**Synthesis of Substituted 2-Aminoimidazoles**

**Significance:** Looper and co-workers described a three-step synthesis of highly substituted 2-aminoimidazoles. The first step consists of the preparation of propargyl cyanamides by copper(I)-catalyzed addition of an iminium generated from condensation of aldehydes ($R^2 = \text{alkyl or aryl}$) with secondary amines. Without further purification, the resulting tertiary amines are subjected to a von Braun reaction. The use of 4-methoxybenzyl-, 2,4- and 3,4-dimethoxybenzyl-substituted propargyl amines lead to the propargyl cyanamides in good yields whereas symmetric $N,N$-dialkylpropargyl amines give exclusively propargyl bromide. Screening of catalysts led to the use of La(OTf)$_3$ for the final addition–hydroamination step. Both acyclic and cyclic secondary amines generated guanidine intermediates which underwent cyclization to the alkyne to afford 2-aminoimidazoles in good yields.

**Comment:** Several alkaloids containing the 2-aminoimidazole ring with interesting structures and biological properties have been isolated from marine sponges (S. M. Weinreb Nat. Prod. Rep. 2007, 24, 931). This scaffold improves physico-chemical properties like lipophilicity, blood-brain barrier passage, cell permeability and bioavailability. Polysubstituted 2-aminoimidazole synthesis remains challenging as the current methods present some disadvantages: i) use of unstable precursors for the condensation of $\alpha$-amino/ $\alpha$-haloketone with a cyanamide or a guanidine derivative respectively; ii) multi-step synthesis for the decoration of the imidazole scaffold. This three-step sequence represents a useful tool for the efficient synthesis of diversely substituted 2-aminoimidazoles from readily available starting materials.

**Ar = 4-MeOC$_6$H$_4$, 2,4-(MeO)$_2$C$_6$H$_3$, 3,4-(MeO)$_2$C$_6$H$_3$

$R^1 = \text{Me, allyl, 4-MeOC$_6$H$_4$CH$_2$, Bn}$

$R^2 = H, n$-Bu, Bn, 4-BnOOC$_6$H$_4$CH$_2$

$R^3 = n$-Bu, Ph, 4-OMeC$_6$H$_4$

$R^4 = \text{Me, allyl}$

$R^5 = \text{Bn, allyl}$

$R^4R^5NH = \text{morpholine, pyrrolidine, isoindoline, 1,2,3,4-tetrahydroisoquinoline}$

also:

$$\text{HN}$$

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