

STEREOSELECTIVE SYNTHESSES OF TRANS- AND CIS-CINNAMIC ACID ESTERS
FROM THE PHENYLALANINE DERIVATIVES.

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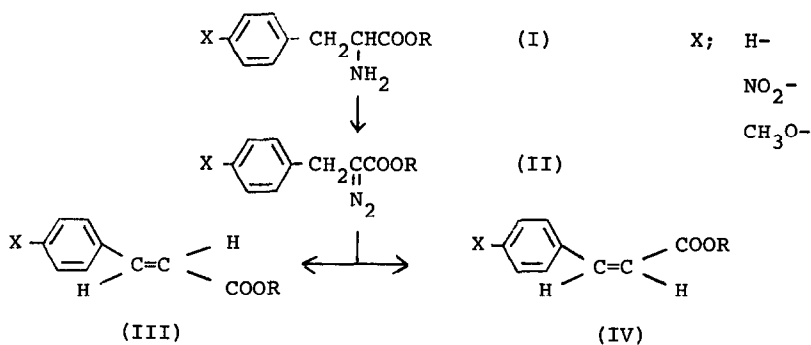
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In a previous study we described a very convenient method for preparation of various α -diazoesters from the corresponding α -amino acids.¹⁾ Reactivities and utilizations of these α -substituted- α -diazoesters have scarcely been examined, though those of ethyl diazoacetate have been widely known. We have been consequently investigating reactivities of the diazoesters and now wish to report stereoselective syntheses of trans- (III) and cis-cinnamic acid esters (IV) from α -diazo- β -phenyl-propionic acid esters (II), which are derived from the phenylalanine derivatives (I).



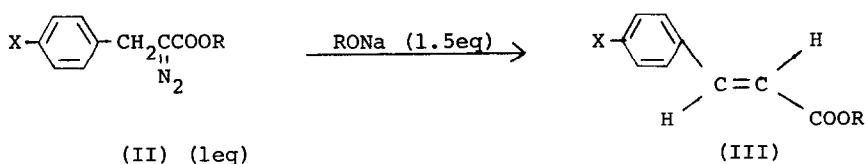
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Studies on enzymatic deamination of phenylalanine to trans-cinnamic acid are well documented,²⁾ but the chemical deaminations of this amino acid and its ester generally yield a variety of products.³⁾ Our detailed examinations on II, however, showed that III and IV could be obtained stereoselectively.

It is well known that 1,2-hydrogen shift to a carbene gives a mixture of isomeric olefins,⁴⁾ and the Cu-catalyzed or photochemical decomposition of II gives a mixture of III and IV. During the course of our investigations on reactivities of α -substituted- α -diazoesters with some basic and acidic reagents, we found that II was decomposed with sodium alkoxide to afford III stereoselectively and also that the decomposition of II in the presence of $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ and dicyclohexylcarbodiimide (DCCD) gave IV solely.

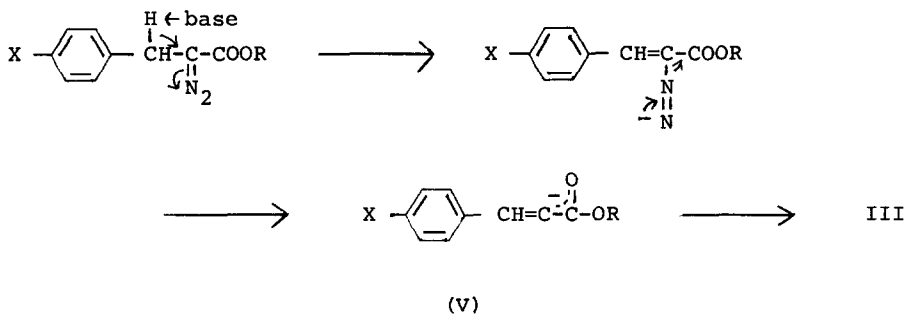
II was readily decomposed by the alkoxide in tetrahydrofuran with evolution of nitrogen to give III,⁵⁾ which was purified on TLC (silica gel, benzene). The yields are given in Table 1 together with reaction conditions employed in each case. The substituents at p-position of the aromatic ring influence the

Table 1.



