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# REGIOSELECTIVE CYCLOADDITION REACTIONS OF ALLYLSILANES AND SILYL ENOL ETHERS WITH NITRONES AND NITRILE OXIDES. SYNTHESIS OF HOMOALLYLAMINES[1)]

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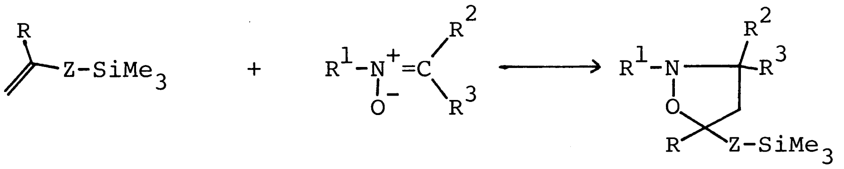
Allylsilanes and silyl enol ethers add to nitrones and nitrile oxides regioselectively to give the corresponding isoxazolidines and isoxazolines in good yield. Hydrogenative cleavage of the N-O bond of [3 + 2] cycloadducts with allylsilanes affords homoallylamines. In contrast, cyanosilane reacts smoothly with nitrones in a 1,3-conjugate mode.

Much attention has been focused on the application of nitrones[2)] and nitrile oxides[3)] as 1,3-dipolar reagents to organic synthesis. On the other hand, allylsilanes, silyl enol ethers and ketene silyl acetals are known as versatile nucleophilic reagents which display high regio- and stereospecificities.[4)] Recently, reactions of ketene silyl acetals with nitrones have been reported to result in the formation of 1,3-conjugate addition products selectively, without cycloaddition reactions.[5)] However in this report we demonstrate that allylsilanes and silyl enol ethers undergo cycloaddition reactions regioselectively as active alkenes, but not as nucleophiles, with 1,3-dipolar reagents such as nitrones and nitrile oxides to afford the corresponding isoxazolidines and isoxazolines, respectively. Moreover, the [3 + 2] cycloadducts with allylsilanes provide a new route to homoallylamines by hydrogenative cleavage of nitrogen-oxygen bond. This is a sharp contrast to reactions of ketene silyl acetals, that are quite similar to silyl enol ethers in structure and reactivities, toward nitrones without 1,3-cycloaddition reaction.[5)] In addition, it has been found that cyanosilane adds to nitrones in a 1,3-conjugate manner.

Allyltrimethylsilane (1a) reacts with nitrones (3) in a sealed tube without solvents or in xylene under thermal conditions (110-135 °C) for 1-2 days to give isoxazolidines (4) in excellent yield. (Eq. 1) The results are summarized in Table 1.

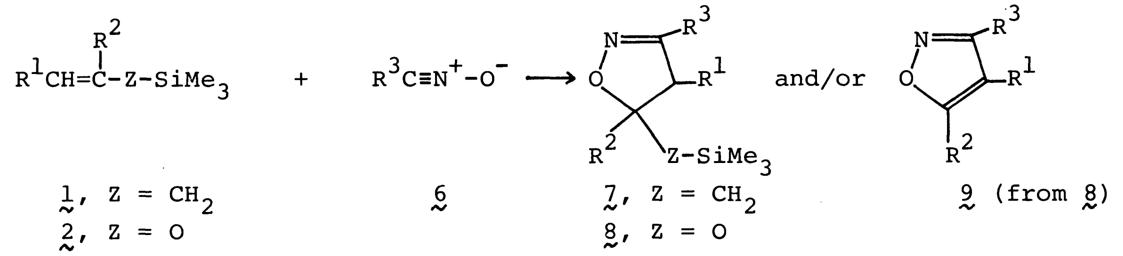


(1)

1, Z = $CH_2$ 　 3 　 4, Z = $CH_2$
2, Z = O 　 　 5, Z = O

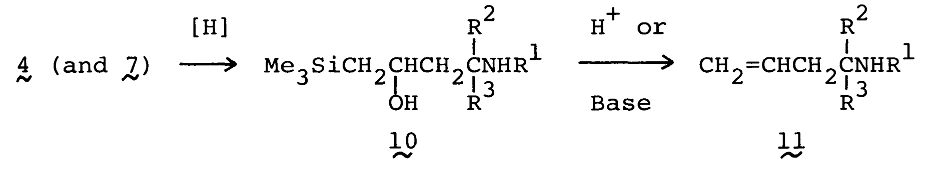
As can be seen from the results recorded in Table 1, in all examples examined, a smooth reaction proceeds to give isoxazolidines (4) exclusively in moderate to excellent yields via regioselective cycloaddition of 1 to 3. Thus, the terminal methylene of 1 binds selectively to the carbon terminus of the 1,3-dipole and internal olefinic carbon connects to the oxygen atom of 1,3-dipole to give the cycloadduct. No 1,3-conjugate allylation products like the reaction with ketene silyl acetals is produced. Similarly, silyl enol ether (2a) reacts with nitrone (3a) at reflux in xylene to afford cycloadduct (5a) exclusively.

