Journal of Organometallic Chemistry, 92 (1975) 43—47

ACTIVATION OF REDUCING AGENTS: SODIUM HYDRIDE-CONTAINING "COMPLEX REDUCING AGENTS"

I. REDUCTION OF AROMATIC HALIDES*

G. GUILLAUMET, L. MORDENTI and P. CAUBERE
Laboratoire de Chimie Organique I, Equipe de Recherche Associée au CNRS No. 476 "Méthodes de Synthèse Organique, Milieux reactionnels", Université de Nancy I, Case Officielle 140, 54037 Nancy Cédex (France)

(Received December 5th, 1974)

Summary

The addition of nickel, cobalt or copper salts to NaH—t-AmONa (Am = amyl) led to the formation of "complex reducing agents" for which the reducing properties depend on the nature of the metal. Reductions of 1-$XC_{10}H_7$ (X = F, Cl, Br, I); 1-XC_6H_4Z (X = Cl, Z = 2-Me, 3-Me, 4-Me; X = Br, Z = 4-Me, 2-OMe, 4-OMe, 2-COOH, 3-COOH, 4-COOH; X = F; Z = 4-OMe) were studied. The results show that the reducing power of "complex reducing agents" is dependent on the nature of the metal, with Ni > Co > Cu.

Introduction

Sodium hydride is commonly used as a base [1]. The reducing properties of this compound in organic chemistry are not well-known and only a few publications about them have been reported [2-5]. The potential of sodium hydride as a reducing agent is not encouraging on account of its very low solubility in the usual solvents and, partly for this reason, its weak reducing power. We intended to examine this problem. Our work on the activation of bases [6] led us to think that the fundamental concept of activation by aggregate formation between two species was general and that, in particular, it should be possible to increase the reducing power of sodium hydride by activation with alcoholates.

In preceding work [2] we have evidence that the reducing properties of NaH in tetrahydrofuran (THF) are dramatically increased by the presence of alcoholates. However, further investigations [7] showed that the reducing power of NaH—RONa in THF is, to some extent, dependent on the origin of the NaH;

---

* This work was supported by DGRST (ASCO Comity) Convention 74-7-0971.

moreover, the scope of application of this system is somewhat limited.

In order to overcome these disadvantages we turned our attention towards new reducing agents composed of mixtures of sodium hydride—sodium alcoholates with metallic salts. These systems have a certain analogy to, for instance, the $LiAlH_4$—$CuCl_2$ [8] and $NaBH_4$—metallic salt systems [9,10].

The idea of utilizing NaH—RONa—metallic salt aggregates as reducing agents originated from work on the reduction of inorganic salts by NaH [7]. We noted that several metallic salts remained unchanged under the action of NaH but reacted rapidly with sodium hydride that was activated by sodium alcoholates. Moreover, the new mixtures thus obtained (for which we propose the name "complex reducing agents") have reducing properties. Bearing in mind that these complexes are very easily prepared and inexpensive, investigations on their properties seemed, to us, interesting. We have first examined the reduction of halogeno compounds. A recent publication on the reduction of aromatic halogeno compounds by NaH in THF [5] prompted us to study the reduction of these compounds in this initial investigation.

Results and discussion

Systematic studies of reductions in an aliphatic series [11] led us to try, for aromatic reductions, the systems NaH—t-AmONa—MY_n, (Am = amyl) where MY_n is $Ni(OAc)_2$, $Co(OAc)_2$, $Cu(OAc)_2$ or Cu_2Cl_2. Complex reducing agents are very easily prepared by adding these metallic salts to sodium hydride activated by t-AmONa [2].

Reduction of 1-halogenonaphthalenes by complex reducing agents NaH—t-AmONa—M(OAc)$_2$ (M = Ni, Co, Cu)

Systematic work, not reported here, allowed us to determine the best ratio of the three constituents of the complex reducing agents for the envisaged reaction. Table 1 reports our essential results. From these results it appears clear that "complex reducing agents" are more powerful ones than NaH alone in THF [5].

We have verified that, with only one exception (vide infra), NaH—$M(OAc)_2$, t-AmONa—$M(OAc)_2$ and NaH—t-AmONa couples do not have the reducing properties displayed by the complex reducing agents under the same reaction conditions. Thus, NaH—t-AmONa reacts with metallic salts to give a black medium with the reducing properties given in Table 1. On the other hand, metallic salts do not react with NaH alone and the medium thus obtained is a simple mixture of NaH and $M(OAc)_2$ with no special properties.

