Mono- and Dicarboxylation of α-Haloalkynes Catalyzed by Nickel Cyanide under Phase-Transfer Conditions

Henri Arzoumanian,* Fabienne Cochini, Didier Nuel, Jean François Petrignani,[†] and Noê Rosas[‡]

Ecole Nationale Supérieure de Synthèses, de Procédés et d'Ingénièrie Chimiques d'Aix-Marseille, URA du CRNS 1410, Université d'Aix-Marseille III, 13397 Marseille, France

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Summary: α-Haloalkynes react with carbon monoxide to give either allenic monoacids or unsaturated diacids in 70–96% overall yields. The reaction is catalyzed by nickel cyanide under phase-transfer conditions (4-methyl-2-pentanone, 5 N NaOH, tetraalkylammonium halide). It is shown that the carbonylation occurs stepwise: first to the allenic monoacid via a nucleophilic substitution, followed by a second carbonylation of this latter. The diacid is obtained with high stereoselectivity.

Transition-metal-mediated carbonylation of acetylenic compounds has been the object of numerous studies.[1-3] They originated from the systematic work of Reppe[4,5] in the early 1940s on the reaction of unsaturated compounds with CO in the presence of $Ni(CO)_4$. The reactions were most often stoichiometric, in which the source of CO was the nickel tetracarbonyl itself.[6-12] When $Ni(CO)_4$ was used catalytically, relatively elevated temperatures and pressures of CO were necessary. Although the selectivities obtained were good and despite some commercial development (e.g. acrylic acid), truly synthetic applications at the laboratory level were never attempted, probably due to safety reasons.

Transition-metal-mediated carbonylation of organic substrates effected under phase-transfer conditions is also a well-studied reaction.[13] Recently Alper and co-workers have shown that, under these conditions, nickel cyanide can advantageously replace nickel tetracarbonyl[14] and become a versatile and much safer catalyst, able to perform carbonylation of various substrates, including alkynes[15] and alkynols.[16]

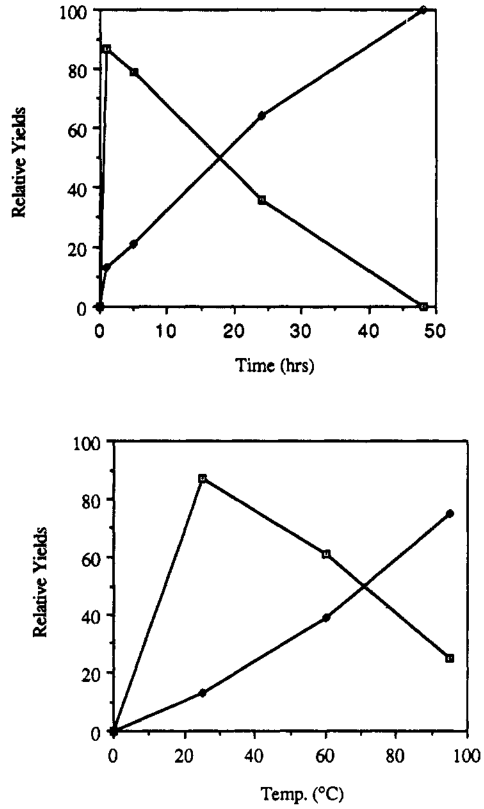
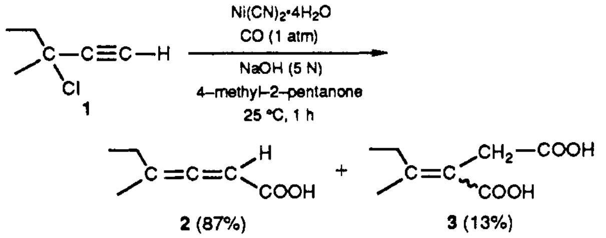


Figure 1. Dependence of the temperature and reaction time for the carbonylation of 1: (◇) monoacid 2; (◆) diacid 3.

We wish to report here the conversion of α-haloalkynes to either mono- or dicarboxylic acids in the presence of nickel cyanide under phase-transfer conditions.

Results and Discussion

Treatment at room temperature of 3-chloro-3-methylpent-1-yne (1) with carbon monoxide (1 atm) in the presence of sodium hydroxide (5 N), 4-methyl-2-pentanone as the organic phase, catalytic amounts of hydrated nickel cyanide, and tetrabutylammonium bromide as the transfer agent resulted, after 1 h and upon workup, in the isolation of 4-methylhexa-2,3-dienoic acid (2) and 3-carboxy-4-methyl-3-hexenoic acid (3) in 94% overall yield.



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[†] Current address: Air Liquide, CRD, B.P. 126, 78350 Jouy en Josas, France.

[‡] On sabbatical leave from the Instituto de Quimica, Universidad Nacional Autonoma de Mexico, Ciudad Universitaria, Mexico.

