A rapid permethylation of complex carbohydrates such as glycolipids and polysaccharides is described. The method is based on the use of Corey's base, created from dimethylsulfoxide and sodium hydride (methylsulfinyl carbanion). [The SCP® indicates that this paper has been cited over 780 times since 1964.]

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I spent 1956-57 as a Fulbright fellow in Roger Jeanloz's laboratory in Boston and learned the difficulty involved in methylation analysis of complex carbohydrates. At that time at least ten grams of pure complex polysaccharides were needed, and several months were required to obtain 'complete' methylation (which even then was not always completed). Methylation of glycolipid was even more difficult as it forms a micelle. Several workers, including myself, tried methylation of glycosphingolipids, but simply failed. Therefore, I was very surprised to hear Richard Kuhn1 and his colleagues had found a way, in 1960, to complete methylation of gangliosides within a few days using dimethylformamide and silver oxide or barium oxide.

In 1963, while I was working at the Tohoku Pharmaceutical College in Sendai, I was trying to de-N-acetylate N-acetyl-hexosamines in glycoproteins and glycolipids from a purely immunochernical interest. A few reactions were tried in dimethylsulfoxide (DMSO) as it had been found that the carbanion was strong and that the methylation could take place effectively even for glycolipids. However, I was not quite sure the method would be superior to that of Kuhn. Moreover, I was not very optimistic that the method could be applied to aminosugar containing complex polymers, as the IR spectra of the methylated glycolipid did not show an absorption band at 1550 cm⁻¹ (due to -NHC=O-) indicating a large extent of N-methylation.

"I thought this would bring us the horrible task of identifying all the N-methylated, partially O-methylated aminosugars. It is now apparent that N-methylation is the most welcome property for GC-MS identification of aminosugar, thanks to the work by Bengt Lindberg2 in Stockholm and by Klaus Stellner,3 once in this laboratory."

"The paper was originally submitted to the Journal of Biochemistry in June 1963, but was soon withdrawn because I received much criticism from someone to whom I had sent my preprint. They were reluctant to believe that such a method was feasible and I thought I needed to reinvestigate in detail. It was my friend Tamio Yamakawa who strongly encouraged me to publish the paper, as the method was good enough at least for glycolipids. I resubmitted it in November 1963. The brief paper was published in February 1964. The method has been greatly elaborated in the paper by PA. Sandford and H.E. Conrad4 which was published in 1966. Since then the method has been widely accepted. Life as a scientist is totally unpredictable. Frankly, I have mixed feelings as the paper cited is in my subsidiary interest, and my interest developed in quite a different area. I would be happier if some of my other papers, such as glycolipid transformation in neoplasia or discovery of cell surface fibronectin, would have been selected as highly cited articles."