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ASYMMETRIC SYNTHESES BY MEANS OF (−)-SPARTEINE MODIFIED ORGANOMETALLIC REAGENTS

H. NOZAKI, T. ARATANI, T. TORAYA and R. NOYORI
Department of Industrial Chemistry, Kyôto University, Kyôto, Japan

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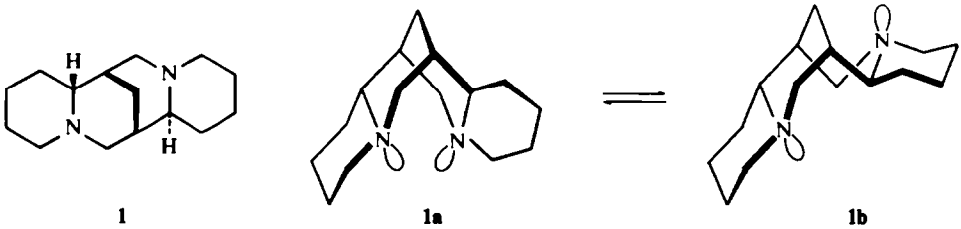
Abstract—Asymmetric induction has been observed in the reactions of organo-lithium and magnesium compounds complexed with a chiral tertiary diamine, (−)-sparteine. Debromination of *gem*-dibromocyclopropanes with such complexed n-BuLi gives optically active allenic hydrocarbons, and this shows that the intermediate leading to allene is lithium carbenoid (or α-bromocyclopropyllithium) rather than free cyclopropylidene. Addition of organolithium or a Grignard reagent to carbonyl compounds proceeds dissymmetrically to afford carbinols of up to 22% optical purity. Finally lithiation of ethylbenzene with n-BuLi has been examined in the presence of (−)-sparteine and the resulting α-phenethyllithium complex yields optically active products.

THE enhanced reactivity of n-BuLi has been discovered in the presence of chelating tertiary diamine, e.g., N,N,N′,N′-tetramethylethylenediamine (TMEDA) to enable the metallation of benzene, toluene and ferrocene.[1] (−)-Sparteine (**1**)* is able to exist in conformational equilibrium of **1a** and **1b** (Scheme 1). Coordination of n-BuLi with this bidentate ligand should give rise to enhanced reactivity and simultaneously create a chiral atmosphere around the Li atom. The latter effect should throw some light on the mechanism of organometallic reactions.

SCHEME 1



1 **1a** **1b**

Asymmetric ring opening of gem-*dibromocyclopropanes leading to allenic hydrocarbons*†

The partial asymmetric synthesis of cyclic allenes from cycloolefin-dibromocarbene adducts proceeds *via* either lithium- or chromium-carbenoid, if the asymmetric metal ligand behaves as an inducing centre. An instance of asymmetric induction in a copper-carbenoid reaction has been recorded.[4]

* The absolute configuration is (6*R*, 7*S*, 9*S*, 11*S*). See Ref 2. The specific rotation is $[\alpha]_D^{21}$ −16·4° (EtOH) or −5·62° (neat).

† Communicated in Ref. 3

Doering–Moore–Skattebøl's allene synthesis depends on the debromination of *gem*-dibromocyclopropanes **2** with alkyllithium.[5] Either α-bromocyclopropyllithium (**3**) or free cyclopropylidene (**4**) have been proposed (Scheme 2) as intermediates. In view of the chirality of 1,3-disubstituted allene, we tried the reaction in the presence of (−)-sparteine.

gem-Dibromides **2a–d** were treated with an equimolar mixture of n-BuLi and (−)-sparteine. Chromatographic separation of the product gave optically active allenes **5a–d** as shown in Table 1. The optical yield was not determined because of the difficulty in resolving the allenic hydrocarbons. Optically pure (+)-cyclonona-1,2-diene (**5c**) prepared from (−) (*R*)-*trans*-cyclooctene was claimed recently to have the rotation of $[\alpha]_D^{25}$ 170–175° (CH_2Cl_2) or 158–162° (neat).[8]

