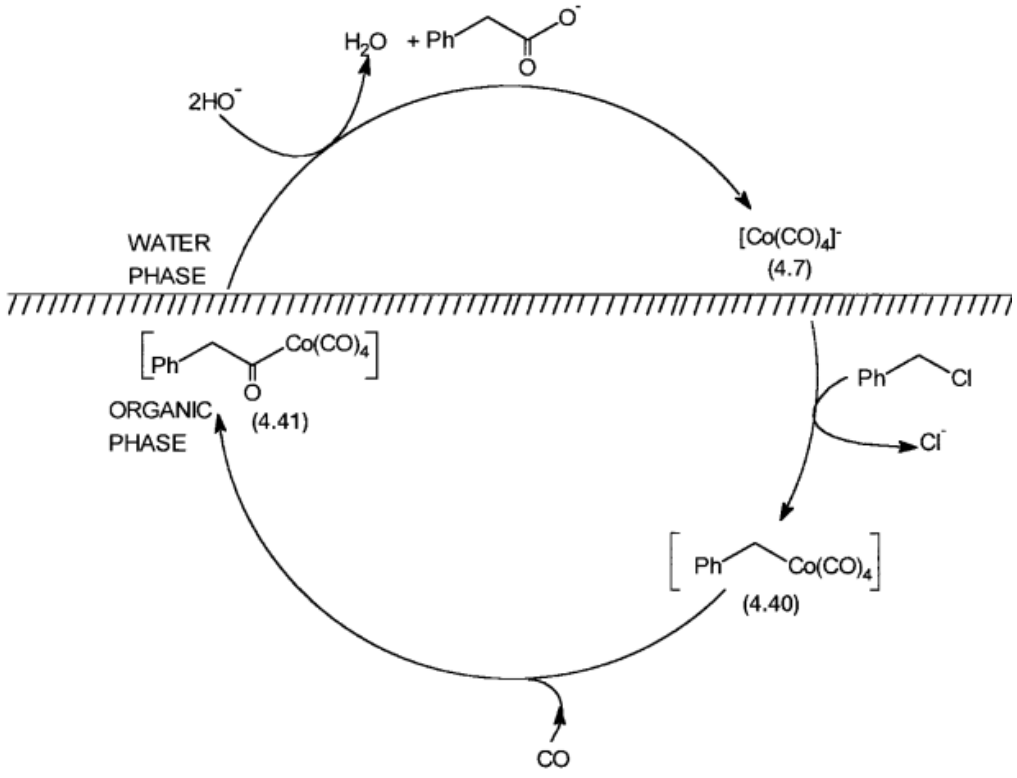
HYDROCARBOXYLATION REACTIONS

There are several fairly small-volume but value-added chemicals which are produced commercially by reactions to carbonylation or hydrocarboxylation.

TABLE Chemicals Manufactured by Carbonylation or Hydrocarboxylation Reactions

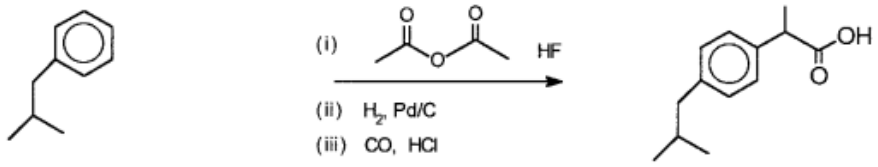
Manufacturer	Product	Process
Montedison	Phenylacetic acid; an intermediate for pesticide and perfumes	Cobalt catalyst; $PhCH_2Cl$, CO, and HO^- are the reactants; $T \sim$ 55°C, P = a few bars; Reaction carried out in a biphasic medium with a *phase-transfer* catalyst
Ube Industries	Oxalate diesters	Palladium catalyst; ROH, CO, and O_2 are reactants. Nitric oxide is used as a co-catalyst; Actual production is probably based on a heterogeneous catalyst
Hoechst	Ibuprofen; an analgesic (see Table 1.1)	Carbonylation of appropriate secondary alcohol with a palladium catalyst



The dashed line, ////////, represents the phase boundary in the biphasic system.

