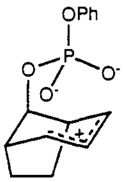
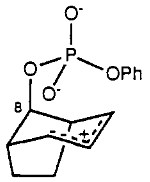
isomer presumably via symmetric zwitterion **7A**. In contrast, the slower racemization of **5b** evidently reflects the relatively large torsional motion (120° rotation about the P–OC(8) bond) and charge separation necessary to effect allylic rearrangement to its enantiomer.[29] Since the kinetic data for **5b** represent the combined barriers to both ionization and rotation, the structure and relative stability of the ion pair(s) from this isomer remain obscure. Heterolysis of **5b** to asymmetric ion pair **7B** followed by collapse back to **5b** without 120° rotation about the P–OC(8) bond would not be detected.



7A



7B

Although the rigid tricyclic structures of **5a** and **5b** allow access to a limited array of allyl carbocation/phosphate anion configurations, it is clear that the proximity of the *P*-oxide group to the double bond in **5a** leads to an enhanced rate of allylic rearrangement.

Acknowledgment. We thank Professor Ronald M. Magid for helpful discussions and the National Institutes of Health for financial support (GM-13956).

Supplementary Material Available: Physical and spectral properties for **3a**,**b**, **4**, **5a**,**b**, **6b**, and synthetic intermediates (5 pages). Ordering information is given on any current masthead page.

---

(29) An alternative mechanism involves inversion of the cyclic phosphate ring to a boat conformation followed by heterolysis and both C–O and O–P bond rotations to attain an open or anti zwitterion with C_s symmetry.

Free-Radical Arylation of Cubane Using Cubyl Lead Acylates

Robert M. Moriarty* and Jaffar S. Khosrowshahi

University of Illinois at Chicago
Department of Chemistry, Box 4348
Chicago, Illinois 60680

Richard S. Miller

Office of Naval Research
800 North Quincy, Arlington, Virginia 22217

Judith Flippen-Andersen and Richard Gilardi

Laboratory for the Structure of Matter
Naval Research Laboratory, Code 6030
Washington, D.C. 20375

Received May 19, 1989

Two methods have been applied recently for functionalization of the cubyl ring system. The first is hypervalent iodine oxidative displacement of the iodo group in a cubyl iodide to yield the derived (*m*-chlorobenzyl)oxy,[1] chloro,[1] acetoxy,[1] tosyloxy,[2] mesyloxy,[2] trifluoroacetoxy,[2] or fluoro[2] analogues. The second involves the elegant ortho-metalation procedure of Eaton et al. upon a cubylcarboxamido precursor and subsequent electrophilic addition.[3]

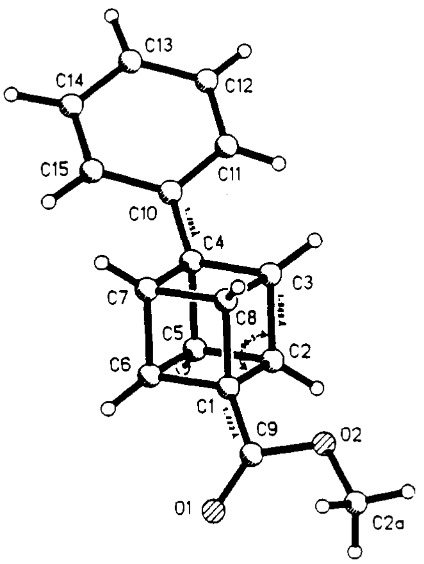
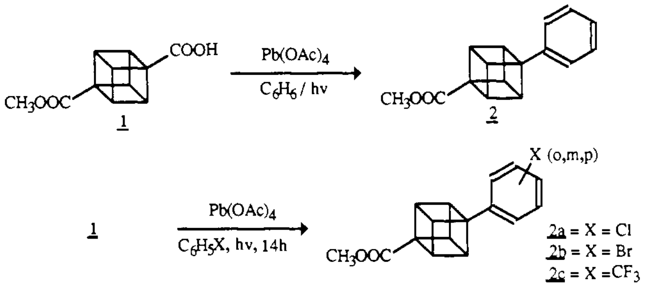


Figure 1. X-ray structure of methyl 1-phenylcubane-4-carboxylate (**2**).