SCHEME 2

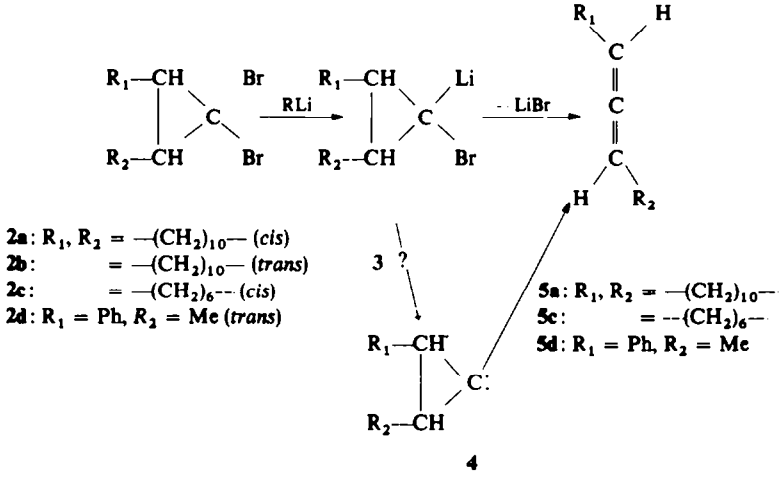


TABLE 1. ASYMMETRIC INDUCTION IN *gem*-DIBROMOCYCLOPROPANE-ALLENE TRANSFORMATION

Method	Dibromide	Product[a]	Yield, %	$[\alpha]_D$, deg.[b]	*c*, g/100 ml
n-BuLi	**2a**	(*S*)-**5a**	70	+1·4	13·1
n-BuLi	**2b**	(*R*)-**5a**	65	−2·8	13·8
n-BuLi	**2c**	(*S*)-**5c**	34	+1·9	6·5
n-BuLi	**2d**	(*S*)-**5d**	54	+2·0	6·1
Cr(II)	**2a**	(*S*)-**5a**	51	+0·43	14·0
Cr(II)	**2b**	(*R*)-**5a**	50	−0·44	15·8

[a] All products gave correct elemental analyses. IR spectra were superimposable on those of authentic samples (Refs 5 and 6). The absolute configuration was assigned on the basis of the sign of optical rotation (*cf* Ref 7).

[b] All rotatory values were obtained in hexane solns with a cell of 5 cm length.

Treatment of racemic allenes **5a, c** with the (−)-sparteine complexed n-BuLi resulted in asymmetric consumption of the allenes in the presence or absence of lithium bromide.* Under the conditions of debromination, however, the extent of

* Dextrotatory allene was recovered in every case, see Experimental.

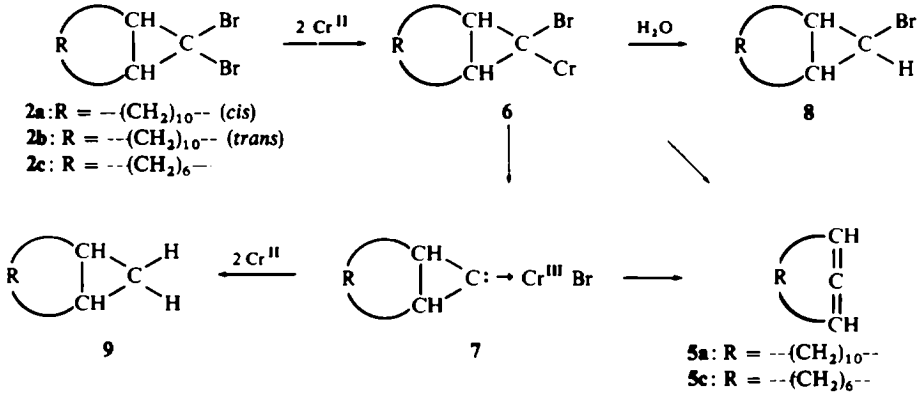
kinetic resolution was not significant, the recovery in per cent and the optical rotation of allenes being 44% for **5a** $[\alpha]_D$ +0·15° (*c* 13, hexane) and 41% for **5c** $[\alpha]_D$ +0·37° (*c* 8·2).

This asymmetric transformation has been successfully extended to another case of allene synthesis. Reduction of *gem*-dibromide **2a–c** with chromous sulphate afforded cyclic allene **5a, c** together with monobromocyclopropane **8** and totally reduced cyclopropane **9** in ratios varying with the length of methylene chain R (Scheme 3).[9]

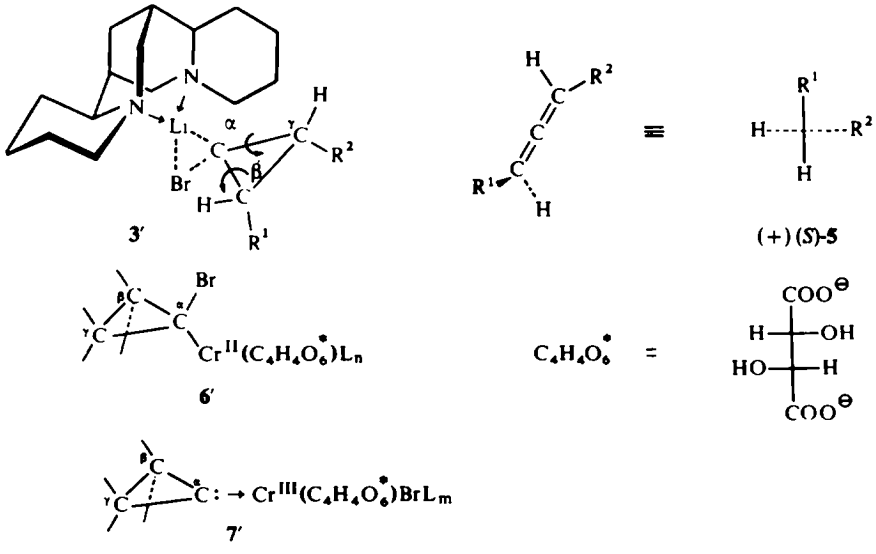
The reaction intermediates are considered to be α-bromo-organochromium (**6**) or cyclopropylidenechromium complex (**7**) rather than a free carbene species.

