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STEREOSELECTIVE SYNTHESIS OF TRISUBSTITUTED OLEFINS *VIA* π-ALLYLIC NICKEL BROMIDE COMPLEXES WITH FUNCTIONAL GROUP

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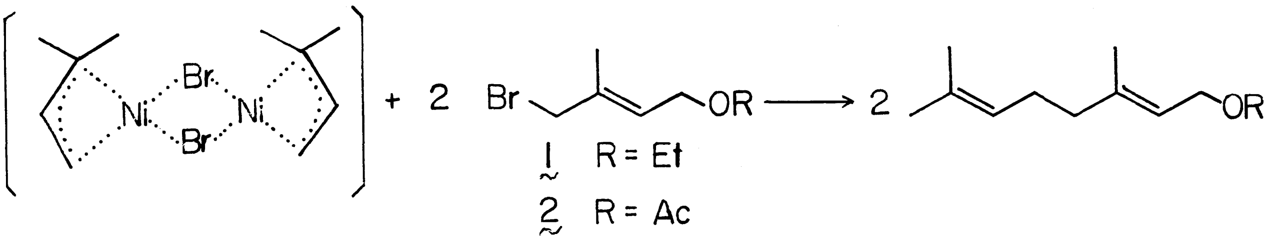
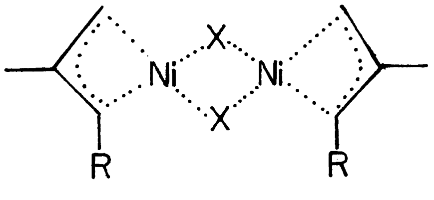
The reaction of several organic halides with the complexes, prepared from 1-bromo-2-methyl-4-phenoxy-2-butene or 4-benzyloxy-1-bromo-2-methyl-2-butene and nickel carbonyl in benzene, afforded trisubstituted (*E*)-olefins, such as 2-methyl-4-phenoxy-1-phenyl-2-butene, geranyl benzyl ether, and farnesyl benzyl ether, stereoselectively.

π-Allylic nickel halide complexes are known as reagents which form carbon-carbon bond.[1] These complexes are prepared by the reaction of allylic halides with nickel carbonyl in benzene under an argon atmosphere, and react with a variety of organic halides in polar, coordinating solvents such as *N,N*-dimethylformamide (DMF) and hexamethylphosphoramide.

We previously reported[2] that the reaction of π-1,1-dimethylallylnickel bromide with 1-bromo-4-ethoxy-2-methyl-2-butene (**1**) and 4-acetoxy-1-bromo-2-methyl-2-butene (**2**) afforded geranyl ethyl ether and geranyl acetate, respectively.



Recently π-allylic nickel halide complexes with functional group were reported in a few papers[3,4] and were used to introduce an acetonyl[3] or ester[4] group into organic substrates. However, these complexes are 2-substituted complexes, and 1,2-disubstituted π-allylnickel halide complex **3** is of great interest in stereoselective synthesis of trisubstituted olefins. Especially when R is suitably protected hydroxymethyl, the complex 3 may act to introduce a functionalized isoprene skeleton into organic substrates. In our earlier investigation$^{2)}$ no stable complexes 3 (R = $EtOCH_2$ or $AcOCH_2$, X = Br) were obtained by the reaction of ethyl ether 1 or acetate 2 with nickel carbonyl.$^{5)}$



