Cobalt Carbonyl Mediated Michael Addition: Direct Synthesis of Esters Containing Other Functional Groups from Activated Olefins

Attila Sisak,* Ferenc Ungváry, and László Markó

Research Group for Petrochemistry of the Hungarian Academy of Sciences, H-8201, Veszprém, Hungary

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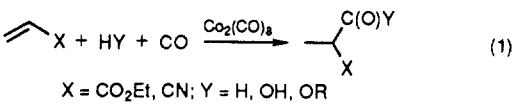
Hydrocarbalkoxylation of acrylonitrile with stoichiometric amounts of alcohols in the presence of catalytic amounts of $Co_2(CO)_8$ and pyridine bases leads to 2,4-dicyano-2-methylbutanoic acid esters. The yield of these Michael adducts shows a maximum as a function of the pyridine/cobalt ratio. Analogous reactions using equimolar amounts of alcohol, acrylonitrile, and an other activated olefin result in products with at least three different functional groups. Acrylonitrile with $pyH[Co(CO)_4]$ gives (1-cyanoethyl)cobalt tetracarbonyl, which is proposed to be the key intermediate of the hydrocarbalkoxylation. This complex may be deprotonated to a "Michael donor" anion, i.e. the Michael adducts are most probably formed in a cobalt-mediated way. The above catalytic system promoted also the Michael addition of some C–H acids to activated olefins under atmospheric conditions.

Introduction

The Michael addition has versatile synthetic utility in the preparative organic chemistry.[1] In the last decade some examples of this reaction performed in the presence of transition-metal complexes were published.[2-4] The metal activates either the C–H acidic component by forming an enolate complex,[2] or it coordinates the olefin, which may be attacked thus by the nucleophilic enolate.[3] The $Fe(CO)_5 + X_2$ (X = halogen) system was claimed to initiate related reactions with a radical chain mechanism.[4]

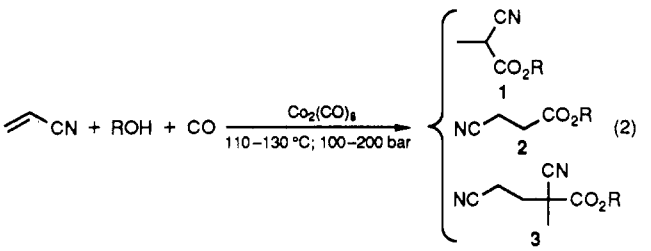
The carbonylation of alkenes with various transition-metal complex catalysts is industrially important.[5] In the presence of dicobalt octacarbonyl at relatively low temperatures electron-deficient olefins are carbonylated predominantly into a branched product,[5a,6] which, as a C–H acidic compound, is a potential Michael donor itself.



(1)

X = CO_2Et, CN; Y = H, OH, OR

Thus, by suitable choice of the reaction conditions, hydrocarbonylation and Michael addition can be made in "one pot" as claimed already in patents.[7,8] In this way, e.g. from acrylonitrile and an alcohol the Michael addition product 2,4-dicyano-2-methylbutanoic acid ester **3** is formed together with the hydrocarbalkoxylated products **1** and **2** (reaction 2).

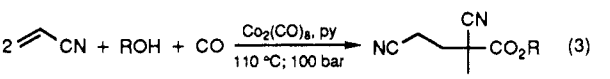


(2)

On the basis of experiences in the carbonylation of electron-deficient olefins[8-10] we studied reaction 2 and related processes in order to develop a useful synthetic method for the preparation of polyfunctional compounds.

Results

We found a dramatic change in product composition of reaction 2 by adding pyridine or related nitrogen bases to the reaction mixture initially. The product composition and the conversion of acrylonitrile as a function of the logarithmic pyridine/cobalt ratio[11] is shown in Figure 1 for R = *i*-Pr. Without added pyridine a low conversion of acrylonitrile and a poor selectivity in either **1**, **2**, or **3** was observed. In the presence of pyridine, however, a much better conversion of acrylonitrile could be achieved and the formation of **1** and **2** was suppressed, i.e. compound **3** became the main product. Use of 1 mol % $Co_2(CO)_8$ and 4 mol % pyridine gave the best conversion of acrylonitrile and the highest selectivity in the formation of compound **3** according to eq 3.



(3)

3a: R = Me
b: R = Et
c: R = *i*-Pr
d: R = 2-Me-butyl
e: R = 2-Et-hexyl
f: R = *c*-Hex
g: R = (–)-menthyl
h: R = benzyl
i: R = 1-Me-benzyl

Substituted pyridines with alkyl groups in the β- and γ-positions and isoquinoline have an effect on the reaction similar to pyridine itself. Toluene, methylene chloride, and alcohols as solvents gave high conversions and support the formation of **3**, but acetone, acetonitrile, and *N*,*N*-di-

(1) Bergman, E. D.; Ginsberg, D.; Pappe, R. *Org. React.* **1959**, *10*, 179. Mackie, R. K.; Smith, D. M. *Guidebook to Organic Syntheses*; Longman: London, 1982. March, J. *Advanced Organic Chemistry*; McGraw-Hill: London, 1977; p 727.

(2) (a) Nelson, J. H.; Howells, P. N.; DeLullo, G. C.; Landen, G. L. *J. Org. Chem.* **1980**, *45*, 1246. (b) Kočovski, P.; Dvořak, D. *Tetrahedron Lett.* **1986**, *27*, 5015. (c) Basato, M.; Corain, B.; De Roni, P.; Favero, G.; Jaforte, R. *J. Organomet. Chem.* **1987**, *42*, 115.

(3) (a) Rosan, A.; Rosenblum, J. *J. Org. Chem.* **1975**, *40*, 3621. (b) Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valey, 1980; pp 609–625.

(4) Amriev, R. A.; Velichko, F. K.; Abdulkina, Z. A.; Freidlina, R. C. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1984**, *33*, 2335 and references therein.

