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# Studies on the Vilsmeier-Haack Reaction. II.[1] Characterization of Thionyl Chloride-Dimethylformamide Complexes

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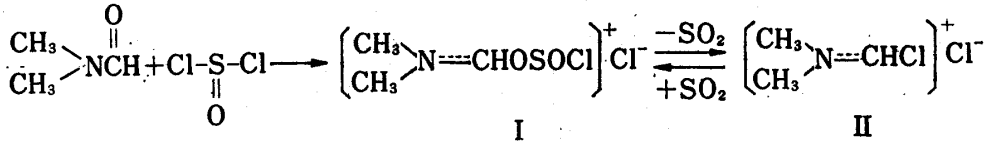
Inorganic acid halides (thionyl chloride, phosgen and phosphorus oxychloride) have been found to react with N,N'-dimethylformamide (DMF) to form active complexes (Vilsmeier-Haack reagents)[3,4,5] which have been found useful as formylating, halogenating and dehydroxylating agents.[6] It has been known that thionyl chloride can combine with DMF to form an intermediate complex (I), and removal of sulfur dioxide from I affords the crystalline complex (II).[4] Although the crystalline II has been frequently used and characterized so far,[4,6] the properties and the utility of I have not yet been demonstrated. In our current studies on the Vilsmeier–Haack reaction,[1,7] the equimolar mixture of thionyl chloride and DMF, corresponding to I, was found to be a good reagent for dehydroxylation reaction which could not be performed by use of the crystalline II.

This paper shows by nuclear magnetic resouance (NMR) spectra that I which could be easily converted into II by evaporation or by heating could be reversibly formed from II by the addition of anhydrous sulfur dioxide.



I II

Chart 1

NMR spectrum of the mixture of thionyl chloride and an equimolar amount of DMF, corresponding to I, indicated that $CH_3$-proton signals appeared at $\delta$ 2.99 and $\delta$ 3.08 (singlet, singlet) and CH-proton signal at $\delta$ 8.26 (singlet). The integration of these peaks showed the ratio of 3:3:1 (Fig. 1, B). The signal of CH-proton of the mixture was different from that of DMF which appeared at $\delta$ 8.12 (singlet) (Fig. 1, A).

Removal of sulfur dioxide from the mixture of thionyl chloride and DMF *in vacuo* produced the hygroscopic crystalline complex (II). NMR spectrum of II indicated that $CH_3$-proton signal appeared at $\delta$ 4.12 (singlet) and CH-proton signal at $\delta$ 11.33 (singlet), and the integration of these peaks showed the ratio of 6:1 (Fig. 1, C). The spectrum was identical with that of chloromethylene dimethylammonium chloride prepared by the reaction of phosgen and DMF.[8]

When II was exposed to an atmosphere of dry sulfur dioxide at room temperature, it turned to a fuming liquid whose properties and reactivities in the dehydroxylation reactions[7]

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7) K. Kikugawa, M. Ichino and T. Kawashima, *Chem. Pharm. Bull.* (Tokyo), **19**, 2466 (1971).
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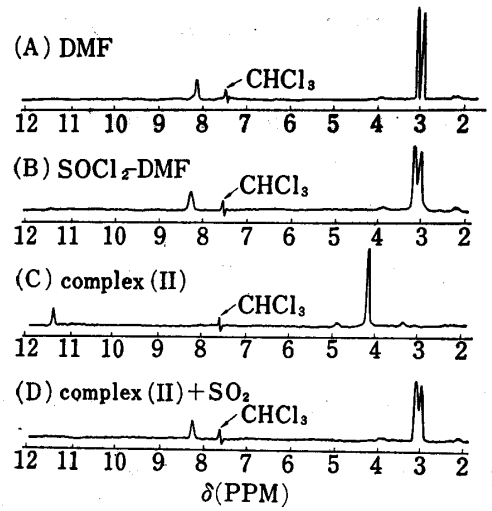


Fig. 1. NMR Spectra of Thionyl Chloride–Dimethylformamide Complexes in $CDCl_3$

were quite same as those of the mixture of thionyl chloride and DMF. NMR spectrum of the liquid (Fig. 1, D) was identical with that of the mixture of thionyl chloride and DMF. The possible structure of I was illustrated above.

