

Nickel catalyzed cascade conversion of propargyl halide and propargyl alcohol into 4,6-dimethyl-5-cyano-2-pyrone in water

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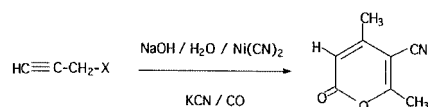
Received (in Cambridge, UK) 24th March 2000, Accepted 30th March 2000

Published on the Web 28th April 2000

Reaction of propargyl halide or alcohol with CO and KCN in the presence of Ni(CN)₂ in a basic aqueous medium affords 4,6-dimethyl-5-cyano-2-pyrone.

Transition-metal mediated carbonylation of various organic substrates constitutes probably one of the most studied and applied reactions in the last decades.¹ Among the numerous metals used, nickel has aroused much interest especially since Alper and Jo² have shown that Ni(CN)₂, under phase transfer conditions, can advantageously replace Ni(CO)₄ and become a versatile catalytic system. In this context, we reported^{3,4} several selective nickel catalyzed mono or dicarbonylations of various alkynyl substrates under phase transfer conditions. More recently,⁵ by working only in water, and in the presence of excess cyanide ions, the same catalyst precursor was shown to transform exclusively α -ketoalkynes into unsaturated hydroxylactams, by a hydrocyanation process, whereas hydroxylactones had been obtained under phase transfer conditions. The apparent change in reaction pathway in going from a biphasic to a monophasic aqueous system prompted us to investigate the reactivity of other alkynyl substrates in water.

We report, here, the reaction of propargyl (prop-2-ynyl) halides or alcohols with CO in the presence of cyanide ions catalyzed by Ni(CN)₂ in water to afford as a sole product 4,6-dimethyl-5-cyano-2-pyrone (Scheme 1).⁶



Scheme 1

Most reported 2-pyrones bear ester groups in the 5-position. Their synthesis from ketone enolate and α,β -acetylenic esters or ester enolates and α,β -acetylenic ketones usually involve several steps.⁷⁻¹¹ More recently a one-pot improved synthesis using the same strategy gave moderate yields.¹² None of these synthetic routes, however, included a carbonylation nor a cyanation step.

In a typical experiment, a 5 M NaOH solution (50 ml) containing 2 mmol of Ni(CN)₂ was kept under CO (1 atm) overnight to give a pale yellow solution, before KCN (15 mmol) was added affording an orange colored solution. Addition of the propargyl substrate (20 mmol) with vigorous stirring, at room temperature, resulted, after 0.5 h, in a cloudy suspension from which the product was extracted with diethyl ether. Evaporation of the solvent afforded the 2-pyrone as a white crystalline solid.† The results given in Table 1 show moderate to good yields for a reaction as yet not optimized.¹³

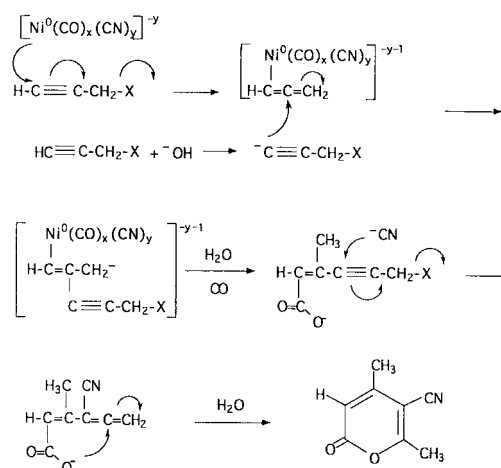
The product obtained indicates a sequential process involving a coupling, a carbonylation, a hydrocyanation and a heterocyclisation by a cascade mechanism with surprising selectivity. Although the nature of the organometallic entity

Table 1 Reaction of propargyl substrates with CO and KCN in the presence of Ni(CN)₂ in water^a

HC≡C-CH ₂ -X	Reaction temperature/°C	Reaction time/min	Isolated yield (%) ^b
X = Br	25	30	86
X = Cl	25	30	63
X = OH	25	30	47

^a Reaction conditions: substrate (20 mmol), 5 M NaOH (50 ml), Ni(CN)₂ (2.0 mmol), KCN (15 mmol), CO (1 atm). ^b Based on available CN.

responsible for these transformations is not established, one can propose a reaction scheme illustrating the 2-pyrone formation (Scheme 2).



Scheme 2

As a first step, one would expect the propargyl halide or alcohol to undergo a nucleophilic attack by the nickel(0) anion, formed *in situ*, in a manner analogous to the reported reaction in a biphasic medium.³ The allenynickel anion obtained could, in turn, undergo another nucleophilic attack on the central, most electrophilic, carbon by an alkynyl anion formed in the aqueous basic environment. This would correspond to the coupling step. A CO insertion into the vinylic C–Ni bond followed by hydrolysis results in the formation of an unsaturated carboxylate anion and concurs with the carbonylation step. The introduction of the cyano group can, then, be depicted as a Michael type nucleophilic attack by cyanide ion, present in the aqueous medium, on the propargyl moiety of the carboxylate anion leading to a cyanoallenyl species which undergoes the final cyclisation to give the observed 2-pyrone product.

Notes and references

† Spectroscopic data for 4,6-dimethyl-5-cyano-2-pyrone: IR (CHCl₃)/cm⁻¹, ν_{CN} , 2231.5, $\nu_{\text{C=O}}$, 1751.3; ¹H NMR (CDCl₃) δ 2.30 (d, 3H, CH-CH₃), 2.54 (s, 3H, O-C-CH₃), 6.07 (q, 1H, CH); ¹³C NMR (CDCl₃) 171.7 (C=O), 158.6 (CH-C-CH₃), 153.2 (O-C-CH₃), 113.9 (CN), 111.1 (CH-C-CH₃), 95.3 (C-CN), 20.5 (CH-C-CH₃), 20.0 (O-C-CH₃). MS (*m/z*) 149 (80%, M⁺), 134 (15%, M⁺ - CH₃), 121 (base peak, M⁺ - CO), 78 (17%, 128 - CH₃O), 43 (62%, 128 - CHCH₃CCN).

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- 13 Under these experimental conditions, substituted homologues react extremely sluggishly and do not afford any detectable amount of 2-pyrone products. This could be due, in part, to the reduced solubility of these substrates in the aqueous medium. Further work, in order to extend the scope of this reaction, is underway.