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A New method for the Regio and Stereoselective hydrocarboxylation of Alkynes using $NaHFe(CO)_4/CH_2Cl_2$ System

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Abstract: The reagent generated in situ in THF using $NaHFe(CO)_4$ and CH_2Cl_2 was used for the regio and stereoselective hydrocarboxylation of terminal and internal alkynes to obtain α,β-unsaturated carboxylic acid derivatives. © 1997 Published by Elsevier Science Ltd. All rights reserved.

Hydrocarboxylation of acetylene is an industrially important reaction for the large scale production of acrylic acid derivatives.[1] Due to the symmetric nature of the acetylene there is no possibility of formation of regio and stereoisomers. In the case of unsymmetrical alkynes, formation of mixtures of regio and stereoisomers hinders the applications. Among the various transition metals, the complexes of Ni,[2] Co,[3] and Pd[4] have been most widely used for the hydrocarboxylation of alkynes. To our knowledge, direct hydrocarboxylation of substituted alkynes mediated by iron carbonyl has not been realised.[5] In continuation of our efforts to effect carbonylation reactions using iron carbonyl reagents,[6] we wish to report that the intermediate generated in the reaction of $NaHFe(CO)_4$ and CH_2Cl_2 in THF is useful for this purpose.

We have observed that the species generated *in situ* by treating $NaHFe(CO)_4$ (1 eq) with CH_2Cl_2 (13 eq) on reaction with terminal and internal alkynes give the hydrocarboxylated products in a regio and stereo controlled fashion after oxidation (Scheme 1). The reaction proceeds satisfactorily under mild conditions at 25°C. The results obtained using various terminal and internal alkynes are summarised in Table 1.

Scheme 1

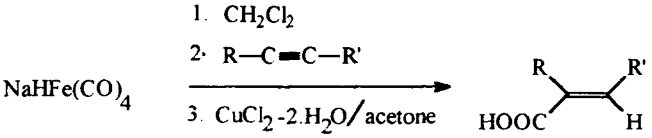
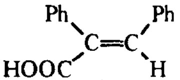
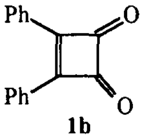
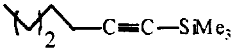
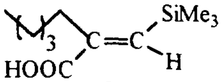
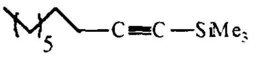
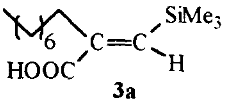
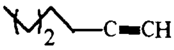
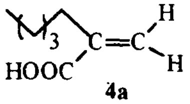
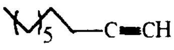
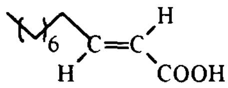


Table 1: Reaction of $NaHFe(CO)_4$ with $CH_2Cl_2/RC{\equiv}CR'$ in THF[a]

S.No	Substrate	Temp.	Product[b]	Yield %[c]
1	$Ph{-}C{\equiv}C{-}Ph$	50°C	 **1a**	60
			 **1b**	21
2		25°C	 **2a**	41
3		25°C	 **3a**	37
4		25°C	 **4a**	50
5		25°C	 **5a**	42

a) All reactions were carried out using $NaHFe(CO)_4$ (6 mmol) [generated by acidification of $Na_2Fe(CO)_4$ with CH_3COOH (6 mmol)] CH_2Cl_2 (5 mL) and alkyne (2.5 mmol).

b) The α,β-unsaturated carboxylic acids were identified by analysis of spectral data (IR, ^1H NMR, ^{13}C NMR and Mass).[8] The compound **1a** was identified by comparing the physical constant and spectral data with reported data.[11a] The regio- and stereoselectivity of the products **2a** and **3a** were confirmed by comparison of the ^{13}C and ^1H NMR spectral data obtained for the corresponding methyl ester with the reported data.[7,4c] The regio- and stereochemistry of products **4a** and **5a** were confirmed by the analysis of spectral data and comparison with the reported data.[2c,4b]

c) Yields are of products isolated by column chromatography and based on the amount of alkynes used.

