[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TENNESSEE A. AND I. STATE UNIVERSITY]

Grignard Reagents and Unsaturated Ethers. VII. The Synthesis, Properties and Reaction of β-Substituted Vinyl Ethers with Aliphatic and Aromatic Grignard Reagents

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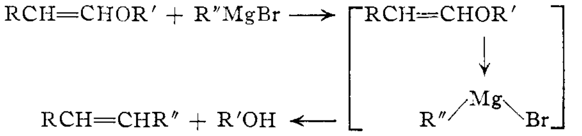
Several new β-substituted vinyl ethers of the type RCH=CHOR′, where R is CH_3, C_2H_5 and n-C_5H_{11}, and R′ is n-C_4H_9, n-C_3H_7 and n-C_7H_{15}, have been synthesized and their physical constants determined. The infrared spectra of the unsaturated ethers have been studied. Reaction of the vinyl ethers with aliphatic and aromatic Grignard reagents yielded primary alcohols, and internal and terminal olefins.

Experiments in an earlier paper[1] of this series demonstrated that aliphatic Grignard reagents react with α-alkyl substituted vinyl ethers to yield ketones. In the present paper an investigation has been undertaken to observe the course of the vinyl ether–Grignard reaction when β-alkyl substituted vinyl ethers are allowed to react with aliphatic and aromatic Grignard reagents. It was suspected that the absence of a substituent in the α-position of the vinyl ether molecule might affect its mode of reaction with Grignard reagents. Products obtained from the reaction of four β-alkyl substituted vinyl ethers with both aliphatic and aromatic Grignard reagents were primary alcohols, and internal and terminal olefins. The difference in the nature of the products formed in these two investigations suggests that the course of the vinyl ether–Grignard reaction is influenced by the position of the alkyl group in the vinyl system. For example, when n-hexylmagnesium bromide reacted with n-butyl ethylvinyl ether, 1-butanol (46%) and 3-decene (66%) were isolated.

Neither the constitution of the Grignard reagent nor the nature of the β-substituted alkyl group altered the mode of cleavage of the vinyl ether molecule by the Grignard reagent. The reaction of n-propyl methylvinyl ether with ethyl- and phenylmagnesium bromides gave 1-propanol (61%) and 2-pentene (64%), and 1-propanol (63%) and 1-phenyl-1-propene (10%), respectively; reaction of n-butyl ethylvinyl and n-butyl n-pentylvinyl ethers with n-hexylmagnesium bromides produced 1-butanol (46%) and 3-decene (66%), and 1-butanol (46%) and 6-tridecene (22%), respectively.

In the vinyl ether–Grignard reactions investigated, it is suspected that the Grignard reagent cleaves the vinyl ether by a 1,2-cleavage mechanism or various combinations of SN2, SN2′ and SN1 mechanisms.



Isolation of 2-pentene (81%) from the reaction of n-hexylmagnesium bromide with n-propyl methylvinyl ether is worthy of mention. The mechanism of formation of 2-pentene is not clearly understood. Further investigation of this reaction is being undertaken.

The infrared spectra of the substituted vinyl ethers were helpful in identifying the ethers.

Experimental[2]

Synthesis of Vinyl Ethers.—n-Propyl ethylvinyl, n-butyl ethylvinyl, n-butyl n-pentylvinyl and n-heptyl n-pentylvinyl ethers were synthesized by the procedure described for n-propyl ethylvinyl ether. Into a flask equipped with inlet and outlet tubes was placed 144 g. (2 moles) of butanal. The flask was immersed in a salt–ice-bath, and dry hydrogen chloride gas was bubbled through the chilled aldehyde for 30 seconds. Stirring was started and 120 g. (2 moles) of n-propyl alcohol added dropwise. Then hydrogen chloride gas was added to the mixture for 4 hours, while keeping the temperature at 0–5°. The top layer was separated and dried over anhydrous calcium chloride. The excess hydrogen chloride was removed by saturating the mixture with dry nitrogen. The crude chloroether was then placed in a flask and, while stirring, 202 g. (2 moles) of triethylamine was added slowly. The mixture was heated gently overnight on a hot-plate. The excess triethylamine was distilled off and the solid residue dissolved in water. The top layer was separated and the bottom layer extracted with several small portions of diethyl ether. The extracts and top layer were combined and dried. After removal of diethyl ether, distillation of the residue through a Todd column (42–60 theoretical plates) gave 68 g. of n-propyl ethylvinyl ether, b.p. 105–107° (748 mm.).

