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SYNTHESIS OF ZINC, CADMIUM, TIN, AND SILICON DERIVATIVES OF CUBANE[1]

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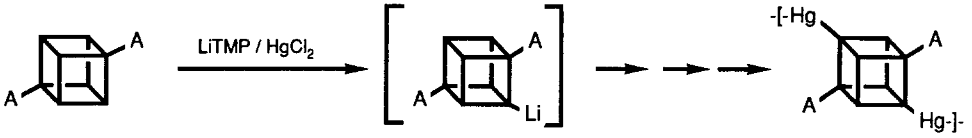
Abstract. Metallocubanes are shown to be available by a transmetalation procedure in which amide-activated cubanes are treated with LiTMP and a metal chloride. They are excellent precursors for new subsituted cubanes.

We have shown that treatment of amidocubanes with lithium tetramethylpiperidide (LiTMP) in the presence of mercury chloride gives high yield ortho-mercuration.[2] The reaction proceeds by way of amide-activated ortho-lithiation, followed by *in situ* trapping (transmetalation) by Hg^{2+} of the small concentration of the lithiated cubane. In the case of the cubane diamide 1, the overall double metalation conversion shown proceeds by iteration of the process, rather than by way of a di-lithiated cubane.

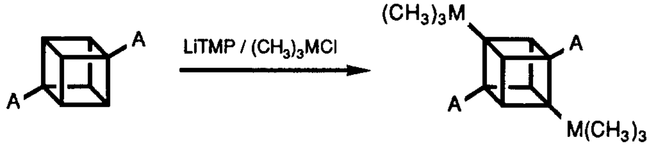


1

A = $C(O)N[CH(CH_3)_2]_2$

Mercurated cubanes in themselves are synthetically useful in important ways (e.g. preparation of halogenated cubanes).[2,3] However, as different metals confer specific kinds of reactivity to the attached organic, we looked to the preparation and use of other metallocubanes. We introduce in this Letter the preparation of the zinc-, cadmium-, tin-, and silicon-substituted cubanes and demonstrate, as an example, the special utility of the zinc compound.

Our methodology for these new metallocubanes is a direct extension of the mercuration procedure, substituting an appropriate metal salt for $HgCl_2$. The reaction of diamide 1 with excess LiTMP and anhydrous $ZnCl_2$ or $CdCl_2$ gave the zinc and cadmium cubanes, respectively, mono or dimetalated depending on reaction time, probably as oligomeric species. Although not isolated, their formation was ascertained by treatment of the crude reaction mixtures with iodine, converting the metallocubanes to the corresponding, known iodocubanes.[2] The combinations LiTMP/$(CH_3)_3SnCl$ and LiTMP/$(CH_3)_4SiCl$[4] gave the trimethyltin- and trimethylsilyl-substituted cubanes 2a,b, respectively. These were isolated and characterized as described in the experimental section overleaf.

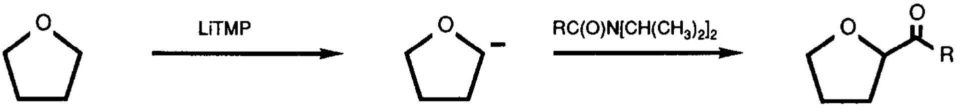


1

2a: M = Sn
2b: M = Si

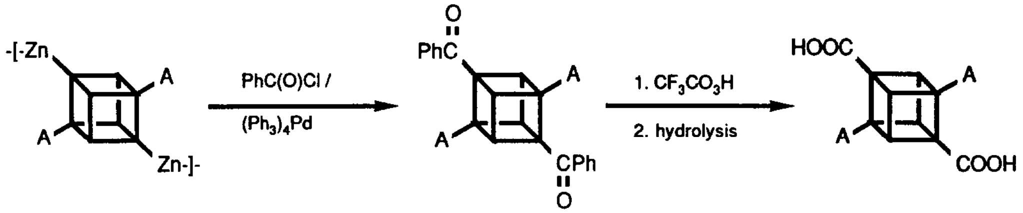
For all these cases the metalation reactions were substantially slower than the mercuration run under equivalent conditions. Longer reaction times -- hours rather than minutes; days in the silyl case -- were needed to obtain fair to good conversions. Warming the reaction mixtures was counterproductive. Reaction of 1 with LiTMP/$ZnCl_2$ at room temperature rather than 0°C gave back primarily unreacted starting material, presumably because the active base had been destroyed by Lewis acid accelerated decomposition of THF by LiTMP. Thus, we found it better to be patient and to run the zincation at 0°C as we had for the mercuration.

[We note in passing that there is significant reaction of LiTMP with THF at room temperature even in the absence of Lewis acids.[5] The THF α-anion (3) so formed is a powerful nucleophile that even under mild conditions will convert an N,N-diisopropylamide to the corresponding ketone. This nucleophile may prove useful in other contexts, but here it was a nuisance.]



3

We expected from classical chemistry that the cubyl zinc compound 4 would be sufficiently reactive to condense with benzoyl chloride. This was not the case. However, successful condensation was achieved by adding $(Ph_3P)_4Pd$ to the reaction system, a procedure following from the work of the Grey and Negishi groups.[6] In this way we obtained 5, the first cubane with four carbon substituents, in 75% yield overall. Baeyer-Villiger oxidation of 5 with peroxytrifluoroacetic acid under standard conditions quantitatively gave 6, the first cubane 1,2,4,7-tetracarboxylic acid derivative [dimethyl ester: mp 215-216°C (dec)]. We shall report in due course on other uses of metalated cubanes.



