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A Convenient One-Pot Preparation of Bicyclic 2-Pyridones from Acyl Isocyanates Utilizing Trimethylsilylketene

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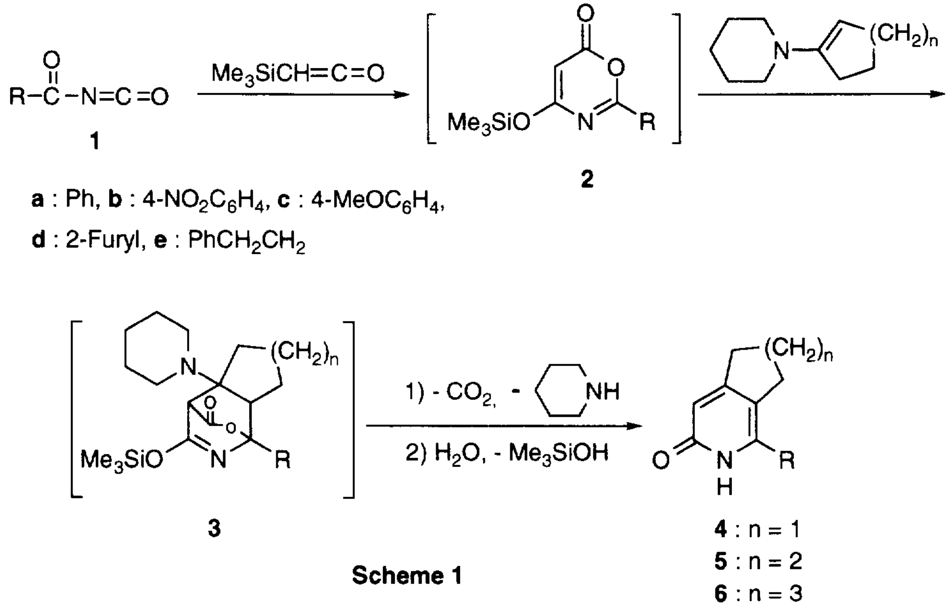
Abstract — *4-Trimethylsiloxy-1,3-oxazin-6-ones, easily generated in situ from trimethylsilylketene and acyl isocyanates, smoothly react with the enamines of cycloalkanones to give bicyclic 2-pyridones.* Copyright © 1996 Elsevier Science Ltd

In the preceding communication,[1] we reported that the reaction of trimethylsilylketene (TMSCH=C=O) with acyl isocyanates, followed by treatment with electron-deficient acetylenes gave 2-pyridones in good yield. As an extension of this work, we now report the convenient one-pot preparation of bicyclic 2-pyridones utilizing TMSCH=C=O.

We have found that 4-trimethylsiloxy-1,3-oxazin-6-ones **2**,[1] easily generated *in situ* from TMSCH=C=O and acyl isocyanates **1**, smoothly undergo the Diels-Alder reaction with the enamines of cycloalkanones to give bicyclic 2-pyridones **4~6**, as shown in Scheme 1.



Scheme 1

A typical experimental procedure is as follows: A mixture of **1a** (149 mg, 1 mmol) and TMSCH=C=O (147 mg, 1.3 mmol) in *o*-dichlorobenzene (3 ml) was heated at 90°C for 3 h under argon. 1-Piperidinocyclohexene (236 mg, 1.4 mmol) was then added and the mixture was stirred at reflux for 2 h. After concentration *in vacuo*, the residue was purified by column chromatography on silica gel (BW-200, Fuji Davison, hexane:AcOEt:MeOH=16:48:3) to give **5a** (143 mg, 63%).

The results are summarized in the Table. Various 1,3-oxazin-6-ones **2** derived from aromatic and heteroaromatic acyl isocyanates smoothly reacted with the piperidine enamines of cyclopentanone, cyclohexanone, and cycloheptanone to give the corresponding bicyclic 2-pyridones. In contrast to the results, the thermolysis of the Diels-Alder adduct derived from 2-trifluoromethyl-4-methyl-1,3-oxazin-6-one and 1-piperidinocyclohexene have been reported to give the amide, 1-(3-trifluoroacetylaminocrotonoyl)piperidine, resulting from the retro-Diels-Alder fission of the adduct and no tetrahydroisoquinoline derivative is formed.[2] Aliphatic acyl isocyanate such as 3-phenylpropionyl isocyanate (**1e**) also underwent the reaction with 1-piperidinocyclopentene to give **4e** in good yield, but cyclohexylcarbonylisocyanate was completely inert. *o*-Dichlorobenzene seems to be the solvent of choice. The morpholino and pyrrolidino enamines could also be used though the yield slightly decreased.

Thus, the present method using TMSCH=C=O makes possible the one-pot conversion of acyl isocyanates to bicyclic 2-pyridones and will provide a convenient methodology for the bicyclic pyridone synthesis.

Table.^{a} Preparation of Bicyclic 2-Pyridones (**4**~**6**)

Compd. No.	R	n	Yield (%)	IR (nujol) cm^{-1}, NHC=O	^1H NMR($CDCl_3$) ppm, C(3)-H	mp^{b,c} (°C)
4a	Ph	1	77	1651	6.42 (s)	218-220
5a		2	63	1651	6.32 (s)	243
6a		3	61	1659	6.36 (s)	212-213
4b	4-$NO_2C_6H_4$	1	96	1647	6.49 (s)	>255
5b		2	45	1657	6.35 (s)	>280
6b		3	55	1657	6.34 (s)	215-218
4c	4-$MeOC_6H_4$	1	69	1657	6.38 (s)	223-235
5c		2	32	1647	6.30 (s)	227-228
6c		3	58	1655	6.33 (s)	237-238
4d	2-Furyl	1	88	1647	6.36 (s)	224
5d		2	75	1686	6.29 (s)	177-178
6d		3	81	1646	6.33 (s)	177-179
4e	$PhCH_2CH_2$	1	70	1655	6.30 (s)	191-193

a) All compounds gave satisfactory elemental analysis. b) Recrystallized from tetrahydrofuran-hexane. c) Melting points were measured on a hot-plate.

References and Notes

1. Takaoka, K.; Aoyama, T.; Shioiri, T. *Tetrahedron Lett.* preceding paper.
2. Steglich, W.; Jeschke, R.; Buschmann, E. *Gazz. Chim. Ital.* **1986**, *116*, 361-372.

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