The Synthesis of Amino Acids *via* Organoboranes

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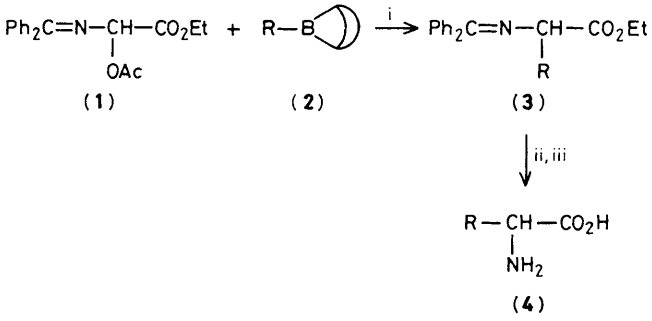
The reaction of the acetate (**1**) with organoboranes provides a convenient, new route to amino acids.

New and general routes to amino acids are of considerable importance owing to the widespread use of these compounds. Syntheses which use functional classes not routinely employed (*e.g.* alkenes) are of special interest since such paths provide the potential for practical syntheses of structurally diversified amino acids. The acetate (**1**), which has recently been prepared and reacted as a glycine cation equivalent with nucleophiles,[1,2] can also be regarded as an α-heteroatom substituted ester. Such compounds are known to react with organoboranes, to form carbon–carbon bonds,[3,4] although this methodology has not been applied to amino acid synthesis. We now report the general synthesis of amino acid derivatives from organoboranes by their carbon–carbon bond-forming reaction with (**1**).

Organoboranes, which are prepared by standard methods from either 9-borabicyclo[3.3.1]nonane (9-BBN)[4a,5] or from



Scheme 1. *Reagents:* i, 2,6-Bu$^t_2$-4-MeC$_6$H$_2$OK, tetrahydrofuran, 0 °C, 2 h, inverse addition; ii, 1 M HCl, diethyl ether; iii, 6 M HCl, heat or LiOH, H_2O.

its 9-methoxy analogue 9-MeOBBN,[4a,6] readily undergo a carbon–carbon bond forming reaction with (**1**)[1] in the presence of a hindered potassium phenoxide[3] to yield the protected higher amino acids (**3**).

Because of the stability of the imines (**3**), the products can be isolated and purified by flash chromatography.† Subsequent two-step hydrolysis then yields the amino acids (**4**).† This methodology provides a general synthesis of amino acids from precursors not normally used for this purpose; these include alkenes, organolithium reagents, aryl halides, or hydrocarbons which can be transformed into organoboranes (See Table 1).

It is important to note that, except for 2-aminodecanoic acid (**4a**), the amino acids prepared by this procedure would be difficult to obtain by normal alkylative chemistry because the alkyl halides needed to prepare (**4b**)—(**4d**) are prone to elimination, or the nucleophilic aromatic substitutions to prepare (**4e**)—(**4g**) are extremely difficult. In conclusion, the easy access to organoboranes as well as their versatile chemistry[4] makes this method an attractive route to various structurally interesting amino acids.

† All new compounds were characterised by analytical and spectral data.

Table 1. Preparation of amino acids by reaction of organoboranes with acetate (**1**).

Starting material[a]	% Yield of (**3**)	Product	R	% Yield[b] of (**4**)
$Me[CH_2]_5CH{=}CH_2$	92	(**4a**)	$Me[CH_2]_7$	74
Cyclohexene	90	(**4b**)	Cyclohexyl	84
α-NpCH=CH_2[c]	68	(**4c**)	α-NpCH_2CH_2	42
Bu^{t}Li	59	(**4d**)	Bu^t	53
PhLi	57	(**4e**)	Ph	55
α-NpBr	64	(**4f**)	α-Np	37
Thiophene	47	(**4g**)	2-Thienyl	40

[a] Starting reagent for the preparation of (**2**). [b] Overall yield from (**1**). [c] α-Np = α-naphthyl.

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References

1 M. J. O'Donnell, W. D. Bennett, and R. L. Polt, *Tetrahedron Lett.*, 1985, **26**, 695.
2 M. J. O'Donnell and J. B. Falmagne, *Tetrahedron Lett.*, 1985, **26**, 699.
3 H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, 1968, **90**, 818; H. C. Brown and M. M. Rogic, *Organomet. Chem. Synth.*, 1972, **1**, 305; M. M. Rogic, *Intra-Sci. Chem. Rep.*, 1973, **7**, 155; M. M. Midland and Y. C. Kwon, *Tetrahedron Lett.*, 1982, **23**, 2077.
4 General references on organoboranes: (a) H. C. Brown, 'Organic Synthesis via Boranes,' Wiley-Interscience, New York, 1975; (b) E. I. Negishi, 'Organometallics in Organic Synthesis,' Wiley-Interscience, New York, 1980; A. Pelter, *Chem. Soc. Rev.*, 1982, **11**, 191; A. Suzuki, *Top. Curr. Chem.*, 1983, **112**, 67.
5 H. C. Brown, 'Hydroboration,' Benjamin/Cummings, Reading, Massachusetts, 1980.
6 G. W. Kramer and H. C. Brown, *J. Organomet. Chem.*, 1974, **73**, 1.