

Nitrene-promoted α -Alkoxylation of Amides with Silyl Ethers

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Thermolysis of a solution of amides, silyl ethers, and ethyl azidoformate caused the introduction of several alkoxy groups into the positions adjacent to the amide nitrogen.

The introduction of oxygen functionalities into an α -position of amino compounds affords attractive synthetic intermediates; such transformation has been so far performed by using peroxides,¹⁾ electrochemical oxidation,²⁾ and metal-catalyzed reactions.³⁾ The previously proposed methods, however, have been limited to the introduction of only some special oxygen functionalities. A nitrene inserts into a C(α)-H bond of ethers and thus constitutes an alternative tool for the preparation of α -oxygenated amino compounds.⁴⁾ We have recently found that the reaction of a nitrene with a mixture of amides and silyl ethers does not bring about α -amination of the silyl ethers, unlike the reaction with ethers, but α -alkoxylation of the amides. Silyl ethers having the functional groups susceptible to oxidation or metal-catalyzed reaction may also be used.

A solution of 1-(trimethylsilyloxy)pentane (1a) (3 mmol) and ethyl azidoformate (2.5 mmol) in DMF (2j) (5 cm³) was heated at 120 °C until evolution of nitrogen gas ceased (2 h). Then, DMF was removed in vacuo and purification of the residue by preparative TLC (ether) afforded N-methyl-N-(pentyloxymethyl)formamide (3aj) (1.14 mmol). Also formed were N,N-dimethyl-N'-(ethoxycarbonyl)urea (0.63 mmol) as an insertion product of the nitrene into the formic C-H bond of DMF and ethyl N-pentyloxy carbamate (0.28 mmol) derived from the attack of the nitrene onto an oxygen atom of 1a. Heating 1a in DMF at 120 °C in the absence of ethyl azidoformate did not form 3aj at all. Both the acetophenone-sensitized photoreaction generating the triplet azido or nitrene⁵⁾ and heating 1a in DMF at 110 °C in the presence of AIBN as a radical initiator were not effective. Thus, a radical pathway via the triplet nitrene may be less possible. A sequence of the attack of singlet nitrene onto the oxygen atom of silyl ethers and migra-

tion of the silyl group is presumable because the thermolysis of ethyl azidoformate in 1a afforded ethyl N-pentyloxy-N-trimethylsilylcarbamate, which, in turn, gave 3aj on heating at 120 °C in DMF.

The results of reaction of silyl ethers and amides in the presence of ethyl azidoformate are shown in Table 1.

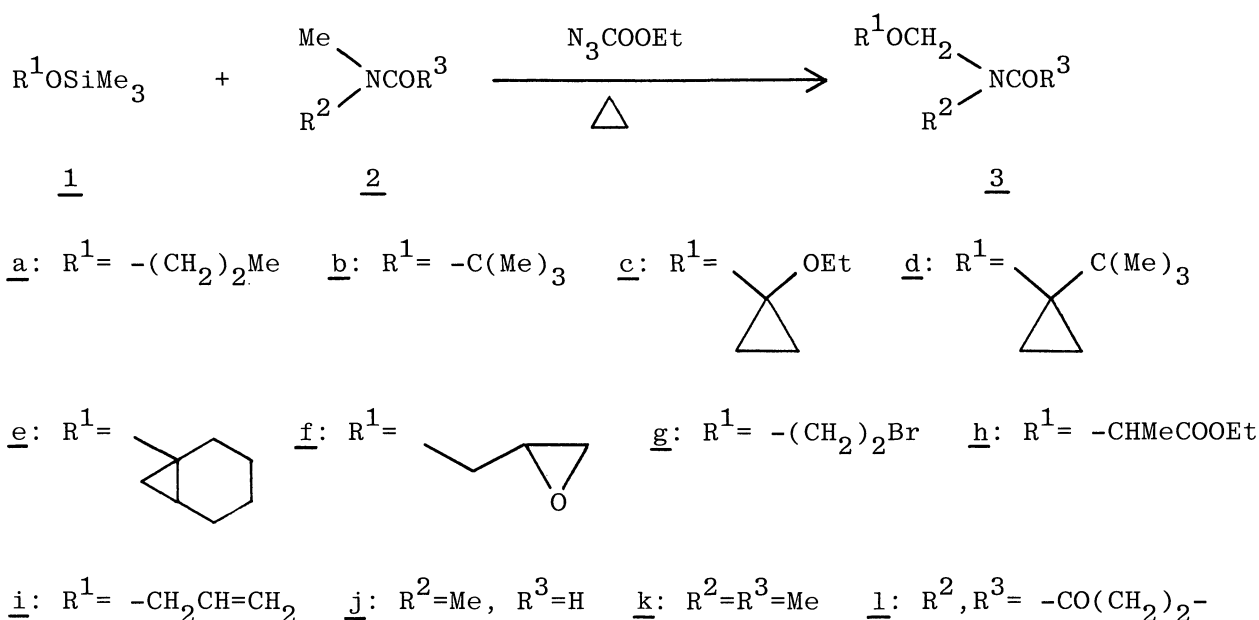


Table 1. α -Alkoxylation of Amides with Silyl Ethers

<u>3</u>	<u>aj</u>	<u>ak</u>	<u>bk</u>	<u>bl</u>	<u>cj</u>	<u>ck</u>	<u>dk</u>	<u>ek</u>	<u>fk</u>	<u>gk</u>	<u>hk</u>	<u>ik</u>
Yield/% ^{a)}	38	41	51	40	47	54	53	49	45	44	47	22

a) Isolated yields based on silyl ethers.

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