82. *Alkyl–Oxygen Fission in Carboxylic Esters. Part VI. Solvolytic Reactions of Esters of Optically Active* cyclo*Hexylphenyl-, Methylphenyl-, and Methyl-α-naphthyl-carbinols.*

By M. P. BALFE, G. H. BEAVEN, and J. KENYON.

First-order rate constants for reactions of the hydrogen phthalate, acetate, and formate of optically active *cyclo*hexylphenylcarbinol (I) with carboxylic acids are compared with constants for similar reactions of esters of methyl-phenyl- (II) and methyl-α-naphthylcarbinols (III). All these reactions are accompanied by racemisation. The tendency to undergo this kind of reaction (alkyl–oxygen fission) is a little less in (I) than in (II), and greatest in (III).

(+)-*cyclo*HEXYLPHENYLCARBINYL HYDROGEN PHTHALATE was prepared as described by Levene and Mikeska (*J. Biol. Chem.*, 1927, **75**, 587), and the corresponding (−)-ester by crystallisation of the strychnine salt of the residual lævorotatory ester. The (+)-phthalate gives the (+)-carbinol on hydrolysis with alkali: from the (+)-carbinol, the (+)-acetate (pyridine–acetic

anhydride), (−)-benzoate (pyridine–benzoyl chloride), and (+)-formate (formic–acetic anhydride) are obtained. The rotatory powers and other characteristics of these compounds are recorded in Table I.

Rate constants for esterifications of the carbinol (Table IV) are derived from changes in rotatory power during the reaction. They are all first-order as the reagent was in excess. The presence of pyridine increases the rate constant of the reaction with acetic anhydride by

TABLE I.

(+)-cyclo*Hexylphenylcarbinol and its esters.*

	M. p.	B. p.	n_D^t.	$[\alpha]_D^{20}$.	Solvent.	c.
Carbinol	72°	—	—	+22·5°	EtOH	5·13
				38·8	Et₂O	4·03
Hydrogen phthalate	127	—	—	22·0	EtOH	5·00
				51·8	CHCl₃	2·22
Acetate	—	170°/20 mm.	1·5125/20°	71·0	EtOH	3·98
Formate	—	180/15 mm.	1·5240/17	75·4	EtOH	2·31
Benzoate	82	—	—	−32·2	EtOH	2·10

TABLE II.

Solvolytic reactions of esters of cyclohexylphenyl-, methylphenyl-, *and* methyl-α-naphthyl-carbinols.

(For concentrations and solvent proportions see Experimental section.)

First-order k * × 10⁵ (in min.⁻¹) in reaction of ester of :

Ester.	Solvent.	Temp.	cycloHexylphenyl-carbinol.	Methylphenyl-carbinol.	Methyl-α-naphthyl-carbinol.
Acetate	AcOH	18°	0	—	—
		100	5	—	—
	AcOH–H₂O	18	0	—	—
		100	70	—	—
	AcOH–p-C₆H₄Me·SO₃Na	100	35	—	—
	H·CO₂H	—	940 at 17°	740 at 19°	11,000 at 15°
				2900 at 27°	63,000 at 21°
Formate	AcOH	100	0	—	—
	AcOH–H₂O	20	0	1·0	—
	H·CO₂H	21	1200 †	2500	—
		26	1700 ‡		
Benzoate	AcOH	20°	—	0	0
		hot	—	0 at 100°	70 at 80°
	AcOH–H₂O	100	—	250	—
Hydrogen phthalate	AcOH–H₂O	100	0	0	100
		23	0	—	—
		100	250	1200	1250
	AcOH–NO₂Me	100	4	—	—
	H·CO₂H	20—45	i	i	i
	MeOH or EtOH	reflux	0	0	0
	MeOH–H₂O	reflux	0	0	60
	EtOH–H₂O	reflux	0	0	50

* 0 = No change in rotatory power during long period; i = too rapid for measurement.
† Table V. ‡ From second branch of mutarotation curve, Table IV.

a factor of 10³; the reaction with formic acid is some 100-fold as fast as the reaction with formic–acetic anhydride.

With thionyl chloride and phosphorus pentachloride (in the absence and in the presence of pyridine) and with aqueous hydrochloric acid, the (+)-carbinol gives partly racemised (+)-chlorides.

