Synthesis of Pyrrolizidinediones from Cyclic N,N-Diacylamino Acids

Hans Jürgen BESTMANN,* Thomas MOENIUS, and Fouad SOLIMAN Institute of Organic Chemistry, University Erlangen-Nürnberg, Henkestraße 42, D-8520 Erlangen, FRG

Cyclic N,N-diacylamino acids can be converted by reaction with N-phenylketeniminylidenetriphenylphosphorane into pyrrolizidinediones.

The OH-group of carboxylic acids can be replaced by the ylide function¹⁾ on reaction of the acid with N-phenylketeniminylidenetriphenylphosphorane 2.²⁾ When cyclic N,N-diacylamino acids 1^{3} are connected with 2 in ethyl acetate (30 min stirring and subsequent 4 h heating under reflux) phosphonium ylides 3 are formed in 80-95% yield. Heating of 3 in refluxing toluene containing 5 vol% ethanol for several hours leads to elimination of phenylisocyanate 4, which reacts with ethanol to give the corresponding urethane. In some cases (see Table 1) the resulting acyl ylide 5 can be isolated after 6 h reaction time. Further heating causes formation of phenylizidinediones 6 via intramolecular Wittig reaction. The addition of catalytic amounts of benzoic acid is sometimes of advantage.⁴⁾



Asymmetric compounds of type 6 can also be synthesized by this method. Furthermore, the table indicates that the activation of the N-CO-group is of decisive importance for the ring closure.⁵⁾

R ¹	R ²	Absolut config.	Yield %	3 <u>Mp</u> a) °C	Yield %	5 <u>Mp</u> a) °C	Yield %	<mark>ь)</mark> 6 <u>Мр</u> °С	[α] ^{R T} _D °	React. time/h ^{e)}
	н	_	95	195	85	204	56	192	-	12
	CH ₃	S	85	145	-	-	60	203	+15,3 ^C) 12
\square	^{CH} 2 ^{-C} 6 ^H 5	S	87	134	-	-	60	141	+13,5 ^d) 12
\square	Н	-	81	199	84	185	28	123	-	200 ^{f)}
сн ₂ -сн ₂	сн ₃	S	88	165	78	147	19	56	+11,8 ^C) 240 ^{f)}

Table 1. Phosphonium ylides **3** and **5** and pyrrolizidinediones **6** obtained from **1** and **2** and via intramolecular Wittig reaction from **5**, respectively

a) Melting under decomposition. b) Relative to **3**. c) In methanol (c 0,5).

d) In THF (c 0,5). e) Reaction time for a solution of 3 in toluene.

f) A catalytic amount of benzoic acid is necessary to obtain cyclization.

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