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DUAL CATALYSIS OF THE MICHAEL REACTION

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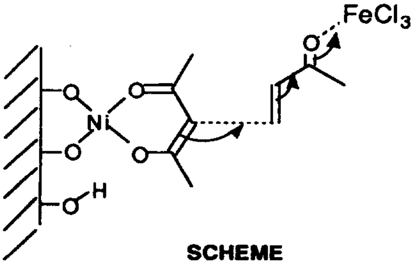
Abstract : The Michael reaction, with conjugate bases of β-diketones as donors and with α,β-unsaturated ketones as acceptors, is efficiently catalyzed by a combination of clay-supported nickel bromide (heterogeneous) and ferric chloride (homogeneous).

In our first attempt at catalysis of the Michael reaction, we sought help for the donor : the fibrous mineral xonotlite doped with potassium t-butoxide served as a solid Brønsted base. Effective and simple procedures were achieved[1]. In our second attempt at catalysis of the Michael reaction, we sought help for the acceptor : Lewis acids, ferric chloride in particular, were effective. Addition of primary and secondary amines was thus catalyzed [2]. It remained to combine the two approaches. We report here the marked improvement in Michael additions from *the joint use of two catalysts*.

Rationale. The design of the catalytic system had to incorporate a solid catalyst since four-body collisions in solution are improbable ! Instead of using a solid base to deprotonate an activated methylene into a negatively-charged Michael donor, as in our initial study [1], we elected to stabilize the conjugate base, i. e. the Michael donor, on the solid surface. Having thus pre-formed the donor, we would bring in the acceptor from the solution. In this manner, nothing prevented homogeneous catalysis for the acceptor side, with a Lewis acid such as ferric chloride. For the first role, of anchoring the Michael donor on the solid catalyst, we were reminded of the very strong complexes between the *acac* ligand and transition metals [3]. For this reason, we elected to impregnate nickel bromide on a clay support. By continuity with the growing list of catalysts of this novel type that includes now "clayfen"[4], "claycop" [5], "clayzic" [6], these catalysts are nicknamed in like manner : "claynick" (∗ in the Table) when the K10 montmorillonite serves as the support; and "kaonick" (§ in the Table), when a kaolinite is chosen as support. Thus the reaction system can be described as in the Scheme :



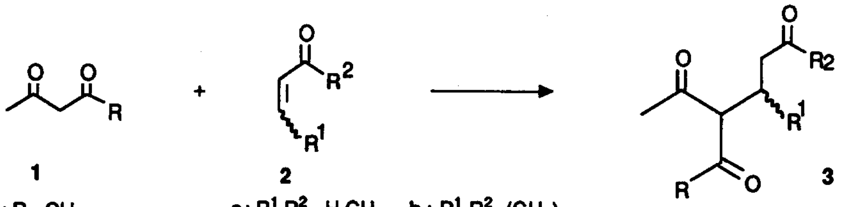
SCHEME

Experimental

Preparation of the catalysts : a solution of anhydrous nickel bromide in acetonitrile (1g in 10 mL; ca. 0.6M) is stirred under moderate heating. Kaolinite (-> "kaonick") or the K10 montmorillonite (Süd-Chemie, Munich) (->"claynick") is added to the suspension in equivalent amount (w/w) as the nickel metal (0.34g). The solvent is evaporated under reduced pressure (rotary evaporator). The residue is dried in an atmospheric oven at 280 °C overnight. It is stored in an oven at 150 °C.

Typical procedure : a mixture of benzalacetone (4 mM) and acetylacetone (20 mM) in dioxane (2 mL) is stirred in a reaction flask at room temperature. A mixture of "claynick" (30 mg) and of ferric chloride (Merck, 20 mg) is added; and stirring is continued under a dry nitrogen atmosphere till completion of the reaction, as monitored by gc. The adduct is isolated by filtration chromatography through a short plug (ca. 4 cm) of silicagel (Riedel-de Haen, 0.063-0.1 mm). After solvent evaporation, crude but practically pure product (by gc and nmr evidence) is obtained. For higher purity the product is distilled or recrystallized.