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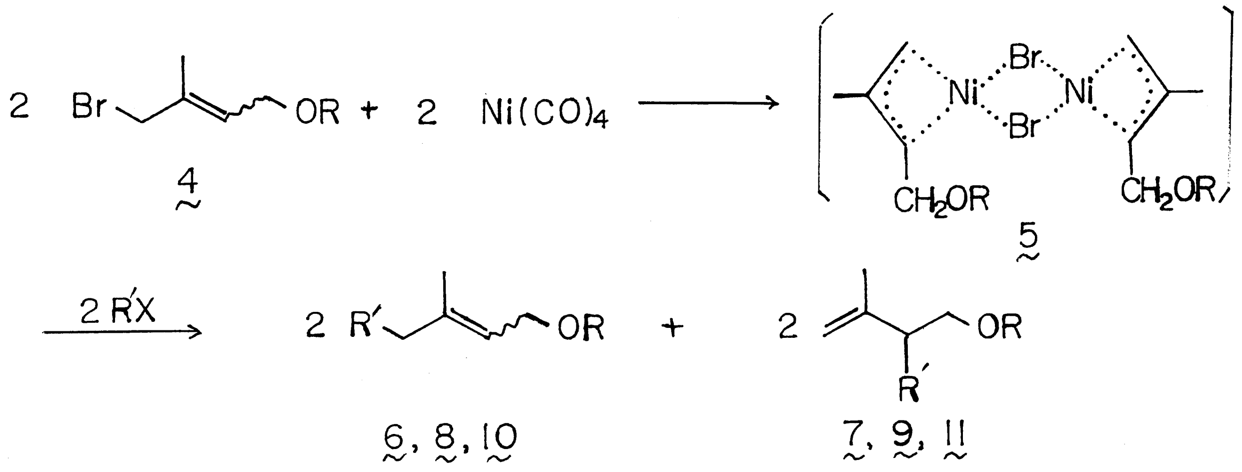
R = $EtOCH_2$, $AcOCH_2$,
$PhOCH_2$, $PhCH_2OCH_2$

X = Cl or Br

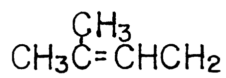
Here we investigated the synthesis of new complexes 3 (R = $PhOCH_2$ or $PhCH_2OCH_2$, X = Br) and the cross-coupling reaction of 3 with several organic halides.

To a solution of nickel carbonyl in benzene 1-bromo-2-methyl-4-phenoxy-2-butene (4a) was added at 50°C over a period of 1.5 hr and the mixture was heated with stirring for further 1.5 hr at 50°C under an argon atmosphere, then the benzene and the remaining nickel carbonyl were removed under reduced pressure to leave crude π-1-(phenoxymethyl)-2-methylallylnickel bromide (5a). Complex 5a was dissolved in DMF and allowed to react with iodobenzene at 40°C for 21 hr. The solution was



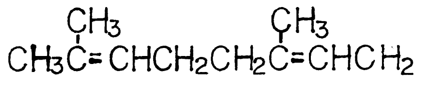
6, 7 R' = C_6H_5

8, 9 R' =



$CH_3\overset{CH_3}{\overset{|}{C}}=CHCH_2$

10, 11 R' =



$CH_3\overset{CH_3}{\overset{|}{C}}=CHCH_2CH_2\overset{CH_3}{\overset{|}{C}}=CHCH_2$

a R = C_6H_5 b R = $C_6H_5CH_2$

poured into cold water, the product was extracted with *n*-hexane and ether (1 : 1), and the extract was dried over anhydrous $MgSO_4$. Distillation gave a mixture of 2-methyl-4-phenoxy-1-phenyl-2-butene (**6a**) as a major product and its isomer, 2-methyl-4-phenoxy-3-phenyl-1-butene (**7a**) as a minor one in 49% yield; bp 135–40°C/0.1 mmHg.[6] Each isomer was isolated by means of column chromatography and the structure was determined by ir and nmr data. These spectrum data of **6a** showed that **6a** consisted of (*E*) and (*Z*) isomers. Good stereo- and regioselectivities were given in this reaction (Table 1).

4-Benzyloxy-1-bromo-2-methyl-2-butene (**4b**) also reacted with nickel carbonyl in benzene under an argon atmosphere at 50°C for 3 hr to give π-1-(benzyloxymethyl)-2-methylallylnickel bromide (**5b**). The reaction of crude complex **5b** with iodobenzene in DMF gave 4-benzyloxy-2-methyl-1-phenyl-2-butene (**6b**) and its isomer, 4-benzyloxy-2-methyl-3-phenyl-1-butene (**7b**) in 81% yield; bp 125–30°C/0.18 mmHg.[6] The product 6b also consisted of (*E*) and (*Z*) isomers.

