19. *The* (+) *and* (−) *γ-Phenyl-α-methylallyl Alcohols.*

By J. Kenyon, S. M. Partridge, and H. Phillips.

Recrystallisation of the cinchonidine salt of *dl*-γ-phenyl-α-methylallyl hydrogen phthalate yields the optically pure (+) hydrogen phthalic ester: the (—) hydrogen phthalic ester can be obtained by recrystallisation of the corresponding brucine salt. The rotatory powers (± 44·6°) of the two hydrogen phthalic esters thus obtained are unchanged when the esters are recrystallised, although *d* + *dl*-hydrogen phthalic esters obtained from incompletely resolved alkaloidal salts can be separated by crystallisation from solvents, notably carbon disulphide, into pure *dl*- and *d*-(+)-hydrogen esters. The specific rotatory powers of the (+) hydrogen ester in various solvents are in Table I. When saponified with sodium carbonate solution, these esters give unexpectedly the *dl*-alcohol. The optically active alcohols can be obtained, however, by saponifying the hydrogen phthalic esters with sodium hydroxide solution: the more concentrated the solution employed, the higher the rotatory powers of the resulting alcohols. Even under the most favourable experimental conditions some racemisation occurs, since the rotatory power and the melting point of the optically active alcohols obtained can be raised by recrystallisation, being finally m. p. 61° and $[\alpha]_{5461}$ + 28·3° (in carbon disulphide) for the alcohol obtained from a mixture of methylene chloride and light petroleum. The recrystallised alcohol when reconverted into its hydrogen phthalic ester gives a product of rotatory power identical with that of the hydrogen phthalic ester from which it has been obtained.

A high concentration of hydroxyl ions thus appears to favour the reaction which leads to the carbinol of the same configuration as the reacting hydrogen phthalic ester, as is the case when the hydrogen phthalic esters of saturated alcohols undergo saponification. At lower concentrations of hydroxyl ions, part of the hydrogen phthalic ester presumably reacts with intermediate formation of a carbonium cation, leading to inversion and racemisation—a type of scission which is possible in esters of substituted allyl alcohols (cf. Burton and Ingold, J., 1928, 904).

Table I.

Specific Rotatory Powers of (+) *γ-Phenyl-α-methylallyl Hydrogen Phthalate in Various Solvents at Room Temperature* (l, 2; c, 5·00).

Solvent.	$[\alpha]_{5893}$.	$[\alpha]_{5780}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	Solvent.	$[\alpha]_{5893}$.	$[\alpha]_{5780}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.
CS_2	+37·38°	+39·00°	+44·71°	+87·4°	$COMe_2$ ...	−10·3°	−11·8°	−12·6°	−22·3°
C_5H_5N	+19·8	+21·2	+24·2	+43·0	Et_2O	−13·9	−14·5	−16·3	−32·2
$C_2H_4O_2$	+19·1	—	+23·8	+47·6	$C_2H_4Br_2$ ...	− 8·9	—	−11·1	−19·6
C_6H_6	+ 4·0	+ 4·7	+ 5·1	+ 7·8	$CH_3{\cdot}CO_2Et$	−19·0	—	−23·7	−41·5
CCl_4	+ 3·3	+ 4·7	+ 4·9	+ 7·2	Dioxan ...	− 7·2	− 8·2	− 9·2	−17·7
$CHCl_3$	+ 1·8	+ 2·0	+ 2·2	+ 5·3	(−) γ-Phenyl-α-methylallyl Hydrogen Phthalate.				
MeOH (*c*, 14·6)	− 7·2	− 7·4	− 8·4	−15·3					
EtOH	−13·5	−14·1	−15·4	−28·0	CS_2........	−36·23	−37·39	−44·53	−88·74

The (+) alcohol thus obtained can be reduced to (—) methyl-β-phenylethylcarbinol having a rotatory power in close agreement with that of the *l*-methyl-β-phenylethylcarbinol obtained by direct resolution (Pickard and Kenyon, J., 1914, **105**, 1124). This affords fairly conclusive evidence that (+) and (—) γ-phenyl-α-methylallyl alcohol have been isolated in an optically pure state. In Table II, the rotatory powers of the (+) alcohol are compared with those of (—) methyl-β-phenylethylcarbinol.

The rotatory powers of (+) butan-2-ol and (+) methylvinylcarbinol are also included in this table because they show (a) that, when the hydrogen atom in the β-position (with

TABLE II.

