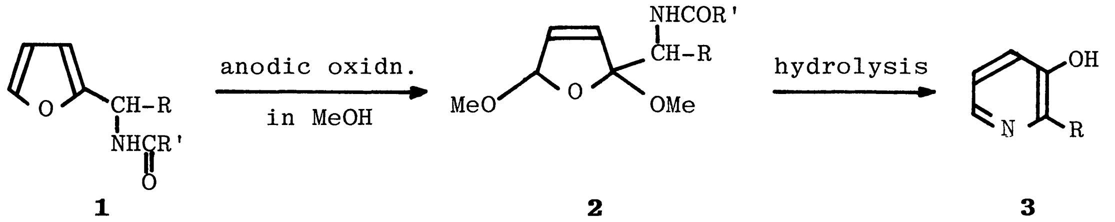
CHEMISTRY LETTERS, pp. 1121-1124, 1981.

ONE STEP SYNTHESIS OF α-AMINOALKYLFURANS AND ITS APPLICATION TO A FACILE SYNTHESIS OF PYRIDOXINE (VITAMIN B_6)[1]

Tatsuya SHONO,* Yoshihiro MATSUMURA, Kenji TSUBATA, and Jiro TAKATA
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Sakyo, Kyoto 606

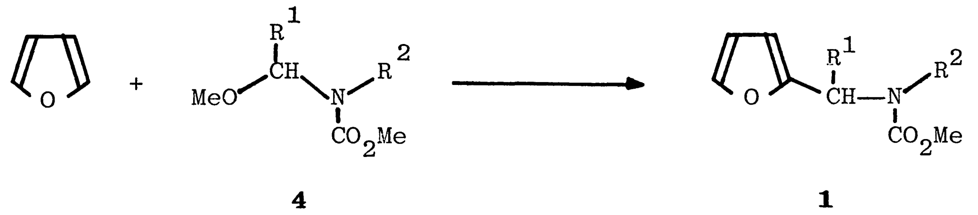
One step synthesis of α-aminoalkylfurans was achieved by the reaction of α-methoxyurethanes or α-methoxyamides with furan. This method was applied to an efficient synthesis of pyridoxine.

One of the remarkable potentialities of α-aminoalkylfurans (**1**) as the starting materials in organic synthesis has been shown in the preparation of 2-alkyl-3-hydroxypyridine derivatives as is exemplified in eq. 1.[2] However, the hitherto known troublesome synthetic methods of **1** make the synthesis of **3** according to the eq. 1 unpractical.



(1)

In our continuing study on the reaction of α-methoxyurethanes (**4**) with a variety of nucleophiles,[3] we have found that the acid-catalyzed reaction of **4** with furan leads to the one-step synthesis of **1** in excellent yields (eq. 2).[4] A similar reaction reported recently[5] prompted us to publish our results.



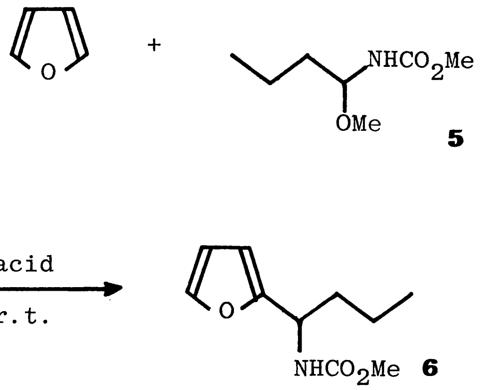
(2)

In the first place, our investigation aimed to clarify the effect of the nature of catalysts on the α-aminoalkylation. Table I shows the effect of the catalysts on the reaction of **5** with furan suggesting that sulfonic acids are the best among the catalysts examined.

Table I. Reaction of **5** with Furan.

