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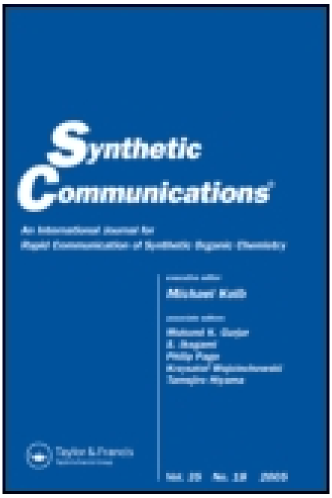

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The Reactivity of Potassium Carbanions with Epoxides

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THE REACTIVITY OF POTASSIUM CARBANIONS WITH EPOXIDES

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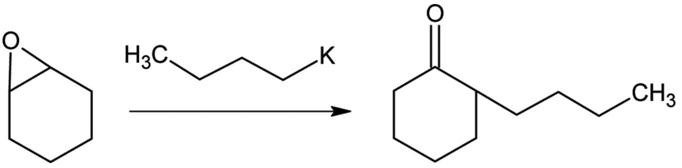
GRAPHICAL ABSTRACT



Abstract *Cyclohexene oxide reacted with n-butylpotassium unexpectedly to produce 2-butylcyclohexanone in a 10% isolated yield of its semicarbazone derivative. Based on previous literature, a three-part mechanism is proposed that implies that a yield greater than 33% is not possible.*

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Keywords 2-Butylcyclohexanone; carbanions; α-cumylpotassium; epoxides; organometallic reagents; semicarbazone

INTRODUCTION

The literature describes the combination of a potassium alkoxide and *n*-butyllithium as a "superbase" or LiCKOR reagent with metalating capabilities.[1] Alkyl potassiums[2–4] prepared in a similar manner[1] have also been reacted with ferrocene,[2] α-olefins,[5] toluene, cross-linked polystyrene derivatives,[3] and saturated ethers to produce metalated products.[2–5] In particular, the reaction of *n*-butylpotassium with cyclohexene oxide was expected to produce cyclohex-2-en-1-ol just as *n*-butyllithium does when reacted with cyclohexene oxide,[6] but the reaction of α-cumylpotassium with cyclohexene oxide to produce *trans*-cumylcyclohexanol by nucleophilic substitution[7] (Scheme 1) indicated that organopotassium species are not simply metalating agents but can be effective nucelophiles.

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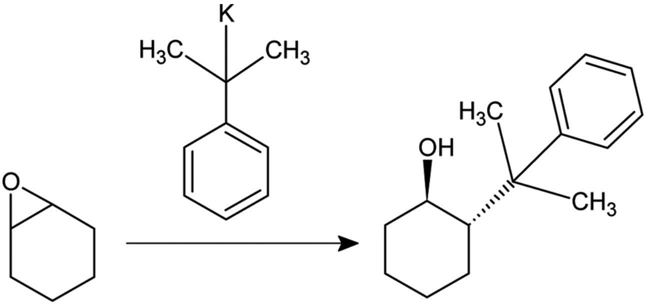

Scheme 1. Synthesis of racemic *trans*-cumylcyclohexanol.

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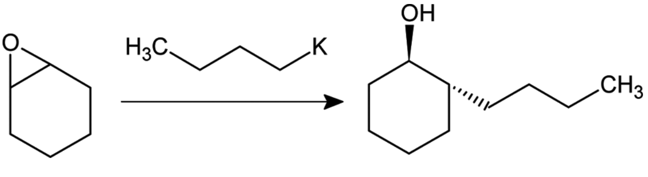
DISCUSSION

