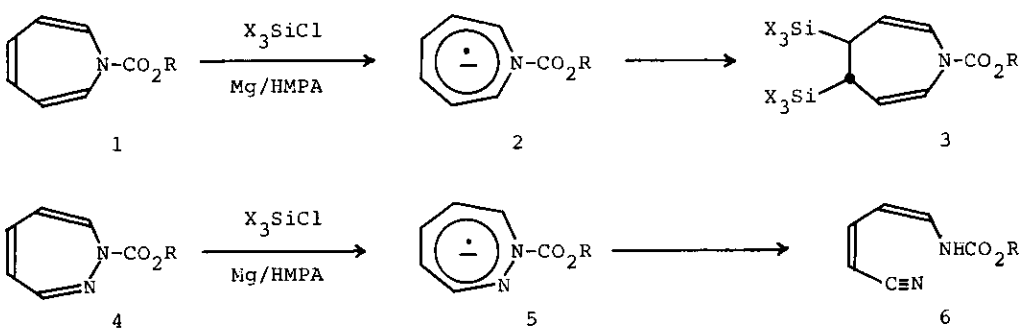
REACTIONS OF PYRAZOLE AND PYRROLE DERIVATIVES WITH TRIMETHYLCHLOROSILANE

Katsuhiro Saito,* Yoichi Horie, Toyonobu Murase, and Kensuke Takahashi
Department of Applied Chemistry, Nagoya Institute of Technology,
Gokiso-cho, Showa-ku, Nagoya 466, Japan

Abstract —— Reactions of 1-carbomethoxypyrazole and 1-carbomethoxypyrrole with trimethylchlorosilane in hexamethylphosphortriamide in the presence of magnesium afforded the parent compounds, respectively, eliminating the substituents. The similar reaction using 1-methylpyrazole gave 1-methyl-5-trimethylsilylpyrazole through a substitution reaction. The reactions are considered to proceed via radical anions of the heterocycles formed by electron transfers from magnesium.

Much effort has been devoted to the investigation of the reactivities of heterocycles from the viewpoint of the synthetic utility of the pharmaceuticals and the elucidation of the electronic natures of the heterocycles. A large number of papers have been published on the addition or substitution reactions of heterocycles with olefins.[1] Reactions of heterocycles with organometallic reagents such as palladium, or ruthenium derivatives have also attracted the attention of chemists and the detailed reaction mechanisms are gradually becoming clear.[2] However, so far as we know, only a little has been documented on the reactions of heterocycles with silane derivatives.



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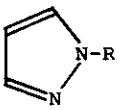
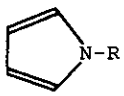
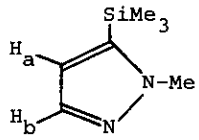


7a: R=H
b: R=CO_2Me
c: R=Me
d: R=Ph



8a: R=H
b: R=CO_2Me
c: R=Me
d: R=Ph



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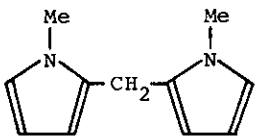

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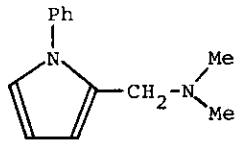

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It is known that chlorosilane derivatives added to olefins in the presence of magnesium in hexamethylphosphortriamide (HMPA).[3] We have reported that reactions of chlorosilane derivatives with azepine derivatives (1) afforded 4,5-double addition products (3) but the similar reactions with diazepine derivatives (4) resulted in the ring cleavage to give nitrileamine derivatives (6).[4] In order to investigate the difference of the reactivities between the seven-membered and the five-membered heterocycles, we studied the reactions of pyrazoles and pyrroles with trimethylchlorosilane in HMPA in the presence of magnesium. Here the results will be discussed.

1-Carbomethoxypyrazole (7b) was reacted with six-molar equivalent amount of trimethylchlorosilane in HMPA in the presence of magnesium at 85°C for 24 h. After decomposition with water the reaction mixture was subjected to thin-layer chromatography to afford pyrazole (7a) in 47% yield. The similar reaction using 1-carbomethoxypyrrole (8b) gave pyrrole (8a) in 57% yield. Pyrrole was not detected in the reaction of 8b under the absence of trimethylchlorosilane, indicating that the presence of trimethylchlorosilane is an essential for this reaction.