TABLE I

PHYSICAL CONSTANTS AND ANALYTICAL DATA OF VINYL ETHERS,[a] RCH=CHOR[1]

R	R[1]	Formula	B.p. °C.	B.p. Mm.	d^{20}_4	$n^{20}D$	Yield,[b] %	Carbon, % Found	Carbon, % Calcd.	Hydrogen, % Found	Hydrogen, % Calcd.
C_2H_5	n-C_3H_7	$C_7H_{14}O$	105–107	748	0.8105	1.4075	32	73.47	73.68	12.29	12.28
C_2H_5	n-C_4H_9	$C_8H_{16}O$	108–111	748	.8240	1.4135	32	74.50	75.00	12.44	12.50
n-C_5H_{11}	n-C_4H_9	$C_{11}H_{22}O$	202–203	750	.8366	1.4283	20[c]	77.31	77.65	12.20	12.94
n-C_5H_{11}	n-C_7H_{15}	$C_{14}H_{28}O$	118–120	5	.8156	1.4403	14	79.08	79.25	13.69	13.21

[a] A Perkin–Elmer model-21 double beam spectrophotometer, with a sodium chloride prism, was used to produce the infrared spectra of the vinyl ethers. The carbon–carbon double bond stretching vibration produced an intense band at 6.05 μ. The absorption peak observed around 10.75 μ probably is due to a C=C—C bending vibration. The strongest band appeared at 9.10 μ and is assigned to the C–O–C stretching vibration. [b] Percentage yields are based on grams of α-chloroether used. [c] Percentage yield is based on grams of n-heptaldehyde used.

Fractional distillation of the vinyl ethers was traced by the infrared spectra of the distillates. Disappearance of the OH absorption bands around 3 and 9.5 μ was observed and indicated separation of the alcohol from the vinyl ether. Appearance of a strong band around 9.10 μ was considered as positive evidence of the ether linkage. An infrared spectrum of an authentic sample of n-butyl vinyl ether was

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[1] C. M. Hill, R. M. Prigmore and G. J. Moore, THIS JOURNAL, **77**, 352 (1955).

[2] Melting points are corrected.

TABLE II

PHYSICAL CONSTANTS AND YIELDS OF REACTION PRODUCTS

Vinyl ether $RCH{=}CHOR^1$ R	R^1	Grignard reagent	Products	B.p., °C.	Mm.	Yield,[a] %
C_2H_5	n-C_4H_9	n-C_6H_{13}	1-Butanol[b]	117–120	749	46
			3-Decene[c]	167–170	749	66
		p-$CH_3OC_6H_4$	1-Butanol[b]	115–118	744	73
			1-p-Anisyl-1-butene[d]	147–149	744	78
CH_3	n-C_3H_7	n-C_6H_{13}	1-Propanol[e]	94–96	748	40
			2-Nonene[f]	164–167	746	31
			2-Pentene[g]	44–47	745	81
		C_2H_5	1-Propanol[e]	98–100	750	61
			2-Pentene[g]	46–48	750	64
		C_6H_5	1-Propanol[e]	97–98	742	63
			1-Phenyl-1-propene[h]	174–178	753	10
n-C_5H_{11}	n-C_7H_{15}	C_2H_5	1-Heptanol[i]	174–176	748	44
			3-Nonene[j]	141–143	748	48
C_2H_5	n-C_3H_7	C_2H_5	1-Propanol[e]	98–100	744	82
			3-Hexene[k]	67–69	744	41
		n-C_6H_{13}	1-Propanol[e]	96–99	749	71
			3-Decene[c]	169–172	751	93
n-C_5H_{11}	n-C_4H_9	n-C_6H_{13}	1-Butanol[l]	110–113	755	46
			6-Tridecene[m]	124–126	2	22
		C_6H_5	1-Butanol[b]	113–	745	9
			1-Phenyl-1-heptene[n]	182– 8	745	53