The possible formation of carbene–chromium complex was recorded during the reduction of polyhalomethanes.[10]

SCHEME 3



SCHEME 4



Treatment of dibromides **2a, b** with chromous (+)-tartarate[11] yielded the corresponding allene **5a** in optically active forms. The results are given in Table 1. Lack of the asymmetric consumption of allenes with chromous (+)-tartarate was confirmed by control experiments.*

Free cyclopropylidene as intermediate must give rise to an optically inactive product. The success of asymmetric induction implies that the reductive ring-enlargement proceeds through chiral carbenoid (carbene–metal complex). This interpretation is in accord with the recent findings by Skell and Engel that free cyclopropylidene in either ground state triplet or lowest singlet state does not isomerize to allene.[13]

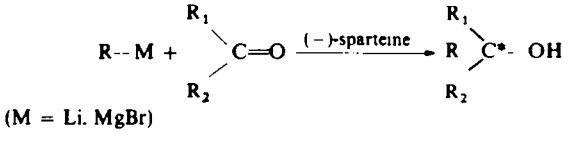
Treatment of *gem*-dihalocyclopropane with alkyllithium was reported to produce α-halocyclopropyllithium.[14] In the present system, coordination of chiral diamine (−)-sparteine to a lithium atom would give rise to the asymmetry-inducing species **3'**, though the situation might be over-simplified (Scheme 4). Conrotation in either a clockwise or a counterclockwise direction around C_α—C_β and C_α--C_γ bonds results in the formation of the respective enantiomeric allene.[15] The selection would be made so as to minimize non-bonded repulsion between the substituents on the cyclopropane and on the metal ligand during the concerted ring opening accompanied by α-elimination of lithium bromide.

Achievement of asymmetric transformation using the chiral chromous salts could similarly be explained by assuming the intervention of the carbenoid **6'** or **7'**.

Asymmetric induction in carbinol synthesis†

It has been found that 1,2-addition of organo-lithium or -magnesium reagent to carbonyl compounds proceeds dissymmetrically in the presence of (−)-sparteine (Scheme 5). Analogous asymmetric synthesis of carbinols was recently recorded to occur in the presence of (+) (2*S*, 3*S*)-N,N,N',N'-tetramethyl-2,3-dimethoxy-1,4-butanediamine.[17]

SCHEME 5



Benzaldehyde reacted with n-BuLi and (−)-sparteine and gave (+)-1-phenyl-1-pentanol of 6% optical purity. Other carbinols obtained similarly are listed in Table 2, which also contains the results with phenyllithium prepared *in situ* by the metallation of benzene with n-BuLi-(−)-sparteine complex.

Applying Ashby's procedure,[19] we have prepared a homogeneous benzene solution of ethylmagnesium bromide (0·5 M) in the presence of an equimolar (−)-sparteine. This solution was added to ethyl benzoylformate and the ethyl 2-hydroxy-2-phenylbutanoate isolated by chromatography showed the dextrotation of 18% optical

* Attempted asymmetric debromination by means of chromous sulphate in the presence of (−) (*R*)-propylenediamine was unsuccessful (*cf* Ref 12).

† Partly communicated in Ref 16.

TABLE 2. ASYMMETRIC CARBINOL SYNTHESIS

R—M	R_1—C(=O)—R_2	Product[a]	Yield, %	$[\alpha]_D$, deg.[b]	c, g/100 ml	Opt. Yield, %
n-BuLi[c]	PhCHO	(*R*)-1-Phenyl-1-pentanol	90	+2·0	25	
				+1·0	(neat)	6[f]
n-BuLi[c]	PhCOMe	(*S*)-2-Phenyl-2-hexanol	83	−1·6	22	
n-BuLi[c]	PhCOCOOEt	(*S*)-Ethyl 2-hydroxy-2-phenylhexanoate	85	+6·6	3·9	
PhLi[c]	EtCHO	(*R*)-1-Phenyl-1-propanol	73	+0·61	26	
				+0·40	(neat)	1·4[g]
PhLi[c]	*t*-BuCOMe	( )-3,3-Dimethyl-2-phenyl-2-butanol	30	+0·93	22	
EtMgBr[d]	PhCHO	(R)-1-Phenyl-1-propanol	15	+9·4	1·7	22[g]
EtMgBr[d]	PhCOMe	(±)-2-Phenyl-2-butanol	11	0	6·5	
EtMgBr[e]	PhCOCOOEt	(*S*)-Ethyl 2-hydroxy-2-phenylbutanoate	48	+7·4	9·7	
				+4·4	(neat)	18[h]

