

DIRECT RADICAL SUBSTITUTION ON THE CUBANE SKELETON

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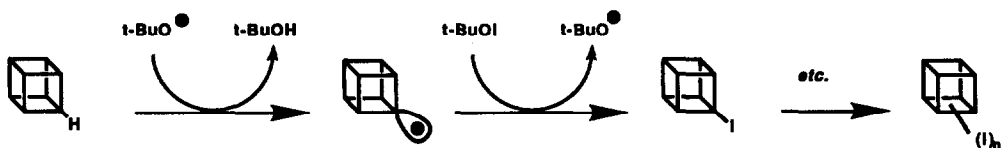
Summary: Radical iodination of cubane and derivatives occurs on irradiation with *tert*-butyl hypoiodite.

Cubyl radicals are certainly intermediate in reductive decarboxylations of cubane peresters,¹ in decarboxylative halogenations of cubane acids,² and in tin hydride reductions of halocubanes.^{2a,3} The geometry of the cage must constrain the cubyl radical to a highly pyramidalized configuration and place the unshared electron in an s-rich orbital. These factors will act to destabilize cubyl radical relative to *tert*-butyl radical.⁴ Although cubyl radical is accessible in decarboxylations and tin hydride reductions, these reactions have powerful driving forces. We were moderately surprised to find that the cubyl radical could be generated by direct homolytic cleavage of the cubyl carbon hydrogen bond in reactions less strongly driven.

The photochemically-induced reaction (tungsten lamp) of *tert*-butyl hypoiodite⁵ with cubane carboxylic acid suspended in 1,1,2-trichloro-1,2,2-trifluoroethane (Freon 113[®]) is known to give iodocubane.^{2a} When extending this procedure to the preparation of 1,4-diiiodocubane from the corresponding diacid, we noticed, in addition to the desired diiodide, formation of higher molecular weight material, principally 1,2,4-triiiodocubane. (Note that only one of the 6 triiodocubanes isomers can be formed by iodination-without-rearrangement of 1,4-diiiodocubane.) In a particular experiment 200 mmol of hypoiodite in 145 ml of Freon 113 and 15.6 mmol of suspended diacid were irradiated for 24 hours using a 200 watt tungsten lamp. Careful column chromatography gave 35% yield of 1,4-diiiodide^{2f} and 45% yield of 1,2,4-triiodide: mp 174-176 °C; ¹H-NMR (500 MHz, CDCl₃) δ 4.5-4.6 ppm (multiplet); ms (EI) base peak 228 (C₈H₅I₃ - I₂). The structure was confirmed by single crystal X-ray analysis.⁶

When the mixture of 1,4-diiiodocubane and 1,2,4-triiiodocubane was irradiated further with additional *tert*-butyl hypoiodite in Freon 113/carbon tetrachloride, the amount of triiodocubane increased at the expense of the diiodide and there appeared slowly new components at longer GC retention times (about 11 minutes on HP-1 versus 5 for the 1,4-diiiodide and 8 for the triiodide) and a trace of yet other products at a much higher retention time (14 minutes). In the mass spectra (GC/MS) of the first group there is a notable fragment ion at mass 354 corresponding to C₄H₄I₄ minus I₂ (*cf.* the mass spectrum of 1,2,4-triiiodocubane quoted above; the parent peak is usually not significant in iodocubanes.) We believe these "11 minute" components are some or all of the isomeric tetraiodocubanes (1,2,4,7-, 1,2,4,6- and 1,2,3,4-) which can arise from iodination of 1,4-diiiodocubane. One was concentrated by repeated chromatography on silica gel. Its structure was defined by NMR analysis as that of the 1,2,4,7-tetraiodide as only this isomer of the three possible can have the observed single line ¹H-NMR spectrum (4.78 ppm). The yet higher retention time material is thought to be a pentaiodocubane or a mixture of the isomers thereof.

Iodination of the cubane system with *tert*-butyl hypoiodite does not require the initial presence of iodine or carboxylic acid substituents on the cubane skeleton. Irradiation of the hydrocarbon cubane in Freon 113 with *tert*-butyl hypoiodite gives very quickly⁷ iodocubane, the three diiodocubanes, at least three triiodocubanes, at least two tetraiodocubanes, etc. The course of the reaction is shown in the scheme below in simple terms; the actual iodinating species and chain carrier may be more complex.^{5b,c}



Various chlorocubanes can be obtained similarly using *tert*-butyl hypochlorite as the halogenating agent. Although many of these compounds are interesting, it is not feasible to separate them from complex mixtures. The synthesis of individual halocubanes is best handled by a combination of ortho-metalation/halogenation chemistry⁸ and Barton thiohydroxamic acid ester decarboxylative halogenation.^{2c,9} Nevertheless, it is clear that cubyl radical can be generated easily by rupture of the CH bond. This might ultimately prove synthetically important for the production of very highly substituted cubanes (for which the isomer number is low) or for fully substituted cubanes.

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- (4) The rate constant for thermolysis at 80 °C of the *tert*-butyl perester of cubane carboxylic acid is about 1/200 that for the *tert*-butyl perester of pivalic acid [Luh, T.-Y.; Stock, L. M.; *J. Org. Chem.* **1978**, *43*, 3271].
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- (6) We are grateful to Richard Gilardi and Cliff George of the Naval Research Laboratory for this determination. Details will be published elsewhere.
- (7) As more iodine substituents are added to the frame, the reaction slows. Iodinations of carbomethoxycubanes are much slower than those of cubane. The electron-withdrawing substituent has a powerful retarding effect.
- (8) For example, Eaton, P. E.; Castaldi, G. *J. Am. Chem. Soc.* **1985**, *107*, 724.
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