(5) (a) Pino, P.; Piacenti, F.; Bianchi, M. Reaction of Carbon Monoxide and Hydrogen with Olefins. The Hydroformylation (Oxo)Reaction. Hydrocarbalkoxylation of Olefins and Related Reactions. In Wender, I., Pino, P., Eds. *Organic Syntheses via Metal Carbonyls*; Wiley: New York, 1977; Vol. 2, pp 44–296. (b) Parshall, G. W. *J. Mol. Catal.* **1978**, *4*, 243. (c) Sheldon, R. A. *Chemicals from Synthesis Gas*; Reidel: Dordrecht, 1983; pp 86–126. (d) Waller, F. J. *J. Mol. Catal.* **1985**, *31*, 123.

(6) Falbe, J. *Carbon Monoxide in Organic Synthesis*; Springer: Berlin, 1970; p 49.

(7) Wakamatsu, S.; Hasaka, S. Japan Pat. 70 31,651, 1970; *Chem. Abstr.* **1971**, *74*, 41946j.

(8) Markó, L.; Sisak, A.; Ungváry, F. DE 3718233 A1, 1987; *Chem. Abstr.* **1988**, *109*, 92294n.

(9) Ungváry, F.; Markó, L. *Organometallics* **1986**, *5*, 2341.

(10) Ungváry, F.; Wojcicki, A. *J. Am. Chem. Soc.* **1987**, *109*, 6848.

(11) This method of representation became known as "ligand concentration control map" and its application was discussed by Heimbach and Schenkluhn.[12]

(12) Heimbach, P.; Schenkluhn, H. *Top. Curr. Chem.* **1980**, *92*, 45.

0022-3263/90/1955-2508$02.50/0

Table I. Hydrocarbalkoxylation of Acrylonitrile[a]

alcohol[b]	solvent	% convn of acrylonitrile	products 1[c]	2[c]	3[c]	others[d]
MeOH (**a**)	toluene	34.2	3.4	2.0	91.1	3.4[e]
EtOH (**b**)	toluene	89.5	17.7	6.0	75.4	4.7
i-PrOH (**c**)	–	68.0	1.0	3.8	95.2	*f*
i-PrOH	toluene	90.5	1.5	6.4	92.1	*f*
i-PrOH	CH_2Cl_2	98.9	3.1	8.0	88.9	*f*
i-PrOH	*i*-PrOH	85.4	2.0	7.2	90.8	*f*
i-PrOH	acetone	67.8	39.9	14.3	45.8	*f*
i-PrOH	acetonitrile	78.3	51.7	13.0	35.3	*f*
i-PrOH	dmf[g]	38.3	55.8	4.7	39.5	*f*
2-Me-butanol (**d**)	toluene	66.2	46.1	9.7	44.2	*f*
2-Et-hexanol[h] (**e**)	toluene	91.1	1.7	6.6	91.6	*f*
c-HexOH[h] (**f**)	toluene	75.4	28.9	5.3	61.7	9.8[i]
(–)-menthol[h] (**g**)	toluene	70.0	1.2	6.6	89.7	2.3[i]
$PhCH_2OH$[h] (**h**)	toluene	91.8	21.0	8.3	60.9	11.8[i]
PhCH(Me)OH[h] (**i**)	toluene	93.5	3.9	7.8	79.3	9.4[i]

[a] 0.1 mol of acrylonitrile; 0.05 mol of alcohol; 1.0 mmol of $Co_2(CO)_8$; 4.0 mmol of pyridine; 2.8 mL of solvent. Reaction time: 6 h; 110 °C; 10 MPa initial CO pressure (cold). [b] The symbol of the alkyl group (see eq 3) is given in parentheses. [c] Based on GC analysis, in mol % of the acrylonitrile incorporated. [d] In wt % of the sum of products unless otherwise noted. [e] Propionitrile. [f] Only traces of other products were found. [g] *N,N*-Dimethylformamide. [h] 0.05 mol of acrylonitrile; 0.025 mol of alcohol; 0.5 mmol of $Co_2(CO)_8$; 2.0 mmol of pyridine. [i] See text.

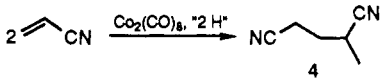
Table II. Combined Hydrocarbethoxylation of Acrylonitrile and a Further Activated Olefin in the Presence of $Co_2(CO)_8$/Pyridine[a]

activated olefin (convn, %)	acrylonitrile convn, %	products (wt %) 1b + 2b	3b	desired product[b]	other products
ethyl acrylate (32)	77	6	44	2-cyano-2-methyl-1,5-pentanedioic acid bis(ethyl ester), **6** (5)	diethyl methylmalonate (2) diethyl succinate (30)
diethyl maleate (38)	57	4	35	1-cyano-1-methylpropanetricarboxylic acid tris(ethyl ester),[c] **7a** (11)	diethyl fumarate (18) diethyl succinate (3) 1,1,2-ethanetricarboxylic acid triethyl ester (2) unknown[d] (27)
methyl vinyl ketone[e] (36)	21	–[f]	–[f]	2-cyano-5-oxo-2-methylhexanoic acid isopropyl ester, **5** (39)	4-isopropoxybutan-2-one (12)
benzylideneacetone (12)	86	15	59	2-cyano-5-oxo-3-phenyl-2-methylhexanoic acid ethyl ester,[c] **8** (10)	unknown[d] (50) unknown[d] (2)

[a] 50–50 mmol of acrylonitrile, other activated olefin, and ethanol, other conditions see in Table I. Data based on GC analysis. [b] See eq 5. [c] Mixture of diastereomers; see the Experimental Section. [d] On the basis of MS the product contains no acrylonitrile. [e] 50 mmol of isopropanol was used. [f] No esters derived from acrylonitrile were found.

methylformamide led to poor selectivity in **3**. The best yields were achieved by applying secondary alcohols, or longer chain primary alcohols as reactants (Table I).

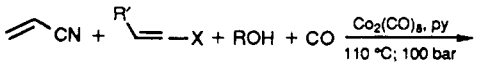
The use of alcohols other than aliphatic ones resulted in the formation of some byproducts, e.g. cyclohexanol was partly dehydrogenated to cyclohexanone and parallel to this α-methylglutaronitrile, **4**, the "hydrodimer" of acrylonitrile was formed (reaction 4).

