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STEREOCHEMISTRY OF P-CHIRAL PHOSPHINYLACETIC ACID ESTERS I
ASYMMETRIC SYNTHESIS OF SUBSTITUTED ALKADIENE-1,2-CARBOXYLIC-1 AND γ-CHIRAL α,β-UNSATURATED CARBOXYLIC ACID ESTERS

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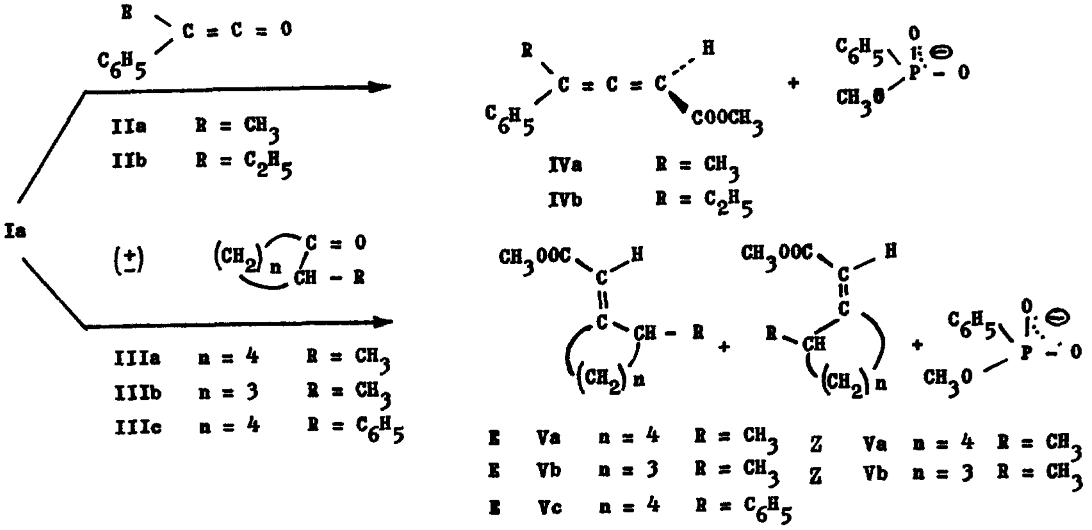
The Horner-Emmons reaction of phosphonate carbanions with carbonyl compounds is well known as an important synthetic approach to olefins[1].

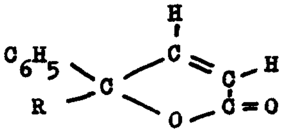
We turned our attention to the possibility of application of P-chiral phosphinylacetic acid ester /I/[2] for asymmetric synthesis of chiral compounds containing olefinic bond. It should be emphasised that in this particular case the group inducing chirality would not be a fragment of the product and its inductive effect would act first of all in the first step of the reaction involving formation of the intermediate oxyanion. The configurational dependence of the substrate /I/ and products would be an important argument in favour of the recognation of stereochemical nonbonding interactions taking place in the intermediates.

In this paper we present our first results concerning the asymmetric synthesis of chiral allene system /IV/ and γ-chiral α,β-unsaturated carboxylic acid esters /V/ in the reaction of carboanion /Ia/ obtained from optically active methyl O-methylphenylphosphinyl acetate $C_6H_5/CH_3O/P/O/-CH_2-COOCH_3$ /I/ with unsymmetric ketenes /IIa and IIb/ and with racemic 2-substituted cycloalkanones /IIIa, IIIb and IIIc/ respectively.



We obtained enantiomerically enriched methyl ester of 3-phenylbutadiene-1,2-carboxylic /IVa/ and 3-phenylpentadiene-1,2-carboxylic-1 /IVb/ acids, using the ketenes /IIa and IIb/[3] and /-//S/ /I/ $[\alpha]_D^{20}$ = - 20.8° [4] as starting materials. The ketenes have smoothly reacted with carbanion /Ia/ in benzene/ether solution at 20° for 3 hours. /IVa/b.p. 105-10°/0.05 mm Hg, /41% yield/, $[\alpha]_D^{20}$ = - 59.6°. /IVb/ b.p. 108-15°/0.1 mm Hg, /42% yield/, $[\alpha]_D^{20}$ = - 35.8°. The optical resolution of 3-phenylbutadiene-1,2-carboxylic-1 acid /IVa H/ and 3-phenylpentadiene-1,2-carboxylic-1 acid /IVb H/[5] and transformation of these acids into methyl esters with diazomethane, made possible to determine the optical purity of the esters prepared in the H-E reaction. It has been found that the ester /-//S//I/ induces the formation of the esters /IVa/ and /IVb/ of configuration /R/. The optical purity of /IVa/ and /IVb/ has not been less then 17% and 12% respectively.

