

This Week's Citation Classic

Metcalfe L D & Schmitz A A. The rapid preparation of fatty acid esters for gas chromatographic analysis. *Anal. Chem.* **33**:363-4, 1961.
[Armour Industrial Chemical Company, McCook, IL]

The routine application of gas chromatography to the determination of the composition of fatty acid samples made it essential to prepare methyl esters rapidly and simply. Boron trifluoride-methanol converts fatty acids to their methyl esters in about two minutes. The esters are comparable to those obtained by other procedures. [The SC® indicates that this paper has been cited over 825 times since 1961.]

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"We were pleased to learn that this publication has become a *Citation Classic*. My observations have led me to the conclusion that if you want to write a highly cited paper, it should be one concerned with methodology in an area of high general interest. Like most authors, I set out to solve a problem in my particular field of interest. The fact that our solution was of great interest to many people was a happy coincidence.

"The story of the paper begins with H.J Harwood, the research director of Armour and Company, asking me to become involved with the National Heart Institute's Lipid Analysis Committee (LAC) in 1957. This committee was organized by Evan Horning, who was with the National Heart Institute at that time. Because of the suspected role that fat played in heart disease, rapid methods for the analysis of fats and fatty acids were urgently needed. The LAC was set up to solve the formidable analytical problems using gas chromatography. Scientists from various universities, government laboratories, and industry made up this rather loose organization.

"In meeting with the LAC, it quickly became apparent that using the primitive gas

chromatograph available to me at that time, our chromatography contribution would be very limited. I decided that the chemical area would be the one where we could make a useful contribution. We did make such a contribution by supplying the Committee with various fats, fatty acids, and methyl esters which were readily available to us at Armour.

"One chemical problem that kept coming up at the LAC meetings in 1958 was the need for a rapid and convenient method for preparing methyl esters of fatty acids. The fatty acids are usually gas chromatographed as their methyl esters. Most of the proposed esterification techniques were cumbersome, slow, or used reagents that were considered hazardous. In any event, the methods were not readily applicable for use with large numbers of routine samples.

"After one of the committee meetings, it occurred to me that an esterification technique using a relatively large amount of a powerful Lewis acid catalyst in methanol might be feasible. As an analytical chemist, I was familiar with an earlier use of boron trifluoride catalyst in a number of analytical techniques involving Karl Fischer reagent.¹ I decided that I would investigate BF₃, as an esterification catalyst for fatty acid methyl ester preparation.

"On recently examining my research notebook of that period, I found my first entry on the use of BF₃-methanol reagent was on January 11, 1959. I was surprised to find that the procedure I used in this early experiment was essentially the same as the one that appeared in the final publication. I never did get to present the new esterification procedure before the LAC.

"Late in 1959, gas chromatography was introduced at Armour Industrial Chemical Company (now Armak Company) as a quality control tool. Preparation of methyl esters for this plant gas chromatography control work involved a two-hour reflux period. We quickly introduced the two minute BF₃-methanol esterification procedure into the plant control laboratory when we became aware of their difficulties.

"Shortly afterward, we submitted a paper for publication in *Analytical Chemistry*. We later published an expanded version that could be applied to most lipids."²

1. Mitchell J, Jr. & Smith D M. *Chemical analysis*. New York: Interscience, 1948. Vol. 5.
2. Metcalfe L D, Schmitz A A & Peika J R. Rapid preparation of fatty acid esters from lipids for gas chromatographic analysis. *Anal. Chem.* **38**:514-15, 1966.