Figure. The Montedison process for the carbonylation of benzyl chloride

Since 1992 Celanese method for producing ibuprofen on a scale of 3500 tons has been in operation. Isobutyl benzene is acylated in this process, and then hydrogenated over a heterogeneous catalyst to give the correct precursor alcohol. The alcohol then is carbonylated. The overall synthetic scheme is shown by reaction 4.14. The conventional process for ibuprofen manufacture was based on six synthetic steps and generated a large amount of salt as a solid waste.



(4.14)

In the Hoechst process, the carbonylation reaction requires the use of $PdCl_2(PPh_3)_2$ as the precatalyst, a CO pressure of around 50 bar, and a temperature of around 130 C. It is achieved in a mixture of organic solvent and hydrochloric acid. The molecular mechanism is not known with certainty. A hypothetical catalytic cycle is shown in Fig, based on the known chemistry of palladium.

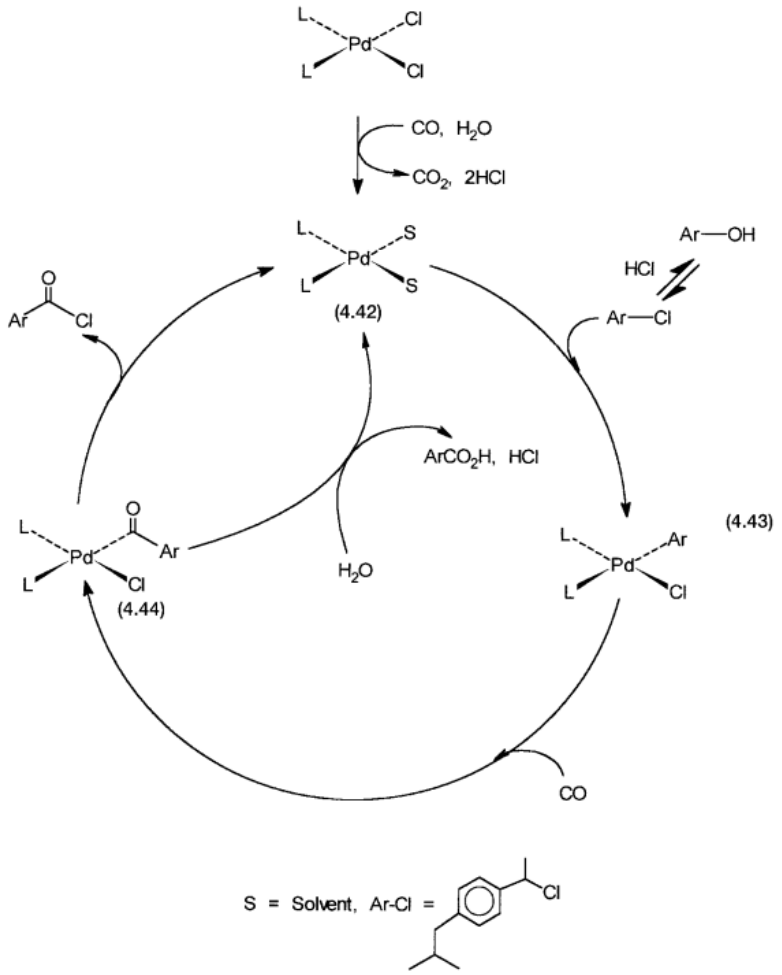


Figure. Hypothetical cycle for Hoechst–Celanase ibuprofen process.

The basic assumptions are as follows: First the precatalyst is reduced to species 4.42 of zero-valent palladium. The addition of oxidative Ar – Cl to 4.42 gives 4.43. The incorporation of CO into the Pd – C bond results in a conversion between 4.43 and 4.44. Finally, from 4.44, ArCOCl is deleted reductively. To give ibuprofen, acid chloride undergoes hydrolysis. Direct reaction between 4.44 and water to give 4.42, ibuprofen, and HCl is also possible.