MECHANOCHEMICAL APPROACH TO THE SYNTHESIS OF 2-UNSUBSTITUTED IMIDAZOLE *N*-OXIDES, CONVENIENT PRECURSORS OF NEW ALKOXYIMIDAZOL-2-YLIDENES (NHCS)

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2-Unsubstituted imidazole *N*-oxides of type **1** are known as useful precursors for the preparation of a wide range of imidazole derivatives [1]. Their *O*-alkylation, leading to imidazolium salts **2**, opens a convenient route to alkoxyimidazol-2-ylidenes **3**, which constitute a new group of nucleophilic carbenes NHCs [2,3] (Fig. 1).

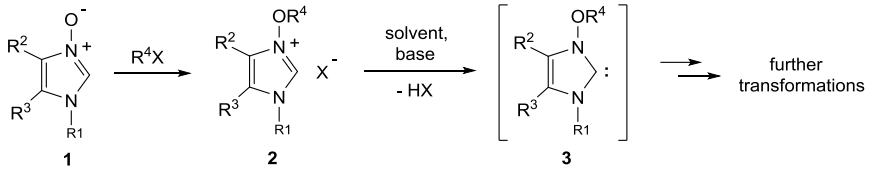

Fig. 1. In situ generation of alkoxy imidazol-2-ylidenes **3** starting with 2-unsubstituted imidazole *N*-oxides **1**.

The best known protocol for synthesis of **1** is heterocyclization of α-hydroxyiminoketones **4** by treatment with formaldimines **5** in boiling EtOH or in AcOH at room temperature [1,2]. In the first case, however, isomerization of the starting *N*-oxide to corresponding imidazol-2-one is a serious disadvantage. Moreover, this method can't be applied for formaldimines derived from aromatic primary amines. On the other hand, reactions performed in acetic acid require longer reaction times (an overnight protocol) and a multi-step workup.

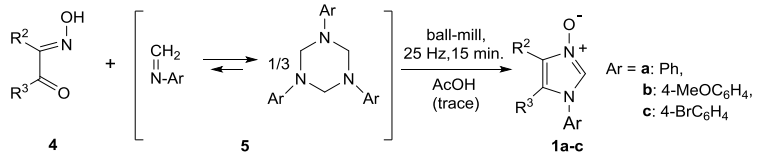

Fig. 2. Mechanochemical synthesis of N(1)-aryl functionalzed imidazole *N*-oxides **1**.

Now, we report mechanochemical approach to the synthesis of imidazole *N*-oxides **1** bearing aryl (Ar) substituent at the N(1). Ball milling of α-hydroxyiminoketone **4** with corresponding formaldimine **5** ($Ar\text{-}NH_2$) led to desired products **1a-c** in 69-80% yield (Scheme 2). The same protocol was applied for N(1)-alkyl substituted imidazole *N*-oxides **1** including optically active derivatives of *trans*-1,2-diaminocyclohexane [3].

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[2] G. Mlostoń, M. Celeda, K. Urbaniak, M. Jasiński, V. Bakhonsky, P. R. Schreiner, H. Heimgartner, Synthesis and selected transformations of 2-unsubstituted 1-(adamantyloxy)imidazole 3-oxides: strightforward access to non-symmetric 1,3-dialkoxy imidazolium salts, Beilstein J. Org. Chem., **15**, 497–505 (2019).

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