First-order rate constants for solvolytic reactions of some of the esters are given in Table II, together with first-order constants for similar reactions of methylphenylcarbinol and methyl-α-naphthylcarbinol, calculated from the data recorded by Balfe *et al.* (*J.*, 1946, 797). It is evident that in the sequence of alcohols arranged in order of diminishing tendency of their esters to react by alkyl–oxygen fission (Balfe *et al.*, *J.*, 1946, 803), cyclohexylphenylcarbinol falls just below methylphenylcarbinol. The present results agree with those previously

reported (*J.*, 1946, 803) in showing that the solvolytic reaction occurs much more readily in acid solvents (particularly formic acid) than in alcohols, and is promoted by addition of water to the medium. Solvolysis of *cyclo*hexylphenylcarbinyl acetate is accelerated by addition of a salt (sodium toluene-*p*-sulphonate) to the medium, and solvolysis of the hydrogen phthalate by addition of nitromethane : presumably, these effects are related to increases in the dielectric constants of the media.

In agreement with the comparatively small tendency to reaction by the alkyl–oxygen fission mechanism in esters of *cyclo*hexylphenylcarbinol, it is found that the carbinol is obtained optically pure on hydrolysis of its hydrogen phthalate by weak alkali (*e.g.*, sodium carbonate solution), a reagent which gives rise to a partly racemised product in the hydrolysis of the hydrogen phthalate of carbinols which have a strong tendency to react by this mechanism (*J.*, 1946, 807).

The hydrogen phthalates of the carbinols described above, when dissolved in an equimolecular proportion of aqueous sodium hydroxide, do not yield the neutral ester and do not react with sodium toluene-*p*-sulphinate, as is to be expected in view of their comparatively small tendency to react by the mechanism which involves alkyl–oxygen fission. α-Naphthylphenylcarbinyl hydrogen phthalate also does not undergo these reactions : it has not been possible to obtain it in optically active forms for study of its solvolytic reactions by the methods described above.

EXPERIMENTAL.

*cyclo*Hexylphenylcarbinol (prepared by Grignard reaction from *cyclo*hexyl bromide; 25% yield) had m. p. 50°; von Auwers and Treppmann (*Ber.*, 1915, **48**, 1220) record m. p. 50—50·5°. Its ($\pm$)-hydrogen phthalate, recrystallised from ethyl alcohol, had m. p. 163—164° (Levene and Mikeska, *loc. cit.*, record m. p. 163°) (Found : equiv. by titration with 0·1N-NaOH, 339. Calc. for $C_{21}H_{22}O_4$: equiv., 338). The cinchonidine salt was recrystallised four times from chloroform–acetone (3 : 1), which raised the rotatory power of the hydrogen phthalate to the maximum value. Levene and Mikeska extracted the solid salt twice with hot acetone and recrystallised the hydrogen phthalate, obtained from the residual salt, from ether. The present procedure gives a product of slightly higher rotatory power. The (−)-hydrogen phthalate, recovered from the mother-liquors, was converted into the strychnine salt, from which, after one recrystallisation from methyl alcohol–acetone (4 : 1), the strychnine salt of the optically pure (−)-hydrogen phthalate was obtained. Cinchonidine was removed by treating its salt, suspended in acetone, with dilute hydrochloric acid and dilution with cold water : the (+)-hydrogen phthalate separated and solidified. Strychnine was precipitated from its salt, in hot ethyl-alcoholic solution, by addition of dilute aqueous ammonia; the filtrate was acidified with dilute hydrochloric acid, and the (−)-hydrogen phthalate separated and solidified. Both the (+)- and the (−)-hydrogen phthalate were obtained in about 35% yield on the ($\pm$)-phthalate used. The (+)- and the (−)-carbinol were obtained from the hydrogen phthalates by steam-distillation from 5N-aqueous sodium hydroxide. Steam-distillation from 1N-sodium carbonate, sodium hydroxide, or sodium ethoxide (in ethyl alcohol) yielded carbinols of the same rotatory power as that from 5N-sodium hydroxide.

Esters were prepared by usual methods (see also p. 376). The (+)-*acetate* had b. p. 162—166°/20 mm., n_D^{25} 1·5106, n_D^{20} 1·5131 (Found : 1·000 g. required 242 mg. of KOH for hydrolysis. $C_{15}H_{20}O_2$ requires 242 mg.). The ($\pm$)-*formate* was obtained from a solution of (+)-carbinol in anhydrous formic acid after 27 days (the solution then being optically inactive); b. p. 169—172°/22 mm., n_D^{25} 1·5250 (Found : 1·000 g. required 219 mg. of KOH for hydrolysis. $C_{14}H_{18}O_2$ requires 218 mg.). The ($\pm$)-*benzoate*, recrystallised from ether–light petroleum, had m. p. 99° (Found : 1·000 g. required 297 mg. of KOH for hydrolysis. $C_{20}H_{22}O_2$ requires 294 mg.). The carbinol did not react with toluene-*p*-sulphonyl chloride. The ($\pm$)-*chloride* [prepared by slow addition of thionyl chloride (5 mols.) to the ($\pm$)-carbinol; solution heated for 1 hour, then treated in usual way] had m. p. 27—29°, b. p. 146—148°/15 mm., n_D^{17} 1·5425 (Found : Cl, 16·9. $C_{13}H_{17}Cl$ requires Cl, 17·0%). Constants of the optically active esters are in Table I. Steam-distillation of a solution of the (−)-benzoate in 5N-sodium hydroxide gave the carbinol with $[\alpha]_D^{20}$ +22·0° in ethyl alcohol, *i.e.*, substantially the same as that from which the benzoate was prepared.

