## NEW 1,3-DIPOLAR CYCLOADDITION LEADING TO 2,5-DIHYDROPYRROLE AND PYRROLIDINE DERIVATIVES

Kazuo ACHIWA and Minoru SEKIYA

Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422

A novel 1,3-cycloaddition of intermediaries derived from N-(benzylidene)trimethylsilylmethylamine and acyl chlorides to conjugated olefins and acetylenes gave pyrrolidine and 2,5-dihydropyrrole derivatives, respectively.

Schiff bases and hexahydro-1,3,5-triazines have been known to give N-(1-chloroalky1)amide by the reaction with acy1 halides. Among them N-chloromethy1amides have been recently reported to function as efficient nucleophiles in the N-alky1amidomethy1ation at the electron-rich carbons.<sup>1)</sup>

We have found that a Schiff base of trimethylsilylamine, i.e. N-(benzylidene)trimethylsilylmethylamine  $(1)^{2}$  reacts with acyl halides in the presence of conjugated alkenes or alkynes to give pyrrolidines (5e,f) or 2,5-dihydropyrroles (5a-d) (See Scheme I).

In a typical experiment, a solution of N-(benzylidene)trimethylsilylmethylamine (1) (5 mmol) in 20 ml of tetrahydrofuran (THF) was added dropwise to a stirred solution of acetyl chloride (5 mmol) and dimethyl acetylenedicarboxylate (5.5 mmol) in 40 ml of THF at 40-45°C over a period of 1 hr. Heating and stirring were continued for 2 hr. After removal of the solvent 5c was obtained in 79% yield by recrystallization of the residure from methanol-isopropyl ether. 5c: mp 145-146°C,  $IR_{max}^{KBr}$  (cm<sup>-1</sup>): 1726 (-COOCH<sub>3</sub>), 1664 (>C=C=), 1652 (>N-COCH<sub>3</sub>); NMR & ppm (CDCl<sub>3</sub>); 1.78 (s), 2.04 (s) (=N-COCH<sub>3</sub>, 3H), 3.59 (s) (-COOCH<sub>3</sub>, 3H), 3.78 (s) (-COOCH<sub>3</sub>, 3H), 4.70 (d, J=4 Hz), 4.73 (d, J=4 Hz) ( $\frac{H}{H} \times_{N=}$ , 2H), 5.74 (t, J=4 Hz), 5.99 (t, J=4 Hz) ( $_{N} \times_{H}^{Ph}$ , 1H), 7.22 (s, aromatic, 5H); Mass M<sup>+</sup>: 303. The long range coupling constant values reported for this type of compounds ( $\underline{H}$ -C-C=C-C-C+<u>H</u>) are J= 0.5-5 Hz.<sup>3</sup>)



When  $\frac{4}{2}$  was absent,  $\frac{1}{2}$  played a role of dipolarophile to give  $\frac{6}{2}$ , as demonstrated by the following experiment. A solution of benzoyl chloride (5 mmol) was added slowly to a solution of N-(benzylidene)trimethylsilylmethylamine (1) (10 mmol) in 40 ml of THF at 40-45°C to give  $\frac{6}{2}$  as a mixture of its geometric isomers in 63% yield.



A recent paper<sup>5d)</sup> has reported a 1,3-dipolar addition of ylides derived by desilylation of trimethylsilylmethyliminium triflate by cesium fluoride. The present reaction may involve a likely intermediate (7) derived from 3 by desilylation, surprisingly in the absence of cesium fluoride, which is virtually unknown in the literature.



Results of extensive experiments are summarized in Table I.