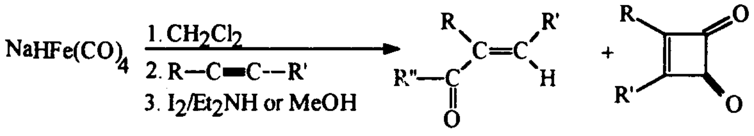
In the case of diphenylacetylene (entry 1, Table 1) the cyclobutenedione **1b** was isolated as a side product (21%).[8] However, in the case of other alkynes (entries 2, 3, and 4), the reaction proceeds well at 25°C to give β–(E)–alkenoic acids and only traces of cyclobutenedione (<2%) was isolated. 1-Decyne, undergoes α-carbonylation (*i.e.* at terminal position) rather than β-carbonylation (entry 5). Earlier, it was reported by Alper *et.al* that regio- and stereoselectivity of certain Pd catalysed hydrocarboxylation was dependent on the steric bulk of substituents.[4b] It seems likely that the increase in the chain length might be responsible for the unusual result with 1-decyne. However, the corresponding silyl derivative of 1-decyne (entry 3, Table 1) undergoes β-carbonylation. Presumably, here the bulky trimethylsilyl group overcomes the effect of chain length. The β-silyl-(E)-α,β-unsaturated carboxylic acids of the type **2a** and **3a** are potential intermediates in many reactions as they contain silyl and carbonyl moieties in the adjacent carbon atoms. Much efforts have been directed previously towards the synthesis of such compounds.[7]

The presence of CH_2Cl_2 as co-reactant is required for this transformation. It was observed that the reaction leads to low yield of carboxylic acid (<10%) in the absence of CH_2Cl_2. Earlier, we have observed that the $NaHFe(CO)_4/CH_3I$ reagent system reacts with alkynes to give mixtures of cyclobutenediones (27-42%) and α,β-unsaturated carboxylic acids (10-22%).[9] Although, we do not have evidence for intermediate species, the difference in the reactivity realised with CH_2Cl_2 is synthetically useful.

The following is the representative procedure for hydrocarboxylation: The $NaHFe(CO)_4$ (6 mmol) in THF (30 mL) [generated by acidification of $Na_2Fe(CO)_4$ (6 mmol) with CH_3COOH (6 mmol, 0.39 g)] was treated with 5 mL of CH_2Cl_2 at 25°C under nitrogen atmosphere. After 1h, diphenylacetylene (2.5 mmol, 0.45 g) was added and the contents were heated to 50°C and stirred for 8 hrs. The metal carbonyl complex was decomposed using $CuCl_2.2H_2O$ (20 mmol, 3.4 g) in acetone (15 mL). Saturated aq.NaCl (30 mL) was added and the resulting solution was extracted with ether, washed with brine (20 mL), dried over anhydrous $MgSO_4$ and concentrated. The residue was subjected to column chromatography. Ethyl acetate (1%) in hexane eluted the cyclobutenedione **1b** (21%, 0.25 g) and α,β unsaturated carboxylic acid **1a** (60%, 0.387) was isolated using ethyl acetate (2%) in hexane.

We have also examined this transformation further to obtain carboxylic acid derivatives. It is well-known that acylferrate anion on treatment with I_2 in the presence of nucleophiles such as CH_3OH, R_2NH undergoes various useful transformations.[10] A similar type of reactivity was anticipated for the intermediate formed in the reaction of $NaHFe(CO)_4/CH_2Cl_2$ with I_2 in the presence of nucleophiles. Regio- and stereoselective synthesis of α,β-unsaturated carboxylic acid derivatives could be achieved if such generalisations could be made. Indeed, this has been observed (Scheme 2). The intermediate generated *in situ* in the reaction of $NaHFe(CO)_4/CH_2Cl_2$/alkyne upon I_2 treatment in the presence of methanol, gives the methyl (E)-2,3-diphenylpropionate **6a** besides the corresponding cyclobutenedione **1b** (Scheme 2). The corresponding amide **7a** was obtained when diethylamine was used instead of MeOH. Similar transformation was also observed with 1-heptyne.[11b]

Scheme 2



R, R'= Ph, R''= OMe	**6a**	55%	**1b**	20%
R, R'= Ph, R''= NEt_2	**7a**	50%	**1b**	20%
R= $CH_3(CH_2)_4$-, R'= H, R''= NEt_2	**8a**	35%		–

The mechanism and intermediates involved in the transformations outlined here are not clearly understood. However, this method of hydrocarboxylation of alkynes should be useful for the regio and stereoselective synthesis of α,β-unsaturated carboxylic acid derivatives from alkynes.

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