The esters /IVa/ and /IVb/ of defined optical purity formed in asymmetric synthesis or by partial optical resolution were converted in acid solution[6,7] at room temperature into optically active lactones /IVa/ and/IVb/. /+//S//IVa/$[\alpha]_D^{20}$ = + 41.7°/12,2% opt. purity/ gave /+//R//VIa/ b.p. 125-30°/0.1 mm Hg, /78% yield/, $[\alpha]_D^{20}$ = + 30.9°. /-//R//IVb/ $[\alpha]_D^{20}$ = - 20.5/7.3% opt. purity/ gave /-//S//VIb/ b.p. 120-25°/0.1 mm Hg, /80% yield $[\alpha]_D^{20}$ = - 19.6°.



We found lactonization of the esters /IVa/ or /IVb/ to be less stereospecific then that of acids /IVa H/ or /IVb H/.

When carbanion /Ia/ obtained from optically active /I/ has been trated with racemic ketones /IIIa/, /IIIb/ in DME at 0°C for 16 hours an optically active mixture of E/Z isomers /Va/ and /Vb/ has been obtained. However in the case of the keton /IIIc/ only E isomer /Va/ has been formed. If /+//R//I/ $[\alpha]_D^{20} = + 20.8^\circ$ and /±/ /IIIa/ were starting materials a mixture of the products /+/E/Z /Va/ /72:28/ b.p. 94-6°/12 mm Hg, /71% yield/, was effectively separated into optically active /+/ E /Va/ $[\alpha]_D^{20} = + 4.5^\circ$ and /+/Z/Va/ $[\alpha]_D^{20} = + 15.7^\circ$ by preparative glc. In order to establish the configuration at the γ-carbon the pure isomers /+/E/Va/ and /+/Z/Va/ were transformed into respective 2-methylcyclohexanones by ozonolysis at - 70°. /+/E/Va/ $[\alpha]_D^{20} = + 4.5^\circ$ gave /-//R//IIIa/ $[\alpha]_D^{20} = - 1.44^\circ$/9.4% opt. purity/, while /+/ Z /Va/ $[\alpha]_D^{20} = + 15.7^\circ$ afforded /+//S//IIIa/ $[\alpha]_D^{20} = + 1.43^\circ$ /9.4% opt. purity/[8]. It is evident that /+/E/Va/ and /+/Z/Va/ obtained from the H-E reaction have opposite configuration. It is noticeable that /-//R//IIIa/ and /+//S//IIIa/ formed on degradation exhibit the same degree optical purity. When carbanion /Ia/ of /-//S//I/ $[\alpha]_D^{20} = - 20.8^\circ$ was reacted with /±//IIIb/ the optically active mixture of /+/E/Z /Vb/ /85:15/ b.p. 88-91°/12 mm Hg, /36% yield/ has been obtained. The isomers /+/ E /Vb/ $[\alpha]_D^{20} = + 19.3^\circ$ and /-/ Z /Vb/ $[\alpha]_D^{20} = - 21.8^\circ$ were separated by preparative glc. Degradation of pure /+//E//Vb/ resulted in the formation of /+/ /S/ 2-methylcyclopentanone $[\alpha]_D^{20} = 12.9^\circ$ [9].

Reaction of carbanion /Ia/ of /-//S//I/ $[\alpha]_D^{20} = - 20.8^\circ$ with /±//Vc/ produced only E /Vc/ isomer b.p. 108-10°/0.2 mm Hg, m.p. 41-42°, /67% yield/, $[\alpha]_D^{20} = - 1.58^\circ$. It is worth-while to notice that some amount of /-//S//IIIc/ m.p. 40-41°, $[\alpha]_D^{20} = - 5.5^\circ$/4.8% opt. purity/[10] was in this case recovered. Oxidation of /-/E/Vc/ gave /+//R//IIIc/ 2-phenylcyclohexanone $[\alpha]_D^{20} = + 32.3^\circ$ /28.0% opt. purity/.

On the basis of the presented experiments the following conclusion can be drawn out: the ester /+//R//I/ induces /R/ configuration /S/ configuration in 2-phenylcyclohexylideneacetic acid methyl ester /Vc/ at the γ-carbon in the E isomer of γ-chiral α, β -unsaturated acid ester /Va//Vb/ while /S/ configuration is induced in the Z isomer /Va/.

If the ozonolysis is fully stereospecific the optical purity of the ketones /IIIa//IIIb/ and /IIIc/ should correspond to the purity of the esters. There is no doubt that observed enantiomeric enrichment of the products is kinetically controlled. Attemped applications of the carbanion /Ia/ to the H-E reactions with /±/ camphor, /±/ 2-t-butylcyclohexanone, /±/ 2-methylcycloheptanone, /±/ 2-methyl-2-phenylcyclohexanone and 2,2-dimethylcyclohexanone have not resulted in the formation of corresponding α,β -unsaturated carboxylic acid esters.

The structure of all products is undoubtful and was established by means of IR, NMR and elementary analysis.

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