

ASYMMETRIC REACTIONS. XLI.*

ASYMMETRIC REDUCTION OF α,β -UNSATURATED KETONES

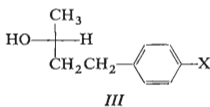
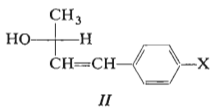
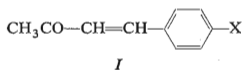
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Asymmetric reduction of substituted benzalacetones (*Ia-g*) with lithium tetrahydridoaluminate in the presence of (-)-quinine in ether gives a mixture of optically active unsaturated (*IIa-g*) and saturated (*IIIa-g*) alcohols to which absolute configuration is assigned.

Our aim was to study the course of the asymmetric lithium tetrahydridoaluminate reduction in the presence of (-)-quinine of α,β -unsaturated ketones in which the phenyl group or the substituted phenyl group is separated from the chirality center in formation by a vinyl group¹. We reduced arylvinyl methyl ketones *Ia-g* which were prepared by condensation of *p*-substituted benzaldehydes with acetone. By asymmetric reduction of ketones *Ia-g* with lithium tetrahydridoaluminate in the presence of (-)-quinine in ether, under the conditions described in², we obtained an optically active mixture of unsaturated (*IIa-g*) and saturated (*IIIa-g*) alcohols, which was separated by repeated crystallisation from light petroleum. The unsaturated



(X = *a* H; *b* CH₃; *c* CH₃O; *d* (CH₃)₂N; *e* Cl; *f* Br; *g* F)

alcohols, representing more than 85% of the mixture, are crystalline, while the saturated alcohols are liquids. Substance *IIId* was isolated by chromatography on alumina. Racemic alcohols were prepared by Braude, Jones and Stern³, alcohol *IIId* is not yet known.

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TABLE I
Substituted Benzalacetones *Ia-g*

Ketone	Yield, %	B.p., °C/Torr	M.p., °C	M.p., °C (ref.)
<i>Ia</i>	71	128–130/11	38	41 (6)
<i>Ib</i>	67	132–134/10	34	34–35 (7)
<i>Ic</i>	62	—	73.5–74	74–75 (8)
<i>Id</i>	74	—	135–136	136 (9)
<i>Ie</i>	82	155–160/17	59	59 (10)
<i>If</i>	69	—	83	83–84 (10)
<i>Ig</i>	65	140–143/15	31–32 ^a	—

^a For C₁₀H₉FO (164.1) calculated: 73.17% C, 5.49% H, 11.59% F; found: 73.28% C, 5.60% H, 11.32% F.

TABLE II
Results of Asymmetric Reduction of Substituted Benzalacetones *Ia-g*

Mixture <i>IIa III</i> B.p., °C/Torr [α] _D ²⁰	<i>II</i>	M.p., °C [α] _D ²⁰ ^a	Formula (m.w.)	Calculated/Found		
				% C	% H	
75–78/0.8 +5.93	<i>IIa</i>	39–41 +9.73 ^b	C ₁₀ H ₁₂ O (148.2)	81.04 81.24	8.16 8.13	—
125/7 +8.9	<i>IIb</i>	39–41 ^c +11.3 ^d	C ₁₁ H ₁₄ O (162.2)	81.44 81.24	8.70 8.70	—
93–96/0.5 +1.2	<i>IIc</i>	79–82 ^e +8.15	C ₁₁ H ₁₄ O ₂ (178.2)	74.13 74.88	7.92 8.10	—
101–102/0.4 +6.2	<i>II d</i>	83–85 ^f +10.02	C ₁₂ H ₁₇ ON (191.3)	75.35 75.35	8.96 8.98	7.32% N 7.11% N
115/2 +1.7	<i>IIe</i>	49–52 ^g +4.84	C ₁₀ H ₁₁ OCl (182.7)	65.73 65.80	6.07 6.13	21.60% Cl 21.45% Cl
87–90/0.6 +1.4	<i>II f</i>	57–59 ^h +2.92	C ₁₀ H ₁₁ OBr (228.1)	53.49 53.22	4.91 4.98	35.28% Br 34.92% Br
85–86/0.7 +1.8	<i>II g</i>	38–40 ⁱ +3.1	C ₁₀ H ₁₁ OF (166.2)	72.33 71.89	6.68 6.57	11.42% F 11.74% F

^a (c 1.5, methanol); ^b [α]_D²⁰ +12.7° (c 4, carbon disulfide), [α]_D²⁰ +18.5° (ethanol), m.p. of racemate⁴ 33.5°C, of antipode⁴ 96°C, [α]_D²⁰ +23.65° (c 5, carbon disulfide); ^c m.p. of racemate³ 43°C; ^d after double crystallisation the rotation value rose to [α]_D²⁰ +19.05° and the m.p. to 50–52.5°C; ^e m.p. of racemate³ 79°C; ^f cyclohexane; ^g m.p. of racemate³ 63°C; ^h m.p. of racemate³ 66°C; ⁱ m.p. of racemate³ 42°C.

