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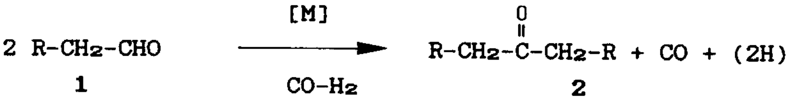
SYNTHESIS OF SYMMETRICAL KETONES FROM ALDEHYDES CATALYSED BY DICOBALTOCTACARBONYL

M. Fontaine, A.F. Noels+*, A. Demonceau+ and A.J. Hubert
Laboratory of Organic Synthesis and Catalysis,
+Laboratory of Macromolecular Chemistry and Organic Catalysis,
University of Liège, Sart Tilman (B.6), B-4000 Liège (Belgium)

Summary : Under a pressure of synthesis gas, dicobaltoctacarbonyl in pyridine selectively catalyses the coupling reaction of aldehydes to ketones.

Aldehydes can be activated by a number of transition-metal complexes. The main reaction pathways are then decarbonylation or hydroacylation in the presence of olefins.[1] Outside the hydroacylation reaction, which has severe limitations,[2] ketone formation from aldehydes is quite unusual. Although dialkylketone formation is known to occur in the hydroformylation of olefins (albeit in low yields, especially with higher olefins),[3] aldehydes as such are not directly involved in the process.

We now wish to report a direct catalytic access to symmetrical ketones from aldehydes according to the equation :



$$\underset{\mathbf{1}}{2\ R\text{-}CH_2\text{-}CHO} \xrightarrow[CO\text{-}H_2]{[M]} \underset{\mathbf{2}}{R\text{-}CH_2\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_2\text{-}R} + CO + (2H)$$

The outcome and yield of the reaction strongly depend on the reaction conditions. The CO-H_2 pressure as well as the presence of pyridine as solvent are required in order to observe a significant production of ketones.

A typical procedure is illustrated hereafter for the synthesis of 1,3-diphenyl-2-propanone (2, R = Ph) from phenylacetaldehyde (1, R = Ph) : 20 mmol of phenylacetaldehyde and 0.96 mmol of dicobaltoctacarbonyl in 25 ml of dry pyridine were heated in a Pyrex jacketed stainless-steel autoclave for 12 h under 10 MPa of synthesis gas (CO:H_2 = 4). After degasing and work-up, the main reaction product was identified as 2 (R = Ph, yield = 55-60%).[4] Toluene (<3%), phenethylalcohol (± 8%), traces of 1,2-diphenylethane, 1,3-diphenylpropane were identified as products[4] together with some high boiling aldols. Interestingly enough, benzaldehyde and benzylalcohol were also present as by-products (total yield <4%). The yield of ketone dropped when the reaction was run in the absence of either carbon monoxide or hydrogen. Blank experiments showed the metal carbonyl to be necessary to observe the formation of the ketone.

The specific effect of pyridine was demonstrated by the fact that solvents covering a wide scale of polarity and basicity afforded no ketone (Table I), the case of N,N-dimethylaniline (same pK_a as pyridine) being particularly noteworthy. Moreover, dilution of pyridine with benzene or dioxane led to a marked decrease of the yield (Table I). Addition of a chelating ligand, 2,2'-bipyridyl, had no influence.

Table I : Influence of Solvent on the Yield of Dibenzylketone[a]

Solvent	Yield (%)[b]	Solvent	Yield (%)[b]
Pyridine	60	Dioxane	0
Pyridine-bipyridyl[c]	60	Benzene	0
Pyridine-dioxane(20/80)	32	Triethylamine	0
Pyridine-benzene(20/80)	17	Acetonitrile	0
N,N-Dimethylaniline	traces	Nitrobenzene	0
N-Methylpyrrolidone	0	Tetrahydrofuran	0

[a] Reaction conditions : T = 140°C; P_{CO-H_2} = 10 MPa ($CO:H_2$ = 4); 0.96 mmol $Co_2(CO)_8$; 20 mmol phenylacetaldehyde; 10 ml solvent; heating time 12 h. [b] The yields were determined by GLC analysis. [c] Ratio Co/bipyridyl = 0.25.