R COC1	Y-C≡C-COOCH <sub>3</sub> or Y-CH=CH-COOCH <sub>3</sub>	Product <sup>b)</sup> (yield %)
PhCOCl	сн <sub>3</sub> оос-с≡с-соосн <sub>3</sub>	$\begin{array}{c} \text{CH}_{3}\text{OOC} \xrightarrow{\text{COOCH}_{3}} \text{Ph} \\ \text{COPh} \end{array} (85) (5a) \end{array}$
PhCH <sub>2</sub> OCOC1	сн <sub>3</sub> оос-с <del>≋</del> с-соосн <sub>3</sub>	CH <sub>3</sub> OOC Ph COOCH <sub>2</sub> Ph (78) (5b)
сн <sub>3</sub> сос1	сн <sub>3</sub> оос-с≡с-соосн <sub>3</sub>	CH <sub>3</sub> OOC Ph (79) (5c) COCH <sub>3</sub>
PhCOCl	н-с <del>≡</del> с-соосн <sub>3</sub>	$\bigvee_{\substack{N\\ COPh}}^{H} (26) (5d)^{c}$
PhCOCl	CH <sub>3</sub> 00C-CH=CH-COOCH <sub>3</sub> (t)	$\overset{CH_{3}OOC}{\underset{\substack{N\\I\\COPh}}{}} \overset{COOCH_{3}}{} (78) (5e)^{d}$
PhCOCl	H <sub>2</sub> C=CH-COOCH <sub>3</sub>	$\sum_{\substack{N \\ COPh}}^{COOCH_3} (65) (5f)^{d}$

Table I. Synthesis<sup>a)</sup> of 2,5-Dihydropyrrole and Pyrrolidine Derivatives

- a) All reactions were carried out with Schiff base (5 mmol), acyl chloride
  (5 mmol), and 1,3-dipolarophile (5.5 mmol) in THF (60 ml) at 40-45°C for 2 hr.
- b) All the products gave satisfactory elemental analyses and spectral data (ir and nmr) consistent with their structures.
- c) As a by-product, 6 was obtained in 30% yield.
- d) The products, 5e and 5f, were obtained in a state of stereochemical purity, investigation of which is under way.

It is noted that this new 1,3-dipolar cycloaddition gave 2,5-dihydropyrrole and pyrrolidine derivatives in good yields by simple procedure and, in contrast to the previously reported cycloaddition<sup>5)</sup> giving N-alkylpyrrolidines, easy removal of the N-acyl-substituent of the products may increase its usefulness for synthesis of N-unsubstituted pyrrolidine derivatives.<sup>6)</sup>

Further active investigations along this line are under way.

## REFERENCES

- a) K. Ikeda, T Morimoto, and M. Sekiya, Chem. Pharm. Bull., <u>28</u>, 1178 (1980).
  b) K. Ikeda, Y. Terao, and M. Sekiya, Chem. Pharm. Bull., 29, 1156 (1981).
- 2) E. Popowski, M. Böttcher, and H. Kelling, Z. Chem., 15, 353 (1975).
- N. F. Chamberlain, "The Practice of NMR Spectroscopy," Plenum Press, New York, 1974, p 305.
- 4) <u>6</u>: Colorless liquid, IR<sup>KBr</sup><sub>max</sub> (cm<sup>-1</sup>): 1640 (≫N-COPh). Hydrogen carbonate, mp 188-189°C (decomp) Anal. Calcd for C<sub>26</sub>H<sub>30</sub>N<sub>2</sub>OSi·CO<sub>3</sub>H<sub>2</sub>: C, 68.04; H, 6.77; N, 5.88. Found: C, 68.05; H, 6.86; N, 5.82.
- 5) a) R. M. Kollog, Tetrahedron, 32, 2165 (1976).
  - b) R. Huisgen, J. Org. Chem., <u>41</u>, 403 (1976).
  - c) H. Hermann, R. Huisgen, and H, Mader, J. Am. Chem. Soc., <u>93</u>, 1779 (1971).
  - d) E. Vedejs and G. R. Martinez, J. Am. Chem. Soc., <u>101</u>, 6452 (1979), and references cited therein.
- 6) a) J. J. Tufariello and G. E. Lee, J. Am. Chem. Soc., 102, 373 (1980).
  - b) G. E. Keck and D. G. Nickell, J. Am. Chem. Soc., <u>102</u>, 3632 (1980), and references cited therein.

(Received May 18, 1981)

1216