instead, directly to **4** by Grob fragmentation.

Acknowledgment. We thank the National Science Foundation for support of this research and for partial funding of the purchase of the Convex C-2 computer on which some of these calculations were performed. We also thank the San Diego Supercomputer Center for a generous allocation of computer time and Professors Philip Eaton[15] and Josef Michl[16] for informing us of the results of their research on **3** and for agreeing to simultaneous publication.

Registry No. 1, 124225-53-2; **2**, 124225-54-3; **3**, 124225-34-9; **4**, 124225-55-4.

Supplementary Material Available: Singlet TCSCF and triplet UHF optimized 3-21G geometries for **1**–**3** and the 3-21G geometry for singlet **4**, optimized with two GVB pairs (7 pages). Ordering information is given on any current masthead page.

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(15) Eaton, P. E.; Tsanaktsidis, J. *J. Am. Chem. Soc.* Third of three papers in this issue.

(16) Hassenrück, K.; Radziszewski, J. G.; Balaji, V.; Murthy, G. S.; McKinley, A. J.; David, D. E.; Lynch, V. M.; Martin, H.-D.; Michl, J. *J. Am. Chem. Soc.* First of three papers in this issue.

The Reactions of 1,4-Dihalocubanes with Organolithiums. The Case for 1,4-Cubadiyl

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Recently Eaton and Maggini reported that reaction of 1,2-diiodocubane with *tert*-butyllithium produces 1,2-dehydrocubane (cubene).[1] We report now our work on the reactions of 1,4-dihalocubanes with organolithiums undertaken in search of "1,4-dehydrocubane".[2]

Addition of 1,4-diiodocubane[3] in THF to an excess of *tert*-butyllithium in THF/pentane at −78 °C followed by carbomethoxylation[4] gives primarily 1,4-dicarbomethoxycubane (from 1,4-dilithiocubane, **2**) and **5** in a ratio of ca. 2:1 (Scheme I).[5] The latter comes via elimination of HI from 4-iodolithiocubane (**1**) giving 4-lithiocubene (**3**), followed by addition of *tert*-butyllithium to this strained olefin (→**4**).[1] No substantial amounts of bicubyls are found. On the other hand, dropwise addition of *tert*-butyllithium *to* a solution of 1,4-diiodocubane in THF at −78 °C followed by carbomethoxylation gives a diverse mixture of products including 4-*tert*-butylcarbomethoxycubane (**6**), 4,4′-dicarbomethoxybicubyl (**7**),[6] and 4-carbomethoxybicubyl (**8**)[5a,7,8] (Scheme II); **6** and the bicubyls **7** and **8** are thought to arise, respectively, from reaction of *tert*-butyllithium, (iodocubyl)lithium (**1**), or cubyllithium with 1,4-dehydrocubane.

When 1,4-dibromocubane or 4-bromoiodocubane is used in place of the 1,4-diiodide in either mode of addition, the principal products are derived via lithiocubene **3**. The rate of formation of 1,4-dehydrocubane by loss of LiBr from 4-bromolithiocubane is apparently slow by comparison to loss of LiI from **1**, as is the rate of bromine–lithium exchange. Evidently, *tert*-butyllithium-induced dehydrobromination (→**3**) can compete effectively. Reaction of 4-chloroiodocubane with *tert*-butyllithium in THF at −78 °C gives 4-chlorolithiocubane. This halolithiocubane is stable at this temperature; it is trapped effectively by carboxylation.

Dropwise addition of *n*-butyllithium (2 equiv) to 1,4-diiodocubane *in ether* at 0 °C followed by carbomethoxylation gives 4.4′-dicarbomethoxybicubyl (**7**, 30% isolated yield) and a little 4-*n*-butylcarbomethoxycubane (**9**).[5a,8] When the addition order is reversed, **9** predominates over **7**. When 4-bromo- or 4-chloroiodocubane was used, similar behavior was observed, but the diester **7** was replaced with halo ester **10** (X = Br or Cl, Scheme III).

