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Nickel Catalyzed Electrosynthesis of Ketones from Organic Halides and Metal Carbonyls.

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Abstract : Ketones can be easily obtained by electroreduction in an undivided cell of an organic halide - metal carbonyl mixture using a Ni-bpy catalytic system in DMF (bpy = 2,2'-bipyridine). The process is especially well convenient for primary benzyl and alkyl halides.
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Introduction :

The most simple reagent for the synthesis of carbonyl compounds is obviously carbon monoxide. However, on account of its low reactivity, the chemistry of carbon monoxide needs the use of either energetic reagents or a catalytic system generally based on transition metal complexes.(1) A number of reactions even combine both approaches in using jointly an organometallic reagent and a CO coordinating transition metal as catalyst or reagent.(1)

The carbonylation of organic halides involves a reductive coupling with the molecule carrying CO. Therefore, except for a transformation of starting halides into carbanion donors such as an organolithium compound and a Grignard reagent,(1,2) these reactions require a reducing agent. For example, hydrogen(3) or formate ions(4) can be used under relatively high temperature and pressure for the synthesis of aldehydes, whereas tributyltin hydride allows the use of milder conditions.(5) The use of zinc-copper couple was also proposed for the synthesis of unsymmetrical ketones from aryl and alkyl iodides.(6) In some examples where symmetrical ketones are obtained with moderate yields the metal carbonyl itself is the reductant.(7)

Aldehydes and ketones are more currently prepared from organic halides and transition metal carbonyl anions. The versatile Collman's reagent $Na_2Fe(CO)_4$(8) and other anionic metal carbonyl like $NaCo(CO)_4$ or $NaHFe(CO)_4$,(9) react with various organic halides to generate alkyl metal carbonyl complexes. Their evolution into acyl metal carbonyl complexes then allows for the obtention of the carbonylated product.(1)

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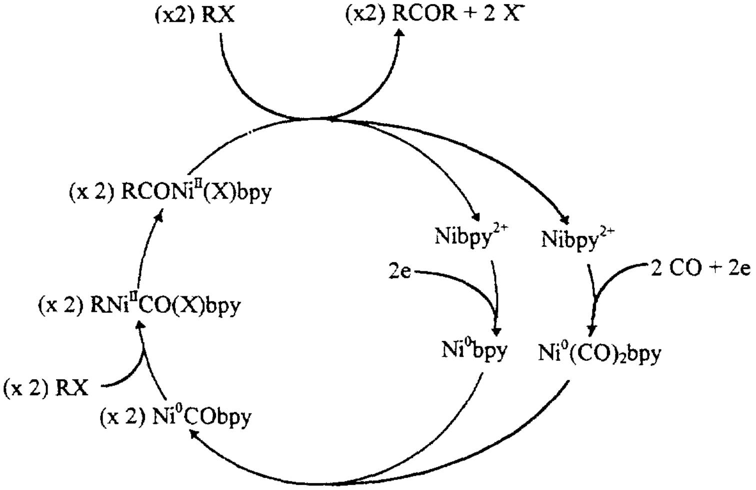
[1] FAX. 01 49 78 11 48

The electrochemical methods have not been much investigated. Two groups reported that the electrolysis of a mixture of an alkyl or benzyl halide and iron pentacarbonyl(10) leads to the corresponding aldehydes after acidic workup. Dibenzylketone can also be obtained with a moderate yield from benzyl bromide.(10b, 11) These reactions involve anionic iron carbonyls species generated from $Fe(CO)_5$(11) which cathodic reduction occurs at -2 V *vs.* SCE.(12)

We recently reported that symmetrical ketones can be obtained electrochemically from organic halides in a DMF solution fed with CO by bubbling at normal pressure.(13) The catalytic system is based on the cathodic reduction of divalent nickel associated with 2,2'-bipyridine (bpy). A detailed mechanistic investigation, which will be published elsewhere, has allowed us to set up the following points. The key catalytic species, active towards the carbon-halogen bond, is a transient 16-electrons mixed Ni^0CObpy complex resulting from CO exchange between two electrogenerated complexes : $Ni^0(CO)_2bpy$ and Ni^0bpy. Scheme 1 presents the postulated catalytic cycle yielding the ketone.



Scheme 1 : Ni-bpy catalyzed electrochemical synthesis of ketones from carbon monoxide and organic halides.

