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1,3-DIPOLAR CYCLOADDITION OF PYRIDINIUM AND DIAZINIUM DICYANOMETHYLIDS WITH BIS(TRIMETHYLSILYL)ACETYLENE: SYNTHESIS OF TRIMETHYLSILYL SUBSTITUTED INDOLIZINES AND BIS(TRIMETHYLSILYL)ACETYLENE AS AN ACETYLENE EQUIVALENT IN 1,3-DIPOLAR CYCLOADDITION

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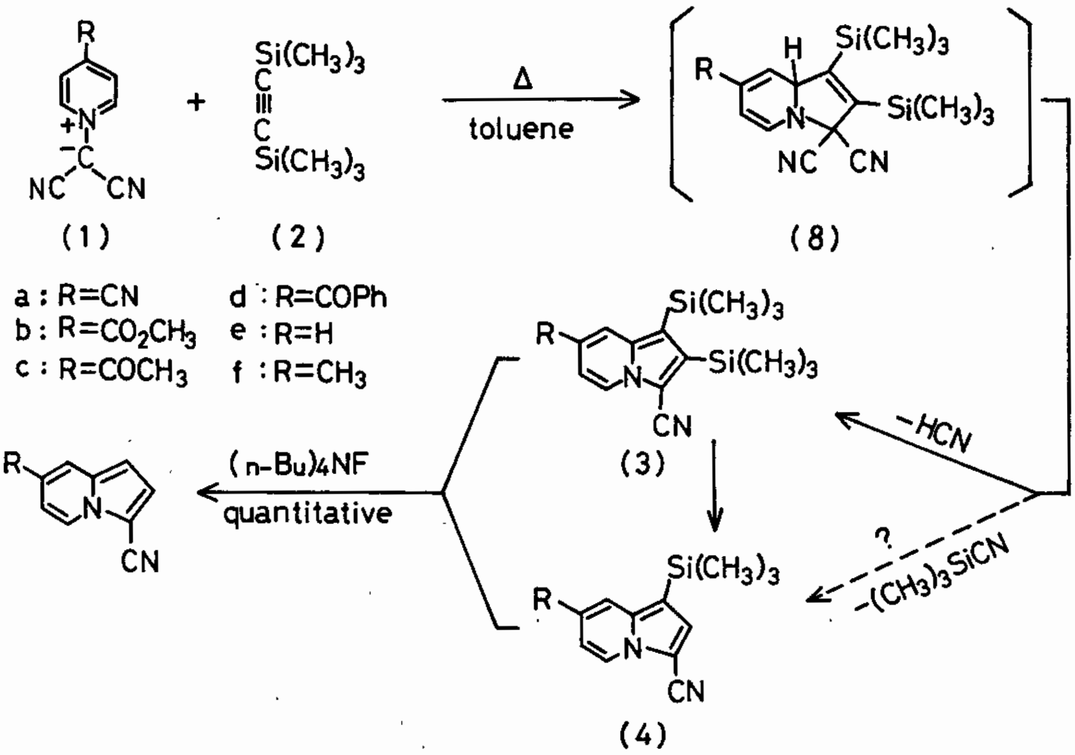
Abstract---Cycloaddition reactions of pyridinium and diazinium dicyanomethylids with bis(trimethylsilyl)acetylene give either the corresponding 1,2-di(trimethylsilyl)-3-cyanoindolizines or the mixtures of these and 1-(trimethylsilyl)-3-cyanoindolizines depending on the substituents and the presence of another nitrogen in the pyridine ring. The trimethylsilyl group was smoothly removed under the catalytic influence of $(n\text{-Bu})_4NF$.

