

α -Amination of Carboxylic Acids: a New Synthesis of α -Amino-acids

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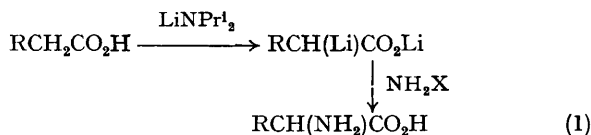
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Summary Amination of α -lithiated carboxylic acid salts provides a new preparative method of α -amino-acids.

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

WE report a new method for the synthesis of α -amino-acids by the amination of α -lithiated acid salts¹ [see reaction (1)].

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



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

For example, phenylacetic acid was lithiated in tetrahydrofuran-hexane using hexamethylphosphoramide as co-solvent,² and treated with *O*-methylhydroxylamine at *ca.* -15° for 2 h. After work-up, α -phenylglycine† was ob-

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† Racemic form.

‡ Yields were determined by an amino-acid analyser. We thank Drs. Y. Oghara and T. Tanimura for the measurement.

§ 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.

¹ 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.

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