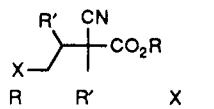


4 (4)

The appearance of **4** and some propionitrile was characteristic in the case of benzyl-type alcohols, accompanied by the formation of dehydrogenated byproducts derived from the alcohol.

Low to fair yields of polyfunctionalized products could be achieved in reaction 5 by using a mixture of acrylonitrile and another activated olefin (Table II).





(5)

	R	R'	X
5	*i*-Pr	H	C(O)Me
6	Et	H	CO_2Et
7a	Et	CO_2Et	CO_2Et
8	Et	Ph	C(O)Me

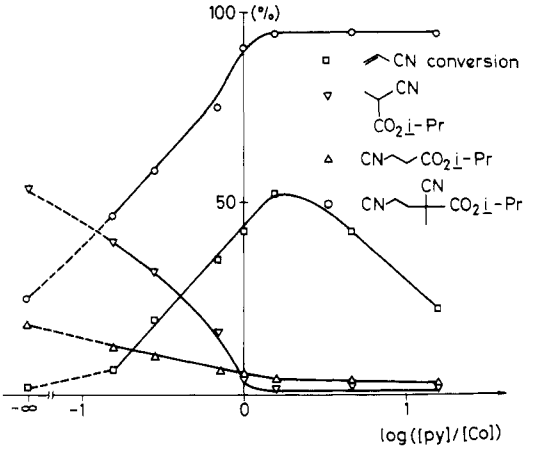
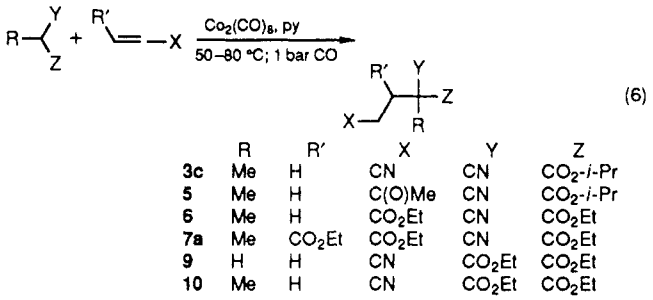


Figure 1. Control map[11] for the hydrocarbisopropoxylation of acrylonitrile with $Co_2(CO)_8$/pyridine catalyst. Reaction conditions: [acrylonitrile]:[2-propanol]:[Co] = 100:50:2; 100 °C; 10 MPa CO pressure (cold); 5 h.

Compound **5** and related ones could be prepared more selectively and in much better yields at milder conditions if a C–H acidic compound was added to the activated olefin according to eq 6 (Table III).

Reaction 6 did not take place in the absence of a base, except in the case of dialkyl maleates as olefin.[13] We

(13) Maleates disproportionate $Co_2(CO)_8$ to $[CoL_3][Co(CO)_nL_{4-n}]_2$ (L = *cis*-$RO_2CCH{=}CHCO_2R$, n = 1, 2).[14]

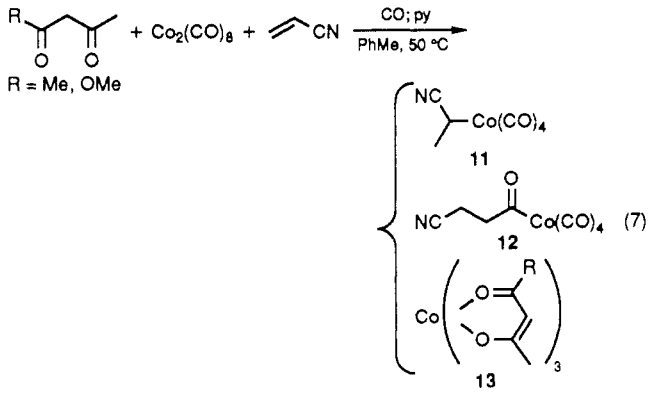


(6)

	R	R′	X	Y	Z
3c	Me	H	CN	CN	CO_2-*i*-Pr
5	Me	H	C(O)Me	CN	CO_2-*i*-Pr
6	Me	H	CO_2Et	CN	CO_2Et
7a	Me	CO_2Et	CO_2Et	CN	CO_2Et
9	H	H	CN	CO_2Et	CO_2Et
10	Me	H	CN	CO_2Et	CO_2Et

generally used pyridine as a base. Without $Co_2(CO)_8$ catalyst only side reactions, e.g. polymerization of acrylonitrile, was observed.[17]

The above cobalt carbonyl catalyzed Michael addition took place only with less enolizable C–H acidic compounds which do not form stable complexes with cobalt. The use of ethyl acetoacetate or acetylacetone did not result in a catalytic reaction, but instead known types of cobalt complexes were formed in a redox process as depicted in eq 7.



(7)

Although some of the products of reactions 3, 5, and 6 (e.g. **3b,c**,[7] **6**,[17a] **10**[17b]) were described earlier, only **9** was fully characterized by spectra.[17c] Analytical and spectral data of the compounds prepared are listed in the Experimental Section and in the supplementary material.

