Stereochemistry of the Acetalization of Hexafluoroacetone with a Bromohydrin

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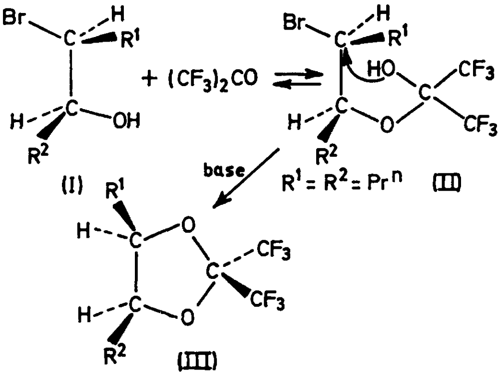
Summary Acetalization of hexafluoroacetone with *threo*- and *erythro*-5-bromo-octan-4-ol has been shown to be highly *trans*-specific by ^{19}F n.m.r., providing a method for establishing the stereochemistry of bromohydrins and their precursors when they are reacted stereospecifically.

The stereochemistry of acetal formation from bromohydrins (synthesized stereospecifically[1]) with hexafluoroacetone is established by the equivalence or non-equivalence, respectively, of the trifluoromethyl groups using ^{19}F n.m.r. spectroscopy. *threo-* and *erythro*-5-Bromo-octan-4-ol, derived from *cis-* and *trans*-oct-4-ene, were each treated (1 equiv) with hexafluoroacetone (1·5 equiv) in pentane containing tri-n-butylamine (1 equiv) in a sealed tube for two days at 75° and yielded acetals of greater than 97% isomeric purity.

Based on the scheme (I) → (II) → (III), the reaction would be predicted to proceed *via trans*-addition. The equilibrium (I) → (II) normally lies far to the right[2,3] and would be driven even further in the presence of base. Any conversion of bromohydrin into epoxide is either very small or gives the same products as shown.



The ^{19}F n.m.r. spectra of the isomeric acetals were run in a Varian Associates XL-100 spectrometer at 94·1 MHz as 20% solutions in $(CD_3)_2CO$ with 5% CCl_3F as the fluorine reference and deuterium as the lock signal. At the resolution used in this work, the four isotopic CCl_3F resonances were observed to have chemical shift differences of about 0·5 Hz and near theoretical values for the relative peak intensities.[4] The chemical shifts, at ambient temperature and without correction for concentration and solvent effects, are referenced to the low-field member of the CCl_3F cluster. The spectrum obtained for the acetal derived from *erythro*-5-bromo-octan-4-ol gave a very narrow triplet (ϕ 80·62 p.p.m.) produced by H–F coupling (J 0·6 Hz) with the methine protons which collapses to a very sharp singlet when the methine protons are decoupled. The acetal derived from the *threo*-bromohydrin gives a spectrum which indicates non-equivalent CF_3 groups typical of *cis*-geometry. A complex but symmetrical pattern (ϕ 79·88 p.p.m.) indicative of an A_3B_3 pattern complicated by H–F coupling, decoupled to a more complex splitting pattern having narrower lines when the methine protons were irradiated. Further interpretation of these data was not attempted.

Thus, addition of hexafluoroacetone to bromohydrins is a highly stereospecific reaction which is useful for characterizing bromohydrins derived from symmetrical alkenes. Extension to other alkenes is under investigation.

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