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HIGHLY SELECTIVE VINYL REARRANGEMENT IN THE REACTION OF ISOPRENE BROMOHYDRIN AND ALLYLIC GRIGNARD REAGENTS

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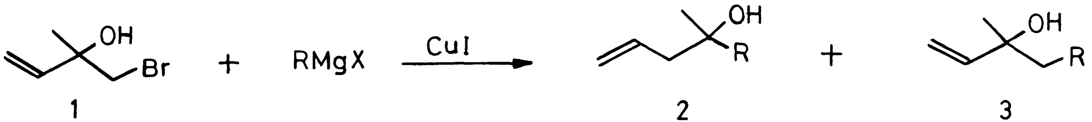
The reaction of isoprene bromohydrin (1-bromo-2-methyl-3-buten-2-ol) (1) with various allylic Grignard reagents in the presence of cuprous iodide gave vinyl group rearranged products (2) highly selectively.

Grignard reaction is one of the most important methods in synthetic chemistry. However, the reaction of halohydrin with Grignard reagent shows complicating features.[1)] It has often been observed that certain bromohydrins undergo isomerization on treatment with Grignard reagents. For instance, the reaction of 2-chlorocyclohexanol with benzylmagnesium chloride gives benzylcyclopentylcarbinol.[2)] Recently, Normant has reported[3)] that the reaction of 2-bromo-1-propanol with vinylic and allylic Grignard reagents in the presence of cuprous bromide gives normal coupling products in good yields, accompanied with a trace of rearranged products. In the present communication, we describe the cuprous iodide catalysed reaction of isoprene bromohydrin (1) with allylic Grignard reagents, which involves the highly selective rearrangement of vinyl group. To our knowledge, this is the first case of vinyl rearrangement in the Grignard reaction of halohydrin.

In the presence of cuprous iodide (0.5 equiv.), 1 (1 equiv.) was added to a solution of Grignard reagent (5 equiv.)[4)] at 0°, and the mixture was stirred overnight at room temperature. The reaction was quenched by the addition of a saturated ammonium chloride solution and the crude products were purified by distillation and subsequent column chromatography on silica gel. The structures of the products were confirmed by elemental analyses and spectral data.[5)] The main product was found to be the vinyl group rearranged one (2), and the normal coupling product (3) was estimated, if any, to be minor. The molar ratios of the products (2:3) were determined by ^{1}H-nmr integrals and VPC (SE-30 column). The results are summarized in Table.



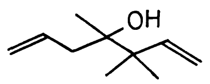
1 2 3

In the reaction of allylic Grignard reagents, the rearranged products 2 were obtained exclusively (entries a, c and d) or selectively (b and e), while, the selectivity decreases in the reaction of phenylmagnesium bromide (f). The observed high selectivities (2 vs. 3) are considered to be partly due to the facile migrating nature of the vinyl group of 1.[6)] It must be noted that in the case of prenyl- (c)

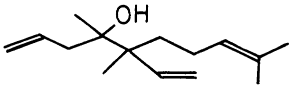
Table. Reaction of isoprene bromohydrin (1) and Grignard reagents in the presence of cuprous iodide

entry	RMgX R	RMgX X	solvent	ratio of 2 : 3	total yield	b.p./Torr
a	allyl	Br	Et$_2$O	100: 0	34%	87-91°/85
b	methallyl	Cl	THF	81:19	42	63-67°/25***
c*	prenyl	Cl	THF	100: 0	10	45-48°/ 8
d**	geranyl	Cl	THF	100: 0	24	125-128°/9
e	benzyl	Cl	Et$_2$O	95: 5	73	84-87°/ 3***
f	phenyl	Br	THF	57:43	78	72-76°/ 2***

* product (2c)



** product (2d)



*** boiling point of a mixture

and geranylmagnesium chloride (d), the reactions occur only at the tertiary carbon atom. This is interpreted in terms of the well-known equilibrium of the substituted allylic Grignard reagents between the primary and the tertiary forms.[7)]

In the absence of the catalyst, present reaction gave a complicating product mixture. Furthermore, the reaction of 1 with alkyl Grignard reagents, such as ethyl- and n-propylmagnesium bromide in the presence of CuI gave no coupling products but vinyl group migrated 4-penten-2-ol in 20-40% yield. In this manner, the reaction behavior of 1 toward Grignard reagents is very diverse. To clarify the reaction mechanism, further investigations are now under way.

