

REACTION OF 1,6-DIHALOPENTACYCLO[5.2.0.0.0^{2,6}.0^{3,9}.0^{5,8}]NONANES WITH
tert-BUTYLLITHIUM:
 IS 1,6-DEHYDROHOMOCUBANE INVOLVED AS A REACTIVE INTERMEDIATE? [†]

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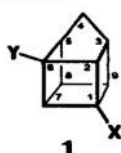
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Summary: Reaction of the 1,6-dihalohomocubanes 1a-g with 5.0 equiv. of *tert*-butyllithium afforded after aqueous workup 1-*tert*-butylhomocubane 5a as the major product in all cases. These results suggest that 1,6-dehydrohomocubane 6 is formed as a short-lived intermediate.

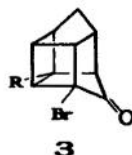
It has recently been demonstrated that the reaction of 1-bromo-7-halohomocubane with *tert*-butyllithium leads to 1(7)-homocubene as a fleeting intermediate.^{1,2} We now report on the reaction of several 1,6-dihalohomocubanes 1a-g with *tert*-butyllithium (*t*-BuLi).

The dihalides 1a-c were synthesized starting from keto-ester 2a³ following conventional reaction paths. The bromo-ester 2b, obtained in 41% yield from treatment of 2a with bromine and triethylamine in CCl₄,⁴ was photocyclized to give 3a (yield 87%, m.p. 107-108°C) by irradiating a methanol solution with a mercury low-pressure lamp in a solidex apparatus. 3a was converted into the dicarboxylic acid 4a in 76% yield (m.p. 190-193°C) by KOH/methanol under reflux, followed by acidic workup. Hunsdiecker degradation of 4a afforded a 62% yield of 1b (m.p. 45-45.5°C), whereas the diiodide 1c was obtained in 34% yield (m.p. 42-43°C) from 4a by reaction with *tert*-butyl hypoiodide in boiling Freon 113 under irradiation with a 150-Watt light bulb.⁵ The dichloride 1a was synthesized in 61% yield (m.p. 37-40°C) from 4a via the dicarboxylic acid dichloride by reaction with the sodium salt of 1-hydroxypyridine-2-thione in boiling CCl₄.^{6,7}

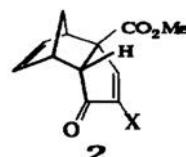
The mixed halides 1d-g were prepared by replacement of the carboxylic group of 3b by either bromine or chlorine using the methods of Barton⁷ with Br-CCl₃ as source for bromine and CCl₄ for chlorine, affording the dibromoketone 3c and the bromochloroketone 3d in yields of 79% and 47%. These ketones were converted into the acids 4b (m.p. 158-160°C) and c (m.p. 156-159°C) in yields of 44% and 66% by treatment with strong alkali. Further application of the Barton procedure to 4b and c (with iodoform as source for iodine) led to the formation of 1d-g in yields of 24, 20, 46, and 12%.



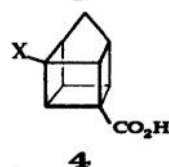
1	a	b	c	d	e	f	g
Y	Cl	Br	I	Br	Br	Cl	Cl
X	Cl	Br	I	Cl	I	Br	I



3	a	b	c	d
R	CO ₂ Me	CO ₂ H	Br	Cl



a: X = H
 b: X = Br



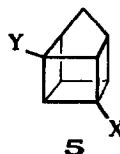
a: X = CO₂H
 b: X = Br
 c: X = Cl

Reaction of 1b with 5.0 equiv. of *t*-BuLi in ether at -78°C for 15 min, warming to room temperature within 1.5 h and an aqueous workup afforded, in addition to some non-volatile material, a 78% yield of 1-*tert*-butylhomocubane 5a.⁸ When deuterium oxide instead of water was added to the reaction mixture of 1b and *t*-BuLi, 1,6-D₂-1-*tert*-butylhomocubane 5b was isolated in 82% yield. The position of the deuterium in 5b was established from the ¹³C NMR spectrum: the signal at δ 42.74 (C-6, C-8) showed only one half of the intensity of the corresponding signal in the ¹³C NMR spectrum of 5a.

The reactions of the dihalides 1c-g with 5.0 equiv. of *t*-BuLi were carried out as described for 1b. In all cases only 5a was isolated, as the sole volatile product, in yields given in Table 1. The same type of result was obtained from reaction of the dichloride 1a with *t*-BuLi. However, complete conversion of 1a was achieved only after a reaction time of 4 h at -78°C . The reaction of 1b with 5.0 equiv. of *sec*-butyllithium gave rise to a 91% yield of 1-*sec*-butylhomocubane.

Table 1. Yields of 5a from 1a-g and 5.0 equiv. of *t*-BuLi

Dihalide 1:	a	b	c	d	e	f	g
% Yield of 5a:	65	78	53	64	57	72	51



- a: X = *t*-Bu, Y = H
 b: X = *t*-Bu, Y = D
 c: X = H, Y = *t*-Bu
 d: X = Li, Y = Cl
 e: X = Cl, Y = Li
 f: X = *t*-Bu, Y = Li

If it is accepted that the lithium-halogen exchange reaction proceeds faster with bromides than with the corresponding chlorides,⁹ 5d should be generated as an intermediate from 1f by reaction with *t*-BuLi, and 5e should be generated from 1d. The simplest interpretation of the experimental results of this investigation is the assumption that 5d and 5e eliminate lithium chloride to give the highly strained 1,6-dehydrohomocubane 6 as a common reactive intermediate. 6 contains the structural subunit of a [3.1.1]propellane; it is trapped by the excess *t*-BuLi, with selective addition of the base to C-1, to give the adduct 5f. NMR spectroscopy of 5a did not furnish any evidence for the formation of 5c, indicating that the attack of the *t*-butyl group at C-1 of 6 is at least 20 times faster than at C-6. This is not fully unexpected, since bond angle deformation is more severe at the propellane central atom C-1 of 6 than at C-6.



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References and Notes:

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