The preparation of indolizines and their aza analogues has been the subject of considerable interest from physical, chemical, and biological points of view.[1] Specifically, most of these heterocycles have been known to undergo either $[8+2]\pi$ or stepwise Michael type addition with electron deficient alkynes and alkenes to give such a novel type of heterocycles as cyclazines.[2] However, to our knowledge, there has never been reported on the synthesis of indolizines bearing organometallic substituents. In the course of our studies[3] on the simple preparation of cycl[2.2.3]azines possessing no substituent in the five membered rings which are needed for our investigations regarding their electronic properties particularly based upon ESR and molecular orbital methods, we have investigated a 1,3-dipolar cycloaddition of cycloimmonium ylids with bis(trimethylsilyl)acetylene. Below, we report a first preparation of trimethylsilyl substituted indolizines and an extremely facile removal of this group without destruction of indolizine nucleus.

Heating of dicyanomethylids (1) with an excess amount of bis(trimethylsilyl)acetylene (2) in refluxing toluene followed by Florisil chromatography produced, depending

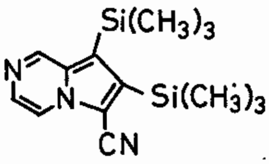


TABLE

R	(3) Yield (%)[a]	(4) Yield(%)
CN	42	—
CO_2CH_3	17 (87)	—
$COCH_3$	22 (69)	—
COPh[b]	19 (58)	0.7(2.3)
H[b]	2 (27)	2.5(31)
CH_3	—	4.4

a. Isolated yield. Parentheses indicate the yields based on the consumed ylids .

b. The mixture was unable to be separated by TLC. The ratio was obtained by ^{1}H-NMR.



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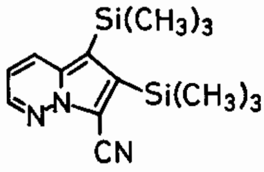

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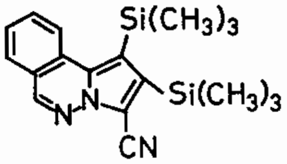

(7)

on the substituents, either the 1,2-di(trimethylsilyl)-3-cyanoindolizines (3)[4] or the mixtures of (3) and the 1-(trimethylsilyl)-3-cyanoindolizines (4)[5] in moderate yields based on the consumed ylids, as summarized in Table.[6]

Generally, the dicyanomethylids having an electron withdrawing group such as cyano group on the pyridine ring afforded better yields of (3). This result is not inconsistent with the qualitative consideration that the present 1,3-dipolar cycloaddition is expected to be controlled by LUMO[dicyanomethylid]-HOMO[bis(trimethylsilyl)acetylene] interaction since (2) is well known to serve as an electron rich alkyne. In agreement with this, the diazinium dicyanomethylids like pyridazinium, pyrazinium, and phthalazinium dicyanomethylids which are regarded as more π-deficient heteroaromatics than the pyridinium ylid, readily underwent cycloaddition onto (2) to yield the corresponding aza-indolizines (5), (6), and (7) in 92, 31 (95),[7] and 68 % yields respectively.

Although no intermediate cycloadducts (8) have been isolated, a probable mechanism for the formation of (3) [and (4)] involves a 1,3-dipolar cycloaddition of (1) to (2) to give an initial adduct (8), followed by formal extrusion of HCN. Although it is equivocal whether (4) forms by elimination of Me_3SiCN from (8) or by removal of Me_3Si group from (3), in some cases e.g. (3b), one of the trimethylsilyl groups is gradually being lost in $CDCl_3$.

Intriguingly, these indolizines, i.e. (3), (4), (5), (6), and (7) underwent a quantitative loss of Me_3Si group(s) under catalytic influence of $(n\text{-}Bu)_4NF$ (1 M solution in THF). In view of the ready availability of both dicyanomethylids and (2), the present method for the preparation of 1,2-unsubstituted indolizines apparently constitutes a complementary method to ours reported previously[8] especially in those cases where the ylids possess either an electron withdrawing group on the pyridine or an additional nitrogen atom in the pyridine ring. Thus, bis(trimethylsilyl)-acetylene should also be regarded as a useful acetylene equivalent in 1,3-dipolar cycloadditions.

