

Complex reducing agents: their applications and their outcome in the field of carbonylations

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Abstract - Works performed in order to increase the single electron transfer ability of NaH and to decrease its basicity led us to discover new reagents : NaH-RONa-MX_n called Complex Reducing Agents (CRA's). A short survey of the reducing properties of CRA's will be given. CRA's prepared in the presence of a ligand led to CRAL's which have proved to be good coupling reagents for aryl or vinyl halides (L = bpy). They also allowed the carbonylation (L = CO) of organic halides under standard pressure. These reactions opened up the field to phase-transfer-catalyzed photostimulated carbonylations as well as to S_{RN}¹ reactions of metalates.

INTRODUCTORY REMARKS CONCERNING THE REDUCING PROPERTIES OF NaH

Examination of the literature concerning NaH shows that this reagent is generally used, in organic chemistry, as a base for proton abstraction. However some data indicate that a few substrates may be reduced by this reagent. Though the yields of such reductions are often far from excellent, these results indicate the potential reducing properties of NaH which, unfortunately, are masked by the basic ones.

So, in order to use NaH as reducing agent, its single electron transfer (SET) ability must be increased and its basic properties must be masked.

Investigations undertaken in order to reach this target led us to discover new reducing agents possessing intriguing as well as interesting properties. In the present paper I shall give a brief survey of how we found these new reagents and I shall develop a few aspects of their properties (more informations may be obtained from reference (1)).

FROM NaH TO COMPLEX REDUCING AGENTS (NaH-RONa-MX_n) VIA NaH-RONa

A series of experiments performed with some organic halides and non-enolisable ketones showed that polar aprotic solvents (and particularly hexamethylphosphoric triamide (HMPA)) favoured SET from NaH but, of course, also increased the basic properties of this reagent (2).

In tetrahydrofuran (THF), NaH was very weakly reactive. However in the presence of sodium alkoxides prepared in situ (one of the best was sodium tert-amyloxyde : tAmONa) a synergy appeared looking like the one discovered some years ago with NaNH₂ (Complex Bases (3)). With NaH, an increase in the reactivity as well as in the SET ability was observed (2b,2c,2d,4). In fact, other things being equal, NaH-RONa in THF had comparable or even better reducing properties than NaH in HMPA.

Unfortunately NaH-RONa was still too basic to find general synthetic applications.

This problem was solved when we found that NaH-RONa reacted with a number of metal salts to give new reagents, we called Complex Reducing Agents (abbreviated CRA). Indeed CRA's were found weaker bases and stronger reducing agents than NaH-RONa. With most part of CRA's the differences observed between the two kinds of reagents were considerable. CRA's can be prepared starting from commercial reagents and starting from the halides or acetates of Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Cd, Zr, Mo, Pd, W. Their properties mainly depend on the nature of the metal and in some degree on the nature of the alkoxide and of the solvent.

Note concerning the nomenclature of CRA's :

Complex Reducing Agents will be sometimes abbreviated as MCRA's (metal atom specified) or as RONa.MCRA's (alkoxide and metal atom specified). If necessary, we shall symbolize RONa.MCRA as NaH-RONa-MX_n although, of course, MX_n is not present as such in the reagent. The abbreviation RONa-MCRA (x/y/z) indicates that NaH/RONa/MX_n (in that order) is equal to

the molar ratio x/y/z. This ratio refers to the one of the starting reagents and has nothing to do with the actual constitution of the CRA.

About the real nature of CRA's, the situation is far from being clear, and we are only at the very beginning of their knowledge. For the present time only $t\text{BuONa.NiCRA}$ (4/2/1) and $t\text{AmONa.ZnCRA}$ (4/1/1) have been studied (5).

From the hydrogen evolution observed during the preparation and from X-ray powder patterns of the solid fractions the following conclusion may be drawn :

At least some $t\text{BuONa.NiCRA}$ (if not all) is crystalline. From the data obtained this reagent appears to be constituted of aggregates formed by association of matrices consisting of Ni atoms surrounded by Na^+ , H^- , $t\text{BuO}^-$, and perhaps AcO^- (the reagent was prepared from $\text{Ni}(\text{OAc})_2$).

Concerning $t\text{AmONa.ZnCRA}$ the situation is still less clear and it appeared that this reagent could be tentatively considered as a mixture of $\text{NaH} [(\text{tAmO})_x \text{Zn}(\text{Na})_x]_n$, a small amount of $[(\text{tAmO})_y (\text{H})_z \text{Zn}(\text{Na})_{y+z}]_n$ and some Zn metal.

