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β-DIALKYLAMINO CONJUGATED ENONES: REDUCTION WITH $NaBH_4$-$FeCl_3$ AND CONVERSION INTO CONJUGATED ENONES

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β-Dialkylamino conjugated enones were reduced to the corresponding saturated γ-amino alcohols with sodium borohydride in the presence of iron (III) chloride. The resulting γ-amino alcohols were converted into conjugated enones by chromic acid oxidation and deamination.

We previously reported the reduction of β-acylamino conjugated enones with sodium borohydride to afford β,γ-unsaturated γ-acylamino alcohols, which were regioselectively hydrolyzed to conjugated enones.1) However, β-dialkylamino conjugated enones resisted to the attack of sodium borohydride similar to that of amide groups. Meanwhile, in the presence of metal halides such as iron (III) chloride, nickel (II) chloride and cobalt (II) chloride, amides were reduced by sodium borohydride to the corresponding amines.2,3) As a vinylogue of amide, it is interesting to reduce β-dialkylamino conjugated enones with sodium borohydride in the presence of metal halides. Also the effects of iron (III) chloride is interesting in the reduction of β-amino conjugated enones, because β-amino conjugated enones usually form the reddish-brown complexes with iron (III) chloride similar to the reddish-brown β-diketonate iron (III) complexes. Here, we wish to communicate the reaction of β-amino conjugated enones with sodium borohydride in the presence of metal halides, especially iron (III) chloride.

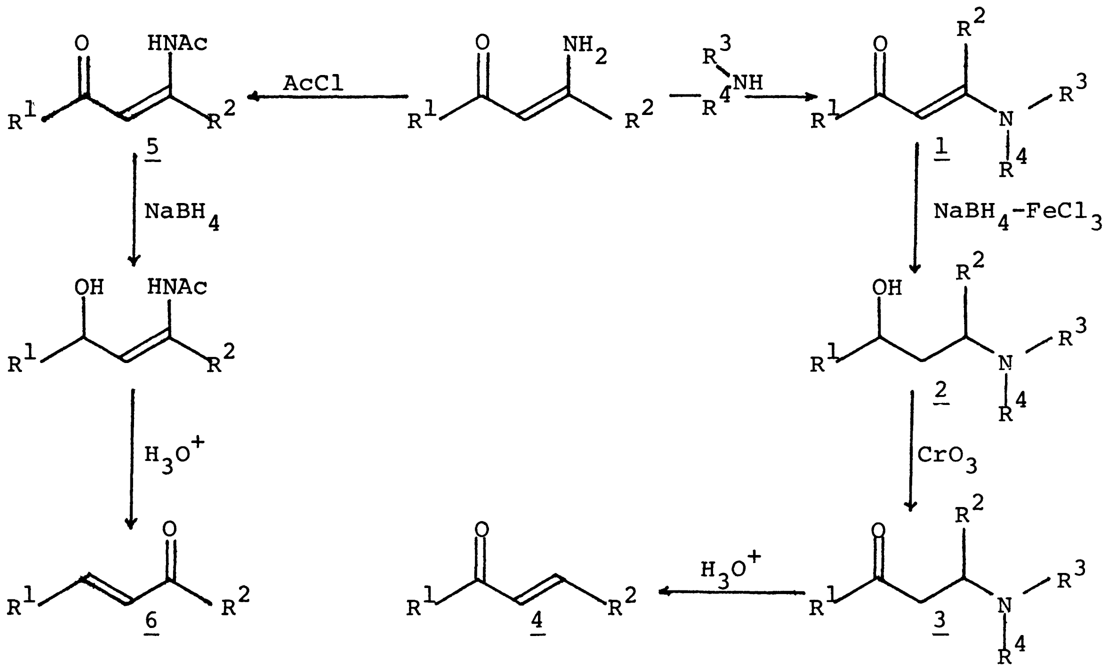
In the cases of nickel (II) chloride, cobalt (II) chloride and zinc (II) chloride, the dramatic effect of metal halide could not be observed in the sodium borohydride reduction of β-amino conjugated enones, as listed in Table 1. The

Table 1

The Reduction of 1-a in Various Molar Ratio of Metal Halides and $NaBH_4$ at 20°C