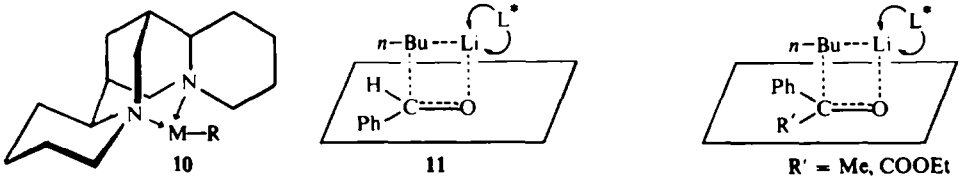
[a] All products gave correct elemental analyses. IR and NMR spectra were compatible with the assigned structures.

[b] Rotatory values were obtained in chloroform solns (5 cm cell) or in neat liquid (1 cm cell).
The reactions were conducted [c] in hexane at −70°, [d] in toluene at −70° or [e] in benzene at 5°.
Optical yields were based on the recorded rotations of [f] $[\alpha]_D^{25}$ 17·6° (neat), [g] $[\alpha]_D^{22}$ 28·1° (neat) and [h] $[\alpha]_D^{20}$ 24·7° (neat). See Ref 18.

purity (Table 2). The same carbinol was previously obtained in a 5% optical yield by asymmetric Grignard reaction in (+) (2*R*,3*R*)-2,3-dimethoxybutane.[20a]

The reacting species involved may be tentatively represented as **10** (Scheme 6).* The absolute configuration of the resulting carbinols implies that the preferred attack occurs as indicated in **11** and **12**, respectively. Correlation between the inducing and induced centres is rather equivocal at present in view of the lack of knowledge on the detailed structure of the reagents and the exact mode of attack.[22]

SCHEME 6



10 M = Li, MgBr

11 L* = (−)-sparteine

12 R' = Me, COOEt

Lithiation of ethylbenzene and formation of asymmetric derivatives

Metallation of toluene with n-BuLi in the presence of TMEDA gave a mixture of lithiotoluenes and a 91% yield of benzyllithium.[23] Ethylbenzene was metallated with n-BuLi and (−)-sparteine (4:1:1 molar ratio) and the resulting lithioethylbenzene **14** was treated with excess of trimethylsilyl chloride (Scheme 7). GC analysis of the

* NMR data are available on $MeSCH_2Li$-TMEDA complex and EtMgBr-TEEDA complex, see Ref 21.

product coupled with NMR revealed that substantial metallation had occurred at aromatic positions as well as on the benzyl nucleus. The distribution is given in Table 3. Similar lack of selectivity was observed recently in the lithiation of alkylbenzenes with n-BuLi-TMEDA complex.[24]

When this mixture **14** was treated with a small amount of trimethylsilyl chloride or carbon dioxide (each *ca* 0·5 molar ratio), the product **15**, containing α-(trimethylsilyl)-ethylbenzene or hydratropic acid (α-**15**: X = $SiMe_3$ or COOH), respectively, showed optical activity (Table 4). Moreover complete conversion of **14** with either of the reagents also gave the optically active compounds with the same sign of rotation.

SCHEME 7

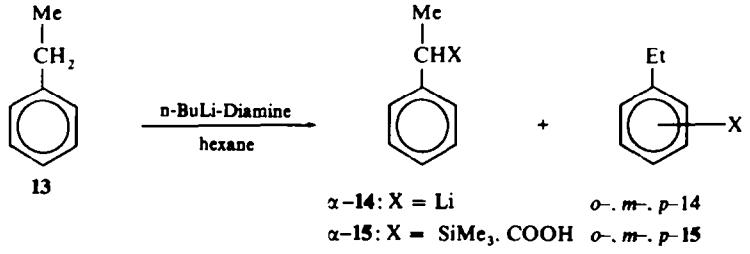


TABLE 3. LITHIATION OF ETHYLBENZENE

Reagent	Metallation temp, °C	Metallation time, hr	Distribution, % α-	o-	m-	p-
n-BuLi-(−)-sparteine[a]	50	2	21	2	55	22
n-BuLi-TMEDA[b]	30	1	37	9	36	17

Distribution of products was determined on GC after [a] trimethylsilylation or [b] carbonation followed by esterification (Ref. 24).

TABLE 4. ASYMMETRIC DERIVATIZATION OF α-PHENETHYLLITHIUM

X	Mixture 15 Yield, %[a]	Mixture 15 $[\alpha]_D$, deg.	Mixture 15 c, g/100 ml	Isomer α-15 Content, %[b]	Isomer α-15 Calc. $[\alpha]_D$, deg.
$SiMe_3$[c]	19	+1·5	14 (PhH)	61	+2·5
$SiMe_3$[d]	70	+0·26	38 (PhH)	21	+1·2
COOH[c]	10	−5·9	8·5 (EtOH)	73	−8·1
COOH[d]	87	−4·3	15 (EtOH)	18	−24

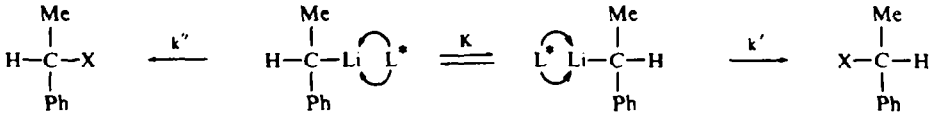
[a] Based on n-BuLi used.
[b] Estimated by GC or NMR analysis.
[c] Partial derivatization.
[d] Total derivatization.

