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N-(TRIMETHYLSILYLMETHYL)PYRIDINIUM TRIFLUOROMETHANESULFONATES AS FACILE PRECURSORS FOR NONSTABILIZED PYRIDINIUM METHYLIDES

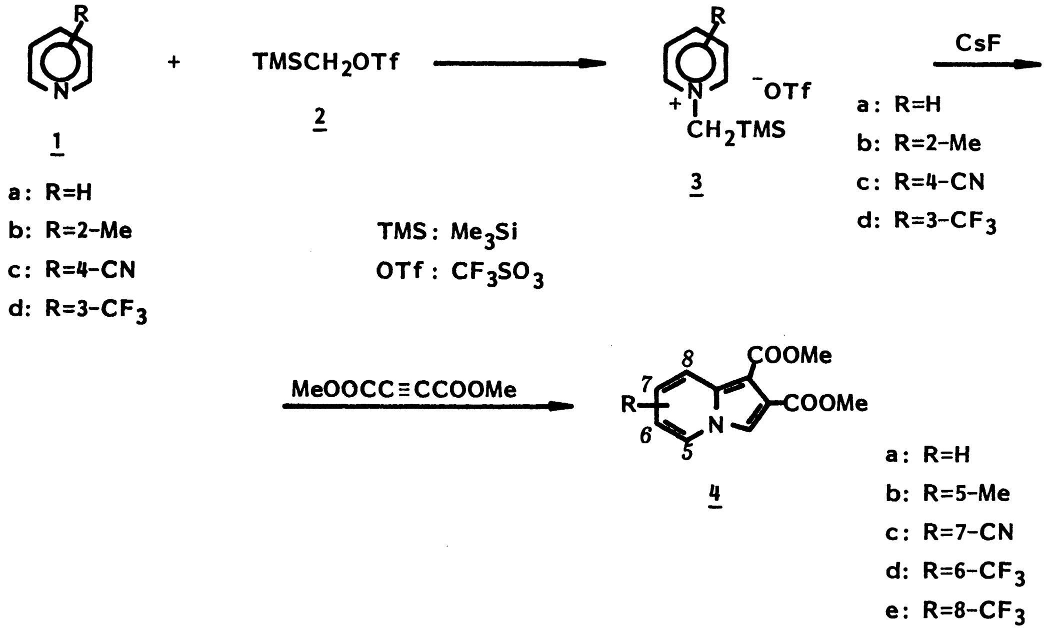
Otohiko TSUGE,* Shuji KANEMASA, Satoru KURAOKA, and Shigeori TAKENAKA
Research Institute of Industrial Science, and Department of Molecular Science
and Technology, Interdisciplinary Graduate School of Engineering Sciences,
Kyushu University, Kasuga, Kasuga 816

As facile precursors for nonstabilized pyridinium methylides N-(trimethylsilylmethyl)pyridinium triflates were synthesized. Cesium fluoride induced desilylation of the precursors liberated the nonstabilized pyridinium methylides which were trapped as the cycloadducts to dimethyl acetylenedicarboxylate.

The vast contribution of ylide chemistry to organic synthesis is well known. A ylide has its characteristic utility based on the different reaction pattern that is dependent upon the kind of positively charged hetero atom of ylide as well as the stabilizing substituents on the ylide carbon.$^{1)}$ Although the nonstabilized species, which carry no substituents capable of stabilizing the dipole, of sulfur and phosphorus ylides have been employed as useful reagents for many years, the first example of nonstabilized nitrogen ylide was only quite recently reported.$^{2)}$ No any practical precursors for nonstabilized ylides of aromatic nitrogen-heterocycles are available.$^{3)}$

The research described herein was aimed at opening the route to nonstabilized ylides of aromatic nitrogen-heterocycles among which several pyridine derivatives were employed.

