Tetrahedron Letters,Vol.27,No.50,pp 6055-6058,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

OXIDATIVE DEIODINATION OF CUBYL IODIDES: A TACTIC FOR THE NUCLEOPHILIC INTRODUCTION OF SUBSTITUENTS ONTO THE CUBANE FRAMEWORK

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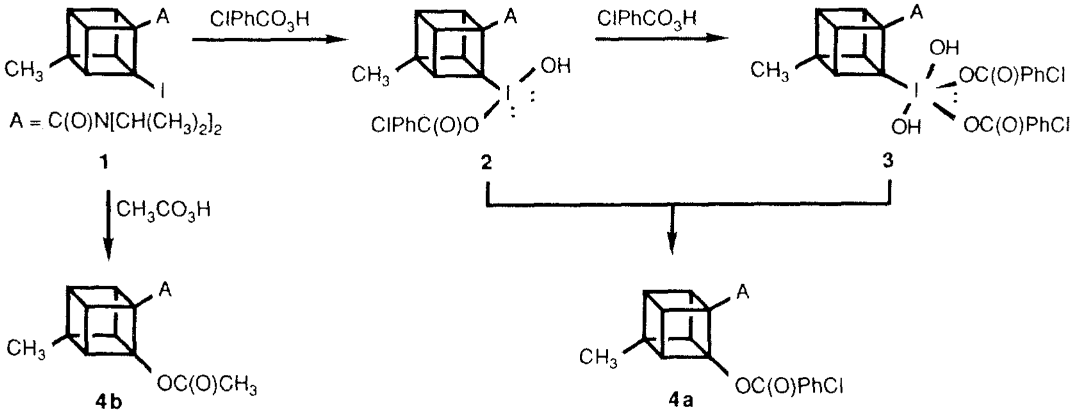
Abstract: Iodocubanes are oxidized by peracids, etc. to relatively stable hypervalent iodine species which upon mild, thermally-induced decomposition produce new cubanes in which the original iodide substituent is replaced.

Oxidation of alkyl iodides with peracids generates a hypervalent iodine substituent which is an exceptional nucleofuge; substitutions, eliminations, and/or rearrangements occur readily.[1] The dramatic increase in nucleofugacity of iodide upon oxidation to a hypervalent state is illustrated by the facile conversion of the otherwise solvolytically very stable 1- and 7-iodobicyclo[2.2.1]heptanes to the corresponding methyl ethers on oxidation of these iodides with m-chloroperbenzoic acid (mCPBA) in methanol.[1b] Such observations suggest that these reactions proceed via carbenium ion-like intermediates, even if at strained bridgehead positions. Extension of this oxidative deiodination/substitution chemistry to iodocubanes might offer an attractive route to substituted cubanes and some insight into the nature of the cubyl carbenium ion. Herein we report on our initial study of hypervalent iodocubanes.

Iodocubanes like 1 are now readily available as a result of the discovery in this Laboratory that LiTMP/$HgCl_2$ effectively mercurates cubyl amides and that the resulting cubane-mercury bond is cleaved easily by iodine.[2] Iodocubane 1 is quite reactive towards mCPBA. When 2 equivalents of mCPBA were added to a solution of 1 in $CDCl_3$ (approx. 10^{-1} M), 1 was consumed completely within 20 minutes (^{1}H-NMR monitoring). Clearly, oxidation had occurred at the iodide substituent for it could be reversed by washing the reaction mixture with aq. $Na_2S_2O_3$. When only one equivalent of the peracid was used, incomplete conversion occurred and an intermediate species could be observed. In analogy with the chemistry of aryliodides,[3,4] we speculate that these two compounds are the 10-I-3 and 12-I-5 hypervalent iodides 2 and 3, respectively,[3,4] but we have not characterized either of them. Both are stable for days at -20°C in $CDCl_3$ solution, but when the solution was heated at 55°C each decomposed within 4 hours with formation of cubyl benzoate 4a and regeneration of some 1. The extent of conversion was variable; at best we achieved 70% of 4a overall from 1. Addition of excess mCPBA did not improve the conversion, possibly because of peracid destruction catalyzed by the reaction by-products.[1a,c]