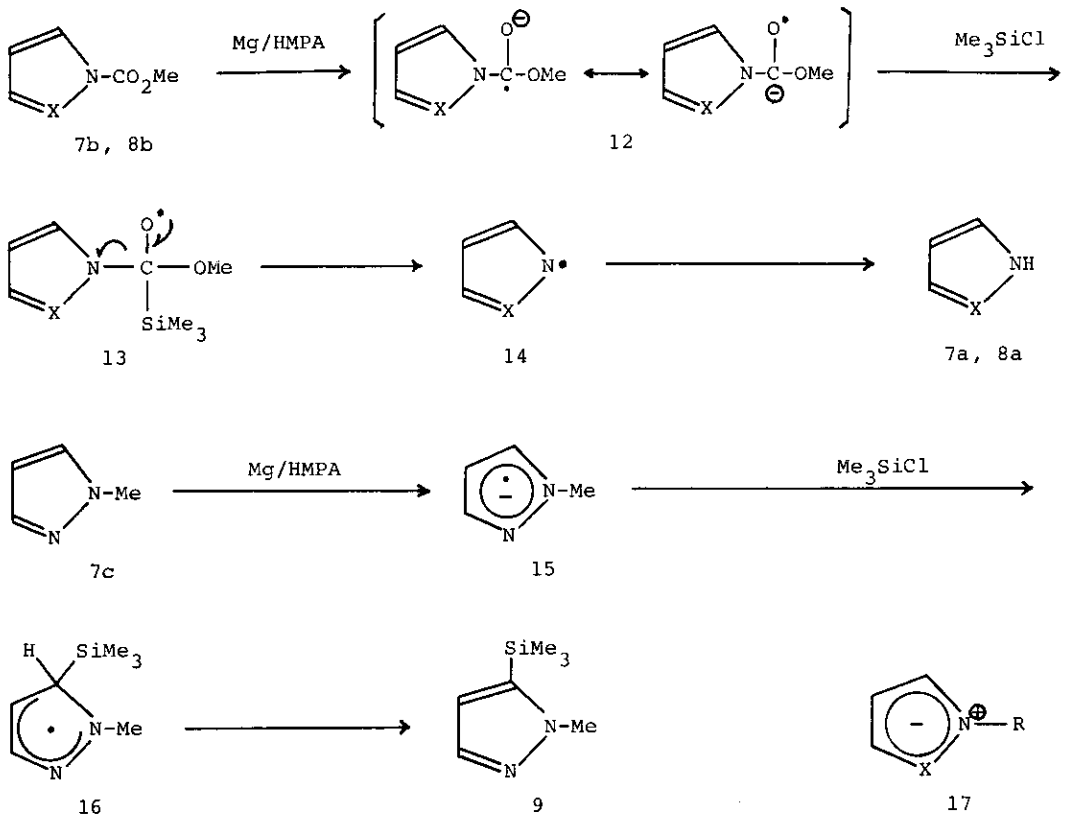
The analogous reaction using 1-methylpyrazole (7c) formed 3% yield of a substituted product, 1-methyl-5-trimethylsilylpyrazole (9). However the same type of reaction using 1-methylpyrrole (8c) afforded no substitution product but gave a symmetric pyrrole derivative (10) in 3% yield. The similar reaction using 1-phenylpyrazole (7d) gave no isolatable product but reaction with 1-phenylpyrrole (8d) produced a pyrrole derivative (11) in 3% yield.

The structures of the products were determined by coincidences with the authentic

samples or deduced on the basis of their spectral properties and confirmed by resemblances of these properties with those of the analogous compounds.[5]

The formations of pyrazole and pyrrole are considered to proceed as follows.[4] An electron transfer from magnesium[3] to 7b or 8b forms a radical anion intermediate 12 which then reacts with trimethylchlorosilane to give the radical intermediate 13 releasing chloride anion. An N-C bond cleavage in 13 generates the radical intermediate 14, which then abstracts hydrogen radical from the solvent to form pyrazole or pyrrole.

The formation of 9 is also considered to proceed via an electron transfer process from magnesium as follows.[4] The electron transfer to 7c generates the radical anion intermediate 15, which reacts with trimethylchlorosilane to form the radical intermediate 16 leaving chloride anion. An elimination of hydrogen radical from 16 affords 9. The formation processes of 10 and 11 are not clear now, but we tentatively suggest a participation of the solvent HMPA as a donner of the methylene and N,N-dimethylaminomethyl groups.



The reactions are completely different from each other in the cases of the seven-membered and the five-membered heterocycles.[4] This difference is considered to be attributable to the aromaticity of the five-membered heterocycles.[6] It is well known that azepines and diazepines behave as polyolefins in chemical reactions.[7] In the reactions with silane derivatives azepines and diazepines acted as polyolefins to accept the electron from magnesium in their ring system to form radical anions 2 and 5, respectively.

Pyrazoles and pyrroles are known to be 6 π-electrons aromatic compounds because of the contribution of the lone pair electrons on the nitrogen atom. Thus the ring systems of these compounds are negatively charged while the nitrogen atoms at 1-positions are positively charged as shown in 17.[6] The contribution of this charge separation is bigger when electron-donating substituents are attached to these compounds, but even electron withdrawing groups such as carbomethoxy group are considered still to alow to form this charge separation. Consequently, the electron transfers from magnesium/HMPA occur at not in the negatively charged ring systems but at the substituents to form the anion radical 12. The poor yield of the substitution product 9 can also be explained by the same argument.

