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CORRELATED INTERNAL ROTATION IN BIS(2,6-DICHLORO-9-TRIPTYCYL)METHANE. TO WHAT EXTENT CAN PHASE ISOMERS BE SEPARATED AND IDENTIFIED ?

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The title compound was separated by HPLC into the stereoisomers (one meso and four racemic compounds) due to the asymmetric bridgehead carbons and the correlated internal rotation. Optical resolution of the racemic compounds was performed by HPLC using a chiral support.

The strictly coupled disrotation around the two adjacent bonds connecting the central to the bridgehead carbon atoms in bis(9-triptycyl)methane and the corresponding ether gives birth to unique stereoisomerism, when the benzene rings are suitably labeled.[1,2] These stereoisomers differ only in the phase relationship between the labeled benzene rings.[3] Since the coupled rotation is rapid, the difference in their physico-chemical properties is considered to be intrinsically small as averaged over many possible conformations. Separation of the 2- and 3-chloro methanes and ethers [1a,c] and the 2,3-dimethyl methane [2b,d] into the racemic and meso isomers was, however, achieved by the liquid chromatographic method. More recently, the racemates of the 2- and 3-chloro substituted methanes and ethers were resolved into the optical antipodes.[1d] The separation and identification are expected to become increasingly difficult when the number of such isomers increases by multiple labeling. We describe here successful separation and partial assignment of all the possible stereoisomers (predicted to consist of one meso and four pairs of dl isomers)[4] of bis(2,6-dichloro-9-triptycyl)methane (**1**).

When the asymmetric centers (the bridgehead carbons in the present case) of two constitutionally equivalent structures (R/S) are connected by a methylene group, two diastereomers, namely, the meso (RS) and racemic (RR/SS) are produced. The former is further divided into a new meso (meso) and a dl pair (dl_1), and the latter into three pairs of new racemic isomers (dl_2, dl_3 and dl_4) in **1** with the strictly geared internal rotation. Accordingly, the meso and dl_1 isomers on the one hand, and the dl_2, dl_3 and dl_4 on the other, should be differentiated experimentally either by starting the preparation from the chiral components or by effecting the mutual interconversion within each generic group by the gear slippage process at elevated temperatures. The six conformers of each isomer are shown in Figure 1 by assuming the C_2 symmetry of the bis(9-triptycyl)methane skeleton.[2c,d] None of the conformers (a ~ f) of dl_1 is identical to another and all the benzene rings are non-equivalent. They are in three dl pairs (g ~ i) in the meso isomer. The CH_2 protons are by symmetry diastereotopic in these two isomers. Conformers j, k, n, p, s and t are doubly degenerate and remaining conformers l, m, o, q, r and u, two in each isomer, have C_2 symmetry in the dl_2, dl_3 and dl_4 isomers. The CH_2 protons are enantiomeric in these cases.

Starting from 9-bromo-2,6-dichloroanthracene which in turn was obtained in three steps from disodium 9,10-anthraquinone-2,6-disulfonate,[5] we obtained **1** in 6% overall yields in a manner similar to the preparation of bis(2- and 3-chloro-