As a test of the generality of the regioselective cycloaddition with 1,3-dipolar reagents the reaction of 1 and 2 with nitrile oxides (6) was examined. Again, regioselective cycloaddition occurred, albeit only with moderate to high yield. (Eq. 2) Results are listed in Table 2.



(2)

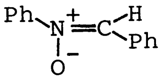
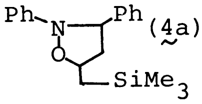
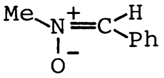
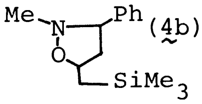
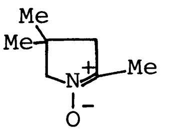
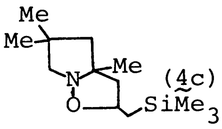
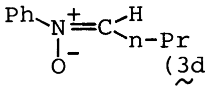
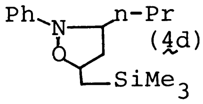
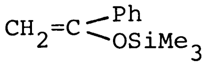
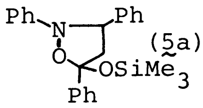
At the stage of isolation, cycloadducts (8) derived from 2 are converted to isoxazoles (9) by elimination of the silyloxy group which would be of synthetically important. More interestingly, the cycloadducts (4 and 7), obtained from 1 can be readily converted to homoallylamines (11) via β-silyl alcohols (10) by hydrogenative cleavage of the oxygen-nitrogen bond catalyzed by Raney-nickel[3a)] or palladium-carbon,[3b)] or by reduction with lithium aluminum hydride in the presence of titanium (IV) chloride[6)] followed by β-elimination of the resulting 10 under the known normal conditions.[7)] (Eq. 3) Thus, 11b ($R^1$ = Me, $R^2$ = Ph, $R^3$ = H) and 11d ($R^1$ = Ph, $R^2$ = n-Pr, $R^3$ = H) were obtained from 4b and 4d in overall 72 and 87% yield, respectively.



$$\text{4 (and 7)} \xrightarrow{[H]} \underset{\textbf{10}}{Me_3SiCH_2\underset{OH}{C}HCH_2\overset{R^2}{\underset{R^3}{C}}NHR^1} \xrightarrow[\text{Base}]{H^+ \text{ or}} \underset{\textbf{11}}{CH_2=CHCH_2\overset{R^2}{\underset{R^3}{C}}NHR^1} \qquad (3)$$

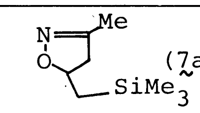
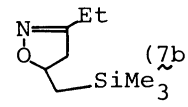
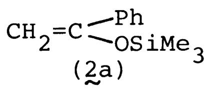
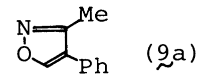
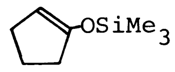
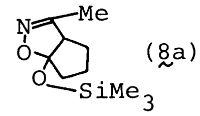
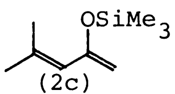
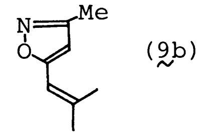
Attempts to obtain 1,3-addition products of 1 and 2 toward 3 were unsuccessful even activated with a variety of Lewis acids and a fluoride ion such as cesium fluoride or tetra-n-butylammonium fluoride.[8)] However in all examples examined, cyanosilane (12) adds to 3 very smoothly under mild conditions without any catalyst in a selective 1,3-conjugate manner to give silyl ether of N-cyanomethylhydroxylamine (13) exclusively in moderate to high yield.[9)] (Eq. 4) For example, yields of 13 were as follows: 82% from 3a, 71% from 3b, and 71% from 3c. These reactions which produce a variety of precursors to heterocyclic compounds are of important in organic synthesis.

