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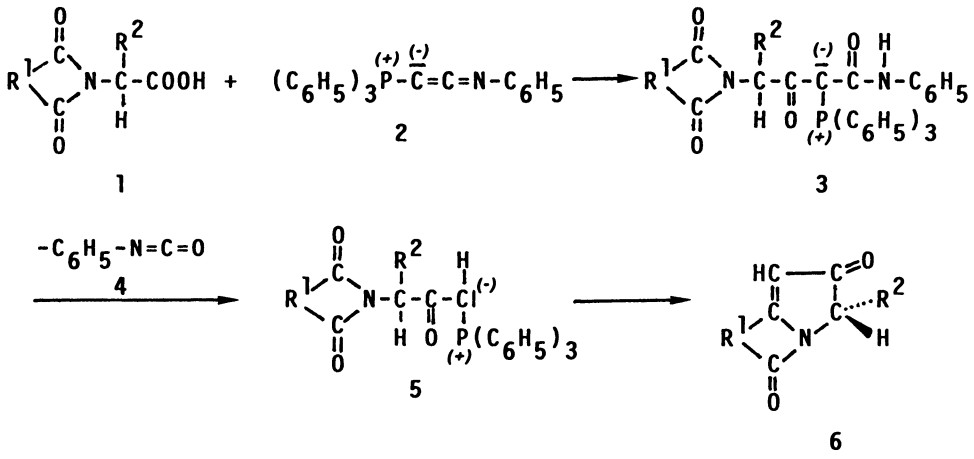
Synthesis of Pyrrolizidinediones from Cyclic N,N-Diacylamino Acids

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 function[1] 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 pyrrolizidinediones **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]

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

R^1	R^2	Absolut config.	**3** Yield %	**3** Mp[a] °C	**5** Yield %	**5** Mp[a] °C	**6** Yield[b] %	**6** Mp °C	$[\alpha]_D^{RT}$/°	React. time/h[e]
	H	-	95	195	85	204	56	192	-	12
	CH_3	S	85	145	-	-	60	203	+15,3[c]	12
	CH_2-C_6H_5	S	87	134	-	-	60	141	+13,5[d]	12
	H	-	81	199	84	185	28	123	-	200[f]
CH_2-CH_2	CH_3	S	88	165	78	147	19	56	+11,8[c]	240[f]

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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