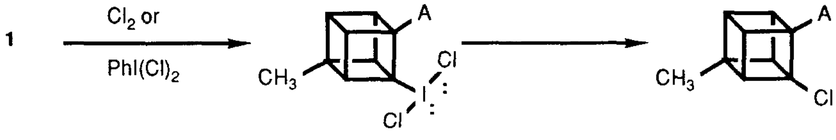


Consistently good conversions of 1 to the cubyl acetate 4b were achieved by oxidizing with excess peracetic acid in acetic acid. Thus, a vigorously stirred solution of 100 mg (0.27 mmol) of 1 in 1 mL of glacial acetic acid was treated with 0.4 mL (2.5 mmol) of commercial (FMC) 40% peracetic acid. Within 30 minutes a white precipitate formed. The mixture was stirred vigorously for 48 hours at ambient temperature, then partitioned between CH_2Cl_2 and 10% aq. Na_2SO_3 . The organic phase was washed with 3% aq. NaOH, dried ($MgSO_4$), and concentrated under vacuum leaving a pale yellow oil contaminated with approx. 10% of 1. Chromatography on silica gel (20 g), eluting with 15 vol.-% EtOAC in $CHCl_3$, gave 55 mg (65%) of 4b as a pale yellow oil, readily identifiable spectroscopically.[5]

In contrast to the results of Kropp and Davidson on the oxidation of 1- and 7-norbornanyl iodides in methanol,[1b] no incorporation of methanol was observed on oxidation of iodocubane 1 therein; only 4a was formed (about 30% conversion). This needs more careful study, but the lack of solvent incorporation suggests that discrete carbenium ion intermediates are not present during the decomposition of the hypervalent iodocubane. In this regard, the reaction appears similar to that of the aryl counterparts for which ion pair and homolytic pathways have been postulated.[6]

Iodocubane 1 can be oxidized with chlorine to the iododichloride 5.[7] In $CDCl_3$, 5 decomposed at room temperature in the dark within 10 hours to give complete conversion to chlorocubane 6. Attempts to introduce other nucleophiles through a ligand exchange on 5 with Ag(I) salts[3a,8] were unsuccessful; the salts seemed only to accelerate the conversion of 5 to 6. Bromine is also capable of oxidation/halide exchange on 1.[9] but the reaction is much more sluggish; 1 in 0.1 M solution in $CDCl_3$

containing 5 equivalents of bromine required 4 days at room temperature for complete transformation of the iodo- to the bromocubane. No intermediate hypervalent species was observed by ^{1}H-NMR; presumably its steady state concentration was too low.

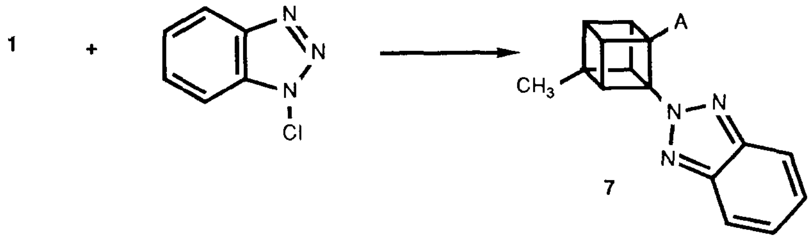


5 6

The stable solid iodobenzene dichloride is a convenient source of chlorine for the oxidation of 1 to 6. When 1.5 equivalents were added to a 0.1 M solution of 1 in $CDCl_3$, all of 1 was converted to 5 within minutes. This indicates that despite the kinetic instability of 5, 1 is more easily oxidized by chlorine than is iodobenzene. This must reflect on the different nature of the cubane-iodine bond[10] relative to that of the aryl iodide. Amide-free iodocubanes behave similarly.

If one could apply with equal success other known[11] hypervalent compounds of iodobenzene as oxidation/substitution agents on iodocubanes it would greatly increase the variety of available cubanes. Our initial studies have shown that iodobenzene diacetate does indeed convert 1 to cubyl acetate 4b, but only after prolonged heating in chloroform. We are of course looking further.

Nitrogen-centered oxidants are being investigated as a route to nitrogen-substituted cubanes. N-chloro- and N-bromo-succinimide reacted slowly with 1, but gave only the corresponding halocubanes. However, 1-chlorobenzotriazole on heating with 1 in chloroform or benzene gave the 2-cubylisobenzotriazole 7 in about 15% yield.[12] A much improved yield, and a cleaner reaction mixture, was obtained by pre-oxidizing 1 with mCPBA, then treating the hypervalent iodide with 1H-benzotriazole. The formation of 7 shows that rather special substituents can be introduced on the cubane nucleus via hypervalent iodocubanes. We believe that "super-nucleofuge"[13] nucleophiles will be particularly effective.



In conclusion, the results presented in this Letter illustrate the power of hypervalent iodine intermediates to encourage, under remarkably mild conditions, what is formally nucleophilic substitution on cubane substrates otherwise virtually inert.[14]

Acknowledgment. We are grateful to the ONR, ARO, and ARADCOM for support of this work. The NSF and the NIH, the latter through The University of Chicago Cancer Center, helped finance the instrument facility essential to this research.

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(Received in USA 17 September 1986)