These procedures correspond formally to carbocationic and carbanionic reactions, respectively. To date, radical reactions have not been applied to cubane functionalization in a systematic way, although the generation, stability, and selectivity of the cubyl radical was first studied 10 years ago.[4,5] Furthermore, regardless of the method used, carbon–carbon bond forming reactions in cubane chemistry are conspicuously absent, except for the recently reported phenylation of cubane, using the cubyl anion formed via reverse transmetalation and subsequent addition to benzyne formed from either dehydrohalogenation of bromobenzene or metal–metal exchange upon 1,2-dibromobenzene.[6] As interesting as this demonstration of arylation is, the structural precondition of a (diisopropylamino)carbonyl group for ortho activation is a limitation.

A desirable goal is the direct arylation of cubane without the necessarily of ortho activation, and we now report this via lead tetraacetate radical oxidative decarboxylation in a reaction akin to Kochi's free-radical halodecarboxylation.[7] Thus, 1,4-cubanedicarboxylic acid methyl ester (**1**),[8] upon reflux and irradiation in benzene solution, yields methyl 1-phenylcubane-4-carboxylate (**2**) in 66% yield.[9] Similarly, chlorobenzene yielded a mixture



---

(1) Eaton, P. E.; Cunkle, E. T. *Tetrahedron Lett.* **1986**, *27*, 6055.

(2) Moriarty, R. M.; Khosrowshahi, J. S.; Penmasta, R. *Tetrahedron Lett.* **1989**, *30*, 791. Moriarty, R. M.; Khosrowshahi, J. S. *Synth. Commun.* In press.

(3) Eaton, P. E.; Castaldi, G. *J. Am. Chem. Soc.* **1985**, *107*, 724. Eaton, P. E.; Cunkle, G. T.; Marchioro, G.; Martin, R. M. *J. Am. Chem. Soc.* **1987**, *109*, 948. Eaton, P. E.; Higuchi, H.; Millikan, R. *Tetrahedron Lett.* **1987**, *28*, 1055.

(4) Luh, T.-Y.; Stock, L. M. *J. Org. Chem.* **1978**, *43*, 3271.

(5) The various decarboxylation methods applied to cubane are the following: RCOOH → RH using *N*-hydroxypyridine-2(1*H*)-thione (Della, E. W.; Tsanaktsides, J. *Aust. J. Chem.* **1986**, *39*, 2061), i.e., the Barton reaction (Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901), and RCOOH → RI (Abeywickrema, R. S.; Della, R. S. *J. Org. Chem.* **1980**, *45*, 4226) using *tert*-butyl hypo iodite (Moriarty, R. M.; Khosrowshahi, J. S.; Dalecki, T. M. *J. Chem. Soc., Chem. Commun.* **1987**, 675) and using $PhI(OAc)_2$–CCl_4–I_2 are all radical processes, but only RX and RH have been obtained to date.

(6) Bashir Hashemi, A. *J. Am. Chem. Soc.* **1988**, *110*, 7234.

(7) Kochi, J. K. *J. Am. Chem. Soc.* **1965**, *87*, 2500. Kochi, J. K. *Free Radicals* Wiley-Interscience: New York, 1973; Vol. II.

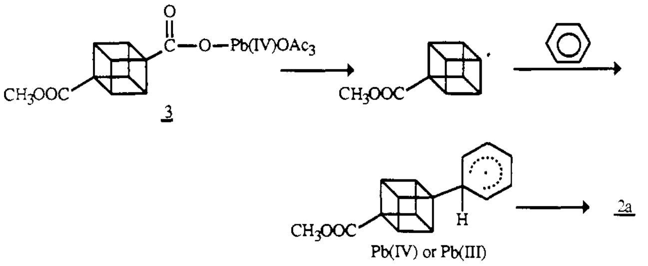
(8) Luh, T.-Y.; Stock, L. M. *J. Org. Chem.* **1972**, *37*, 338.

0002-7863/89/1511-8943$01.50/0

of ortho-, meta-, and para-substituted analogues, **1** → **2a** (ortho:meta:para = 36:5:58); bromobenzene, **1** → **2b** (ortho:para = 37:63); α,α,α-trifluorotoluene, **1** → **2c** (meta:para = 50:50). In the case of *o*-dichlorobenzene, a mixture of methyl 1-(*o*-dichlorophenyl)cubane-4-carboxylates is obtained.

