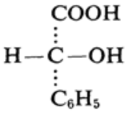
The Anomalous Adsorption of Enantiomers of Mandelic Acid and Atrolactic Acid on the Optically-Active Adsorbent

By Masaaki OHARA, Kosuke OHTA and Takao KWAN

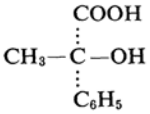
(Received July 1, 1963)

The present paper is concerned with the selective adsorption of enantiomers of mandelic acid (I) and atrolactic acid (II) on a starch column.



$$\begin{array}{c} COOH \\ \vdots \\ H-C-OH \\ \vdots \\ C_6H_5 \end{array}$$

(I)



$$\begin{array}{c} COOH \\ \vdots \\ CH_3-C-OH \\ \vdots \\ C_6H_5 \end{array}$$

(II)

As has been described in a previous paper,[1] the (−) isomer of mandelic acid is eluted from a starch column earlier than the (+) isomer. A similar selectivity in the adsorption was found with the homologues of mandelic acid except with atrolactic acid (II), where the (+) isomer was eluted earlier than the (−) isomer. The apparently anomalous selectivity in the adsorption of these enantiomers will be discussed here.

Experimental and Results

Racemic mandelic acid or atrolactic acid (0.5 g.) in 50% aqueous methanol was adsorbed at room temperature on a starch column 1.6× 60 cm. and chromatographed with the same solvent. The optical rotation of the eluted was measured by a Zeiss-Kreis polarimeter. The concentration of the acid in the fraction was determined by absorption at 257 mμ.

In Fig. 1 the specific rotations of mandelic acid as well as of atrolactic acid are plotted against the fraction numbers. The observed angle of rotation, α, and the concentration of the adsorbates, c, in g. per 100 ml. of an aqueous methanol solution are given for some of the fractions.

As shown in the figure with atrolactic acid the (+) isomer is eluted earlier, while with mandelic acid the (−) isomer is eluted earlier, in accordance with the previous observation.[1] Over 90% of the acids were recovered in either case. Judging from the reversal order of the elution of the enantiomers of mandelic acid

TABLE I. THE ELUTION OF SEVERAL HOMOLOGUES OF MANDELIC ACID ON A STARCH COLUMN (15~18°C)

Racemate	The sign of the isomer eluted earlier	The sign of the isomer eluted later
Mandelic acid	(−)	(+)
Atrolactic acid	(+)	(−)
Methyl mandelate	(−)	(+)
Acetyl mandelic acid	(+)	(−)
β-Phenyl lactic acid	(+)	(−)
Tropic acid	(−)	(+)

---

[1] M. Ohara, I. Fujita and T. Kwan, This Bulletin, 35, 2049 (1962).

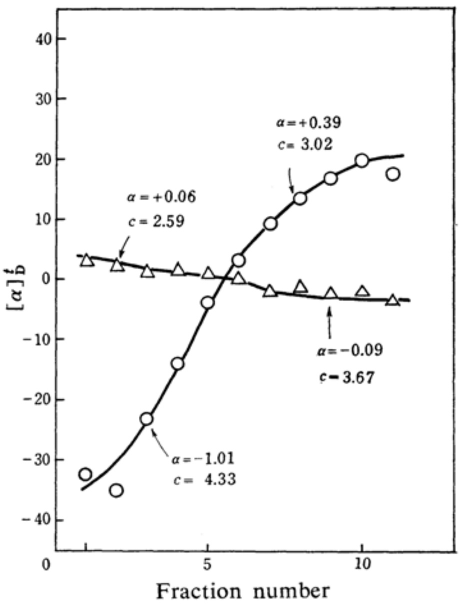


Fig. 1. The specific rotation $[\alpha]^t_D$ of mandelic acid and atrolactic acid against fraction numbers (t, 15∼18°C).

○ Mandelic acid

△ Atrolactic acid

and atrolactic acid, it can be considered that the adsorption affinity of mandelic acid and that of atrolactic acid are reversed with respect to their enantiomers.

$(+)$ mandelic acid $>$ $(-)$ mandelic acid

$(+)$ atrolactic acid $<$ $(-)$ atrolactic acid

Several homologues of mandelic acid were investigated in a similar manner. The order of appearance is shown in Table I.