The reaction of *n*-butylpotassium with cyclohexene oxide was studied. If *n*-butylpotassium were to react with cyclohexene oxide by the same substitution mechanism as α-cumylpotassium, the expected product would be *trans*-2-butylcyclohexan-1-ol (Scheme 2). The reaction of 1.2 equivalents of potassium-*tert*-amylate and 1 equivalent of *n*-butyllithium and cyclohexene oxide afforded not only the expected elimination product (cyclohex-2-en-1-ol) but also new signals corresponding to 2-butylcyclohexanone by ^{13}C NMR that agreed with the literature values,[8] but there was no evidence of the predicted substitution product. To verify the identity and quantify this unique product, 2-butylcyclohexanone was isolated in a 2% yield by radial chromatography and mass analyzed. Noting the volatility of this spearmint-scented ketone, semi-carbazide was added to the crude reaction mixture to give a 10% yield of the semicarbazone with a melting point for the recrystallized product in ethanol of 134 °C (lit. 138.5–150 °C[9–12]). ^{13}C NMR data for the semicarbazone could not be found in the literature, but the ^{13}C NMR of the synthesized semicarbazone, included in the Supporting Information (available online), agreed with a simulated spectrum calculated using ^{13}C NMR Predictor Software from ACD Labs. A review of the literature gave insight into the mechanism for the conversion of cyclohexene oxide to 2-butylcyclohexanone. First, the work done by Hodgson et al. describes that in the presence of a strong base epoxides can rearrange to enolates through a carbene intermediate[13] (Scheme 3). Second, work conducted by Oku et al. describes that ketones can be produced when carbenes react with secondary alkoxides by hydride abstraction[14] (Scheme 4). The literature led us to postulate the following three-step mechanism: First, 2-butylcyclohexanone is produced by opening the epoxide ring of cyclohexene oxide by an S_N2 substitution with



Scheme 2. Predicted product of reaction of *n*-butylpotassium and cyclohexene oxide, racemic *trans*-2-butylcyclohexanol.

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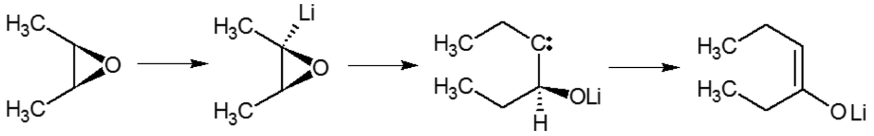
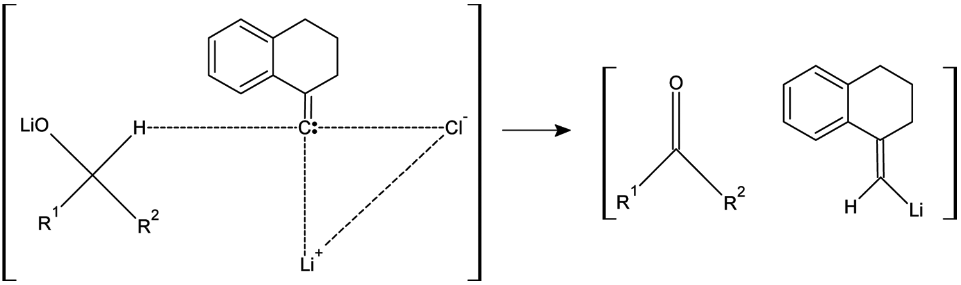
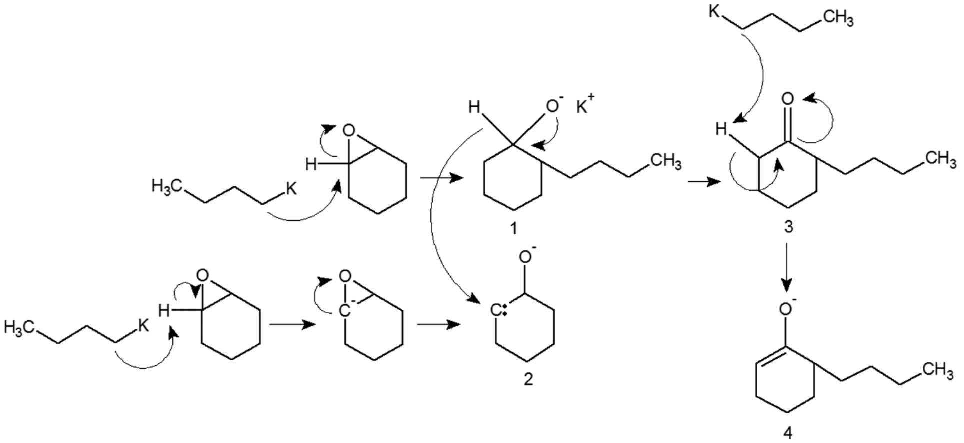


Scheme 3. Rearrangement of an epoxide in the presence of a strong base.



