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PREPARATION OF 3-AZABICYCLO [3.2.0] HEPTENONES BY INTRAMOLECULAR [2+2] CYCLOADDITION

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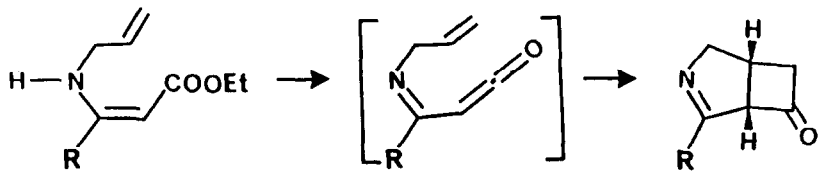
Abstract :
Pyrolysis of N-allyl enaminoesters is a general method for the stereoselective synthesis of 3-azabicyclo[3.2.0] heptenones ; the reaction involves a [2+2] intramolecular cycloaddition of an intermediate iminoketene.

Thermal intramolecular [2+2] cycloaddition of ketenes is a valuable method for the synthesis of bicyclo[3.2.0] heptanones[1]. In addition, it has been reported that molecules containing the 3-azabicyclo[3.2.0] heptane skeleton can be antifungal substances[2] or highly active compounds in the central nervous system[3]. Recently, we presented preliminary experiments on the access to 3-azabicycloheptenones 3 from allylenaminoesters 1 through the intramolecular [2+2] cycloaddition



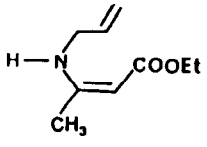
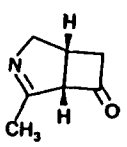
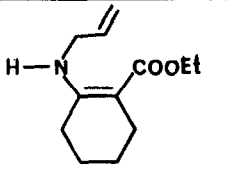
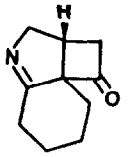
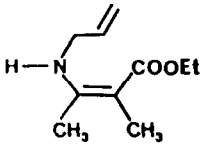
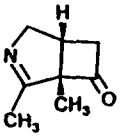
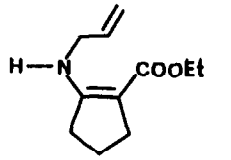
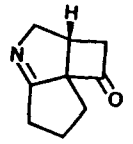
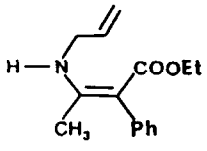
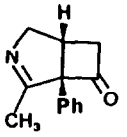
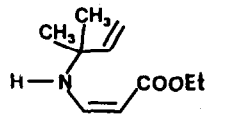
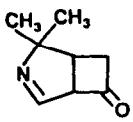
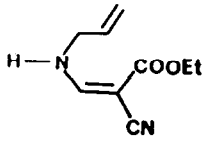
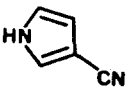
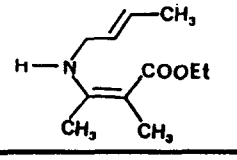
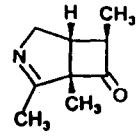
Scheme 1

of the intermediate iminoketene 2 (scheme 1)[4]. Similar approaches to heterobicyclo[3.2.0] skeletons have just been applied to oxygen[5,6] and nitrogen[6] derivatives. In this paper, we show that pyrolysis of N-allyl enaminoesters can be regarded as a simple and powerful method of preparative value for the synthesis of aza-polyheterocyclic compounds.

We observed that the best results in selectivity and yields (Table 1) were obtained when the pyrolysis was performed as follows: a solution of enaminoester in THF (2.10^{-3} mole.l^{-1} ; 2-7 g) was dropped through a hot vertical Pyrex tube (60 cm, 400°C) filled with Pyrex balls, at low pressure (10^{-2} torr) ; the cycloaddition product could be isolated by distillation under reduced pressure.

Four points emerge from table : (i) the high yield of products if we take into account the recovered starting material ; (ii) the generality of the method that can lead to highly strained

Table 1

Entry	Enaminoester	Product	Yield[a]	Entry	Enaminoester	Product	Yield
1			46(82)	5			b) 33(90)
2			62(75)	6			b) 32(87)
3			60(67)	7			67(78)
4			30(84)	8			46(59)

a) Yields of isolated products are calculated from starting material[7] *; the percentage of conversion is indicated in brackets. b) partial polymerization occurs during distillation.*

polycyclic derivatives (entries 5-6) ; the only exception is observed in entry 4 where a retro [2+2] cycloaddition takes place with the cyano derivatives ; (iii) the regioselectivity of this [2+2] cycloaddition (entries 1-8) ; (iiii) the stereospecificity of the reaction as indicated by the result of entry 8.

This reaction represents a short and efficient two step route to variously substituted 3-azabicycloheptenones from readily available β-ketoesters and allylamines.

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7. All new compounds have been fully characterized by IR, ^{1}H NMR (300 MHz), ^{13}C NMR.

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