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ACTIVATION OF REDUCING AGENTS. SODIUM HYDRIDE-CONTAINING "COMPLEX REDUCING AGENTS"
IV[1]. KETONE, ALKENE AND ALKYNE REDUCTIONS

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Addition of metal salts is known to modify the reducing ability of metal hydrides. Recently, much attention has been paid to reducing agents which consist of mixtures of metal hydrides and metals salts.[2-7] During the last few years, part of our interest had been focused upon the activation of reducing ability of sodium hydride. In preceding work[8], we have demonstrated that the reducing properties of NaH in THF are dramatically increased by the presence of sodium alcoholates. However, the scope of application of this reducing system is somewhat limited and its reducing ability is, to some extent, dependent on the origin of NaH.[9]

We recently described preparation of new reducing systems consisting of mixtures of sodium hydride, sodium alcoholates and metallic salts. By analogy with "Complex Bases" $NaNH_2$-RONa[10], the new reagents "NaH-RONa-MX_n" were designated "Complex Reducing Agents" (abbreviated : CRA).[11] They have been shown to be very effective for the reduction of aryl halides (M = Ni, Co, Cu ; X = OAc, halogen).[11] In addition, they reduce gem-dihalogenocyclopropane compounds to the corresponding monohalogeno derivatives.[12] Finally, we have described the preparation of carbonyl complexes, at atmospheric pressure and low temperature, from reaction of CO with NaH-t-AmylONa-MX_n (M = Ni, Co, Fe).[13] *In this communication, we wish to report that the basic properties of NaH and RONa are strongly masked in NiCRA and we present some arguments supporting the hypothesis of nickel hydride species generation. Ketone, alkene and alkyne reductions exemplify the usefulness of NaH as an inexpensive source of hydrogen.*

NiCRA are easily generated by dropwise addition, at 60°C, of the activating alcohol to a stirred THF suspension of NaH and $Ni(OAc)_2$ in adequate ratios. A deep black color rapidly develops. After refluxing for 3-4 hours under nitrogen, the reagent is ready for use.

Ketone reduction

It appeared from our earlier work[11, 12] that good reducing properties of CRA required excess sodium hydride and that sodium alcoholate was necessary.[14] A serious limitation would therefore be anticipated with base-sensitive substrates, if the classical basic properties of these components were preserved in the reagent. In fact, the basic character of NaH and t-AmylONa is strongly "masked" in CRA. Thus, as seen from Table I, enolizable ketones can be reduced by NaH-t-AmylONa-$Ni(OAc)_2$ in good yields. In all cases, conversion to alcohol passes through a maximum, then decreases, i.e. a reoxidation occurs.[15] Addition of LiCl or LiBr to the reaction mixture prevents this reoxidation. This effect is particularly helpful for the reduction of 4-t-butylcyclohexanone (Table I).

Although the actual reducing species have not been identified, it is suggested that they are some kind of nickel hydride[15]. This hypothesis is also consistent with the results of alkene and alkyne reductions (vide infra).

Table I : Reduction of ketones by NaH-t-AmylONa-Ni$(OAc)_2$ in THF[a]

Compound	Temp. (°C)	Time (h)	Alcohol yield (%)
Di-n-butylketone	40	20	95-100[b] (90)[c]
Di-t-butylketone	65	23	95-100[b] (85)[c]
Methylphenylketone	40	13	95[b] (75)[c]
Cyclohexanone	40	20	95[b] (75)[c]
4-t-butylcyclohexanone	40	20	55[b,d] (48)[c]
4-t-butylcyclohexanone[e]	40	20	95-100[b,f] (88)[c]

[a] NaH/t-AmylONa/Ni$(OAc)_2$/ketone (in mmol) = 40/10/10/10 ; all reactions were performed under nitrogen, in 40-50 ml THF. Reduction is followed by dropwise addition of EtOH at 0°C, and then by hydrolysis in water. [b] Determined by GLPC with calibrated internal standards (hydrocarbons C_{10}-C_{18}). [c] Isolated yields. [d] cis/trans = 53/47. [e] LiCl or LiBr (20 mM) was added together with ketone. [f] Cis/trans = 5/95.

Alkene reduction

Exploratory experiments conducted with cyclooctene indicated that anisole was a better solvent than pyridine, THF, DME, hexane, benzene or toluene[16], and that t-BuOH was a better activating alcohol than t-AmylOH. Some results are provided in Table II. Substitution at the double bond dramatically decreases the reactivity. Thus, 1-alkenes are easily reduced to alkanes, but reduction of 2-alkenes requires longer reaction times. During the reactions, a small amount of isomerization is observed in some cases. Cyclooctene is unexpectedly less reactive than cyclohexene. In this way, these reductions do not parallel the catalytic P_1 or P_2 nickel hydrogenation described by C.A. Brown[17]. The overall obtained results favorably compare with the reported reduction of alkenes by $TiCl_4$-$AlLiH_4$[7].

