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A FACILE SYNTHESIS OF 1,5-DIENES BY A REGIOSELECTIVE ALLYLATION OF THE ALLYLIC CARBANIONS GENERATED FROM ALLYL PHENYL SELENIDES

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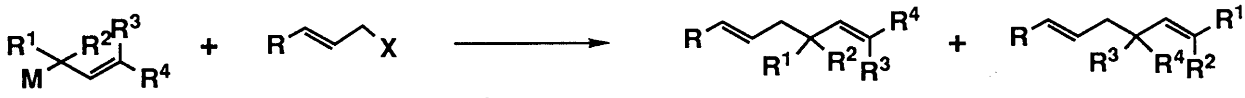
Allyl-allyl or benzyl coupling reactions were effected by allyl carbanions, generated from allyl phenyl selenides and n-butyllithium, and allylic or benzylic halides. The ambident selectivities of the allyl carbanions are depending on the solvent system.

KEYWORDS allyl selenide; allyllithium; allyl carbanion; coupling reaction; 1,5-diene; regioselective allylation

1,5-Diene systems are widely distributed in natural products, especially terpenes such as cembranoids.[1] The carbon-carbon bond formation between α-hetero atom (Se or S) stabilized allyllithium and allylic halides is one of the useful methods for the synthesis of the natural products containing 1,5-diene moiety. [2,3] However, the reductive elimination of the hetero atoms was necessary for the synthesis of 1,5-diene moiety in many cases.[3] A more direct method, the coupling reaction of the allylic anion without hetero atom stabilization with allyl halides, is useful for the synthesis. Allyl- and crotylmagnesium halides and allylzinc halides were reacted with various allyl- and benzyl halides to give the 1,5-diene compounds in poor to moderate yields.[4] The yields were variable depending on the nature of the allyl halides and the reaction conditions. Some highly regioselective allyl-allyl coupling reactions by the use of allylic indate[5], boronate[6] and other organometallic reagents[7] have been reported.



M=metal

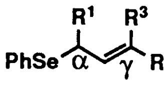
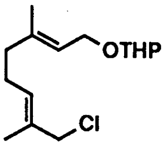
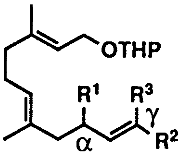
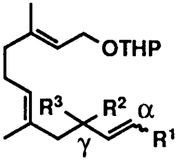
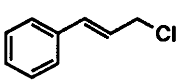
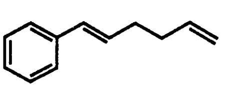
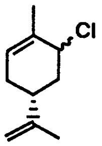
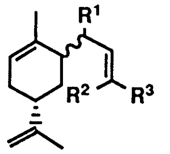
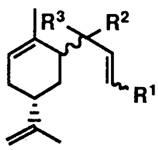
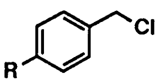
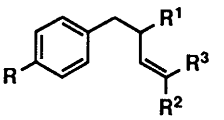
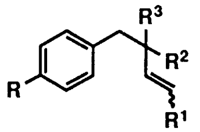
Chart 1

Usually, allyllithium derivatives are more reactive than the allylmagnesium and allylzinc compounds for the Wurtz reaction.[4a] A few examples of the reaction of allylic lithiums and allyl halides have been reported.[8] Clarembeau and Krief [9,10] reported an efficient method for the synthesis of various allyl carbanions by the reaction of allyl phenyl selenides with n-butyllithium. They also reported the reactions of the allylic and benzylic carbanion with benzaldehyde[9,10] and alkyl halides.[11] However, to our knowledge, there are no reports on the reactions of the allyl carbanions with allyl or benzyl halides, giving 1,5-diene derivatives. We report in this communication an efficient method for the synthesis of various 1,5-dienes by the reaction of allyl halides and allyl carbanions prepared from allylselenides as described above.