The X-ray structure[10] of **2** is given in Figure 1. In addition to confirming the structure, the X-ray determination provides a value for the relatively short cubyl–phenyl distance, 1.482 (4) Å. In contrast, five X-ray determinations[11] of the adamantyl–phenyl distance range from 1.531 to 1.536 Å [average: 1.534 Å]. The shortened distance in **2** may be attributed to increased s character in the exocyclic cubyl orbital, which causes a cubyl–phenyl bond to more closely resemble a single bond between two sp^2 C atoms, rather than an sp^2–sp^3 bond. The cubyl–cubyl distances thus far observed have been even shorter: 1.475 (3) Å in pure cubylcubane crystals[12] and 1.458 (8) and 1.474 (5) Å in a cocrystal of two cubylcubanes.[13] This may be due to more favorable steric interactions in the perfectly staggered cubylcubane molecule; nonbonded C···C and H···H distances across the link are extremely long (3.4–3.6 Å). In **2**, there are two short C···C distances across the phenyl–cubyl link, both 3.18 (1) Å (the van der Waals C···C distance is 3.4 Å, and the distances below this limit are considered repulsive).

The mechanism of the reaction **1** → **2**, **2a**, **b** and **1** → **2c** proceeds via the cubyl radical. Thus, lead-mixed acylate **3** has been synthesized separately and shown to decompose in the appropriate aromatic solvent to yield products **2a**,**b**. Furthermore,



3 can be iodinated upon treatment with I_2 to yield methyl 4-iodocubane carboxylate[2] and also reacts with $(C_6H_5Se)_2$ to yield methyl 4-(phenylseleno)cubanecarboxylate. The reactions with I_2 and $(C_6H_5Se)_2$ are not in agreement with possible carbocationic intermediates ($R^\bullet \rightarrow Pb(IV) \rightarrow R^+ + Pb(III)$). Furthermore, arylation with $CF_3C_6H_5$ (**1** → **2c**) effectively distinguishes between the radical reaction and carbocationic processes since the CF_3 group is radical stabilizing and carbocation destabilizing as has been demonstrated in radical cyclizations.[14] Reaction **1** → **2a–d** is formally and mechanistically analogous to $Pb(OAc)_4$ arylation of apocamphane-1-carboxylic acid, for which a radical process has been established.[15]

The key reaction intermediate, namely, the cubyl radical, was found by Stock and Luh to form 4600-fold less rapidly than the *tert*-butyl radical and 3285-fold more slowly than 1-adamantyl.[4]

The observed ortho:meta:para ratios are essentially in agreement with expectation based upon polar and steric considerations. The electrophilicity of the cubyl is intermediary between sp^3 and sp^2 (electrophilicity of radicals varies in the series p/sp^3 < sp^2 < sp). Thus, partial rate factors for nuclear substitution of chlorobenzene by the cyclohexyl radicals, the phenyl radical, and the phenylethynyl are f_o:f_m:f_p = 5.6:3.5:2.5, 1.3:1.0:1.4, and 0.8:0.4:0.7.[16a,b] In the case of typical sp^3-centered radicals such as CH_3 or cyclohexyl, ortho substitution predominates,[17] but in the cubyl system, steric effects reverse this pattern. In the case of $CF_3C_6H_5$, the observed meta:para ratio of **1** is close to that observed with the cyclohexyl radical and $CF_3C_6H_5$ of 1.2.[16a] The relatively large amount of meta substitution in this case agrees with calculated (RHG4-31G) radical stabilization energies of substituents such as CH_3 (+3.27 kcal/mol), Cl (+2.57 kcal/mol), and CF_3 (−1.34 kcal/mol).[16c]

Acknowledgment. We thank the Office of Naval Research for support of this work under Contract FED ONR 0001486K0619. In addition, valuable discussions with Professor Harold Shechter of The Ohio State University contributed to this study.

Supplementary Material Available: Footnote 9, giving experimental details for the syntheses of **2** and **3** from **1**, footnote 10, giving X-ray data for **2**, and tables of atomic positional parameters, Cartesian coordinates, bond distances, bond angles, torsion angles, and anisotropic thermal parameters for **2** (5 pages); table of observed and calculated structure factors (6 pages). Ordering information is given on any current masthead page.

---

(9) See supplementary material.

(10) See supplementary material.

(11) Okaya, Y.; Lin, S. Y.; Chiou, D. M.; Le Noble, W. J. *Acta Crystallogr.* **1980**, *B36*, 977–9. Okaya, Y.; Maluszynska, H.; Chiou, D. M.; Le Noble, W. J. *Acta Crystallogr.* **1978**, *B34*, 3434–6. Okaya, Y.; Chiou, D. M.; Le Noble, W. J. *Acta Crystallogr.* **1979**, *B35*, 2268–71.

(12) Gilardi, R.; Tsanaktsidis, J.; Eaton, P. X-Ray diffraction analysis of pure sublimed cubylcubane crystals. To be published.