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1. F.J. Swinbourne, J.H. Hunt, and G. Klinkert, *Adv. Heterocycl. Chem.*, **22**, 103 (1978).
2. W. Flitsch and U. Kramer, *Adv. Heterocycl. Chem.*, **22**, 322 (1978).
3. For example: T. Uchida and K. Matsumoto, *Chem. Lett.*, 1980, 149.
4. Satisfactory elemental analyses were obtained for all new compounds except the mixtures of (**3d**, **e**) and (**4d**, **e**).
5. The assignment of the position of trimethylsilyl group is at present equivocal. e.g. (**4f**), ^{1}H-nmr(CDCl$_3$) 0.36(s, 9H, Si(C$\underline{H}_3$)$_3$), 2.31(s, 3H, C$\underline{H}_3$), 6.31(s, 1H, H-2), 6.55(dd, 1H, $J_{5,6}$=7.2 Hz, $J_{6,8}$=1.7 Hz, H-6), 7.17(bs, 1H, H-8), 8.09(d, 1H, H-5, $J_{5,6}$=7.2 Hz); ^{13}C-nmr(CDCl$_3$) -0.91(q, Si($\underline{C}$H$_3$)$_3$), 21.05(q, $\underline{C}$H$_3$), 98.40(s, C-3), 105.58(d, C-2), 115.47(s, $\underline{C}$N), 115.70(d, C-6), 117.53(d, C-8), 124.32(d, C-5), 132.35(s, C-1), 134.90(s, C-7), 137.38(s, C-8a).
6. Typical spectroscopic and physical data: (**3b**), m.p. 160-161 °C; i.r.(KBr) 1715, 2250 cm^{-1}; ^{1}H-nmr(CDCl$_3$) 0.46 and 0.50(each s, 9H x 2, 2 x Si(C$\underline{H}_3$)$_3$), 3.90(s, 3H, CO$_2$C$\underline{H}_3$), 7.36(dd, 1H, $J_{5,6}$=7.4 Hz, $J_{6,8}$=1.2 Hz, H-6), 8.32(dd, 1H, $J_{5,6}$=7.4 Hz, $J_{5,8}$=1.2 Hz, H-5), 8.52(brd, 1H, $J_{6,8}$=1.2 Hz, H-8); ^{13}C-nmr(CDCl$_3$) 1.79 and 2.71(each q, Si($\underline{C}$H$_3$)$_3$), 52.56(q, CO$_2\underline{C}$H$_3$), 105.24(s, C-3), 111.75(d, C-6), 114.94 (s, $\underline{C}$N), 120.90(s, C-2), 123.39(s, C-1), 123.50(d, C-8), 124.72(d,C-5), 140.92 (s, C-7), 141.06(s, C-8a). (**6**), m.p. 73-74 °C; i.r.(KBr) 2250 cm^{-1}, ^{1}H-nmr (CDCl$_3$) 0.43 and 0.50(each s, 9H x 2, 2 x Si(C$\underline{H}_3$)$_3$), 6.77(dd, 1H, $J_{6,7}$=4.3 Hz, $J_{7,8}$=9.3 Hz, H-7), 8.06(dd, 1H, $J_{6,8}$=1.5 Hz, $J_{7,8}$=9.3 Hz, H-8), 8.26(dd, 1H, $J_{6,7}$=4.3 Hz, $J_{6,8}$=1.5 Hz , H-6); ^{13}C-nmr(CDCl$_3$) 1.76 and 2.71(each q, Si($\underline{C}$H$_3$)$_3$), 108.52(s, C-3), 113.88(d, C-7), 114.37(s, $\underline{C}$N), 116.26(s, C-2), 135.13(s, C-8a), 143.15(d, C-6).
7. The yield based on the consumed ylid.
8. K. Matsumoto, T. Uchida, and L. A. Paquette, *Synthesis*, 1979, 746.

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