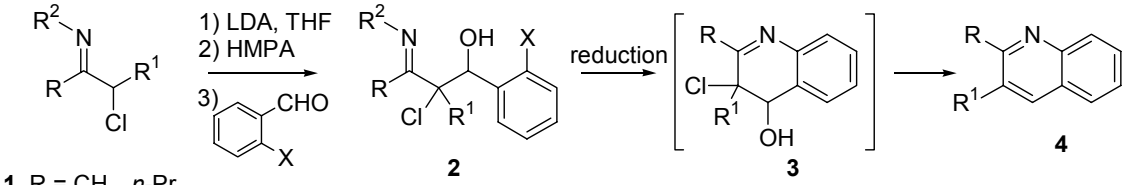
Use of 1-Azaallylic Anions Toward the Synthesis of 2-Alkyl- and 2-Arylquinolines

Nicola Giubellina, Wim Aelterman and Norbert De Kimpe

Department of Organic Chemistry, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium

The synthesis of quinoline derivatives has been of considerable interest to organic and medicinal chemists for many years, since a large number of natural products and drugs contain this heterocyclic nucleus. Thus, development of new and alternative quinoline derivatives is a continuing and urgent requirement. Herein is presented a simple and efficient synthesis of new 2-arylquinolines **4** starting from 3,3-dichloro- and 3-chloro-1-azaallylic anions **1**.

α,α-Dichlorinated imines **1** (R = C_6H_5, 4-ClC_6H_4; R^1 = Cl; R^2 = *i*-Pr), readily available upon condensation of α,α-dichloroacetophenones and *i*-propylamine in the presence of Ti(IV) chloride, are quantitatively deprotonated with lithium amides in THF at low temperature in the presence of an equimolar amount of hexamethylphosphor(V) amide (HMPA). Addition of the lithium 1-azaallylic anions to aromatic aldehydes, bearing an amino equivalent at the ortho position (X = N_3, NO_2), gave aldol adducts **2** in good to very good yield (67-100 %). The latter, when reduced at the masked amino functionality, spontaneously ring closed to dihydroquinolines **3**, which, via imino reduction and elimination of hydrogen chloride and water, gave 3-chloroquinolines **4** in satisfactory overall yields upon flash chromatographic purification (30-45 %).



1 ,R = CH_3, *n*-Pr, C_6H_5, 4-ClC_6H_4
R^1 = CH_3, Cl
R^2 = Et, *i*-Pr, *t*-Bu

X : N_3, NO_2

2 **3** **4**

Chlorinated imines **1** (R = Me, *n*-Pr, 4-ClC_6H_4; R^1 = CH_3, Cl ; R^2 = Et, *i*-Pr, *t*-Bu), when reacted with ortho-azidobenzyl iodide, gave stable α-chlorinated azidoimines in excellent yields (89-94 %). Reduction of the latter azides with tin(II) chloride afforded quinolines **4** (16-45 %) along with the analogous 3,4-dihydro- and 1,2,3,4-tetrahydroquinoline derivatives (0-60 % and 0-27 % yield, respectively). Therefore, new entries toward new potentially biologically active 2-aryl-3-methyl- and 2-aryl-3-chloroquinolines are presented.