Acid (equiv.)	Reaction Time (h)	Yield (%) of **6**
p-TsOH (0.1)	2.5	84
MsOH* (0.1)	2.5	83
conc. H_2SO_4 (0.1)	2.5	76
conc. HCl (0.1)	2.5	64
AcOH (1.0)	48	~0
$TiCl_4$ (0.2)	2	73
$SnCl_4$ (0.2)	2	59
$BF_3 \cdot OEt_2$ (0.2)	2	57
$ZnCl_2$ (0.2)	2	very low

* MsOH = methanesulfonic acid

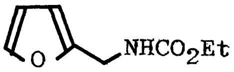
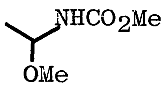
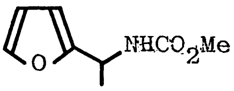
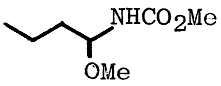
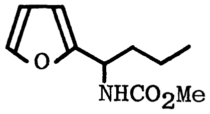
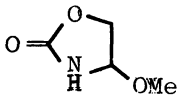
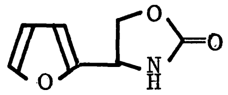
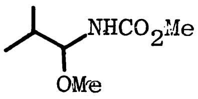
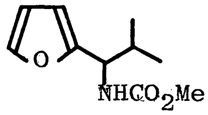
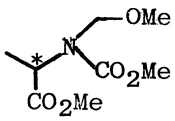
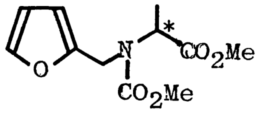
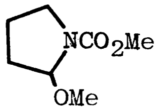
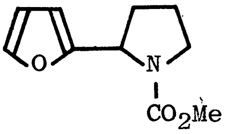
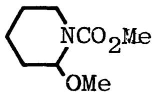
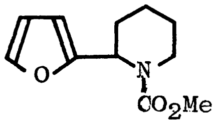
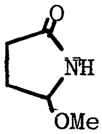
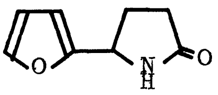
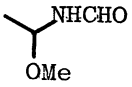
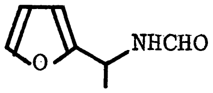
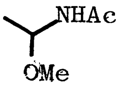
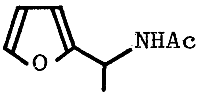


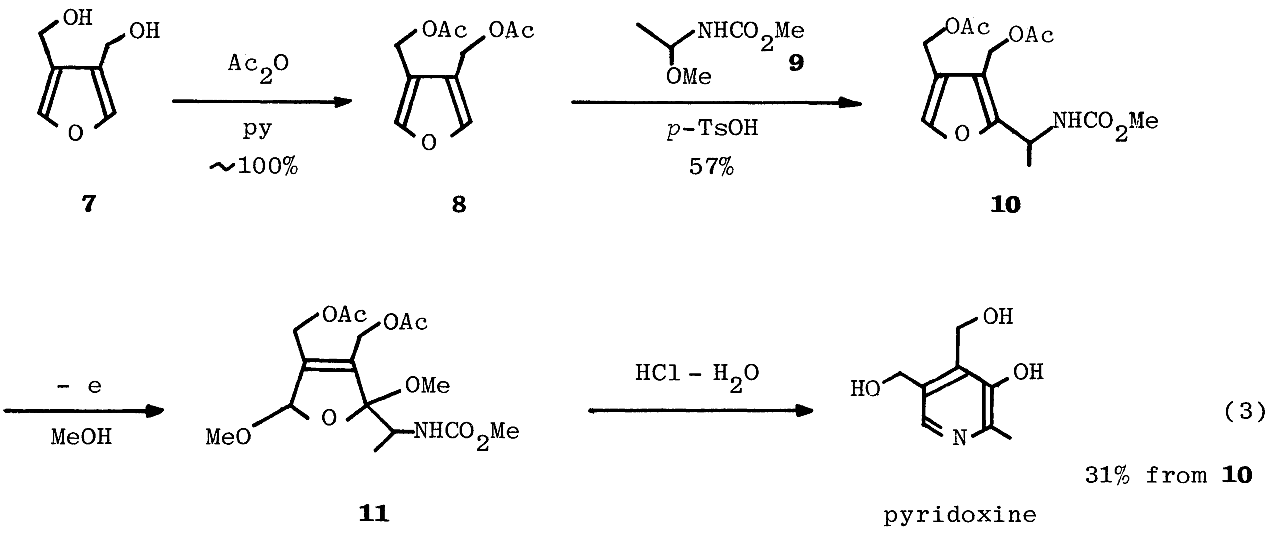
A general procedure using *p*-toluenesulfonic acid (*p*-TsOH) as the catalyst is as follows. To a solution of **4** (1 mmol) in furan (2 g) was added a catalytic amount of *p*-TsOH, and the reaction mixture was stirred at room temperature during the period stated in Table II. When the reaction was completed, an excess of sodium bicarbonate was added to the solution, and furan was evaporated successively. The product **1** was isolated by preparative thin-layer silica gel chromatograph. All the results are summarized in Table II.[6]

