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ACTIVATION OF REDUCING AGENTS. SODIUM HYDRIDE CONTAINING COMPLEX REDUCING AGENTS 21. REGIOSELECTIVE REDUCTION OF ALKENE OXIDES

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Abstract : *It is shown that epoxides are reduced by ZnCRA and NiCRA. Interestingly, the simple change in the nature of the metal included in the reagent, changes the regiochemistry of the reduction.*

We have previously shown[1] that Complex Reducing Agents (CRA)[2] are unexpensive and versatile reagents. In continuing our exploration of their properties, we turned towards the reduction of epoxides into the corresponding saturated alcohols. A very interesting aspect of this important synthetic transformation is the regioselective opening in case of unsymmetrical epoxides.[3] From the literature, it appears that new reagents could be of interest to improve the regioselectivity and/or to replace expensive reducing agents by unexpensive ones.

We wish to report here the first results obtained with ZnCRA and NiCRA showing that the use of these reagents could be an interesting approach to solve this problem.

The results obtained are given in the Table. Two essential features emerge :
i) ZnCRA and NiCRA easily reduce epoxides in good yields ; ii) simple change in the nature of the metal included in CRA's, changes the regioselectivity of the reduction.

We have verified that the expected amount of hydrogen[4] was evolved during the preparation of CRA's. Thus hydrogenolysis due to some quenched hydrogen cannot be invoked to explain the reductions observed.

From not reported experiments it appeared that : i) ZnCRA may be indifferently prepared from $ZnCl_2$ or $Zn(OAc)_2$. On the contrary much better results were obtained when NiCRA was prepared from $NiCl_2$ than from $Ni(OAc)_2$; ii) DME led to better results than THF ; iii) $\overset{t}{Am}ONa$ must be prefered to $\overset{t}{Bu}ONa$ as activating agent.

The data given in the Table, deserve some further comments.

Excess of NaH was sometimes used (see Table) in order to increase the reduction rate. Taking into account our previous results[1], the weaker reducing properties of NiCRA compared to ZnCRA was unexpected. Some various degree of electrophilic assistance cannot be invoked to explain this reversal of reactivity since, in both reagents, the metal (Ni and Zn) is formally in a zero-valent oxidation state.[4] Moreover if such an assistance had taken place, the reductions would have taken a different pathway.[5]

For the present time, the change in regioselectivity is difficult to explain. It could be admitted, as a working hypothesis, that ZnCRA behave as nucleophilic hydrides, attacking the less hindered side of the epoxide. On the other hand, with NiCRA complexes looking like the ones proposed by Bartok and Notheisz[6] to explain the stereochemistry of the hydrogenolysis of epoxides, could intervene.

General procedure :

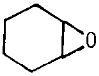
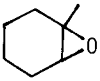
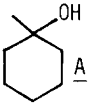
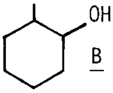
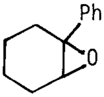
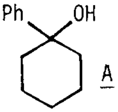
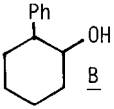
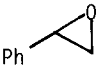
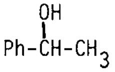
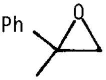
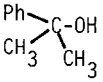
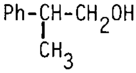
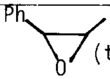
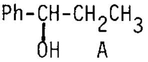
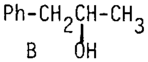
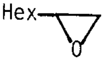
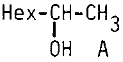
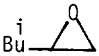
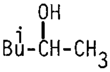
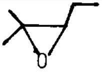
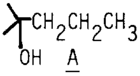
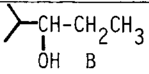
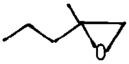
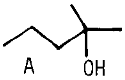
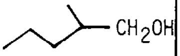
As previously described[4] the CRA are prepared in DME by addition of A^{t}mONa in a stirred mixture of NaH and metallic salt at 65°C.

The epoxide (10 mmol) and the adequate internal standard in 10 ml of DME was then added to the reagent.

The reaction was monitored by GC analysis of small syringed aliquots on either a Carlo Erba GI 452 or a Spectra Physics 7100 apparatus (flame ionization) equipped with 2 m 10 % OV 101 or SE 30 capillary column.

After completion of the reaction the excess of NaH was carefully destroyed by dropwise addition of the stoechiometric amount of water. The organic phase was filtered, and dried over magnesium sulfate. After removing of the solvent, the alcohols were isolated by flash chromatography on silica column. They were characterized by direct comparison (G.C., ^{1}H NMR) with authentic samples.

TABLE : Reduction of epoxides to alcohols with MCRA [x/y/z] at 65°C in DME

Epoxide	Nature of CRA M ; (x/y/z)[a]	t (h)	Alcohol[b]	Yield %[c]	Ratio of Alcohols[d] %
	Zn ; (4/2/1)	2.5	c.$C_6H_{11}OH$	94	-
	Ni ; (4/2/1)	17	c.$C_6H_{11}OH$	97	-
	Zn ; (4/2/1)	5	 A  B	92	A/B = 100
	Ni ; (8/2/1)	40		95	A/B = 20/80
	Zn ; (4/2/1)	5	 A  B	87	A/B = 100
	Ni ; (4/2/1)	13		95	A/B = 10/90
	Zn ; (4/2/1)	1.5	 $Ph-\overset{OH}{CH}-CH_3$	96	-
	Ni ; (4/2/1)	2	$Ph-CH_2-CH_2OH$	90[e]	-
	Zn ; (4/2/1)	1		95	-
	Ni ; (4/2/1)	3.5	 $Ph-\underset{CH_3}{CH}-CH_2OH$	93	-
 (trans)	Zn ; (4/2/1)	6	 $Ph-\underset{OH}{CH}-CH_2CH_3$ A  $Ph-CH_2\underset{OH}{CH}-CH_3$ B	95	A/B = 100
	Ni ; (4/2/1)	18		95	A/B = 35/65
	Zn ; (4/2/1)	3	 $Hex-\underset{OH}{CH}-CH_3$ A $Hex-CH_2CH_2OH$ B	99	A/B = 100
	Ni ; (8/2/1)	17		99	A/B = 30/70
	Zn ; (8/2/1)	1.5	 $^{i}Bu-\overset{OH}{CH}-CH_3$ A $^{i}Bu-CH_2-CH_2OH$ B	91	A/B = 100
	Ni ; (8/2/1)	27		89	A/B = 40/60
	Zn ; (8/2/1)	17	 A  B	85	A/B = 70/30
	Ni ; (8/2/1)	32		83	A/B = 40/60
	Zn ; (8/2/1)	12	 A  B	90	A/B = 100
	Ni ; (8/2/1)	32		85	A/B = 40/60

a) The molar ratio epoxide/metal was always equal to 1

b) Identified by comparison of retention times with those of authentic samples

c) Isolated yields after flash chromatography

d) Determined by G.C. and NMR analyses of the crude product

e) 5 % of ethylbenzene were observed.

References

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2) In the present paper we have adopted the convention given in ref. (1). Thus a CRA prepared from NaH, RONa (alkoxide) and a metal salt MX_n will be abbreviated MCRA [x/y/z] where the molar ratio NaH/RONa/MX_n (in that order) is equal to x/y/z.

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