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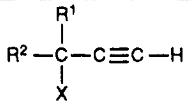
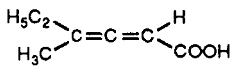
Table I. Carbonylation of α-Haloalkynes[a]

							product distribn	
entry no.	R^1	R^2	X	temp, °C	time, h	yield,[b] %	monoacid	diacid (*E*/*Z*)
1	C_2H_5	CH_3	Cl (**1**)	25	1	94	87 (**2**)	13 (5/95)[c] (**3**)
2	C_2H_5	CH_3	Cl (**1**)	60	1	92	61 (**2**)	39 (**3**)
3	C_2H_5	CH_3	Cl (**1**)	95	1	91	24 (**2**)	76 (7/93) (**3**)
4	C_2H_5	CH_3	Cl (**1**)	25	5	93	79 (**2**)	21 (**3**)
5	C_2H_5	CH_3	Cl (**1**)	25	24	94	36 (**2**)	64 (**3**)
6	C_2H_5	CH_3	Cl (**1**)	25	48	96		100 (9/91) (**3**)
7	C_2H_5	CH_3	Br (**9**)	25	48	94	13 (**2**)	87 (10/90) (**3**)
8	C_2H_5	CH_3	Cl (**1**)[d]	25	48	94	5 (**2**)	95 (10/90) (**3**)
9	C_2H_5	CH_3	Cl (**1**)[e]	25	48	71	52 (**2**)	48 (88/12) (**3**)
10	CH_3	CH_3	Cl (**10**)	25	1	71	48 (**11**)	52 (**12**)
11	H	H	Cl (**13**)	65	2	85	15[f] (**14**)	85 (**15**)
12	H	H	Br (**16**)	65	2	68	32[f] (**14**)	68 (**15**)
13				25	24	94		100 (12/88) (**3**)

[a] Reaction conditions: α-haloalkyne, 14 mmol; 4-methyl-2-pentanone, 50 mL; 5 N NaOH, 20 mL; $Ni(CN)_2{\cdot}4H_2O$, 1.0 mmol, tetrabutylammonium bromide, 0.3 mmol; CO, 1 atm; 25 °C. [b] Isolated yields. [c] Ratio established by ^1H NMR spectroscopy and based on reported data.[16] [d] Phase-transfer agent tetrabutylammonium chloride. [e] Phase transfer agent cetyltrimethylammonium bromide. [f] Could not be obtained in pure form;[18] estimated from the yield of isolated diacid.

Compounds **2** and **3** have been previously reported as the carbonylation products of alkynols. Allenic acid **2** was the major product of the stoichiometric reaction of 3-methylpent-1-yn-3-ol with nickel tetracarbonyl,[8] whereas the diacid **3** was the only product reported for nickel- and phase-transfer-catalyzed carbonylation of the same alkynol at 95 °C.[16] Also relevant to the present work, it has been reported[10] that propargyl chloride is carbonylated stoichiometrically with nickel tetracarbonyl to give butane 2,3-dienoic acid (**14**) and itaconic acid (**15**) depending on the amount of water present in the medium.

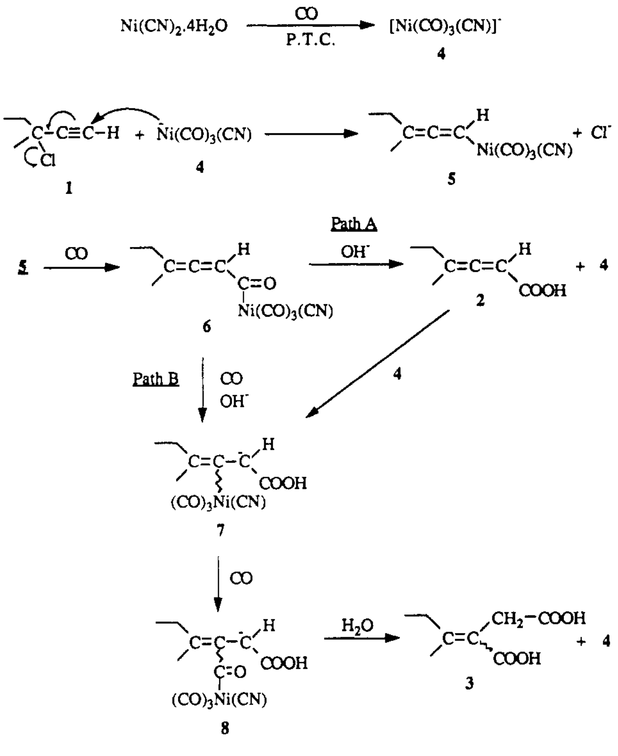
In each case the reaction pathways proposed were different, but none suggested that **3** could arise simply by carbonylation of **2**.[17] In the present study, the interpretation of the results was more compatible with the intermediacy of **2**.

Indeed, by an increase in either the reaction time or the reaction temperature, the ratio **3**/**2** increased to practically complete disappearance of **2**, as is shown in Figure 1. This strongly suggested that the allenic structure was first formed, followed by a second carbonylation to give **3**. Supporting evidence for this was given by reacting **2** under identical reaction conditions and obtaining **3** quantitatively (entry 13 in Table I). The reaction seems general and was performed on other α-haloalkynes, as is shown in Table I. A plausible mechanism is given in Scheme I.

