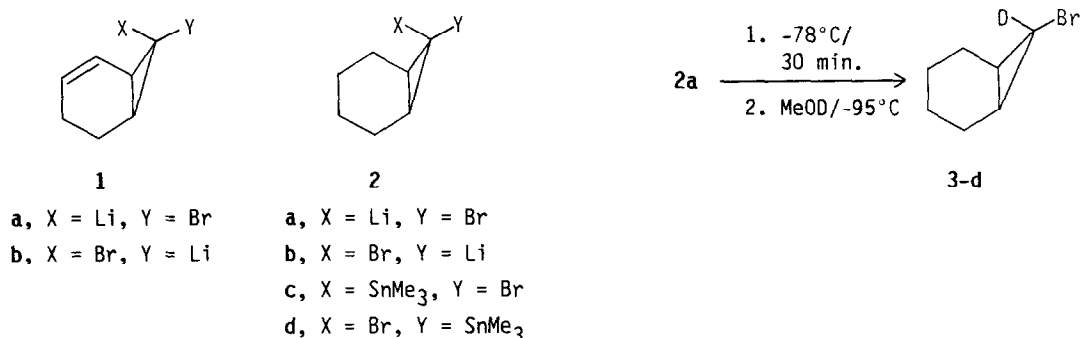# LITHIUM NORCARANYLIDENOIDS.
## ALKYLATION AND EPIMERIZATION[1]

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Summary: The epimeric 7-bromo-7-lithionorcaranes have been stereospecifically generated; the exo-bromo isomer is stable at -78°C, while the endo- bromo isomer is reactive. The stereochemistry of its reaction with nBuLi involves inversion.

The recent report[2] of a partially invertive alkylation of a lithium vinylidenoid with tBuLi prompts us to communicate similar results in a cyclopropylidenoid system. Our interest in the stereospecifically generated carbenoids 2a[3-5] and 2b[3-5] was stimulated by our studies[6] of the Skattebol rearrangement[7] of 1a and 1b, where it appeared reasonable that rearrangement of the latter was preceded by its epimerization to the former.


1	2	3-d
a, X = Li, Y = Br	a, X = Li, Y = Br	
b, X = Br, Y = Li	b, X = Br, Y = Li	
	c, X = SnMe$_3$, Y = Br	
	d, X = Br, Y = SnMe$_3$	

Generation of carbenoid 2a from stannane 2c was effected at -95°C[8] in THF (5 eq. nBuLi, 5 min.). When 2a was warmed to -78°C for 30 min., followed by recooling to -95°C and quenching with MeOD, only 3-d resulted. Thus, 2a was stable at -78°C. Epimeric carbenoid 2b, synthesized from 2d[8] at -95°C in THF (3 eq. nBuLi, 20 min.),[9] behaved quite differently at -78°C. Now, quenching of the recooled 2b solution with MeOD (-95°C) gave, depending upon reaction time, up to 5 main products (eqn. 1).[10,11] The overall yield of these products was 60-70%.


(1)

| 2b | | 4 | 4-d | 3-d | 5-d | 6 |
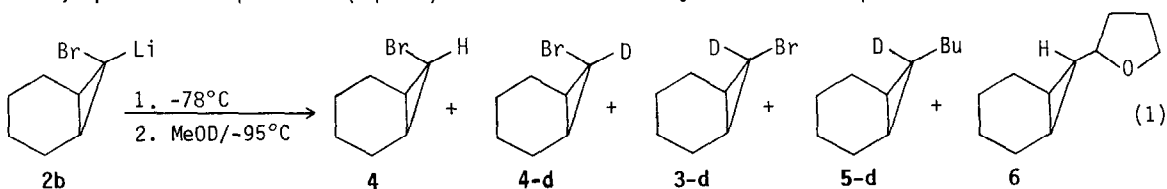
The ratios of the products were determined by analytical gc for reaction times varying from 0-8 min. at -78°C. Reasonable pseudo-first-order kinetics[13] were observed: k_{obs} (loss of 4-d) = (5.9 ± 0.4) x 10^{-3} sec^{-1}; k_{obs} (production of 5-d and 6) = (5.8 ± 0.4) x 10^{-3} sec^{-1}. From the ratios of 3-d:5-d:6, their relative rates of formation were calculated (using [THF] = 12 M; [nBuLi] = 0.05 M[13]): $k_1/k_3 \approx 1.3$ M; $k_2/k_3 \approx 160$.
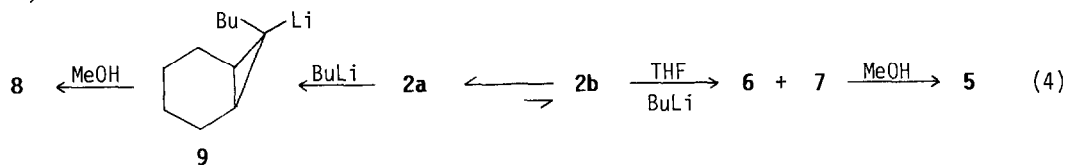