	$[\alpha]^{20°}_{5461}$.	$\alpha_{4358}/\alpha_{5461}$.	$[M]^{20°}_{5461}$.
(−) $CH_2Ph{\cdot}CH_2{\cdot}CHMe{\cdot}OH$	− 16·75°	1·670	− 25·12°
(−) $CH_3{\cdot}CH_2{\cdot}CHMe{\cdot}OH$	− 16·10	1·662	− 11·91
(+) $CHPh{:}CH{\cdot}CHMe{\cdot}OH$	+ 39·48	2·06	+ 58·43
(+) $CH_2{:}CH{\cdot}CHMe{\cdot}OH$ *	+ 40·38	1·802	+ 29·07

* Kenyon and Snellgrove, J., 1925, **127**, 1169.

respect to the hydroxyl group) in both the saturated and the unsaturated aliphatic alcohol is replaced by a phenyl group, the molecular rotatory powers are approximately doubled, (b) that the introduction of a Δ^{α}-bond into both the aliphatic and the semi-aromatic alcohol not only more than doubles the rotatory power but also reverses its sign. In compiling this table it has been assumed that (−) methylvinylcarbinol has the same configuration as (+) butan-2-ol, since (−) *n*-butylvinylcarbinol has been proved to have the same configuration as (+) ethyl-*n*-butylcarbinol (Levene and Haller, *J. Biol. Chem.*, 1929, **83**, 579; Johnson and Kenyon, J., 1932, 722).

In Table III, the properties of (+) γ-phenyl-α-methylallyl alcohol and its derivatives are compared with those of the corresponding saturated alcohol, (+) methyl-β-phenylethylcarbinol.

TABLE III.

	(+) Methyl-β-phenylethyl-carbinol.	(+) γ-Phenyl-α-methylallyl alcohol.
(+) Alcohol		
$\alpha^{50°}_{5461}$	+ 16·94° *	+ 42·0°
$\alpha^{50°}_{4358}/\alpha^{50°}_{5461}$	1·680	2·06
Acetate of (+) alcohol		
$\alpha^{20°}_{5461}$	1·72° †	− 166·0°
$\alpha^{20°}_{4358}/\alpha^{20°}_{5461}$	0·2	1·928
Hydrogen phthalate of (+) alcohol		
$[\alpha]_{5893}$ (*c*, 5 in ethyl alcohol)	+ 54·4°	− 15·4°
M. p.	oil	92—93·5°
Hydrogen phthalate of *dl*-alcohol		
M. p.	oil	68·5°

* Pickard and Kenyon, *loc. cit.* † Hewitt and Kenyon, J., 1925, **127**, 1094.

TABLE IV.

Variation of Rotatory Power of (+) *γ-Phenyl-α-methylallyl Alcohol with Temperature* (1, 0·5).

t.	α_{5780}.	α_{5461}.	α_{4358}.	*t*.	α_{5780}.	α_{5461}.	α_{4358}.
51°	+ 17·96°	+ 21·00°	+ 43·23°	74·5°	+ 16·54	+ 19·26°	+ 39·65°
59·5	17·66	20·68	41·56	95·0	15·28	17·82	35·63

TABLE V.

Specific Rotatory Powers of (+) *γ-Phenyl-α-methylallyl Alcohol in Various Solvents* (1, 2·0) *at Room Temperature.*

Solvent.	G. per 100 c.c. soln.	α_{5893}.	α_{5780}.	α_{5461}.	α_{4358}.	Solvent.	G. per 100 c.c. soln.	α_{5893}.	α_{5780}.	α_{5461}.	α_{4358}.
C_5H_5N	5·000	+28·8°	+32·3°	+36·5°	+73·3°	C_6H_6	4·070	+18·2°	+19·4°	+22·2°	+43·0°
$CHCl_3$	5·000	24·7	26·5	30·9	60·7	$COMe_2$	5·000	16·8	19·1	21·8	45·0
CS_2	5·000	23·65	25·0	28·3	59·3	(−) γ-Phenyl-α-methylallyl Alcohol.					
Et_2O	5·000	22·2	24·8	28·5	54·5	CS_2	4·498	−23·55	−24·1	−28·0	−56·0
EtOH	5·000	18·5	20·8	23·7	49·0						

EXPERIMENTAL.

