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Dibenzyl ($^{12}CH_2{}^{13}CH_2$) Sulphoxide — An Example of Optical Activity due to Isotopic Dissymmetry of Carbon

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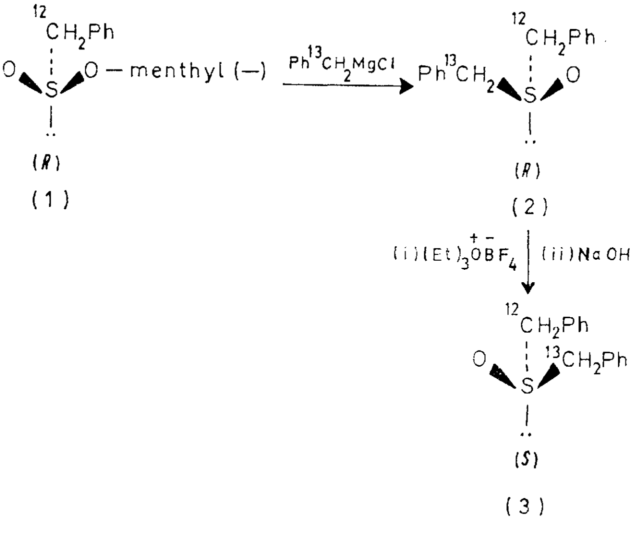
Summary (*R*)-Dibenzyl sulphoxide ($Ph^{12}CH_2SO^{13}CH_2Ph$), $[\alpha]_{280} = +0{\cdot}71$, has been obtained by treatment of (*R*)-(+)-menthyl toluene-ω-sulphinate with $Ph^{13}CH_2MgCl$ and converted into the enantiomer by *O*-alkylation and hydrolysis.

OPTICAL activity due to isotopic dissymmetry has been reported for hydrogen isotopes[1] and for oxygen isotopes.[2] Recent availability of ^{13}C compounds of high isotopic purity suggested the possibility of obtaining compounds showing optical activity due to isotopic dissymmetry of carbon. Because the expected degree of activity was small, a suitable system required a stereospecific conversion occurring in high yield, preferably with known steric course from a starting material of high enantiomeric purity and known absolute configuration yielding a readily purifiable product. Ideally, as an additional authentification of any optical activity discernible, the product should itself be capable of being converted stereospecifically into other simple asymmetric derivatives and should also be capable of being converted in a non-destructive procedure into an achiral compound. These criteria have been embraced in a synthesis of [α-^{13}C]dibenzyl sulphoxide from menthyl toluene-ω-sulphinate (Scheme).



[α-^{13}C]Benzyl chloride, of *ca.* 90% isotopic purity, was treated with magnesium in ether under nitrogen and subsequent reaction with menthyl toluene-ω-sulphinate (**1**)† at −40 °C gave the sulphoxide (**2**) (47%) after chromatography twice on silica gel in ether–light petroleum. The product was thrice recrystallised from ethanol-water, conditions shown by optical rotatory dispersion to remove all detectable menthyl ester from a specimen of the isotopically normal (inactive) sulphoxide artificially contaminated with 0·5% of the active menthyl ester. The sulphoxide thus obtained had the o.r.d. shown in the Table.

Table.

Optical rotatory dispersion of (*R*)- and (*S*)-Ph^{12}CH$_2$SO^{13}CH$_2$Ph

λ	280	285	290	295	300	310	320
(*R*)-Sulphoxide[a]	+0·71		+0·35		+0·13	+0·04	0
(*S*)-Sulphoxide[b]	−0·49	−0·36	−0·26	−0·17	−0·10	—	—
(+)/(−)	0·69	—	0·74		0·77	—	—

[a] 56·2 mg ml^{-1} in CHCl$_3$ [b] 40·4 mg ml^{-1} in CHCl$_3$.

Reaction at nuclear carbon in reactions of benzylic Grignard reagents is well known.[4] In this instance, such reaction would lead to optically-active benzyl *o*- and/or *p*-tolyl sulphoxides of high rotatory power[5] and the product would thus show spurious activity. Isotopically normal dibenzyl sulphoxide, obtained from the menthyl ester in an identical manner, showed no rotation in the range 280—320 nm.

The absolute configuration of the sulphoxide may be assigned as (*R*). Displacement of menthol from the (*R*)-sulphinate occurs with inversion of configuration.[3]

Treatment of sulphoxides with triethyloxonium fluoroborate and subsequent alkaline hydrolysis of the *O*-alkyl sulphoxonium salt[6] inverts the configuration at sulphur. Application of this procedure to the ^{13}C sulphoxide gave, after four recrystallizations from aqueous ethanol, inverted sulphoxide (**3**) in 44% yield (*ca.* 70% inversion). The o.r.d. is given in the Table.

Treatment of the sulphoxide with *N*-aminophthalimide and lead tetra-acetate in dichloromethane[7] gave the *N*-phthalimidosulphoximine (71%). This reaction is known[8] to occur stereospecifically with retention of configuration at sulphur. The sulphoximine, however, absorbed too strongly in the range 280—320 nm for rotation measurements to be made.

The 100 MHz ^{1}H n.m.r. spectrum (CDCl$_3$, Me$_4$Si) of the ^{13}C-sulphoxide gave, besides the aromatic protons at δ 7·34, two quartets, part of an ABX spectrum, centred at δ 4·59 and 3·18 [^{13}CH$_2$, J (^{13}CH) 141, J_{HH} 13] and a second set of closely spaced quartets centred at δ 3·89 [^{12}CH$_2$, J (^{13}CH) 3·5, J_{HH} 13]. The ^{13}C content was 92% as calculated from the areas of the ^{13}CH$_2$ and ^{12}CH$_2$ absorptions. The n.m.r. spectrum (CDCl$_3$, Me$_4$Si) of the ^{13}C-sulphoximine gave single peaks for the benzyl protons at δ 5·18, 4·48, and 3·88.

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† (*R*)-menthyl toluene-ω-sulphinate had the physical constants obtained previously.[3] The optical purity was estimated to be > 91% by conversion with *p*-tolylmagnesium bromide into benzyl *p*-tolyl sulphoxide.

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