

Reaction between 3-hydroxy pyridine alkyl isocyanides and dialkyl acetylenedicarboxylate: synthesis of 4H-chromenes

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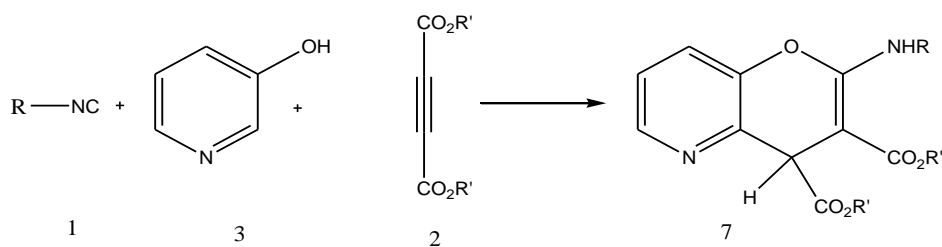
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Abstract- The reactive intermediate generated by the addition of tert-butyl and 1,1,3,3-tetramethyl butyl isocyanide and cyclohexyl isocyanide to dialkyl acetylenedicarboxylate was trapped by 3-hydroxy pyridine to produce highly functionalized 4H-chromenes in fairly good yields.

Keywords: 3-hydroxy pyridine , dialkyl acetylene dicarboxylates ,alkyl isocyanide ,multi component reaction,4H-chromenes

Introduction:

Multi component reaction (MCRs) have attracted much attention in combinatorial chemistry .Of importance in this area are the isocyanide based MCRs such as the versatile Ugi and Passerini reaction [1]. The addition of nucleophilic carbens such as isocyanides to dialkyl acetelendicarboxylates has been investigated in detail [2]. In recent years, isocyanide-based multi component condensation reactions(IMCRs) by virtue of their synthetic potential ,their inherent atom efficiency , convergent nature , ease of implementation, and the generation of molecular diversity , have attracted much attention because of the advantages that they offer to the field of combinatorial chemistry [3,4]. We now report an efficient synthetic route to poly substituted benzo chromenes using alkyl isocyanides and alkyl acetylene dicarboxylates in the presence of 3-pyridinol.



Scheme 1.

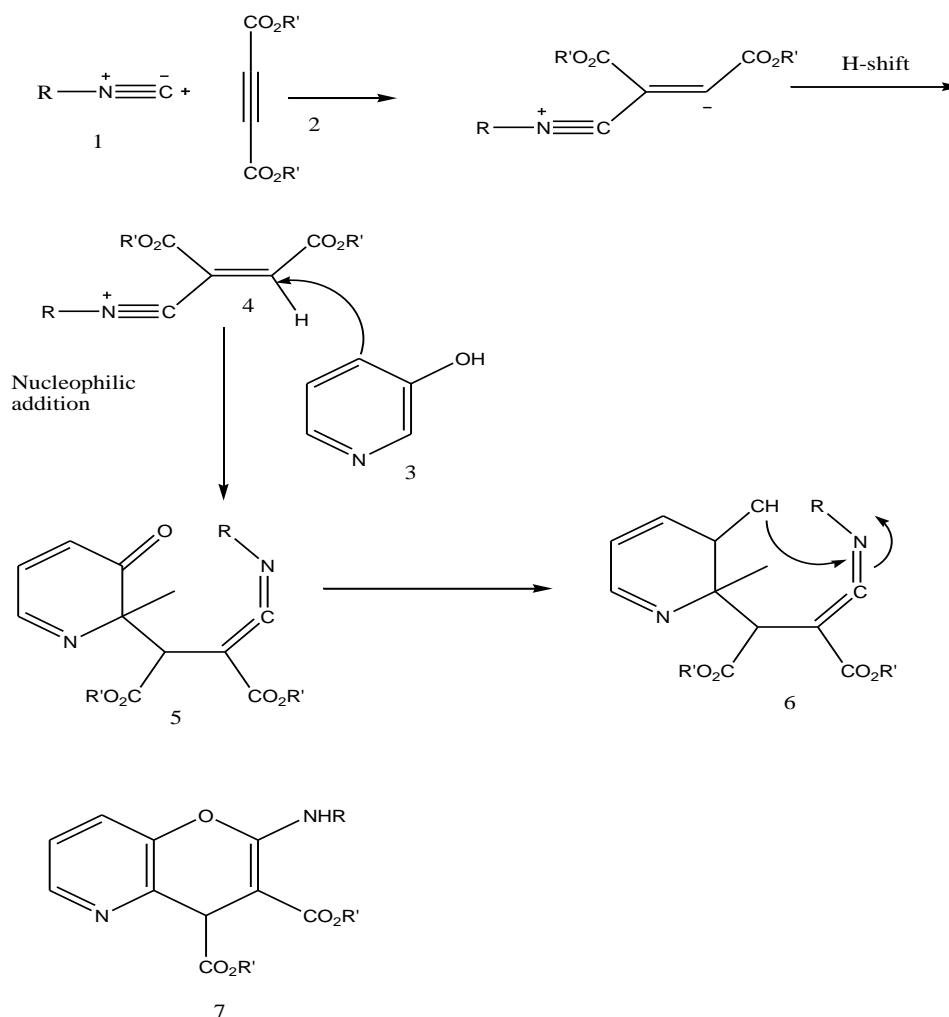
Experimental:

To a stirred solution of 3-pyridinol (0.095,1mmol) in CH₂CL₂(5ml) and tert-butyl isocyanide (0.083,1mmol) in 5ml of CH₂CL₂ ,dimethylacetylene dicarboxylate (DMAD) (0.14, 1mmol) was added .