dl-γ-Phenyl-α-methylallyl alcohol (119 g.), prepared by the addition of cinnamaldehyde (126 g.) to the Grignard reagent obtained from magnesium (24 g.) and methyl bromide (98 g.), had b. p. 129—131°/11 mm. It set to a mass of small, irregular, prismatic needles, m. p. 30—31·5°. Its phenylurethane separated from ether and petroleum in fine hairy needles, m. p. 93—94° (Klages, *Ber.*, 1902, **35**, 2650, gives m. p. 94—95°), and its p-*xenylurethane* from benzene in rosettes of small needles, m. p. 162—163° (Found : N, 4·3. $C_{23}H_{21}O_2N$ requires N, 4·1%).

Attempts were made to separate *dl*-γ-phenyl-α-methylallyl alcohol into *cis*- and *trans*-forms by (a) fractional distillation, (b) partial fusion of the solidified alcohol and draining of the liquefied portion, and (c) crystallisation from methylene chloride and light petroleum. The various fractions of the alcohol from (a) and (b) all had m. p. 30—31·5°; the alcohol after crystallisation from methylene chloride and light petroleum, from which it separated in spherical clusters of fine needles, had m. p. 33°.

dl-*γ-Phenyl-α-methylallyl* p-*nitrobenzoate* was prepared from *p*-nitrobenzoyl chloride (18·8 g.), *dl*-γ-phenyl-α-methylallyl alcohol (14·8 g.), and pyridine (10 g.). The solid product was taken up in ether and sodium carbonate solution. The dried ethereal solution was evaporated to small bulk and mixed with light petroleum; the *p*-nitrobenzoate (22 g., m. p. 56—58°) on re-crystallisation formed almost colourless, short, fine needles, m. p. 58—59° (Found: N, 4·7. $C_{17}H_{15}O_4N$ requires N, 4·7%).

dl-*γ-Phenyl-α-methylallyl Hydrogen Phthalate.*—(i) A mixture of the alcohol (148 g.), phthalic anhydride (148 g.), and pyridine (100 g.), heated for 1½ hours on the steam-bath, became a homogeneous viscous liquid. Next day the product was dissolved in acetone (500 c.c.) and mixed with ice-cold dilute hydrochloric acid; the liberated oil, when stirred with a large volume of water, soon set to a crystalline mass (218 g., m. p. 85—90°). The hydrogen phthalic ester separated from carbon disulphide or from ether–light petroleum in irregular glassy rhombs, m. p. 92—93·5°.

(ii) Phthalic anhydride (3·5 g.) was added to the Grignard complex obtained by the interaction in ethereal solution of magnesium (0·3 g.), methyl iodide (3·6 g.), and subsequently of cinnamaldehyde (3·2 g.) and the resultant paste was triturated for a few minutes until it changed into a yellowish-brown powder easily removable by filtration. This was taken up in ether and dilute sodium carbonate solution: the sodium carbonate extracts on addition of hydrochloric acid gave an oil which rapidly crystallised. The hydrogen phthalic ester (2·5 g., m. p. 90—91°) separated from carbon disulphide in glassy rhombs, m. p. and mixed m. p. 92—93° (Found by titration with sodium hydroxide: *M*, 293. $C_{18}H_{16}O_4$ requires *M*, 296). Repeated crystallisation of *dl*-γ-phenyl-α-methylallyl hydrogen phthalate did not alter its m. p. and the *dl*-γ-phenyl-α-methylallyl alcohol obtained from it by saponification had b. p. 129°/10 mm., m. p. 30—31·5°, $d_{4^\circ}^{17\cdot2^\circ}$ 1·072, $d_{4^\circ}^{27\cdot4^\circ}$ 1·040, $d_{4^\circ}^{36\cdot5^\circ}$ 1·012, $d_{4^\circ}^{43\cdot2^\circ}$ 0·990, $n_D^{10^\circ}$ 1·5741, $n_D^{20^\circ}$ 1·5692, $n_D^{62^\circ}$ 1·5521, [*P*] 367·4 (mean value between 17° and 43°) (calc., 372·1).

