Sulfur ylides

## 10.\* Modified method for the synthesis of pyrrolizine- and indolizinediones

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A modified method for the synthesis of derivatives of pyrrolizinedione and indolizinedione was proposed. The method is based on the intramolecular cyclization of keto-stabilized sulfur ylides generated *in situ* from diazo ketones and Me<sub>2</sub>S in the presence of  $Rh_2(OAc)_4$ .

**Key words:** keto-stabilized sulfonium ylides, diazo ketone, dimethyl sulfide,  $Rh_2(OAc)_4$ , intramolecular cyclization, 3-benzyl-1-methylthio-3*H*-pyrrole[2,1-*a*]isoindole-2,5-dione, 1-methylthio-3,4-dihydropyrido[2,1-*a*]isoindole-2,6-dione.

Earlier,<sup>2,3</sup> we have developed a method for the synthesis of pyrrolizinedione **1** and indolizinedione **2** through intramolecular cyclization of sulfur ylides **3**, which are derived from  $\alpha$ - and  $\beta$ -(*N*-phthaloyl)amino acids **4**. The method includes the conversion of *N*-protected amino acids **4** into acid chlorides, which react with CH<sub>2</sub>N<sub>2</sub> to give diazo ketones **5**. The latter are treated successively with HBr and Me<sub>2</sub>S to form sulfonium salts **6**, whose deprotonation yields the corresponding ylides **3** (Scheme 1).

It is known<sup>4</sup> that sulfur ylides can also be obtained immediately from diazo compounds by reacting them with sulfides in the presence of catalysts, usually Rh or Cu compounds. To simplify the scheme of preparing cyclization products 1 and 2 and increase their yields, we studied the intramolecular cyclization of sulfur ylides 3 generated



Reagents and conditions: *i*. SOCl<sub>2</sub>; *ii*. CH<sub>2</sub>N<sub>2</sub>; *iii*. HBr; *iv*. Me<sub>2</sub>S; *v*. NaOH, K<sub>2</sub>CO<sub>3</sub>, CHCl<sub>3</sub>; *vi*. BzOH, PhMe, 110 °C; *vii*. Me<sub>2</sub>S, Rh<sub>2</sub>(OAc)<sub>4</sub>, PhMe, 40 °C.

\* For Part 9, see Ref. 1.

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*in situ* from diazo ketones **5** and Me<sub>2</sub>S in the presence of  $Rh_2(OAc)_4$ . A mixture of diazo ketone **5** and Me<sub>2</sub>S with a catalytic amount of  $Rh_2(OAc)_4$  was heated in toluene at 40 °C until the diazo ketone was completely consumed (monitoring by TLC). Then a necessary amount of benzoic acid was added, and cyclization was carried out under reflux.

Thus, we shortened the original scheme by three steps and performed cyclization without isolating ylides from the reaction mixture. As a result, the yields of pyrrolizinedione 1 and indolizinedione 2 from the starting diazo ketones were increased by about 20% (from 41 to 63%for 1 and from 49 to 68% for 2).

## Experimental

The course of the reaction was monitored and the purity of the products was checked by TLC on Silufol UV-254 plates (visualization under UV light or by heating the plates with a sprayed solution of ninhydrin to 100-120 °C). The reaction products were isolated by column chromatography on silica gel.

 $Me_2S$  and BzOH (both high-purity grade) were used without additional purification. Toluene was refluxed over Na and distilled. The other solvents were purified by distillation. The catalyst  $Rh_2(OAc)_4$  was prepared according to the known procedure.<sup>5</sup> The starting diazo ketones were synthesized as described in Ref. 2.

3-Benzyl-1-methylthio-3*H*-pyrrolo[2,1-*a*]isoindole-2,5-dione (1) and 1-methylthio-3,4-dihydropyrido[2,1-*a*]isoindole-2,6-dione (2) (general procedure). Rhodium acetate  $Rh_2(OAc)_4$  (0.004 g, 0.009 mmol) was added in one portion to a stirred solution of diazo ketone 5 (2.05 mmol) and Me<sub>2</sub>S (1 g, 16.10 mmol) in 10 mL of anhydrous toluene. The crimson reaction mixture was stirred at 40 °C until the diazo ketone was completely consumed (TLC,  $CHCl_3-Me_2CO$  (9 : 1), visualization with ninhydrin). The solution gradually turned yellow. Then BzOH (0.25 g, 2.05 mmol) was added, and the resulting solution was refluxed for 1 h. The solvent was evaporated, and the products were isolated by column chromatography (AcOEt-hexane, 1 : 1). The yields of compounds 1 and 2 were 63 and 68%, respectively. The spectral characteristics of the products are consistent with the previous data.<sup>3</sup>

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