SOME GENERAL CONSIDERATIONS OF THE PROPERTIES OF CRA'S

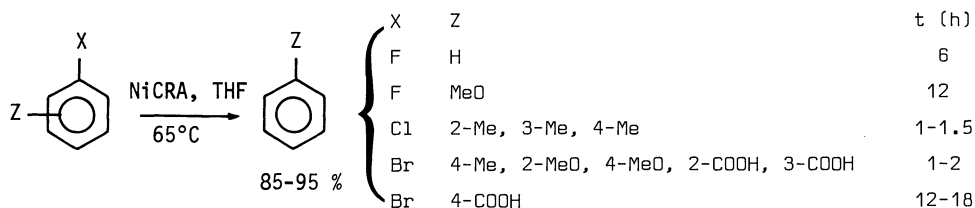
The main interesting characteristics of CRA's may be summarized as follows :

- They are unexpensive reagents readily prepared from commercial grade starting materials. Thus it is sufficient to add, in a given solvent, anhydrous MX_n to NaH-RONa or to add ROH to the suspension obtained by mixing NaH and MX_n . The reagents are ready for use after short warming (6).
- The reducing properties being dependent on the nature of the metal, of the alkoxide and of the solvent, a palette of reducing agents with graduated properties can be obtained. Selective reduction can be thus performed.
- CRA's can constitute a source of metals in low degree of oxidation state. So they may be used in the preparation of selective catalysts for heterogeneous hydrogenation (7). Moreover, prepared in the presence of a ligand to quench the metal species, they allow to prepare new reagents abbreviated CRAL or MCRAL (ligand specified) which some properties will be given below.

A SHORT VIEW ON THE REDUCING PROPERTIES OF CRA'S

Exemplification of the reducing power which may be reached with CRA's is given in Scheme 1 where the reduction of aryl halides is reported (8).

Scheme 1



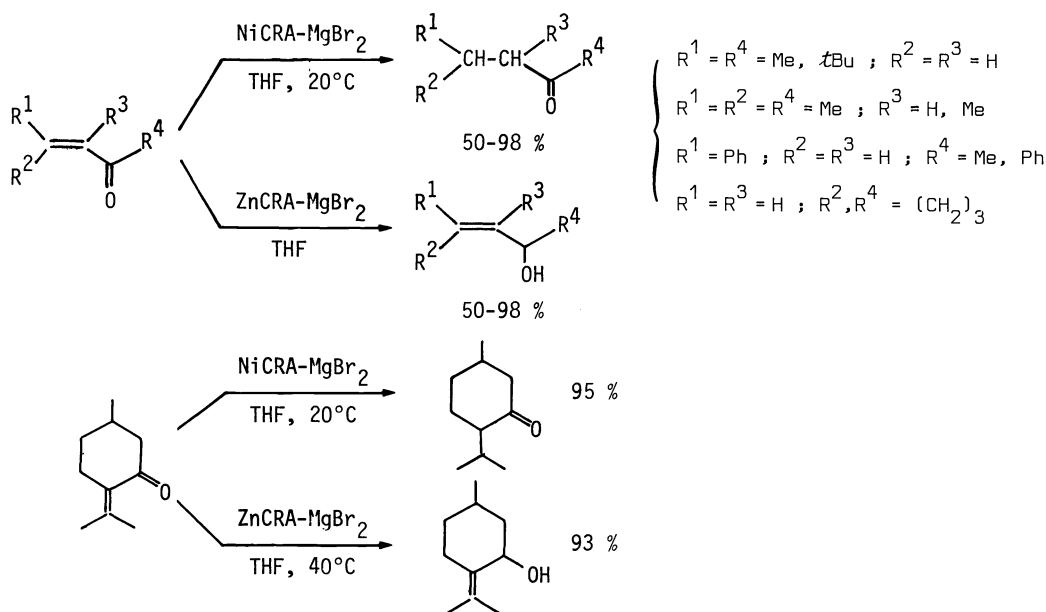
Besides the fact that substituted aryl chlorides and bromides are easily reduced, it must be emphasized that fluorides are also transformed without difficulty.

Of course primary, secondary, tertiary as well as vinyl halides (fluorides excepted) are also easily reduced. Moreover, using appropriate MCRA's, selective reductions can be performed (9).

Good illustration of the selectivity and versatility of CRA's was given with the reduction of carbonyl derivatives. It was found that in the presence of additive salts, such as MgBr_2 , ketones and aldehydes were easily reduced by NiCRA or ZnCRA (10). Note that this property shows that CRA's are weak bases. Another interesting point also emerged from our studies. Indeed we showed that NiCRA 's also reduced carbon-carbon double bond and, in certain cases, preferably to carbonyl group. The reverse was true with ZnCRA 's which in fact were not able to reduce ethylenic linkage.