(+) *γ-Phenyl-α-methylallyl Hydrogen Phthalate.*—Cinchonidine (30 g.) was dissolved in a hot solution of the *dl*-hydrogen phthalic ester (30 g.) in ethyl acetate (90 c.c.). The cinchonidine salt of (+) γ-phenyl-α-methylallyl hydrogen phthalate (25 g.) separated on cooling: it was obtained optically pure in tufts of fibrous needles (7·5 g.), m. p. 179° (decomp.), with $[\alpha]_{5893}$ − 28·9°, $[\alpha]_{5780}$ − 30·1°, $[\alpha]_{5461}$ − 36·4°, $[\alpha]_{4358}$ − 59·2° (*c*, 5·050; *l*, 2) in chloroform solution. On decomposition with dilute hydrochloric acid it yielded (+) γ-phenyl-α-methylallyl hydrogen phthalate, which crystallised from carbon disulphide and light petroleum in felted masses of fine hairy needles, m. p. 68·5° (unchanged after 18 months). The rotatory powers are in Table I.

(+) *γ-Phenyl-α-methylallyl Alcohol.*—The alcohol of highest rotatory power was obtained when the following procedures were followed: (a) the (+) hydrogen phthalic ester (30 g.) was heated for 1 hour on the steam-bath with 5*N*-sodium hydroxide (45 c.c.), and the mixture distilled in steam. Extraction of the distillate yielded the (+) alcohol (13 g.), b. p. 128°/10 mm., m. p. 49—50°, $\alpha_{5893}^{20^\circ}$ +6·4°, $\alpha_{5461}^{20^\circ}$ + 7·5°, $\alpha_{4358}^{20^\circ}$ + 14·4° (*l*, 0·25). After being kept in a closed vessel for nearly two years, the alcohol had $\alpha_{5893}^{26^\circ}$ + 11·86° (*l*, 0·5).

(b) The (−) hydrogen phthalic ester (12 g.) in hot ethyl alcohol (40 c.c.) was mixed with 5*N*-sodium hydroxide (30 c.c.) and heated under reflux for 15 minutes. Distillation in steam removed the alcohol, which solidified in the distillate. After drying, it had m. p. 55° and $[\alpha]_{5461}$ − 21·2° in carbon disulphide solution (*c*, 5·00; *l*, 2).

Even under these conditions some racemisation occurred, since both the rotatory power and the m. p. of the alcohol were raised by crystallisation. That from experiment (b) after one crystallisation from methylene chloride–light petroleum had m. p. 61°, $n_D^{66^\circ}$ 1·5486, and $[\alpha]_{5461}$ − 28·0° (*c*, 5·00; *l*, 2) in carbon disulphide solution. The maximum values obtained are in Tables IV and V.

(−) *γ-Phenyl-α-methylallyl Hydrogen Phthalate.*—The first filtrate from the crystallisation of the cinchonidine salt yielded a hydrogen phthalic ester (18 g.) with $[\alpha]_{5461}$ − 24° (*c*, 5 in carbon disulphide). In a solution of this in acetone (30 c.c.), brucine (24 g.) was dissolved. On cooling, the brucine salt of (−) γ-phenyl-α-methylallyl hydrogen phthalate separated in small needles; it was obtained optically pure after two further crystallisations from acetone; decomp. about 110°, $[\alpha]_{5893}$ − 31·0°, $[\alpha]_{5780}$ − 36·9°, $[\alpha]_{5461}$ − 48·7°, $[\alpha]_{4358}$ − 102·0° (*c*, 5·325; *l*, 2) in chloroform solution. On decomposition of the brucine salt with hydrochloric acid (—) γ-phenyl-α-methylallyl hydrogen phthalate was obtained. It separated from carbon disulphide and light petroleum in masses of felted needles, m. p. 68·5°.

The optically active forms of γ-phenyl-α-methylallyl hydrogen phthalate are much more soluble than the inactive variety : when carbon disulphide solutions containing equal amounts of the *d*- and the *l*-form were mixed, the crystals which separated were glassy rhombs of the *dl*-hydrogen phthalic ester, m. p. 92—93°.

(—) γ-Phenyl-α-methylallyl alcohol, obtained from the (—) hydrogen phthalic ester, crystallised from methylene chloride and light petroleum in large hexagonal plates or long four-sided prisms, m. p. 61°. Equal amounts of (+) and (—) γ-phenyl-α-methylallyl alcohol of m. p. 61° were fused together; after solidification the *dl*-product had m. p. 33·5°.