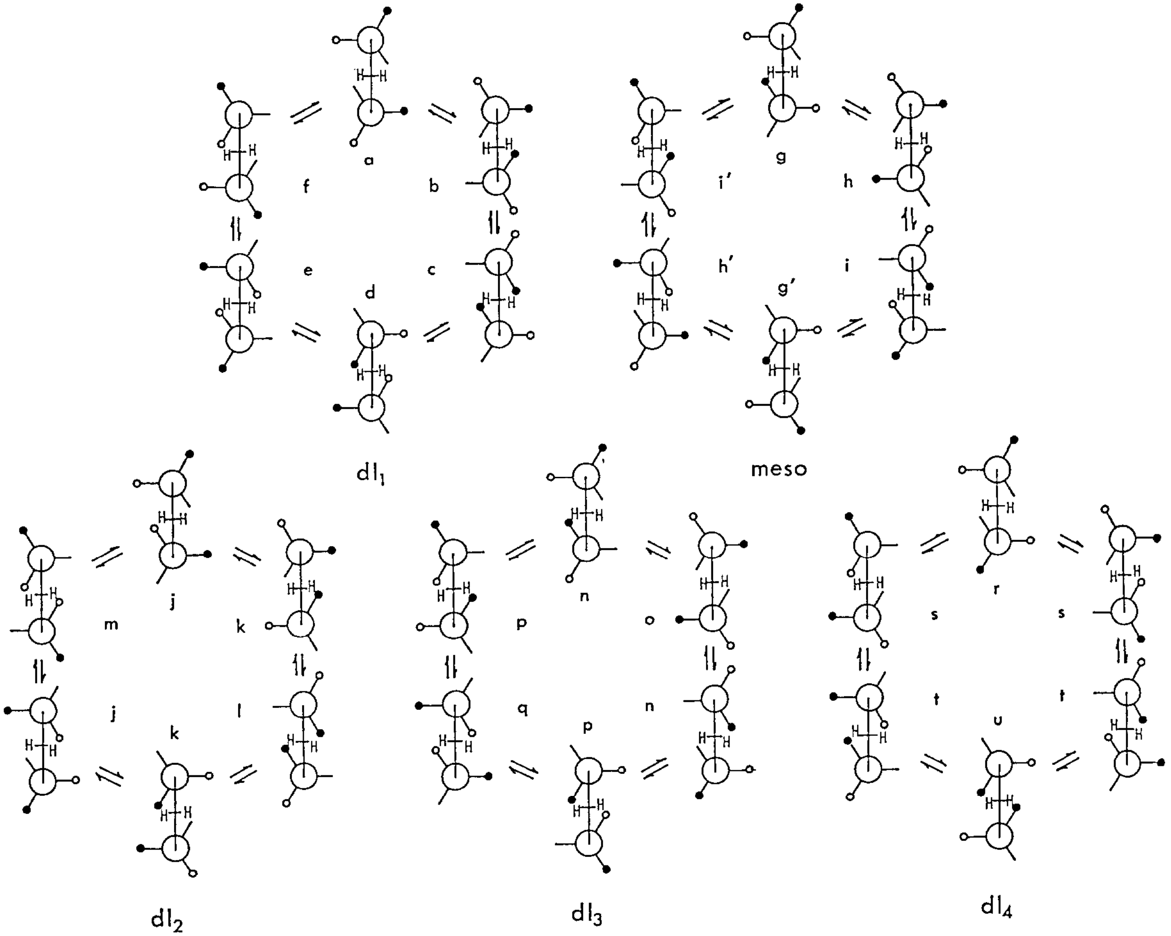


Figure 1. Gearing conformers a ~ u in the five diastereomers of **1**. The 2- and 6-chloro substituents are given by • and ∘, respectively. Only the RR configuration is shown here for dl_2 ~ dl_4.

9-triptycyl)methanes.[1a,c] HPLC of 1 on microsilica with 1% chloroform-hexane elution gave five peaks as shown in Figure 2a.[6] The base-line separation of the last two fractions was effected on a reversed-phase column with methanol-water (5:1 v/v) elution (Figure 2b).[6] Colorless granules, mp 317 ~ 318°C,[7] obtained from fraction 2 was heated under reflux in o-dichlorobenzene for 5 hr to give a chromatogram showing only peaks 2 and 3 in an intensity ratio of 1:2. Fraction 2 showed only eight quaternary ring carbons, six (attached to the bridgehead carbons) in the δ 140 ~ 150 region and two (attached to chlorine atoms) in the vicinity of δ 130, in the ^{13}C NMR spectrum. Fraction 3 revealed twelve and four signals in the corresponding spectral regions, respectively. Thus fractions 2 and 3 were unequivocally assigned to the meso and dl_1, respectively.

One (mp 268 ~ 269°C) of the remaining three isomers of the other group is unusual in that it has a much smaller retention volume than the other two, actually smallest among the five diastereomers. A rough estimation of the orientation of the C-Cl bond dipoles from molecular models indicates that dl_2 may be less polar and resemble the meso isomer, whereas dl_3 and dl_4 could be

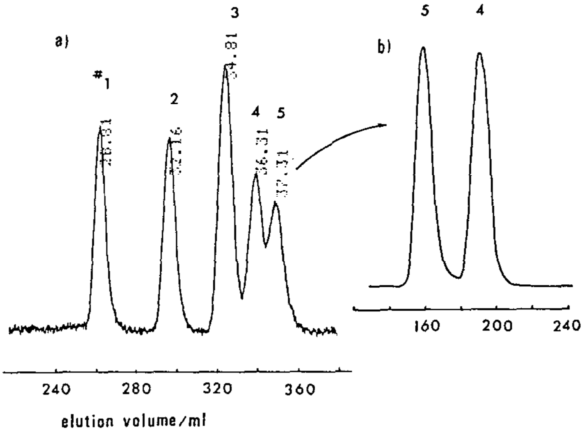
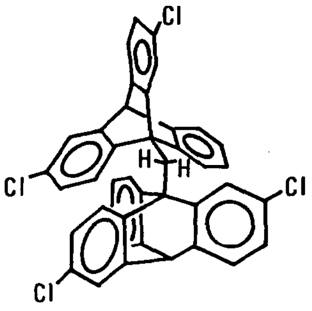


Figure 2. HPLC separation of the five diastereomers of 1. Columns were (a) µPorasil (3/8 in.×1ft) + Develosil(10×250 mm) and (b) µBondapak(3/8 in.×1ft).



