Helicenes. Resolution on Chiral Charge-transfer Complexing Agents Using High Performance Liquid Chromatography

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Summary The ten known carbohelicenes were rapidly and completely resolved by high performance liquid chromatography (h.p.l.c.) on short columns containing the optically active charge transfer (C.T.) complexing agent 2-(2,4,5,7-tetranitro-9-fluorenylideneamino-oxy)propionic acid (TAPA) or its 2-butyric acid homologue (TABA).

IN CONTINUATION of our studies on the separation of enantiomers by gas chromatography using selective interactions between chiral solutes and solvents,[1] we now report on the resolution of optical isomers by h.p.l.c.

Resolution of the helicenes, according to Wynberg's summary[2] 'has proved to be both exciting and frustrating.' Newman *et al.*,[3] who prepared the first (hexa) helicene, also showed that the compound could be resolved by crystallization from a solution containing optically active TAPA. Attempts to extend this approach to gravity liquid chromatography have not been too satisfactory, yielding at best only partial resolution, in spite of very long operation times.[4,5]

TABLE

Resolution of the enantiomers of penta- to tetradeca-helicenes by h.p.l.c. using short packed columns coated with a chiral complex forming agent.

Helicene	$\dfrac{k'^{a}}{k'_{\mathrm{ref}}}$	r^{b}	$[\alpha]^{23}_{28}{}^{c}$
Penta[d]	—	1·041	−1190
			+1970
Hexa[e]	1·52	1·112	+3570
	1·69		−3540
Hepta[e]	2·30	1·131	+4360
	2·60		−4570
Octa[e]	2·46	1·147	+6010
	2·82		−5520
Nona[e]	3·20	1·184	+7140
	3·79		−7380
Deca[e]	4·78	1·161	+5600
	5·55		−6100
Undeca[e]	5·10	1·158	+7200
	5·90		−6910
Dodeca[e]	5·76	1·200	+6300
	6·91		−6850
Trideca[e]	7·04	1·234	+6870
	8·69		−6050
Tetradeca[e]	7·77	1·268	+7620
	9·85		−7530

[a] On a TAPA column (20 cm × 2·3 mm i.d.), calculated with respect to pentahelicene (which was not resolved), $k'_{\mathrm{ref}} = 2·68$ at $u = 0·256$ cm s^{-1}. k' = capacity factor. [b] $r = k'$ (−)-(M)/k'-(+)-(P), the resolution coefficient for the two enantiomers. [c] Tentative [α] values measured on μg quantities, the concentration of which was determined by u.v. spectroscopy. Some samples contained impurities which may have interfered with the measurements. [d] Using (−)-TABA. Some racemization occurred during concentration of the sample. [e] Using (+)-TAPA.

We have recently been investigating h.p.l.c. technology, particularly for the resolution of optical isomers. This preparatory work has led to the introduction of complex-forming stationary phases,[6] and has resulted in the resolution of the helicenes (see Table).

Slurry-packed[7] silica gel (7μ) columns (20 or 40 cm × 2·3 mm i.d.) were coated *in situ*[8] with 10—25% of optically active TABA or TAPA (the acceptors). Helicenes (the donors) were eluted with cyclohexane–CH_2Cl_2, in which both TABA and TAPA are insoluble.