II		Reaction conditions	III yield (%)
X	R		
H	CH ₃	r.temp. 3 hr.	72
NO ₂	C ₂ H ₅	-78° → r.temp. 1 hr.	59
CH ₃ O	C ₂ H ₅	50° 1.5 hr.	72

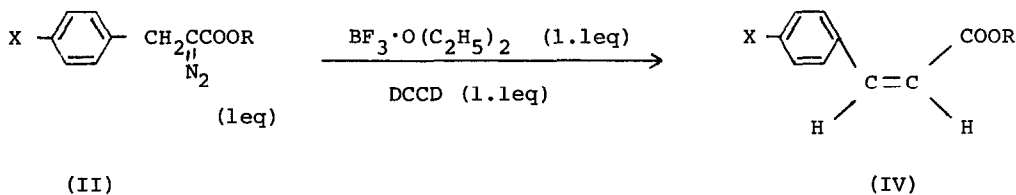
removability of hydrogen from the β -carbon and stronger reaction conditions are required in proportion to the increase of the electron density at the β -carbon. This result is tentatively rationalized by the following mechanism. The reaction may be initiated by the proton abstraction from the β -carbon with an alkoxide, followed by removal of a molecule of nitrogen to give the intermediate (V),



which is subsequently converted into thermodynamically stable III.

When II was treated with $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$ in the presence of DCCD in CH_2Cl_2 at $0-5^\circ$, IV⁶⁾ was obtained in a fairly good yield after purification on column chromatography (silica gel, benzene). The yields are given in Table 2. In the absence of DCCD, the reaction occurred even at -78° with vigorous evolution of nitrogen to give a complex mixture of several kinds of products. Assuming that

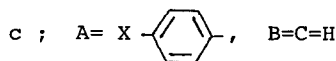
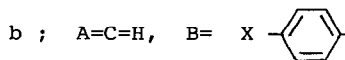
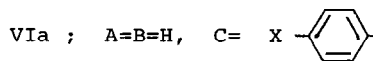
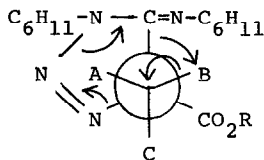
Table 2



II		IV
X	R	yield (%)
H	C_2H_5	80
NO_2	C_2H_5	68
CH_3O	C_2H_5	71

DCCD simply weakened the acidity of BF_3 , we attempted to use pyridine, $\text{C}_6\text{H}_5\text{N}=\text{CHC}_6\text{H}_5$ or $(\text{C}_6\text{H}_5)_3\text{P}$ instead of DCCD, but the results obtained were similar to that of the absence of DCCD. Therefore this reaction evidently needs DCCD. Though the mechanism of this reaction has not been clarified yet, the intermediate of the reaction is presumably a cycloaddition product, a 1,2,3-triazoline derivative (VIa,b or c).⁷⁾ Of the three possible conformations (VIa,b and c),

VIa must be most preferable because of the least steric repulsion between the aromatic ring and cyclohexane ring. The concomitant elimination of DCCD (as the BF_3 complex) and nitrogen from VIa thus gives IV stereoselectively.



References

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K. Koga, C.C. Wu and S. Yamada, *Chem. Pharm. Bull.*, 20, 1272, 1282 (1972).
- 4) W. Kirmse, "Carbene Chemistry", Academic Press, New York (1964).
- 5) The vpc of the crude reaction mixture showed that the content of IV in III was less than 1 %.
- 6) The vpc of the crude reaction mixture showed that the content of III in IV. was less than 2 %.
- 7) Such a cycloaddition between carbodiimides and diazomethane was already reported by Rotter; R. Rotter, *Monatshfte für Chemie* 47, 353 (1926).