

REDUCTIVE COUPLING OF ALLYLIC HALIDES
BY CHLOROTRIS(TRIPHENYLPHOSPHINE)COBALT(I)

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Summary : Reactions of geranyl and farnesyl halide, and their geometrical isomers with chlorotris(triphenylphosphine)cobalt(I) gave the corresponding geometrically pure coupling products under mild and non-basic conditions. Squalenes were stereospecifically synthesized by this method.

Coupling of allylic halides is an important synthetic reaction forming 1,5-diene system, which is frequently encountered in structures of natural products. In recent years the coupling of allylic halides using low-valent transition metal reagents has been extensively studied. In many cases a higher valent transition metal compound with a reducing agent was employed for coupling reactions¹, and in some cases the transition metal carbonyls² and lanthanide compounds³ were also used. However, few example of the allylic coupling promoted by low-valent cobalt is available⁴.

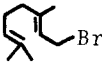
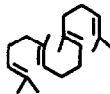
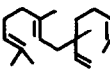
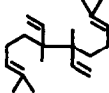
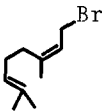
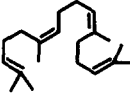
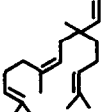

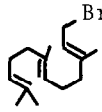
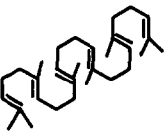
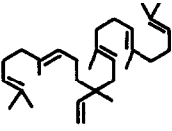
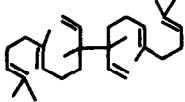
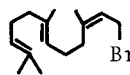
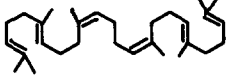
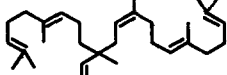

In the course of our investigation⁵ on the reactions of mono-valent cobalt complex, chlorotris(triphenylphosphine)cobalt(I), we have found that $\text{CoCl}(\text{Ph}_3\text{P})_3$ effects the reductive coupling of allylic halides. The reaction is characterized by the following advantages. The reaction can be carried out under mild and non-basic conditions in various organic solvents without generation of the mono-valent cobalt in situ prior to the reaction since the reagent is fairly stable complex. The reaction proceeds with preservation of the stereochemistry of carbon-carbon double bond of allylic halides to give geometrically pure 1,5-dienes.

In this paper we wish to describe the coupling reactions of terpenoid allylic

halides such as geranyl and farnesyl halide, and their geometrical isomers with $\text{CoCl}(\text{Ph}_3\text{P})_3$.

A typical experimental procedure is as follows : to a stirred suspension of $\text{CoCl}(\text{Ph}_3\text{P})_3$ ⁶ (1.08 g, 1.2 mmol) in 11 ml of degassed benzene was added 242 mg of geranyl bromide (1.1 mmol) under argon atmosphere and the mixture was stirred for 0.5 h at room temperature. The reaction mixture was filtered and the filtrate was treated with methyl iodide (5 ml) for 10 min at room temperature⁷. Precipitates were filtered off and the filtrate was concentrated under reduced pressure. Flash chromatography of the residue using n-hexane as an eluent afforded 2, 3 and 4 in 66, 16 and 7% yield, respectively. The results of the other coupling reactions are summarized in the Table.

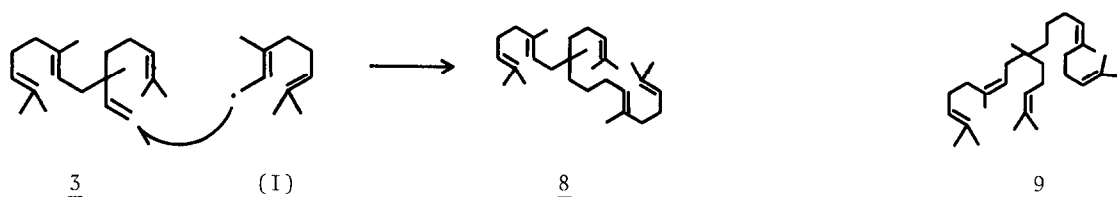
Table Examples of Coupling of Allylic Bromides Using $\text{CoCl}(\text{Ph}_3\text{P})_3$ ^a

Allylic Bromide ^b	Products(Yield)				
 <u>1</u>	 <u>2</u> (66%)	+	 <u>3</u> (16%)	+	 <u>4</u> (7%)
 <u>5</u>	 <u>6</u> (63%)	+	 <u>7</u> (16%)	+	 <u>4</u> (9%)
 <u>10</u>	 <u>11</u> (55%)	+	 <u>12</u> (22%)	+	 <u>13</u> (12%)
 <u>14</u>	 <u>15</u> (51%)	+	 <u>16</u> (19%)	+	 <u>13</u> (8%)

a. Reactions were carried out in degassed benzene at room temperature.

b. Prepared by the reaction of corresponding alcohols with PBr_3 in ether.

Both reactions of 1 and its geometrical isomer 5 with the reagent in benzene afforded head-to-head coupling product (2 from 1, 6 from 5) as the major product with the regioselectivity of 70%. Regarding the stereochemical feature of the reaction, the geometry of the double bond of the allylic bromides was retained in the coupled products; any geometrical isomers of 2 and 6 were not detected in each reaction mixture. The reaction of the corresponding allylic chlorides gave the same coupling products in similar ratio and yields although it required somewhat prolonged reaction time. The yield and product distribution were almost unaffected by changing the reaction medium from benzene to n-hexane, toluene and dimethoxyethane, respectively. However, when the reaction was carried out in an aprotic polar solvent such as N,N-dimethylformamide(DMF) and hexamethylphosphoramide, a trimer (8 from 1 or 9 from 5) was formed in addition to the dimeric coupled products with change of the product ratio. The stereochemistry of the trimers (8) and (9) reflected those of allylic halides used. The reaction of 1 in DMF gave 2(53%), 3(10%), 4(14%) and the trimer (8)^{8,9}(10% yield). Similarly the trimer (9)¹⁰(11%) was obtained from 5 in addition to 6(48%), 7(8%) and 4(18%). Formation of 8 can be explained by the addition of geranyl radical species (I) derived from initially formed organocobalt intermediate¹¹, to the least hindered olefin of 3 in an anti-Markownikoff's manner followed by hydrogen abstraction from the solvent.



Squalenes were effectively synthesized by this method. (E,E)-Farnesyl bromide (10) was converted to (E,E,E,E)-squalene (11) in 55% yield in stereospecific manner. (E,Z,Z,E)-Squalene (15) was also formed in 51% yield from (Z,E)-farnesyl bromide (14). Present reaction provides a new and convenient synthetic method for the stereospecific preparation of 1,5-diene system.

References and Notes

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7. Triphenylphosphine liberated during the reaction was removed as methyl-triphenylphosphonium iodide.
8. New compounds gave satisfactory high resolution mass measurements.
9. 8 ; $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ_{ppm} 0.90(3H,s), 1.21(6H,m), 1.60(15H,s), 1.69(9H,s), 1.90-2.09(14H,m), 5.06(5H,m).
10. 9 ; $^1\text{H-NMR}$ (100 MHz, CDCl_3) δ_{ppm} 0.90(3H,s), 1.21(6H,m), 1.60(9H,s), 1.69(15H,s), 1.90-2.09(14H,m), 5.06(5H,m).
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