143. *The Optical Rotatory Powers of* (+)-γ-*Methyl*-n-*heptane.*

By J. KENYON and B. C. PLATT.

The specific rotatory power of (+)-γ-methyl-*n*-heptane [(+)-methylethyl-*n*-butylmethane] in the homogeneous state remains practically constant with change of temperature; on the other hand, it changes considerably when determined in non-polar solvents.

FROM a survey of the accumulated data bearing on the influence of temperature on liquid optically active compounds in the homogeneous state, and of the effect of solvents on optically active compounds in solution, the following main generalisations of a qualitative character can be drawn : (i) For compounds of the same type, *e.g.*, saturated aliphatic alcohols or ethers, the influence of temperature is greater the smaller the molecular weight. (ii) The presence of unsaturated groups or of aromatic radicals generally increases, often to a very marked degree, the influence of temperature on rotatory power and rotatory dispersion : a carbalkoxyl group generally exerts a similar influence. (iii) The influence of polar solvents is generally directly proportional to their dipole moments (as is shown by the extensive measurements of, *inter alia*, Rule and his co-workers). (iv) The influence of non-polar solvents on the rotatory power of many types of compounds is often considerable.

It therefore seemed desirable to study a case in which as many as possible of these disturbing influences should be absent or reduced to a minimum : a saturated aliphatic hydrocarbon of low molecular weight fulfils most of these requirements, for it possesses little or no dipole moment and its power of associating either with itself or with a solvent must be very low.

Accordingly, (+)-γ-methyl-*n*-heptane was prepared, and its rotatory powers for light of various wave-lengths in the visible spectrum determined, both in the homogeneous condition at different temperatures and in various solvents at room temperature.

Over a range of 31° the specific rotatory powers of the hydrocarbon remained almost constant, supporting the view that the substance is not associated to any marked degree and that the alteration in observed rotatory power follows *pari passu* the alteration in density as the temperature changes.

On the other hand, the specific rotatory powers of the hydrocarbon suffered considerable alteration when they were determined in methylene chloride and the non-polar solvents benzene and carbon disulphide. Even in the same solvent—carbon disulphide—the specific rotatory power underwent a 10% alteration in value when the concentration of the solute was changed from 4·4% to 2·2%. It is thus clearly established that even under the most favourable conditions for the avoidance of polar influences a solvent does not act as a mere inert diluent for the solute.

Although the dipole moment of γ-methyl-*n*-heptane has not been determined, strong support for presuming it to be zero is found in the observations of Smyth and Stoops (*J. Amer. Chem. Soc.*, 1928, **50**, 1883), who record that nine isomeric heptanes—including in particular, β-methyl-*n*-hexane—all possess zero dipole moments.

The (+)-γ-methyl-*n*-heptane was prepared by the following reactions :

$$\underset{\substack{(dl\text{-})\\ \text{(I.)}}}{\mathrm{CHEtBu^{\alpha}{\cdot}CO_2H}} \rightarrow \underset{\substack{(+)\\ \text{(II.)}}}{\mathrm{CHEtBu{\cdot}CO_2H}} \rightarrow \underset{\substack{(+)\\ \text{(III.)}}}{\mathrm{CHEtBu{\cdot}CO_2Et}} \rightarrow \underset{\substack{(+)\\ \text{(IV.)}}}{\mathrm{CHEtBu{\cdot}CH_2{\cdot}OH}} \rightarrow$$

$$\underset{\substack{(+)\\ \text{(V.)}}}{\mathrm{CHEtBu{\cdot}CH_2I}} \rightarrow \underset{\substack{(+)\\ \text{(VI.)}}}{\mathrm{CHEtBu{\cdot}CH_3}}$$

Numerous attempts were made to resolve *dl*-β-ethyl-*n*-hexanol (as IV), but although crystalline alkaloidal salts of its *hydrogen phthalate* and hydrogen 3-nitrophthalate were readily obtained, repeated crystallisation of these from various solvents failed to yield the alcohol with more than 5% of its maximum rotatory power.