Sodium alcoholates react with metallic acetates but we observed no reduction of halogeno compounds by these mixtures. The work of Whitesides et al. [12] point out that metallic alcoholates are certainly formed. Lastly, NaH—t-AmONa gave reduction of 1-iodonaphthalene in 1 hour in 92% yield. This is the only case of a reduction reaction in the absence of the metallic salts. However, with 1-bromonaphthalene activated sodium hydride gives naphthalene in very low yield after 17 hours of reaction. The most powerful complex reducing agent is NaH—t-AmONa—$Ni(OAc)_2$ (runs 1-4), which even reduces 1-fluoronaphthalene. The reducing power of NaH—t-AmONa—$Co(OAc)_2$ is weaker (runs 5-8), as indicated by the cases of 1-chloro- and 1-fluoro-naphthalene. With the latter, reac-

TABLE 1

$$\underset{\text{(I)}}{\text{1-XC}_8\text{H}_7}\ \text{(10 mmol)} + \text{NaH—t-AmONa—M(OAc)}_2{}^{a} \xrightarrow[\text{THF}]{65^{\circ}\text{C}} \underset{\text{(II)}}{\text{C}_8\text{H}_8}$$

Runs	M	X	time (h)	II[b] (%)
1	Ni	I	1	87-93
2	Ni	Br	1	85-90
3	Ni	Cl	1	95-97
4	Ni	F	6	94-96
5	Co	I	1	87
6	Co	Br	4-5	90-95
7	Co	Cl	18	95
8	Co	F		[e]
9	Cu	I	1	75-80[c]
10	Cu	Br	17	60-65[d]
11	Cu	Cl		[e]

[a] For M = Ni, Co, the ratio (in mmol) NaH/t-AmONa/M(OAc)$_2$ is 40/20/10. For M = Cu, this ratio is 60/20/10. [b] Isolated by column chromatography. [c] 10 to 15% of 1,1'-binaphthyl was formed. [d] 20% of 1,1'-binaphthyl was formed. [e] Small quantities of II formed.

tion is very slow and a large part of the halogeno compound remains unchanged after 92 hours. Finally, the weakest reducing agent is NaH—t-AmONa—Cu(OAc)$_2$ (runs 9-11). Thus, after 40 hours the reduction of 1-chloronaphthalene had progressed very little. Moreover, with this complex reducing agent, we have observed the formation of 1,1'-binaphthyl, probably as the result of an Ullman reaction [13]; a study of this reaction is underway now.

At present, the nature of the complex reducing agents and their reduction mechanisms are not clear. On this subject, we report the following reaction which illustrates the complexity of the problem. The reduction of 1-bromonaphthalene (10 mmol) with NaH—t-AmONa—Cu$_2$Cl$_2$ (6/2/1) gave a mixture of naphthalene (65%) and 1,1'-binaphthyl (15%) with little reproducibility of reaction times (51 to 72 h). On the other hand, with a 8/2/1 ratio of the same constituents of the "complex reducing agent" when the reaction times are lowered to 24-40 hours, the reproducibility is no better. It is very difficult to find an explanation for these results. Particularly, if we compare the data of Table 1, we do not see why a longer reaction time and a larger amount of NaH are required in the case of Cu$^{\text{I}}$ than in the case of Cu$^{\text{II}}$, for the same reduction yield.

Note that the differences in reactivities of the complex reducing agents, according to the nature of the metal, may have application in synthesis enabling one to carry out selective reductions.

Reduction of substituted halogenated aromatic compounds by the complex reducing agent NaH—t-AmONa—Ni(OAc)$_2$

Nelson and Gribble [5] found that halogeno-aromatic compounds substituted in the ring by OCH$_3$ do not react readily with NaH alone in refluxing THF, and, when the substituent is COOH, reaction hardly occurs at all. In many cases, reductions were not possible at all. We have tested the reactivity of our more powerful complex reducing agents with compounds of this type. The results obtained are summarized in Table 2.

TABLE 2

$$\underset{\text{(III)}}{1\text{-X-}C_6H_4Z}\ \text{(10 mmol)} + \text{NaH—t-AmONa—Ni(OAc)}_2{}^{a} \xrightarrow[\text{THF}]{65^{\circ}\text{C}} \underset{\text{(IV)}}{C_6H_5Z}$$

Runs	X	Z	time (h)	IV (%)
12[a]	Br	4-CH_3	1	82-83[b]
13[a]	Cl	2-CH_3	1	88-95[b]
14[a]	Cl	3-CH_3	1	87-96[b]
15[a]	Cl	4-CH_3	1-1½	88-93[b]
16[a]	Br	2-OCH_3	1	95[b]
17[a]	Br	4-OCH_3	1	85-92[b]
18[a]	F	4-OCH_3	12	87-97[b]
19[c]	Br	2-COOH	1-2	94-96[d]
20[c]	Br	3-COOH	1-2	93-96[d]
21[c]	Br	4-COOH	12-18	86-96[d]

[a] NaH/t-AmONa/$Ni(OAc)_2$, ratio 40/20/10. [b] Yield determined by VPC with internal standard (*o*-xylene or cycloheptanone). [c] NaH/t-AmONa/$Ni(OAc)_2$, ratio 50/20/10 (10 mmol of NaH are necessary to transform the acid into salt). [d] Isolated by column chromatography.

