Application of a New Resolution Method to Chiral Epoxides, Arene Oxides, and Alcohols

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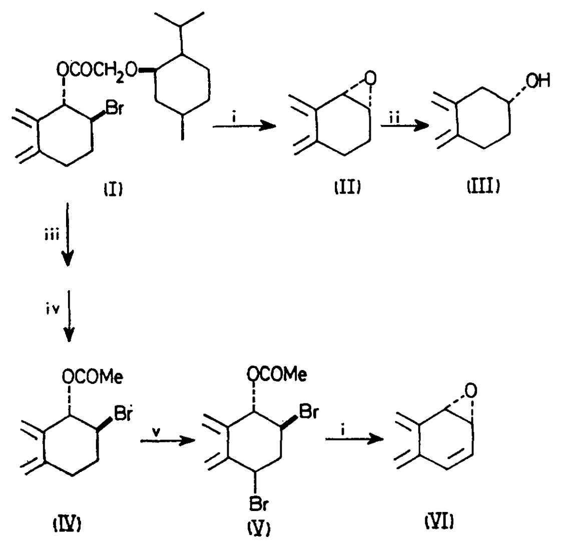
Summary A chromatographic method for separating the diastereomers of *trans*-2-bromo-1-menthoxyacetoxy-1,2,3,4-tetrahydronaphthalene (or the tetrahydroanthracene analogue) has facilitated the synthesis of 1,2-epoxy-1,2,3,4-tetrahydro-2-hydroxy-1,2,3,4-tetrahydro-, and arene 1,2-oxide derivatives of naphthalene or anthracene in high optical yield.

ARENE-OXIDES have been established as initial intermediates during the metabolism of aromatic rings by plants, animals and micro-organisms.[1] However, the study of stereopreference for a particular enantiotopic face of an arene or of enantioselectivity during further enzymatic transformation of the arene oxide intermediates has to date been virtually precluded as a result of the chemical instability

TABLE. Specific rotation of chromatographic fractions and further reaction products[a] [absolute stereochemistry]

Parent hydrocarbon	(I) ⟶	(II) ⟶	(III)	
Naphthalene	−140[1*R*:2*R*]	+126[1*R*:2*S*]		
Naphthalene	−122[1*R*:2*R*]	+108[1R:2*S*]	−44[2*S*][b]	
Anthracene	−118[1*R*:2*R*]	+133[1*R*:2*S*]	−47[2*S*][c]	
	(I) ⟶	(IV ⟶	(V) ⟶	(VI)
Naphthalene	−25[1*S*:2*S*]	+15[1*S*:2*S*]	+12[1*S*:2*S*]	−21[1*S*:2*R*]
Anthracene	−118[1*R*:2*R*]	−129[1*R*:2*R*]	−203[1*R*:2*R*]	+214[1*R*:2*S*]
Anthracene	−11[1*S*:2*S*]	+127[1*S*:2*S*]	+174[1*S*:2*S*]	−203[1*S*:2*R*]

[a] $[\alpha]_{589}°$ in $CHCl_3$. [b] ⩾ 63% optical purity. [c] ⩾ 90% optical purity.



i, NaOMe; ii, LiAlH₄; iii, B_2H_6; iv, $(MeCO)_2O$; v, *N*-bromosuccinimide

and unavailability of discrete arene-oxide enantiomers.[2] We now report a convenient synthetic route to epoxides, arene oxides and alcohols of high optical purity.

trans-1-Hydroxy-2-bromo-1,2,3,4-tetrahydronaphthalene or *trans*-1-hydroxy-2-bromo-1,2,3,4-tetrahydroanthracene were each treated with (−)-menthoxyacetyl chloride in pyridine to give a diastereomeric mixture of bromomenthoxyacetates (I). These diastereomers were separated by short column chromatography[3] [Kieselgel G (Merck)] using light petroleum–ether (90:10) as eluent. The specific rotation of several chromatographic fractions obtained after one passage down the column (120 mm diameter) is shown in the Table. The optical purity and absolute configuration determinations are based upon the known[2,4] stereochemistry of the alcohols (III). The efficiency of separation depended upon the column loading and as expected, *trans*-1-menthoxyacetoxy-2-bromo-1,2,3,4-tetrahydronaphthalene was obtained in a higher state of diastereomeric purity ($[\alpha]_D$ −147°) by a further pass down the column.

The chemical reaction sequences (I) → (II) → (III) and (IV) → (V) → (VI) were carried out using the same or slight modifications of the previously reported synthesis of naphthalene 1,2-oxide.[5] The interchange of ester groups [(I) → (IV)] which was effected by using the selective reducing properties of diborane followed by acetylation, was necessary since *N*-bromosuccinimide bromination occurred preferentially at the menthoxyacetoxy side chain.

Whereas optically active naphthalene 1,2-oxide showed the low thermal stability normally associated with non-K region arene oxides, the separated enantiomers of anthracene 1,2-oxide proved to be stable at ambient temperature for several weeks. The optical rotation of (+)-anthracene 1,2-oxide ($[\alpha]_{589}$ + 214°) could not be increased by multiple recrystallization and it is considered that this constitutes the first example of an optically pure arene oxide. This optical rotation also remained constant during an extended period of observation (> 24 h) indicating that the arene-oxide ⇌ oxepin equilibrium does not occur to any detectable degree in anthracene-1,2-oxide.

The application of this resolution technique to other epoxides, arene oxides and alcohols in the polycyclic hydrocarbon series and an associated biological study of the optically active arene oxides is currently under way.

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