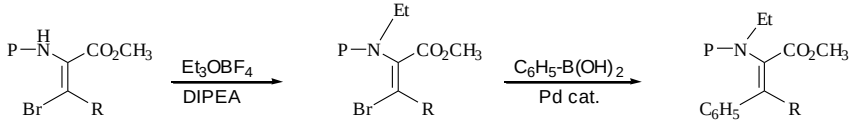
Synthesis of New *N*-Ethyl Dehydroamino Acids

A. C. Suarez, J. Andrade, L. S. Monteiro
Chemistry Centre, University of Minho, Gualtar, 4710-057 Braga, Portugal
anacarolina.ms@hotmail.com

Non-proteinogenic amino acids are an important class of organic compounds that can have intrinsic biological activity or can be found in peptides with antiviral, antitumor, anti-inflammatory or immunosuppressive activities. Among non-proteinogenic amino acids are *N*-alkylamino acids and dehydroamino acids which can be found in many biologically important peptides.[1] Recently we reported the use of a combination of alkylation[2] and dehydration methodologies[3] to obtain, for the first time, non-natural amino acids which incorporate both the *N*-ethyl and α,β-dehydro moieties.[4] Herein, we report the application of this *N*-alkylation procedure to several β,β-dibromodehydroalanine, β-bromo dehydroaminobutyric acid and β-bromo dehydrophenylalanine derivatives, protected with standard amine protecting groups and their subsequent use in Suzuki-Miyaura cross-couplings reactions (Scheme 1).



R = Br, CH_3, C_6H_5. R = Br, CH_3, C_6H_5. R = CH_3, C_6H_5.

P = $Z(NO_2)$, Z, Boc, Nosyl, Tos.

Scheme 1 - *N*-Ethylation and cross-coupling with phenyl boronic acid of β-bromodehydroamino acid derivatives.

Acknowledgment*: FCT-Portugal and FEDER/COMPETE through CQ-UM. The NMR spectrometer Bruker Avance II$^+$ 400 is part of the National NMR Network and was purchased in the framework of the National Programme for Scientific Re-equipment, contract REDE/1517/RMN/2005, with funds from POCI 2010, FEDER and FCT*

References

[1] Goodman T.; Moroder, L. *Synthesis of Peptides and Peptidomimetics*, *Houben-Weyl*, Thieme, Stuttgart, Germany, **2003**, vol. E22c, pp. 215–271.
[2] Belsito, E. L.; De Marco, R.; Di Gioia, M. L.; Liguori, A.; Perri, F.; Viscomi, M. C. *Eur. J. Org. Chem*. **2010**, 4245-4252.
[3] a) Ferreira, P. M. T.; Maia, H. L. S.; Monteiro, L. S.; Sacramento, J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3697-3703. b) Ferreira, P. M. T.; Monteiro, L. S.; Pereira, G.; Silva, L.; Ribeiro, L.; Sacramento, J. *Eur. J. Org. Chem*. **2007**, 5934-5949.
[4] Monteiro, L. S; Kołomańska, J.; Suarez A. C. *Eur. J. Org. Chem*. **2010**, 6731-6735.