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# CHEMISTRY OF O-SILYLATED KETENE ACETALS[1]: AN EFFICIENT SYNTHESIS OF α-THIO-N-HETEROCYCLES FROM ω-AMIDOSULFOXIDES BY A NOVEL INTRAMOLECULAR PUMMERER-TYPE REARRANGEMENT

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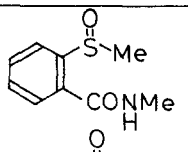
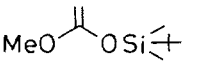
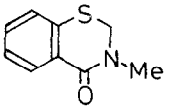
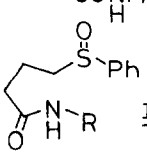
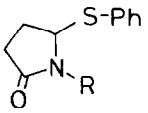
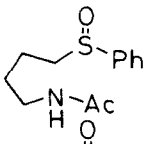
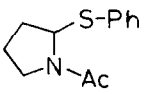
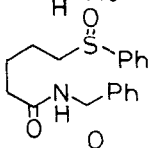
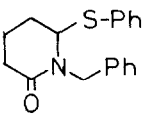
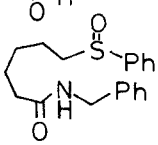
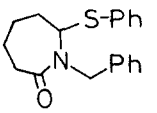
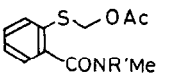
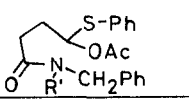
Summary: Treatment of ω-amidosulfoxides with O-silylated ketene acetals in dry acetonitrile in the presence of a catalytic amount of zinc iodide causes a novel intramolecular Pummerer-type rearrangement to give α-thio-N-heterocycles in high yields.

There has been a growing interest in the intramolecular cyclizations of ω-amino(or amido)olefins, which give pyrrolidines and piperidines bearing functionalities at the α-position to the nitrogen atom.[2] Although similar intramolecular cyclization of ω-amidosulfoxides leading to the α-thio-N-heterocycles (intramolecular Pummerer reaction) has been reported with hot acetic anhydride[3] or with trimethylsilyl trifluoromethanesulfonate (TMSOTf)/triethylamine,[4] these methods are not good enough because of either the competition with the normal intermolecular Pummerer reaction or other side reactions. Thus, the reaction of methyl o-methylcarbamoylphenyl sulfoxide (1a) with acetic anhydride gave no cyclized product (2a), but the normal intermolecular Pummerer reaction products (3a and 3a') exclusively.[3a] Recently, we have reported that treatment of sulfoxides with O-silylated ketene acetal (4) caused a Pummerer-type rearrangement to give α-siloxy sulfides under nearly neutral conditions.[5] As an extension of this reaction, we now report a novel and efficient intramolecular Pummerer-type rearrangement of ω-amidosulfoxides (1a-f), which gives α-thio-N-heterocycles (2a-f) in high yields.

We first examined the conversion of N-benzyl-4-(phenylsulfinyl)butanamide (1b) into 5-(phenylthio)-2-pyrrolidone (2b) by the use of acetic anhydride, TMSOTf/triethylamine, and O-methyl-O-tert-butyldimethylsilyl ketene acetal (4). The use of 4 was found to be quite efficient for the synthesis of 2b, although the former two conditions resulted in either formation of the normal intermolecular Pummerer reaction products (3b and 3b') or formation of complex mixtures. Typically, a mixture of 1b, 4, and zinc iodide in dry acetonitrile was stirred at room temperature for 1h. After the usual work-up, a quantitative yield of 2b was obtained. Various types of ω-amidosulfoxides (1a and 1c-f)[6] similarly reacted with 4 to give the corresponding α-thio-N-heterocycles (2a and 2c-f). The results are summarized in the Table.

Since the α-thio-N-heterocycles (2) are known as useful intermediates for pyrrolizidines and indolizines,[7] the present reaction would provide a versatile synthesis of these alkaloids.

Table Synthesis of α-Thio-N-heterocycles (2a-f) from ω-Amidosulfoxides (1a-f)

| Entry | Sulfoxides | Conditions[a] | Products (Yield)[b] |
|---|---|---|---|
| 1 |  1a |  4, r.t. 5h |  2a (85%) |
| 2 |  1b (R=$CH_2Ph$) | 4, r.t. 1h |  2b (R=$CH_2Ph$, quant) |
| 3 | 1c (R=$CH_2CO_2Et$) | 4, r.t. 14h | 2c (R=$CH_2CO_2Et$, 88%) |
| 4 |  1d | 4, r.t. 25h |  2d (57%) |
| 5 |  1e | 4, r.t. 4h |  2e (54%) |
| 6 |  1f | 4, r.t. 18h |  2f (57%) |
| | 1a | $Ac_2O$, 120°, 3h[3a] |  3a (R'=H, 52%) + 3a' (R'=Ac, 48%) |
| | 1c | $Ac_2O$, reflux, 3.5h |  3b (R'=H, 18%) + 3b' (R'=Ac, 62%) |

a) The reactions were carried out on 0.2-1 mmol scale of sulfoxides with 1.3-2 equiv of 4 in the presence of a catalytic amount (0.1 eq.) of $ZnI_2$. b) Isolated yields by column chromatography (silica gel) are given. The microanalyses for all products were in satisfactory agreement with the calculated values.

References and Notes


1) For a review, see: Y. Kita, O. Tamura, and Y. Tamura, Yuki Gosei Kagaku Kyokai Shi, 44, 1118 (1986).

2) a) For a review, see: Asymmetric synthesis, J. D. Morrison ed., P. A. Bartlett, Vol. 3, p 411-454, Academic Press, Inc. (London) LTD., 1984; b) S. Knapp, K. E. Rodriques, A. T. Levorse, and R. M. Ornaf, Tetrahedron Lett., 26, 1803 (1985); c) N. Knouzi, M. Vaultier, L. Toupet, and R. Carrie, ibid., 28, 1757 (1987) and references cited therein; d) A. Toshimitsu, K. Terao, and S. Uemura, J. Org. Chem., 52, 2018 (1987) and references cited therein.

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6) The unknown starting sulfoxides (1b-f) were readily prepared by standard methods and will be described in the forthcoming full paper.

7) a) D. A. Burnett, J. -K. Choi, D. J. Hart, and Y. -M. Tsai, J. Am. Chem. Soc., 106, 8201 (1984); b) S. Kano, Y. Yuasa, K. Asami, and S. Shibuya, Chem. Lett., 1986, 735; c) T. Kametani, H. Yukawa, and T. Honda, J. Chem. Soc., Chem. Commun., 1986, 651.


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