Tetrahedron Letters,Vol.25,No.51,pp 5917-5920,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

INTRAMOLECULAR AMIDOSELENATION LEADING TO LACTAMS BY THE REACTION OF N-ALKYLALKENAMIDES WITH BENZENESELENENYL CHLORIDE[1]

Akio Toshimitsu,* Keiji Terao, and Sakae Uemura

Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan

The reaction of N-alkylalkenamides (1)~(4) with benzeneselenenyl chloride affords γ- or δ-lactams (7)~(10) in good to excellent yields through the intramolecular attack of the nitrogen atom of the amide group on episelenonium ion intermediates.

Organoselenium-induced cyclization of olefinic alcohols has been extensively studied to produce cyclic ethers.[2] Analogous cyclization of olefinic acids has also been studied to afford lactones[3] by the formation of alkyl carbon-oxygen bond. These reactions have been utilized in the syntheses of natural products and related compounds.[4] On the other hand, organoselenium-induced cyclization by the formation of carbon-nitrogen bond has so far been limited to the reactions of olefinic urethanes[5] or 1-aza-4-cyclooctene[6] with organoselenium reagent to afford pyrrolidine or piperidine derivatives. The incorporation of carbonyl group in the cyclic system, namely, the formation of lactams has not yet been reported. In view of the important role of lactams, for instance, in the field of biologically active compounds, we would like to describe here the first example of organoselenium-induced cyclization leading to lactams by the reaction of N-alkylalkenamides with benzeneselenenyl chloride.

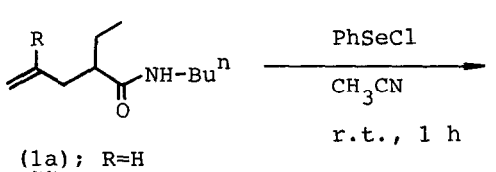
In a typical reaction, benzeneselenenyl chloride (1 mmol) was added to a solution of N-butyl-2-ethyl-4-pentenamide (1a) (1 mmol) in acetonitrile (10 ml) and the resulting solution was stirred at ambient temperature for 1 h. After the usual work-up, N-butyl-α-ethyl-δ-(phenylseleno)-γ-valerolactam (7a) (0.87 mmol; 87%) was isolated in a pure form by column chromatography [alumina Woelm B (type W 200) activity grade V]. Similarly γ-lactam (7b) and δ-lactam (8) were produced from 1b and 2 respectively in isolated yields of 94% and 73%.

These lactams were produced by the Markovnikov type attack of a nitrogen atom of the amide group on episelenonium ion intermediates. Although 7a and 7b were found to be mixtures of stereoisomers (1:1), 8 consisted of one stereoisomer (by ^{13}C n.m.r.). A large coupling constant between methine protons in 8 (7.8 Hz) indicates that phenylseleno and phenyl substituents are both on pseudoequatorial positions. The trans relation of phenylseleno and phenyl substituents (erythro configuration) in 8 is a result of trans-addition of phenylseleno and amide groups to the trans cinnamyl moiety. We tentatively assigned the pseudoequatorial configuration of the ethyl group in 8 considering the thermodynamical stability.

When the reaction was applied to the amide possessing cyclic alkene (3), a stereoisomeric mixture of γ-lactams possessing bicyclo[3.3.0] skeleton, (9), was produced in 73% yield. The configuration of phenylseleno group in 9 was assigned as exo, based on the trans-stereoselectivity of the amidoselenation reaction. In the case where olefinic lactam (4) was used as a starting material, bicyclic lactams having bridgehead nitrogen atom, (10a) + (10b), were produced in 91% yield. Major isomer (3:1) was tentatively assigned as 10a which would be free from the steric interaction between the (phenylseleno)-methyl group and C-3 hydrogen.

In the amidoselenation reactions already reported by us[1] and others[7], a cyano group was used as a nucleophile which was afterward hydrolysed to give the amide functional group. The formation of lactams described herein provides the first example of the reaction of amide with episelenonium ion to form the nitrogen-carbon bond. The substituent on a nitrogen atom plays an important role, as N-phenyl analogue of 1a, namely 5, did not afford a lactam by the reaction with benzeneselenenyl chloride. The substituent on carbon atoms between the carbonyl group and double bond also plays an important role. The formation of a lactam was not detected by the reaction of benzeneselenenyl chloride with 6 which possessed no substituent on these carbons.

All of the lactams containing the phenylseleno group thus prepared were unstable to silica-gel and decomposed during the attempted thin layer and column chromatography. It was necessary to use aluminium oxide chromatography for the monitoring the reaction and also for the isolation of 7~10.

