

A NEW TRIMETHYLSILYL TRIFLATE-CATALYZED 1,3-DIPOLAR CYCLOADDITION
LEADING TO PYRROLIDINES

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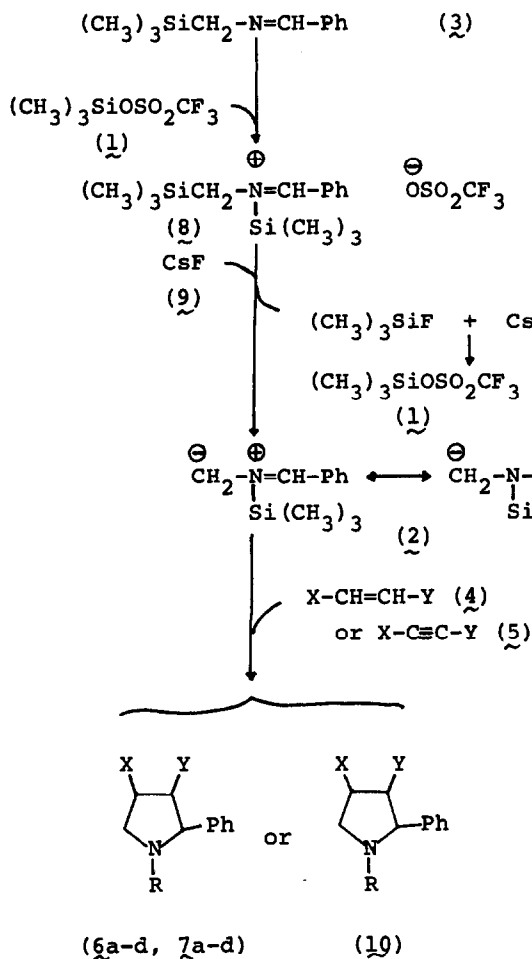
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Summary: Pyrrolidines were obtained by a new, trimethylsilyl triflate-catalyzed cycloaddition of an intermediary N-trimethylsilylated methyleneiminium ylide, a 1,3-dipole, to olefinic and acetylenic dipolarophiles.

Trimethylsilyl triflate (1) has been known as an efficient catalyst for the carbon-carbon bond forming reactions, in the course of which its regeneration by the fission of silicon-carbon bond has been reported only in the use of allyltrimethylsilanes as reagents.¹⁾ We now wish to describe a new cycloaddition of an intermediary N-trimethylsilylated methyleneiminium ylide, a 1,3-dipole (2), formed from N-(benzylidene)trimethylsilylmethylamine (3) in the presence of trimethylsilyl triflate as a catalyst.²⁾ Olefinic and acetylenic dipolarophiles (4 and 5) react to give N-trimethylsilylated pyrrolidine derivatives (6), which are easily transformed into N-unsubstituted ones (7). Path of the formation of the 1,3-dipole (2) is represented in Scheme I. The catalytic process involves a new fission of silicon-carbon bond of the N-trimethylsilylmethyliminium salt (8). The reaction is more accelerated by addition of cesium fluoride (9), which aids in the fission of silicon-carbon bond as previously known.³⁾ A typical experiment using dimethyl fumarate as a dipolarophile is shown below. As an efficient solvent hexamethylphosphoramide (HMPA) was selected.

To a stirred mixture of trimethylsilyl triflate (1) (1 mmole), cesium fluoride (9) (1 mmole) and 10 ml of HMPA a solution of dimethyl fumarate (5 mmole) and N-(benzylidene)trimethylsilylmethylamine (3) (5 mmole) in 10 ml of HMPA was dropwise added. The whole was then heated at 60-65°C with stirring for 20 hr under a nitrogen atmosphere. The mixture was treated with a potassium bicarbonate solution and then extracted with benzene. After removal of benzene from the solution dried over magnesium sulfate the residual oil was submitted to silica gel chromatography using ether as an eluent. Dimethyl 2-phenyl-3,4-pyrrolidinedicarbonylate (7a) was obtained as a colorless oil in 91% yield.⁴⁾ When cesium fluoride was absent, the yield was lowered into 80%. 7a; PMR δ ppm(CDCl₃) 2.32 (s) (1H, >NH),

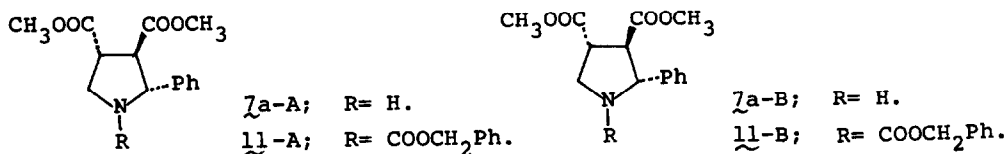
Scheme I.