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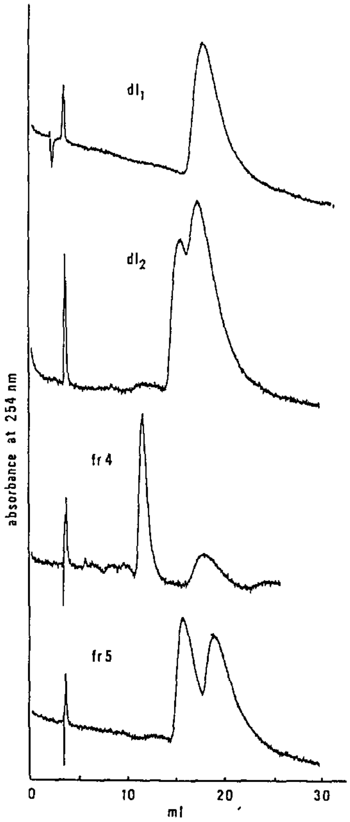

Figure 3. Optical resolution of the dl isomers of 1 by HPLC on a 4.6 × 250 mm column of microsilica coated with (+)-poly(triphenylmethyl methacrylate)(25 wt %) and kept at 13 ~ 14°C with 0.7 ml/min of methanol elution.

more polar and like dl_1 (see Figure 1).[8] Therefore, fraction 1 was tentatively assigned to dl_2. Fraction 4 (mp 278 ~ 280°C) and 5 (mp 202 ~ 204°C) still remain to be assigned to dl_3 and dl_4.

Optical resolution of the $dl_1 \sim dl_4$ diastereomers was attempted by HPLC using a column of silanized silica gel coated with chiral poly(triphenylmethyl methacrylate).[9] As seen in Figure 3, the three isomers in the second group were more or less separable into the optical antipodes, whereas dl_1 showed no sign of resolution. It may be the case that the R and S configurations at the bridgehead of dl_1 control more strongly the chiral recognition by the column and obscure the enantiomerism produced by less perturbing phase relationship between the chloro-substituted benzene rings.

References and Notes

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2) (a) W. D. Hounshell, C. A. Johnson, A. Guenzi, F. Cozzi, and K. Mislow, *Proc. Natl. Acad. Sci. U.S.A.*, **77**, 6961 (1980). (b) F. Cozzi, A. Guenzi, C. A. Johnson, K. Mislow, W. D. Hounshell, and J. F. Blount, *J. Am. Chem. Soc.*, **103**, 957 (1981). (c) H.-B. Bürgi, W. D. Hounshell, R. B. Nachbar, Jr., and K. Mislow, *J. Am. Chem. Soc.*, **105**, 1427 (1983). (d) A. Guenzi, C. A. Johnson, F. Cozzi, and K. Mislow, *J. Am. Chem. Soc.*, **105**, 1438 (1983).
3) Term "Phase isomerism" was adopted to describe the phenomenon giving birth to stereoisomers in which only the phase relationship between the labeled cogs is different in the rapidly rotating molecular gears[1] and corresponds to "residual isomerism" in the Mislow's papers.[2]
4) The number of isomers corresponds to substitution patterns #11 and 15 in ref. 2d.
5) Chlorination with $NaClO_3/HCl$, reduction with Al cyclohexoxide in cyclohexanol, and bromination with cupric bromide in chlorobenzene. The synthetic procedure of one-step addition of two benzyne molecules to the bis(9-anthryl)methane did not allow us to obtain the RS and RR/SS series separately.
6) HPLC was performed on a Waters model ALC/GPC 244 high-performance liquid chromatographic system. Flow rates were 4 ml/min.
7) Fractions 1 ~ 5 of **1** gave satisfactory analytical and ^1H and ^{13}C NMR data, except that the CH_2 protons of the dl_1 and meso isomers showed only a slightly broadened singlet at δ 4.69 and 4.71, respectively, in $CDCl_3$ at 100 MHz.
8) Conformers l and m are effectively non-polar.
9) Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, S. Murata, R. Noyori, and H. Takaya, *J. Am. Chem. Soc.*, **103**, 6971 (1981).

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