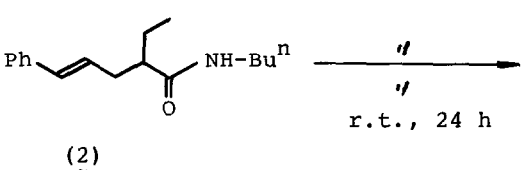


(1a); R=H

(1b); R=Me

(7a); R=H 87% $\nu_{C=O}$ 1705 cm^{-1}

(7b); R=Me 94% $\nu_{C=O}$ 1705 cm^{-1}



(2)

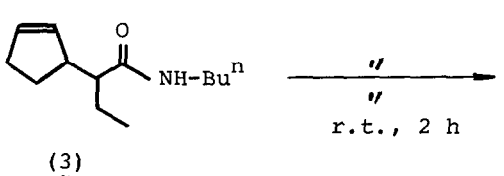
(8) 73%

$\nu_{C=O}$ 1645 cm^{-1}

δ_H (100 MHz)

3.43(1H, ddd, J=10.3, 7.8, 3.9 Hz)

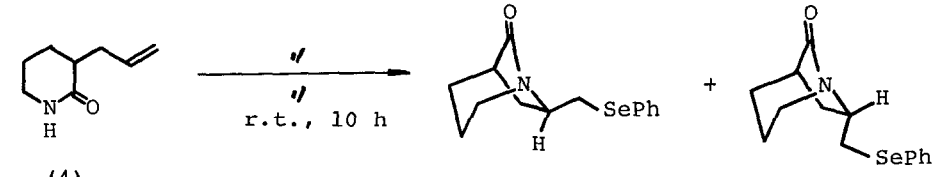
4.49(1H, d, J=7.8 Hz)



(3)

(9) 73% (77:23)

$\nu_{C=O}$ 1705 cm^{-1}

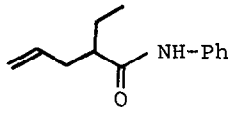


(4)

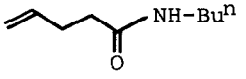
(10a)

(10b)

91% (75:25)



(5)



(6)

As alkenamides, (1)~(4), are easily prepared by the allylation of amides, this selenium-induced cyclization reaction provides a convenient method for the conversion of amides to lactams.

Acknowledgement One of the authors (A.T.) is grateful to the Ministry of Education, Science, and Calture, Japan for financial support to this work (Grant-in-Aids for Encouragement of Young Scientist, No59750671).

References

1. Amidoselenation reaction; Part IV.
   Part I; A.Toshimitsu, T.Aoai, S.Uemura, and M.Okano, J. Chem. Soc., Chem. Commun., 1980, 1041.
   Part II; A.Toshimitsu, H.Owada, T.Aoai, S.Uemura, and M.Okano, ibid., 1981, 546.
   Part III; A.Toshimitsu, T.Aoai, H.Owada, S.Uemura, and M.Okano, J. Org. Chem., 46, 4727(1981).
2. (a) K.C.Nicolaou, R.L.Magolda, W.J.Sipio, W.E.Barnette, Z.Lysenko, and M.M.Joullie, J. Am. Chem. Soc., 102, 3784(1980).
   (b) D.L.J.Clive, G.Chittattu, and C.K.Wong, Can. J. Chem, 55, 3894(1977).
   (c) D.L.J.Clive, G.Chittattu, N.J.Curtis, W.A.Kiel, and C.K.Wong, J. Chem. Soc., Chem. Commun., 1977, 725.
   (d) R.M.Scarborough,Jr., A.B.Smith III, W.E.Barnette, and K.C.Nicolaou, J. Org. Chem., 44, 1742(1979).
   (e) A.Toshimitsu, T.Aoai, S.Uemura, and M.Okano, ibid., 46, 3021(1981).
3. (a) K.C.Nicolaou, S.P.Seitz, W.J.Sipio, and J.F.Blount, J. Am. Chem. Soc., 101, 3884(1979).
   (b) D.L.J.Clive, C.G.Russell, G.Chittattu, and A.Singh, Tetrahedron, 36, 1399(1980).
4. (a) K.C.Nicolaou, W.E.Barnette, and R.L.Magolda, J. Am. Chem. Soc., 103, 3480(1981).
   (b) J.D.White, S.C.Choudhry, and M.-c.Kang, Tetrahedron Lett., 25, 3671 (1984).
5. (a) D.L.J.Clive, C.K.Wong, W.A.Kiel, and S.M.Menchen, J. Chem. Soc., Chem. Commun., 1978, 379.
   (b) K.C.Nicolaou, D.A.Claremon, W.E.Barnette, and S.P.Seitz, J. Am. Chem. Soc., 101, 3704(1979).
   (c) D.L.J.Clive, V.Farina, A.Singh, C.K.Wong, W.A.Kiel, and S.M.Menchen, J. Org. Chem., 45, 2120(1980).
   (d) R.R.Webb II and S.Danishefsky, Tetrahedron Lett., 24, 1357(1983).
6. S.R.Wilson and R.A.Sawicki, J. Org. Chem., 44, 287(1979).
7. A.Bewick, D.E.Coe, G.B.Fuller, and J.M.Mellor, Tetrahedron Lett., 21, 3827 (1980).

(Received in Japan 6 September 1984)