Scheme I
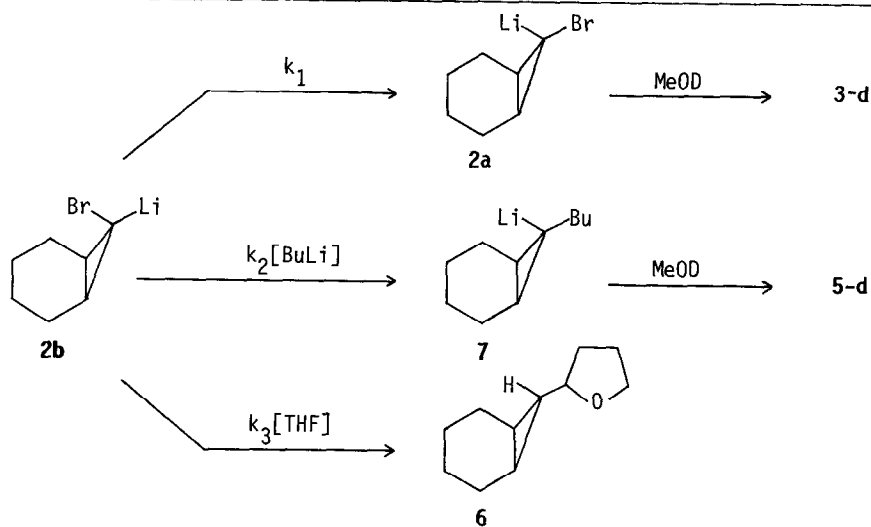
Mechanistically, the results can be interpreted in terms of three parallel competitive pathways for the demise of 2b (Scheme I). From such a scheme, one can calculate $k_1 \approx 3.5$ x 10^{-4} sec^{-1}.[14] The important conclusions are: (1) epimerization of 2b to the more stable 2a is relatively slow at -78°C, although rapid enough to be consistent with the aforementioned 1b to 1a conversion;[6] this means that previously encountered apparent epimerizations should be reevaluated to see whether they might have proceeded via bimolecular exchange;[8] and (2) 2b undergoes stereoselective solvent insertion[18] and stereospecific alkylation; alkylation involves a nucleophilic attack[19] with inversion of configuration.

The higher temperature chemistry of carbenoid 2a was investigated briefly. In addition to other products,[3a] those shown in eqns. (2) and (3) were found in the indicated ratios for
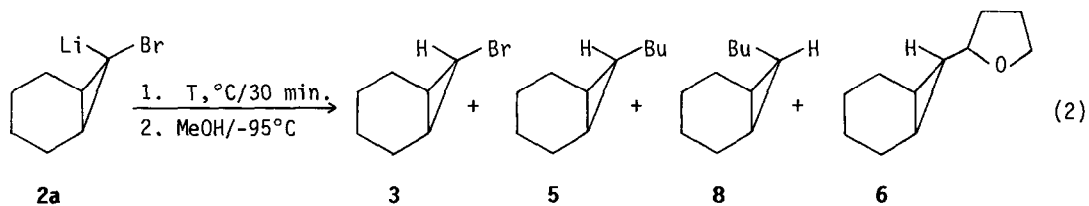
	3		5		8		6	
-50°C:	18	:	6	:	8	:	13	
-25°C:	0	:	8	:	7	:	19	(3)

reactions at -50°C and -25°C, respectively. Also, nBu_3SnMe and nBu_4Sn were both formed at -50°C, and only nBu_4Sn at -25°C. It can be seen that carbenoid butylation is fairly stereo-random at -50° to -25°C. In our view, these results are best explained by assuming 2a is in equilibrium with its less stable, more reactive epimer, 2b, which is the source of 5 and 6 (eqn. 4).

$$8 \xleftarrow{\text{MeOH}} 9 \xleftarrow{\text{BuLi}} 2a \underset{\longrightarrow}{\longleftarrow} 2b \xrightarrow[\text{BuLi}]{\text{THF}} 6 + 7 \xrightarrow{\text{MeOH}} 5 \qquad (4)$$

Further studies of the kinetic behavior of lithium carbenoids will be reported in due course.