An alternative method of preparing γ-methyl-*n*-heptane (Duveen and Kenyon, *Bull. Soc. chim.*, 1938, **5**, 1120) by the attempted complete resolution of γ-methylheptan-δ-ol, CHMeEt·CHPr$^{\alpha}$·OH, proved unsatisfactory, for it was found, after conversion of the group —CH(OH)Pr into —CH_2Pr, whereby one centre of asymmetry is destroyed, that the optical activity of the resultant hydrocarbon was less than 10% of its maximum value.

TABLE I.

Specific Rotatory Powers (l = 2) *and Densities of* (+)-n-*Heptane-γ-carboxylic Acid at Various Temperatures.*

t.	$d_{4^\circ}^{t^\circ}$.	$[\alpha]_{6438}^{t^\circ}$.	$[\alpha]_{5893}^{t^\circ}$.	$[\alpha]_{5780}^{t^\circ}$.	$[\alpha]_{5461}^{t^\circ}$.	$[\alpha]_{5086}^{t^\circ}$.	$[\alpha]_{4358}^{t^\circ}$.
14°	0·9112	+ 7·65°	+ 9·00°	+ 9·47°	+ 10·64°	+ 12·43°	+ 18·19°
20	0·9064	7·34	8·95	9·43	10·62	—	17·50
31	0·8975	7·38	8·89	9·37	10·56	12·25	17·55
48	0·8840	7·43	8·78	9·22	10·38	—	16·74
68	0·8678	7·14	8·71	9·17	10·28	12·26	14·81
90	0·8500	—	8·61	9·18	10·21	12·20	—
15*	0·9104	—	8·92	9·43	10·64	12·33	17·36

* Recooled.

Corresponding (—)*Acid.*

16	—	— 7·25	— 8·75	— 9·14	— 10·32	— 12·04	— 17·13

These rotatory powers are accurately expressed by the equation

$$[\alpha]_{\lambda}^{20^\circ} = 2\cdot923/(\lambda^2 - 0\cdot0230),\ \text{whence}\ \lambda_0 = 1516\ \text{A.},$$

and those of the corresponding ethyl ester (Table III) by the equation

$$[\alpha]_{\lambda}^{20^\circ} = -\ 2\cdot173/(\lambda^2 - 0\cdot0273),\ \text{whence}\ \lambda_0 = 1662\ \text{A.}$$

TABLE II.

Specific Rotatory Powers of (—)-n-*Heptane-γ-carboxylic Acid* ($[\alpha]_{5461}^{16}$ — 10·32°) *in Various Solvents* (l = 2).

Solvent.	*t.*	*c.*	$[\alpha]_{6438}^{t^\circ}$.	$[\alpha]_{5893}^{t^\circ}$.	$[\alpha]_{5780}^{t^\circ}$.	$[\alpha]_{5461}^{t^\circ}$.	$[\alpha]_{5086}^{t^\circ}$.	$[\alpha]_{4358}^{t^\circ}$.
Et_2O	20°	5·008	— 8·59°	— 9·88°	— 10·30°	— 12·28°	— 14·87°	— 18·37°
CH_2Cl_2	20	4·990	6·91	8·62	9·12	9·41	11·42	16·43
$CHCl_3$	20	5·079	5·12	7·88	8·17	8·86	10·14	13·98
1 : 4-Dioxan	21	5·043	6·45	6·94	7·54	8·64	9·92	12·60
CCl_4	20	5·087	6·29	7·08	7·27	7·67	9·04	12·78
CS_2	19	5·075	—	6·60	6·80	7·39	8·28	11·22
C_6H_6	18	5·127	4·29	5·66	5·85	6·24	7·31	9·85
C_6H_5Me	19	4·994	4·01	5·01	5·41	6·11	7·0	10·0

TABLE III.

Observed Rotatory Powers of Ethyl (—)-n-*Heptane-γ-carboxylate at Various Temperatures* (l = 2).

t.	α_{6438}.	α_{5893}.	α_{5780}.	α_{5461}.	α_{5086}.	α_{4358}.
17°	— 9·74°	— 11·76°	— 12·28°	— 13·86°	— 16·15°	— 23·10°
24	—	11·72	—	—	16·03	—
29·5	9·68	11·62	12·21	13·72	16·01	22·70
59	9·34	11·40	—	13·43	15·59	22·10
89	8·90	11·11	11·88	13·03	15·53	—
18*	9·86	11·76	12·23	13·81	16·23	22·56

* Recooled.

