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1-t-BUTOXYCYCLOHEXENES FROM REACTIONS OF 1-HALOCYCLOHEXENES AND POTASSIUM t-BUTOXIDE. EVIDENCE FOR 1,2-CYCLOHEXADIENE AND CYCLOHEXYNE INTERMEDIATES

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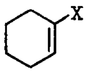
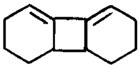
Compelling evidence indicates that reactions of phenyllithium in ether at > 100° with 1-chlorocyclopentene, 1-chlorocyclohexene (1), and 1-chlorocycloheptene occur predominantly, and probably exclusively, by elimination-addition mechanisms involving cycloalkynes.[1] In marked contrast, equally compelling evidence indicates that reactions of the 2-halo-3-(2-hydroxyethoxy)-cyclohexenes with potassium t-butoxide (KO-t-Bu) in dimethyl sulfoxide (DMSO) that give cyclohexenone ethylene ketal and 2,5-dioxabicyclo[4.4.0]dec-7-ene in combined yields of > 70% can be explained on the basis of mechanisms that do not involve a cyclohexyne.[2] Further, the interesting tricyclic hydrocarbons 5 and 6, which were obtained in yields of 7 and 30% from reactions of 1-bromocyclohexene (2) with KO-t-Bu in DMSO[3] and 1-chlorocycloheptene with sodamide in liquid ammonia,[4] have been explained as arising from dimerization of intermediate 1,2-cycloalkadienes.



1: X = Cl   3: X = I
2: X = Br   4: X = O-t-Bu



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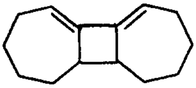

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This observed diversity of reactions made clear the need of a systematic investigation of reactions of 1-halocycloalkenes with a strong base system. Experience with reactions of substituted 1-halocyclohexenes[2] indicated that study of reactions of the 1-halocyclohexenes 1-3 with KO-t-Bu would be more feasible, and probably more informative, than with either an alkali metal amide or phenyllithium.

1-Chlorocyclohexene (1) was converted to 1-lithiocyclohexene,[5] and addition of halogen gave 2, bp 72-74°/36 mm,[6] and 3, bp 53-55°/5 mm, in > 70% yield.[7] Treatment of 1, 2, and 3 in DMSO at 65° with 1.1 equiv of KO-t-Bu·HO-t-Bu for 30, 3.2 and 2 hr, respectively, (or 2.2 equiv of resublimed KO-t-Bu for < 7 min) gave, in addition to a complex mixture of hydrocarbons,[8] a 5-12%

yield of 1-*t*-butoxycyclohexene (4), bp 87-89°/40 mm.[7] Similar yields of 4 were obtained from 2 and 3 on treatment with 1.1 equiv of KO-*t*-Bu in 80:20% by volume DMSO-HO-*t*-Bu. Change of solvent to boiling THF for 2 and 3 or diglyme at 130° for 1 raised the yield of the ether to *ca*. 60%.

Formation of 4 could be rationalized on the basis of numerous mechanisms. That more than one is operative was indicated when we found that treatment of the different 1-halo-4-methyl-cyclohexenes[7] with KO-*t*-Bu in DMSO, THF, or diglyme gave different mixtures of 1- and 2-*t*-butoxy-4-methylcyclohexene (Table I).[9] Significantly, 2-1-^{14}C and 3-1-^{14}C with KO-*t*-Bu in THF gave essentially the same proportions of ether by direct substitution[10] as were obtained when the corresponding 1-halo-4-methylcyclohexenes were treated under the same conditions.

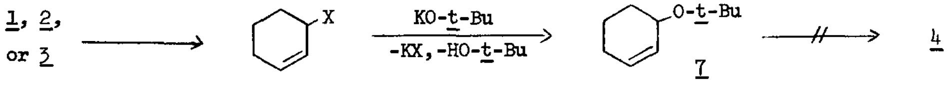
Table I: Composition of 1- and 2-*t*-Butoxy-4-methylcyclohexenes from Reactions of 1-Halo-4-methylcyclohexenes with KO-*t*-Bu [a]

Halogen	Solvent	% 1-ether [b]	% 2-ether [b]
Cl	DMSO	98	2
Cl	Diglyme [c]	90	10
Br	DMSO [d]	86	14
Br	80% DMSO: 20% HO-*t*-Bu	80	20
Br	THF	58	42
I	DMSO [d]	72	28
I	80% DMSO: 20% HO-*t*-Bu	69	31
I	80% DMSO: 20% HO-*t*-Bu [c]	74	26
I	THF	56	44
I	Diglyme [c]	68	32

[a] Reactions were carried out under nitrogen at 65° unless noted otherwise. Ether yields ranged from 8-20% in DMSO or DMSO·HO-*t*-Bu and 20-53% in THF or Diglyme. [b] Analyzed as ketones by vpc after hydrolysis with HCl. [c] At 130°. [d] Reactions carried out in the presence of oxygen gave the same distribution of ethers.

