

A NEW SYNTHESIS OF TRANS-STILBENES

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A recent publication on a deamination reaction (1) prompted us to publish a preliminary communication about a new synthesis of stilbenes, which also comprises a deamination reaction, but in acidic conditions.

Very few cases of olefine synthesis produced by the action of acids on amides have been published (2). During research work carried out in this Laboratory, it was necessary to hydrolyze 1-(3,4-dimethoxy-phenyl)-2-phenyl-1-acetylamine ethane under acidic conditions. The product obtained was mainly trans 3,4-dimethoxystilbene and some of the expected amine. This stilbene was identified by its infrared and ultraviolet spectra (3). The oxidation of 3,4-dimethoxystilbene gave a mixture of benzoic and veratric acids, identified by paper chromatography (4).

This unexpected result led us to investigate the reaction more exhaustively. Therefore, other amides, with or without methoxy groups in the benzene rings, were subjected to hydrolysis with hydrochloric acid. The amides studied so far show that both the presence of the methoxy group in the benzene ring and the nature of the acyl group are important for the synthesis of stilbenes.

Acid hydrolysis of the formyl and acetyl derivatives of 1,2-diphenyl-ethylamine give only 1,2-diphenylethylamine hydrochloride. However, hydrolysis of 1-(p-anisyl)-2-phenyl-1-acetylamine ethane gives about 95% of 4-methoxy stilbene.

An increase in the number of methoxy groups promotes the elimination reaction, giving generally better yields of stilbenes and reducing the reaction time.

The nature of the acyl group has a strong influence on the reaction. Formyl derivatives give the amine hydrochloride on hydrolysis. Thus, acid hydrolysis of 1-(p-anisyl) 2-phenyl-1-formylamino-ethane gives the amine hydrochloride (5) as the main product and only traces of 4-methoxystilbene. On the other hand, benzoyl derivatives favour the elimination reaction. After refluxing 1,2-diphenyl 1-benzoylaminoethane with hydrochloric acid during 168 hours, about 12 % of trans stilbene is obtained.

Hydrochloric acid concentration is very important too, since stilbene formation increases with acid concentration. Very satisfactory yields were obtained using 1:1 (v/v) dilutions of HCl D: 1.19. Since only trans stilbenes are produced, the reaction seems to be stereospecific, of E₂ type.

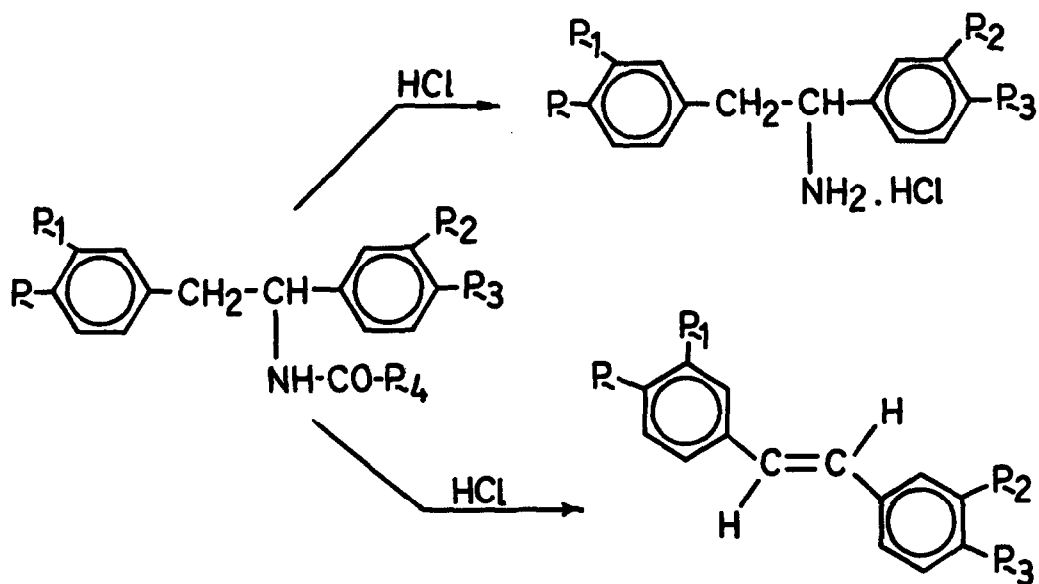


Table I gives the results obtained in some experiments.

TABLE I

AMIDES					STILBENES		Reflux. in hours
R	R ₁	R ₂	R ₃	R ₄	. %	m.p.	
H	H	H	H	H	--	--	
H	H	H	H	CH ₃	--	--	4 $\frac{1}{2}$
H	H	H	H	C ₆ H ₅	12.6	119-121°	168
H	H	H	OCH ₃	H	--	--	
H	H	H	OCH ₃	CH ₃	95.0	131-3°	4
H	H	OCH ₃	OCH ₃	H	traces		$\frac{1}{2}$
H	H	OCH ₃	OCH ₃	CH ₃	84.0	106-8°	1 $\frac{1}{2}$
OCH ₃	H	OCH ₃	OCH ₃	CH ₃	92.7	133-5° (a)	1
OCH ₃	OCH ₃	H	OCH ₃	CH ₃	97.5	133-5° (a)	1 $\frac{1}{4}$
OCH ₃	H	H	OCH ₃	CH ₃	32.5	196-8°	4
OCH ₃	H	H	OCH ₃	C ₆ H ₅	50.0	213-4° (b)	24
OCH ₃	OCH ₃	OCH ₃	OCH ₃	H	traces		2
OCH ₃	OCH ₃	OCH ₃	OCH ₃	CH ₃	93.7	151-3°	2

The stilbenes column (% and m.p.) refers to crude products.

a) Recrystallized from EtOH gave m.p.: 138.5-139° (Anal. calcd. for C₁₇H₁₈O₃: C, 75.5 H, 6.7; found: C, 75.3 H, 6.42) I.R. (nujol): 1613, 1515 (arom. conj.); 1266, 1152, 1139, 1025 (Ar-OCH₃); 961 ($\text{H}-\text{C}=\overset{\text{H}}{\text{C}}$); 840, 803 (1,2,4-trisubst. phenyl) and 822 cm⁻¹ (p-disubst. phenyl).

b) Recrystallized from EtOH.

Experimental conditions: The amide (2.5 g) suspended in conc. HCl (25 ml) and water (25 ml), was refluxed on an oil bath at 140° with stirring. At the end of the reaction the suspension was filtered while hot, and the solid washed three times with boiling water. If necessary the product was crystallized from boiling EtOH.

By concentrating the acid solution in a rotatory evaporator the amine hydrochloride was obtained.

Further investigation is being carried out at this laboratory to determine the scope of the reaction.

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