

Binaphthyl-2,2'-diyl Hydrogen Phosphate. A New Chiral Atropisomeric Selector for the Resolution of Helicenes Using High Performance Liquid Chromatography

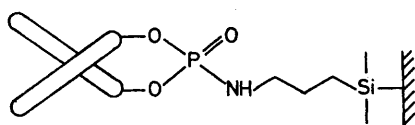
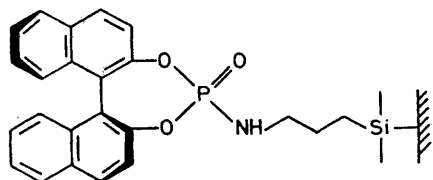
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Summary On chiral cyclic atropisomeric binaphthyl-2,2'-diyl hydrogen phosphate linked to silica gel, dinaphtho-[1,2-*d*;1',2'-*d'*]benzo[1,2-*b*;4,3-*b'*]dithiophen (I), 8,20-dibromodiphenanthro[4,3-*a*;4',3'-*j'*]chrysene (II), a dibromohexahelicene (III), and hexa-, hepta-, octa-, nona-,

trideca-, and tetradeca-carbohelicenes were partially resolved, and 9,10-diaza[7,8; 11,12]dibenzoheptahelicene (IV) completely resolved using high performance liquid chromatography (h.p.l.c.).

PREVIOUSLY, we have reported^{1,2} on the resolution of carbohelicene selectands† on the chiral charge transfer selector‡ 2-(2,4,5,7-tetranitrofluoren-9-ylideneamino-oxy)-propionic acid (TAPA) and its homologues. We now report the introduction of a new cyclic selector binaphthyl-2,2'-diyl hydrogen phosphate (BPA)‡ for the resolution of helicenes, especially those containing heteroatoms or electron-donating substituents.



P(+)-BPA

Although BPA was first synthesized in 1928,³ its only application to enantiomer resolutions was the preferential ion pair crystallization with one enantiomer of 7 aromatic amino-compounds using P(+) BPA.⁴ No resolutions of axially chiral compounds using BPA or its application to chromatographic systems have been reported before.

The binaphthyl unit of BPA together with its 7-membered phosphadioxepin ring (which helps to fix the spatial conformation of its binaphthyl planes) form a pentahelicene-like configuration. One might expect the easy resolution of all racemic helicenes on this selector. However on a linked BPA§ column only the hepta-, trideca-, and tetradeca-carbohelicenes showed small resolution effects (shoulder preceding main peak) at room temperature (see Table). By decreasing the column temperature to 2 °C resolution effects were also observed for the hexa-, octa-, and nona-carbohelicenes and the resolution factors for those previously mentioned were increased. The highest resolution factor was observed for the heptahelicene which was ca. 25%

† Selector and selectands are terms for resolving agent and sample input, respectively. These terms were introduced by us at the 11th International Symposium on Chromatography, Birmingham 1976 (ref. 2).

‡ Because of the cyclic, helicene-like character of BPA we use for this selector the helicene nomenclature established by the 'helicity rule.' A right handed helix is denoted by P (plus) and a left handed helix by M (minus).

§ BPA was synthesized and resolved according to the procedure in ref. 4 and linked as described in ref. 2. P(+) BPA has m.p. 217°C and gave satisfactory elemental analysis; i.r. (KBr) 1305, 1230, 1205, 1050, 990, 960, 950, and 890 cm⁻¹; [α]_D²⁵ +575° (MeOH). The optical purity of P(+) BPA was also confirmed by the n.m.r. spectrum of its methyl ester protons (34μ equiv.) in the presence of the chiral shift reagent tris[trifluoroacetyl-(+)-camphor]europium (34μ equiv.): δ_{Me} (CDCl₃), (+)BPA-Me ester 4.50 and 4.68; (±)BPA-Me ester 4.50 and 4.55; 4.68 and 4.73 (Δδ 3.0 Hz for the Me doublets). (The ¹H n.m.r. work was carried out at the Weizmann Institute of Science, Rehovot, Israel.)

TABLE.