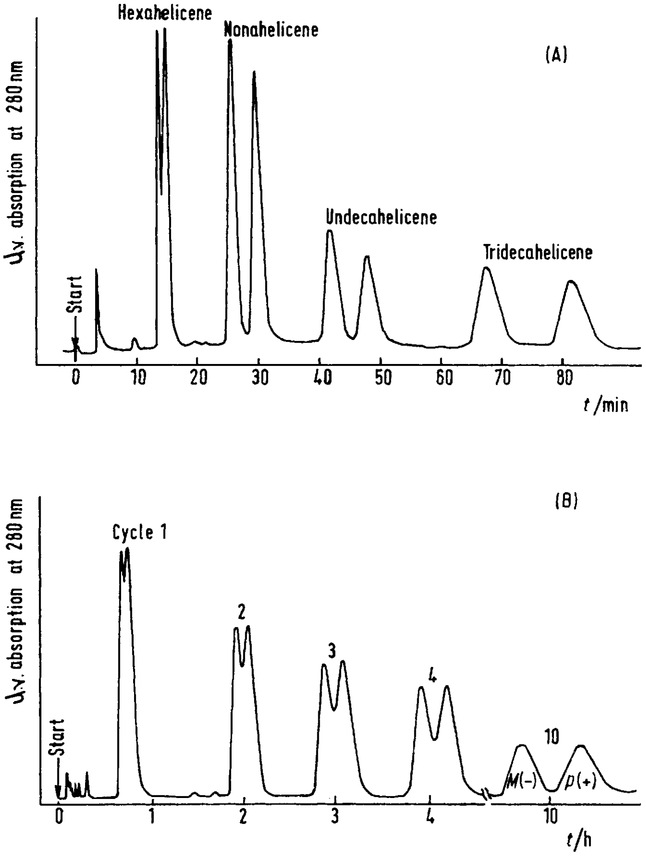

FIGURE. Typical chromatograms of helicenes. (A) Resolution of racemic hexa-, nona-, undeca-, and trideca-helicenes. For chromatographic conditions, see text and Table. (B) Resolution of penta-helicene using recycling.

Authentic samples of helicenes were supplied by various laboratories. The optical rotation of the isomers corresponding to the two peaks was measured for each of the helicenes. On (+)-TAPA, as well as (+)-TABA, the (+)-(P) isomer always precedes the (−)-(M) compound.[9] The quantities collected (μg) sufficed for the determination of [α] on a Perkin Elmer laser ultramicropolarimeter (λ 6328 Å), but the values are subject to a relatively large error and are therefore still tentative. The specific rotations compare well with the maxima values for the sodium D-line where available in the literature;[9–11] the difference in wavelength of measurement should be taken into account {*e.g.* for (−)-decahelicene, $[\alpha]_{6328} = -6100°$; $[\alpha]_{\mathrm{D}} = -7800°$, our measurements}.

Additional proof that resolution had occurred was obtained by the injection of enriched mixtures of some of the helicenes on columns coated, respectively, with the (+) and the (−) C.T. complexing agent, and observing peak inversion. Incidentally the use of such pairs of columns may be very useful for the recognition of the presence of chiral and achiral impurities, as well as their separation.

The hexa- to tetradeca-helicenes were readily resolved with TAPA at ambient temperature. The Figure (A) shows a chromatogram for a mixture containing 2 μg each of hexa-, nona-, undeca-, and trideca-helicene. Complete resolution (R_S[12] 1·25) was achieved in 10—60 min, depending on the compound considered. The resolution coefficients (*r*) increase in general with the number of rings with the exception of deca- and undeca-helicene. The relatively high *r* value for nona-helicene, in which the *ortho* edges in the terminal positions of the helix are 'para' to one another, is interesting.

Pentahelicene showed no separation on TAPA; however, on TABA in which the alkyl substituent at the asymmetric carbon is increased by a methylene group, a beginning of resolution was detected. At 0 °C and with recycling on a 2 × 20 cm column, complete resolution was achieved in this case also, after 10 cycles (Figure, B). The k' (solute capacity factor) on (−)-TABA was 3·91 and 4·05 for (−)-(*M*)- and (+)-(*P*)-penta-helicene, respectively; u = 0·242 cm s^{-1}.

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[11] Optically pure octa-, nona-, deca-, undeca-, and trideca-helicenes have recently been synthesised starting from optically pure hexahelicene-2-carboxylic acid (V. Libert, and R. H. Martin, personal communication).

[12] R_S is the resolution function, the total measure of component peak separation at their apexes and baselines; see L. R. Snyder and J. J. Kirkland, 'Introduction to Modern Liquid Chromatography,' Wiley, New York, 1974, p. 35.