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CYCLIC AMINIMIDES CONTAINING THE 3-OXO-5-THIOXO-1,2,4-TRIAZOLIDINE SKELETON; REARRANGEMENTS OF 5-THIOURAZOLE DERIVATIVES

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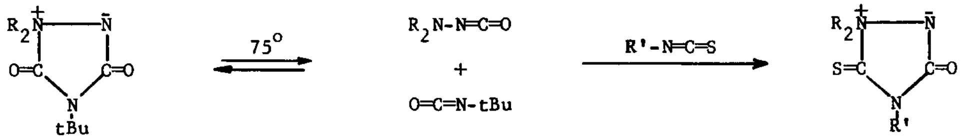
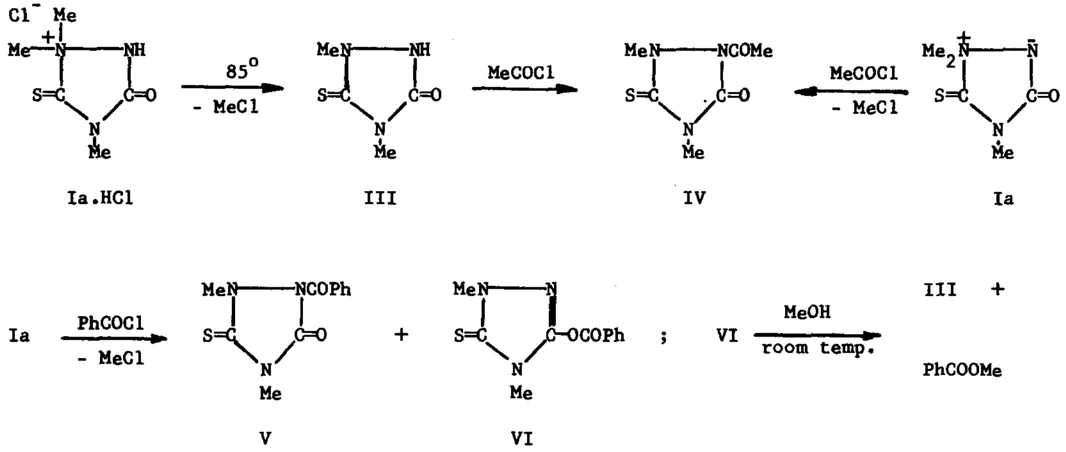
N,N-Dialkylaminoisocyanates, when generated in the presence of isothiocyanates, add to form cyclic aminimides of the type I,[1] 1,1,4-trialkyl-1,2,4-triazolidin-3-on-5-thion-1,2-aminimides, in good yields. For example, 0.03 mol of the aminoisocyanate precursor IIa, 1,1-dimethyl-4-tert.-butyl-1,2,4-triazolidin-3,5-dion-1,2-aminimide, and 0.09 mol of methyl isothiocyanate were heated to reflux in 25 ml of benzene for three hours to give a 86% yield of Ia, mp. 146-8° (dec)[2]:



IIa a : R = R' = Me. Ia

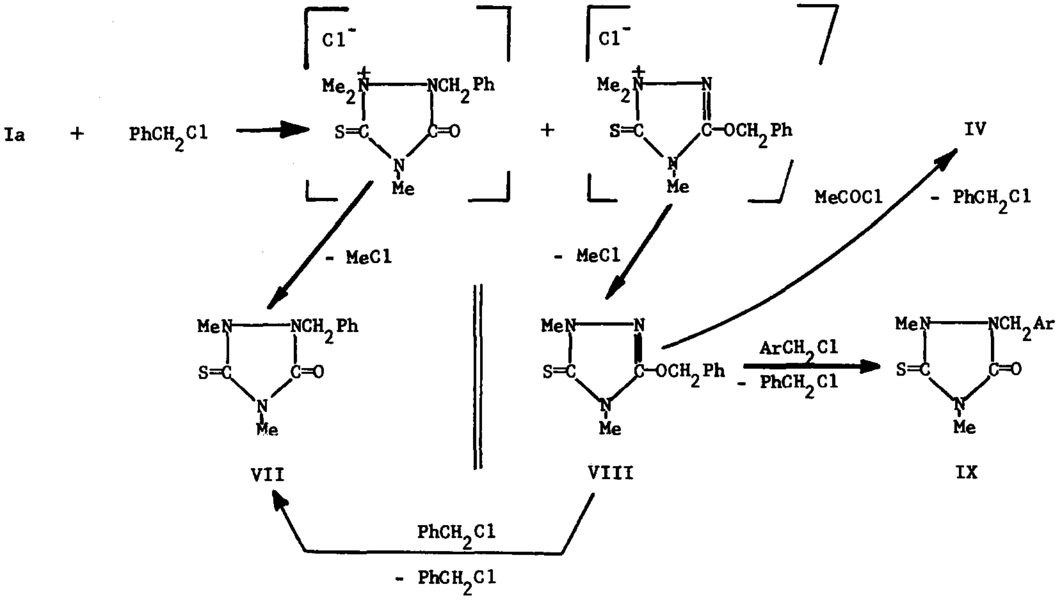
The aminimide Ia has a carbonyl stretching frequency of 1710 cm^{-1} ($CHCl_3$), nmr signals at δ3.42 (s, 6H) and 3.38 (s, 3H) ($CDCl_3$), and a parent m/e of 159. The mass spectrum shows metastable ion peaks for the loss of MeNCO and MeNCS, the former presumably due to a 1,2-methyl shift before fragmentation. Other mass spectral signals indicate the loss of NCO, HNCO, and Me_2N_2. Other aminimides of the type I were prepared analogously[2], including those with R = Et and R' = Me (mp 121-3°, dec); R = Et and R' = benzyl (mp 143-5° dec); R = Me and R' = benzyl (mp 125-7° dec). The aminimide Ia is used here to exemplify the chemistry of the compounds.