Corresponding (+)*Ester.*

17	—	+ 12·15	+ 12·83	+ 14·42	—	+ 23·75

TABLE IV.

Specific Rotatory Powers of Ethyl (—)-n-*Heptane*-γ-*carboxylate* ($\alpha^{17^\circ}_{5461}$ — 13·86; l = 2) *in Various Solvents* (l = 2).

Solvent.	*t.*	*c.*	$[\alpha]^{t^\circ}_{6438}$.	$[\alpha]^{t^\circ}_{5893}$.	$[\alpha]^{t^\circ}_{5780}$.	$[\alpha]^{t^\circ}_{5461}$.	$[\alpha]^{t^\circ}_{5086}$.	$[\alpha]^{t^\circ}_{4358}$.
Et_2O	21°	5·047	— 6·94°	— 7·73°	— 8·53°	— 9·62°	— 11·20°	— 13·8°
CS_2	23	5·025	6·27	7·16	7·36	8·26	9·95	13·3
$C_6H_5{\cdot}NO_2$	20	5·010	6·49	6·79	7·29	8·39	9·08	—
CH_2Cl_2	18	5·027	—	6·66	7·16	7·76	9·05	13·0
1 : 4-Dioxan	22	5·041	6·15	6·45	6·55	7·34	8·84	11·3
$CHCl_3$	18	5·054	5·34	6·13	6·13	6·83	8·61	10·8
CCl_4	20	5·067	—	5·92	6·61	7·30	8·00	11·0
C_6H_5Me	22	5·035	4·47	4·17	—	5·26	5·86	8·34
C_6H_6	20	5·065	3·85	4·05	4·15	4·74	5·53	7·60

TABLE V.

Observed Rotatory Powers and Densities of (+)-β-*Ethyl*-n-*hexanol at Various Temperatures* (l = 2).

t.	$d^{t^\circ}_{4^\circ}$.	α_{6438}.	α_{5893}.	α_{5780}.	α_{5461}.	α_{5086}.
19°	0·8342	+ 5·92°	+ 7·10°	+ 7·53°	+ 8·48°	+ 9·82°
30	0·8611	5·85	6·94	7·27	8·20	9·68
37	0·8205	5·68	6·89	7·17	8·09	9·46
44	0·8150	5·61	6·76	7·09	8·04	9·34
94	0·7770	5·01	6·10	6·40	7·19	8·41
20*	0·8334	5·80	7·12	7·56	8·49	9·84

* Recooled.

TABLE VI.

Specific Rotatory Powers of (+)-β-*Ethyl*-n-*hexanol in Various Solvents* (l = 2).

Solvent.	*t.*	*c.*	$[\alpha]_{6438}$.	$[\alpha]_{5893}$.	$[\alpha]_{5780}$.	$[\alpha]_{5461}$.	$[\alpha]_{5086}$.	$[\alpha]_{4358}$.
Et_2O	20°	5·069	+ 3·46°	+ 4·93°	+ 5·92°	+ 6·51°	+ 6·91°	+ 9·97°
CH_2Cl_2	20	5 049	—	3·47	4·26	4·86	5·15	8·32
$CHCl_3$	19	5·002	2·40	3·60	—	4·30	5·00	5·70
C_5H_5N	19	4·926	2·36	3·05	3·16	4·04	4·24	6·6
CCl_4	23	4·951	—	3·17	—	3·76	4·16	6·95
CS_2	18	4·975	—	3·42	—	3·62	4·52	5·53
C_6H_6	20	5·060	—	2·57	—	3·16	4·35	7·12

TABLE VII.