I was also found to convert into II by heating and the extent of the conversion could be known by the integration of $CH_3$- and CH-protons of both species. NMR spectrum of the deuterated chloroform solution of I, which had been refluxed for an hour, showed about 50% of I was converted into II. Thus, the temperature of the reaction in which the unstable I acts as an active species[1,7] should be well controlled in order to avoid the conversion of I into II.

## Experimental

**NMR Spectra**——Spectra were taken with Varian T-60 spectrometer, in $CDCl_3$ (20%) with an internal standard of TMS.

**Complex (I)**——From Thionyl Chloride and DMF: Highly purified thionyl chloride (1.19 g, 10 mmoles) was added to 0.73 ml (10 mmoles) of DMF at room temperature and the mixture corresponded to I was obtained. NMR spectrum of the complex showed $CH_3$-protons at $\delta$ 2.99 and $\delta$ 3.08 (singlet, singlet) and CH-proton at $\delta$ 8.26 (singlet). The integration of these peaks showed the ratio of 3:3:1 (Fig. 1, B). Although the signals of $CH_3$-protons of the complex were similar to those of DMF which appeared at $\delta$ 2.95 and $\delta$ 3.03 (singlet, singlet), the signal of CH-proton of the complex differed from that of DMF which appeared at $\delta$ 8.12 (singlet) (Fig. 1, A). The spectrum of the mixture which was stored at room temperature overnight was quite identical with that of the freshly prepared mixture.

From the Complex (II) and Sulfur Dioxide: Crystalline complex (II) (1.25 g) was exposed to an atmosphere of dry sulfur dioxide at room temperature, and 1.9 g of fuming liquid was obtained. The NMR spectrum of the liquid was identical with that of the mixture of thionyl chloride and DMF; $CH_3$-proton signals appeared at $\delta$ 3.01 and $\delta$ 3.10 (singlet, singlet) and CH-proton signal at $\delta$ 8.30 (singlet) showing relative intensities of 3:3:1 (Fig. 1, D). The liquid could be converted into II *in vacuo* as well as the mixture of thionyl chloride and DMF.

**Complex (II)**——Sulfur dioxide was removed *in vacuo* at 40—50° for 5 hours from I (1.9 g, 10 mmoles) prepared from thionyl chloride and DMF, and 1.25 g (10 mmoles) of the crystalline II was obtained. II thus prepared was found free from $SO_2$ function in view of the fact that the aqueous mixture of it did not consume any iodine. NMR spectrum of II showed $CH_3$-protons at $\delta$ 4.12 (singlet) and CH-proton at $\delta$ 11.33 (singlet) showing relative intensities of 6:1 (Fig. 1, C). The chloroform (10 ml) containing 10 mmoles of the mixture of thionyl chloride and DMF was refluxed for an hour and was evaporated to dryness *in vacuo* produced 1.20 g of the crystalline II showing the same spectrum.

**Conversion of the Complex (I) to the Complex (II) by Heating**——NMR spectra of the refluxed solutions of I (1.9 g) in 10 ml of deuterated chloroform were measured. The signals of $CH_3$- and CH-protons corresponding to I ($\delta$ 2.99, $\delta$ 3.08 and $\delta$ 8.26) gradually diminished and the signals of $CH_3$- and CH-protons corresponding to II ($\delta$ 4.12 and $\delta$ 11.33) appeared as the time of reflux proceeded. From the intensities of the signals about 25 and 50% of I were converted into II in the solution refluxed for 10 min and 1 hour respectively.

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