Anhydrous HCl in chloroform converts Ia to the hydrochloride, melting at 85° with evolution of MeCl to give 1,4-dimethyl-5-thiourazole[2] III, mp 183-5°. III was independently synthesized using Tisler's method[3]. Compound III and its acetyl derivative IV were identical with the corresponding synthetic samples. Treating Ia with acetyl chloride gave MeCl and IV (94% yield) in an exothermic reaction. Under controlled conditions at 90°, benzoyl chloride gave MeCl and two isomeric benzoyl-thiourazoles, the N-benzoyl derivative V[2] and the O-benzoyl derivative VI, which were separated by chromatography on silica gel. Two carbonyl bands at 1770 and 1712 cm^{-1} appear in the ir spectrum ($CHCl_3$) of V, one at 1774 cm^{-1} in that of VI. At room temperature, methanol reacts with VI to give III and methyl benzoate, while V is inert. Heating VI to 105° in C_2Cl_4 for 20 hrs converts it quantitatively to V. Thus, both spectra and reactivites agree with the structure assignments for V and VI[4]. The various acyl compounds presumably are formed via intermediate 1,1-dimethyltriazolidinium chlorides and displacement by Cl^- on one of the methyl groups on the ammonium nitrogen N-1.

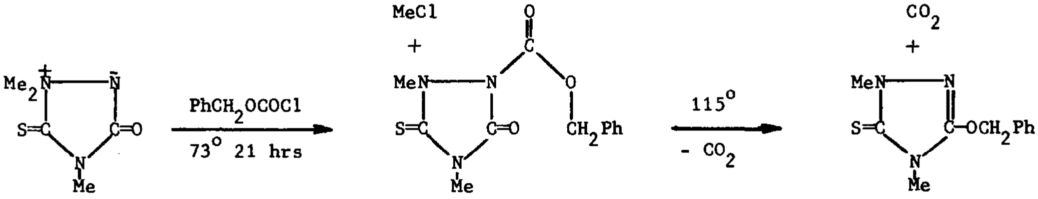


Treating Ia with benzyl chloride gave MeCl and two isomeric benzyl 1,4-dimethyl-5-thiourazoles[2], VII and VIII. The N-benzyl derivative VII, mp 94-5°, has a carbonyl absorption at 1725 cm^{-1} in its ir spectrum and the most prominent peaks in the mass spectrum correspond to the parent ion and to loss of the benzyl group. The O-benzyl derivative VIII, mp 161-2°, has no C=O absorption, but a strong ir band at 1660 cm^{-1}. Heated pure, the isomers do not interconvert, but heating with benzyl chloride transforms VIII into VII. Heating VIII overnight to 105° with o-methylbenzyl chloride (α-chloro-o-xylene) gives IX, 1,4-dimethyl-2-(o-methylbenzyl)-5-thiourazole[2] and one equivalent of benzyl chloride is liberated (determined by nmr). The N-(o-methylbenzyl)-thiourazole IX has a carbonyl band at 1730 cm^{-1} ($CHCl_3$) and mass and nmr spectra analogous to those of the corresponding 2-benzyl-1,4-dimethyl-5-thiourazole VII.

Treating VIII with acetyl chloride gave one equivalent of benzyl chloride and the 2-acetyl derivative IV. The reaction of Ia with o-methylbenzyl chloride gave IX and the O-benzyl derivative[2] X, which in turn gave VII on treatment with benzyl chloride. Thus, the reactions of the O-benzyl derivatives VIII or X with RCl or RCOCl attaches the electrophile to N-2 and the group on the oxygen on C-3 is lost as the chloride. The process resembles the Hilbert-Johnson reaction[5] as well as the conversion of tetrazole ethers to N-substituted tetrazolones[6]. Hassner has discussed various plausible mechanisms for the latter reaction[6] - it remains to be seen which one applies to our reaction.



Whatever the mechanisms of the acyl migration and the alkyl replacement reactions will ultimately turn out to be, the reactions can be combined to obtain pure O-benzyl compounds, such as VIII. Heating Ia with benzyl chloroformate for 21 hrs to 73° - a temperature sufficient to rearrange the O-acyl derivative of 1,4-dimethyl-5-thiourazole to the N-acyl compound - gave MeCl and benzyl 1,4-dimethyl-5-thiourazol-2-carboxylate[2] (XI). Heating this in C_2Cl_4 to 115° resulted in the evolution of CO_2 and the formation of VIII which, in the absence of an electrophile, is stable at that temperature.



Ia XI VIII

Compound XI has carbonyl absortions at 1806 and 1765 cm^{-1} (CHCl$_3$), the expected nmr spectrum and a mass spectrum showing the parent m/e peak of 279 as well as fragments corresponding to loss of CO$_2$ (formation of VIII), CO$_2$ + CH$_2$Ph, CH$_2$PH, Ph, MeNCS, MeNNCO, CO$_2$, and MeN$_2$.

Thermal rearrangements of Ia are presently under investigation.

References and Notes

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