Specific Rotatory Powers and Densities of (+)-γ-*Methyl*-n-*heptane at Various Temperatures* (l = 0·5).

t.	$d^{t^\circ}_{4^\circ}$.	$[\alpha]^{t^\circ}_{6438}$.	$[\alpha]^{t^\circ}_{5893}$.	$[\alpha]^{t^\circ}_{5780}$.	$[\alpha]^{t^\circ}_{5461}$.	$[\alpha]^{t^\circ}_{5086}$.	$[\alpha]^{t^\circ}_{4358}$.	$\alpha_{4358}/\alpha_{5461}$.
18°	0·7075	+ 5·18°	+ 6·70°	+ 7·10°	+ 7·95°	+ 9·33°	+ 12·6°	1·60
25·5	0·7014	5·22	—	—	7·87	9·32	12·9	1·63
34	0·6948	—	6·62	7·00	7·89	9·21	12·6	1·60
49	0·6827	—	6·71	6·94	7·74	9·17	—	—
19*	0·7066	—	6·71	6·97	7·93	—	12·8	1·61

* Recooled.

Refractive indices, n_λ.

18		1·3990	1·4002	1·4009	1·4024	1·4042	1·4094

TABLE VIII.

Specific Rotatory Powers of (+)-γ-*Methyl*-n-*heptane in Various Solvents* (l = 1).

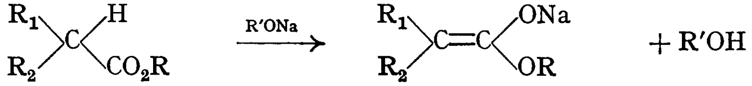
Solvent.	*t.*	*c.*	$[\alpha]^{t^\circ}_{6438}$.	$[\alpha]^{t^\circ}_{5893}$.	$[\alpha]^{t^\circ}_{5780}$.	$[\alpha]^{t^\circ}_{5461}$.	$[\alpha]^{t^\circ}_{5086}$.	$[\alpha]^{t^\circ}_{4358}$.
CH_2Cl_2	23°	4·842	+ 4·13°	—	+ 5·99°	+ 6·82°	+ 8·05°	+ 12·2°
C_6H_6	18	4·476	—	+ 5·36°	5·36	5·59	7·82	11·8
CS_2	19	4·359	—	4·36	4·59	5·51	6·43	—
CS_2	20	2·179	—	4·59	—	5·05	5·50	—

Note on the Reduction of Esters of n-*Heptane-γ-carboxylic Acid to* β-*Ethyl*-n-*hexanol.*—Since the standard method of reducing the ethyl ester by means of sodium and ethyl alcohol (Bouveault and Blanc, *Compt. rend.*, 1903, **136**, 1676) failed to produce β-ethyl-*n*-hexanol in yields of more than 15—30%, various modifications of procedure which have, from time to time, been suggested were tried. The ethyl ester was reduced by means of sodium and *n*-butyl or *iso*amyl alcohol; the n-*butyl*, iso*amyl* and *phenyl* esters were reduced with sodium and *n*-butyl, *iso*amyl, and ethyl alcohols respectively (Rupe and Läuger, *Helv. Chim. Acta*, 1920, **3**, 272); the ethyl ester in toluene solution was reduced with powdered sodium and specially dried ethyl alcohol (Ford and Marvel, " Organic Syntheses," Vol. X, 62). The various yields obtained are given below.

Ester.	Alcohol.	Yield, %.	Ester.	Alcohol.	Yield, %.
Ethyl	Ethyl 99%	25	*n*-Butyl	*n*-Butyl	23
,,	,, (specially dried) + C_6H_6 or PhMe	23	*iso*Amyl	*iso*Amyl	30
,,	*n*-Butyl	60	Phenyl	Ethyl	38
,,	*iso*Amyl	37			

Unfortunately, when the reduction of ethyl (—)-*n*-heptane-γ-carboxylate was effected by means of sodium and *n*-butyl alcohol, the resultant (—)-β-ethyl-*n*-hexanol possessed a rotatory power only 20% of that of the alcohol produced by an alternative method of reduction.

This extensive racemisation suggests that, during the reduction of carboxylic esters by means of sodium and alcohol, the following reaction must occur to a considerable extent:



Support for this view was provided by the following experimental results: Ethyl (—)-*n*-heptane-γ-carboxylate was heated under reflux for 3 hours with sodium *n*-butoxide in *n*-butyl alcohol and the recovered (—)acid possessed only 20% of its original optical activity; (—)-β-ethyl-*n*-hexanol, after being heated under reflux for 3 hours with a solution of sodium *n*-butoxide in *n*-butyl alcohol, retained 80% of its original optical activity.