It is most likely that the first step consists of a nucleophilic attack of the tricarbonylcyanonickelate ion (**4**) on the terminal alkynyl carbon, if one considers chloride as being a much better leaving group than hydroxide.[19] Furthermore, an initial addition onto the triple bond would result in the formation of a monoacid different from **2**.[16] This first step followed by a CO insertion into the allenyl–nickel bond gives the acyl complex **6**.

Two paths can now be envisaged for the second carbonylation. They differ in the mode of the nucleophilic attack by the nickel carbonyl entity onto the center carbon of the allenyl function. In path A, there is liberation of **2** prior to a new attack by $Ni(CO)_3CN^-$ to give intermediate **7**, whereas in path B there is a concerted base-induced cleavage and intramolecular attack of nickel to give **7**. The difference between paths A and B could possibly have consequences on the stereochemistry of the second carbonylation step and be reflected in the *E*/*Z* ratio.

Scheme I. Mechanism for the Catalytic Carbonylation of α-Haloalkynes



Comparison of the *E*/*Z* ratio of **3** obtained in entry 1 (Table I; via either path A or B) and in entry 13 (Table I; only via path A) showed respectively *E*/*Z* = 5/95 and 12/88; this would tend toward a preference for path A, but the small difference leaves a certain degree of uncertainty.

More interesting, however, is the comparison of the *E*/*Z* ratio of **3** obtained either from the α-haloalkyne or from the alkynol[16] (5/95 vs 50/50). This difference is only compatible with a radically different reaction pathway and

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(17) This was suggested in ref 10 but discarded as improbable under their reaction conditions.

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(19) Another possible route could have been an initial rearrangement of the α-haloalkyne into a haloallene prior to the carbonylation. This was shown not to be the case: Arzoumanian, H.; Cochini, F.; Nuel, D.; Rosas, N. To be submitted for publication.

again supports the mechanism described in Scheme I. The high selectivity obtained in the case of α-haloalkynes can be rationalized if we consider the introduction of the second CO as being sterically more constraining on species **2** or **6** compared to an allylic system, as in the case of alkynols,[16] where the entering nucleophile is too far away to differentiate between the size of a methyl and an ethyl group.

It is interesting to note that, in contrast to the carbonylation of alkynols, the E/Z ratio was not influenced by the counterion of the phase-transfer agent used (see entries 6 and 8) or by the nature of the halogen on the substrate (see entries 6 and 7); on the other hand, changing the nature of the transfer agent (TBAC vs CTAB) resulted not only in a slower reaction but also in the total inversion of the stereochemistry (entries 6 or 8 and 9). This may be the direct consequence of two different steric requirements of the attacking nickelate ion pairs. An additional reason for the difference in behavior for the two transfer agents could be that they might operate by different mechanisms.[21]

Experimental Section

General Data. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. NMR spectra were recorded on a Bruker AC-100 or a Bruker AMX-400 spectrophotometer. The chemical shifts (ppm) were determined relative to $(CH_3)_4Si$. IR spectra were recorded on a Nicolet MX5 spectrometer. Thin-layer or column chromatography was performed on silica gel (Merck). Reactions were done in a 100-mL double-walled, thermostated reactor equipped with a magnetic stirrer and inlet tube for gas bubbling. α-Haloalkynes, except propargyl bromide and chloride, were prepared according to reported methods.[20]

General Procedure for the Nickel Cyanide and Phase-Transfer-Catalyzed Carbonylation of α-Haloalkynes. 4-Methyl-2-pentanone (50 mL) and 5 N NaOH (20 mL) were degassed and saturated with CO under atmospheric pressure before $Ni(CN)_2 \cdot 4H_2O$ (1.0 mmol) and tetrabutylammonium bromide (0.3 mmol) were introduced, and the mixture was kept at room temperature overnight with stirring while CO was slowly (2–3 mL/min) bubbled through the solution. To the yellow two-phase mixture was then added 14 mmol of α-haloalkyne. Stirring and flow of CO were maintained for the desired time and at a given temperature. Separation of the aqueous phase and acidification (pH ~1), followed by extraction with diethyl ether (2 × 25 mL), drying ($MgSO_4$) of the combined extracts, and rotary evaporation yielded the products. Either recrystallization (methanol/diethyl ether, 50/50), for the diacid, or distillation, for the monoacid, gave analytically pure samples. All products were known materials and had spectral and physical characteristics in accordance with literature values.[8,10,16]

Registry No. **1**, 14179-94-3; **2**, 65359-70-8; (*Z*)-**3**, 132885-49-5; (*E*)-**3**, 132885-52-0; **9**, 40185-84-0; **10**, 1111-97-3; **11**, 60221-74-1; **12**, 584-27-0; **13**, 624-65-7; **14**, 5732-10-5; **15**, 97-65-4; **16**, 106-96-7; $CH_3C(CH_3)CH_2COCH_3$, 108-10-1; $NBu_4{}^+Br^-$, 1643-19-2; $NBu_4{}^+Cl^-$, 1112-67-0; $Me_3N(CH_2)_{15}CH_3{}^+Br^-$, 57-09-0; $Ni(CN)_2$, 557-19-7.

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