One drawback to the method was the difficulty to control the content of CO in the solution. Actually CO is poorly soluble and dissolves slowly in DMF.(14) The choice of the current intensity which commands the rate of consumption of CO is then crucial.

Indeed, when CO is in excess, *i.e.* more than two equivalents *vs.* the instantaneous concentration of Ni^0bpy, the electroreduction of $Nibpy^{2+}$ only leads to the stable known $Ni^0(CO)_2bpy$ complex(15) which does not react (or only slowly) with organic halides. On the other hand, when CO lacks, the electrogenerated Ni^0bpy complex reacts with RX and yields, as already shown,(16) the dimer RR instead of the ketone RCOR.

In order to improve this Ni-catalyzed reaction, we changed CO into a metal carbonyl. This could offer both advantages : to choose at will the available amount of CO and to control its activity. This activity will depend on the respective CO-donor / acceptor abilities of the metal carbonyl and the zerovalent nickel-bpy complexes.

Results and discussion :

To DMF, was added a supporting electrolyte (Bu_4NBF_4), a metal carbonyl, the catalytic precursor $NiBr_2bpy$ and the organic halide. The undivided cell described elsewhere(17) was fitted with a sacrificial metallic rod anode surrounded by a cylindrical nickel grid cathode.

The electrolyses were carried out at room temperature at constant current intensity by using a direct-current power supply until the halide was fully consumed. The overall reaction is :

$$2\,RX + 2e \xrightarrow[\text{DMF, NiBr}_2\text{bpy (cat.)}]{M(CO)_n} RCOR + 2\,X^- \quad (1)$$

We started with the synthesis of dibenzylketone from benzyl chloride in order to find the best experimental conditions. We first examined the influence of the nature of the metal carbonyl complex used as source of CO. The results presented in Table 1 show that all the tested metal carbonyls are efficient for this reaction.(18) Bibenzyl and toluene (not measured) were minor products in all cases.

Table 1 : Synthesis of dibenzylketone from benzylchloride and various metal carbonyls.

$M(CO)_n$	GC yields (%) $PhCH_2COCH_2Ph$	$PhCH_2CH_2Ph$	Faradaïc yields (%)
$Fe(CO)_5$	97	2	60
$Fe_3(CO)_{12}$	99	traces	40
$W(CO)_6$	95	5	80
$Cr(CO)_6$	75	8	20
$Mo(CO)_6$	92	6	30
$Co_2(CO)_8$	84	14	35

General conditions : DMF (50 ml), Bu_4NBF_4 1.5 mmol, $PhCH_2Cl$ 20 mmol, $M(CO)_n$ 3 mmol, $NiBr_2bpy$ 3 mmol, stainless steel anode (Fe_{64}/Ni_{36}), I = 0.5 A (25mA.cm^{-2}), nickel grid cathode.

Regarding both the chemical and faradaïc yields, $W(CO)_6$ gave the best results. However we chose to carry on this study with $Fe(CO)_5$, which is cheap and easy to handle since it is a liquid. We have then studied the influence of the current intensity, the nature of the sacrificial anode and the amount of the catalytic precursor.

The results concerning the current density are given in Table 2. It comes out that the chemical yield in dibenzylketone becomes excellent when the current density is high enough. However the faradaïc yields decrease as the current intensity is increased. This results from a side electroreaction where Ni^{2+} and Fe^{2+} ions released by the stainless steel anode are reduced into metal. For the further experiments we have chosen, as a good compromise a cathodic current density of 25 mA.cm^{-2} (I = 0.5 A).

Table 2 : Influence of the current density on the electrosynthesis of $PhCH_2COCH_2Ph$ from $PhCH_2Cl$ and $Fe(CO)_5$.

Current density (mA.cm^{-2})	GC yields (%) $PhCH_2COCH_2Ph$	$PhCH_2CH_2Ph$	Faradaïc yields (%)
10	75	3	50
20	80	5	75
25	>95	2	55
30	>95	2	44
40	>95	traces	33

General conditions : DMF (50 ml), Bu_4NBF_4 1.5 mmol, $PhCH_2Cl$ 20 mmol, $Fe(CO)_5$ 3 mmol, $NiBr_2bpy$ 3 mmol, stainless steel anode (Fe_{64}/Ni_{36}), nickel grid cathode.