It thus appeared desirable to effect the reduction of the optically active ester in a non-alkaline medium, and accordingly Prins's method (*Rec. Trav. chim.*, 1923, **42**, 1050) of using sodium and cold, very dilute acetic acid in the presence of sodium acetate was adopted.

EXPERIMENTAL.

dl-n-*Heptane-γ-carboxylic Acid.*—(*a*) Potassium permanganate (340 g.) in water (3000 c.c.) was added to a well-stirred mixture of commercial β-ethyl-*n*-hexanol (130 g.) and sodium hydroxide (30 g.) dissolved in water (250 c.c.). After 12 hours' stirring, the mixture was acidified with sulphuric acid and sulphur dioxide, and extracted with ether; this yielded *n*-heptane-γ-carboxylic acid (107 g. = 74%); b. p. 119—121°/14 mm., b. p. 218°/760 mm., $n_D^{18^\circ}$ 1·4255.

(*b*) Potassium permanganate (150 g.) in water (2500 c.c.) was added to a well-stirred mixture of α-ethyl-*n*-hexanal (a commercial specimen, b. p. 158—160°, 128 g.), anhydrous sodium carbonate (23 g.), and water (300 c.c.). After 7 hours' stirring, *n*-heptane-γ-carboxylic acid (113 g. = 78%) was obtained.

(—)-n-*Heptane-γ-carboxylic Acid.*—Quinine (324 g.) was dissolved in a hot solution of the *dl*-acid (144 g.) in 50% aqueous acetone (1500 c.c.), and the salt which separated overnight was recrystallised six times from aqueous acetone. The resulting quinine (—)-*n*-heptane-γ-carboxylate (140 g.) had m. p. 64—65°; $[\alpha]_{5893}$ —112·0°, $[\alpha]_{5461}$ — 136·0°, $[\alpha]_{4358}$ — 270° (*c*, 5·084; *l* = 2, in ethyl alcohol); on decomposition it yielded the (—)acid, b. p. 218—220°, the rotatory powers of which are recorded in Tables I and II.

(+)-n-*Heptane-γ-carboxylic Acid.*—The dextrorotatory acid (80 g.), obtained by decomposition of the more soluble fractions of the quinine salt described above, was combined with cinchonidine (161 g.) in aqueous-acetone solution; the resulting salt after four recrystallisations from aqueous acetone yielded the cinchonidine salt of (+)-*n*-heptane-γ-carboxylic acid (135 g.), m. p. 67—69°; $[\alpha]_{5893}$ — 74·8°, $[\alpha]_{5461}$ — 89·1°, $[\alpha]_{4358}$ — 165·5° (*c*, 4·646; *l* = 2, in ethyl alcohol). The (+)acid obtained from this salt had b. p. 218—220°, $d_{4^\circ}^{20^\circ}$ 0·9064; its rotatory powers are included in Table I. Its ethyl ester, prepared in excellent yield by the Fischer–Speier method, had b. p. 96—97°/35 mm., $n_D^{13°}$ 1·4185, $d_{4°}^{17°}$ 0·8641; its rotatory powers are given in Table III.

(+)-β-Ethyl-*n*-hexanol was prepared according to Prins's method (*loc. cit.*): ethyl (+)-*n*-heptane-γ-carboxylate (34 g.) in ether (100 c.c.) was mixed with a solution of sodium acetate (28 g.) in water (30 c.c.), and sodium (25 g.) in small pieces was added from time to time during 5 days, the reaction mixture being kept at 0° and maintained slightly acid by additions of 80% acetic acid. Several such experiments were carried out, and the combined products worked up; two main fractions were obtained, b. p. 84—92°/18 mm. (80 g.) and b. p. 117—137°/3 mm. (23 g.). Saponification of the former with alcoholic sodium hydroxide (150 c.c. of 3N) yielded (+)-β-ethyl-*n*-hexanol (15 g.), b. p. 92—94°/22 mm., $n_D^{17°}$ 1·4325; its rotatory powers are given in Tables V and VI. Acidification of the sodium hydroxide solution yielded (+)-*n*-heptane-γ-carboxylic acid (52 g.), the rotatory powers of which were 97% of that of the original acid.