(13) Gilardi, R.; Maggini, M.; Eaton, P. E. *J. Am. Chem. Soc.* **1988**, *110*, 7232.

(14) Morikawa, T.; Mshiwaki, T.; Kobayashi, Y. *Tetrahedron Lett.* **1989**, *30*, 2407.

(15) Davies, D. I.; Waring, C. *J. Chem. Soc., Chem. Commun.* **1965**, 263.

(16) (a) Shelton, J. R., Uzelmeier, C. W., *J. Am. Chem. Soc.* **1966**, *88*, 5222. (b) For a discussion, see: Perkins, M. J. Aromatic Substitution. *Free Radicals*; Chap. 16, John Wiley & Sons: New York, 1973; Vol. II, pp 248–9. (c) Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062.

(17) Hay, J. M. *Reactive Free Radicals*; Academic Press: New York, 1974; pp 116–7.

Microscale Glycosidic Cleavage of Oligosaccharide Bromobenzoates for Circular Dichroism Analysis

Makoto Ojika, Harold V. Meyers, Mayland Chang, and Koji Nakanishi*

Department of Chemistry, Columbia University
New York, New York 10027

Received July 28, 1989

Glycoproteins and glycolipids play important roles in biological processes.[1] Despite developments in chemical methodology,[2] ^{1}H NMR,[3] and GC/MS,[4] structure determinations of complex carbohydrates remain difficult because of their great number of possible isomers[5] and the microgram quantities in which many are obtained.

Approaches to determine oligosaccharide glycosidic linkages based on the CD exciton chirality method have been demonstrated.[6-8] In our recent approach, tagging free hydroxyls of an

---

(1) *Biology of Carbohydrates*; Ginsberg, V., Robbins, P. W., Eds.; Wiley: New York, 1984; Vol. 2.

(2) Bennek, J. A.; Rice, M. J.; Gray, G. R. *Carbohydr. Res.* **1986**, *157*, 125.

(3) For applications of 3D NMR to oligosaccharide structural studies, see: (a) Fesik, S. W.; Gampe, R. T., Jr.; Zuiderweg, E. R. P. *J. Am. Chem. Soc.* **1989**, *111*, 770. (b) Vuister, G. W.; de Waard, P.; Boelens, R.; Vliegenthart, J. F. G.; Kaptein, R. *Ibid.* **1989**, *111*, 772.

(4) (a) Lindberg, B. *Chem. Soc. Rev.* **1981**, *10*, 409. (b) *Analysis of Carbohydrates by GLC and MS*; Biermann, C. J., McGinnis, G. D., Eds.; CRC Press: Boca Raton, FL, 1989.

(5) Three monomers XYZ give rise to six isomeric tripeptides/trinucleotides but to 1056 isomeric trisaccharides: Clamp, J. *Biochem. Soc. Symp.* **1974**, *No. 40*, 3 (see: Sharon, N.; Lis, H. *Chem. Eng. News* **1981**, *March 30*, 21 and references therein).

(6) (a) Nakanishi, K.; Kuroyanagi, M.; Nambu, H.; Oltz, E. M.; Takeda, R.; Verdine, G. L.; Zask, A. *Pure Appl. Chem.* **1984**, *56*, 1031. (b) Nakanishi, K.; Park, M. H.; Takeda, R.; Vázquez, J. T.; Wiesler, W. T. *Stereochemistry of Organic and Bioorganic Transformations*; Bartmann, W., Ed.; Verlag Chemie: Weinheim, 1986; pp 303–319. (c) Chang, M.; Meyers, H. V.; Nakanishi, K.; Ojika, M.; Park, J. H.; Park, M. H.; Takeda, R.; Vázquez, J. T.; Wiesler, W. T. *Pure Appl. Chem.* **1989**, *61*, 1193.

(7) For additivity in CD amplitudes of split curves in monochromophoric acylates (a–c) and benzylates (d), see: (a) Lichtenthaler, F. W.; Sakakibara, T.; Oeser, E. *Carbohydr. Res.* **1977**, *59*, 47. (b) Liu, H. W.; Nakanishi, K. *J. Am. Chem. Soc.* **1982**, *104*, 1178. (c) Golik, J.; Liu, H. W.; DiNovi, M.; Furukawa, J.; Nakanishi, K. *Carbohydr. Res.* **1983**, *118*, 135. (d) Takeda, R.; Zask, A.; Nakanishi, K. *J. Am. Chem. Soc.* **1987**, *109*, 914.