We know from the behavior of monohalocubanes that direct alkyllithium/halocubane coupling or halogen–metal exchange followed by coupling cannot account for the products formed in reactions of the dihalides. Iodocubane undergoes ready halogen–metal exchange with *n*- or *tert*-butyllithium, but little (*n*-butyl) or no coupling (*tert*-butyl) product is formed. Bromocubane does not undergo halogen–metal exchange or coupling noticeably with *n*-butyllithium in ether at 0 °C; an even greater lack of reactivity can be expected for chlorocubane.

The disparate behavior of the individual monohalocubanes toward *n*-butyllithium contrasts sharply with the similar behavior observed within the set of the 4-haloiodocubanes. It seems likely therefore that, after initial lithium-for-iodine exchange (→**11**), a common halogen-free intermediate is formed. As 1,4-dilithiocubane (**2**, see Scheme I) is not reactive in Wurtz-type coupling reactions, we propose that formation of **11** is followed by its slow decomposition to 1,4-dehydrocubane. This very reactive intermediate is trapped by *n*-butyllithium, when present in excess. Otherwise, it is trapped instead by yet undecomposed **11**. The 4′-halolithiobicubyl so formed remains as such until quenched or, in the case of X = I, undergoes iodine–metal exchange, to give 4,4′-dilithiobicubyl and ultimately the diester **7**.[9]

The intermediacy of a halogen-free species in these reactions was confirmed on finding that treatment of any of the 4-X-iodocubanes (X = I, Cl, or Br) with excess phenyllithium in ether at room temperature gives the same product, 4-phenyliodocubane (**12**, mp 84.5–85 °C), in good yield.[10] These reactions must be initiated by iodine-for-lithium exchange (generating iodobenzene); subsequent loss of LiX gives 1,4-dehydrocubane; phenyllithium adds to it, and the product is iodinated by reverse Li-for-I exchange with iodobenzene (Scheme IV).[11]

To test for the presence of a symmetric intermediate, we synthesized[12] specifically labeled 2-deuterio-4-bromoiodocubane and

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(1) Eaton, P. E.; Maggini, M. *J. Am. Chem. Soc.* **1988**, *110*, 7230.

(2) The formation of single bonds in highly strained molecules by through-space dehalogenation has a checkered history. Claims for formation of [2.2.2]propellane from a 1,4-dihalobicyclo[2.2.2]octane by electrolysis (Wiberg, K. B.; Epling, G. A.; Jason, M. *J. Am. Chem. Soc.* **1974**, *96*, 912) or by reaction with *tert*-butyllithium (Wiberg, K. B.; Pratt, W. E.; Bailey, W. F. *J. Am. Chem. Soc.* **1977**, *99*, 2297) have been withdrawn (Wiberg, K. B.; Pratt, W. E.; Matturro, M. G. *J. Org. Chem.* **1982**, *47*, 2720. See also: Adcock, W.; Iyer, V. S.; Kitching, W.; Young, D. *Ibid.* **1985**, *50*, 3706). There is evidence for the formation of [2.2.1]propellanes (Walker, F. H.; Wiberg, K. B.; Michl, J. *J. Am. Chem. Soc.* **1982**, *104*, 2056 and references therein) and [2.1.1]propellanes (Wiberg, K. B.; Walker, F. H.; Pratt, W. E.; Michl, J. *Ibid.* **1983**, *105*, 3638) by dehalogenation of the appropriate bridgehead diiodides. [1.1.1]Propellane has been made from 1,3-dibromobicyclo[1.1.1]pentane and fully characterized (Wiberg, K. B.; Walker, F. H. *Ibid.* **1982**, *104*, 5239). The formation of trishomo[2.2.2]propellane (or "its diradical or zwitterionic equivalent") has been suggested to account for the chemistry of 1,5-diiodotrishomobarrelene (de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809).