Optically active chlorides (*cyclo*hexylphenylchloromethanes) were prepared from (+)- or (−)-carbinols (Table I) unless otherwise stated. During distillation, the chlorides suffered some racemisation, apparently not caused by decomposition since chlorine contents were satisfactory. Levene and Mikeska (*loc. cit.*), from carbinols of lower optical purity, obtained chlorides with proportionally higher rotatory powers, probably on account of lower distillation temperatures (b. p. *ca.* 110°/1 mm.).

Optically active chlorides were prepared as follows (see Table III for physical constants). (*a*) 1·4 G. of (+)-carbinol, 1 c.c. of thionyl chloride, procedure as above. (*b*) 2·5 G. of (−)-carbinol and 2·4 g. of pyridine (2 mols.), 1·3 c.c. of thionyl chloride added, procedure as above. (*c*) 2·5 G. of (−)-carbinol were added gradually to a suspension of phosphorus pentachloride (4·2 g., 1 mol.) in ether (50 c.c.) at 0°; after 3 hours at room temperature, the product was isolated in the usual way. (*d*) 2·5 G. of (−)-carbinol with 2·4 g. pyridine (2 mols.) were added to 4·2 g. of phosphorus pentachloride (2 mols.), and then treated as in (*c*). (*e*) 2·0 G. of carbinol, $[\alpha]_D^{20}$ −20·6° (in EtOH), were triturated with 10 c.c. of 10N-hydrochloric (10 mols.) : the oil solidified, 1·7 g. of recrystallised chloride being obtained.

Rate Constants.—Individual values of k were calculated from the rotation changes for each time interval. They fall in a satisfactory distribution about the mean, which was also confirmed by calculation

of k from the time of half-reaction, read from a straight line drawn through log a–time plots. Rate constants for the reactions of the acetates of methylphenyl- and methyl-a-naphthyl-carbinols are taken from Downer (Thesis, London, 1942) : they are supported by calculation from half-reaction time. For other reactions of these two carbinols the constants are calculated only from half-reaction times interpolated in the data of Balfe *et al.* (*J.*, 1946, 797), the observations being inadequate for calculation of individual constants : they cannot be of a high order of accuracy, but are probably adequate for the present comparative use. [The data given by Balfe *et al.* (*J.*, 1946, 797) for the reaction of (+)-methyl-phenylcarbinyl acetate with formic acid were erroneously transcribed : to all the observations at 19°, except the first, add 2·0° to each a; to all the observations at 27°, except the first, add 0·5° to each a.]

Table IV summarises the data for the formation of esters, and Table V the data for solvolytic reactions. In the reaction of (+)-carbinol with formic acid, the rotatory power first rises (formation

TABLE III.

(±)- and (−)-cyclo*Hexylphenylchloromethane.*

| | | Crude chloride. | | | | Redistilled chloride. | | | |
	Yield, % .	$[a]_D^t$ in Et$_2$O.	n_D^t.	B. p.	$[a]_D^t$ in Et$_2$O :		c.	n_D^t.	M. p.
(a)	98	+44·8°/15°	1·544/15°	144°/14 mm.	+39·1°/15°		1·4	—	30°
(b)	87	−62·0°/18°	1·546/18°	145°/15 mm.	−30·8°/19°		1·4	1·544/19°	30
(c)	96	−2·9°/19°	1·541/19°	—	−0·76°/19°		1·4	1·543/19°	27—30
(d)	93	−4·5°/18°	1·541/18°	138°/20 mm.	−1·7°/18°		1·5	1·544/18°	29—30
(e)	84	—	—	—	−15·7°/20°		7·0	—	28

TABLE IV.

