

# THE GOESSMANN GAZETTE

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Present  
Research Group of  
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## LOUIS A. CARPINO RECEIVES HIRSCHMANN AWARD IN PEPTIDE CHEMISTRY

Louis A. Carpino, Professor of Organic Chemistry, has been awarded the 1992 Ralph F. Hirschmann American Chemical Society Award in Peptide Chemistry, which is sponsored by Merck, Sharp & Dohme Research Laboratories. As one colleague quoted in *Chemical and Engineering News* of October 7, 1991, states, "It is difficult even to conceive of the idea that one chemist should have introduced so many of the intermediates that have made modern peptide synthesis possible and has now added another one. However, Louis Carpino has done it."

Carpino has been on the faculty since 1954 and is currently being honored for two key discoveries in the development of protecting groups for peptide synthesis. Today the majority of chemists doing peptide synthesis use either the *tert*-butyloxycarbonyl (BOC) or 9-fluorenylmethoxycarbonyl (Fmoc)

group, both designed by Carpino, as alpha protectants for the assembly of peptides and small proteins.

The work which led to the Hirschmann Award is a good example of two consecutive serendipitous discoveries in the field of amino group protection. When Professor Carpino came to UMass in 1954, one of his research goals was to synthesize the first examples of a class of compounds, monosubstituted diimides ( $RN=NH$ ), considered too unstable to be isolated under normal conditions. It was thought that it might be possible to generate a stable diimide salt, for example by treatment of known esters such as  $R-N=NCOOBn$  with HBr, a typical deblocking agent for the carbobenzoxy group (COOBn, CBZ). Professor Carpino had in mind doing IR studies, possibly at low temperatures, to verify the postulated intermediates. Indeed this project allowed the

University via Research Corporation and NSF support to obtain its first IR spectrometer, the old Perkin-Elmer 21. NMR studies would have been equally useful, but at that time NMR was not even "just around the corner." It was several years before the first commercial NMR spectrometer, the Varian A-60, like the PE-21 now only a museum piece, became available.

Unfortunately (or fortunately, in view of the eventual results), the azo linkage in  $R-N=NCOOBn$  acted to oxidize the deblocking agent HBr, thus dashing hopes for removing the CBZ group and retaining the azo linkage. Professor Carpino therefore sought a protecting group which would be cleaved by a weaker acid which happened also to be non-reducing. The carbo-*t*-butoxy group (COOCMe<sub>3</sub>, BOC) fit the bill in combination with trifluoroacetic acid (TFA). Following Carpino's initial work

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