From the empirically deduced relationships² it is known that methyl aryl and cyclohexyl aryl ketones afford on reduction with lithium tetrahydridoaluminate in the presence of (-)-quinine in ether dextrorotatory alcohols of R configuration. Therefore it may be expected that the dextrorotatory unsaturated alcohols *IIa-g* also have the absolute R configuration. This assumption was confirmed by their hydrogenation which gave levorotatory saturated alcohols *IIIa,b,d* (from alcohols *IIa,b,d*), and the levorotatory alcohol *IIIa* of known configuration⁴ from the alcohols *IIe,f*, in consequence of simultaneous hydrogenolytic elimination of the halogen atom. When alcohol *IIc* was hydrogenated *p*-methoxy-*n*-butylbenzene was obtained. All unsaturated alcohols *IIa-g*, although of the same absolute configuration, have the opposite sign than the saturated alcohols *IIIa-g*. This observation was made by Kenyon and coworkers⁵ for the pair of alcohols *IIa, IIIa*.

Ultraviolet spectra of unsaturated alcohols *IIa-g* measured in ethanol have absorption maxima in the 250–280 nm region; ORD curves of the partially optically active alcohols obtained, display a positive monotonous course in the same solvent. Only in the case of the optically almost pure alcohol *IIb* an inflexion may be observed on the curve (about 290 nm), and the curve changes its direction to the negative region about 240 nm. These results confirm the finding that the dextrorotatory unsaturated alcohols *IIa-g* have the same absolute configuration.

TABLE III
Results of Catalytic Hydrogenation of Unsaturated Alcohols *IIa-f*

Alcohol		B.p., °C/Torr [α] _D ²⁰ (c2, methanol)	Formula (m.w.)	Found/Calculated	
Unsaturated	saturated			% C	% H
<i>IIa</i>	<i>IIIa</i>	104/10 -10.21 ^a	C ₁₀ H ₁₄ O (150.2)	79.95 79.90	9.39 9.30
<i>IIb</i>	<i>IIIb</i>	115–116/12 -7.96	C ₁₁ H ₁₆ O (164.2)	80.43 80.20	9.82 9.93
<i>IIc</i>	—	98–99/11 ^b	—	—	—
<i>IIId</i>	<i>IIIId</i>	168/14 -7.10	C ₁₂ H ₁₉ NO ^c (193.3)	73.57 74.80	9.91 10.11
<i>IIe</i>	<i>IIIa</i>	113/16 -5.30	C ₁₀ H ₁₄ O (150.2)	79.95 79.86	9.39 9.33
<i>IIIf</i>	<i>IIIa</i>	102/9 -3.95	C ₁₀ H ₁₄ O (150.2)	79.95 79.58	9.39 9.46

^a Literature⁴ gives [α]_D²⁰ -19.45° (ethanol) for optically pure antipode; ^b the product is *p*-methoxy-*n*-butylbenzene; ^c calculated: 7.25% N; found: 7.22% N.

EXPERIMENTAL

The melting and the boiling points are not corrected. Samples for analysis were dried *in vacuo* (oil pump) at room temperature for 8 h. Optical rotations were measured on a polarimeter with a $\pm 0.02^\circ$ accuracy, ORD curves on a Jasco UV 5 apparatus.

Substituted Benzalacetones *Ia-g*

Aromatic aldehyde (472 mmol), acetone (1.3 mol), and 15 ml of a 10% NaOH were diluted with water to 1000 ml volume and the mixture was shaken at room temperature for 4 h. After neutralisation with hydrochloric acid the organic layer was separated, dried over anhydrous magnesium sulfate, and the product distilled or crystallised from ethanol (Table I).

Asymmetric Reduction of Benzalacetones *Ia-g*

To a solution of 0.42 g (11 mmol) of lithium tetrahydridoaluminate in 100 ml of ether 3.56 (11 mmol) of (-)-quinine were added. After 10 min stirring a solution of 10 mmol of ketone in 20 ml of ether was added dropwise and the mixture refluxed for 4 h. After cooling the reaction mixture was decomposed with 10 ml of water and 10 ml of 20% H_2SO_4 . The non-aqueous layer was shaken three times with 10% H_2SO_4 , washed with water, dried over magnesium sulfate, and evaporated. The residual mixture of alcohols *Ila-g* and *Illa-g* was distilled. After dilution of the distillate with light petroleum the separated alcohols *Ila-g* were crystallised from the same solvent. The purity of compounds *Ila-g* was checked by gas chromatography on a column filled with 20% Carbowax 20 M on celite (Table II). Unsaturated alcohols *Ila-f* were hydrogenated on palladized charcoal at atmospheric pressure and room temperature (Table III).

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