Table 1. Reactions of π-Allylic Nickel Bromides with Organic Halides

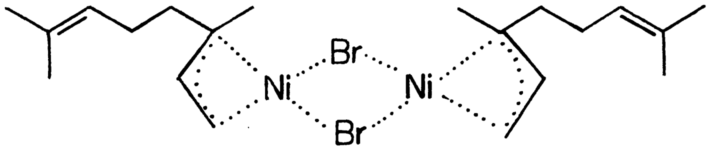
Complex	Halide	Solvent	Time (hr)	Temp. (°C)	Products (ratio, %)[a]		Yield (%)	(E) :	(Z)[a]
5a	Iodobenzene	DMF	21	40	**6a**(92)	**7a**(8)	49	84	16
5a	Prenyl bromide	THF	18	40	**8a**(93)	**9a**(7)	40	87	13
5b	Iodobenzene	DMF	40	50	**6b**(95)	**7b**(5)	81	86	14
5b	Prenyl bromide	THF	19	50	**8b**(88)	**9b**(12)	45	89	11
5b	Geranyl bromide	THF	21	50	**10b**(97)	**11b**(3)	37	93	7[b]

a) These ratios are calculated by glc peak areas.

b) This ratio refers to only C-2 double bond of **10b**.

π-Allylic nickel halides also react with allylic halides to give 1,5-diene derivatives.[7] This suggests that the reaction of polyprenyl halides with complex **5a** or **5b** gives polyprenyl phenyl or benzyl ether which is elongated by the isoprene skeleton. Thus the complex **5a** and prenyl bromide reacted in tetrahydrofuran (THF) to give geranyl phenyl ether (**8a**) and its isomer, 2,6-dimethyl-3-phenoxymethyl-1,5-heptadiene (**9a**) in 40% yield; bp 114–8°C/0.3 mmHg.[6] Geranyl benzyl ether[8] (**8b**) and its isomer **9b** were obtained from **5b** and prenyl bromide in the same procedure in 45% yield; bp 94–6°C/0.13 mmHg.[6]

A sesquiterpene, farnesyl benzyl ether (**10b**) and its isomer **11b** were obtained by the reaction of complex 5b with geranyl bromide in THF in 37% yield: bp 140–5°C/0.3 mmHg.[6] The farnesyl benzyl ether consisted of following four isomers: (2*Z*, 6*Z*)-, (2*Z*, 6*E*)-, (2*E*, 6*Z*)-, and (2*E*, 6*E*)-farnesyl benzyl ether in the ratio of 0.1 : 6.7 : 22.2 : 71.0. Each isomer was identified with an authentic sample by comparison on glc. A partial loss of the stereochemistry of C-6 double bond which originated from geranyl bromide would be probably due to halogen-metal exchange, that is, geranyl bromide is partly isomerized to neryl bromide *in situ via* π-geranylnickel bromide complex (12).



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As described above new π-allylic nickel bromides with functional group such as 5a and 5b are highly effective compounds which afford trisubstituted olefins stereoselectively. The usage of these complexes can realize a new stereoselective synthesis of acyclic terpenes.

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References and Notes

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5) The complex 3 (R = AcOCH$_2$, X = Cl) was reported by F. Guerrieri *et al.*, but experimental detail was not described and we could not obtained the complex by the reaction of 4-acetoxy-1-chloro-2-methyl-2-butene with nickel carbonyl in benzene. F. Guerrieri and G. P. Chiusoli, Chim. Ind. (Milan), **51**, 1252 (1969).

6) Each yield and boiling point refer to the mixture of isomers.

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8) Geranyl benzyl ether was lead to geraniol in 96% yield by the treatment with lithium in ethylamine at −78°C. (the Benkeser reduction) cf. E. E. van Tamelen, P. McCurry, and U. Huber, Proc. Nat. Acad. Sci. USA, **68**, 1294 (1971).

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