Table II : Reduction of alkenes with NaH-*t*-BuONa-Ni(OAc)$_2$ in anisole[a]

Compound	Temp. (°C)	Time (h)	Alkane yield (%)[b]
1-Hexene	55-60	10-15	95-100
trans-2-Hexene	55-60	20-25	95-100
1-Octene	70-75	5-10	95-100
trans-2-Octene	70-75	45-50	95-100
Cyclohexene	65-70	60-70	95
1-Methylcyclohexene	65-70	60-70	25-30[c]
Methylenecyclohexane	65-70	25-30	75[d]
Cyclooctene	75-80	140-150	90

[a] NaH/*t*-BuONa/Ni(OAc)$_2$/alkene (in mmol) = 40/20/10/10. All reactions were performed under nitrogen in 50 ml anisole. [b] Determined by GLPC analysis with internal standards. [c] Unreacted 1-methylcyclohexene = 70 %. [d] Isomerization to 1-methylcyclohexene is observed.

Alkyne reductions

Reductions of 1-alkynes to alkanes are easily achieved under the same conditions. Selective partial reductions of alkynes to alkenes may be achieved (see Table III) at lower temperatures, by replacing anisole with THF and *t*-BuOH with *t*-AmylOH. These reductions are selective syn additions. Thus, 2-hexyne give *cis*-2-hexene in very good yield. With diphenyl acetylene, the reduction is certainly a syn addition but isomerization to the more stable isomer cannot be suppressed.

Table III : Reduction of alkynes by NaH-RONa-Ni(OAc)$_2$[a]

Compound	Solvent	R(RONa)	Temp. (°C)	Time (h)	Major product	yield[b]
1-Hexyne	Anisole	*t*-Bu	55-60	15-20	n-Hexane	100
1-Octyne	Anisole	*t*-Amyl	60-65	35-40	n-Octane	80[c]
1-Octyne	THF	*t*-Amyl	20-25	40-45	1-Octene	100
2-Hexyne	THF	*t*-Amyl	35-40	35-40	cis-2-Hexene	95-100
Diphenylacetylene	THF	*t*-Amyl	35-40	15-20	cis-Stilbene trans-Stilbene Bibenzyl	63-67 10-15 13-17

[a] NaH/RONa/Ni(OAc)$_2$/Alkyne (in mmol) = 40/20/10/10. All reactions were performed in 50 ml solvent under nitrogen. [b] Determined by GLPC with internal standards. [c] 2-Octenes appear during the reaction.

The stereochemistry of these reductions and the previously observed isomerization of alkenes are consistent with the intermediacy of nickel hydride as the reducing species.[18]

The mechanism of these reactions may be very complicated and the nature of active species remains to be thoroughly investigated. We are continuing to examine the versatile properties of CRA in order further to extend their scope and efficiency and to clarify the nature of active species.

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REFERENCES AND NOTES

(1) For part III, see ref. 13. Part of this report, together with refs 11 and 12 represents the research work of L.M. for her Ph. D. Thesis.

(2) M.N. Rerick in "Reduction", R.L. Augustine, Ed. Marcel Dekker, New York, N.Y. 1968

(3) J.E. McMurry and M.P. Fleming, J. Am. Chem. Soc., 96, 4708 (1974).

(4) J.E. McMurry and M.P. Fleming, J. Org. Chem., 40, 2555 (1975).

(5) M.F. Semmelhack and R.D. Stauffer, J. Org. Chem., 40, 3619 (1975).

(6) E.C. Ashby and J.J. Lin, Tetrahedron Lett., 4453 (1975).

(7) P.W. Chum and S. Wilson, Tetrahedron Lett., 15 (1976).

(8) J. Moreau and P. Caubère, Tetrahedron, 27, 5741 (1971) and references cited therein.

(9) Unpublished results.

(10) P. Caubère, Accounts Chem. Res., 7, 301 (1974).

(11) G. Guillaumet, L. Mordenti and P. Caubère, J. Organometal. Chem., 92, 43 (1975).

(12) G. Guillaumet, L. Mordenti and P. Caubère, J. Organometal. Chem., 102, 353 (1975).

(13) B. Loubinoux, B. Fixari, J.J. Brunet and P. Caubère, J. Organometal. Chem., 105, C 22 (1976)

(14) While this work was in progress, reports claiming ketone, alkene and alkyne reductions by NaH-$FeCl_3$ appeared : T. Fujisawa, K. Sugimoto and H. Ohta, J. Org. Chem., 41, 1667 (1976) ; T. Fujisawa, K. Sugimoto and H. Ohta, Chem. Lett., 581 (1976) (see also C.A., 85, 142799w (1976). It must be noted that large excesses of NaH and $FeCl_3$ (molar ratios NaH/$FeCl_3$/substrate = 21/7/1) must be employed in the method of Fujisawa, Sugimoto and Ohta.

(15) This reaction has precedent in the work of Eliel : E. Eliel and S.H. Shroeter, J. Am. Chem. Soc., 87, 5031 (1965). Catalytic hydrogenation with Raney Nickel has been suggested to involve nickel hydride species : P.W. Jolly and G. Wilke, The Organic Chemistry of Nickel, Academic Press 1974, Vol. 1, p. 144.

(16) Aromatic solvents were not detectably reduced in 100 hours.

(17) C.A. Brown and W.K. Ahuja, J. Org. Chem., 38, 2226 (1973) and references cited therein.

(18) P.W. Jolly and G. Wilke, The Organic Chemistry of Nickel, Academic Press, 1975, Vol. 2. For a comprehensive review on nickel hydrides, see also D.R. Fahey, J. Organomet. Chem. Rev., A, 7, 245 (1972).