(1*S*,2*S*)-(+)- and (1*R*,2*R*)-(−)-1,2-Diphenylcyclopropane from their Racemic Mixture by Liquid Chromatography on Triacetylcellulose

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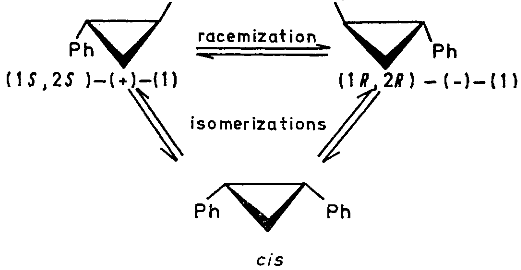
Summary The title compounds were isolated with 86 and 100% enantiomeric purity, respectively, and characterised by their rotations and c.d.-spectra.

The detailed mechanism of the stereomutation of cyclopropanes has interested chemists for a long time and cyclopropane isomerisations are among the most widely studied of all unimolecular reactions. In order to evaluate the mechanistic possibilities (*e.g.* stereo-random trimethylene biradical, single and double methylene rotation in a 0,0-diradical *etc.*) the study of optically active cyclopropanes



(1)

has proven to be an essential tool (*e.g.* reaction 1).[1] These compounds were prepared by conventional asymmetric syntheses, involving standard resolution techniques and stereospecific chemical transformations. It would, of course, be a useful achievement if some of these materials could be obtained conveniently in high enantiomeric purity from their racemic mixtures by simple chromatographic techniques.

We report here the isolation and characterisation of the title compounds (+)- and (−)-(**1**) (equation 1) from racemic material[2] by liquid chromatography. (±)- (**1**) was conveniently separated on microcrystalline, swollen triacetylcellulose[3] (2 columns of 30 cm length, 25 mm inner diameter, particle size 0·03—0·06 mm, flow rate 140 ml h^{-1}, *P ca.* 10 atm, 22 °C) using absolute ethanol as eluant. Both the angle of rotation and absorbance were recorded continuously (*cf.* Figure). 150 mg samples of (±)-(**1**) led to the isolation of 30 mg of (+)-(**1**), $[\alpha]_D^{22}$ 362°, $[\alpha]_{365}^{22}$ 1715° (CHCl$_3$, *c* 0·038) and 55 mg of (−)-(**1**), m.p. 31—32 °C, $[\alpha]_D^{22}$ − 407°, $[\alpha]_{365}^{22}$ − 1886° (CHCl$_3$, *c* 0·028) with 86 and 100% enantiomeric purity, respectively. The enantiomeric purities were determined independently by a new method[4] using analytical chromatograms (*cf.* Figure) of the two samples isolated by preparative separation. Since the overlap of the (+)- and (−)- peaks in the Figure is weak, the areas under the α/v curve represent good approximations for the relative concentrations of the enantiomers. This approximate method yields enantiomeric purities for samples of (+)- and (−)- (**1**) of 84 and 100%, respectively, which are close to the purities given above. Further support for the optical purities is derived from the c.d.-spectra of (+)- (**1**): θ_{230} 80,500 deg cm^2 dmol^{-1}, θ_{262} 11,500, θ_{269} 15,300, θ_{276} 12,500 (n-hexane, 1·51 × 10^{-4} mol l^{-1}),† and θ_{235} 49,000 (CHCl$_3$, 1·96 × 10^{-3} mol l^{-1}), and (−)-(**1**), $[\theta]_{230}$ −98,000, $[\theta]_{262}$ −13,000, $[\theta]_{268}$ −17,500, $[\theta]_{276}$ −14,500 (n-hexane, 1·51 × 10^{-4} mol l^{-1}), and $[\theta]_{235}$ −65,000 (CHCl$_3$, 1·44 × 10^{-3} mol l^{-1}), whose absolute configurations have already been determined by chemical correlation.[5a,b,6] Both enantiomers were completely free from impurities as determined by v.p.c. and h.p.l.c. The ^{1}H n.m.r. spectra in CDCl$_3$ showed a small impurity at δ 1·5, probably owing to a trace of water.

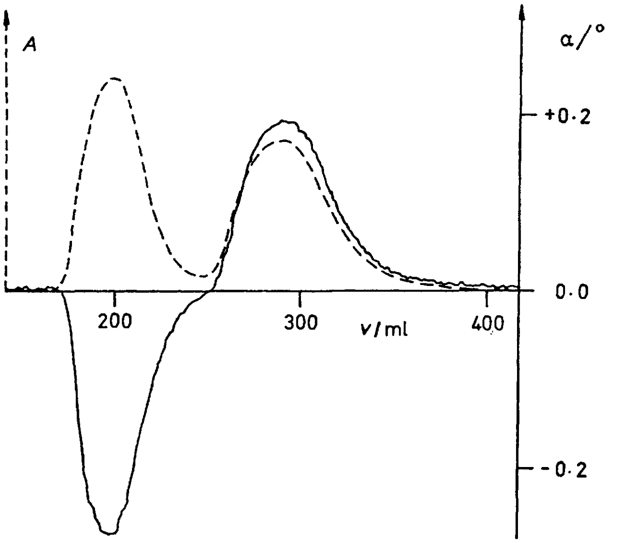


FIGURE. Analytical chromatogram of 15 mg of (1*R*,2*R*)-(−)- and (1*S*,2*S*)-(+)-(**1**) in absolute ethanol. α: angle of rotation at 365 nm; *A*: absorbance at 254 nm; *v*: volume of eluate; injection at v = 0; see text for further details.

The isolation of optically pure (−)- (**1**) allows an evaluation of earlier literature data in which the preparation of (+)- and (−)- (**1**) was carried out *via* asymmetric synthesis. It turns out that most preparations gave only low optical yields (8—25%)[5] with one exception[6] in which (+)- and (−)-(**1**) were prepared conventionally in high optical purities (100 and 64%, respectively) *via* degradation of the corresponding 2-phenylcyclopropane carboxylic acids.‡

Thus, liquid chromatography on triacetylcellulose seems to be effective in separating phenyl-substituted compounds of widely differing structures.[3,4]

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† The measured values are not corrected for 100% optical purity.

‡ Since no criteria for the optical purity were then available, the authors (ref. 6) might not have realized that they actually had obtained pure (+)-(**1**).

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