(3) (a) Tsanaktsidis, J.; Eaton, P. E. *Tetrahedron Lett.* In press. (b) Della, E. W.; Tsanaktsidis, J. *Aust. J. Chem.* **1989**, *42*, 61.

(4) Quenching with CO_2, acidification, and diazomethane esterification.

(5) (a) Not insignificant amounts of various reduction products are also formed. (b) Small amounts of 2- and 3-*tert*-butylcarbomethoxycubanes are formed, probably from partial protonation of **4** prior to carboxylation. Some 4-*tert*-butylcarbomethoxycubane is also produced, most likely arising from 1,4-dehydrocubane. (c) The structures of these products and others reported here were determined by mass spectroscopy and analysis of the high-field NMR spectra.

(6) The structure of **7**, the first 4,4′-disubstituted bicubyl, was confirmed by single-crystal X-ray diffraction (Eaton, P. E.; Tsanaktsidis, J.; Pramod, K.; Gilardi, R. Manuscript in preparation). Cf.: Gilardi, R.; Maggini, M.; Eaton, P. E. *J. Am. Chem. Soc.* **1988**, *110*, 7232.

(7) Including 4-(α-tetrahydrofuranyl)carbomethoxycubane, whose origin is obscure; it is not seen in any of the other experiments reported here.

(8) Quenching with methanol gives the corresponding compounds with H in place of CO_2Me; e.g., bicubyl, mp 178–180 °C,[1] was isolated in 42% yield.

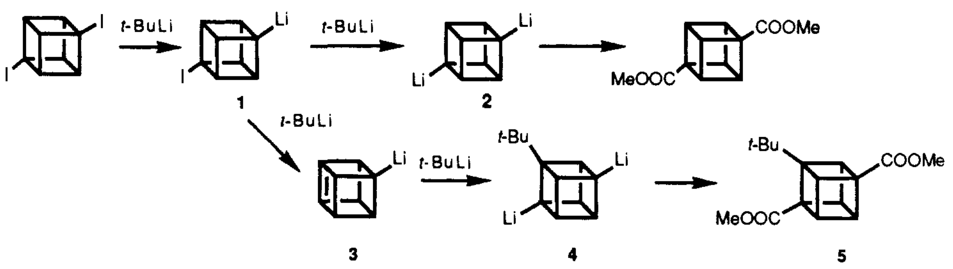
(9) The bicubyllithiums can, and do, add to 1,4-dehydrocubane, producing oligomeric cubanes.

(10) Reduction fortunately is much less a problem here (cf. ref 5a). We thank D. S. Reddy and A. Bashir-Hashemi for early experiments into these reactions.

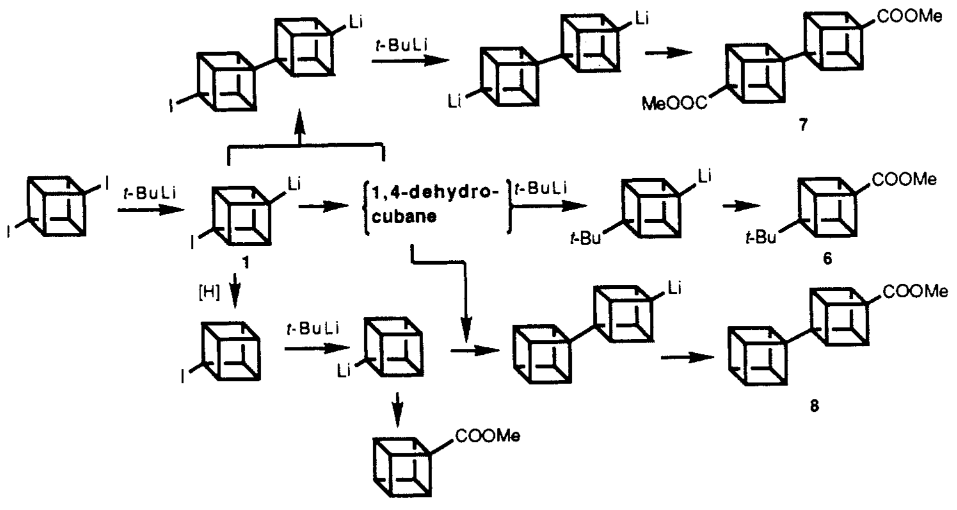
(11) Reaction of cubyllithium with iodobenzene in ether at room temperature generates iodocubane cleanly. Phenyllithium and iodocubane do not react under these conditions.

