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THE CHIRAL STABILITIES OF "TRIMERIC KETONE PEROXIDES"

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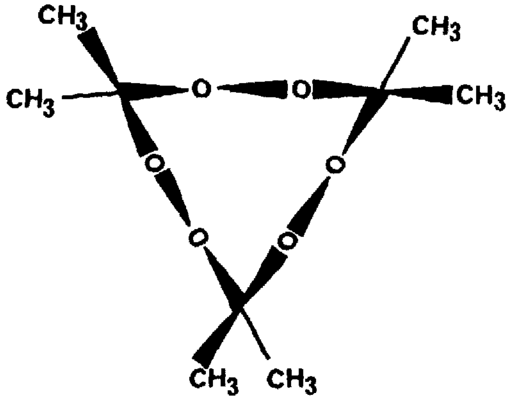
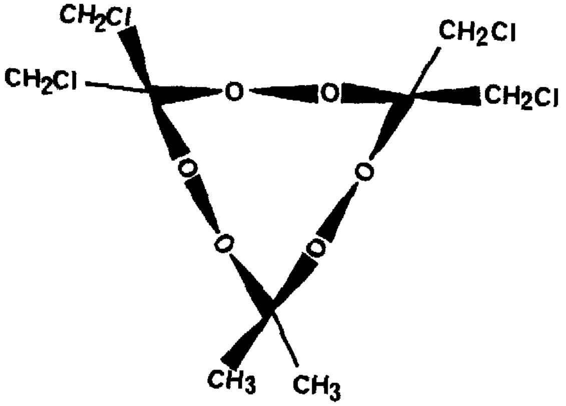
Summary The 251 MHz ^{1}H NMR spectrum of the methylene protons of the all-cis isomer of trimeric chloroacetone peroxide shows an AB quartet which remains sharp even at 155°C, indicating that the free-energy barrier for enantiomerization is higher than 24 kcal/mol, and that trimeric ketone peroxides are potentially resolvable at room temperature.

Ketones are known to form heterocyclic nine-membered trimeric peroxides upon reaction with hydrogen peroxide in the presence of mineral acids.[1] Although these compounds are explosive, they are synthetically useful.[2] The molecules of the crystalline compound (I) obtained from acetone have approximately D_3 symmetry, and the crystals of I are built up of pairs of enantiomeric molecules.[3] Although I does not contain any asymmetric carbon atom, it is a chiral molecule. Since we expected that the barrier to enantiomerization in I would be relatively high and might allow resolution of the compound at room temperature, we have investigated the enantiomerization barrier in I and related compounds by NMR methods. Actually, it has already been reported that the mixed peroxide (II) from 1,3-dichloroacetone and acetone gives an AB quartet for the methylene protons at room temperature.[4] The authors indicated that this could be due to either restricted rotation of the CH_2Cl group, or to an asymmetry of the ring system, but the effect was not investigated further.[5]

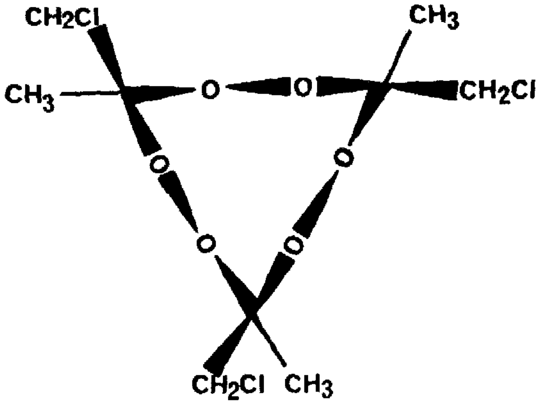
Another derivative of I with diastereotopic protons is the trimeric peroxide of chloroacetone (III).[6] It has been reported that III (mp 120° - 126.5°C) gives a single resonance for the methylene protons in CCl_4 solution at room temperature. We have repeated the preparation of III (yield 10%) and find that the compound gives a single methyl signal and a just resolvable AB quartet for the methylene group in CCl_4 at 60 MHz; in $CDCl_3$, however, the AB quartet is well



