

ACTIVATION OF REDUCING AGENTS. SODIUM HYDRIDE CONTAINING COMPLEX REDUCING AGENTS 29.

EPIMERIZATION OF ALCOHOLS BY NICKEL-CONTAINING COMPLEX REDUCING AGENTS (NiCRA)

G. FECHOU LI, R. VANDERESSE, Y. FORT and P. CAUBERE*

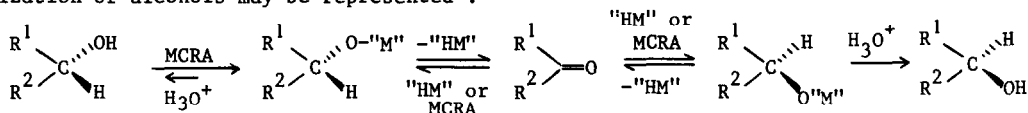
Laboratoire de Chimie Organique I, associé au CNRS - Université de Nancy I

B.P. 239, 54506 VANDOEUVRE LES NANCY (FRANCE)

Abstract : Epimerization of selected alcohols has been easily achieved by nickel-containing Complex Reducing Agents (termed NiCRA) prepared from 2,5-dimethyl-2,5-hexanediol. It is shown that these reactions are under thermodynamic control.

During the study of the stereoselective reduction of ketones by Complex Reducing Agents (MCRA)¹ we observed an epimerization of the alcohol formed, when M was a transition metal such as Ni or Co.

In fact this result was not unexpected since NiCRA or CoCRA have the interesting property of containing in the same reagent an oxidative as well as a reductive parts. Indeed the reductive properties of CRA are now well established. On the other hand, it is also well known that transition metal alkoxides easily eliminate metal hydride to lead to a carbonyl derivative. So epimerization of alcohols may be represented :

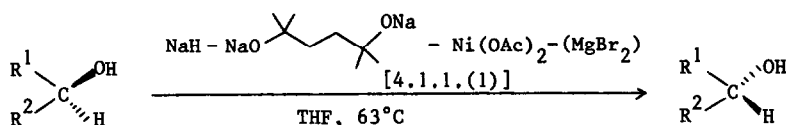


In order to establish the possibilities offered by MCRA in the epimerization of alcohols, we have performed the reactions reported in the Table. The reagents appear to be very efficient. The addition of MgBr₂ may be of some help with a number of alcohols. This salt is well known to increase the reduction rates as well as the yields of the alcohols formed². In the present epimerizations it avoids the formation of undesirable ketones.

Starting from "kinetic" alcohols, we have verified that these epimerizations are under thermodynamic control. Interestingly, based upon the data of the Table, it appears that the thermodynamic to kinetic alcohol ratios are different from those obtained by classical Meerwein-Ponndorf-Oppenauer equilibration³. Obviously, this result can be explained by the nature of the species formed during the NiCRA-epimerization. This point is currently being developed.

General procedure : To a suspension of dry Ni(OAc)₂ (10 mmol) and degreased NaH (60 mmol) in THF (20 ml) under nitrogen at 63°C was added a solution of 2,5-dimethyl-2,5-hexanediol (10 mmol) in THF (10 ml). After stirring 2 hours at 63°C, MgBr₂ (10 mmol) in THF (10 ml) was added if necessary. The substrate (10 mmol) and the adequate internal standard (C₇-C₁₅) in THF (10 ml) was then added over a period of 2-3 minutes. The reaction was monitored by GC analysis of small aliquots by comparison with authentic samples using Girdel 300 chromatograph (flame ionization) equipped with 50 m Carbowax 20 M capillary column. After classical work up¹, the product was isolated by flash chromatography or preparative HPLC and characterized by direct comparison (GC, ¹H NMR, IR) with authentic samples.

TABLE :



"Kinetic" starting alcohol (10 mmol)	MgBr ₂ (eq)	Time (h)	Yield of ketone(%) (a)	Total yield of alcohol (%) (a)	Thermodynamic/ kinetic isomer ratios (a)	Literature ratio (b)
Cis-4-t-butyl-cyclohexanol	0	18	-	99	98/2	79/21
	1	18	-	99	98/2	(3a)
Trans-3,3,5-trimethyl-cyclohexanol	0	5	10	89	97/3	94/6
	1	3	2	97	98/2	(3b)
Cis-2-methyl-cyclohexanol	0	5	9	90	94/6	94/6
	1	24	-	99	94/6	(3a)
Trans-3-methyl-cyclohexanol	0	3	8	91	94/6	77/23
	1	4	-	99	90/10	(3a)
Cis-4-methyl-cyclohexanol	0	3	tr.	99	90/10	70/30
	1	3	-	99	90/10	(3a)
Endo-norborneol	0	4	8	91	89/11	80/20
	1	4	tr.	99	89/11	(3c)
Iso-borneol (exo)	0	42	2	97	76/24	71/29
	1	28	tr.	99	77/23	(3c)
(α)-3-cholestanol	0	2	10	89	95/5	84/16
	1	2	1-2	97	94/6	(3d)

(a) Yields determined by GC analysis

(b) Merwein-Pondorff-Oppenauer equilibration with aluminium isopropoxide-isopropyl alcohol-acetone at 88-89°C.

Acknowledgements :

G.F. wishes to acknowledge support from the Sonatrach Research and Development Center (Boumerdes, Algeria).

REFERENCES

1. A. FEHOUILI, Y. FORT, R. VANDERESSE and P. CAUBERE, in the press : Tetrahedron Lett., 1988.
2. J.J. BRUNET, L. MORDENTI and P. CAUBERE, J. Org. Chem. **43**, 4804 (1978).
3. a) E.L. ELIEL and R.S. RO, J. Amer. Chem. Soc. **79**, 5992 (1957) ; b) E.L. ELIEL and H. HAUBENSTOCK, J. Org. Chem. **26**, 3504 (1961) ; c) C.F. WILCOX, M. SEXTON and M.F. WILCOX, J. Org. Chem. **28**, 1079 (1963) ; d) H.R. NACE and G.L. O'CONNOR, J. Amer. Chem. Soc. **73**, 5824 (1951).

(Received in France 6 November 1987)