Tetrahedron Letters,Vol.26,No.37,pp 4475-4478,1985 0030-4039/85 $3.00 + .00
Printed in Great Britain

β-LACTAMS VIA PHOTOCHEMICAL REACTION OF MONOTHIOIMIDES

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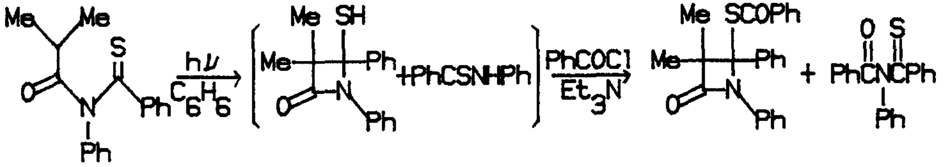
Summary: Photolysis of acyclic monothioimides gave β-lactams and thioamides via Type II reaction involving γ-hydrogen abstraction by thiocarbonyl group.

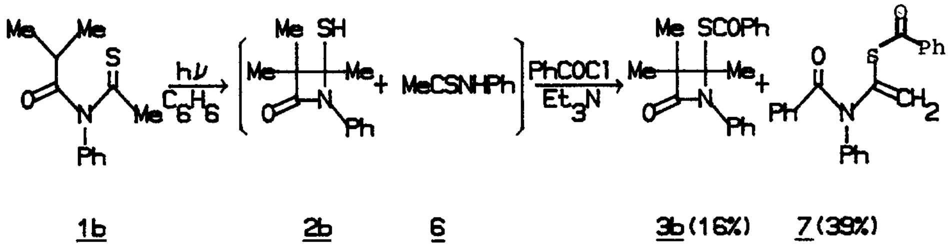
Photochemical reactions of thioketones and thioesters were well studied.1) However, those of thiocompounds corresponding to amides or imides are a little.2) Previously we reported some types of photochemical reactions of acyclic mono- or dithioimides, such as, δ-hydrogen abstraction of N-thioacyl(thio)ureas,3) [2+2]photocycloaddition of N-thiobenzoylmethacrylamides,4) and β-hydrogen abstraction of monothioimides. Now we wish to report a photochemical synthesis of β-lactams involving γ-hydrogen abstraction of acyclic monothioimides.5)

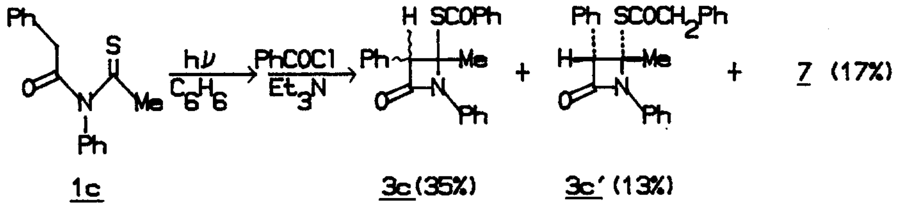
When N-isobutyroyl-N-phenylthiobenzamide (1a) was irradiated in benzene with a 1kw high pressure mercury lamp under argon, ir and nmr spectrum of the reaction mixture indicated the formation of β-lactam (2a) and thiobenzamide (4). The β-lactam was too unstable to isolate as such. Benzoylation of the reaction mixture with benzoyl chloride and triethylamine gave S-benzoyl β-lactam (3a) in 29% and N-thiobenzoyl-N-phenylthiobenzamide (5) in 70%. The formation of 5 was reasonably explained in terms of benzoylation of 4 which was produced by Type II cleavage of 1a. Photolysis of the monothioimide (1b)



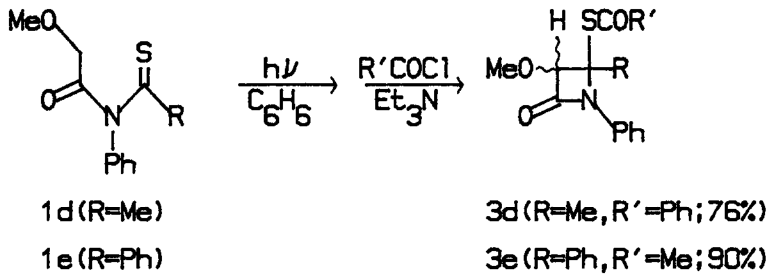
1a 2a 4 3a(29%) 5(70%)

followed by benzoylation gave the β-lactam 3b in 16% and 7 in 39%. The formation of 7 from 6 was confirmed by the fact that 7 was independently synthesized from 6 by benzoylation. In the case of 1c, S-benzoyl β-lactams (3c, about 1:1 mixture of stereoisomers), S-phenylacetyl β-lactam (3c'), and 7 were obtained in the respective yields of 35%, 13%, and 17%.[6)]