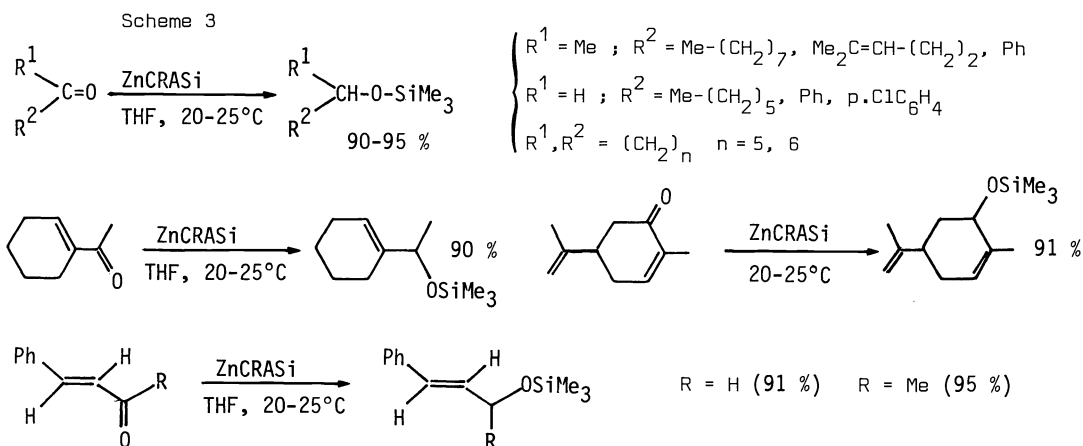
So we were encouraged to attempt the regioselective reduction of α,β -unsaturated ketones. A number of experiments are reported in Scheme 2 (11). They show that the regioselectivity of the unexpensive NiCRA's and ZnCRA's is such that they may be classified among the best reducing agents for this kind of reductions.

Scheme 2



The huge possibilities offered by CRA's in obtaining new reagents is well illustrated by the following results.

When Me_3SiCl was added to ZnCRA (12) an hydrosilylating agent (called ZnCRASi) was obtained. It very specifically hydrosilylated the carbonyl group of ketones and aldehydes as reported in Scheme 3.

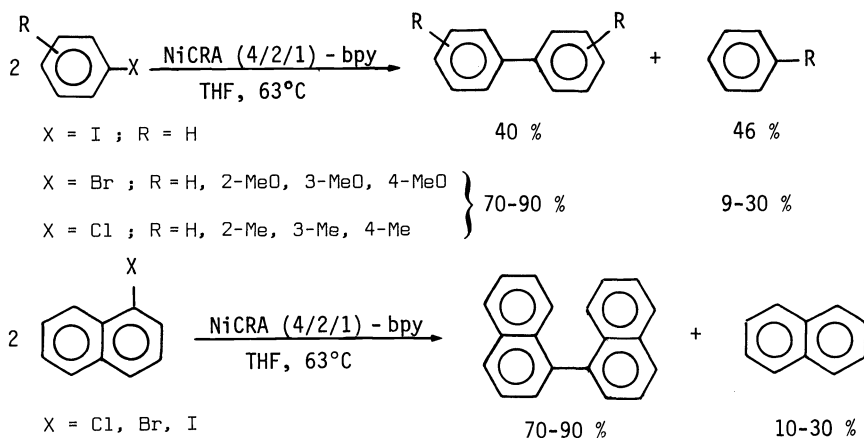


MCRAL'S AS SYMMETRICAL COUPLING REAGENTS OF ORGANIC HALIDES

During exploratory experiments, NiX_2 used in the preparation of CRA was replaced by $(\text{Ph}_3\text{P})_2\text{NiCl}_2$. Interestingly, when the new reagent was tested against aromatic halides, we observed that the reducing properties were partially replaced by coupling properties. We supposed that in the presence of Ph_3P (from $(\text{Ph}_3\text{P})_2\text{NiCl}_2$) a fraction of the low oxidation state metal species was trapped as complexes capable to couple organic halides. In order to verify this hypothesis we first prepared $t\text{AmONa.NiCRA}$ (4/2/1) in the presence of Ph_3P (4 equivalents). Addition of 1-bromonaphtalene to the reagent thus obtained (NiCRA-PPh_3) led to 70 % of 1,1'-binaphthyl and only 25 % of naphtalene (9a). The only drawback in this reaction was some classical transfer of phenyl group from Ph_3P . In order to avoid this side

reaction, the phosphine was replaced by 2,2'-bipyridine (bpy) (2 equivalents). NiCRA (4/2/1) - bpy thus obtained coupled aryl halides with satisfying yields as it may be seen from Scheme 4 (9a, 13).

