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Photolysis of Cubyl Iodides: Access to the Cubyl Cation

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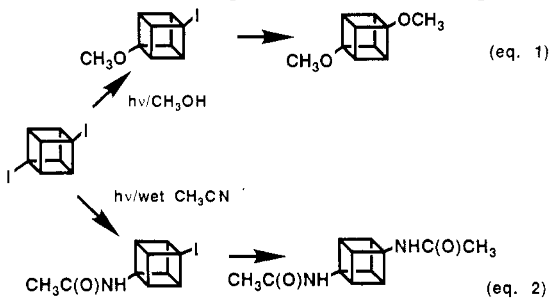
Many diverse methods have been developed for preparation of cubyl iodides, indeed probably more than for any other nonaromatic system. These include iodinolysis of metalated cubanes,[2] halogen exchange,[3] direct radical iodination,[4] and various decarboxylative iodinations.[5-7] What use can be made of iodo substituents on cubane? Clearly, S_N2 reactions are out of the question; backside displacement by an external nucleophile is geometrically impossible. S_N1 reactions can be expected to be difficult; the cubyl cation is very high in energy (vide infra). Cubyl iodides are in fact very stable compounds and show no tendency to decompose under ordinary conditions. This, of course, is the primary reason that so many methods for their production are successful. For example, the preparation of 1,4-diiodocubane given in the Experimental Section is successful only because cubyl iodides are stable to visible light, unlike so many other tertiary iodides, e.g., 1-adamantyl iodide (cf. the discussion in ref 5).

Under certain conditions cubyl iodides do react with cleavage of the cubane–iodine bond. Eaton and Cunkle have shown that iodine replacement can occur after oxidation of the iodine substituent to the hypervalent species.[8] In such conversions the oxidation of iodine weakens the carbon–iodine bond and activates it for dissociation. Whether or not there is significant charge development at the cubyl carbon during these transformations of the hypervalent iodide species is not yet clear, but we believe the reaction can best be described in carbonium ion terms.

In this paper we demonstrate a different way to activate iodide on the cubane nucleus for the introduction of other substituents. The scheme is an extension of the pioneering work of Kropp on the photochemical behavior of alkyl iodides,[9] particularly such bridgehead systems as 1-norbornyl iodide and 1-adamantyl iodide. Ultraviolet irradiation of such compounds dissolved in nucleophilic solvents results in "solvolysis". Kropp has formulated the process as occurring through initial excitation of the C–I bond, homolytic dissociation to a caged radical pair, and finally internal electron transfer to give iodide ion and the carbocation, which is then trapped by solvent.[10]

Is it possible to extend Kropp's elegant method to formation of a cubyl cation? By any description *cubyl cation is very much higher in energy than even the bridgehead 1-norbornyl cation.* Its distortion from planarity is much larger,[11] and its geometry is very far indeed from the "ideal" of the planar *tert*-butyl cation.[12] Hyperconjugative stabilization is unlikely as it would involve contributions from the extreme anti-Bredt's rule olefin cubene,[13] certain to be particularly unfavorable. Furthermore, versus the 1-norbornyl carbon, the much greater degree of rehybridization of cubyl carbon away from sp^3, increasing the s character in the exo skeletal bond (31% versus 27% in the hydrocarbons), would more strongly destabilize the cubyl cation as the positive charge is in an s-richer orbital closer to the positively charged nucleus.

Nonetheless, we have found that photolysis of cubyl iodides in nucleophilic solvents provides fairly effectively for iodide substitution reactions. In illustration we report here two examples using 1,4-diiodocubane (eq 1 and 2).



These reactions were run at 40 °C with light centered at 254 nm from a low-pressure source. Details are provided in the Experimental Section. The conversions, an etherification and an amidation, produce strategically important cubanes. Isolated yields of products having *both* iodides replaced are in the 50–55% range; 10–15% of the mixed substituent cubanes can be obtained from the same runs. It is not advantageous to press for complete conversions. Approximately double the yield of mixed substituted compounds can be obtained from runs optimized for the purpose. As could be expected, similar conversions go in higher yield when starting with mono-iodocubane.