Formation of esters of cyclo*hexylphenylcarbinol.*

Carbinol, g.	Reactants.	Temp.	Initial a (l, 2 dm.).	1st-Order k : Mean.	From $t_{\frac{1}{2}}$.	$t_{\frac{1}{2}}$, mins.
1·55	Ac$_2$O (10 c.c.) ; pyridine (15 c.c.)	23°	+5·28°	2·3 × 10^{-2}	2·2 × 10^{-2}	31
1·195	Ac$_2$O (25 c.c.)	21	+2·53	7·6 × 10^{-5}	7·4 × 10^{-5}	9300
1·07	HCO·OAc (15 c.c.)	23	+4·47	1·1 × 10^{-4}	1·2 × 10^{-4}	6000
1·00	H·CO$_2$H (25 c.c.)	26	+1·88	5·5 × 10^{-2} *	—	13

* Corrected for racemisation of formate.

TABLE V.

Solvolytic reactions of esters of cyclo*hexylphenylcarbinol.*

Ester.	Reactant.	Temp.	Initial a_D^{20} (2 dm.).	1st-Order k, in min.$^{-1}$. Mean.	From $t_{\frac{1}{2}}$.	$t_{\frac{1}{2}}$
Acetate ([a]^{18} +66° in EtOH), 3·01 g.	AcOH (100 c.c.)	100°	+2·78°	5·0 × 10^{-5}	4·8 × 10^{-5}	242 hrs.
Acetate, as above, 2·30 g.	AcOH (90 c.c.) +H$_2$O (10 c.c.)	100	+3·88	7·2 × 10^{-4}	7·0 × 10^{-4}	16·5 ,,
Acetate, as above, 1·72 g.	AcOH (100 c.c.) + p-C$_6$H$_4$Me·SO$_3$Na (14·4 g.)	100	+2·73	3·5 × 10^{-4}	3·5 × 10^{-4}	33 ,,
Acetate, as above, 2·58 g.	H·CO$_2$H (100 c.c.)	17	+4·51	1·0 × 10^{-2}	0·9 × 10^{-2}	74 mins.
(+)-Formate, 1·30 g.	H·CO$_2$H (100 c.c.)	21	+2·24	1·3 × 10^{-2}	1·2 × 10^{-2}	57 ,,
(−)-Hydrogen phthalate, 4·04 g.	AcOH (80 c.c.) +H$_2$O (20 c.c.)	100	−3·23	—	2·5 × 10^{-2}	46 hrs.
(−)-Hydrogen phthalate, 4·11 g.	AcOH (20 c.c.) +NO$_2$Me (80 c.c.)	100	−2·41	3·6 × 10^{-5}	3·6 × 10^{-5}	320 hrs.

of formate) then falls to zero (solvolysis of formate). The log a–time plot gave two straight lines from which k's for the two stages were calculated.

a-*Naphthylphenylcarbinol* (experiments by Dr. R. E. Dabby).—The carbinol (Acree, *Ber.*, 1904, **37**, 2757) yielded a *hydrogen phthalate*, needles, m. p. 158° (Found : equiv., 384. C$_{25}$H$_{18}$O$_4$ requires equiv., 382), and a *hydrogen succinate*, short needles, m. p. 122° (Found : equiv., 338. C$_{21}$H$_{18}$O$_4$ requires equiv., 334), by the usual methods. The carbinol on reaction with acetyl chloride or acetic anhydride in presence of pyridine gave the *acetate*, needles, m. p. 80° (Found : C, 82·5; H, 5·9. C$_{19}$H$_{16}$O$_2$ requires C, 81·9; H, 6·0%). When heated at 150° for 35 hours it was converted into *di-(a-naphthyl-phenylcarbinyl) ether*, which was isolated, by extraction with ethyl ether, concentration, and dilution with benzene, as glistening needles, m. p. 172—173° (Found : C, 90·0; H, 5·7. C$_{34}$H$_{26}$O requires C,

90·1; H, 5·8%). From a solution of the hydrogen phthalate (4·0 g.) and sodium toluene-*p*-sulphinate (2·2 g.) in formic acid (50 c.c.), heated under reflux for 8 hours, and then diluted with water, a solid separated which was washed with water and recrystallised from ethyl alcohol, yielding *α-naphthyl-phenylcarbinyl* p-*tolyl sulphone* (3·3 g.), plates, m. p. 122° (Found : S, 8·3. $C_{24}H_{20}O_2$ requires S, 8·5%). From a solution of the hydrogen phthalate (5·0 g.) in ethyl alcohol (75 c.c.), heated under reflux for 18 hours and then concentrated, diluted with ether, and extracted with aqueous ammonia (to remove unchanged phthalate), an ethereal solution of *ethyl α-naphthylphenylcarbinyl ether* was obtained, which was dried and concentrated, yielding the ether, b. p. 203°/14 mm., short needles, m. p. 47° (Found : C, 87·2; H, 7·1. $C_{19}H_{18}O$ requires C, 87·0; H, 6·9%).