Good results were also obtained with nickel instead of (Fe_{64}/Ni_{36}) stainless steel anode, but iron or ($Fe_{74}/Ni_8/Cr_{18}$) stainless steel gave lower chemical yields (~ 60%). With aluminium or magnesium we observed a drift of the cathode potential towards negative values (<-2V *vs.* SCE) and toluene became the main product.

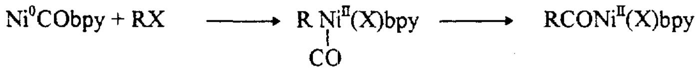
The study of the initial ratio of $Fe(CO)_5$ *vs.* $PhCH_2Cl$ showed that five moles of ketone can be formed per mole of iron carbonyl. This behavior is noticeable since analogous chemical reactions generally requires one mole of the neutral or anionic metal carbonyl complex (or extra CO) to produce one mole of carbonylated product. This can be accounted for by the formation of various $Fe_x(CO)_y$ complexes, such as $Fe_2(CO)_9$, $Fe_3(CO)_{12}$, as CO is consumed. The fact that all the CO molecules are available in our conditions is of interest with respect to the lower cost and no need to dispose of the toxic metal carbonyl in the reaction mixture.

The role of the nickel salt is crucial since no ketone was obtained when the electrolysis was carried out without $NiBr_2bpy$. Excellent yields were obtained with a 10-20% ratio (*vs.* RX) of catalyst. The reaction was also efficient when $NiBr_2bpy$ was replaced by a (1/1) $NiBr_2$ -1,10-phenanthroline mixture (15% *vs.* $PhCH_2Cl$). We have not yet fully explored the mechanism of the reaction. Nevertheless we can put forwards the following points. All along the electrolyses the potential of the cathode keeps between -1 and -1.3 V (*vs.* SCE). This indicates that the reaction does not proceed through the reduction of $Fe(CO)_5$ into anionic species which occurs at much more negative potentials.(12)

The electrochemical step at -1.2 V involves the well known reduction of the catalytic precursor $Nibpy^{2+}$ (19) (eq.2) as the first reaction followed by CO capture from the iron (or other metal) carbonyl complex (eq.3). As mentioned above the mixed (16-electrons) NiCObpy complex is very likely the active species to react with the organic halide. An oxidative addition, then a migration of the organic group leads to an acyl nickel complex which is likely the key-intermediate for the ensuing formation of the ketone (eq.4).

$$Nibpy^{2+} + 2\,e \longrightarrow Ni^{0}bpy \qquad (2)$$

$$Ni^{0}bpy + Fe(CO)_5 \longrightarrow Ni^{0}CObpy + Fe_x(CO)_y \qquad (3)$$



$$Ni^{0}CObpy + RX \longrightarrow R\underset{\overset{|}{CO}}{Ni^{II}}(X)bpy \longrightarrow RCONi^{II}(X)bpy \qquad (4)$$

We finally tested the method with various organic halides. Results are given in Table 3.

Table 3 : Ni-bpy catalyzed electrosyntheses of symmetrical ketones from organic halides and iron pentacarbonyl. [a]

RX (benzyl halides)	RCOR isolated yield (%)	RX (alkyl halides)	RCOR isolated yield (%)
$PhCH_2Cl$	90	$CH_3(CH_2)_5I$	80
$PhCH_2Br$	70	$CH_3(CH_2)_7I$	82
2 $ClC_6H_4CH_2Cl$	68	$CH_3(CH_2)_5Br$	24 [b]
3 $ClC_6H_4CH_2Cl$	70	$CH_3(CH_2)_5Br$ [c]	40 [b]
4 $ClC_6H_4CH_2Cl$	75	$CH_3(CH_2)_7Br$ [c]	62 [b]
$PhCH(CH_3)Cl$	traces	$CH_3(CH_2)_7Br$ [d]	48 [b]
$PhCH(CH_3)Br$	5 [b]		

RX (aryl halides)	RCOR isolated yield (%)	RX (aryl halides)	RCOR isolated yield (%)
PhI	15	2 $CH_3OC_6H_4Br$	32 [b]
2 $CH_3OC_6H_4I$	50	3 $CH_3OC_6H_4I$	traces
2 ClC_6H_4I	traces	4 $CH_3OC_6H_4I$	traces
2 $NH_2C_6H_4I$	35	2,5 $(CH_3O)_2C_6H_3I$	25

(a) General conditions : DMF (50 ml), Bu_4NBF_4 1.5 mmol, RX 20 mmol, $Fe(CO)_5$ 3 mmol, $NiBr_2bpy$ 3 mmol, stainless steel anode (Fe_{64}/Ni_{36}), nickel grid cathode, I = 0.5 A, (b) GC yields, (c) Bu_4NI 1.5 mmol as supporting electrolyte, (d) KI 4 mmol as supporting electrolyte.