Discussion

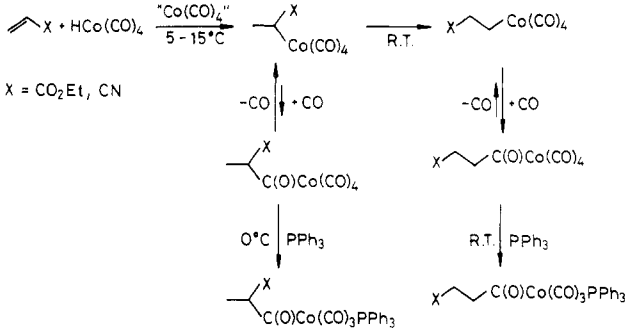
The mechanism of the $Co_2(CO)_8$-catalyzed hydrocarbalkoxylation of alkenes is not well understood yet.[5] Important mechanistic details of the related hydroformylation, however, became known recently.[9,18] It has been stated that in the reaction of $HCo(CO)_4$ with electron-deficient olefins in the presence of $Co_2(CO)_8$ the "branched" alkylcobalt tetracarbonyl is the kinetically controlled product. This isomerizes to the "linear" alkylcobalt complex which in turn gives the corresponding acylcobalt tetracarbonyl as the termodynamically controlled product. In spite of its lability the "branched" acylcobalt complex may exist in a small equilibrium concentration since it could be trapped in form of its triphenylphosphine derivative (Scheme I).[9]

Table III. Michael Additions Catalyzed by $Co_2(CO)_8$/Pyridine

C–H acidic component (convn, %)	olefin (convn, %)	method[a]	product (yield, %)[b]
1c (75.0)	acrylonitrile (93.0)	A	**3c** (67.9)
1c (83.7)	methyl vinyl ketone (100)	B	**5** (81.9)
1c (9.7)	ethyl acrylate (12.2)	B	**6** (9.6)
1b (53.6)	diethyl maleate (77.6)	B[c]	**7a** (51.4)
diethyl malonate (59.8)	acrylonitrile (73.5)	A	**9** (48.6)
diethyl methylmalonate (92.4)	acrylonitrile (93.5)	B	**10** (85.9)

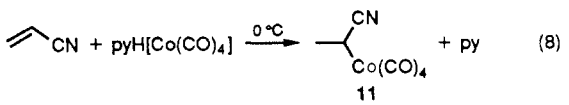
[a] Method A: 5 mmol of C–H acidic compound; 5 mmol of olefin; 0.25 mmol of pyridine; 0.25 mmol of $Co_2(CO)_8$; 5.0 mL of toluene; reaction time 2 h; 55 °C; CO atmosphere. Method B: 25 mmol of C–H acidic compound; 25 mmol olefin; 0.61 mmol of $Co_2(CO)_8$; 1.24 mmol of pyridine; 10.0 mL of 1,4-dioxane; reaction time 3 h; 75 °C. [b] Determined by GC analysis, based on the consumed C–H acidic compound. [c] Reaction time 8 h.

Scheme I



In the case of hydrocarbalkoxylation it can be anticipated that the same acylcobalt carbonyls are formed which then react with the alcohol giving the branched (**1**) and the linear (**2**) products.

The reaction of an activated olefin and $HCo(CO)_4$ provides some information for the understanding of the striking effect of pyridine on the rate and product composition in reaction 3. Pyridine and $HCo(CO)_4$ give, even at −78 °C, pyridinium tetracarbonylcobaltate(1−), pyH[$Co(CO)_4$], which reacts with activated olefins according to eq 8 under mild conditions and, more remarkably, in the absence of $Co_2(CO)_8$. This latter suggests the existence of another way for the formation of the key intermediate, (1-cyanoethyl)cobalt tetracarbonyl (**11**), than was found in the absence of pyridine.



(8)

Pyridine, like its derivatives, promotes the alcoholysis of acylcobalt tetracarbonyls formed from compound **11**. The ethanolysis of **11** under CO atmosphere at room temperature gave the corresponding α- and β-substituted esters, **1b** (86%) and **2b** (14%), respectively.[19] In mixtures

(14) (a) Csizmadia, J.; Ungváry, F.; Markó, L. *Trans. Met. Chem.* **1976**, *1*, 170. (b) Ungváry, F.; Gallucci, J.; Wojcicki, A., to be published.

(15) The lack of polymerization of acrylonitrile in the presence of $Co_2(CO)_8$ could be explained by the radical trap character of the latter, which has been demonstrated in some cases.[16]

(16) (a) Ungváry, F.; Markó, L. *J. Organomet. Chem.* **1980**, *193*, 383. (b) Jaitner, P.; Huber, W.; Gieren, A.; Betz, H. *J. Organomet. Chem.* **1986**, *311*, 379.

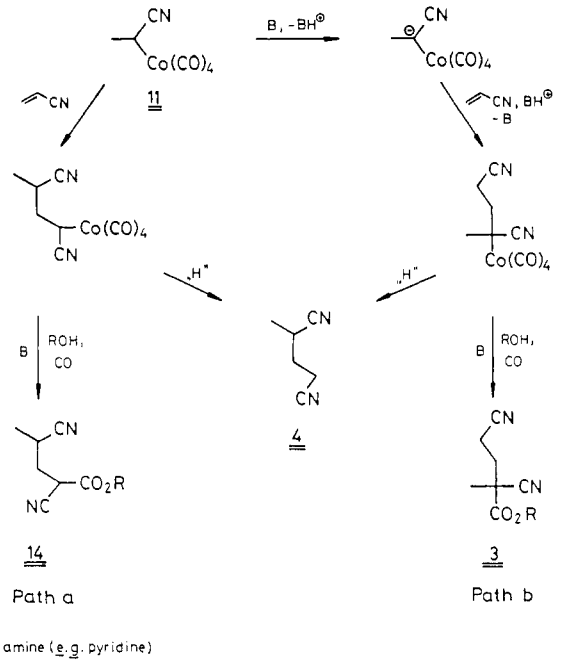
(17) (a) Kazuo, K. *Chem. Pharm. Bull.* **1960**, *8*, 110. (b) Colonge, J.; Constantini, M.; Ducloux, M. *Bull. Soc. Chim. Fr.* **1966**, 2005. (c) Freidlina, R. K.; Vinogradova, L. V.; Velichko, F. K. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1980**, 1210.

(18) (a) Ungváry, F.; Markó, L. *Organometallics* **1982**, *1*, 1120. (b) Bockman, T. M.; Garst, J. F.; King, R. B.; Markó, L.; Ungváry, F. *J. Organomet. Chem.* **1985**, *279*, 165. (c) Kovács, I.; Ungváry, F.; Markó, L. *Organometallics* **1986**, *5*, 209.

(19) The pyridine-promoted alcoholysis of acylcobalt tetracarbonyls probably does not proceed via acylpyridinium salt,[21] because carbon monoxide inhibits the reaction.[22]

(20) Imyanitov, N. S.; Bogoradovskaya, N. M.; Semenova, T. A. *Kinet. Katal.* **1978**, *19*, 573.