The optical yield of (−) (*R*)-hydratropic acid was calculated to be 30% based on the reported value of $[\alpha]_D^{20}$ 81·1° (EtOH).[25]

These transformations belong to a kind of asymmetric synthesis and are not a case of kinetic resolution.[20a] Based on the planarity of benzyl anion,[26] the asymmetric induction observed may be explained as shown in Scheme 8. The diastereomeric pair of α-phenethyllithium-(−)-sparteine complex (α-**14′** and α-**14″**) exists in

equilibrium and the reaction with electrophile proceeds in proportion to the different rate k′ and k″ leading to the corresponding enantiomer α–15′a and α–15″, respectively. At the present stage, the absolute configuration of α-(trimethylsilyl)-ethylbenzene is still an open question.

SCHEME 8



L* = (−)-sparteine

EXPERIMENTAL

All b.ps are uncorrected. Microanalyses were performed by Mrs. K. Fujimoto of Prof. Sisido's Laboratory. IR spectra were recorded with a Shimadzu IR-27-G spectrophotometer as liquid films unless otherwise stated. NMR spectra were taken on a JEOL C-60-H spectrometer in CCl_4 solns using TMS as an internal standard. NMR signals in singlet are designated as s, doublet as d, triplet as t and multiplet as m. Optical rotations were measured with a Yanagimoto OR-20 polarimeter at room temp (20°). GC analyses and separations were performed on a Yanagimoto Model GCG-3D using columns packed with HVSG or Apiezon L Grease. All operations involving n-BuLi, EtMgBr or chromous salts were carried out under N_2 atmosphere.

Asymmetric synthesis of allenic hydrocarbons

(a) *Debromination of* gem-*dibromocyclopropanes with* n-BuLi *in the presence of* (−)-*sparteine*. A mixture of n-BuLi (11 mmoles) and (−)-sparteine (2·6 g, 11 mmoles) in hexane (100 ml) was added to a stirred soln of *cis*-13,13-dibromobicyclo[10.1.0]-tridecane (3·9 g, 11·5 mmoles) in hexane (75 ml) at −70° in the course of 1 hr. Soon after the addition was complete, the mixture was quenched with NH_4Cl aq and extracted with hexane. Combined extracts were washed with HCl aq to remove (−)-sparteine, then with water and dried on Na_2SO_4. The evaporated residue was chromatographed on alumina column (hexane elution) and distilled to give (+)-*cyclotrideca*-1,2-*diene* (1·37 g, 70%), b.p. 100°/4 mm, $[\alpha]_D$ + 1·40° (*c*, 27, hexane). The IR and NMR spectra were superimposable on those of racemic sample. Purification on GC (HVSG 2 m, 190°) gave a sample of $[\alpha]_D$ + 1·38° (*c*, 13, hexane). (Found: C, 87·6; H, 12·6. Calc. for $C_{13}H_{22}$: C, 87·6; H, 12·4%).

Similar treatment of trans-13,13-*dibromobicyclo*[10,1.0]*tridecane*, cis-9,9-*dibromobicyclo*[6.1.0]*nonane* and trans-1,1-*dibromo*-2-*methyl*-3-*phenylcyclopropane* gave (−)-*cyclotrideca*-1,2-*diene*, (+)-*cyclonona*-1,2-*diene* and (+)-1-*phenylbuta*-1,2-*diene*, respectively. The results are summarized in Table 1. NMR of $PhCH^{(C)}{=}C{=}CH^{(B)}CH_3^{(A)}$ is given below: δ 1·75 (quartet, 3H, H_A), 5·40 (quintet, 1H, H_B), 5·96 (sextet, 1H, H_C) and 7·12 (narrow m, 5H, aromatic H); J_{AB} = 7 Hz, J_{BC} = 7 Hz and J_{AC} = 2 Hz.

(b) *Kinetic resolution of allenic hydrocarbons by means of* n-BuLi-(−)-*sparteine complex*. To a mixture of n-BuLi (11 mmoles) and (−)-sparteine (2·6 g, 11 mmoles) in hexane (75 ml) was added a hexane (50 ml) soln of racemic cyclotrideca-1,2-diene (2·0 g, 11 mmoles) and 1,1-dibromo-2-n-hexylcyclopropane (1·1 g, 4 mmoles) at −60° during 1 hr. Stirring was continued for 2 hr at −50° and additional 3 hr at room temp. Work-up followed by fractional distillation gave (+)-*cyclotrideca*-1,2-*diene* (1·32 g, 66% recovery), $[\alpha]_D$ + 9·7° (*c* 26, hexane). Preparative GC gave a sample of $[\alpha]_D$ + 9·1° (*c* 13).