Primary benzylic halides are efficiently converted into the corresponding symmetrical ketones. The dimer $ArCH_2CH_2Ar$ and the hydrocarbon $ArCH_3$ were minor products in all cases. The reaction is also efficient with primary aliphatic iodides, or even bromides provided that iodide anions are added to the medium.

Secondary alkyl or benzyl halides do not give the ketone. For example phenethyl chloride or bromide are mainly converted into the reductive dimerization product $PhCH(CH_3)CH(CH_3)Ph$.
The method is not applicable to either aryl halides unless an electron donating group is present at the ortho-position to the carbon-halogen bond. The diaryl ketone is then obtained with moderate yields. In all cases we got a mixture of ArCOAr, ArAr, ArH and $ArCO_2H$. A preliminary study on the reactivity of aryl halides indicates that the first oxidative addition (eq.2) occurs but the further steps in the process are not as efficient as with primary benzyl halides.

Conclusion :

We have shown that the $Nibpy^{2+}$ electroreduction into a zerovalent nickel complex provides a good catalytic system to achieve the synthesis of symmetrical ketones from alkyl and benzyl halides and metal carbonyl complexes used as source of carbon monoxide. The method as well as the electrochemical device are very simple. The experimental conditions are mild since the syntheses are carried out at room temperature without the need for any "energetic reagent".

We now attempt to synthesize unsymmetrical ketones by the same process, starting from mixtures of two organic halides or from an halocarbon and a nucleophilic reagent. Preliminary results have already shown that aryl-alkyl ketones can be obtained in good yields.

Experimental section :

Electrolyses were conducted according to the conditions described above up to the complete conversion of the organic halide. The progress of the reaction was monitored by GC analysis of samples.
The ketones were recovered by suitable water-organic solvent extraction, purification on a silica gel column and characterized by GC-MS by EI (Finnigan Ion Trap Detector 800), ^1H NMR($CDCl_3$/TMS, 200MHz), ^{13}C NMR ($CDCl_3$/TMS, 50MHz) and IR. Except for one, all the ketones obtained are known products and the analytical data given below are satisfactory.

CAUTION : $Fe(CO)_5$ is toxic and easily flammable. It must be handled with care.

1,3-diphenylpropan-2-one R.N. [102-04-5]; IR : ν_{CO} : 1715 cm^{-1} ; Mass., m/z (rel. intensity) : 118(15), 92(16), 91(100), 65(26); ^{13}C NMR (δ ppm) : 205.9 (1C, C=O), 134.0-127.1 (12C), 49.1 (2C, CH_2); ^1H NMR (δ ppm) : 7.3-7.0 (m, 10H), 3.6 (s, 4H).

benzophenone R.N. [119-61-9]; IR : ν_{CO} : 1655cm^{-1}; Mass., m/z (rel. intensity) : 182(47), 105(100), 77(88), 51(67), ^{13}C NMR (δ ppm) : 196.6 (1C, C=O), 137.5-128.2 (12C); ^{1}H NMR (δ ppm) : 8.0-7.7 (m, 10H).

1,1'-dimethoxybenzophenone R.N. [13102-33-5]; IR : ν_{CO} : 1660 cm^{-1}; Mass., m/z (rel. intensity) : 243(46), 225(7), 181(10), 139(12), 135(80), 121(19), 92(75), 77(100), 64(30), 63(31), 51(28); ^{13}C NMR (δ ppm) : 196 (1C, C=O), 158.2 (2C, C-O), 132.5-111.4 (10C), 55.6 (2C, O-CH$_3$); ^{1}H NMR (δ ppm) : 7.4-6.8 (m, 8H), 3.6 (s, 6H).