It is clear that the reducing power of "complex reducing agents" is much higher than that of NaH alone in refluxing THF. With the latter, for instance, 8 days are necessary to reduce *o*-bromobenzoic acid incompletely [5].

Conclusion

From these results it appears that the complex reducing agents NaH—RONa—MY_n are reagents that are very easy to prepare. Their reducing properties are obviously not limited to aromatic halogenated derivatives and before long we shall publish results obtained with an aliphatic series.

At present we cannot discuss any reduction mechanism. However, the field of application appears to be very wide. Thus, we have seen that the reducing properties of complex reducing agents change with the nature of the metal of MY_n, and we know also that the nature of Y is important [11]. Moreover, by analogy with complex bases [6], we can predict that it will be possible to modify the reducing properties by modification of the nature of the alcoholate, the relative proportions of the complex constituents, and the solvent. In other words, with complex reducing agents, it is possible with the help of all these factors to obtain a wide range of reagents with variable reducing power. This is very important for investigations in the field of selective reduction, as we shall show in future publications.

Experimental

Fluka sodium hydride 50-60% in oil was used, washed several times with THF. All the reactions were carried out in a nitrogen-R atmosphere. The metallic salts used (Prolabo) were dried 12-15 h at 100-110°C in vacuum. Infrared spectra were recorded with a Perkin—Elmer 457 spectrometer, UV spectra with a Beckman DK 2A spectrophotometer, and NMR spectra with a Jeol C 60 HL instrument (using TMS as internal standard).

Analytical VPC analyses were carried out with Girdel 75 CDPT and 3000 FF 1E instruments (carbowax 20 M or SE 30 columns). For column chromatography, we used Woelm silica gel 0.063-0.2 mm and light petroleum or light petroleum—ether mixtures as eluents. The quantities of the reagents and substrates are given in Tables 1 and 2.

Preparation of complex reducing agents

To a vigorously stirred NaH suspension, t-amyl alcohol is added rapidly, and the mixture refluxed for 2 h. With the temperature slightly decreased, the metallic salt is added and the mass kept at 55-60°C for 4 h, still with good stirring. The total amount of THF used is 30 ml. (We must mention the black colour, characteristic of complex reducing agents, which rapidly appears with copper and cobalt salts, whereas it takes about 15-40 min in the case of nickel acetate.)

Reduction

After the preceding operations, the temperature is raised to 65°C, and the halogen derivative, dissolved or suspended in 10-15 ml THF, is added over 3 to 4 min. After this addition, the reaction mixture is stirred at 65°C for the times mentioned in Tables 1 and 2. After cooling it is poured onto ice and extracted with ether. (Note the necessity of acidification before extraction, in runs 19, 20 and 21.)

After evaporation of solvents, the compounds (toluene and anisole) were identified by means of VPC by comparison with authentic samples and the yields were determined using internal standards.

The isolated compounds (naphthalene, 1,1'-binaphthyl, and benzoic acid) had melting points and spectral characteristics in agreement with the data of the literature.

Acknowledgements

One of us (L.M.) thanks DGRST (Comite ASCO) for financial support. We thank M.P. Bourguignon, too, for the recording of NMR spectra.

References

1 J. Plesek and S. Hermanek, Sodium Hydride, Iliffe, London, 1968.
2 J. Moreau and P. Caubère, Tetrahedron, 27 (1971) 5741 and refs. therein.
3 M. Natsume, S. Kumadaki, Y. Kanda and K. Kiuchi, Tetrahedron Lett., (1973) 2335 and refs. therein.
4 Young-Jin Lee and W.D. Closson, Tetrahedron Lett., (1974) 381 and refs. therein.
5 R.B. Nelson and G.W. Gribble, J. Org. Chem., 39 (1974) 1425 and refs. therein.
6 P. Caubère, Accounts Chem. Res., (1974) 301.
7 Unpublished work.
8 T. Mukaiyama, K. Narasaka, K. Maekawa and M. Furusato, Bull. Chem. Soc. Jap., 44 (1971) 2285.
9 S. Susuki, Z. Imai, Y. Susuki, T. Sato and Y. Miyaji, Chem. Abstr., 74 (1971) 3400u.
10 C.A. Brown and V.K. Ahuja, J. Org. Chem., 38 (1973) 2226.
11 To be published.
12 G.M. Whitesides, J.S. Sadowski and J. Lilburn, J. Amer. Chem. Soc., 96 (1974) 2829.
13 P.E. Fanta, Synthesis, (1974) 9.