Results



1 a: R= CH_3 b : R= OC_2H_5

2 a : R^1,R^2= H,CH_3 b : R^1,R^2=$(CH_2)_3$ c : R^1,R^2= C_6H_5,CH_3 d : R^1,R^2= C_6H_5,C_6H_5

3

1	2	catalyst	temperature, °C	1 / 2 ^{a}	time, h	yield,%
1a	2a	*	20	1	24	90
1b	2a	*	20	1	21	98
1a	2b	*	20	1	26	95
1a	2c	§	20	5	20	82
1b	2c	*	reflux	5	4	85
1b	2b	*	20	1	6	97
1a	2d	§	80	5	23	71^b
1b	2d	§	80	2	45	40^b

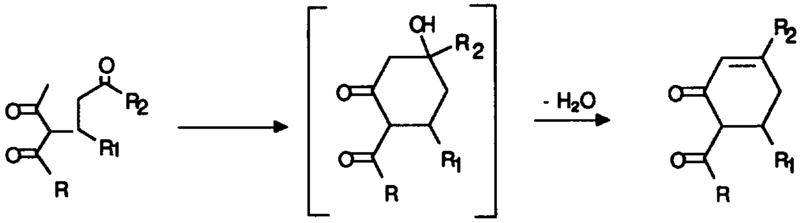
* : "claynick"+ $FeCl_3$; § : "kaonick" + $FeCl_3$; *a* : molar ratio ; *b* : recrystallized product

Table : Michael reactions catalyzed by Ni (II), impregnated on clays, in conjunction with ferric chloride.

Reaction products. The known products give consistent IR (measured on a Nicolet MX-S-IRFT spectrometer) and ^1H and ^{13}C NMR (recorded with a Bruker 200 MHz spectrometer) spectra. δ's for the diastereomers were assigned by two dimensional NMR using correlation spectrum (COSY) and heteronuclear ^{13}C-^1H shift correlation (HSC) spectra [7] jointly.

3-acetyl heptane-2,6 dione (3a)[1,8,9]: the two keto and enol forms were identified. **3-carboxyethyl heptane-2,6-dione (3b)** [1,8,9]. **3-(3-oxocyclohexyl) pentane-2,4-dione (4a)** [8]. **Cyclohexaneacetic acid, α acetyl-3-oxo, ethyl ester (4b)** [8,10] : the two enantiomers give duplicated NMR spectra. **3-acetyl-4-phenyl heptane-2,6-dione (5a)**: m.p. 92-94 °C. IR (CCl_4) ν (cm^{-1}): 1700, 1725; ^1H NMR ($CDCl_3$) δ (ppm) 1.86 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.70 (m, 2H, CH_2CO), 4.02 (m, 1H, $C\underline{H}C_6H_5$), 4.20 (d, 1H, CHCO), 7.24(m, 5H, arom.). **3-carboxyethyl-4-phenyl heptane-2,6-dione (5b)**: (oily) a mixture of diastereomers with relative configuration syn or anti ([11] for a definition): IR: (CCl_4) ν (cm^{-1}): 1717, 1740; ^1H NMR ($CDCl_3$) δ (ppm) 0.95 and 1.28 (two t, 3H, $C\underline{H}_3CH_2O$), 1.96 and 1.98 (two s, 3H, CH_3CO), 2.25 (s, 3H, CH_3CO), 2.79 and 2.88 (two d, 2H, CH_2CO), 3.88 and 4.18 (two q, 2H, $OC\underline{H}_2CH_3$), 3.84-3.97 (m, 2H, CHCO and $C\underline{H}C_6H_5$), 7.24 (m, 5H, C_6H_5).**4-acetyl-1,3-diphenylhexane-1,5-dione (6a)**[12,13,14]: m.p.142-143°C. **4-carboxyethyl-1,3-diphenyl hexane-1,5-dione (6b)** [12,14] : a mixture of syn-anti diastereomers : ^1H NMR ($CDCl_3$) δ (ppm) 0.98 and 1.26 (two t, 3H, $OCH_2C\underline{H}_3$), 2.02 and 2.31 (two s, 3H, CH_3CO), 3.37 and 3.39 (two m, 2H, CH_2CO), 3.98 and 4.19 (two q, 2H, OCH_2CH_3), 4.04 (two d, 1H, CHCO), 4.20 (m, 1H, CHC_6H_5), 7.20-7.89 (m, 10H, two C_6H_5). ^{13}C NMR (CDCl3) δ (ppm) 13.70 and 14.03; 29.58 and 30.00; 40.53 and 40.61; 42.72 and 42.82; 61.34 and 61.65; 64.80 and 65.44; 127.08 -128.65, 133.05, 136.79 (aromatic); 168.02 and 168.51, 197.63 and 197.96, 202.06 and 202.45 (CO).

Discussion. In some cases, with acceptors such as benzalacetone or chalcone, the main by-product results from annulation :



In general however, reactions run under the conditions stated are clean and do not give rise to secondary products. Control experiments, not reported here, show that indeed there is synergy between the two catalysts "claynick" or "kaonick" for the donor and ferric chloride for the acceptor. The procedures reported here commend themselves for their operational simplicity, *by the absence of a strong base requirement*, and by the mild conditions.

To sum up, whenever β-diketones are the activated methylenes serving as Michael donors an efficient catalytic system combining clay-supported nickel bromide and ferric chloride enables additions with the triple avantage of (i) **dispensing with a base; (ii) mild reaction conditions; (iii) ease of set-up and work-up.**

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