(+)-β-Ethyl-*n*-hexyl iodide, obtained by heating a mixture of (+)-β-ethyl-*n*-hexanol (18 g.), red phosphorus (1·5 g.), and iodine (17·6 g.) at 150° for 3 hours, had b. p. 100—103°/18 mm., $n_D^{15°}$ 1·4938, and $\alpha_{5893}^{18°}$ + 3·13°, $\alpha_{5780}^{18°}$ + 3·27° (*l*, 0·5). [Levene, Rothen, and Meyer, *J. Biol. Chem.*, 1936, **115**, 412, give for the (−) iodide: $n_D^{25°}$ 1·4897, $\alpha_{5893}^{25°}$ − 3·46° (*l*, 1·0).]

(+)-γ-*Methyl*-n-*heptane*.—Zinc dust (27 g.) was added to a solution of the (+)iodide (18 g.) in glacial acetic acid (150 c.c.), and the mixture heated on the steam-bath until the zinc was almost completely dissolved (7 hours). On working up, there was obtained (+)-γ-methyl-*n*-heptane, b. p. 115—122°, α_{5893}^{18} + 1·21°, α_{5461}^{18} + 1·36° (*l*, 0·25). After being heated at 100° for 3 hours in the presence of sodium, this had b. p. 115—118° (3 g.), $n_D^{18°}$ 1·4000 (Smittenburg, Hoog, and Henkes, *J. Amer. Chem. Soc.*, 1938, **60**, 18, give $n_D^{20°}$ 1·3988; and Levene, *J. Biol. Chem.*, 1922, **54**, 351, gives $n_D^{20°}$ 1·3980), and almost unaltered rotatory powers (see Table VII) (Found: C, 84·3; H, 15·8. Calc.: C, 84·2; H, 15·8%).

n-*Butyl* dl-n-*heptane*-γ-*carboxylate*, prepared by the Fischer–Speier method in 82% yield, has b. p. 110—111°/18 mm., $n_D^{21°}$ 1·4225 (Found: C, 71·9; H, 12·0. $C_{12}H_{24}O_2$ requires C, 72·0; H, 12·0%); the iso*amyl* ester, prepared similarly in 84% yield, has b. p. 120—121°/16 mm., $n_D^{16°}$ 1·4247 (Found: C, 72·8; H, 12·2. $C_{13}H_{26}O_2$ requires C, 72·8; H, 12·2%); and the *phenyl* ester, prepared by the action of the acid chloride on a solution of phenol in pyridine (yield 70%), has b. p. 138—141°/12 mm., $n_D^{21°}$ 1·4818 (Found: C, 76·7; H, 9·2. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

Attempted Resolution of dl-β-*Ethyl*-n-*hexanol*.—The commercial alcohol (b. p. 180—181°, 65 g.) was heated for 2½ hours on the steam-bath with a suspension of phthalic anhydride (74 g.) in pyridine (40 g.); dl-β-*ethyl*-n-*hexyl hydrogen phthalate* (140 g.) was obtained as a crystalline mass, m. p. 14—16° (Found: C, 68·7; H, 8·1; *M*, 283, by titration with NaOH. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0%; *M*, 278). In a similar manner the hydrogen 3-nitrophthalic ester, m. p. 108—110°, was prepared and, by the usual method, the *p*-xenylurethane, m. p. 81—82°. For the last two compounds m. p.'s 107—108° and 80°, respectively, are recorded by Morgan, Hardy, and Procter (*J. Soc. Chem. Ind.*, 1932, **51**, 7).

Decomposition of brucine β-ethyl-*n*-hexyl phthalate which had been recrystallised five times from acetone yielded a hydrogen phthalic ester with $[\alpha]_{5461}$ + 1·73° (*c*, 5·0; *l* = 2, in carbon disulphide), which on hydrolysis gave (−)-β-ethyl-*n*-hexanol, b. p. 178—179°, with $\alpha_{5461}^{18°}$ − 0·11°, $\alpha_{4358}^{18°}$ − 0·27° (*l*, 0·5).

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BATTERSEA POLYTECHNIC, LONDON, S.W. 11.

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