4 5 6

Experimental. Zincation of 1(→ 4); benzoylation of 4 (→ 5): All reactions were done under argon until the point of workup; anhydrous, low-oxygen conditions are prerequisites for success. n-Butyl lithium in hexane (3.00 ml, 2.60M, 7.54 mmol) was added dropwise with stirring to dry 2,2,6,6-tetramethylpiperidine (1.30 ml, 7.54 mmol) in dry THF (5 ml, distilled from sodium benzophenone ketyl) cooled to -70°C. The internal temperature was not allowed to exceed -45°C. The solution was gradually warmed to 0°C and stirred there for 1.5 h, after which it was transferred by cannula into a 25 ml flask containing a magnetically stirred mixture of finely powdered, anhydrous ZnCl$_2$ (200 mg, 1.47 mmol, freshly sublimed) and diamide 1 (150 mg, 0.420 mmol). This mixture was stirred for 8 h at 0-3°C to form 4, then cooled to -40°C and held there as benzoyl chloride (1.3 ml, 11 mmol, freshly distilled under N$_2$) was added dropwise with vigorous stirring, followed by the addition in one portion of (Ph$_3$P)$_4$Pd (120 mg, 0.10 mmol). The reaction mixture was allowed to warm to room temperature overnight, and then poured into CH$_2$Cl$_2$ (200 ml). The mixture was washed twice with cold, aq. 10% NaOH (30 ml), once with 1F H$_2$SO$_4$ (20 ml), then with brine, and dried (MgSO$_4$). Evaporation of solvent *in vacuo* left a brown, viscous oil. Trituration with dry acetone gave 5 (112 mg). The mother liquor was chromatographed on silica gel (70-230 mesh) with ØH/CH$_2$Cl$_2$/EtOAc (10:2:1) to afford an additional 66 mg of 5 (total yield 178 mg, 75%); a small amount of monobenzoyl compound in the middle cut, and 15 mg (10%) of starting material in the last fraction. Compound 5: colorless prisms from THF/hexane (1:2); mp 197-202°C (dec); ^{1}HMR (500 MHz, CDCl$_3$) δ 7.83, 7.53 and 7.46 (5H, Ar-H), 4.80 (s, 4H, cubyl-H), 3.24 and 3.09 (septets, J = 6 Hz, 2H each, amide C$\underline{H}$(CH$_3$)$_2$), 1.50 and 1.20 ppm (doublets, J = 6 Hz, 12H each, amide CH(C$\underline{H}_3$)$_2$); ^{13}CMR (100 MHz, CDCl$_3$) δ 195.3, 166.3, 134.1, 133.7, 128.8, 128.5, 61.7, 60.8, 49.0, 47.1, 45.9, 21.3, 19.8 ppm; IR (CHCl$_3$) ν 1657(s), 1621 cm^{-1} (s); MS (CI, isobutane) 567 (M+1)$^+$. Anal: calcd for $C_{26}H_{42}N_2O_4$ (MW = 566): C, 76.29: H, 7.47%; found; C, 76.35: H, 7.35%.

The bis-(trimethylstannyl)-(2a) and bis-(trimethylsilyl)-(2b) cubanes were prepared similarly, substituting $(CH_3)_3SnCl$ or $(CH_3)_3SiCl$, as appropriate, for $ZnCl_2$. For these cases, after the metalation, the reaction mixtures were poured into CH_2Cl_2/aq. K_2HPO_4 buffer (pH 7) at -10°C. Standard work-up procedures were used. No attempts were made to optimize yields beyond noting that longer reaction times were useful. Compound 2a: colorless fine crystals from $CHCl_3$; mp 235°C (dec); ^{1}HMR δ 4.90 (s, 4H, cubyl-H), 3.59 and 3.29 (septets, J = 6 Hz, 2H each, amide $C\underline{H}(CH_3)_2$), 1.38 and 1.20 (doublets, J = 6 Hz, 12H each, amide $CH(C\underline{H}_3)_2$), 0.04 ppm (s, 18H, $Sn(CH_3)_3$); ^{13}CMR δ 171.0, 62.1, 52.4, 48.8, 47.0, 46.2, 21.5, 20.8, -8.0 ppm; MS (CI, isobutane) 687 $(M + 1)^+$; calcd for $C_{28}H_{50}N_2O_2{}^{120}Sn_2$, 686. Compound 2b: colorless powder from CH_2Cl_2; mp 220°C (dec); ^{1}HMR δ 4.18 (s, 4H, cubyl-H), 3.47 and 3.31 (septets, J = 6 Hz, 2H each, amide $C\underline{H}(CH_3)_2$), 1.34 and 1.21 (doublets, J = 6 Hz, 12H each, amide $CH(C\underline{H}_3)_2$), 0.10 ppm (s, 18H, $Si(CH_3)_3$); ^{13}CMR δ 171.3, 62.6, 57.4, 49.6, 48.5, 46.0, 22.3, 21.2, -2.2 ppm; MS m/e 503 $(M + 1)^+$; calcd for $C_{28}H_{50}N_2O_2Si_2$, 502.

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References and Notes.

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