0002-7863/90/1512-876$02.50/0

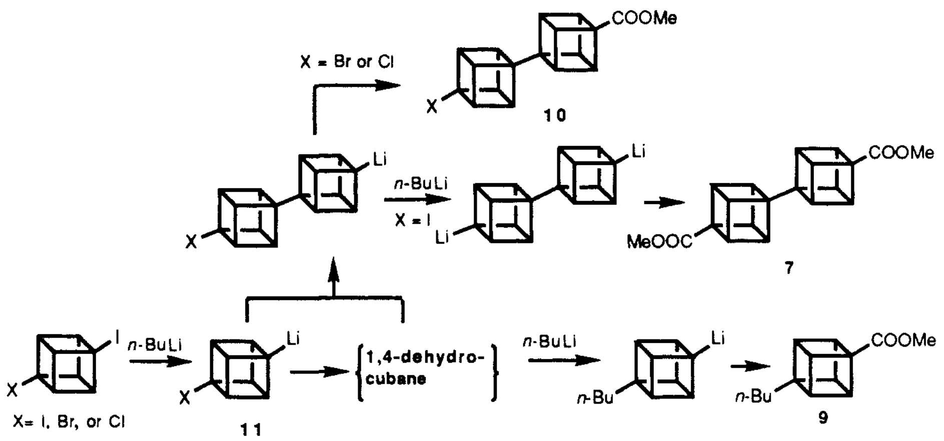
Scheme I



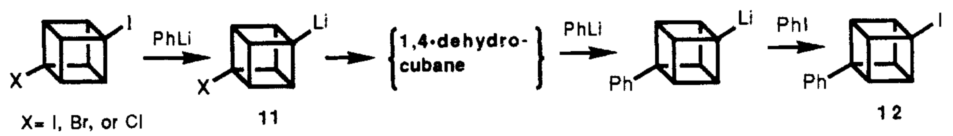
Scheme II



Scheme III



Scheme IV



reacted it with excess *n*-butyllithium. The mixture was quenched with elemental iodine to obtain products suitable for deuterium NMR analysis.[13] An approximately 60:40 mixture of the 2-deuterio-4-*n*-butylcubyl iodide (^{2}H NMR: δ 4.2 ppm) and the 3-deuterio isomer (δ 3.9 ppm) was obtained, indicating that substantial symmetrization does indeed occur along the critical reaction pathway. The lack of complete scrambling may be due to a cage or aggregation effect.

Several symmetrical halogen- and lithium-free structures for 1,4-dehydrocubane can be drawn to account for our observations. 1,4-Cubylane (**13**), a triply bridged [2.2.2]propellane, would have a weak (the phases of the required orbitals are mismatched), inordinately long "internal" bond. As ab initio calculations place bonded propellane structures of any geometry at higher energy than 1,4-cubadiyl (**14**), this latter structure is thought to better

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(12) Eaton, P. E.; Tsanaktsidis, J., details to be published elsewhere.