2,2',5,5'-tetramethoxybenzophenone IR : ν_{CO} : 1655 cm^{-1}; Mass., m/z (rel. intensity) : 302(100), 285(8), 271(10), 241(7), 185(6), 165(82), 151(52), 122(53), 107(74), 92(29), 79(78), 77(79), 63(16), 51(35); ^{13}C NMR (δ ppm) : 194.5 (1C, C=O), 153.1-152.4 (4C, C-O), 130.5-112.9 (8C), 56.2-55.5 (4C, O-CH$_3$); ^{1}H NMR (δ ppm) : 7.2-6.7 (m, 6H), 3.7 (s, 6H), 3.5 (s, 6H); Calcd for $C_{17}H_{18}O_5$: C, 66.55; H, 6.14. Found : C, 66.61; H, 6.17.

2,2'-diaminobenzophenone R.N. [606-10-0]; IR : ν_{CO} : 1620 cm^{-1}; Mass., m/z (rel. intensity) : 212(21), 195(8), 167(5), 140(6), 120(23), 106(6), 92(29), 84(15), 77(5), 65(100), 52(11); ^{13}C NMR (δ ppm) : 200.2 (1C, C=O), 149.3 (2C, C-N), 133.3-115.9 (10C); ^{1}H NMR (δ ppm) : 7.3-6.5 (m, 8H), 5.4 (s, 4H).

Tridecan-7-one R.N. [462-18-0]; IR : ν_{CO} : 1720 cm^{-1}; Mass., m/z (rel. intensity) : 199(100), 113(21), 55(11); ^{13}C NMR (δ ppm) : 211.3 (1C, C=O), 42.5 (2C, CH$_2$-CO), 31.3-22.2 (8C, CH$_2$), 13.7 (2C, CH$_3$); ^{1}H NMR (δ ppm) : 2.3 (t, 4H, J = 7 Hz), 1.52-1.42 (m, 4H), 1.1-1.3 (m, 12H), 0.8 (t, 6H, J = 6 Hz).

Heptadecan-9-one R.N. [540-08-9]; IR : ν_{CO} : 1715 cm^{-1}; Mass., m/z (rel. intensity) : 255(39), 169(6), 156(16), 141(88), 123(17), 113(16), 109(9), 100(12), 96(26), 81(41), 71(79), 67(19), 57(100), 55(62); ^{13}C NMR (δ ppm) : 216.7 (1C, C=O), 42.6 (2C, CH$_2$-CO), 31.6 à 22.5 (10C, CH$_2$), 13.9 (2C, CH$_3$); ^{1}H NMR (δ ppm) : 2.3 (t, 4H, J = 7,5 Hz), 1.52-1.45 (m, 4H), 1.1-1.3 (m, 20H), 0.8 (t, 6H, J = 6.3 Hz).

1,3-bis-(2-chlorophenyl)propan-2-one R.N. [85150-76-1]; IR : ν_{CO} : 1730 cm^{-1}; Mass., m/z (rel. intensity) : 125(100), 89(73), 63(23); ^{13}C NMR (δ ppm) : 203.1(1C, C=O), 134.5 (2C, C-Cl), 132.6-127.0 (10C), 45.2 (2C, CH$_2$); ^{1}H NMR (δ ppm) : 7.3-7.2 (m, 8H), 3.9 (s, 4H).

1,3-bis-(3-chlorophenyl)propan-2-one R.N. [59757-95-8]; IR : ν_{CO} : 1725 cm^{-1}; Mass., m/z (rel. intensity) : 125(100), 89(71), 63(24); ^{13}C NMR (δ ppm) : 203.8 (1C, C=O), 135.4 (2C, C-Cl), 134.4-127.3 (10C), 48.6 (2C, CH$_2$); ^{1}H NMR (δ ppm) : 7.2-7.0 (m, 8H), 3.6 (s, 4H).

1,3-bis-(4-chlorophenyl)propan-2-one R.N. [65622-34-6]; IR : ν_{CO} : 1725 cm^{-1}; Mass., m/z (rel. intensity) : 125(100), 89(43), 63(13); ^{13}C NMR (δ ppm) : 204.2 (1C, C=O), 133.5-127.0 (12C), 48.1 (2C, CH$_2$); ^{1}H NMR (δ ppm) :7.3- 7.0 (m, 8H), 3.6 (s, 4H).

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