

DIRECT TRANSFORMATION OF AMINO ACIDS INTO DIAZIRINES AND $^{15}\text{N}_2$ -DIAZIRINES AND THEIR APPLICATION AS HYPERPOLARIZED MARKERS

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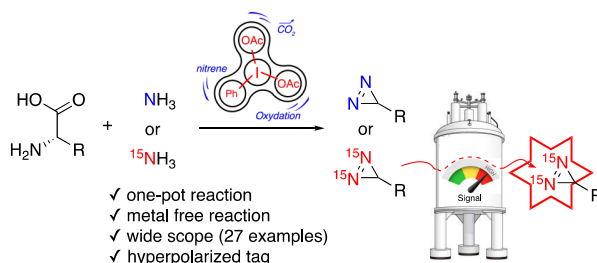
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Diazirines are small 3-membered ring heterocyclic compounds bearing a nitrogen-nitrogen double bond and an sp^3 carbon that are cyclic and substituted analogues of diazomethane [1]. Usually, diazirines are synthesized from carbonyl derivatives in 3 or 4 steps [2].

In 2016, T. Theis showed that $^{15}\text{N}_2$ -diazirines could be used in SABRE-SHEATH hyperpolarization in NMR and MRI with a possible application for *in vivo* imaging [3]. However, as for their unlabelled counterpart, there is a lack of efficient method for $^{15}\text{N}_2$ -diazirine synthesis.

Here, we report a new procedure for a one-pot and metal-free synthesis of ($^{15}\text{N}_2$ -labeled) diazirines from unprotected amino acids. Our methodology proved to be efficient on most proteinogenic amino acids and on non-proteinogenic one as well, providing good to excellent yields.



The reaction conditions for the formation of ($^{15}\text{N}_2$ -labeled) diazirines, first insights onto the reaction mechanism and hyperpolarization results will be presented and discussed.

[1] Schmitz, E.; Ohme, R. *Chemische Berichte*, **1961**, 94, 2166-2173.

[2] (a) Graham, W. H. *J. Am. Chem. Soc.*, **1966**, 88, 4677-4681, (b) Smith, R. A. G.; Knowles, J. R. *J.C.S. Perkin II*, **1975**, 686-694, (c) Protasova, I.; Bulat, B.; Jung, N.; Bräse, S. *Org. Lett.*, **2017**, 19, 34-37.

[3] Theis, T.; Ortiz Jr., G. X.; Logan, A. W. J.; Clayton, K. E.; Feng, Y.; Huhn, W. P.; Blum, V.; Malcolmson, S. J.; Chekmenev, E. Y.; Wang, Q.; Warren, W. S. *Science Advances*, **2016**, 2, e1501438.