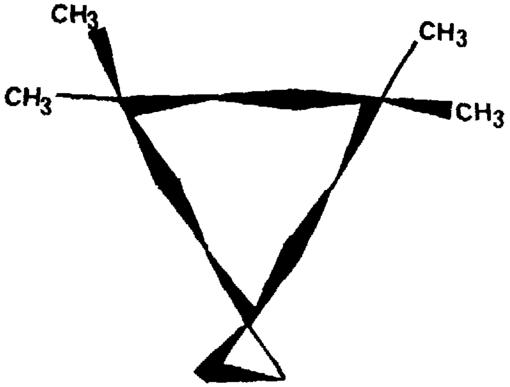
I



II



III



IV

resolved (ν_{AB} = 8.5 Hz, J_{AB} = 11.2 Hz). We have studied the temperature dependence of the AB quartet in **III** at 251 MHz in bromobenzene as a solvent. Although the relative chemical shifts of the AB protons decreased with increasing temperature, a sharp AB quartet (ν_{AB} = 30.0 Hz, J_{AB} = 11.2 Hz) was still visible at 155°C, the highest temperature investigated. The ^1H NMR spectrum of **III** was also investigated in $CHCl_2F$ in the temperature range -30° to -150°C, but no dynamic NMR effect was observed.

The presence of only a single methyl line and a single AB quartet is indicative of the all-*cis*-isomer, as shown in structure **III**. The low yield of **III** is also in agreement with this assignment, as the only other isomer (*cis*, *cis*, *trans*) has three times the probability of being formed as compared to the all-cis compound, on the likely assumption that enthalpy differences between the two isomers are negligible. The trimeric ketone peroxide residue obtained after the crystallization of III showed several overlapping AB quartets in the methylene region. Additionally, the ^{13}C NMR spectrum of III in $CDCl_3$ has single resonances at 17.2 ppm (CH_3), 42.6 ppm (CH_2Cl), and at 111.0 ppm (quaternary carbon) downfield from tetramethylsilane. There is thus little doubt that III has the all-cis configuration.

Restricted rotation in III almost certainly has a barrier lower than 10 kcal/mol. Ring inversion in III, on the other hand, is expected to have a quite high barrier because the methyl groups have to point inwards in intermediate conformations and the short C-O and O-O bonds make this effect be even more important than in the corresponding hexamethylcyclononane conformation. Although 1,1,4,4,7,7-hexamethylcyclononane is not known, the closely related spiro compound IV has been reported[7] to have a coalescence temperature above 80°C for the methyl groups. Compound III thus should have an even higher ring inversion barrier than has IV. The observed line widths of the AB quartet of III at 155°C was less than 2 Hz, and this leads to a minimum free-energy barrier for ring inversion in this compound of 24 kcal/mol. If entropy effects are small and can be neglected, the average lifetime before inversion of III should be more than a day at 20°C. The rate of racemization of I should be closely similar to that of III, as shown by an examination of molecular models.[8] Thus, I and related compounds potentially can be resolved into optically active forms at room temperature, although the lack of a reactive functional group makes a direct resolution a difficult task. Attempts to prepare optically active forms of trimeric ketone peroxides are being made.

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(5) The analogy given in reference 4 for possible restricted rotation in **II** [F. Kaplan and D. Weisleder, J. Amer. Chem. Soc., **88**, 4103 (1966)] actually refers to diastereotopic protons in a CH_2Cl group in a compound with an asymmetric carbon atom, and is not a case of restricted rotation with a high barrier. Thus, the only reasonable source of asymmetry in **II** that is sufficiently long lived to give rise to diastereotopic protons is the chirality of the ring skeleton.

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(8) Unfortunately, the sharp ^1H resonance of the diastereotopic methyl groups of **I** did not split in the presence of the chiral shift reagent, tris(3-(trifluoromethylhydroxymethylene)-d-campharato)europium(**III**), and thus this method could not be used to investigate the chiral properties of **I**. This failure may be due to the low basicity of the peroxide group, which would lead to a very weak complex with the shift reagent.