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SELECTIVE INSERTION OF CYCLOPROPYLIDENES IN THE FORMATION OF BICYCLOBUTANES

R. B. Reinarz* and G. J. Fonken

Department of Chemistry, The University of Texas at Austin

Austin, Texas 78712

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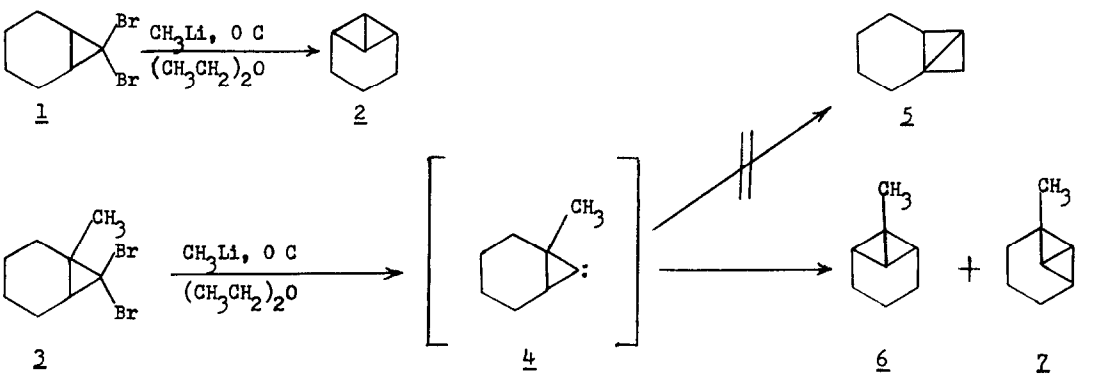
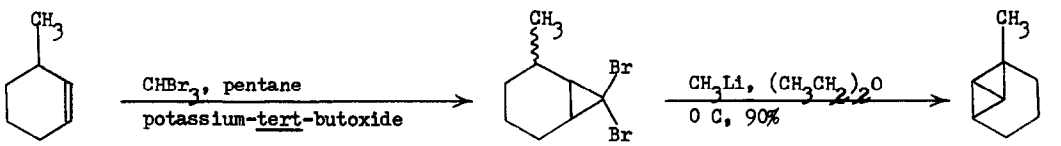
Reaction of methyl lithium with 7,7-dibromobicyclo[4.1.0]heptane (1) has been shown to yield a variety of products which are explained via a cyclopropylidene intermediate[1,2,3,4]. Depending upon the reaction conditions, tricyclo[4.1.0.$0^{2,7}$]heptane (2) was formed in low yields (<25%) along with an array of both intermolecular and intramolecular insertion products[1]. Among the products anticipated from the reaction of methyl lithium with gem-dibromocyclopropanes of similar carbocyclic structure are bicyclobutanes. For comparison to 1, the C-1 methyl homolog, 7,7-dibromo-1-methylbicyclo[4.1.0]heptane (3) was prepared by dibromocarbene addition to 1-methylcyclohexene. On reaction of 3 with methyl lithium, it was assumed that cyclopropylidene 4 would be formed. Although insertion of cyclopropylidenes have been shown to favor substituted C-H bonds[3,5,6], there was a possibility also for some primary insertion into the C-1 methyl group to yield 5. Only bicyclobutanes 1-methyltricyclo[4.1.0.$0^{2,7}$]heptane (6--60%) and 2-methyltricyclo[4.1.0.$0^{2,7}$]heptane (7--40%) were produced, however.



The structure assigned to the major product 6 was based on the following spectral characteristics: NMR in CCl_4 [2.17 δ (multiplet, 2H), 1.52 δ (singlet, 3H), 1.27 δ (singlet, 6H), 1.01 δ (multiplet, 1H)]; IR, neat [1164 cm^{-1}, 809 cm^{-1}, 772 cm^{-1}(strong)]; mass spectrum with parent peak at 108; elemental analysis; comparison to the known compound[7]. The identification of the second isomer 7 was confirmed by spectral data: NMR in CCl_4 [2.30 δ (multiplet, 1H), 1.31 δ (multiplet, 8H), 1.05 δ (singlet, 3H)]; IR, neat [1162 cm^{-1}, 1009 cm^{-1}, 830 cm^{-1}, 738 cm^{-1}(strong)]; mass spectrum with parent peak at 108; elemental analysis. Only two compounds were formed, both bicyclobutanes, indicating that alkyl substitution at C-1 influences product distribution to favor only bicyclobutanes. The two bicyclobutanes were formed by insertion into secondary C-H bonds at C-2 (6) and C-5 (7) with no insertion detected into the primary methyl group at C-1 which would have formed 5.