(13) The products are iodine free if the quenching is done with methanol or carbon dioxide.

represent 1,4-dehydrocubane.[14a] Interestingly, the singlet state of this diyl is calculated to be more stable than its triplet by over 10 kcal/mol, suggesting substantial through-bond interaction. At an extreme, one could envision this interaction proceeding to Grob fragmentation and formation of the diolefin **15**. The strained, bridgehead double bonds in **15** would be open to nucleophilic attack. Whether or not this could lead to reclosure to the cubane nucleus is moot. We would expect **15** to react readily with Diels–Alder dienes. However, when furan or 9,10-diphenylisobenzofuran is present during reaction of 1,4-diiodocubane with *n*-butyllithium, neither diene is incorporated. Thus, singlet 1,4-cubadiyl is the likely structure for the intermediate in the principal chemistry presented here.

Acknowledgment. The National Institutes of Health (GM-36436) and the Office of Naval Research provided the principal support for this work. We are grateful to Professor Borden for enlightening discussions about 1,4-dehydrocubane and thank both him and Professor Michl for prepublication access to their manuscripts.[14]

Registry No. 5, 124225-26-9; **6**, 124225-27-0; **7**, 124225-28-1; **8**, 124225-29-2; **9**, 124225-30-5; **10** (X = Br), 124225-31-6; **10** (X = Cl), 124225-32-7; **12**, 124225-33-8; **14**, 124225-34-9; 1,4-diiodocubane, 97229-08-8; 1,4-dibromocubane, 59346-70-2; 4-bromoiodocubane, 111873-47-3; 4-chloroiodocubane, 124225-25-8; 1,4-dicarbomethoxycubane, 29412-62-2; 4-chlorolithiocubane, 124225-35-0; bicubyl, 116503-50-5; 2-deuterio-4-bromoiodocubane, 124225-36-1; 2-dieuterio-4-*n*-butylcubyliodide, 124225-37-2; 3-deuterio-4-*n*-butylcubyliodide, 124225-38-3.

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[14] (a) Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* Second of three papers in this issue. (b) Hassenrück, K.; Radziszewski, J. G.; Balaji, V.; Murthy, G. S.; McKinley, A. J.; David, D. E.; Lynch, V. M.; Martin, H.-D.; Michl, J. *Ibid.* First of three papers in this issue.

A Practical and General Enantioselective Synthesis of Chiral Propa-1,2-dienyl and Propargyl Carbinols

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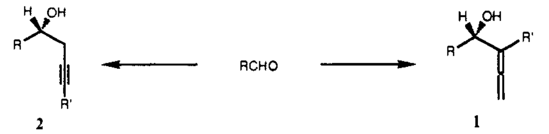
We report here a new and effective method for the enantioselective addition of propa-1,2-dienyl and propargyl groups to aldehydes to form chiral alcohols as shown in eq 1. The method

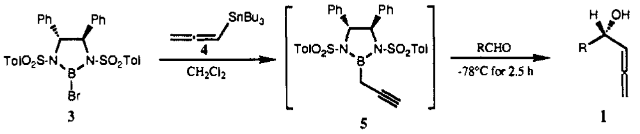


(1)

R = Aryl, alkyl, cycloalkyl; R' = H or alkyl

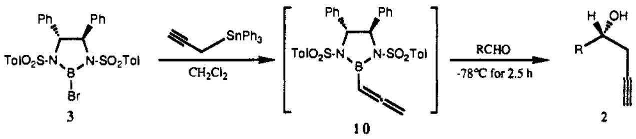
is successful with a wide variety of aldehydes and affords products of high enantiomeric purity. The absolute configuration of the reaction product in each case is predictable from the absolute configuration of the reagent and a well-defined model of the transition state. Further, either the *R* and *S* form of the alcohols **1** and **2** may be synthesized since the required reagents are readily accessible from the available enantiomers of 1,2-diphenyl-1,2-diaminoethane (stilbenediamine, stien).[1] Previous publications from this laboratory have described the use of the stien controller group in a number of other useful enantiocontrolled processes, including Diels–Alder,[1] aldol,[1] carbonyl allylation,[2] and olefin dihydroxylation reactions.[3] All of these reactions are characterized by stereochemical predictability, high yield and enantioselectivity, and efficient recovery of the chiral controller group.