Scheme II



of acrylonitrile, $HCo(CO)_4$, pyridine, and alcohols at higher temperature (50 °C) some **3** was formed in addition to **1** and **2**, indicating that the presence of pyridine promotes the Michael addition as well.

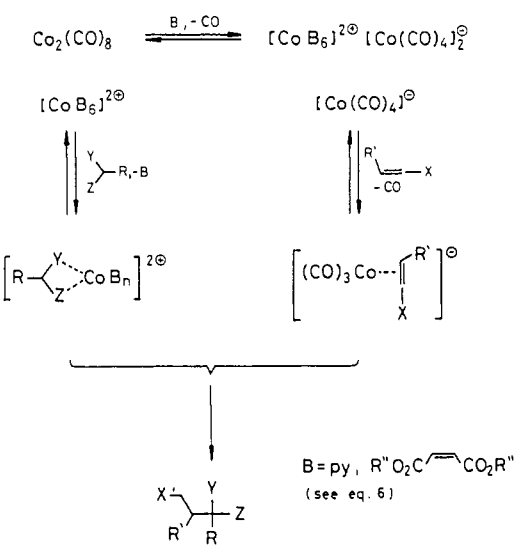
Reaction of acrylonitrile with an alkylcobalt carbonyl was proposed by Dubois and Garrou[22] as a possible step in the hydrodimerization of acrylonitrile to **4** under hydroformylation conditions. They suggested insertion of the olefin into the cobalt carbon bond, and subsequent hydrogenation to **4** (path a in Scheme II, cf. ref 3b). In the presence of an amine we propose deprotonation of **11**, which is followed by Michael addition (path b in Scheme II).

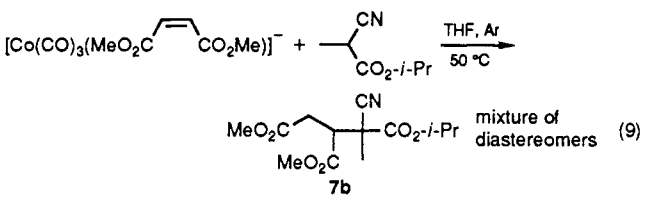
It is obvious from Scheme II that both the "insertion" (path a) and the "addition" (path b) ways can lead to **4**, but only path b may give product **3** in the presence of an alcohol and pyridine as a base. No traces of the isomer **14** were observed even in the case alcohols, which are good hydrogen donors (e.g. cyclohexanol) and, accordingly, gave **4** as a byproduct.

In addition to the above discussed model reactions and analogous processes Figure 1 gives also useful clues to the understanding of reaction 2. The nearly proportional decrease of the shares of **1c** and **2c** in the product in favor of **3c** indicates that the attack of pyridine takes place on a common intermediate of **1c** and of **2c**, i.e., most probably on **11**. Thus the partial catalytic cycles leading to **1c** and **2c** become less, the cycle leading to **3** becomes more populated with the increasing relative concentration of the base. This is in accord with the proposed path b in Scheme II.

The good yields in reaction 6 at much milder conditions than in reactions 3 and 4 suggest that the $Co_2(CO)_8$ + pyridine catalyst can effectively promote the formation of the Michael adducts in another way, too. In this case the simultaneous attack of base and cobalt on the C–H acid may give a powerful nucleophile (cf. ref 2c). At the same time, the olefin may be activated against nucleophilic attack[3b] by being coordinated to cobalt. The probable role of olefin-substituted carbonyl cobaltate ions[10] is demonstrated by the model reaction 9, which gave the Michael addition product **7b** in a yield of 52%. A possible interpretation of reaction 6 is shown in Scheme III. The cobalt(2+) salt of tetracarbonylcobaltate(1–) resulting from the disproportionation of $Co_2(CO)_8$ may activate both reactants by coordination (cf. refs. 2, 3, 10). This way of activation probably contributes to the good selectivity for compounds **3** in reaction 3 as well, at higher pyridine–cobalt ratios.

Scheme III





(9)

Conclusion

The "one-pot" combined hydrocarbalkoxylation–Michael addition reaction (eqs 3 and 5) offers a relatively simple synthetic tool to prepare polyfunctionalized compounds from common starting materials. Furthermore, our results gave a new example for the control of homogeneous catalytic systems by basic additives (cf. ref 12).

Experimental Section

General Techniques. NMR spectra were recorded on a Tesla BS-487/C spectrometer (^1H) and on a Varian CFT-20 spectrometer (^{13}C) with TMS as internal standard. IR spectra were obtained using NaCl windows and CaF_2 cuvettes on a Carl Zeiss Jena Specord IR 75 spectrophotometer. GC and GC–MS analyses were performed on a Hewlett-Packard HP 5830A type gas chromatograph, and on a JEOL IMS 01-SG-2 spectrometer, respectively, using SP-2100 fused silica capillary columns.

Materials. Starting materials were commercial products except $Co_2(CO)_8$,[23] $HCo(CO)_4$,[24] $Na[Co(CO)_3(dimethyl\ maleate)]$[10] and ethyl 2-cyanopropionate,[25] which were prepared according to the published procedures.

General Procedure for Reaction 3. In a 22-mL stainless steel autoclave equipped with manometer and valve were added under argon 342 mg (1.0 mmol) of $Co_2(CO)_8$, 6.6 mL (0.1 mol) of

(21) Sisak, A.; Ungváry, F., unpublished kinetic results.
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(23) Szabó, P.; Markó, L.; Bor, G. *Chem. Technol. (Leipzig)* **1961**, *13*, 549.
(24) Sternberg, H. W.; Wender, I.; Orchin, M. *Inorg. Synth.* **1957**, *5*, 192.
(25) Vogel, A. I. *Practical Organic Chemistry*, 3rd ed.; Longman: London, 1961; p 484.

acrylonitrile, 0.05 mol of alcohol (see Table I), 2.8 mL of solvent, and 0.32 mL (4.0 mmol) of pyridine. The autoclave was purged twice with CO, pressurized to 10–12 MPa, and shaken for 6 h in a heating mantle thermostated at 110 °C. (The pressure should be maintained above 4 MPa during the reaction.) After cooling the pressure was released, and the reaction mixture was analyzed by GC–MS and/or fractionated in vacuo (purity data are based on GC).