References and Notes

1. We gratefully acknowledge partial support of this work by the National Science Foundation.

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7. Skattebol, L. Tetrahedron 1967, 23, 1107.

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9. The amount of nBuLi used was determined by what was required for complete disappearance of 2d in reasonable time (given the difficulty of maintaining the -95°C temperature bath for long times[8]). Thus 2d still remained after 40 min. with 2 eq. nBuLi, and after 10 min. with 3 eq. nBuLi.

10. Almost all the 4 was produced in the initial exchange reaction at -95°C. Thus MeOD quenching of the 2d/nBuLi/-95°C reaction after 6 min. at -95°C gave the same deuterium incorporation result as after 20 min. at -95°C, namely a ca. 55:45 ratio of 4-d:4; the amount of 4 remained approximately constant over time at -78°C, while 4-d decreased (in accord with it being the quench product from 2b). The production of 4, suggestive of electron transfer in the -95°C carbenoid formation step, is apparently related to the amount of n-BuLi used; further studies are in progress.

11. In addition to these products, <5% of the two binorcaranylidene dimers[3a,12] were formed (but not included in our analysis). Intramolecular insertion products[3a] do not arise from 2b.

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13. Formation of 6 is pseudo-first-order, while production of 5-d is approximately so under our

conditions. We use an $[nBuLi]_i = 0.076$ $\underline{M}$. After formation of **2b**, $[nBuLi] = 0.05$ $\underline{M}$. This represents a $\underline{ca.}$ 8 fold excess over that amount of **2b** which reacts with nBuLi to eventually give **5-d**. However, the situation is complicated by the loss of some nBuLi via its reaction with nBuSnMe$_3$ to give nBu$_2$SnMe$_2$. In any event, we do not observe the fall-off in the production of **5-d** which would be expected if the pseudo-first-order approximation were grossly incorrect.

14. This represents an "overall" rate constant; we cannot yet address kinetic questions involving aggregation effects,[15] ion pair behavior,[16,17] etc.

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19. At times there appears to be some confusion regarding the overall mechanism of carbenoid alkylation. Because a carbenoid is ambiphilic,[20] it might nucleophilically attack RX (itself generated via the initial metal-halogen exchange with RLi). While such a reaction is possible,[21] it is not the source of alkylated cyclopropane. Thus we have found that **i** + CH$_3$Li in CH$_3$I/Et$_2$O ($[CD_3I]/[CH_3Li] = 5.1$) at room temperature gave **iv** (7% isolated) with only $\underline{ca.}$ 8% CD$_3$ (92% CH$_3$), with that amount having arisen from reaction of the CD$_3$Li generated in the final step. In the absence of MeI, the epimeric 10-bromo-10-methyl-[4.3.1]propellanes were formed in a 12:1 ratio, with **vi** predominating. While **vi** was
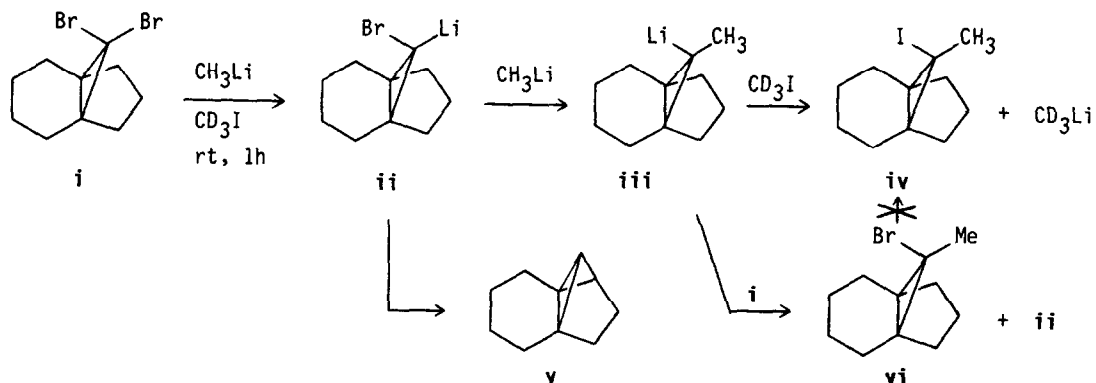
produced in ~1% yield in the **presence** of MeI, a control experiment showed it did not give **iv** under the reaction conditions. As reported,[22] **v** was always the major product (63% isolated). In view of the work on **2**, it is clear that the stereochemistry of **iv** and the regiochemistry of C-H insertion are due to the predominance of carbenoid **ii**, which is thermodynamically preferred over its epimer. Lastly, for the carbenoid generation method used herein, nucleophilic attack on RX is precluded by its absence.

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