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Optical Resolution of Heterohelicenes by High Performance Liquid Chromatography

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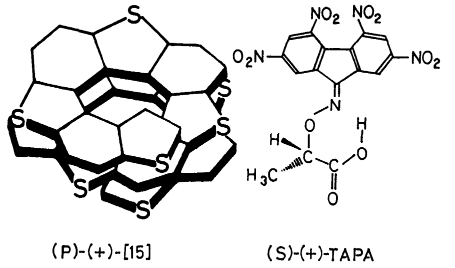
Synopsis. Heterohelicenes up to 15 rings were resolved by high performance liquid chromatography (HPLC) on silica gel covalently linked with a chiral charge transfer complexing agent 2-(2,4,5,7-tetranitro-9-fluorenylideneamino-oxy)propionic acid(TAPA). The efficiency of resolution was discussed in terms of the helical structure of heterohelicenes.

In the course of our work on heterohelicenes, optical resolution was found to be necessary, since their chiroptical properties require isolation of the pure enantiomers. Mikes *et al.* reported the resolution of helicenes by HPLC on a short column containing chiral reagents which function as a selector,[1)] and achieved resolution for carbohelicene series. However, they examined only a few heterohelicenes containing sulfur atoms in a molecule, separation between enantiomers being poor.



(P)-(+)-[15] (S)-(+)-TAPA

Fig. 1

We describe here a better resolution of heterohelicenes up to 15 rings consisting of alternant thiophene and benzene nucleus (Fig. 1) by HPLC with a chiral TAPA-bonded silica-gel column. TAPA is a chiral charge transfer (CT) complexing agent in which tetranitrofluorenylidene moiety provides a strong binding power, oxypropionic acid moiety playing the chiral recognition for the electron donating heterohelicenes.

The chromatogram of [7] to [15] heterohelicenes (Fig. 2) was obtained by using a 30 cm silica-gel (5 μ) column linked with 11% (*S*)-(+)-TAPA. The parameters for resolution are given together with the optical rotations of alternatives isolated by the preparative HPLC in Table 1. The capacity factor k' denoting the ratio of partition coefficients between stationary and mobile phase depends upon the strength of CT interaction of a selector with a selectand. Higher heterohelicene having more powerful electron donating ability gave a larger k' value. (*S*)-(+)-TAPA interacted more strongly with (*M*)-(−)-heterohelicene than with its antipode.

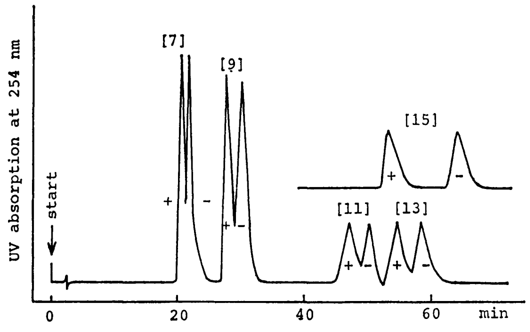


Fig. 2. Chromatogram of heterohelicenes. Column: 11% (*S*)-(+)-TAPA bonded on 5 μ silica gel, mobile phase: 50% dichloromethane–hexane.

Table 1. Resolution of heterohelicenes by HPLC using a (*S*)-(+)-TAPA-bonded silica-gel column

Heterohelicene	k'	r[a)]	$[\alpha]^{23}_{500}$
[7]	5.97 6.42	1.076	2990 −2980
[9]	8.24 9.38	1.138	3760 −3700
[11]	16.88 18.09	1.072	4440 −4550
[13]	19.68 21.20	1.077	8170 −8290
[15]	19.15 23.02	1.202	b) b)

a) $r=k'_-/k'_+$, where k'_- is k' for a minus enantiomer and k'_+ for a plus enantiomer. b) Amount separated too small to measure $[\alpha]^{23}_{500}$.

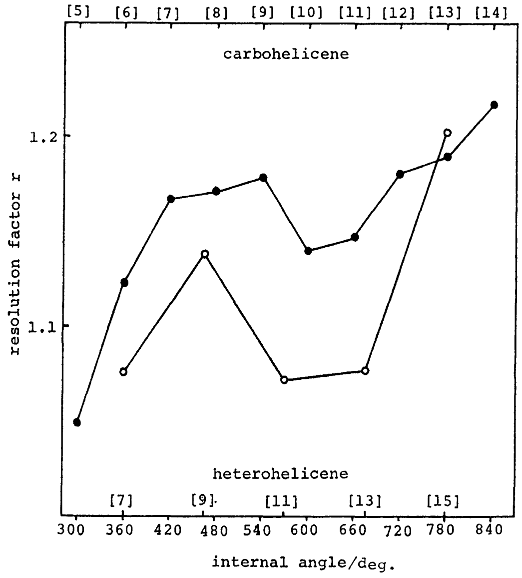


Fig. 3. Relationship between resolution factor and internal angle of helicenes. The data for carbohelicenes were quoted from the literature.[1)]
○: Heterohelicene, ●: carbohelicene.

The absolute values of $[\alpha]_{500}^{23}$ for each antipode were almost the same, indicating that satisfactory separation was achieved. $[\alpha]_{500}^{23}$ increased abruptly with an increase in the number of rings.

Figure 3 shows the relationship of the resolution factor r against the internal angle evaluated by allocating 45° for a thiophene ring and 60° for a benzene ring.[2] The curve for heterohelicenes as well as that for carbohelicenes have no monotonically increasing slope with the progression of helix, but a concave in the range 540°—720° where separation is worse. The range of angle corresponds to a helix possessing 1—1.5 turns. This might be explained in terms of the steric repulsion of the methyl group attached to an asymmetric carbon atom of TAPA against the terminal ring of helicenes, in which a chiral recognition is effectuated. The steric repulsion should give a predominant influence on the r value, since this value refers to the difference in the diastereomeric interaction of TAPA with each enantiomer. On the other hand the k' values are mainly determined by the strength of CT interaction. [11] and [13] heterohelicene have a relatively large k', but small r value, as compared with those of [9] and [15] respectively. Thus, helicenes of the helical structure with 1.5—2 turns undergo a stronger CT interaction owing to the smaller repulsion, resulting in smaller chiral selection from TAPA.

Experimental

Materials. The synthesis of heterohelicenes has been reported.[3] Chiral (*R*)-(−)- and (*S*)-(+)-TAPA were prepared according to the method of Block and Newman.[4] Aminated silica gel (5 μ, Polygosil 60-5 NH_2, Macherey-Nagel Co.) was used as a fixer of TAPA. Silica gel covalently linked with chiral TAPA was prepared according to the method of Mikes.[1] A TAPA content in the silica gel was calculated from the nitrogen content obtained by elemental analysis.

Apparatus. HPLC system (Model 204, Waters assoc.), slurry packing apparatus (Model 124, Chemco), and columns (0.39 cm O. D. × 30 cm I. D. and 0.8 cm × 25 cm) were used. Optical rotations were measured on an automatic recording spectropolarimeter (Model J-20A. Japan Spectroscopic Co.).

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