As 3-*t*-butoxycyclohexene (7)[7] is not converted to 4 under the reaction conditions, mechanisms involving 7, such as eq. 1, could be eliminated from further consideration as pathways to 4.

(1)



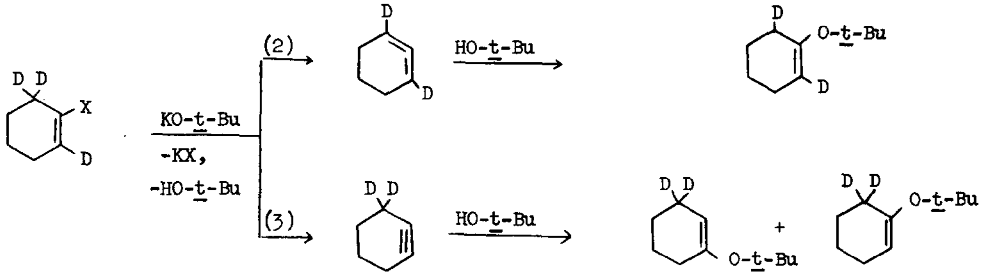
After it was determined that 1-*t*-butoxycyclohexene (4) undergoes no exchange with solvent under the reaction conditions, 1 was treated with KO-*t*-Bu·DO-*t*-Bu in DMSO-d_6. Also, 1-2,6,6-d_3[1a] and 3-2,6,6-d_3 were prepared and treated with KO-*t*-Bu·HO-*t*-Bu in DMSO. The ether products were analyzed by mass spectrometry (ms) and NMR. They were then converted to cyclohexanone by treatment with 1.5 *M* HCl in THF, and each of the cyclohexanone samples was treated twice with 0.1 *M* aqueous NaOH and analyzed by ms. The results of these experiments, which are summarized in Table II, showed that formation of 4 occurs with incorporation on one hydrogen from the solvent at either C_2 or C_6 of the ether, and that the amount of ether which incorporates hydrogen from the solvent at its vinyl position is twice the amount of ether formed by rearrangement (*i.e.*, ether in which C_1 corresponds to C_2 of the 1-halocyclohexene).

Table II: Summary of Reactions in DMSO that gave 1-*t*-Butoxycyclohexene (4) Labelled with Deuterium [a]

1-Halocyclohexene	1-*t*-Butoxycyclohexene	Cyclohexanone
1 [b]	93%d_1, 7%d_2	$>$ 99%d_0
1-2,6,6-d_3 [c,d]	7%d_1, 93%d_2; $<$0.10 H at C_2	98%d_0, 2%d_2
3-2,6,6-d_3 [c]	$>$99%d_2; 0.6H at C_2	64%d_0, 2%d_1, 34%d_2

[a] Run at 65° under nitrogen. [b] DMSO-d_6 solvent. [c] Starting material was 95%d_3, $<$0.5%d_0 and d_1. [d] Recovered starting material was 90%d_3, $<$0.5%d_0 and d_1.

These results are incompatible with formation of a significant amount of 4 by an elimination-addition mechanism involving bicyclo[3.1.0]hex-5-ene[11] or bicyclo[2.2.0]hex-1-ene, an SN-type mechanism, or addition-elimination mechanisms that occur with or without rearrangement. They are completely consistent with formation of 4 by means of two concurrent elimination-addition mechanisms involving 1,2-cyclohexadiene (eq. 2) and cyclohexyne (eq. 3).



The data summarized in Table I can now be interpreted as showing that change of halogen from bromide or iodide to chloride, use of DMSO in place of an ether solvent, and elevated temperatures favor formation of 1-t-butoxycyclohexene via 1,2-cyclohexadiene.

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References and Notes

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(7) Preparation and characterization are described in the Ph.D. Thesis of F. P. C., University of California, Davis, 1967. See Diss. Abstr., 29, 934 (1968).

(8) A. T. Bottini, F. P. Corson, R. Fitzgerald, and K. A. Frost, Jr., accompanying paper.

(9) P. Caubere and J. J. Brunet [Tetrahedron Letters, No. 39, 3323 (1969)] have observed similar rearrangements in reactions of amines and thiolates with 1-chloro-4-methylcyclohexene effected by NaO-t-Bu·$NaNH_2$.

(10) Labelled cyclohexanone, obtained by acid hydrolysis of 4-x-^{14}C, was degraded to cadaverine and carbon dioxide and radioassayed as described by J. D. Roberts et al., J. Amer. Chem. Soc., 78, 601 (1956).

(11) Cf. T. C. Shields and P. D. Gardner, J. Amer. Chem. Soc., 89, 5425 (1967).