Tandem Synthesis of 1,2-Dihydropyridines from Amines, Isocyanides and Acetylenic Esters

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Dihydropyridines have long been recognized as versatile synthetic intermediates [1] that provide ready access to a variety of substituted N-heterocycles such as piperidines and pyridines. The majority of synthetic approaches to 1,2-dihydropyridines has relied on nucleophilic addition to N-alkyl or N-acylpyridinium salts. However, regioisomeric mixtures of addition products are often obtained if unsymmetrically substituted pyridinium salts are employed.

As a part of our current studies on the development of new routes in heterocyclic synthesis [2], we report the results of our studies involving the reaction of the zwitterionic intermediates derived from alkyl isocyanides and acetylenic esters with dialkyl 2-(alkyl(aryl)amino)but-2-enedioates [generated in situ from primary alkyl(aryl)amines and acetylenic esters, which constitutes a synthesis of highly functionalized 1,2-dihydropyridines in good yields.

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\begin{align*}
R_1^1N=\overset{\ominus}{\overset{\oplus}{C}} + \overset{\ominus}{\overset{\oplus}{R_2^2\text{CO}_2}} + R_3^3\text{NH}_2 + \overset{\ominus}{\overset{\oplus}{R_4^4\text{CO}_2}} &\xrightarrow{\text{r.t, 10 h, CH}_2\text{Cl}_2} \overset{N}{\overset{\ominus}{\overset{\oplus}{R_2^2\text{CO}_2}}}NHR_1^1 \overset{\ominus}{\overset{\oplus}{R_3^3\text{CO}_2}} \overset{\ominus}{\overset{\oplus}{R_4^4\text{CO}_2}}
\end{align*}
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The reaction proceeded smoothly in CH₂Cl₂ at r.t temperature in good yields and finished within 10 h. The structures of dihydropyridine derivatives were deduced from their elemental analyses and their IR, ¹H NMR, ¹³C NMR and single-crystal X-ray analyses.

REFERENCES