

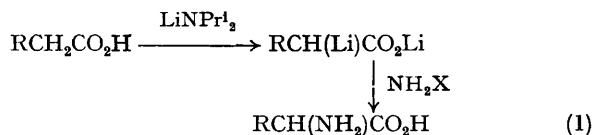
## $\alpha$ -Amination of Carboxylic Acids: a New Synthesis of $\alpha$ -Amino-acids

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**Summary** Amination of  $\alpha$ -lithiated carboxylic acid salts provides a new preparative method of  $\alpha$ -amino-acids.

We report a new method for the synthesis of  $\alpha$ -amino-acids by the amination of  $\alpha$ -lithiated acid salts<sup>1</sup> [see reaction (1)].



For example, phenylacetic acid was lithiated in tetrahydrofuran-hexane using hexamethylphosphoramide as co-solvent,<sup>2</sup> and treated with *O*-methylhydroxylamine at *ca.*  $-15^\circ$  for 2 h. After work-up,  $\alpha$ -phenylglycine<sup>†</sup> was ob-

tained in 55.5% yield, with 32.8% recovery of the starting acid.

Isovaleric acid was aminated under the same conditions to give valine<sup>†</sup> in 33.9% yield. In an attempt to improve the yield, several aminating reagents were investigated:  $\dagger$  *O*-ethylhydroxylamine (22.2%), *O*-isopropylhydroxylamine (25.4%), *O*-*t*-butylhydroxylamine (18.3%), *O*-benzylhydroxylamine (trace), chloramine (7.7%), *O*-mesitoylhydroxylamine (4.3%), *O*-(3,5-dinitromesitoyl)hydroxylamine<sup>§</sup> (5.3%), and hydroxylamine *O*-sulphonic acid (trace).

This is the first method reported for the preparation of  $\alpha$ -amino-acids from carboxylic acids by a one stage procedure. Application of the method to the synthesis of other amino-acids is under way.

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<sup>†</sup> Racemic form.

<sup>‡</sup> Yields were determined by an amino-acid analyser. We thank Drs. Y. Ogiwara and T. Tanimura for the measurement.

<sup>§</sup> M.p. 150–153° (decomp.), prepared from mesitoic acid by successive treatment with fuming nitric acid, thionyl chloride, *t*-butyl *N*-hydroxycarbamate, and hydrogen chloride.

<sup>1</sup> Cf. P. L. Creger, *J. Amer. Chem. Soc.*, 1967, **89**, 2500; 1970, **92**, 1396, 1397; G. W. Moersch and A. R. Burkett, *J. Org. Chem.*, 1971, **36**, 1149.

<sup>2</sup> P. E. Pfeffer and L. S. Silbert, *J. Org. Chem.*, 1970, **35**, 262; P. E. Pfeffer and L. S. Silbert, *Tetrahedron Letters*, 1970, 699.