

ASYMMETRIC REDUCTIONS USING OPTICALLY ACTIVE ALKOXYLITHIUMALUMINIUMDEUTERIDE* **

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The use of chiral reducing agent lithiumaluminiumdeuteride — (—)-quinine for the reductions of aromatic aldehydes and ketones is described. The CD measurements of the resulting partially optically active 1-deuterio alcohols were performed.

We have studied the reductions of ketones by various alkoxyolithiumaluminiumhydrides and compared the chiroptical properties of the resulting alcohols¹. Within the scope of the work performed we reduced a series of arenecarbaldehydes *Ia–Id*, methyl aryl *Iia–Iid*, cyclohexyl aryl *IIia, IIib* and diaryl ketones *IVa–IVd* using a reducing agent prepared from equimolar amounts of lithiumaluminiumdeuteride and (—)-quinine.*** The results thus obtained are summarized in Table I.

The reductions of arenecarbaldehydes *Ia–Id* lead to the dextrorotatory 1-deuterio alcohols *Va–Vd* with optical yields 16 to 40%. We assume the absolute configuration of all the members of this series to be *S*(+) due to the stereospecific course of the reduction and the known³ *S*(+) configuration of [1-²H]phenylmethanol as well. Having measured the CD curves we have found distinct positive Cotton effect of *S*(+)-[1-²H]phenylmethanol (*Va*) and of *S*(+)-[1-²H]*p*-tolylmethanol (*Vb*) in the region of ¹*L*_b-band of the benzene ring (Table II).

Dextrorotatory alcohols resulted from the reductions of methyl aryl ketones *Iia–Iid* and cyclohexyl aryl ketones *IIia, IIib*. Optical rotations and CD curves were comparable with those of the nondeuterated alcohols obtained in a similar way¹ (Table II). Using this analogy we predict [1-²H]arylethanols *VIa–Vid* and cyclohexylaryl[1-²H]methanols *VIIa, VIIb* to be of *R*(+) configuration. We have observed the characteristic effect of the methyl group situated in *ortho*-position of the benzene ring (compounds *VIb, Vid, VIIb*), which at the same absolute configuration of the alcohol investigated causes a change of sign of the Cotton effect in 265 nm UV region.

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*** Recently Mosher and coworkers² published a paper motivated similarly to ours.

We assume diaryl[1-²H]methanols *VIIIa–VIIId* to be of *S* configuration using the analogy to the non-deuterated ones⁴. Phenyl-*p*-tolyl[1-²H]methanol (*VIIIa*) though inactive at the sodium D-line exhibits significant Cotton effect on the CD curve (Table II).

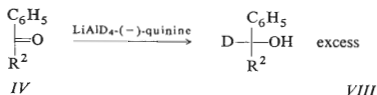
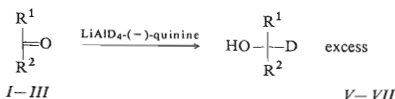
TABLE I
Asymmetric Reductions Using Lithiumaluminiumdeuteride and (–)-Quinine

Compound	Yield %	B.p., °C/Torr	M.p., °C	$[\alpha]_D^{20}$	Absol. config.	Optical purity, %
<i>Va</i>	78	65–70/15	—	0.71 ^{oa}	S(+)	35 ^b , 43 ^c
<i>Vb</i>	69	—	52–54	1.71 ^{od}	S(+)	16 ^b
<i>Vc</i>	52	50–60/15	—	0.42 ^{oa}	S(+)	20 ^b
<i>Vd</i>	57	88–90/15	—	0.10 ^{oa}	S(+)	32 ^b
<i>VIa</i>	81	70–73/11	—	9.71 ^{oa}	R(+)	20 ^e
<i>VIb</i>	73	80–82/12	—	27.10 ^{oa}	R(+)	56 ^e
<i>VIc</i>	88	97–98/12	—	28.46 ^{oa}	R(+)	46 ^e
<i>VIId</i>	87	—	63–65	20.41 ^{of}	R(+)	—
<i>VIIa</i>	88	—	42–44	15.00 ^{of}	R(+)	—
<i>VIIb</i>	85	105–107/0.02	—	4.55 ^{of}	R(+)	—
<i>VIIIa</i>	75	—	44–46	0.00 ^{od}	S	—
<i>VIIIb</i>	88	—	60–63	3.50 ^{od}	S(+)	—
<i>VIIIc</i>	81	—	65–72	–22.19 ^{od}	S(–)	—
<i>VIIIId</i>	75	100–101/0.1	—	–26.72 ^{of}	S(–)	—

^a Neat, *l* = 1. ^b Based on the NMR spectrum of the MTPA derivative. The signals of the trifluoromethyl group were investigated. ^c Based on optical rotation. ^d Chloroform, *c* = 2. ^e Based on the NMR spectrum of the MTPA derivative. The signals of the benzylic hydrogen were investigated. ^f Methanol, *c* = 2.

TABLE II
CD Data of Partially Optically Active 1-Deuterio Alcohols

Compound	λ_{max} , nm	θ	Compound	λ_{max} , nm	θ
<i>Va</i>	259	+11	<i>VIIa</i>	261	–220
<i>Vb</i>	265	+25	<i>VIIIb</i>	265	+38
<i>VIa</i>	260	–100	<i>VIIIa</i>	265	+250
<i>VIb</i>	265	+42	<i>VIIIb</i>	260	+120
<i>VIc</i>	263	–46	<i>VIIIc</i>	295	+900
<i>VIId</i>	280	+102	<i>VIIIId</i>	280	+370
				232	+4 000



	R ¹	R ²		R ¹	R ²
I, Va	H	phenyl	III, VIIa	cyclohexyl	phenyl
I, Vb	H	<i>p</i> -tolyl	III, VIIb	cyclohexyl	<i>o</i> -tolyl
I, Vc	H	α -furyl	IV, VIIIa	phenyl	<i>p</i> -tolyl
I, Vd	H	α -thienyl	IV, VIIIb	phenyl	<i>p</i> -methoxyphenyl
II, VIa	CH ₃	phenyl	IV, VIIIc	phenyl	α -naphthyl
II, VIb	CH ₃	<i>o</i> -tolyl	IV, VIII d	phenyl	2,4,6-trimethylphenyl
II, VIc	CH ₃	<i>p</i> -tolyl			
II, VI d	CH ₃	2,4,6-trimethylphenyl			

EXPERIMENTAL

CD curves were measured on Roussel Jouan Dichrographe in the methanolic solution at concentrations approximately 1 mg/ml. NMR determinations of optical purities were carried out using Varian XL-100-15 spectrometer through ¹H and ¹⁹F spectral region. Asymmetric reductions were carried out as standard procedure described previously¹. Melting points reported in Table I are uncorrected.

Optical purity of the partially optically active alcohols was determined from the NMR spectra of diastereoisomeric esters with MTPA using the method of Mosher and coworkers⁵.

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