Resolution of the enantiomers of helicenes by h.p.l.c. using a chiral binaphthyl-2,2'-diyl hydrogen phosphate selector

Helicene	<i>k'</i> ^a (2 °C)	<i>r</i> ^b (25 °C)	<i>r</i> ^b (2 °C)
Dithia-hepta (I) ^c ..	5.15 5.44	1.04	1.06
Dibromo-double (III) ^d	16.1 18.2	1.12	1.13
Dibromo-hexa (II) ^e ..	35.8 39.2	1.08	1.09
Diaza-hepta (IV) ^f ..	52.4 59.8	1.12	1.14
Hexa ^g	3.77 3.92	—	1.04
Hepta ^g	4.79 5.08	1.04	1.06
Octa ^g	5.38 5.62	—	1.04
Nona ^g	7.00 7.23	—	1.03
Trideca ^g	16.10 16.73	1.03	1.04
Tetradeca ^g	17.38 18.29	1.04	1.05

^a On P(+) BPA linked through a 3-aminopropyl spacer to 5 μ silica gel (column 20 × 0.23 cm i.d.), mobile phase n-hexane, *k'* = capacity factor = (retention volume of peak - dead volume)/(dead volume). ^b *r* = resolution factor = (*k'* of more retained enantiomer)/(*k'* of less retained enantiomer). For helicene structures see ^c M. B. Groen, H. Schadenberg, and H. Wynberg, *J. Org. Chem.*, 1971, **36**, 2797; ^d R. H. Martin, C. Eyndels and E. Defay, *Tetrahedron Letters*, 1972, 2731; ^e hexahelicene (50 μg) was brominated in carbon tetrachloride at 70 °C during 1 h; the mass spectra of the h.p.l.c. purified product confirmed the dibromination (see text), but the position of the bromine atoms has not yet been determined; ^f H. Rau and O. Schuster, *Angew. Chem.*, 1976, **88**, 90; ^g H. Martin, *Angew. Chem. Internat. Edn.*, 1974, **13**, 649 (an excellent review of the helicenes, especially carbohelicenes).

resolved (*R*_s¶ 0.27). A heteroheptahelicene containing two sulphur atoms (I) showed similar chromatographic behaviour to the heptahelicene containing all benzene rings.

Significantly better resolutions were obtained with a dibromo double (II) and a diaza dibenzo hepta (IV) helicene (see Table and Figure). At 2 °C base line resolution (*R*_s 1.26) of compound (IV) was achieved.

These results suggested that increasing the electron-donating capacity of the helicenes would lead to their better resolution. Hexahelicene was therefore brominated to give the dibromo derivative (III) (*m/e* 484, 486, and 488).

¶ *R*_s is the resolution function: (difference in the retention times of the two enantiomers)/(sum of the peak widths at half height).

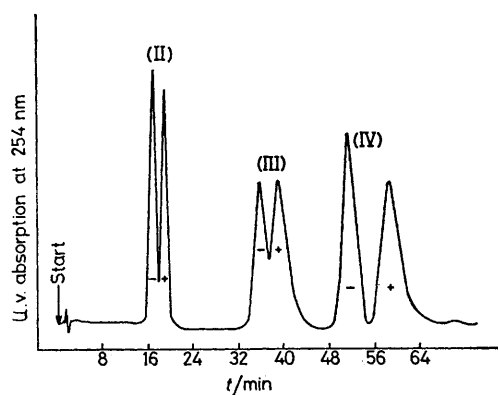


FIGURE. Resolution of helicenes containing heteroatoms or electron donating substituents on a linked P(+) BPA column. Mobile phase, n-hexane. Flow rate 0.5 ml/min.

Whereas no resolution effect could be observed for hexahelicene at room temperature, the dibromo derivative could be *ca.* 50% resolved (R_s 0.48). At 2 °C the resolution was further improved (see Table and Figure).

Polarimetric measurements of the peaks collected after chromatography showed that the M(-) helicene enantiomer always precedes the P(+) isomer on P(+) BPA. Additional proof that resolution had occurred was obtained by injecting the enantiomers collected from the P(+) BPA column on M(-) BPA and observing peak inversion.

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