2,4-Dicyano-2-methylbutanoic acid esters, 3, are pale yellow oils.

(a) Methyl ester: >95%; bp 115–116 °C (0.4 kPa); IR ν (CN) 2248, (CO) 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 3 H), 2.0–2.6 (m, 4 H), 3.77 (s, 3 H) ppm.

(b) Ethyl ester: >95%; bp 123–127 °C (0.4 kPa);[26] MS (*m/e*, 70 eV) 153 (2), 135 (8), 107 (26), 68 (100), 41 (33), identical with that of the authentic sample.[7]

(c) Isopropyl ester: >98%; bp 122–128 °C (0.4 kPa);[27] IR ν (CN) 2250, (CO) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (d, J = 6 Hz, 6 H), 1.57 (s, 3 H), 2.0–2.6 (m, 4 H), 5.03 (septet, J = 6 Hz, 1 H) ppm; ^{13}C NMR ($CDCl_3$) δ 13.7, 21.3, 23.2, 32.9, 43.2, 71.3, 117.9, 118.5, 167.3 ppm; MS (*m/e*, 70 eV) 179 (11), 135 (36), 107 (87), 68 (37), 43 (100).

(d) 2-Methylbutyl ester: >97%; bp 129–136 °C (0.06 kPa); ν (CN) 2249, (CO) 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–1.05 (m, 6 H), 1.15–1.8 (m, 3 H), 1.57 (s, 3 H), 2.05–2.65 (m, 4 H), 4.00 (d, J = 6 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 13.8, 16.2, 16.5, 23.4, 25.8, 33.1, 34.0, 43.2, 71.7, 117.8, 118.4, 168.0 ppm; MS (*m/e*, 70 eV) 193 (2), 153 (9), 126 (32), 107 (23), 71 (61), 70 (63), 43 (100).

(e) 2-Ethylhexyl ester: not isolated; MS (*m/e*, 70 eV) 235 (2), 153 (18), 112 (26), 107 (17), 70 (87), 57 (100), analogous to that of **3b,c**.

(f) Cyclohexyl ester: not isolated; MS (*m/e*, 70 eV) 189 (1), 153 (24), 107 (26), 83 (100), 67 (61), 55 (56), analogous to that of the above MS spectra.

(g) (−)-Menthyl ester: >90%; bp 195–208 °C (0.05 kPa); mixture of diastereomers (^1H NMR, ^{13}C NMR[28]); IR ν (CN) 2247, (CO) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.68 (d, J = 7 Hz, 3 H), 0.83 (d, J = 7 Hz, 6 H), 1.2–2.6 (m, 13 H), 1.56 (s, broad, 3 H), 4.67 (m, 1 H) ppm; ^{13}C NMR ($CDCl_3$) δ 13.7, 16.0, 20.7, 21.9, 23.2 (broad), 26.3, 31.4, 32.8–33.1 (double), 34.0, 40.2, 43.2–43.3 (double), 46.7, 77.9, 117.8, 118.3, 167.4 ppm; MS (*m/e*, 70 eV), 223 (1), 153 (19), 138 (52), 95 (100), 81 (68), 55 (28).

(h) Benzyl ester: not isolated; MS (*m/e*, 70 eV) 242 (18) M^+, 197 (4), 107 (48), 91 (100), 65 (15), analogous to that of **3i**.

(i) 1-Methylbenzyl ester: 85%, bp 179–190 °C (0.5 kPa); mixture of diastereomers (GC, ^1H NMR); IR ν (CN) 2245, (CO) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, broad, 3 H), 1.55 (m, 3 H), 2.0–2.6 (m, 4 H), 5.8 (m, 1 H), 7.0 (s, broad, 5 H) ppm; MS (*m/e*, 70 eV) 256 (18) M^+, 211 (14), 107 (16), 105 (100), 104 (59), 77 (20).

General Procedure for Reaction 5. The above procedure for reaction 3 was modified so that instead of 0.1 mol of acrylonitrile, 0.05 mol of acrylonitrile and 0.05 mol of another activated olefin were added (see Table II). The products were not isolated, except **5**, and their structures were assigned on the basis of comparison of the GC–MS data with those of the authentic samples (see below).

2-Cyano-5-oxo-2-methylhexanoic acid isopropyl ester (5): >97%; colorless oil; bp 123–125 °C (1.4 kPa); IR ν (CN) 2238, (CO) 1740, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (d, J = 6 Hz, 6 H), 1.49 (s, 3 H), 2.0 (m, 2 H), 2.08 (s, 3 H), 2.55 (m, 2 H), 4.97 (septet, J = 6 Hz, 1 H) ppm; ^{13}C NMR ($CDCl_3$) δ 21.4, 23.3, 29.8, 31.5, 39.0, 43.3, 70.8, 119.6, 168.3, 205.0 ppm; MS (*m/e*, 70 eV) 152 (36), 124 (22), 71 (16), 58 (38), 43 (100).

2-Cyano-5-oxo-3-phenyl-2-methylhexanoic acid ethyl ester (8): not isolated; tentative assignment of the structure was made on the basis of the MS (*m/e*, 70 eV): 273 (3) M^+, 228 (53), 200 (47), 147 (100), 43 (98), 29 (27).

General Procedure for Reaction 6. In a 2-necked 50-mL flask equipped with reflux condenser, silicon septum, and magnetic stirrer were added 0.025 mol of C–H acidic compound and 0.025 mol of olefin (see Table III), 10 mL of 1,4-dioxane, 200 mg (0.58 mmol) of $Co_2(CO)_8$, and 0.10 mL (1.24 mmol) of pyridine. The flask was heated to 75 °C in a water bath, and the reaction mixture was stirred (for 3 h), while the reaction could be followed by GC analysis.