Table I



aldehyde	isolated yield, %	% ee of **1**	abs config
n-$C_5H_{11}CHO$	82	>99	*S*
$(CH_3)_2CHCHO$	74	>99	*S*
c-$C_6H_{11}CHO$	78	>99	*S*
$(CH_3)_3CCHO$	78	>99	*S*
PhCHO	72	>99	*R*
PhCH═CHCHO	74	>99	*S*

Table II



aldehyde	isolated yield, %	% ee of **2**	abs config
n-$C_5H_{11}CHO$	81	91	*S*
$(CH_3)_2CHCHO$	76	94	*R*
c-$C_6H_{11}CHO$	82	92	*R*
$(CH_3)_3CCHO$	74	98	*R*
PhCHO	76	96	*R*
PhCH═CHCHO	79	98	*R*

An enantiospecific route to the propadienyl carbinols **1**, R = H, was developed as follows. The (*R*,*R*)-bromoborane reagent **3** was prepared as described earlier[2] from the bis-*p*-toluenesulfonamide of (*R*,*R*)-1,2-diphenyl-1,2-diaminoethane and boron tribromide in dry CH_2Cl_2 at 20 °C and, after removal of volatile components under vacuum, was used in the same flask. Reaction of bromoborane **3** with 0.95 equiv of propadienyltri-*n*-butylstannane (**4**)[4] in CH_2Cl_2 at 0 °C for 4 h and 23 °C for 0.5 h produced the propargylborane derivative **5** which was used in situ for reaction with various aldehydes (0.9 equiv) at −78 °C for 2.5 h. The results obtained with a series of six aldehydes are summarized in Table I. In addition, parallel experiments were performed with the (*S*,*S*) enantiomer of **5** and the six aldehydes shown in Table I to give the enantiomeric series of propa-1,2-dienyl carbinols. The adducts of general formula **1** and their enantiomers were each converted to the (*R*)-(+)-α-methoxy-α-(trifluoromethyl) phenyl acetate (MTPA) esters[5] and analyzed by 500 MHz ^1H NMR spectroscopy, which allowed clear distinction between the two diastereomers. For each reaction shown in Table I (and the other enantiomeric series as well) only a single enantiomeric product could be detected, with enantioexcesses definitely greater than 99% in each case. Absolute configurations were determined by optical rotation for the previously known alcohols (**1**, R = C_6H_5, R = cyclohexyl and R = *n*-alkyl).[6] The reaction products **1** were isolated in the indicated yields with purity of 98–99%, the contaminant being the isomeric propargyl carbinol (1–2%).[7]

The extraordinary enantiospecificity of the carbonyl addition to form the propadiene carbinols **1** is unprecedented.[6] Because

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[1] Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.

[2] Corey, E. J.; Yu, C.-M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495.

[3] Corey, E. J.; Jardine, P. D.-S.; Virgil, S.; Yuen, P. W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243–9244.

[4] Propadienyltri-*n*-butylstannane (**4**) (colorless liquid) was prepared by reaction of ethereal propargyl magnesium bromide with tri-*n*-butylchlorostannane followed by heating the crude product at reflux in methanol for 30 min and was obtained in 78% yield after distillation at 92–95 °C (0.2 Torr). See: (a) Ueno, Y.; Okawara, M. *J. Am. Chem. Soc.* **1979**, *101*, 1893. (b) Boaretto, A.; Marton, D.; Tagliavini, G. *J. Organomet. Chem.* **1985**, *297*, 149.

[5] Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

[6] Boldrini, G. P.; Lodi, L.; Tagliavini, E.; Tarasco, C.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1987**, *52*, 5447.

[7] The recovery of the chiral controller, the bis-*p*-toluenesulfonamide of 1,2-diphenyl-1,2-diaminoethane, was also excellent (>90%).

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