Optical isomers with the same sign can not always be assigned to the same configuration. In Table I it may be seen that atrolactic acid, acetyl mandelic acid and β-phenyl lactic acid are different with respect to the sign of the isomer eluted earlier. The literature shows, however, that the $(+)$ isomers of the latter two have the same configuration as the $(-)$ isomer of mandelic acid.[2,3] On the other hand, optical isomers of mandelic acid and atrolactic acid with the same sign have generally been assigned to the same configuration.[3-6] Therefore, the fact that the $(+)$ isomer of atrolactic acid is eluted earlier may be considered peculiar with regard to the relative adsorption affinity of enantiomers or may raise some question of the configurational interaction between the adsorbate molecule and the surface of starch.

Discussion

The configurational relation of the enantiomers of mandelic acid and its homologues has been established so far by the chemically correlative method. For instance, Brewster[5] clarified the configurational correlation of mandelic acid with atrolactic acid by means of a diastereoisomer, i. e., *threo*-1, 2 diphenyl propanediol. Support for this conclusion was provideded by Cram and his co-workers[6] through a similar stereochemical course. The physical method was also applied in determining the configurational relationship; the change in the molecular rotation of several of their derivatives were investigated,[3] leading to results consistent with the chemical method. Another physical method, the quasi-racemate one, was also tried, but it was found ineffective.[7]

On the other hand, the so-called adsorption affinity method has sometimes been proposed; in this method the adsorbability of one optical isomer in preference to its enantiomer was investigated on a certain optically-active adsorbent. For instance, it was adopted by Beckett and his co-workers[8] in such systems as quinine-quinidine or cinchonine-cinchonidine adsorbed on quinine-pretreated silica gel. They were successful in correlating the configuration of the adsorbent to the strongly-adsorbed epimers. In this case, the adsorbent molecule is similar to the adsorbate molecule in size. Thus the method may resemble the quasi-racemate method.[7]

In contrast, in cases where adsorbents are macromolecules, the adsorption affinity may be conceptually included in the biological method in view of the specificity-like enzyme action. An investigation of the adsorbed configuration of enantiomers along such lines may be found the work of Balandin and his co-workers.[9]

Now, the observed reversal order of elution with mandelic acid and atrolactic acid seems to be incosistent with their *established* configurational correlations; one has to seek an interpretation of the *anomalous* selectivity in the relative configuration of the adsorbate-adsorbent complex. On the other hand, if we assume that the substitution of H for CH_3 with mandelic acid has little effect on the

---

[2] G. W. Clough, *J. Chem. Soc.*, **27**, 2805 (1925).

[3] K. Freudenberg, J. Todd and R. Seidler, *Liebig Ann.*, **501**, 199 (1933).

[4] V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953).

[5] J. H. Brewster, *J. Am. Chem. Soc.*, **78**, 4061 (1956).

[6] D. J. Cram and K. R. Kopecky, ibid., **81**, 2748 (1959); D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, ibid., **81**, 5754 (1959).

[7] K. Mislow and M. Heffler, ibid., **74**, 3668 (1952).

[8] A. H. Beckett and P. Anderson, *Nature*, **179**, 1074 (1957).

[9] A. A. Balandin, E. I. Klabunovskii and Yu. I. Petrov, *Doklady Akad. Nauk. S. S. S. R.*, **127**, 557 (1959).

adsorption on starch, then the *established* relation between the sign and the configuration with enantiomers of mandelic acid and atrolactic acid will be false.

Two tentative explanations to this anomaly have been proposed. One is that the true configurational relationship of enantiomers is a reverse one, being consistent with the order of adsorption affinity. Another is associated with the structure-sensitive properties of starch.

When the above-mentioned configuration relationship is admitted as having been established, the relationship between the adsorption affinity and the configuration of the enantiomers is reversed.

In the latter explanation, when a three-point adsorption model, as was mentioned by, for instance, Ogston,(10) is adopted and when the common functional groups (-OH, -COOH, and -C_6H_5) are responsible to the adsorption force, it is impossible to expect the reversal effect in the adsorption of the enantiomers of mandelic acid and atrolactic acid. Perhaps a kind of multiple interaction would have to be assumed between the adsorbate and the surface of the starch.

At present it is difficult to determine what kind of interaction is responsible for the specific adsorption of mandelic acid and atrolactic acid.

Division of Physicochemical Technology
Faculty of Pharmaceutical Sciences
The University of Tokyo
Hongo, Tokyo

---

10) A. G. Ogston, *Nature*, **162**, 963 (1948).