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THE MECHANISM OF THE COUPLING REACTION BETWEEN IODOCYCLOPROPANES AND METHYLLITHIUM (1)

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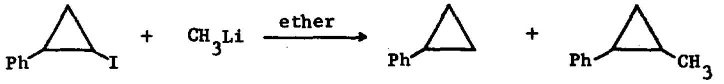
The reaction of *trans*- or *cis*-1-iodo-2-phenylcyclopropane (**1a**,**b**) with methyllithium in ether yields phenylcyclopropane (**2**) and, with 100% retention of configuration, *trans*- or *cis*-1-methyl-2-phenylcyclopropane (**3a**,**b**). The reaction is quantitative, produces roughly equal amounts of **2** and **3a** or **3b**, and is over in less than five minutes at room temperature (3a). The epimeric 7-iodonorcaranes behave similarly, although their reaction with methyllithium is very much slower (50-70% reaction after two hours) (3b).



1a *trans*
b *cis*

2

3a *trans*
b cis

Scheme **1** illustrates plausible mechanisms for the production of **2** and **3**. Compound **2** is shown as arising from halogen-metal exchange followed by protonation of cyclopropyllithium **4** upon aqueous work-up (see below). Compound **3** can arise in either of two ways:

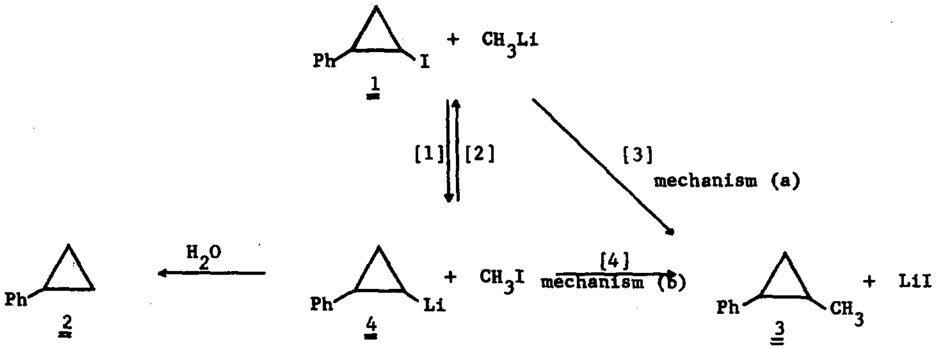
(a) by a one-step Wurtz coupling of the reactants, reaction [3];

(b) by a two-step process involving cyclopropyllithium **4**, reactions [1] and [4].

To account for the observed stereospecificity, reaction [3] would have to proceed with complete retention of configuration were mechanism (a) followed, whereas reactions [1] and [4] would have to proceed with the same stereochemistry, either both retention or both inversion, were mechanism (b) correct. Of the two possibilities for mechanism (b), the double retention mechanism is by far the more likely since halogen-metal exchange of bromocyclopropanes with organometallic reagents is known to proceed with complete (or nearly complete) retention of configuration (4).

The sequence [1],[4] (mechanism (b)) was our original choice, since reaction of **1a** with a

Scheme 1



10 to 15-fold excess of methyllithium produces equal amounts of 2 and 3a, but the same experiment in the presence of a 45-fold excess of methyl iodide gives 2 and 3a in a ratio of 1:23 (5). It is possible, however, that mechanism (a) is responsible for 3, and that the effect of excess methyl iodide is simply to displace the [1],[2] equilibrium in the direction of 1 + CH_3Li. We now present evidence which suggests that mechanism (b) is, in fact, the sole route to coupling product 3.

Our solution to this problem requires a knowledge of two partition factors in Scheme 1: k_1/k_3 (the partitioning of 1 + CH_3Li between reactions [1] and [3]) and k_4/k_2 (the partitioning of 4 + CH_3I between reactions [4] and [2]). In order to determine these competition factors, one must perform the experiments under conditions where the two competing reactions are irreversible.

As was reported in the preceding communication (6), 0.0045 mole of iodo compound 1 reacts with 0.01 mole of methyllithium(lithium iodide) in the presence of methylene chloride, hexane, and ether yielding only phenylcyclopropane (2); even in the presence of 0.01 mole of methyl iodide, 2 is the only product. Since 2-phenylcyclopropyllithium (4) is not appreciably protonated by ether (6), we take this as evidence that reaction [1] has occurred and that 4 is protonated by methylene chloride before it can react with methyl iodide. Thus, the partitioning of reactions [1] and [3] is strongly in favor of the halogen-metal exchange process, $k_1 \gg k_3$.

If we can now show that k_2 is not large relative to k_4, but is in fact of comparable magnitude, then we can say that mechanism (b) is the exclusive route to methylcyclopropane 3. In order to determine k_4/k_2, we must observe the reaction of 4 + CH_3I under conditions where reaction [2] is irreversible. One way to do this is to remove methyllithium from the reaction as it is formed.

Reaction of 0.002 mole of iodo compound 1 with 0.0077 mole of methyllithium(lithium iodide) in the presence of a huge excess of methyl iodide (1.0 mole) in ether leads to only 5-10% reaction of 1, the exclusive product being methyl cyclopropane 3. A gas (presumably ethane) is evolved during this reaction but not during the reactions in which methyl iodide is present in low concentrations or not at all. Thus, methyllithium reacts with methyl iodide much faster than it does with iodocyclopropane 1. Therefore, the ratio of methyl compound 3 to iodo compound 1 formed from lithium reagent 4 with a similarly huge excess of methyl iodide will give the desired partition factor, k_4/k_2.

Cyclopropyllithium 4 is prepared by reaction of 1-chloro-2-phenylcyclopropane (*cis*/*trans* = *ca*. 7) with lithium (1% sodium) shot (7) in ether; an aliquot from this solution when quenched with iodine gives 1-iodo-2-phenylcyclopropane (1b/1a = *ca*. 5) along with 16% of phenylcyclopropane (8). Addition of 0.0032 mole of lithium reagent 4, thus prepared, to 1.0 mole of methyl iodide in ether produces about 60% of compound 3 and 40% of compound 1. Therefore, k_4/k_2 is *ca*. 1.5.

The combination of $k_1 \gg k_3$ with $k_4 > k_2$ insures that 1-methyl-2-phenylcyclopropane (3) arises exclusively by mechanism (b), halogen-metal exchange followed by coupling of 2-phenylcyclopropyllithium (4) with methyl iodide.

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