Table 1. Reaction of allylsilanes (1) and silyl enol ethers (2) with nitrones (3)

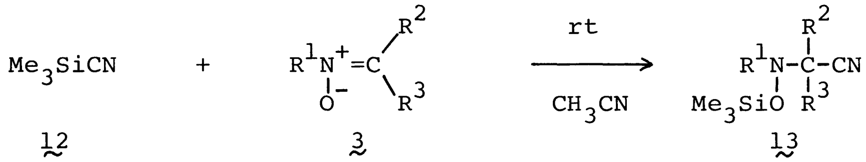
| Entry | 1 or 2 | Nitrone (3) | Reaction conditions$^{a)}$ | Product | Yield/%$^{c)}$ |
|---|---|---|---|---|---|
| 1 | $CH_2=CHCH_2SiMe_3$ (1a) |  (3a) | 110 °C, 36 h |  | 91 |
| 2 | 1a |  (3b) | 120 °C, 40 h |  | 94 |
| 3 | 1a |  (3c) | 120 °C, 40 h |  | 88 |
| 4 | 1a |  (3d) | 120 °C, 40 h |  | 83 |
| 5 |  (2a) | 3a | reflux, 48 h$^{b)}$ |  | 65 |

a) In a sealed tube. b) In xylene. c) Yield after isolation by TLC.

Table 2. Reaction of allylsilanes (1) and silyl enol ethers (2) with nitrile oxides (6)

| Entry | 1 or 2 | Nitrile oxide (6) | Reaction conditions$^{a)}$ | Product | Yield/%$^{c)}$ |
|---|---|---|---|---|---|
| 1 | $CH_2=CHCH_2SiMe_3$ (1a) | $CH_3C\equiv N^+-O^-$ (6a) | reflux, 12 h$^{a)}$ |  | 80 |
| 2 | 1a | $CH_3CH_2C\equiv N^+-O^-$ (6b) | reflux, 12 h$^{a)}$ |  | 73 |
| 3 |  (2a) | 6a | reflux, 40 h$^{b)}$ |  | 54 |
| 4 |  (2b) | 6a | reflux, 40 h$^{a)}$ |  | 46 |
| 5 |  (2c) | 6a | reflux, 60 h$^{b)}$ |  | 38 |

a) In benzene. b) In xylene. c) Yield after isolation by TLC.



$$\underset{\mathbf{12}}{\mathrm{Me_3SiCN}} + \underset{\mathbf{3}}{R^1\overset{+}{N}(O^-){=}C(R^2)R^3} \xrightarrow[\mathrm{CH_3CN}]{\mathrm{rt}} \underset{\mathbf{13}}{R^1N(OSiMe_3){-}C(R^2)(R^3){-}CN} \quad (4)$$

Thus, it is noted that allylsilanes and silyl enol ethers which are known as highly nucleophilic reagents react with nitrones and nitrile oxides to afford the corresponding [3 + 2] cycloadducts, isoxazolidines and isoxazolines, with excellent regioselectivity, but not 1,3-conjugate addition products. In sharp contrast, the reaction of cyanosilane with nitrones proceeds smoothly in 1,3-conjugate addition manner. The cycloadducts with allylsilanes can be converted to the corresponding homoallylamines. Applications of these reactions to organic synthesis will be the subject of further studies in this laboratory.

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References

1) Chemistry of Organosilicon Compounds 205.
2) For examples, see P. Deshong and J. M. Leginus, Tetrahedron Lett., 25, 5355 (1984); J. Org. Chem., 49, 3421 (1984) and references cited therein. Reviews: A. Padwa, Angew. Chem., Int. Ed. Engl., 15, 123 (1976); R. Huisgen, ibid., 2, 565 (1963); D. C. Black, R. F. Crozier, and V. C. Davis, Synthesis, 1975, 205.
3) a) D. P. Curran, S. A. Scanga, and C. J. Fenk, J. Org. Chem., 49, 3474 (1984) and references cited therein; b) Review: A. P. Kozikowski, Accounts Chem. Res., 17, 410 (1984).
4) For leading articles in this area, see E. W. Colvin, "Silicon in Organic Synthesis," Butterworth, London (1981), Chapters 9 and 17; W. P. Weber, "Silicon Reagents for Organic Synthesis,: Springer-Verlag, Berlin (1983), Chapters 11-16; T. H. Chan and I. Fleming, Synthesis, 1979, 761; H. Sakurai, Pure Appl. Chem., 54, 1 (1982); A. Hosomi and H. Sakurai, J. Syn. Org. Chem., Japan, 43, 406 (1985).
5) S. Tomoda, Y. Takeuchi, and Y. Nomura, Chem. Lett., 1982, 1787.
6) G. A. Olah, J. Am. Chem. Soc., 81, 3165 (1959).
7) D. J. Peterson, J. Org. Chem., 33, 780 (1968); P. F. Hudrlik, D. Peterson, and R. J. Rona, ibid., 40, 2263 (1975).
8) Use of the fluoride ion enables **1** to react with **3** deoxygenatively in a 1,3-conjugate addition manner to give homoallylamines (**11**), though the yields are not so high as the stepwise procedure described in this work.
9) After our work had been completed, we learned that **12** had reacted with **6a** in a 1,3-conjugate mode. R. F. Cunico and L. Bedell, J. Organomet. Chem., 281, 135 (1985).

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