The reactions of the allylic carbanions prepared from allyl selenides and n-butyllithium at -78 ° C with various allyl- and benzyl halides afforded excellent yields of the 1,5-dienes together with n-butyl phenyl selenide. These results are summarized in Table I. Allyl Grignard reaction with *p*-methoxybenzyl chloride (**9**) gave the coupling product (**22**), but only in 26% yield.[12] However, the reaction of the allylic carbanion prepared from the allylselenide (**1**) with the benzyl chloride (**9**) gave **22** in 76% yield (entry 11). The primary, secondary, benzyl and cinnamyl chlorides (**5,7,8,9** and **6**) were easily reacted with the allylic carbanions in good yields. Even the highly substituted allylic carbanion from **4** underwent a similar reaction with excellent yields. (entries 4,9 and 14) All these reactions selectively proceeded at the α-position of the allylic halides with excellent yields, and also proceeded with good regioselectivities of the allylic carbanions. It is well known that an allyllithium reacts with nucleophiles as the ambident carbanion, and its regioselectivities depend on the nature of the nucleophiles and reaction conditions.[4a,9]

In most of our cases, the carbanion derived from the primary and the secondary allyl selenides (**2** and **3**) reacted with the various allyl halides (**5-9**) to give almost the same distribution of the coupling products (entries 2,3; 7,8; and 12,13). From these results, it can be partly assumed that the ambident allylic carbanions generated from the two allylselenides (**2** and **3**) reacted mainly at the secondary carbon. The carbanion derived from **4** also predominantly reacted with the primary; the benzylic halides (**5** and **9**) at the tertiary position, however, reacted with the secondary halide (**7**) at the primary carbon. These results could be assumed to be due to the steric hindrance.

TABLE I. Allyl-Allyl (Benzyl) Coupling Reactions between Allyl(or Benzyl)chlorides and Allyl Selenides[a]

Entry	Selenide	Chloride	Products[b] α-Attack[c]	Products[b] γ-Attack[c]	Ratio[d]	Yield (%)[e]
						
1	**1** $R^1=R^2=R^3=H$	**5**	**10** $R^1=R^2=R^3=H$			74
2	**2** $R^1=H$, $R^2,R^3=H,Me$ (E/Z 77/23)	**5**	**11** $R^1=H$, $R^2,R^3=H,Me$	**12** $R^1=H$, $R^2,R^3=H,Me$	**11**/**12** 30/70	85
3	**3** $R^1=Me$, $R^2=R^3=H$	**5**	**12** $R^1=Me$, $R^2=R^3=H$	**11** $R^1=Me$, $R^2=R^3=H$	**11**/**12** 30/70	98
4	**4** $R^1=H$, $R^2=R^3=Me$	**5**	**13** $R^1=H$, $R^2=R^3=Me$	**14** $R^1=H$, $R^2=R^3=Me$	**13**/**14** 40/60	98
						
5	**1**	**6**	**15**			72
						
6	**1**	**7**[f]	**16** $R^1=R^2=R^3=H$			75
7	**2**	**7**	**17** $R^1=H$, $R^2,R^3=H,Me$	**18** $R^1=H$, $R^2,R^3=H,Me$	**17**/**18** 14/86	92
8	**3**	**7**	**18** $R^1=Me$, $R^2=R^3=H$	**17** $R^1=Me$, $R^2=R^3=H$	**17**/**18** 28/72	76
9	**4**	**7**	**19** $R^1=H$, $R^2=R^3=Me$	**20** $R^1=H$, $R^2=R^3=Me$	**19**/**20** 87/13	99
						
10	**1**	**8** R=H	**21** $R^1=R^2=R^3=H$			71
11	**1**	**9** R=OMe	**22** $R^1=R^2=R^3=H$			76
12	**2**	**9** R=OMe	**23** $R^1=H$, $R^2,R^3=H,Me$	**24** $R^1=H$, $R^2,R^3=H,Me$	**23**/**24** 20/80	75
13	**3**	**9**	**24** $R^1=Me$, $R^2=R^3=H$	**23** $R^1=Me$, $R^2=R^3=H$	**23**/**24** 33/67	82
14	**4**	**9**	**25** $R^1=H$, $R^2=R^3=Me$	**26** $R^1=H$, $R^2=R^3=Me$	**25**/**26** 20/80	95

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a) All reactions were carried out in THF at -78 °C, and were performed within 30 min.

b) These products were obtained as a mixture, and are not separable. The geometry of the double bond of the introduced allylic part has not been determined.

c) α-Attack and γ-attack mean the attacking position of the allyl selenides to the electrophiles.

