Tetrahedron Letters, Vol.22, No.25, pp 2411 - 2412, 1981
Printed in Great Britain

0040-4039/81/252411-02$02.00/0

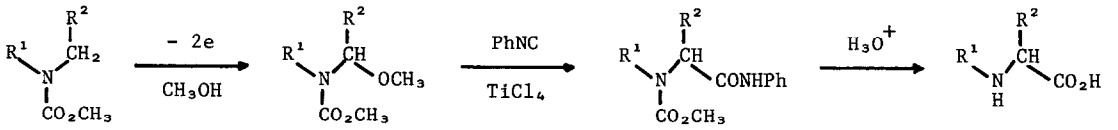
A NEW SYNTHETIC METHOD OF α-AMINO ACIDS FROM α-METHOXYURETHANES[1]

Tatsuya Shono,* Yoshihiro Matsumura, and Kenji Tsubata
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Sakyo, Kyoto 606, Japan

Reaction of α-methoxyurethanes with phenylisocyanide gave the corresponding amides of α-amino acid in reasonable yields.

As a part of our continuing study[2] on the synthetic application of α-methoxyurethanes (**2**) being easily obtainable by the anodic oxidation of urethanes (**1**) in methanol,[3] we have found that in the presence of a Lewis acid catalyst, phenylisocyanide reacts with **2** to afford α-amino acid derivatives **3** (Scheme 1). A recent communication[4] describing the synthesis of α-amino cyanides from α-methoxyamides and trimethylsilylcyanide prompted us to report our results.

Scheme 1

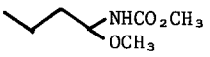
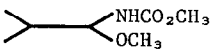
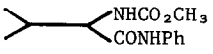
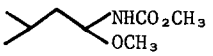
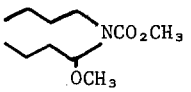
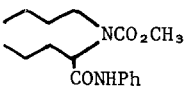
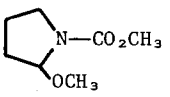
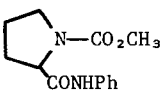
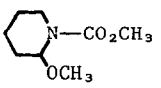
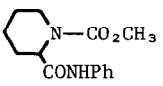
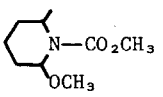
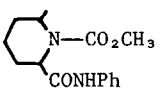
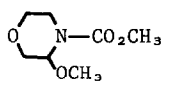
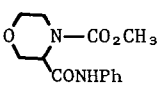
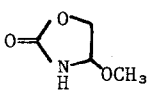
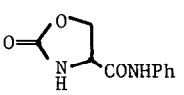
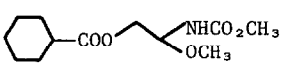
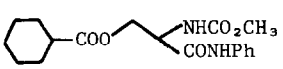


1 **2** **3** **4**

The synthesis of valine is shown below as a typical example. To a stirred solution of titanium tetrachloride (5 mmol) in methylene chloride (10 ml) was added a solution of **2** (R^1 = H, R^2 = i-Pr) (5 mmol) in methylene chloride (3 ml) at - 70 °C. After the reaction mixture was stirred for 5 minutes, phenylisocyanide (6.8 mmol) was added, and the reaction was completed after the reaction mixture was allowed to stand for 3 hr at - 70 °C. Then, diluted hydrochloric acid was added into the reaction mixture and the organic layer was extracted with methylene chloride. Isolation of **3** (R^1 = H, R^2 = i-Pr) was achieved by column chromatography (82% yield). The conversion of **3** to **4** was accomplished as follows. Hydrolysis of **3** (R^1 = H, R^2 = i-Pr) by refluxing it in 47% hydrobromic acid for 4 hr afforded *d,l*-valine in a 63% yield. Other results are summarized in Table I.[5]

Since a variety of α-methoxyurethanes can easily be synthesized by the anodic oxidation of urethanes, the synthesis of other essential amino acids is achievable by this method.

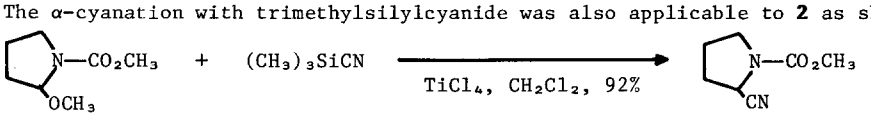
Table I. Reaction of α-Methoxyurethanes with Phenylisocyanide.

Run	**2**	Yield of **2** (%)	**3**	Yield of **3** (%)
1.		50		64
2.		70		82[a]
3.		77		72[b]
4.		75		49
5.		80		64
6.		86		73
7.		69		50
8.		55		48
9.		89		34
10.		39		49

a) Hydrolysis gave valine in a 63% yield. b) Leucine was obtained by hydrolysis in a 62% yield.

References and Notes

1. Electroorganic Chemistry. 52.
2. T. Shono, Y. Matsumura, and K. Tsubata, *J. Am. Chem. Soc.*, in press.
3. T. Shono, Y. Matsumura, and H. Hamaguchi, *J. Am. Chem. Soc.*, **97**, 4264 (1975).
4. V. Asher, C. BeCu, M. J. O. Anteunis, and R. Callens, *Tetrahedron Lett.*, **22**, 141 (1981). The α-cyanation with trimethylsilylcyanide was also applicable to **2** as shown below.



5. Spectroscopic data and elemental analyses of all the products coincided with assigned structures.

(Received in Japan 26 March 1981)