Reformatsky Reaction

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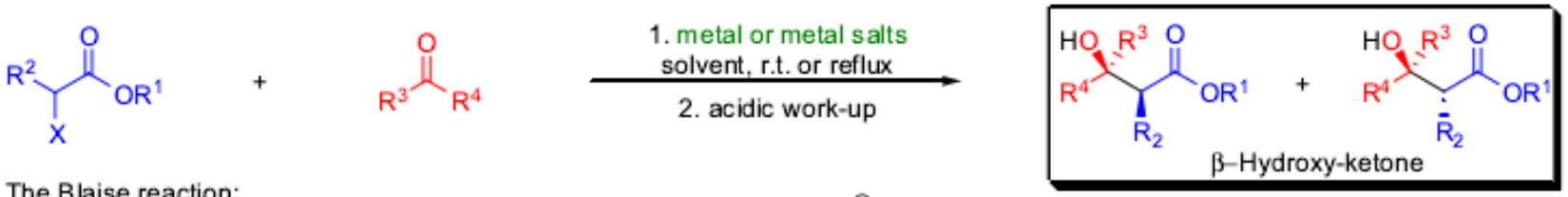
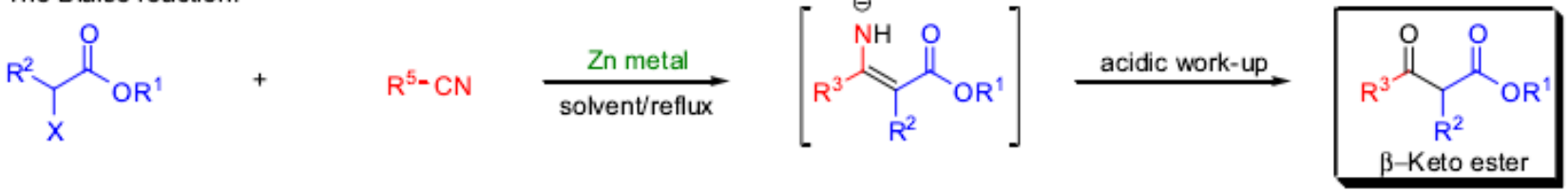
In 1887

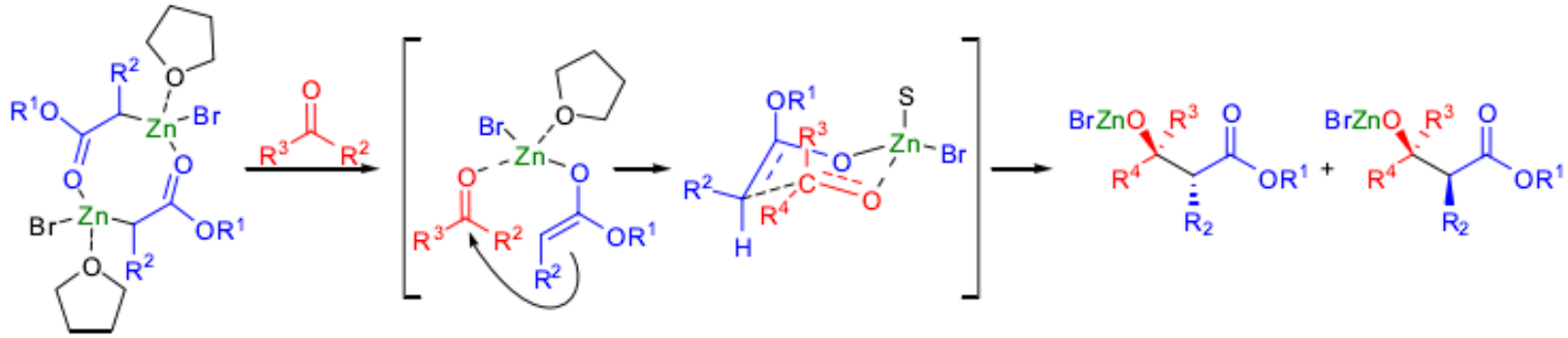


The Blaise reaction:



X = Cl, Br, I; R^1 = alkyl; R^2 = H, alkyl, aryl; R^3, R^4 = H, alkyl, aryl; R^5 = alkyl, aryl; solvent: Et_2O, THF, 1,4-dioxane, DME, benzene, toluene, MeCN, DMF, DMSO; metal: Zn, Mg, Cd, Ba, In, Ge, Co, Ni, Ce; metal salt: SmI_2, $CrCl_2$, $TiCl_2$, CeX_3, Na_2Te, R_3SnLi, R_3Sb/I_2, Et_2AlCl;

Mechanism:



General Features :

1) the reaction is most commonly carried out in a single step by addition of the α-halo ester and the carbonyl compound to the suspension of the activated zinc, but preforming the organozinc reagent prior to the addition of the electrophile is also possible;
2) most often ether solvents are used such as diethyl ether, tetrahydrofuran, 1,4-dioxane and dimethoxyethane, but mixtures of these solvents with aromatic hydrocarbons and more polar solvents such as acetonitrile, dimethyl formamide, dimethyl sulphoxide, and hexamethylphosphoric triamide are also used;
3) organozinc reagents can be formed from 2-bromoalkanoates, α-bromo ketones, alkyl 2-bromomethyl-2-alkenoates, and alkyl 4-bromo-2-alkenoates ;
4) in addition to aldehydes and ketones, Reformatsky reagents also react with esters, acid chlorides,epoxides,nitrones,aziridines,imines,and nitriles (Blaise reaction). The scope of the Reformatsky reaction was considerably extended by the development zinc-activation procedures.

Activated zinc metal can be formed in two ways:

1) by removal of the deactivating zinc oxide layer from the metal surface employing reagents such as iodine, 1,2-dibromoethane, copper(I) halides, mercuric halides or by using zinc-copper or zinc-silver couple;

2) by reduction of zinc halides in solution by various reducing agents such as potassium (Rieke zinc), sodium-or lithium naphthalide and potassium-graphite Laminate (C8K) to form finely dispersed zinc metal. Metals other than zinc were also used including lithium, magnesium, cadmium, barium, indium, germanium, nickel, cobalt, and cerium. A major breakthrough in the Reformatsky reaction was the application of metal salts with favorable reduction potentials, the most important ones being samarium(II) iodide, chromium(II) chloride, and titanium(II) chloride. These reactions often can be carried out under mild conditions and afford the products with high stereoselectivity. In addition to these metal salts, cerium(III) halides, disodium telluride, trialkylantimony/iodine, and diethylaluminum chloride can also be employed.

Synthetic Applications: