

Summary and Conclusions

The rate constants of both unimolecular and bimolecular reactions can be calculated analytically when the initial concentration or time cannot be determined. This method, however, is not to be recommended when it is possible to determine the initial concentration accurately by direct means, since it has greater probable error.

The commonly used simple arithmetical average of rate constants is entirely incorrect and should never be used except for averaging rate constants calculated from entirely independent data, and then only when the probable errors are nearly alike. The method of least squares should be used with caution. The graphical method may be used in all cases where each point on the graph represents entirely independent data.

The author recommends that one should first determine whether the rate law holds within experimental error. Then, in case it does, one should take more data in such a manner that a number of values of k can be calculated from entirely independent data for approximately the optimum concentration change. These values of k may be averaged graphically or by taking the simple arithmetical average.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MANITOBA]

THE PHYSICAL IDENTITY OF ENANTIOMERS. THE CAMPHORIC ACIDS

BY ALAN NEWTON CAMPBELL

RECEIVED JANUARY 20, 1931

PUBLISHED MAY 6, 1931

In a recent paper¹ the author in collaboration with another was able to produce evidence that the *d*- and *l*-mandelic acids are not absolutely identical in their physical properties. Private criticism made at that time rested upon the contention that the *d*-form was not quite pure, despite the facts that the rotation of *d*-form was normal, and that the rotatory dispersions or rather differences in rotation for the two lines used, were the same, which would not be the case if one form were impure. Nevertheless, in view of this contention, it was thought advisable to prepare the next pair of enantiomers from independent optically active sources of opposite rotation. I am indebted to Dr. Kenyon for the suggestion that I should use the *d*- and *l*-camphors, or rather the camphoric acids obtainable from them. I have been exclusively occupied for the past fifteen months with this work, most of the time being spent on preparation and purification. As I surmise that criticism will, as usual, be directed rather to this question of purity than to ability to determine physical constants, I give a detailed statement of the methods of preparation and purification.

¹ Campbell and Garrow, *Trans. Faraday Soc.*, **26**, 560 (1930).

Preparation and Purification

Pure *d*-camphor was purchased from British Drug Houses (m. p. 176.3° (uncorr.)); three hundred grams of *d*-camphor was heated with 2400 cc. of nitric acid (*d* 1.42) and 1600 cc. water for sixty-five hours on the water-bath. The product was cooled and the crude *d*-camphoric acid filtered off.

The crude product was purified as follows. It was dissolved in 10% caustic soda and extracted with ether to remove unchanged camphor. The acid was reprecipitated with hydrochloric acid, dried and converted into its anhydride by refluxing with acetyl chloride. Excess acetyl chloride was removed by shaking with cold water. The anhydride was then dissolved in boiling alcohol and the solution allowed to crystallize. The purified anhydride was then hydrolyzed by boiling with potassium carbonate solution. *d*-Camphoric acid was precipitated from the alkaline solution by addition of hydrochloric acid. The precipitate was filtered and washed, and then recrystallized ten times from boiling water, the first crop of crystals being always rejected; 50 g. of *d*-camphoric acid was eventually obtained.

In order to decide whether this repeated recrystallization would constitute a purification from the opposite enantiomer, supposing it to be present, the solubility diagram for *d*-, *l*- and *r*-camphoric acids was determined, for 16°. The results were

	Dextro	Solid phase	
		Inactive	Inactive and dextro
Solubilities, g. per 100 g. of water	{ 0.679	{ 0.12 <i>d</i> 0.12 <i>l</i>	{ 0.63 <i>d</i> 0.04 <i>l</i>

When these figures are plotted Fig. 1 is obtained.

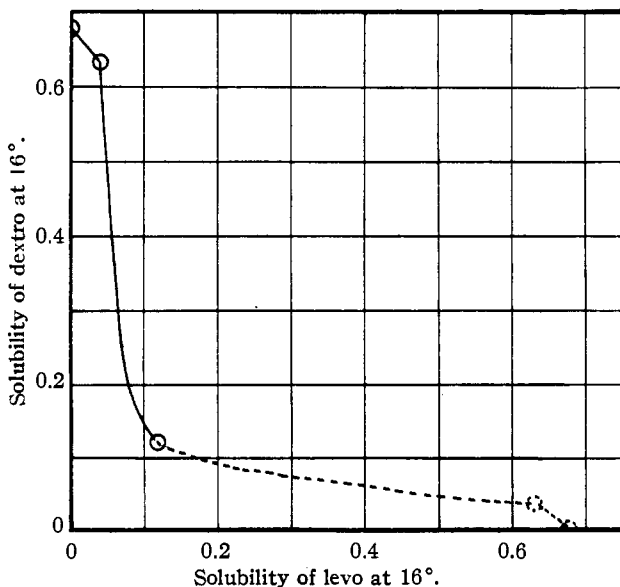


Fig. 1.

The titration of the two acids eventually obtained, by standard baryta, gave equivalent weights of 99.90 (levo) and 100.00 (dextro); calcd., $\frac{1}{2} \cdot 200.13$.

From the diagram it is apparent that the solid phase in contact with solution throughout the greater course of the curve is the racemic form. It therefore follows that if a solution of the *d*-form contains any appreciable quantity of the *l*-form, racemic form will separate from the solution (at room temperature) until the solution contains 0.63 g. of dextro and 0.04 g. of levo per 100 g. of water. Further evaporation will result in the deposition of *d*- and *l*- in the above proportions. Further than this, therefore, the purification of dextro cannot be carried. If, however, as has hitherto been stated, enantiomers are completely identical, then the complete solubility diagram will be perfectly symmetrical, and the recrystallization of the levo form will also result in a product which will be impure with opposite enantiomer, to precisely the same extent. Hence any objections urged against the differences in physical properties on the score of impurity fall to the ground.

Each recrystallization was allowed to stand overnight, in contact with the mother liquor, after separation and rejection of the crystals first appearing. Under these circumstances it is improbable that equilibrium was not attained, in view of the relatively large amount of active form separating from the solution.

The form of the solubility diagram bears out the contention of Ross and Summerville² that the racemate is a very stable one.

It was at first attempted to prepare *l*-camphoric acid from *l*-camphor, but it was found that commercial *l*-camphor was hopelessly impure. Recourse was therefore had to *l*-borneol as the starting material. *l*-Borneol was obtained from British Drug Houses, and it had the following physical constants: m. p. 203.5°; $[\alpha]_D^{16} -37.6$ (in alcohol). The *l*-borneol was purified by the method of Haller.³ The *l*-borneol acetate was distilled under reduced pressure, before freezing, to free it from non-volatile impurities. The purified *l*-borneol was then oxidized with nitric acid and purified in the above manner. The product eventually obtained had a chemical equivalent of 99.90, as against 100.00 for the *d*-form (calcd. 100.07).

In connection with the question of purity, the appearance of the preparations was well worth noting. They consisted entirely of large, clear, well-shaped crystals, of an average diameter of 5 mm. Apart from occasional twinning, they were well-shaped rhombohedra, having the hemihedral facets well developed. Admixture with the opposite enantiomer would have resulted in the formation of the racemic form, with a holohedral structure. After examining such a preparation carefully with a low-power lens, it is impossible to believe that it is not homogeneous.

Melting Points of the Camphoric Acids.—These were determined by the method described in the previous paper.¹ The precautions there described were repeated in the present instance. The following figures were obtained for the melting points of successive crops of crystals.

² Ross and Summerville, *J. Chem. Soc.*, 2778 (1926).

³ Haller, *Ann. chim. phys.*, [6] 27, 422 (1892).

TABLE I
MELTING POINTS

All these figures are uncorrected and therefore low, but the same thermometer was used for all determinations.

Dextro.....	187.5	188.0	186.0	186.0	186.0
Levo.....	183-189 ^a	186.5 ^b	186.5 ^b	186.5 ^b	186.5 ^b

^a Large but distorted crystals deposited slowly from aqueous solution of crude product. ^b Successive recrystallizations of product.

Solubilities.—The solubilities were determined in water, since, though the solubility in acetone is conveniently large, camphoric acid forms a compound with acetone (private communication from Professor Smits). All solutions were filtered in the thermostat, by means of an apparatus previously described,⁴ the saturated solution was weighed, and a weighed portion titrated with baryta. Solubilities are expressed, as usual, in grams per 100 g. of solvent.

TABLE II
SOLUBILITIES IN WATER

Temp., °C.	Dextro	Levo	Temp., °C.	Dextro	Levo
16.0	0.665		25.5		0.705
16.0	.657		29.9		.710
18.0	.715		30.0	0.802	
20.1		0.682	35.0	.92	
24.8	.74		35.5		.77
25.0	.765		40.0	1.00	.88

These results, when plotted, yield Fig. 2.

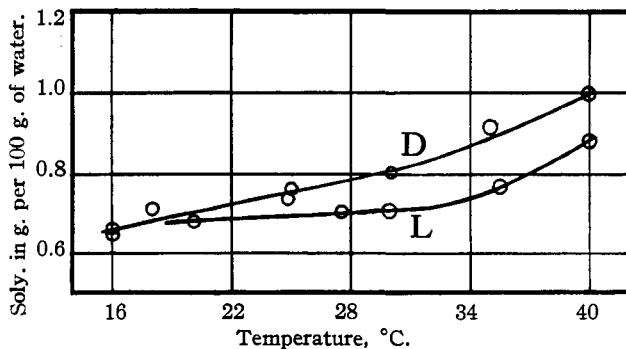


Fig. 2.—Solubilities of *d*- and *l*-camphoric acids in water: D, dextro; L, levo.

Specific Rotatory Power.—The instrument which I used in Aberdeen and the method of work are described in the previous paper.¹ Since coming to Winnipeg, I have used an identical instrument, except that it has no

⁴ Campbell, *J. Chem. Soc.*, 179 (1930).

spectrometric attachment. Determinations with this instrument were therefore made with sodium light. Solutions were made up by weighing in the first place, but in order to be entirely independent of graduated apparatus, the densities of the solutions were determined in a pycnometer holding 11.660 cc. of water at 4°. A weighed portion of the solution was then titrated with baryta and calculated by the formula

$$[\alpha]_{\lambda}^t = \frac{\alpha \times 100}{l \times d \times p}$$

Specific Rotatory Power in Water.—A single determination of this was made, with the result $[\alpha]_{\lambda=5960}^{16} + 46.3^{\circ}$.

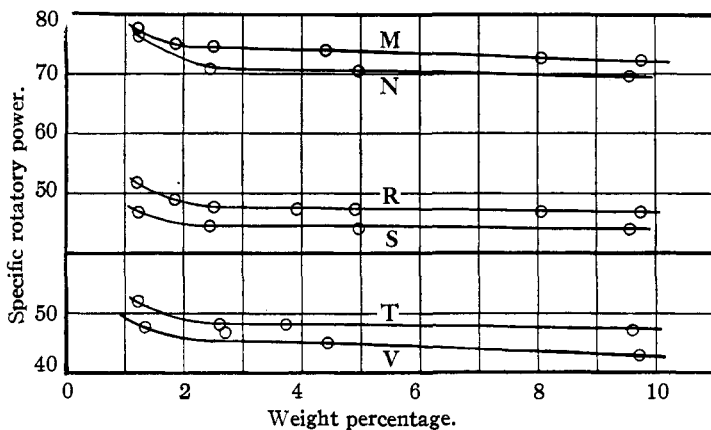
Specific Rotatory Power in Alcohol.—The alcohol used was the ordinary rectified alcohol, having d_4^{18} 0.80275. It therefore contained 96.99% of alcohol by weight. An 8-liter glass jar was filled with this alcohol, in order that identical solvent might be used throughout. In a few experiments carried out in Winnipeg I was of course obliged to use a different sample of alcohol, but it had an almost identical density and was used for both forms. The specific rotatory powers, at 18°, were as given in Table III.

TABLE III

ρ	Dextro		Levo		Dispersion, $[\alpha]_{\lambda=5960} - [\alpha]_{\lambda=4610}$
	$\lambda = 5960$	$\lambda = 4610$	$\lambda = 5960$	$\lambda = 4610$	
1.21	+51.8	+77.5			25.7
1.24			-47.0	-76.5	29.5
1.86	+49.0	+75.0			26.0
2.44			-44.7	-70.9	26.2
2.50	+47.7	+74.4			26.7
3.92	+47.5	+73.8			26.3
4.90	+47.3	+73.5			26.2
4.95			-44.4	-70.4	26.0
8.05	+46.9	+72.7			24.8
9.55			-44.05	-69.5	25.45
9.75	+46.7	+72.1			25.4
ρ			Dextro		Levo
			$\lambda = 5896$		$\lambda = 5896$
1.22			+52.0		
1.33					-48.0
2.51			+48.3		
2.52					-47.0
3.73			+48.3		
4.43					-45.0
9.6			+47.3		
9.70					-43.0

When these figures are plotted the curves of Fig. 3 are obtained. The dispersions appear to be identical, while the rotations differ. Apart from the evidence of purity which this affords, it may have a theoretical sig-

nificance. According to Hunter⁵ dispersion is a more fundamentally constitutive property than rotation and, if this view is correct, it would seem to indicate that the difference between enantiomers is not constitutive, in the ordinary sense of that word, as indeed it could not be, but of a more superficial character.



M, Dextro, $\lambda = 4610$; N, levo, $\lambda = 4610$. R, Dextro, $\lambda = 5960$; S, levo, $\lambda = 5960$. T, Dextro, $\lambda = 5986, 5890$; V, levo, $\lambda = 5986, 5890$.

Fig. 3.

Conclusion.—The theoretical implications of these results have already been discussed in the previous paper.¹

Summary of Results

1. Dextro and levo camphoric acids have been prepared in a state of purity.
2. The melting points, solubilities and specific rotatory powers of the two forms have been determined and compared.

UNIVERSITY OF ABERDEEN
UNIVERSITY OF MANITOBA
WINNIPEG, CANADA

⁵ Hunter, *J. Chem. Soc.*, 123, 1671 (1923).