3.15⁵) (s) (3-COOCH₃, cis to 2-phenyl), 3.65 (s) (3-COOCH₃, trans to 2-phenyl) (3H), 3.71 (s) (4-COOCH₃) (3H), 3.1-4.0 (m) (3-H, 4-H, and 5-H₂) (4H), 4.29 (d, J= 6.8Hz) (2-H, trans to 3-H), 4.52 (d, J= 8.1Hz) (2-H, cis to 3-H) (1H, cis/trans= 1.2), 7.1-7.4 (m) (5H, aromatic protons). This assignment was made by comparison of PMR spectrum of a pure isomer (7a-A) obtained in the following procedure. From the product 7a as an isomeric mixture 7a-A was obtained in a pure state by fractional crystallization of

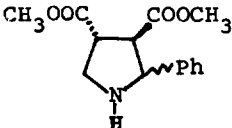
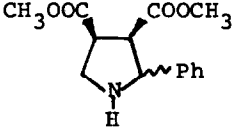
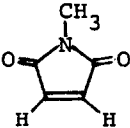
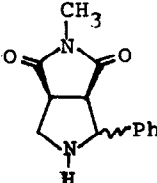
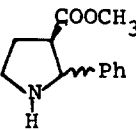
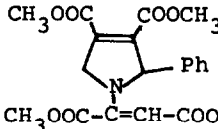
- 6a; X=Y= COOCH₃ (trans), R= Si(CH₃)₃.
 6b; X=Y= COOCH₃ (cis), R= Si(CH₃)₃.
 6c; X=Y= $\begin{matrix} \text{CO} \\ \diagup \\ \text{N-CH}_3 \\ \diagdown \\ \text{CO} \end{matrix}$, R= Si(CH₃)₃.
 6d; X= H, Y= COOCH₃, R= Si(CH₃)₃.
 7a; X=Y= COOCH₃ (trans), R= H.
 7b; X=Y= COOCH₃ (cis), R= H.
 7c; X=Y= $\begin{matrix} \text{CO} \\ \diagup \\ \text{N-CH}_3 \\ \diagdown \\ \text{CO} \end{matrix}$, R= H.
 7d; X= H, Y= COOCH₃, R= H.
 10; X=Y= COOCH₃, R= CH₃OOC-C≡CH-COOCH₃.

the N-benzoyloxycarbonylated products (11-A and 11-B) of 7a followed by catalytic hydrogenation of the isolated 11-A⁶) over palladium-on-charcoal.



Results of extensive experiments are summarized in Table I.

Table I. Synthesis of Pyrrolidines by the 1,3-Dipolar Cycloaddition^{a)}

| X-CH=CH-Y or X-C≡C-Y | Product ^{b)} | Yield(%) | 2-Phenyl and 3-COOCH ₃ ^{c)} cis : trans |
|---|---|----------|--|
| $\begin{array}{c} \text{CH}_3\text{OOC} \\ \\ \text{H}-\text{C}=\text{C}-\text{H} \\ \\ \text{COOCH}_3 \end{array}$ |  | 91 | 5 : 4 |
| $\begin{array}{c} \text{CH}_3\text{OOC} \\ \\ \text{H}-\text{C}=\text{C}-\text{COOCH}_3 \\ \\ \text{H} \end{array}$ |  | 83 | 2 : 3 |
|  |  | 85 | 1 : 2 |
| $\text{CH}_2=\text{CH}-\text{COOCH}_3$ |  | 83 | 5 : 4 |
| $\text{CH}_3\text{OOC}-\text{C}\equiv\text{C}-\text{COOCH}_3$ ^{d)} |  | 92 | — |

a) All the reactions were carried out with *N*-(benzylidene)trimethylsilylmethylamine (5 mmole), 1,3-dipolarophile (5 mmole), trimethylsilyl triflate (1 mmole) and cesium fluoride (1 mmole) in HMPA at 60-65°C for 20 hr, unless otherwise noted.

b) All the products gave satisfactory elemental analyses and spectral data (ir and nmr) consistent with their structures.

c) The ratios were determined by PMR measurement.

d) In this run, 10 mmole of dimethyl acetylenedicarboxylate was used, since its two molar equiv. were consumed in the reaction to give the *N*-substituted product as indicated.

It should be noted that this new 1,3-dipolar cycloaddition involving new catalytic fission of silicon-carbon bond of the N-trimethylsilylmethyliminium is admirably suited for synthesizing N-unsubstituted pyrrolidines in excellent yields by simple procedure in contrast to the previously reported methods.^{2,3)}

Further active investigations along this line are under way.

REFERENCES AND NOTES

- 1) T. Tsunoda, M. Suzuki and R. Noyori, *Tetrahedron Letters*, 21, 71 (1980).
- 2) Non-catalytic fission of silicon-carbon bond of λ has been reported. K. Achiwa and M. Sekiya, *Chemistry Letters*, 1981, 1213 (1981).
- 3) a) Y. Terao, N. Imai, K. Achiwa and M. Sekiya, *Chem. Pharm. Bull.*, in press.
b) E. Vedejs and G. R. Mattinez, *J. Am. Chem. Soc.*, 102, 7993 (1980) and references cited therein.
- 4) An analytical sample was obtained by flash bulb-to-bulb distillation (bp 240°C (0.2 mmHg)). λ a; Anal. Calcd for $C_{14}H_{17}O_4N$: C, 63.86; H, 6.51; N, 5.32. Found c, 64.09; H, 6.58; N, 5.28.
- 5) PMR signals of methyl esters oriented cis to phenyl group on the 5-membered ring usually shift to near 3.1 ppm due to the shielding effect of phenyl group. M. Joucla, D. Gree and J. Hamelin, *Tetrahedron*, 29, 2315 (1973).
- 6) λ 1-A; mp 101-102°C, Anal. Calcd for $C_{22}H_{23}O_6N$; C, 66.49; H, 5.83; N, 3.52; Found C, 66.77; H, 6.08; N, 3.52.
PMR δ ppm(CDCl₃) 3.39 (3-COOCH₃, cis to 2-phenyl).

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