Similar treatment on racemic *cyclonona*-1,2-*diene* gave a sample showing $[\alpha]_D$ + 6·7° (*c* 9·8, hexane) in 52% recovery.

(c) *Optically active cyclotrideca*-1,2-*diene by debromination with chromous* (+)-*tartarate*. 0·8 N $CrSO_4$ soln (100 ml, 80 mmoles) was added to a mixture of (+)-tartaric acid (12 g, 80 mmoles) and NaOH (6·4 g, 160 mmoles) with cooling. The sky blue ppt was washed with deaerated water (50 ml × 2) and suspended in a mixture of water (85 ml) and DMF (75 ml). To this suspension *cis*-13,13-dibromobicyclo-[10.1.0]tridecane (4·0 g, 12 mmoles) was added all at once and the mixture was heated at 80° for 13 hr with vigorous stirring. The cooled mixture was extracted with hexane and the extracts were washed with NaOH aq and then

water. Concentration followed by distillation gave (+)-*cyclotrideca-1,2-diene* (1·1 g, 51%), $[\alpha]_D$ +0·45° (*c* 18, hexane). A sample purified on GC showed $[\alpha]_D$ +0·43° (*c* 14). Similar treatment of *trans*-dibromide **2b** gave laevorotatory allene as shown in Table 1.

Asymmetric synthesis of carbinols

(a) *Addition of* n-BuLi *to carbonyl compounds in the presence of* (−)-*sparteine.* A soln of benzaldehyde (3·0 g, 28 mmoles) in hexane (20 ml) was added to a stirred mixture of n-BuLi (53 mmoles) and (−)-sparteine (12·5 g, 53 mmoles) in hexane (150 ml) at −70° in the course of 10 min. The mixture was stirred overnight and allowed to warm up to room temp. Work-up followed by distillation gave (+)-*1-phenyl-1-pentanol* (4·2 g, 90%), b.p. 91°/4 mm. A sample collected by preparative GC showed $[\alpha]_D$ +1·02° (neat), +1·99° (*c* 25·0, $CHCl_3$) or +1·46° (*c* 26·6, EtOH). IR: 3360, 1040 and 1010 cm^{-1}. NMR: δ 0·75–1·80 (m, 9H), 3·25 (m, 1H), 4·43 (broad t, 1H) and 7·20 (s, 5H). (Found: C, 80·6; H, 9·9. Calc. for $C_{11}H_{16}O$: C, 80·4; H, 9·8%).

Similar reaction of n-BuLi with acetophenone and ethyl benzoylformate (inverse addition) gave (−)-*2-phenyl-2-hexanol*, b.p. 71–72°/0·5 mm, and (+)-*ethyl 2-hydroxy-2- phenylhexanoate*, b.p. 105°/0·2 mm, respectively. The optical rotations are shown in Table 2.

(b) *Addition of* PhLi-(−)-*sparteine complex prepared* in situ. A soln of n-BuLi (35 mmoles) and (−)-sparteine (8·0 g, 34 mmoles) in hexane (90 ml) was added to a mixture of benzene (15 ml, 190 mmoles) and hexane (50 ml). The mixture was stirred for 45 min at 80° for completion of the conversion of n-BuLi to PhLi. To the resultant soln a hexane (20 ml) soln of pinacolone (3·5 g, 35 mmoles) was added at −78° during 1 hr and the mixture was stirred overnight. The enolized ketone was removed by treatment with CO_2 gas followed by alkaline washing. Work-up gave (+)-*3,3-dimethyl-2-phenyl-2-butanol* (1·84 g, 30%), b.p. 70°/4 mm, $[\alpha]_D$ +0·80° (neat) or +0·93° (*c* 22, $CHCl_3$). IR: 3500 and 1070 cm^{-1}. NMR: δ 0·90 (s, 9H), 1·55 (s, 3H), 1·80 (s, 1H) and 7·1–7·5 (m, 5H). (Found: C, 80·6; H, 10·5. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·2%).

Similar reaction between PhLi and propionaldehyde gave (+)-*1-phenyl-1-propanol*, b.p. 105°/20 mm, as shown in Table 2.