These results demonstrate again the power of the Kropp method and *extend its applicability to one of the most extreme structural cases.* Despite the geometric and electronic destabilizations expected for cubyl carbonium ion, photochemical fracture of a cubyl C–I bond apparently provides sufficient energy for its production.[10]

It is known that irradiation of bridgehead halides in methanol gives, in addition to the carbonium ion derived methyl ether, some reduction to hydrocarbon. This is thought to result primarily from those bridgehead radicals that escape the initial cage prior to electron transfer. As

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[10] We note that the reaction mechanism could be formulated instead as a radical nucleophilic substitution ($S_{RN}1$), but this seems unlikely given the conditions and reagents (cf. Santiago, A. N.; Iyer, A. S.; Adcock, W.; Rossi, R. A. *J. Am. Chem. Soc.* **1987**, *53*, 3016 and references 5–10 therein).

[11] Note, however, that the internuclear lines give a false picture for the bonding and geometry in cubane. Bent bonding is important; the endocyclic interorbital angle is not 90°; it has been estimated to be 107° (Mislow, K. *Tetrahedron Lett.* **1964**, 1415) by calculation from ^{13}C–H coupling constant data and is, on average, 105° (minimum of 96°, maximum of 112°) by difference Fourier synthesis from X-ray analysis of the 1,4-diacid (Ermer, O.; Lex, J. *Angew. Chem.* **1987**, *26*, 447).

[12] The destabilization of cubyl cation relative to *tert*-butyl cation has been estimated to be 25.9 kcal/mol by ab initio methods (Borden, W. T., private communication).

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has been suggested by others,[9a,14] the ratio of methyl ether to hydrocarbon might be related to the relative energies of the cation and radical. In the 1-adamantyl case, the ratio is about 95:5;[14] in the 1-norbornyl system, 76:12.[9a] We find that on irradiation of cubyl iodide in methanol under similar conditions, the ratio of methoxycubane to cubane is >95:5.[15] *The trend from adamantyl to norbornyl to cubyl is not in agreement with expectation from simple geometric and electronic arguments.* What is needed now is a more quantitative picture, both from experiment and theory, of the relative energies of the radical and cation species involved.

Experimental Section

1,4-Diiodocubane. This procedure is derived from that in the literature for monoiodocubane.[5] *tert*-Butyl hypochlorite (3.8 g, 35 mmol) was added with stirring to a mixture of mercuric iodide (7.95 g, 17.5 mmol) and Freon 113 (25 mL) held at 0 °C. The precipitated mercuric chloride was removed after 2 h. The filtrate was added to a stirred suspension of 1,4-dicarboxycubane[16] (1.34 g, 7.0 mmol) in the same solvent (20 mL), and the mixture was irradiated overnight at 40 °C with a 200-W tungsten lamp. The mixture was then filtered, and the residue washed with acetone. The combined filtrate and wash was taken to dryness on a rotary evaporator under vacuum, keeping the bath temperature below 20 °C. The residue was dissolved in a small volume of methylene chloride. The solution was washed with aqueous 10% sodium thiosulfate solution to remove iodine and then dried ($MgSO_4$). The solvent was removed; the residue was purified by chromatography on silica gel, eluting with hexanes, to give the white, crystalline diiodide (1.79 g, 72%): mp 227–228 °C dec (lit.[3] mp 226–227 °C dec); ^{1}H NMR ($CDCl_3$) δ 4.37 (s); ^{13}C NMR ($CDCl_3$) δ 57.4 (d), 35.6 (s). Some higher iodides are also formed.[4]

4-Methoxyiodocubane and 1,4-Dimethoxycubane. 1,4-Diiodocubane (71 mg) was kept suspended in dry methanol (6.0 mL) under nitrogen in a 10-mL quartz tube with a magnetic stirrer. The tube, centered in a Rayonet (The Southern New England Ultraviolet Co.) RPR-204 reactor equipped with 2537-Å low-pressure lamps, was irradiated at ambient temperature (ca. 40 °C). The progress of the irradiation was monitored by GLC (flame detection; OV-101) at 1-h intervals (removing HI before injection). After 6 h about 32% of the soluble product mixture was 4-methoxyiodocubane. Further irradiation gave significant conversion to 1,4-dimethoxycubane. After 12 h the reaction was stopped. A few drops of aqueous 10% Na_2CO_3 solution was added, and the solvent was removed under reduced pressure. The crude product was dissolved in 5 mL of dichloromethane; the solution was absorbed onto a silica gel column (10 g). This was eluted with hexane (100 mL) to remove residual diiodocubane and then with toluene (50 ml) to get 4-methoxyiodocubane (5 mg, 10%): mp 86–87 °C; IR (KBr) ν 2996, 1352, 1316, 1305, 1130, 1118, and 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.32 (3 H, s, OMe), 4.03 (3 H, m), 4.30 (3 H, d of d); MS (EI), *m/e* 217 (5), 204 (51), 165 (4), 152 (4), 118 (95), 89 (base), 77 (68).