As shown in Table II, amides and a lactam also gave the corresponding products.

Finally, we applied this reaction to the synthesis of pyridoxine (eq. 3). A solution of **9** (2 mmol) and *p*-TsOH (0.05 equiv.) in **8** (10 mmol) prepared from **7** was stirred at 0 - 5 °C for 2 h to yield **10**,[6,7] which was transformed to pyridoxine in two steps.[8] Thus, **10** was electrochemically oxidized in methanol to give **11**, which was hydrolyzed with hydrochloric acid (1 N) to produce pyridoxine hydrochloride.

Table II. Reaction of α-Methoxyurethanes (**4**) with Furan.

Run	**4**	Amount of *p*-TsOH (equiv.)	Reaction Temp.	Reaction Time (h)	Product (**1**)	Yield of **1** (%)
1.		0.1	r.t.	1.5		84
2.		0.1	r.t.	20		76
3.		0.1	r.t.	2.5		84
4.		0.1	r.t.	21		71
5.		0.05	r.t.	20		76
6.		0.05	reflux	23		66
7.		0.05	r.t.	25		89
8.		1.0	r.t.	0.75		72
9.		0.25	r.t.	5.5		67
10.		0.1	reflux	7		59
11.		0.1	r.t.	46		67



References

(1) Electroorganic Chemistry. 55.

(2) (a) N. Clauson-Kaas, N. Elming, and Z. Tyle, *Acta Chem. Scand.*, **9**, 1 (1955).
(b) J. T. Nielsen, N. Elming, and N. Clauson-Kaas, *ibid.*, **9**, 9 (1955).
(c) N. Clauson-Kaas and P. Nedenskov, *ibid.*, **9**, 14 (1955).
(d) P. Nedenskov, N. Elming, J. T. Nielsen, and N. Clauson-Kaas, *ibid.*, **9**, 17 (1955).
(e) N. Elming and N. Clauson-Kaas, *ibid.*, **9**, 23 (1955).

(3) (a) T. Shono, Y. Matsumura, and H. Hamaguchi, *J. Am. Chem. Soc.*, **97**, 4264 (1975).
(b) T. Shono, Y. Matsumura, and K. Tsubata, *J. Am. Chem. Soc.*, **103**, 1172 (1981).

(4) Some reactions of **4** having carbomethoxy group as R^1 have been reported.
(a) E. Goldstein and D. Ben-Ishai, *Tetrahedron Lett.*, **1969**, 2631.
(b) D. Ben-Ishai, I. Sataty, and Z. Bernstein, *Tetrahedron*, **32**, 1571 (1976).

(5) V. Asher, C. Becu, M. J. O. Anteunis, and R. Callens, *Tetrahedron Lett.*, **22**, 141 (1981).

(6) Spectroscopic data and elemental analyses of all the products coincided with assigned structures.

(7) Excess of **8** was recovered in a 93% yield.

(8) This transformation was carried out according to the method described in the literature.[2a]

(Received May 29, 1981)