EXPERIMENTAL

Melting points were recorded on a Yanagimoto micro melting point apparatus and were uncorrected. Nmr spectra were measured with a Varian XL 200 or a Hitachi R-20B spectrometers with tetramethylsilane as an internal standard. Ir and uv spectra were measured with a JASCO A-102 and Hitachi 200-10 spectrophotometers, respectively. Mass spectra were measured with a Hitachi M-52 or a JMX-DX300 spectrometers. Wako gel B5F was used for thin-layer chromatography. HMPA was dried over Molecular Sieves 3A 1/16.

Reaction of 1-Carbomethoxypyrazole (7b) with Trimethylchlorosilane. A mixture of 7b (630 mg, 5 mmol), trimethylchlorosilane (3270 mg, 30 mmol), magnesium (180 mg, 7.5 m gram atom) in HMPA (5 ml) was heated at 85°C for 24 h. The reaction mixture was decomposed with water, extracted with ethyl acetate, washed with brine and water, and dried over anhydrous sodium sulfate. After filtration the solvent was removed on a rotary evaporator. The residual oil was subjected to thin-layer chromatography on silca gel using diethyl ether as a developing solvent to give pyrazole (160 mg, 47.1%, R_f=0.50).

Reaction of 1-Carbomethoxypyrrole (8b) with Trimethylchlorosilane. A mixture of

8b (625 mg, 5 mmol), trimethylchlorosilane (3270 mg, 30 mmol), magnesium (180 mg, 7.5 m gram atom) in HMPA (5 ml) was heated at 85°C for 20 h. The reaction mixture was treated by the same method as above to give pyrrole (192 mg, 57.3%).

Reaction of 1-Methylpyrazole (7c) with Trimethylchlorosilane. A mixture of 7 (820 mg, 10 mmol), trimethylchlorosilane (2730 mg, 25 mmol), magnesium (600 mg, 25 m gram atom) in HMPA (15 ml) was stirred at room temperature for 24 h. After the usual treatment the oily mixture was subjected to thin-layer chromatography on silica gel using benzene-diethyl ether (1:1) as a developing solvent to give an oil 9 (48 mg, 3.1%, R_f=0.75).

9: Hrms 154.0917. Calcd for $C_7H_{14}N_2Si$: M, 154.0926. Mass m/z (rel intensity): 154 (M^+, 32), 139 (100), 59 (11). Uv (EtOH): 228 nm (sh. log ε, 3.99). Ir (oil): 3130, 2950 cm^{-1}. Nmr ($CDCl_3$): δ 0.33 (s, 9H), 3.99 (s, 3H), 6.38 (d, 1H, H_a, J=1.0 Hz), 7.50 (d, 1H, H_b, J=1.0 Hz).

Reaction of 1-Methylpyrrole (8c) with Trimethylchlorosilane. A mixture of 8c (10.0 g, 123 mmol), trimethylchlorosilane (40.0 g, 369 mmol), magnesium (4.48 g, 185 m gram atom), in HMPA (100 ml) was heated at 60°C for 50 h. After the usual treatment, the oily mixture was subjected to thin-layer chromatography on silica gel using benzene as a developing solvent to give colorless crystals 10 (331 mg, 3.0%, R_f=0.65). Recrystallization from cyclohexane gave pure crystals 10.

10: mp 77-78°C. Found: C; 75.99, H; 8.09, N; 16.01%. Calcd for $C_{11}H_{14}N_2$: C; 75.82, H; 8.10, N; 16.08%. Mass m/z (rel intensity): 174 (M^+, 100), 159 (6), 94 (22). Uv (EtOH): 222 nm (log ε, 4.08). Ir (KBr): 3130. 3100, 2950 cm^{-1}. Nmr ($CDCl_3$): δ 3.51 (s, 6H), 3.87 (s, 2H), 5.84 (m, 1H), 6.05 (m, 1H), 6.57 (m, 1H).

Reaction of 1-Phenylpyrrole (8d) with Trimethylchlorosilane. A mixture of 8d (5.0 g, 35 mmol), trimethylchlorosilane (11.4 g, 105 mmol), magnesium (1.28 g, 53 m gram atom), in HMPA (50 ml) was heated at 100°C for 24 h. After the usual treatment the oily mixture was subjected to thin-layer chromatography on silica gel using benzene-diethyl ether (3:7) as a developing solvent to give an oil 11 (160 mg, 3.0%, R_f=0.55).

11: Hrms: 200.13209. Calcd for $C_{13}H_{16}N_2$: M, 200.13202. Mass m/z (rel intensity): 200 (M^+, 15), 169 (12), 156 (100). Uv (EtOH): 237 nm (log ε, 4.36). Ir (oil): 3130, 2950 cm^{-1}. Nmr ($CDCl_3$): δ 2.16 (s, 6H), 3.27 (s, 2H), 6.23 (m, 2H), 6.83 (m, 1H), 7.2-7.6 (m, 5H).

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