Elution with 9:1 toluene/ethyl acetate (50 mL) gave 17 mg (52%) of 1,4-dimethoxycubane: mp 79–80 °C; IR (KBr) ν 2990, 1470, 1323, 1211, 1132, 1024 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.32 (6 H, s, OMe), 3.9 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 46.1 (d), 51.6 (q), and 92.9 (s); MS (EI), *m/e* 149 (11), 133 (11), 121 (28), 108 (58), 91 (30), 78 (base).

4-Iodoacetamidocubane and 1,4-Diacetamidocubane. 1,4-Diiodocubane (1.2 g, 3.3 mmol) was suspended under nitrogen in 250 mL of ACS grade acetonitrile in a 300-mL, quartz, round-bottomed flask equipped with magnetic stirrer. Water (2 mL) was added, and the flask placed in a Rayonet apparatus (as above) and irradiated. The course of the reaction was monitored at 8-h intervals by thin-layer chromatography on silica gel. After 48 h, the starting material was essentially gone. The acetonitrile was removed under reduced pressure. The black gummy residue was washed with saturated aqueous solutions of sodium thiosulphate and potassium carbonate, leaving a brown powder. TLC on silica gel showed two major components. The crude was absorbed onto a silica gel column. Elution with chloroform gave 4-iodoacetamidocubane (113 mg, 12%): mp 210–213 °C dec; ^{1}H NMR (DMSO-d_6) δ 1.88 (3 H, s, $COCH_3$), 4.15 (3 H, d, cubyl H) 4.2 (3 H, d, cubyl H), 8.5 (1 H, s, NH); ^{13}C NMR (DMSO-d_6) δ 22.39 (q), 39.7 (s), 52.4 (d), 52.6 (d), 62.7 (s), 168.8 (s); IR (KBr) ν 3250 (s, N—H), 1650 (s, C=O) 1505 (m), 1375 (m), 1345 (w), 1306 (m) cm^{-1}. Elution with chloroform/methanol (9:1) gave 1,4-diacetamidocubane (370 mg, 50%): mp 276–281 °C dec; ^{1}H NMR (DMSO-d_6) δ 1.80 (6 H, s, CH_3), 3.80 (6 H, s, cubyl CH), 8.5 (s, 2 H, NH); ^{13}C NMR (DMSO-d_6) δ 22.17 (q), 47.1 (d), 66.08 (s), 168.3 (s); IR (KBr) ν 3250 (s, N—H), 1650 (s, C=O), 1555 (m) cm^{-1}.

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Preparation and Utilization of a Macromolecular Analogue of *N-tert*-Butyl-*N*-ethylamine as a Reusable Amide Base

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Recently, examples of synthetically useful aldol and related reactions in which the stabilized carbanion intermediates were generated by polymeric analogues of strong bases have been reported. In particular, the polymeric species that were employed as bases involve alkali-metal derivatives of polystyrene or KF adsorbed on basic alumina.[1-4] Of specific interest to our work were the examples of the derivatized polystyrenes, which have been prepared by several procedures. Included among these procedures were the deprotonation of pendant aryl rings by *n*-BuLi–TMEDA, metal–halogen exchange between *n*-BuLi and halogenated polystyrenes, transmetalation reactions of alkyllithium reagents and mercurated polystyrenes, and deprotonation of polymer-bound weak acids. Of the metalated derivatives that have been prepared, the use of weak acids as precursors for regenerable bases were the ones that were synthetically useful in forming stabilized carbanions. Specific examples of such species included

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