2-Cyano-2-methyl-1,5-pentanedioic acid bis(ethyl ester) (6): not isolated; MS (*m/e*, 70 eV) 227 (5) M^+, 182 (100), 154 (78), 126 (36), 109 (43), 96 (47), 29 (37), identical with that of the authentic sample, prepared by the procedure given if ref 17a.

1-Cyano-1-methylpropanetricarboxylic acid tris(ethyl ester) (7a): >95%; bp 165–182 °C (0.05 kPa); mixture of diastereomers (GC, ^{13}C NMR); IR ν (CN) 2235, (CO) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (m, 9 H), 1.54 (s, broad, 3 H), 2.75 (m, 2 H), 3.45 (m, 1 H), 4.15 (m, 3 H) ppm; ^{13}C NMR ($CDCl_3$, all signals are double, except the highest field one, with the intensity ratio of 1:0.8) δ 14.0 (broad), 20.5–22.1, 32.8–33.5, 45.2–45.5, 46.5–46.9, 61.0–61.2, 61.8–61.9, 63.1–63.4, 118.0–118.2, 167.5–168.2, 169.6–170.2, 170.4–170.6 ppm; MS (*m/e*, 70 eV), 299 (2) M^+, 254 (100), 226 (85), 198 (56), 180 (80), 153 (40), 29 (41).

4-Cyano-2-(ethoxycarbonyl)butanoic acid ethyl ester (9): boiling point, IR, and MS data were identical with previously reported ones.[17c]

4-Cyano-2-(ethoxycarbonyl)-2-methylbutanoic acid ethyl ester (10): >95%; bp 132 °C (0.05 kPa);[29] IR ν (CN) 2247, (CO) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (t, J = 6 Hz, 6 H), 1.34 (s, 3 H), 1.9–2.5 (m, 4 H), 4.09 (q, J = 6 Hz, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 13.0, 14.0, 20.1, 31.6, 52.7, 61.6, 119.2, 170.9 ppm.

Preparation of (1-Cyanoethyl)cobalt Tetracarbonyl (11). To 4.0 mL of 0.75 M solution of $HCo(CO)_4$ in *n*-pentane was added 250 μL (3.1 mmol) of pyridine at −78 °C, under CO atmosphere with continuous stirring. An orange-yellow precipitate was formed immediately. The solvent was decanted; the precipitate was washed twice with cold *n*-pentane and dried in vacuo at −20 °C. The residue was dissolved in 100 mL of dichloromethane, 1.0 mL (15 mmol) of acrylonitrile was added, and the reaction mixture was stirred at 0 °C under argon for 8 h. After the mixture was stored in the refrigerator (~5 °C) overnight, it was cooled to −78 °C in order to remove the $Co_2(CO)_8$ byproduct by crystallization. The yield of the (1-cyanoethyl)cobalt tetracarbonyl, **11**, as dichloromethane solution is 54% (based on Co analysis of the solution).

The procedure using 100 mL of toluene instead of dichloromethane gave quite similar results: IR ν (CO) (toluene) 2108.9 (m), 2044 (s) (sh), 2029 (vs), 2020 (vs) cm^{-1}.

Alcoholysis of 11. A 5.0-mL sample of a 0.017 M solution of **11** in toluene was reacted with 0.2 mL (3.4 mmol) of ethanol and 8.0 μL (0.1 mmol) of pyridine under a CO atmosphere at 15 °C. The reaction was followed by IR spectroscopy and was complete within 2 h. The only volatile product detected by GC–MS was **1b**. In a repeated experiment at 25 °C the ratio of **1b** and **2b** was 7:1.

Reaction of $[Co(CO)_3$(dimethyl maleate)$]^-$ with 1c. To 4.0 mL of 0.045 M Na[$Co(CO)_3$(dimethyl maleate)] in THF (prepared as described in ref 10) was added 250 mg (1.8 mmol) of **1c** under argon. The reaction mixture was refluxed for 2 h while the orange-red color turned to deep brown. The GC–MS analysis of the reaction mixture showed that dimethyl maleate was converted to diastereomers of 1-cyano-1-methylpropanetricarboxylic acid 1-(isopropyl ester) 2,3-bis(methyl ester) (**7b**) with 52% yield: MS (*m/e*, 70 eV) 254 (10), 226 (69), 212 (67), 180 (36), 167 (91), 139 (57), 43 (100). Dimethyl fumarate was found as byproduct.

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Registry No. **1b**, 1572-99-2; **1c**, 30378-24-6; **1d**, 125847-85-0; **1f**, 125847-86-1; **1h**, 125847-87-2; **2b**, 10137-67-4; **2c**, 125847-88-3; **2d**, 125847-89-4; **2e**, 89829-27-6; **2f**, 125847-90-7; **2g**, 125847-91-8; **2h**, 125847-92-9; **2i**, 125847-93-0; **3a**, 55084-12-3; **3b**, 30378-23-5; **3c**, 30378-25-7; **3d**, 125847-79-2; **3e**, 125847-80-5; **3f**, 125847-81-6; **3g**, 125847-82-7; **3h**, 125847-83-8; **3i**, 125847-84-9; **5**, 115906-96-2;

(26) Published bp: 129–135.5 °C (0.53 kPa).[7]
(27) Published bp: 100–125 °C (0.4 kPa).[7]
(28) The induced diastereoselectivity on the 2-carbon atom was ~15% based on ^{13}C NMR data recorded under NOE suppressed conditions.
(29) Published bp: 162 °C (2.5 kPa).[17b]

6, 91341-03-6; 7a, 115906-95-1; 8, 115906-97-3; 9, 17216-62-5; 10, 10444-11-8; 11, 125847-78-1; MeOH, 67-56-1; EtOH, 64-17-5; *i*-PrOH, 67-63-0; 2-Me-butyl-OH, 137-32-6; 2-Et-hexyl-OH, 104-76-7; c-HexOH, 108-93-0; (−)-menthyl-OH, 2216-51-5; benzyl-OH, 100-51-6; 1-Me-benzyl-OH, 98-85-1; $CO_2(CO)_8$, 10210-68-1; acrylonitrile, 107-13-1; ethyl acrylate, 140-88-5; diethyl maleate, 141-05-9; methyl vinyl ketone, 78-94-4; benzylidene acetone, 122-57-6; diethyl succinate, 123-25-1; diethyl fumarate, 623-91-6; 4-isopropoxybutan-2-one, 32541-58-5; diethyl malonate, 105-53-3; diethyl methylmalonate, 609-08-5.