It also appeared that among the different N-containing heterocycles tested so far, none had the efficiency of pyridine for promoting the reaction (Table II). Moreover, hindering the nitrogen center of the pyridine ring also drastically reduced the yield of dibenzylketone (DBK). Then, formation of aldols and, in the case of lutidine more particularly, of 2,4-diphenylbutanal was observed (≈30%).

Preliminary results indicated that the reaction could be extended to other aldehydes, although with somewhat lower yields (not optimised), e.g. 50% of 1,5-diphenyl-3-pentanone from 3-phenylpropionaldehyde.[4]

Cross experiments with phenylacetaldehyde and 3-phenylpropionaldehyde yielded a mixture of the homo and cross-coupled ketones, namely dibenzylketone(DBK), 1,5-diphenyl-3-pentanone and 1,4-diphenyl-2-butanone[4]

Table II : Effect of Various Amines as Solvent on the Yield of DBK[a]

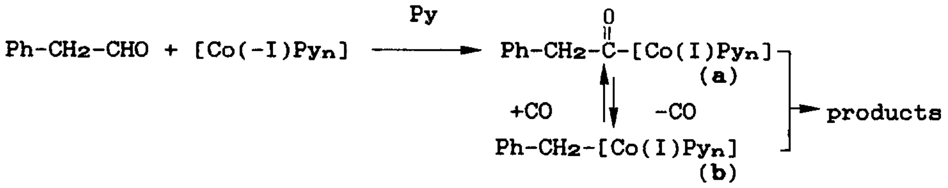
Solvent	Yield (%)[b]	Solvent	Yield (%)[b]
Pyridine	60	2-Methoxypyridine	0
4-Picoline	60	Quinoline	8
2-Picoline	7	Pyrazine	0
2,4-Lutidine	9	Pyridazine	<2
2,6-Lutidine	9	Piperidine	0

[a,b]See Table I.

in a ratio of respectively 1:4:4 (overall yield = 50%). Benzaldehyde did not react and, with aliphatic aldehydes such as heptanal, aldol condensations took over and reduced the yield of ketones to 10-20% (not optimised). Carbonyls of Ir, Rh, Mn, Ru, Fe, W, Mo, did not promote the formation of 2 to any considerable extent. Instead, with group 9 metals, new, heavier products different from the aldols are formed. Those reactions are presently investigated. Interestingly, carrying out the reaction in the presence of styrene (styrene : phenylacetaldehyde = 0.5) did not affect the synthesis of dibenzylketone. In particular no product resulting from a possible intermolecular addition of the aldehyde to the double bond was detected. Instead, the olefin was reduced, which rules out a hydroacylation mechanism.

The reaction is probably homolytic in nature. The formation of DBK is totally quenched by addition of a 10 mol % of CCl_4 or of a Cu(II) salt. The structure of the by-products also fit within the context of a radical reaction. Many aldehydes are decarbonylated by the addition of free radical sources.[5] Recently, the synthetic interest of acyl-cobalt derivatives to promote radical reactions via homolytic cleavage of the cobalt-carbon bond has been stressed by Pattenden and al.[6] In our case, the specific role of pyridine is less clear. On the one hand, cobalt-catalysed hydroformylation reactions are known to be slow in the presence of excess pyridine[7] but on the other hand, the beneficial effect of pyridine (together with a small amount of hydrogen) has been noted in hydroesterification reactions.[8]

It is well known that nitrogen-centered bases disproportionate dicobaltoctacarbonyl into Co(II)/Co(-I) species and that solvents (ligands) critically influence the evolution of the resulting ion-pairs.[9] In this context, a plausible scheme is the oxidative addition of the aldehyde to the metal center (possibly a cobalt anion) to yield an acyl-cobalt (**a**) in equilibrium with alkyl-species (**b**), the relative amount of (**a**) and (**b**) being regulated *inter alia* by the CO pressure.



Although a detailed understanding of the reaction mechanism must await further study, the absence of products resulting from coupling of free radicals with the radicophilic pyridine is suggestive of a specific inner-sphere mechanism.

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