References and Notes

1) For a review: M.Tiffeneau, Bull.Soc.Chim.Fr.[5],12,453(1945).
2) J.W.Cook,C.L.Hewett,and C.A.Lawrence, J.Chem.Soc.,1936,71.
3) J.F.Normant,T.Mulamba,F.Scott,A.Alexakis,and G.Cahiez,Tetrahedron Lett.,1978,3711.
4) The use of 2 equiv. of Grignard reagent caused a lowering of the total yield, while, the molar ratio (2 : 3) being essentially unchanged.
5) 2a and 2f are identical to samples prepared by known procedures; 2a: M.Fetizon, M.Golfier,and J-M.Louis,Tetrahedron,31,171(1975), 2f: V.I.Esafov,Zh.Obshch.Khim., 33,3755(1963). Spectral data of new compounds (2b - 2e) are as follows; 2b: ir (neat) 3440,1640,995,910,888 cm^{-1}, ^{1}H-nmr(CDCl$_3$,δ) 1.10(3H,s,Me),1.70(1H,s,OH), 1.81(3H,d,J=1Hz,=$\overset{|}{\mathrm{C}}$-Me),2.12(2H,s,-CH$_2$-),2.19(2H,d,J=7Hz,CH$_2$=CH-C$\underline{\mathrm{H}}_2$-),4.6-6.3(5H, m,olefin); 2c: ir(neat) 3500,1638,998,910, ^{1}H-nmr(CDCl$_3$) 1.09(6H,s,-$\overset{|}{\mathrm{C}}$Me$_2$),1.13(3H, s,-$\overset{|}{\mathrm{C}}$(OH)Me),1.52(1H,s,OH),2.25(2H,dd,J=7,2Hz,CH$_2$=CH-C$\underline{\mathrm{H}}_2$-),4.8-6.3(6H,m,olefin); 2d: ir(neat) 3500,1638,996,910, ^{1}H-nmr(CDCl$_3$) 1.04(3H,s,-$\underset{|}{\overset{|}{\mathrm{C}}}$-Me),1.13(3H,s,-$\overset{|}{\mathrm{C}}$(OH)Me), 1.53(1H,s,OH),1.60(3H,s,=$\overset{|}{\mathrm{C}}$-Me),1.68(3H,s,=$\overset{|}{\mathrm{C}}$-Me),1.5-2.1(4H,m,-CH$_2$-),2.25(2H,d,J= 7Hz,CH$_2$=CH-C$\underline{\mathrm{H}}_2$-),4.6-6.3(7H,m,olefin); 2e: ir(neat) 3400,1638,1600,1498,995,910, 735,698, ^{1}H-nmr(CDCl$_3$) 1.11(3H,s,Me),1.68(1H,s,OH),2.24(2H,d,J=7Hz,CH$_2$=CH-C$\underline{\mathrm{H}}_2$-), 2.75(2H,s,PhC$\underline{\mathrm{H}}_2$-),4.8-6.4(3H,m,olefin),7.21(5H,m,Ph).
6) A communication dealing with the migration of ethynyl group of halohydrin magnesium salts has been reported: J.J.Riehl,A.Smolokiewicz,and L.Thil, Tetrahedron Lett.,1974,1451.
7) The regioselective alkylations (at the primary carbon atom) of substituted allylic Grignard reagents in the presence of a Cu(I) salt have recently been reported: F.D-Boumechal,R.Lorne,and G.Linstrumelle, Tetrahedron Lett.,1977, 1181; G.Cahiez,A.Alexakis,and J.F.Normant, Synthesis, 1978, 598.

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