The reaction mixture was then allowed to warm up to room temperature and stand for 24 h. The solvent was removed under reduced pressure, and the residual was purified by thin layer chromatography using n-hexan –EtoAC (1:1) as eluent .

Result :

Compound 7 result from nucleophilic addition of alkyl isocyanide to the acetylenic system and subsequent protonation of the 1:1 adduct by the OH –acid .then the positively charged ion 4 is attacked by the anion of the OH-acid to form ketenimine 5.such an addition product may tautomerize to 6 and then cyclize under the reaction conditions employed to product 7.



Scheme2

Conclusion:

In conclusion, we have found an efficient synthetic method for the preparation of some 4H-chromenes. The present method carries the advantage that not only is the reaction performed under neutral conditions and without anhydrous conditions at room temperature ,but also the starting materials and reagents can be mixed without any activation or modification.

Diethyl2-(tert-Butylamino)-4H-pyrano[3,2-b]pyridine-3,4-dicarboxylate (1a) . Yellow oil , $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 1.10 (t, $J=7.1$, 3H), 1.17 (t, $J=7.13$,H), 1.50(s,9H),4.02-4.28(m, 4H),5.29(s,1H), 7.45(d, $J=6.4$,1H), 7.62(dd, $J=6.4$, 7.4 ,1H) , 9.60(d, $J= 7.4$,1H); IR (KBr) δ :3436, 2855, 1734, 1631, 1094 cm^{-1} . Anal. calcd for $\text{C}_{18}\text{H}_{26}\text{N}_2$: C 61.70, H 7.48, N 7.99; found C61.68, H 7.49, N 7.98(HRMS calcd for $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5$ 350.1842, found 350.1839)

Diethyl2-(1,1,3,3-Tetramethyl-butylamino)-4H-pyrano[3,2-b]pyridine-3,4-dicarboxylat (2a).Yellow oil , $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 0.81(s , 9H), 0.90 (t, $J=7.1$,3H), 1.18 (t, $J=7.1$, 3H),1.33(s,6H),1.94(s,2H), 4.12-4.32(m, 4H),5.56(s,1H), 7.28(d, $J= 6.3$,1H) 7.62(dd, $J=6.3,7.5,1\text{H}$) , 9.03(d, $J=7.5,1\text{H}$); IR (KBr) δ :3435, 2924, 1733, 1629, 1186 cm^{-1} . Anal. calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2$: C 65.32, H 7.97, N 6.93; found C65.26, H 7.95, N 8.6.96 (HRMS calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_5$ 404.2311, found 404.2313).

Diethyl 2- (Cyclohexylamino) -4H-pyrano [3,2-b] pyridine-3,4-dicarboxylate(3a). Yellow oil , $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 0.82-0.99(m , 10H), 1.18 (t, $J=7.1$, 3H), 1.25 (t, $J=7.1$, 3H), 3.02 (m, 1H), 4.11-4.28(m, 4H),5.44(s,1H), 7.42(d, $J= 6.6$,1H) 7.62(dd, $J= 6.6,7.1$,1H), 9.03(d, $J=7.1$,1H); IR (KBr) δ :3409, 2932, 1731, 1622, 1106 cm^{-1} . Anal. calcd for $\text{C}_{20}\text{H}_{26}\text{N}_2$: C 64.15, H 7.00, N 7.48; found C 64.19, H 6.68, N 7.47 (HRMS calcd for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_5$ 374.1842, found 374.1840).

Dimethyl 2 -(Cyclohexylamino)- 4H-pyrano [3,2-b] pyridine-3,4-dicarboxylate (4a). Yellow oil , $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 0.84-0.86(m , 10H), 3.11 (m, 1H),3.64(s,3H),3.75(s,3H), 5.44(s,1H),7.23(d, $J=6.8$,1H),7.45(dd, $J=6.8,7.2$,1H) , 9.03(d, $J=7.2$,1H); IR (KBr) δ :3409, 2932, 1731, 1622, 1106 cm^{-1} ; MS(70 eV) m/z (%): 346 (M^+ , 20), 320 (15), 179 (80),111(74),83(67),57(100). Anal. calcd for $\text{C}_{18}\text{H}_{22}\text{N}_2$: C 62.42, H 6.40, N 8.09; found C 62.39, H 6.42, N 8.11 (HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5$ 346.1529, found 346.1526).

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