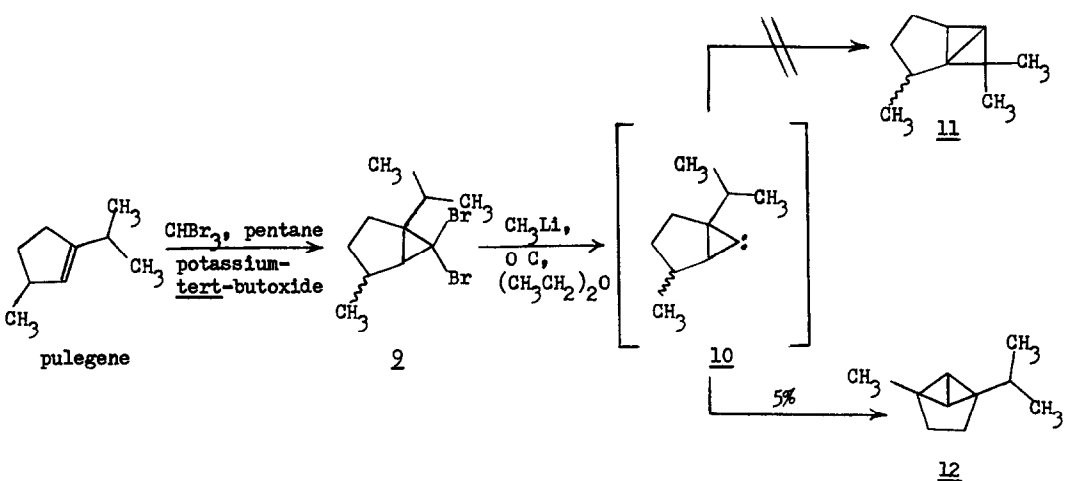
An isomer of 3, 7,7-dibromo-2-methylbicyclo[4.1.0]heptane (8) was synthesized by addition of dibromocarbene to 3-methylcyclohexene (9). This reaction would conceivably yield two isomers; one with the C-2 methyl group syn and the other with the methyl group anti to the cyclopropane ring. The anti isomer was the expected predominate product and has the necessary configuration which, on reaction with methyl lithium, would lead to 2-methyltricyclo[4.1.0.$0^{2,7}$]heptane (7). Expectation of 7 was based on evidence that cyclopropylidenes have been shown to favor insertion into substituted C-H bonds of similar structures[5,8]. Upon reaction of 8 with methyl lithium, it was anticipated that insertion into the tertiary C-H bond at C-2 would be favored. Indeed, a 90% yield of 7 was obtained with no evidence for intermolecular insertions into solvent or methyl bromide.



2 8 7

This example is especially significant since the bicyclobutane is available in large yield. Also, the compound is the same as the lesser product from the reaction of 3 with methyl lithium. The NMR, IR, and mass spectrum are identical for the products from both reactions and are consistent with the assigned structure.

In addition, the reaction of methyl lithium with 6,6-dibromobicyclo[3.1.0]hexane has been reported to yield a mixture of a dimer, trimers, and tetramers depending upon the reaction conditions[1,2]. These products were explained as arising from an intermediate 1,2-cyclohexadiene[9,10,11]. The proposed mechanism for 1,2-cyclohexadiene formation was rationalized via a rearrangement of an α-bromolithium species and very unlikely through a cyclopropylidene[10]. Corroborative evidence was obtained from the reaction of 1-bromocyclohexene with potassium-tert-butoxide for the existence of 1,2-cyclohexadiene as an intermediate which could be captured with a dienophile[12]. The alternate pathway, through cyclopropylidene formation, was considered for further testing since recent evidence has accumulated that cyclopropylidenes favor insertion into substituted C-H bonds[5,6,8,13]. Therefore, it was felt that if 6,6-dibromo-1-isopropyl-4-methylbicyclo[3.1.0]hexane (9), on reaction with methyl lithium, yields any cyclopropylidene (10), adducts 11 or 12 would be formed by insertion of 10 into either tertiary C-H bond. A single monomeric product, 1-isopropyl-4-methyltricyclo[2.1.1.$0^{5,6}$]hexane (12), was obtained in low yield plus polymers of presently unknown stereochemistry. This result is especially significant since the reaction provides the first example of the generation and trapping of a cyclopropylidene intermediate in the 6,6-gem-dibromobicyclo[3.1.0]hexane series since 12 could best be explained via the pathway involving cyclopropylidene 10[8].



Evidence for the proposed structure of 12 is as follows: NMR in CCl_4 [1.80 δ (heptet, J=6 hz, 1H), 1.51 δ (singlet, 2H), 1.28 δ (singlet, 4H), 1.15 δ (singlet, 3H), 0.91 δ (doublet, J=6 hz, 6H)]; IR, neat [1385 cm^{-1}, 1365 cm^{-1}, 975 cm^{-1}, 804 cm^{-1}(strong)]; mass spectrum with parent peak at 136; suitable elemental analysis. Moreover, the compound reacted explosively with iodine which

is characteristic of bicyclobutanes[8,14,15].

Since 9 was obtained from the addition of dibromocarbene to pulegene[16,17], there were two possible isomers, one with the C-4 methyl group syn to the cyclopropane ring and the other with the C-4 methyl group anti. Based on steric considerations, the isomer with the C-4 methyl group anti to the cyclopropane ring should be disfavored. If so, the anti isomer, which has the necessary configuration for the insertion reaction, would be available in lesser quantity and explain the low yield of 12. Thus, the isolation of 12 is evidence that, at least in this example, the cyclopropylidene is the logical intermediate.

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*Author to whom correspondence should be addressed at Department of Chemistry, North Texas State University, Denton, Texas 76203.

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