(c) *Addition of* EtMgBr *prepared in the presence of* (−)-*sparteine.* A benzene (2 ml) soln of EtBr (5·5 g, 50 mmoles) was added dropwise to a suspension of Mg turnings (1·35 g, 55 mmoles) in (−)-sparteine (12 g, 50 mmoles). The reaction was initiated by a catalytic amount of EtMgBr in ether and the reaction was controlled by addition of benzene (100 ml). The resulting pale green soln was added to a soln of ethyl benzoylformate (6·92 g, 40 mmoles) in benzene (50 ml) at 5° in the course of 30 min and the mixture was stirred overnight. Work-up followed by column chromatography on silica gel (benzene elution) gave (+)-*ethyl 2-hydroxy-2-phenylbutanoate* (3·9 g, 48%), b.p. 140°/20 mm, $[\alpha]_D$ +4·38° (neat) or +7·36° (*c* 9·7, $CHCl_3$). IR: 3530, 1730, 1250 and 1020 cm^{-1}. NMR: δ 0·85 (t, 3H), 1·20 (t, 3H), 2·00 (oct, 2H), 3·65 (s, 1H), 4·14 (q, 2H) and 7·10–7·65 (m, 5H). (Found: C, 69·3; H, 7·8. Calc. for $C_{12}H_{16}O_3$: C, 69·2; H, 7·7%).

Similar reaction of EtMgBr with benzaldehyde and acetophenone gave (+)-*1-phenyl-1-propanol* and (±)-*2-phenyl-2-butanol*, respectively, as shown in Table 2.

Lithiation of ethylbenzene and formation of asymmetric derivatives

(a) *Metallation followed by trimethylsilylation.* A hexane soln of n-BuLi (0·21 *N*, 110 ml, 23 mmoles) and (−)-sparteine (5·1 g, 22 mmoles) was added to a mixture of ethylbenzene (11 g, 100 mmoles) and hexane (40 ml) at room temp. The mixture was heated at 50° for 2 hr with stirring for the completion of metallation. To the resulting red soln a hexane (20 ml) soln of Me_3SiCl (3·3 g, 30 mmoles) was added at −75° during 45 min and the mixture was stirred overnight while warming to room temp. Work-up followed by fractional distillation gave a mixture of *trimethylsilylated ethylbenzene* (2·86 g, 70%), b.p. 80–95°/20 mm, $[\alpha]_D$ +0·26° (*c* 38, PhH). The composition of product was determined on Golay Column GC (Castro Wax 0·25 mm × 45 m, 150°) and the results are recorded in Table 3. Relative retention time of each component was as follows: *m*-isomer 0·92, α-isomer 1·00, *p*-isomer 1·12, and *o*-isomer 1·23. (Found: C, 74·0; H, 10·3. Calc. for $C_{11}H_{18}Si$: C, 74·1; H, 10·2%).

Similarly prepared lithioethylbenzene was treated with Me_3SiCl (*ca* 0·5 molar ratio to n-BuLi) to give a mixture of trimethylsilyl-ethylbenzene (19% yield based on n-BuLi) showing $[\alpha]_D$ +1·54° (*c* 14·3, PhH). The content of α-trimethylsilylethylbenzene was 61% (by GC) or 57% (by NMR). NMR of the mixture consisted two parts, that of α-isomer: δ 0·00 (s, $SiMe_3$), 1·40 (d, Me), 2·15 (q, CH) and 6·80–7·40 (m, aromatic H); that of *o*-, *m*- and *p*-isomer: δ 0·30 (s, $SiMe_3$), 1·30 (t, Me), 2·70 (q, CH_2) and aromatic protons.

(b) *Lithiation followed by carbonation.* A hexane soln of n-BuLi (0·54 N, 100 ml, 54 mmoles) and (−)-sparteine (12 g, 51 mmoles) was added to a mixture of ethylbenzene (20 g, 190 mmoles) and hexane (40 ml) at

room temp and the mixture was heated at 70° for 1 hr. To the resultant soln dry CO_2 gas (*ca* 600 ml) was introduced gradually at −65° and the mixture was stirred overnight. Work-up followed by repeated distillation gave a mixture of *hydratropic acid and ethylbenzoic acids* (0·80 g, 10% based on n-BuLi), b.p. 140°/20 mm, $[\alpha]_D$ −5·9° (*c* 8·5, EtOH). The content of hydratropic acid (73%) was determined on NMR. NMR of the mixture consisted of two parts, that of hydratropic acid: δ 1·47 (d, Me), 3·65 (q, CH), 7·0–8·1 (m, Ar) and 11·8 (s, COOH); that of ethylbenzoic acids: δ 1·21 (t, Me), 2·65 (q, CH_2) and aromatic and acidic protons. (Found: C, 72·0; H, 6·5. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%).

Similarly prepared lithioethylbenzene was treated with excess of dry CO_2 gas to give a mixture of hydratropic acid and ethylbenzoic acids in 87% yield. This sample showed $[\alpha]_D$ −4·3° (*c* 15, EtOH) or −5·5° (neat) and the content of hydratropic acid was 18% based on NMR analysis.

