers was separated by preparative TLC on silica GF_{254} with 10% ethyl acetate/benzene and the pure diastereoisomers were obtained. The TLC slow diastereoisomer was hydrolysed and the pure acid IV was isolated. This was dissolved in pentane, treated with excess of Na_2CO_3 and methane sulphonyl chloride and stirred at room temperature for over 24 hrs. The intermediate mesyl derivative V underwent an internal nucleophilic displacement by the

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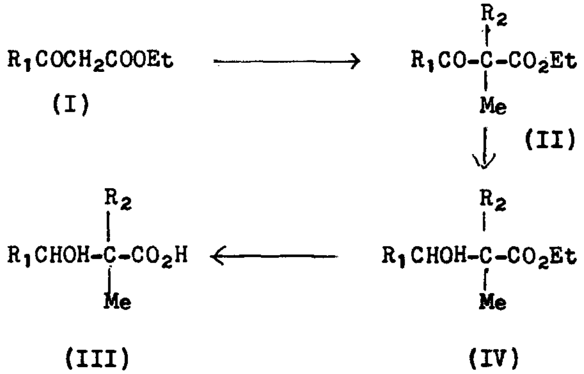
carboxylate group into the β - lactone, VI which could be purified by distillation under reduced pressure. On refluxing this in collidine under N_2 for 1 hr. the trans olefine VII(a) was obtained in a purity > 95%, as shown by the n.m.r. of the methyl protons[6] and v.p.c. analysis. Likewise similar processing of the TLC fast diastereoisomer resulted in the formation of pure cis - olefine X(a) via the mesylate VIII and lactone IX.



R_1COCH_2COOEt (I)

$R_1CO\text{-}\overset{R_2}{\underset{Me}{C}}\text{-}CO_2Et$ (II)

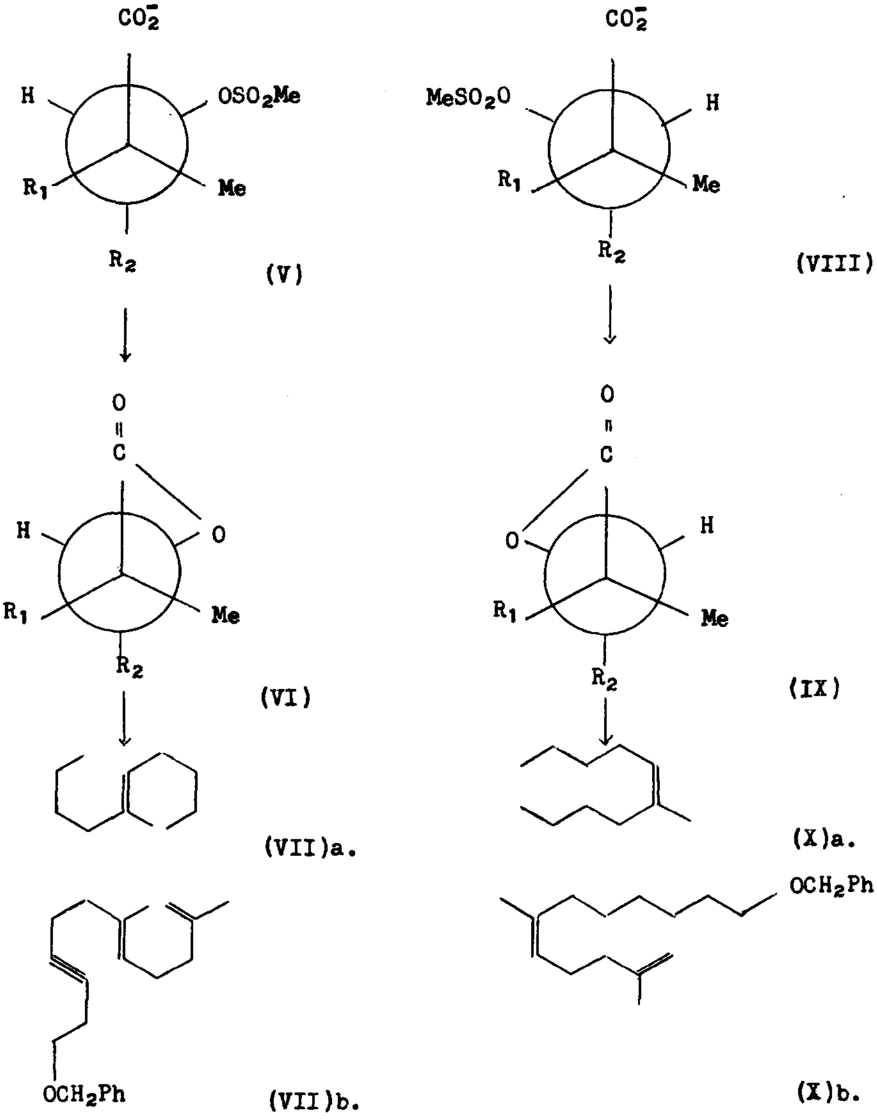
$R_1CHOH\text{-}\overset{R_2}{\underset{Me}{C}}\text{-}CO_2Et$ (IV)

$R_1CHOH\text{-}\overset{R_2}{\underset{Me}{C}}\text{-}CO_2H$ (III)

The keto ester I(b) was synthesised from 5-methylhex-5-enone by reaction with diethylcarbonate in the presence of NaH and the resulting ketoester[8] was alkylated with 6-benzyloxy-1-bromo-3-hexyne[7] and methyl iodide to IV(b). IV(b) was reduced with sodium borohydride and separated by TLC on silica GF_{254} with 5% ethyl acetate/benzene and converted to VII(b)[9] and X(b) as in the model system.

The above decomposition of β - lactones appears to be a general method for the formation of cis or trans - trisubstituted olefines. The yield from the hydroxy ester to olefine was 43%.

The methyl ester of II(a) could be hydrolysed by methanolic aqueous alkali at room temperature to the keto acid. Reduction of the potassium salt of the keto acid with potassium borohydride in the presence of KCl resulted in the



(V) (VIII)

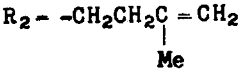
(VI) (IX)

(VII)a. (X)a.

(VII)b. (X)b.

Series (a) $R_1 = R_2 = n\text{-}C_4H_9$

(b) $R_1 = -CH_2CH_2C \equiv CCH_2CH_2OCH_2Ph$



$R_2 = -CH_2CH_2\underset{\displaystyle Me}{\underset{|}{C}} = CH_2$

formation of 70% of the TLC slow diastereoisomer which was estimated, after esterification with diazomethane as the methyl hydroxy ester. Similarly reduction of the potassium salt with potassium borohydride in the presence of LiCl resulted in the formation of 63% of the TLC fast isomer. By the above method of separation and processing the formation of pure trans - olefine or cis - olefine as the major product of the sequence can be effected.

Satisfactory analyses have been obtained for new compounds.

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