Scheme 4



Note that the best results were obtained from aryl chlorides. Moreover aryl bromides are easily coupled even when an ortho substituent is present. Finally iodides led to the lowest yields. This behaviour is the reverse of what is observed when classical nickel reagents are used to couple aryl halides.

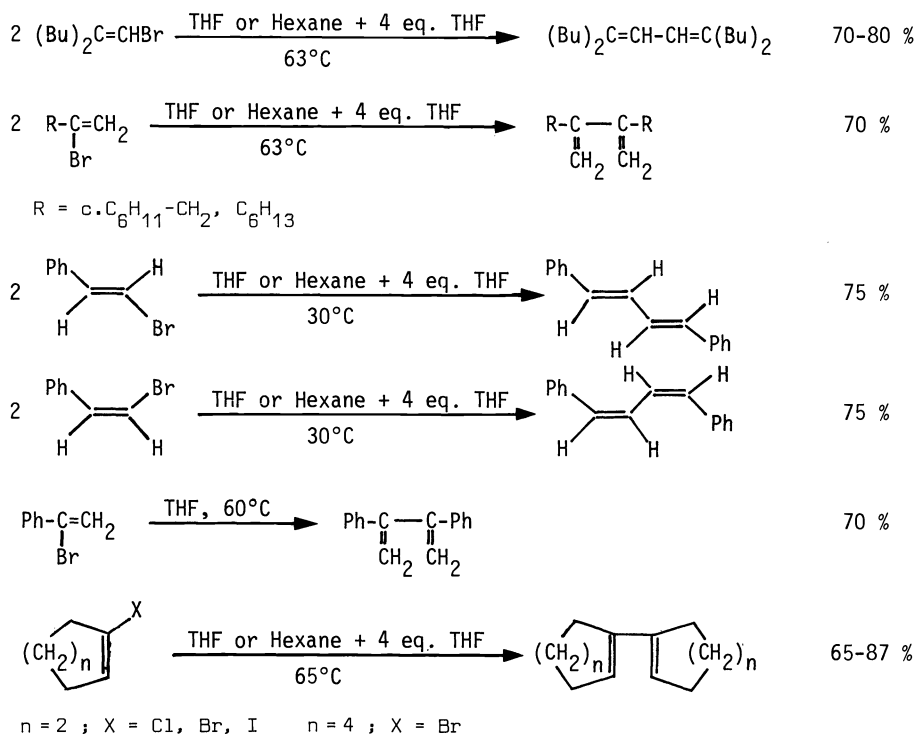
The side reduction may be slightly decreased using NiCRA (2/2/1) - bpy. However the reaction times were considerably increased.

A completely different situation was found with vinyl halides. Indeed, these halides were strongly reduced by NiCRA (4/2/1) - bpy and NiCRA (2/2/1) - bpy had to be used.

From the results reported in Scheme 5 it appears that our reagent is very efficient for the coupling of vinyl halides (13, 14).

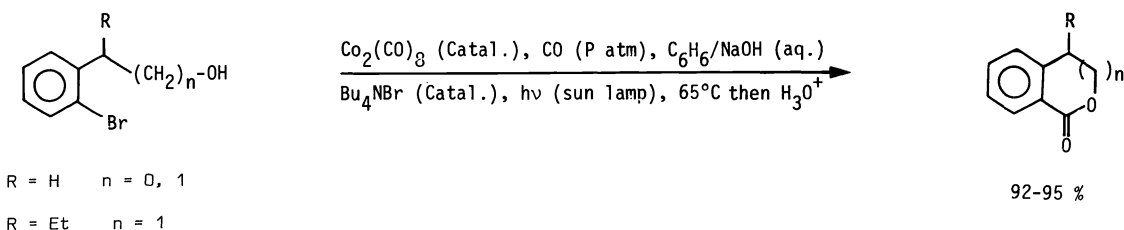
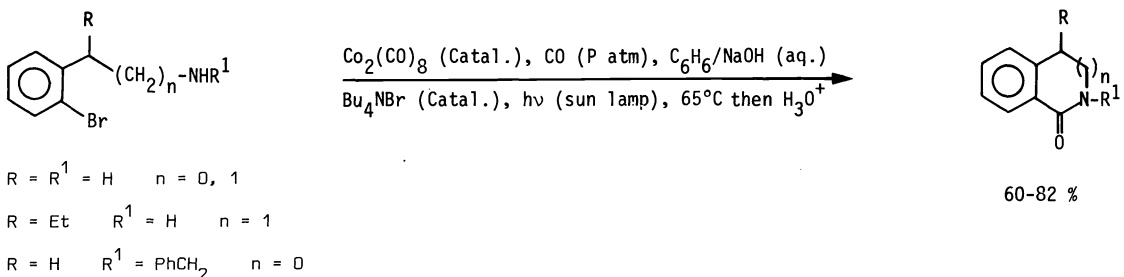
Scheme 5