Metal Halide	Ratio	Ratio of $NaBH_4$	Time	Yield of 2-a
none	——	3.0	16 h	30 %
$NiCl_2 \cdot 6H_2O$	1.0	3.0	20 min	50 %
$CoCl_2 \cdot 6H_2O$	1.0	3.0	20 min	50 %
$ZnCl_2$	1.0	3.0	20 min	40 %
$FeCl_2 \cdot nH_2O$	1.0	3.0	20 min	98 %
$FeCl_3 \cdot 6H_2O$	1.0	3.0	20 min	100 %
$FeCl_3 \cdot 6H_2O$	1.0	2.0	20 min	98 %
$FeCl_3 \cdot 6H_2O$	1.0	1.0	20 min	73 %
$FeCl_3 \cdot 6H_2O$	1.0	0.5	20 min	10 %
$FeCl_3 \cdot 6H_2O$	1.0	2.5	16 h	100 %
$FeCl_3 \cdot 6H_2O$	1.0	1.0	16 h	96 %
$FeCl_3 \cdot 6H_2O$	1.0	0.5	16 h	50 %
$FeCl_3 \cdot 6H_2O$	0.33	2.5	16 h	85 %
$FeCl_3 \cdot 6H_2O$	0.037	2.5	16 h	65 %

pale-green mixture of iron (II) chloride and β-dialkylamino conjugated enones was reduced to saturated γ-amino alcohols in good yield. By the gradual addition of sodium borohydride to reddish-brown solution of β-dialkylamino conjugated enones and iron (III) chloride, the color changed to pale-green and the reduction proceeded smoothly to give the saturated γ-amino alcohols. For example, to a solution of 4-pyrrolidinyl-3-penten-2-one (1-a) in methanol was added equimolar amount of iron (III) chloride to give reddish-brown solution, which was treated with equimolar amount of sodium borohydride for 3 hr with stirring. The mixture was diluted with water, and 4-pyrrolidinyl-2-pentanol (2-a) was extracted with dichloromethane. The structure of 2-a was confirmed with nmr and ir spectral data.



a: $R^1=R^2=$ Me $R^3,R^4=(CH_2)_4$

b: $R^1=R^2=R^3=R^4=$ Me

c: $R^1=R^2=$ Me $R^3,R^4=(CH_2)_5$

d: $R^1=$ Ph $R^2=$ Me $R^3,R^4=(CH_2)_4$

e: $R^1=$ Ph $R^2=$ H $R^3,R^4=(CH_2)_4$

f: $R^1=$ Ph $R^2=$ H $R^3,R^4=(CH_2)_5$

g: $R^1=$ Ph $R^2=$ H $R^3,R^4=(CH_2)_2O(CH_2)_2$

h: $R^1=R^2=$ Me $R^3=R^4=$ H

i: $R^1=R^2=$ Me $R^3=$ Bu $R^4=$ H

Table 2

The Yields of Saturated γ-Amino Alcohols (2)

Comp.	R^1	R^2	R^3	R^4	Temp.	Time	Yield of 2
1-a	Me	Me	$(CH_2)_4$		20 °C	3 h	100 %
1-b	Me	Me	Me	Me	20 °C	3 h	66 %
1-c	Me	Me	$(CH_2)_5$		20 °C	3 h	73 %
1-d	Ph	Me	$(CH_2)_4$		60 °C	16 h	70 %
1-e	Ph	H	$(CH_2)_4$		60 °C	16 h	30 %
1-f	Ph	H	$(CH_2)_5$		60 °C	16 h	40 %
1-g	Ph	H	$(CH_2)_2O(CH_2)_2$		60 °C	16 h	45 %
1-h	Me	Me	H	H	60 °C	16 h	0 %
1-i	Me	Me	Bu	H	60 °C	16 h	0 %

Similarly, 4-dimethylamino-3-penten-2-one (1-b), 4-piperidino-3-penten-2-one (1-c), 3-pyrrolidinyl-1-phenyl-2-buten-1-one (1-d), 3-pyrrolidinyl-1-phenyl-2-propen-1-one (1-e), 3-piperidino-1-phenyl-2-propen-1-one (1-f) and 3-morpholino-1-phenyl-2-propen-1-one (1-g) gave the corresponding saturated γ-amino alcohols as shown in Table 2. β-Amino conjugated enones (1-h and 1-i), which have an N-H group, were not reduced with sodium borohydride even in the presence of iron (III) chloride, because of the formation of stable complexes. From the investigation of this reduction in various ratio of β-amino conjugated enones, iron (III) chloride and sodium borohydride, optimal condition was concluded to be equimolar amount of iron (III) chloride and 2 molar amounts of sodium borohydride.

Furthermore, the oxidation of the resulting γ-amino alcohols with chromic acid provided the corresponding β-amino ketones (3), which was easily deaminated into conjugated enones (4) by the treatment with sulfuric acid. For example, 3-pyrrolidinyl-1-phenyl-1-butanol (2-d) was converted into 1-phenyl-2-buten-1-one (4-d) in 90 % yield by the treatment with chromic anhydride in acetone in the presence of sulfuric acid. These conjugated enones (4) had the alternative structure from the conjugated enones (6), which was prepared from β-acylamino conjugated enones (5) by sodium borohydride reduction followed by acidic hydrolysis.[1) These results concluded that β-amino conjugated enones were quite important compounds for the specific synthesis of conjugated enones by reducing with sodium borohydride.

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