Pyridine 1a was allowed to react with an equivalent of trimethylsilylmethyl triflate 2$^{4)}$ in dry dichloromethane at room temperature for 1 h and the solvent was removed off under reduced pressure to give a quantitative yield of N-(trimethylsilylmethyl)pyridinium triflate 3a (mp 97 °C) whose structure



was confirmed by the spectral and analytical data.[5] The salt 3a is nonhygroscopic solid and is soluble in most organic solvents such as benzene, acetone, dichloromethane, chloroform, ether, tetrahydrofuran, and 1,2-dimethoxyethane. Similarly 2-methyl- 3b (mp 92-93 °C, 96%), 4-cyano- 3c (mp 242 °C, 83%), and 3-trifluoromethyl-N-(trimethylsilylmethyl)pyridinium triflates 3d (mp 93-94 °C, 99%) were obtained from 2-picoline 1b, 4-cyano- 1c, and 3-trifluoromethylpyridines 1d, respectively.

Successful formation and isolation of the pyridinium salts 3 are very much owing to both high alkylating ability of 2 and low silylophilicity of triflate ion. Neither chloromethyl- nor iodomethyltrimethylsilane could replace the triflate 2 as an alkylating agent.

Treatment of 3 with cesium fluoride liberated nonstabilized pyridinium methylides A as transient 1,3-dipolar species that were trapped as the [3 + 2] cycloadducts to dimethyl acetylenedicarboxylate. Equimolar amounts of 3a, cesium fluoride, and the acetylenedicarboxylate in dry 1,2-dimethoxyethane were heated under reflux for 24 h. The mixture was poured into water, extracted with chloroform, the chloroform was evaporated, and the residue was subjected to silica gel chromatography to give dimethyl indolizine-1,2-dicarboxylate 4a in 82% yield.[6] Similarly the 5-methyl- 4b (47%), 7-cyano- 4c (36%), and a mixture (5 : 1) of 6- and 8-trifluoromethylindolizines 4d and 4e (53%) were produced in the reactions of 3b, 3c, and 3d, respectively.

Our generative method of nonstabilized methylides has some advantages as follows: 1) nitrogen-heterocycles with low basicity may be convertible into the ylide precursors, 2) the precursors are highly soluble in most organic solvents, 3) the methylides can be generated by action of silylophiles under mild conditions, 4) desilylation leads to the exclusive formation of methylides.[7]

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3) Participation of pyridinium methylide in the reactions with aromatic aldehyde was reported, but no further application to other organic synthesis is known: From N-methylpyridinium bromide and piperidine (F. Krohnke, Angew. Chem., 65, 605 (1953); R. K. Howe and K. W. Ratts, Tetrahedron Lett., 1967, 4743), and from pyridine and bromoacetic acid (K. W. Ratts, R. K. Howe, and W. G. Phillips, J. Am. Chem. Soc., 91, 6115 (1969); W. G. Phillips and K. W. Ratts, Tetrahedron Lett., 1969, 1383).

4) S. Ambasht, S. Kichiu, P. E. Peterson, and J. Gueen, Synthesis, 1980, 318.

5) All new compounds reported herein provided satisfactory elemental analyses.
3a: IR (KBr) 1270, 1150, 1030, and 860 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 0.01 (9H, s, Me$_3$Si), 4.35 (2H, s, CH$_2$), 8.00 (2H, t, J=7.0 Hz, 3- and 5-H), 8.40 (1H, t, J=7.0 Hz, 4-H), and 8.76 ppm (2H, d, J=7.0 Hz, 2- and 6-H); Mass m/e 166 (M^+).

6) The indolizine 4a (mp 82-83 °C) is a known compound which has been reported to melt at 88-90 °C (R. A. Abramovitch and V. Alexanian, J. Org. Chem., 41, 2144 (1976)).

7) Dehydrohalogenation of N-alkylpyridinium halides with other alkyl substituents at the 2- and/or 4-positions hardly forms the pyridinium methylides because proton elimination occurs at the latter alkyl groups.

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