Coupling of vinyl halides by NiCRA (2/2/1) - bpy



As an extension of these results we were able to prepare benzolactams and lactones (Scheme 11) starting from aryl halides bearing amino or hydroxy groups on a side chain α to the halogen.

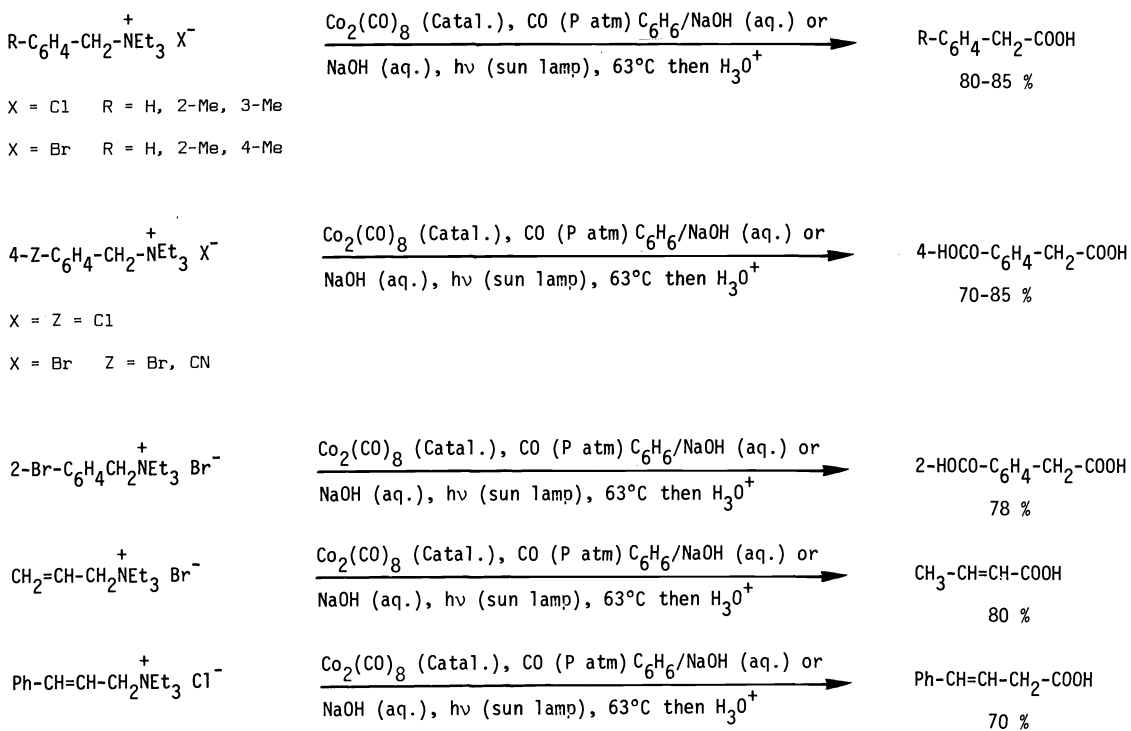
Scheme 11



In any case, the results obtained compare very favourably with those obtained with palladium species. Indeed the present method is much less expensive, the reactions are carried out under milder conditions and yields are of the same magnitude and often higher.

A number of observations carried out during these studies also led us to show that benzyl and allyl triethylammonium salts can be carbonylated under PTC conditions by photostimulated $S_{RN}1$ process (19). The results obtained are reported in Scheme 12.

Scheme 12



CONCLUSION

We started from NaH and we showed that this hydride can donate its electrons, but its proton affinity impedes from using it as a SET reagent in organic chemistry. When activated by alkoxides its SET tendency becomes better but the basicity of NaH-RONa still constitutes a considerable drawback.

In CRA's a synergism between NaH-RONa and metal species seems to arise, the result of which being the formation of a weak basic reagent possessing a strong ability in donating electrons to organic substrates.

This brief survey on some of the properties of CRA's shows how rich their chemistry is. In fact we are far from having exhausted the possibilities they offer.

ACKNOWLEDGEMENT

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