Supplementary Material Available: Mass spectral data of some byproducts of reactions 3 and 5 (2 pages). Ordering information is given on any current masthead page.

2-Aryl-4-quinolones and Fused Quinolines from β-Chloroarylidenemalonates and Related Chloro Esters

Osmo E. O. Hormi,* Carita Peltonen, and Laila Heikkilä

Department of Organic Chemistry, Åbo Akademi, Akademigatan 1, SF-20500 Åbo, Finland

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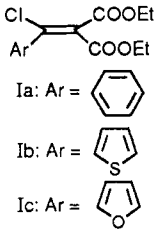
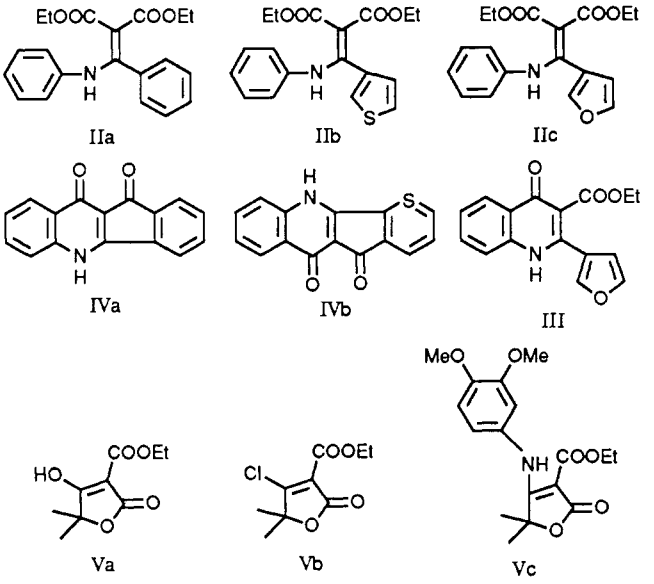
The β-chloroarylidenemalonates I were transformed to the anilinoarylidenemalonates II in 50–70% yield. Thermolysis of the β-anilinofurfurylidenemalonate IIc at 250 °C gave 3-(ethoxycarbonyl)-2-(2-furyl)-4-quinolone III in 85% yield. Treatment of the anilinomalonates IIa and IIb with polyphosphoric acid at 210–230 °C gave the indeno[1,2-*b*]quinoline IVa in 75% yield and its thiophene analogue IVb in 50% yield. The hydroxybutenolide Va was prepared from 2-bromo-2-methylpropanoyl chloride and (ethoxymagnesio)malonate in 72% yield, and Va was then transformed to the chlorobutenolide Vb in 75% yield. The treatment Vb with 3,4-dimethoxyaniline in the presence of triethylamine followed by cyclization of the intermediate anilinobutenolide Vc gave the furo[3,4-*b*]quinolinedione VI in 48% yield.

We have been investigating the utilization of β-chloroarylidenemalonates[1] and related chloro esters I as starting materials in synthetic work, partly because they are accessible in large quantities from readily available acylmalonates[2] and especially because the high level of functionality that is present in these chloro esters leads to chemical reactivity not otherwise attainable. The esters possess three features of functionality: the ester groups, the double bond, and the substituent (Ar in I).



In previous papers we have demonstrated the significance and the powerful nature of the three functionalities. We have shown that the chloro esters can be converted into various substances,[2a,3] some of which are natural products.

As a complement to our continuing investigations we now describe a utilization of the chloro esters in the synthesis of the 2-(2-furyl)-4-quinolone III, indeno[1,2-*b*]-quinolines and related fused heterocycles IVa and IVb via the intermediate β-anilinoarylidenemalonates II. As a further application of the method we also describe a synthesis of the furoquinoline VI via the anilinobutenolide Vc.



Our interest in the synthesis of the 2-aryl-4-quinolones was stimulated by a recent observation of Chen et al. that only a few examples of the synthesis of 2-aryl-4-quinolones have been described.[4] The authors indicate that problems are encountered during the preparation of the required β-anilinoacrylate intermediates such as the β-anilinoarylidene malonates II.

With our earlier experiences on the nucleophilic vinylic substitution (S_NV) reactions[5] between various chloro esters and nucleophiles in mind we hoped that the anilino esters

(1) We think that it is more convenient and descriptive to use nonsystematic nomenclature for the compounds I and II. Their systematic names are as follows: Ia, ethyl 3-chloro-2-(ethoxycarbonyl)-3-phenylpropenoate; Ib, ethyl 3-chloro-2-(ethoxycarbonyl)-3-(2-thienyl)-propenoate; Ic, ethyl 3-chloro-2-(ethoxycarbonyl)-3-(2-furyl)-propenoate; IIa, ethyl 2-(ethoxycarbonyl)-3-(*N*-phenylamino)-3-phenylpropenoate; IIb, ethyl 2-(ethoxycarbonyl)-3-(*N*-phenylamino)-3-(2-thienyl)propenoate; IIc, ethyl 2-(ethoxycarbonyl)-3-(2-furyl)-3-(*N*-phenylamino)propenoate.

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(4) Chen, B.-c.; Huang, X.; Wang, J. *Synthesis* **1987**, 482. See also: Huang, X.; Chen, B.-c. *Synthesis* **1987**, 480.

(5) Recent reviews of the S_NV mechanism: (a) Rappoport, Z. *Recl. Trav. Chim., Pays-Bas* **1985**, *104*, 309. (b) Bernasconi, C. F. *Tetrahedron* **1989**, *45*, 4017.

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