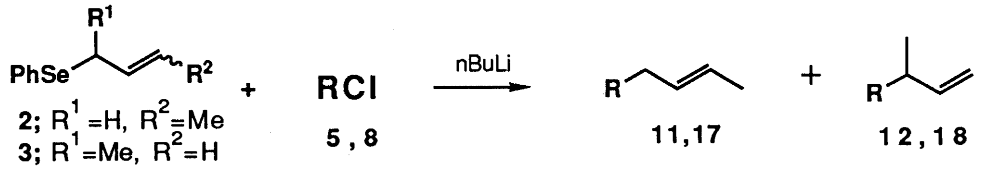
d) These ratios were determined by the ^{1}H-NMR spectra of the mixture.

e) Isolated yield. n-Butyl phenyl selenide was also isolated in 80-99% yields.

f) Synthesized from *d*-carvone by the method of Collington (see ref 13); mixture of the stereoisomers.

The nature of the solvent also plays an important role in the selectivity. The reaction of the allylic carbanions prepared from **2** and **3** with allyl halides (**5** and **7**) in THF or DME mainly afforded the coupling products **12** and **18**, respectively. When the hexane containing 3 equiv. of THF was used as the reaction solvent, the yields of **11** and **17** were remarkably increased (Table II, entries 4,5,7,9 and 11). The temperature dependence of this reaction was not observed. The selectivity and the mechanism have not been clarified; however, we assume the allyllithium intermediate[9] (**A**) as shown in Chart 2. Equilibrium is not established between **2** and **3** below room temperature. We are currently investigating the selectivities and the limitations of these reactions.

TABLE II. Solvent and Temperature Effects on the Coupling Reaction



Entry	Selenide	Halide	Solvent	Additive	Temp.(°C)	Products (11/12 or 17/18)	
						Ratio a)	Yield (%)
1	3	5	THF		-78	30/70	98
2	3	5	THF		r.t.	35/65	68
3	3	5	DME		-78	32/68	50
4	3	5	Hexane	THF(3eq.)	-30~-20	70/30	63
5	3	5	Hexane	THF(3eq.)	r.t.	78/22	53
6	2	5	THF		-78	30/70	85
7	2	5	Hexane	THF(3eq.)	-30~-20	61/39	54
8	3	8	THF		-78	28/72	76
9	3	8	Hexane	THF(3eq.)	-30~-20	70/30	76
10	2	8	THF		-78	14/86	92
11	2	8	Hexane	THF(3eq.)	-30~-20	60/40	47

a) The ratio was determined from the ^{1}H-NMR spectrum of the mixture of **11/12** or **17/18**.

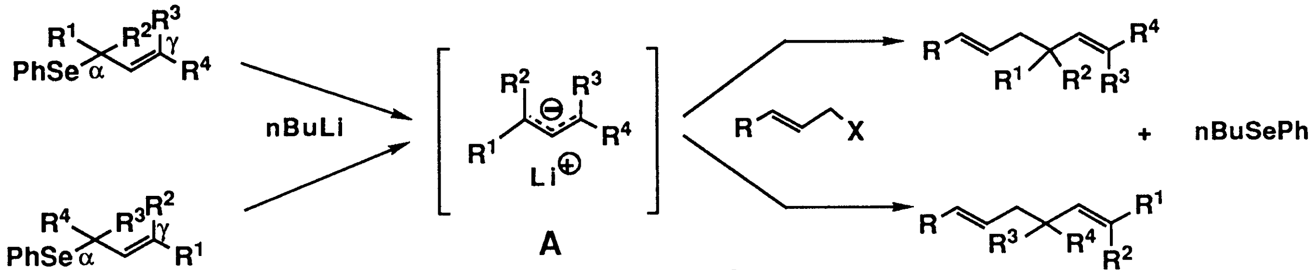


Chart 2

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