(+) γ-Phenyl-α-methylallyl alcohol, $[\alpha]_{5461}$ + 28·3° (*c*, 5·0; *l*, 2 in carbon disulphide solution), was reconverted into its hydrogen phthalic ester; this had m. p. 68° and $[\alpha]_{5461}$ + 44·7° (*c*, 2·905; *l*, 2) in carbon disulphide solution.

The p-*xenylurethane* of (+) *γ-phenyl-α-methylallyl alcohol* formed needles, m. p. 179—180°, from methylene chloride and light petroleum; it had $[\alpha]_{5893}$ + 163·3°, $[\alpha]_{5780}$ + 176·6°, $[\alpha]_{5461}$ + 200·1°, $[\alpha]_{4358}$ + 408° (*c*, 0·6385; *l*, 2) in chloroform solution (Found : N, 4·2. $C_{23}H_{21}O_2N$ requires N, 4·1%).

(+) γ-Phenyl-α-methylallyl acetate, prepared by gently heating a mixture of the (+) alcohol (5 g.), pyridine (4 g.), and acetic anhydride (5 g.), had b. p. 132—133°/9 mm., $n_D^{12°}$ 1·5369, $\alpha_{5893}^{20°}$ + 34·16°, $\alpha_{5780}^{20°}$ + 35·78°, $\alpha_{5461}^{20°}$ +41·51°, $\alpha_{4358}^{20°}$ + 80·0° (*l*, 0·25); in chloroform solution (*c*, 5·020; *l*, 2) it had $[\alpha]_{5893}$ + 132·8°, $[\alpha]_{5750}$ + 86·2°, $[\alpha]_{5461}$ + 108·7°, $[\alpha]_{4358}$ + 308·3°.

(+) *γ-Phenyl-α-methylallyl* p-*nitrobenzoate* formed leaflets, m. p. 41°, from ether–light petroleum (Found : N, 4·8. $C_{17}H_{15}O_4N$ requires N, 4·7%); it had $[\alpha]_{5893}$ — 27·0°, $[\alpha]_{5780}$ — 27·5°, $[\alpha]_{5461}$ — 33·5°, $[\alpha]_{4358}$ — 87·4° (*c*, 4·450; *l*, 2) in chloroform solution.

Reduction of (+) *γ-Phenyl-α-methylallyl Alcohol to* (—) *Methyl-β-phenylethylcarbinol.*—The alcohol (4·4 g. with $[\alpha]_{5893}$ + 23·65° in carbon disulphide solution) was reduced with hydrogen in the presence of a platinum catalyst prepared by the method of Adams, Voorhees, and Skriner (" Organic Syntheses," 8, 92). The calculated volume of hydrogen was absorbed within 1 hour. The resulting (—) methyl-β-phenylethylcarbinol, which had no action on bromine solution, had b. p. 127°/16 mm., and $\alpha_{5893}^{18°}$ — 3·42°, $\alpha_{5780}^{18°}$ — 3·59°, $\alpha_{5461}^{18°}$ — 4·04°, $\alpha_{4358}^{18°}$ — 6·69° (*l*, 0·25). Its *phenylurethane* (Found : N, 5·4. $C_{17}H_{19}O_2N$ requires N, 5·2%) had m. p. 47—48° alone or mixed with a specimen prepared from the alcohol of Pickard and Kenyon. The rotatory powers given by Pickard and Kenyon (*loc. cit.*) for this alcohol prepared by direct resolution are $\alpha_{5461}^{18·5°}$ — 4·10°, $\alpha_{4358}^{18·5°}$ — 6·85° (*l*, 0·25). The specimen prepared by Pickard and Kenyon was found after some 22 years to have (without redistillation) the following rotatory powers : $\alpha_{5461}^{19°}$ — 3·88°, $\alpha_{4358}^{19°}$ — 6·52° (*l*, 0·25).

In view of the change in the sign of rotatory power undergone by (+) γ-phenyl-α-methylallyl alcohol after its conversion into (—) methyl-β-phenylethylcarbinol it is interesting to note that, whereas the less soluble cinchonidine salt of the hydrogen phthalic ester of the former gives rise to the (+) alcohol and the less soluble brucine salt of the hydrogen phthalic ester to the (—) alcohol, the converse is the case with the latter, the less soluble cinchonidine salt of the hydrogen phthalic ester yielding the (—) alcohol and the corresponding brucine salt the (+) alcohol.

Thanks are due to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries, Ltd., for grants.

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, November 7th,* 1935.]