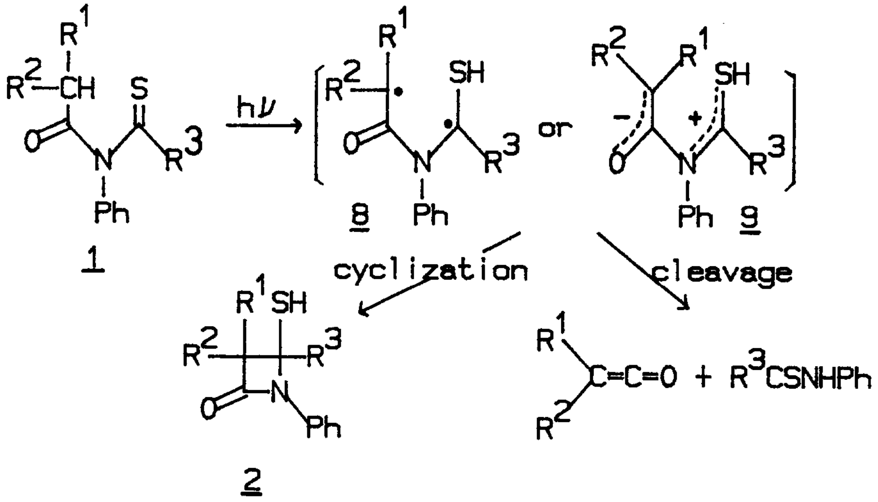




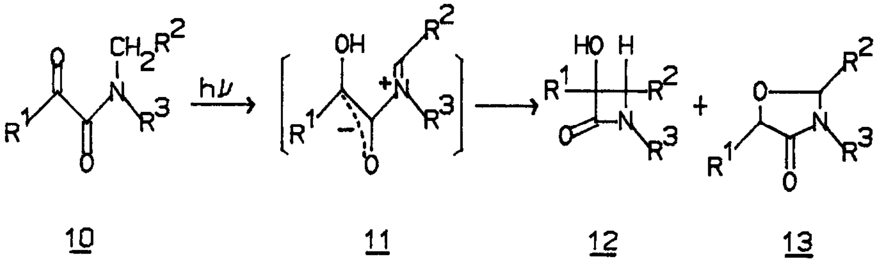
Photolysis of methoxy acetyl derivative (1d) gave β-lactam (3d) in high yield (76%) in the same manner. In this case, only cis isomer was obtained.[6)] Photolysis of 1e followed by acetylation with acetyl chloride and triethyamine gave S-acetyl β-lactam (3e) as a mixture of two stereoisomers (cis, 63% : trans, 27%) in 90% yield.



For the mechanism, Type II reaction is postulated as shown below. The intermediacy of the zwitterion 9 is included by the following reason. Previously we reported the photochemical reaction of α-oxoamides (10) which gave β-lactams (12) and oxazolidinones (13) via zwitterionic intermediate



11.[7] Zwitterion 9 resembles 11. Zwitterion 9 may be more stable than 11 because of the sulfur atom at cation center and the absence of a hydroxy group at the anion center as compared with zwitterion 11. The formation of the ketenes (Type II cleavage products) was supported by the fact that S-phenylacetyl β-lactam (3c') was obtained in the photolysis of 1c. For the formation of 4 and 6, direct homolysis of C-N bond of the monothioimide (1) could not be excluded. In the present reaction, Type II cyclization occurred as a main process. On the other hand, Mazzocchi et al. reported the photochemistry of acyclic imides.[8] The imides have been shown to undergo Type II eliminations across the imide moiety in addition to those on the C-alkyl chain and α-cleavage reaction. The differences in the photochemical behavior between acyclic imides and acyclic monothioimides can not be explained at present.



In conclusion, acyclic monothioimides undergo photochemical γ-hydrogen abstraction to produce β-lactams (Type II cyclization products), ketenes, and thioamide (Type II cleavage products). The present reaction provides not only the first example of γ-hydrogen abstraction of thioimide derivatives but also a useful synthetic method of some β-lactams possessing sulfur atoms at the C-4 possition.

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(Received in Japan 30 April 1985)