NEW REACTION OF KETOSTABILIZED SULFUR YLIDS. A CONVENIENT METHOD FOR THE PREPARATION OF PYRROLIZIDINEDIONES

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We have discovered a new reaction of ketostabilized sulfur ylids containing the phthalimide group. The reaction yields pyrrolizidinedione derivatives, which cannot be obtained by reported methods [1]. Bromoketones (II) were synthesized from N-phthalyl- α -amino acids according to a standard procedure [2]. The reaction of (II) with Me₂S gives sulfonium salts (III). Deprotonation of (III) gives sulfur ylids (IV). Heating (IV) in acetonitrile leads to the formation of the product of the intramolecular condensation (I) in 35-40% yield.



 $R \,=\, Me(a), \ CH_2C_6H_5(b), \ CH(CH_3)_2 \ (c).$

Since the IR and PMR spectra for all the intermediates (II), (III), (IV), and pyrrolizidinediones (I) are generally similar, we only present the data for compounds obtained from $L-\alpha$ -alanine.

 $\frac{1-\text{Bromo-3-phthalimido-2-butanone (IIa)}{2^3} \text{ was obtained in 65\% yield, mp 67-68°C, } [\alpha]_D^{2^3} = -33.9° (c 4.01, CHCl_3). IR spectrum (v, cm⁻¹): 1770, 1735, 1705, 1610. PMR spectrum (\delta, ppm): 1.58 d (J = 7 Hz, CH_3), 3.93 s (CH_2Br), 5.12 q (J = 7 Hz, CH), 7.73 s (C_6H_4).$

 $\frac{3-\text{Phthalimido-2-butanone-l-dimethylsulfonium bromide (IIIa)}{\text{mp 131-132°C. IR spectrum (v, cm⁻¹): 1770, 1735, 1705, 1610. PMR spectrum (<math>\delta$, ppm): 1.23 d (J = 7 Hz, CH₃), 2.58 s ((CH₃)₂S), 4.59 s (CH₂Br), 4.83 q (J = 7 Hz, CH), 7.37 s (C₆H₄).

 $\frac{3-\text{Phthalimido-2-butanone-l-dimethylsulfurane} (IVa)}{(c 1.07, CHCl_3)} \text{ was obtained in 90% yield, } [\alpha]_D^{23} = -74.5^\circ (c 1.07, CHCl_3). \text{ IR spectrum } (v, cm^{-1}): 1775, 1705, 1555. \text{ PMR spectrum } (\delta, ppm): 1.58 \text{ d} (J = 7 \text{ Hz}, CH_3), 2.83 \text{ s} ((CH_3)_2\text{S}), 3.65 \text{ s} (^{-}\text{CH}), 4.58 \text{ q} (J = 7 \text{ Hz}, CH), 7.77 \text{ m} (C_6\text{H}_4).$

 $\frac{1-\text{Thiomethy}1-3-\text{methy}1-3\text{H-pyrrol}[2,1-a]\text{izoindole}-2,5-\text{dione (Ia)} \text{ mp } 145-147\,^{\circ}\text{C}, \ [\alpha]_D^{23} = -3.1^{\circ} \text{ (c } 1.67, \text{ CHCl}_3\text{)}. \text{ IR spectrum } (\nu, \text{ cm}^{-1}): 1776, 1740, 1714, 1604. \text{ PMR spectrum } (\delta, \text{ ppm}): 1.67 \text{ d } (\text{J} = 7 \text{ Hz}, \text{CH}_3\text{)}, 2.54^{\circ}\text{s} \text{ (SCH}_3\text{)}, 4.40 \text{ q } (\text{J} = 7 \text{ Hz}, \text{CH}), 7.75 \text{ m and } 8.24 \text{ m } (C_6\text{H}_4\text{)}.$ Found: C 63.62; H 4.48; N 5.69; S12.98%; m/z 245. Calculated for $C_{1.3}\text{H}_{1.1}\text{NO}_2\text{S}:$ C 63.65; H 4.52; N 5.71; S 13.07%.

Analogously, L-phenylalanine gave (Ib), mp 129-131°C, $[\alpha]_D^{25} = -16.4^\circ$ (c 2.6, CHCl₃) and D,L-valine gave (Ic), mp 78-80°C. The structure of (Ic) was confirmed by x-ray diffraction structural analysis.

LITERATURE CITED

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