Scheme 4. Conversion of secondary alkoxide to ketone via hydride abstraction.

n-butylpotassium to make the alkoxide of *trans*-2-butylcyclohexan-1-ol (**1**) as predicted. Next, a second equivalent of *n*-butylpotassium reacts with cyclohexene oxide to produce a carbene alkoxide (**2**) as postulated by Hodgson. Finally, the carbene alkoxide (**2**) oxidizes the alkoxide of *trans*-2-butylcyclohexan-1-ol (1) to 2-butylcyclohexanone (**3**) as observed in Oku's chemistry, which is then converted to the corresponding enolate (**4**) by a third equivalent of *n*-butylpotassium (Scheme 5). In addition to the volatility of 2-butylcyclohexanone, the incomplete isolation of its semicarbazone after recrystallization, and the competing elimination of cyclohexene oxide to cyclohex-2-en-1-ol, the proposed mechanism also explains why a yield greater than 33% is not possible. We continue to study the range of the



Scheme 5. Proposed mechanism for the production of 2-butylcyclohexanone.

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reactivity of organopotassium species with epoxides, including how to isolate the proposed initial ring-opening products.

EXPERIMENTAL

Synthesis of 2-Butylcyclohexanone

To a clean and dry 100-mL, round-bottom flask with magnetic stir bar and rubber septum were added 40 mL of 1.2 M potassium *tert*-amylate (48 mmol) and 16 mL of 2.5 M *n*-butyllithium (40 mmol) dropwise via syringe under nitrogen gas. After 15 min, the reaction formed a white precipitate and 3.74 g of cyclohexene oxide (38.1 mmol) was added dropwise. The reaction was stirred a further 2 h, and then 30 mL of deionized water were added and the yellow organic layer was washed with more water (2 × 30 mL). The combined aqueous layers were extracted with dichloromethane (3 × 30 mL), and the combined organic layers were dried over potassium carbonate and decanted into a round-bottom flask. The solvent was removed via vacuum distillation on a rotary evaporator, and the remaining light yellow oil was distilled bulb to bulb utilizing a Kugelrohr apparatus to give 1.18 g of crude product. Radial chromatography was performed on the distillate to identify and quantify the percentage yield of 2-butyl cyclohexanone as follows: A 5% ethyl acetate/hexane solution was prepared and utilized to moisten the 0.25 in rotating silica plate. To the moistened silica plate was added 0.28 g of crude sample. An ultraviolet light was utilized to observe and collect the first band as it eluted from the plate. The solvent was evaporated utilizing aspirator pressure giving 0.03 g (2%) of isolated product. The ^{1}H NMR, ^{13}C NMR, and mass spectrum analysis coincide with the literature data.[8]

Synthesis of 2-Butylcyclohexanone Semicarbazone

To a clean and dry 100-mL round-bottom flask with magnetic stir bar and rubber septum were added 10 mL of 1.2 M potassium *tert*-amylate (12 mmol) and 0.99 g of cyclohexene oxide (10.1 mmol) via syringe under nitrogen gas. To the flask was added 4 mL of 2.5 M *n*-butyllithium (10 mmol) dropwise. The reaction was stirred for a further 1 h, and then 30 mL of deionized water was added and the yellow organic layer was washed with more water (2 × 30 mL). The combined aqueous layers were extracted with hexane (3 × 30 mL), and the combined organic layers were poured into a 250-mL, round-bottom flask. To the flask were added 1.57 g of sodium acetate and 0.98 g semi-carbazide, and it was shaken vigorously until a white solid formed. The remaining solvent was evaporated via vacuum distillation on a rotary evaporator and the remaining light yellow oil was allowed to cool until crystals formed. The remaining crystals were then washed with cold ethanol to give 0.19 g of semicarbazone or 0.154 g of 2-butylcyclohexanone (10%). The semicarbazone was recrystallized using ethanol to give fine white crystals: mp 134 °C (lit. mp. 138.5–139.5 °C) ^{13}C NMR ($CDCl_3$) $\delta = 14.105$, 22.867, 23.754, 25.144, 26.306, 29.458, 30.700, 33.018, 43.996, 155.652, 157.915.

SUPPORTING INFORMATION

^{1}H and ^{13}C NMR spectra can be found online in the Supporting Information for this article.

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