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REFERENCES

1 [a] G. G. Eberhardt and W. A. Butte, *J. Org. Chem.* **29**, 2928 (1964); G. G. Eberhardt, *Organometal. Chem. Rev.* **1**, 491 (1966);
[b] A. W. Langer, Jr., *Trans. N. Y. Acad. Sci. (II)* **27**, 741 (1965)

2 [a] S. Okuda, H. Kataoka and K. Tsuda, *Chem. Pharm. Bull. Tokyo* **13**, 491 (1965);
[b] F. Bohlmann, D. Schumann and C. Arndt, *Tetrahedron Letters* 2705 (1965)

3 H. Nozaki, T. Aratani and R. Noyori, *Ibid.* 2087 (1968)

4 H. Nozaki, H. Takaya, S. Moriuti and R. Noyori, *Tetrahedron* **24**, 3655 (1968)

5 W. von E. Doering and P. M. LaFlamme, *Ibid.* **2**, 75 (1958); L. Skattebøl, *Acta Chem. Scand.* **17**, 1683 (1963); W. R. Moore and H. R. Ward, *J. Org. Chem.* **27**, 4179 (1962)

6 [a] H. Nozaki, S. Katô and R. Noyori, *Canad. J. Chem.* **44**, 1021 (1966);
[b] P. Rona and P. Crabbé, *J. Am. Chem. Soc.* **91**, 3289 (1969)

7 G. Lowe, *Chem. Commun.* 411 (1965); see also W. M. Jones and J. M. Walbrick, *Tetrahedron Letters* 5229 (1968)

8 A. C. Cope, W. R. Moore, R. D. Bach and H. J. S. Winkler, *J. Am. Chem. Soc.* **92**, 1243 (1970)

9 H. Nozaki, T. Aratani and R. Noyori, *Tetrahedron* **23**, 3645 (1967)

10 C. E. Castro and W. C. Kray, Jr., *J. Am. Chem. Soc.* **88**, 4447 (1966); A. Zurqiyah and C. E. Castro, *J. Org. Chem.* **34**, 1504 (1969)

11 *Gmelins Handbuch der anorganischen Chemie* (8 Auflage), *Chrom* Teil B, p. 424. Verlag Chemie (1962)

12 J. K. Kochi, D. M. Singleton and L. J. Andrews, *Tetrahedron* **24**, 3503 (1968)

13 R. R. Engel and P. S. Skell, *J. Am. Chem. Soc.* **88**, 3749 (1966); *Idem, Ibid.* **89**, 2912 (1967); see also H. R. Ward and E. Karafiath, *Ibid.* **91**, 7475 (1969)

14 [a] G. Köbrich and W. Goyert, *Tetrahedron* **24**, 4327 (1968);
[b] H. R. Ward, R. G. Lawler and H. Y. Loken, *J. Am. Chem. Soc.* **90**, 7359 (1968)

15 W. M. Jones and J. W. Wilson, Jr., *Tetrahedron Letters* 1587 (1965); J. M. Walbrick, J. W. Wilson, Jr. and W. M. Jones, *J. Am. Chem. Soc.* **90**, 2895 (1968); W. M. Jones and J. M. Walbrick, *J. Org. Chem.* **34**, 2217 (1969)

16 H. Nozaki, T. Aratani and T. Toraya, *Tetrahedron Letters* 4097 (1968)

17 D. Seebach, H. Dörr, B. Bastani and V. Ehrig, *Angew. Chem. Internat. Edit.* **8**, 982 (1969)

18 [a] R. MacLeod, F. J. Welch and H. S. Mosher, *J. Am. Chem. Soc.* **82**, 876 (1960)
[b] A. McKenzie and A. Ritchie, *Ber. Dtsch. Chem. Ges.* **70**, 23 (1937)

19 E. C. Ashby and R. Reed, *J. Org. Chem.* **31**, 971 (1966)

20 [a] H. L. Cohen and G. F. Wright, *Ibid.* **18**, 432 (1953); N. Allentoff and G. F. Wright, *Ibid.* **22**, 1 (1957);
[b] T. D. Inch, G. J. Lewis, G. L. Sainsbury and D. J. Sellers, *Tetrahedron Letters* 3657 (1969)

21 [a] D. J. Peterson, *J. Org. Chem.* **32**, 1717 (1967);
[b] D. F. Evans and M. S. Khan, *J. Chem. Soc. (A)* 1648 (1967)

22 [a] T. Eicher, *The chemistry of the carbonyl group* (Edited by S. Patai) p. 621. Interscience, New York (1966);
[b] E. C. Ashby, *Quart. Rev.* **21**, 259 (1967); H. O. House and J. E. Oliver, *J. Org. Chem.* **33**, 929 (1968)

23 A. J. Chalk and T. J. Hoogeboom, *J. Organometal. Chem.* **11**, 615 (1968)

24 C. D. Broaddus, *J. Org. Chem.* **35**, 10 (1970)

25 C. Aaron, D. Dull, J. L. Schmiegel, D. Jaeger, Y. Ohashi and H. S. Mosher, *Ibid.* **32**, 2797 (1967)

26 D. J. Cram, *Fundamentals of Carbanion Chemistry*. Academic Press, New York (1965)