[a] Yields are based on grams of vinyl ether used. [b] *MR*D calcd. 22.20, found 22.05; observed m.p. of 3,5-dinitrobenzoate was 62–63°; lit. value is 64° by S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1953, p. 201. [c] Ozonation of a sample of this olefin and decomposition of the ozonide with water and zinc dust gave propionaldehyde and enanthaldehyde whose 2,4-dinitrophenylhydrazones melted at 138–139° and 106–107°, respectively; reported m.p. 155° and 108° by footnote *b*, p. 207. The hydrazone of propionaldehyde was analyzed for nitrogen. *Anal.* Calcd. for $C_9H_{10}N_4O_4$: N, 23.51. Found: N, 23.00. [d] Observed physical constants: d^{20}_4 0.8904, $n^{20}\text{D}$ 1.4587; *MR*D calcd. 49.87, found 49.71. The infrared spectrum of this compound showed a strong C=C absorption band. This band was not present in the spectrum of the dibromide. Decomposition of the ozonide of this olefin gave propionaldehyde, b.p. 46–48° (753 mm.), 2,4-dinitrophenylhydrazone, m.p. 151° (lit. value 155° by footnote *b*, p. 207); and anisaldehyde, b.p. 179–181° (753 mm.), d^{20}_4 0.8825, $n^{20}\text{D}$ 1.4222, 2,4-dinitrophenylhydrazone, m.p. 250–251° (lit. value 254° by footnote *b*, p. 207). [e] *MR*D calcd. 17.58, found 17.53; m.p. of 3,5-dinitrobenzoate was 71–71.5°; lit. value is 74° by footnote *b;* mixed m.p. with an authentic sample of the benzoate showed no depression. [f] Observed physical constants were d^{20}_4 0.8208, $n^{20}\text{D}$ 1.4105; reported values are d 0.738, $n^{20}\text{D}$ 1.420 by M. Bourguel, *Bull. soc. chim.*, 41, 1475 (1927). A sample of this olefin was treated with an oxygen–ozone stream as above. Ozonolysis products were acetaldehyde and enanthaldehyde; their 2,4-dinitrophenylhydrazones melted at 139–140° and 106–107°, respectively; reported values are 138–139° and 108° by C. M. Hill, *et al.*, THIS JOURNAL, **77**, 3892 (1955), and footnote *b*, p. 207. [g] Observed physical constants were: d^{20}_4 0.6571, $n^{20}\text{D}$ 1.3684, *MR*D calcd. 24.82, found 24.01. The 2,3-dibromide was prepared and its infrared spectrum compared with that of an authentic sample of 2,3-dibromopentane; the two spectra were identical. Observed physical constants of the dibromide were: b.p. 171–173 (751 mm.), d^{25} 1.625, $n^{20}\text{D}$ 1.4999; reported d^{20}_4 1.6789 and $n^{20}\text{D}$ 1.5079 by M. L. Sherrill, M. E. Smith and D. D. Thompson, THIS JOURNAL, **56**, 612 (1934). *Anal.* Calcd. for $C_5H_{10}Br_2$: Br, 69.56. Found: Br, 69.90. [h] The ozonide of this compound was decomposed as described above. The ozonolysis products were acetaldehyde and benzaldehyde; their 2,4-dinitrophenylhydrazones melted at 166° and 236–237°, respectively; lit. values are 168° and 237° by footnote *b*, p. 207. Mixed melting points of these hydrazones with authentic hydrazones were not depressed. [i] Observed physical constants were d^{20}_4 0.8409, $n^{20}\text{D}$ 1.4351, *MR*D observed 35.99, calcd. 35.55. The 3,5-dinitrobenzoate melted at 41°; reported m.p. is 47° by footnote *b*. The infrared spectrum of the isolated 1-heptanol was identical to that of an authentic specimen of 1-heptanol. [j] Physical constants: d^{20}_4 0.8489, $n^{20}\text{D}$ 1.4290. Decomposition of the ozonide with zinc dust and water gave propionaldehyde, b.p. 48–49° (746 mm.), $n^{20}\text{D}$ 1.3635, and caproaldehyde, b.p. 132–134° (746 mm.), $n^{20}\text{D}$ 1.4258; melting points of their 2,4-dinitrophenylhydrazones were 151–152° and 102–103°, respectively; lit. values are 155° and 106° by footnote *b*, p. 207. [k] This compound was identified by its ozonolysis product, propionaldehyde, b.p. 49–51° (749 mm.), d^{20}_4 0.8091, $n^{20}\text{D}$ 1.3660; m.p. of the 2,4-dinitrophenylhydrazone was 151–152°; lit. value is 155° by footnote *b*, p. 207. [l] The 3,5-dinitrobenzoate melted at 66–67°; reported m.p. is 64° by footnote *b*. The infrared spectrum of the isolated alcohol was identical to that of an authentic sample of 1-butanol. [m] Observed physical constants were: d^{20}_4 0.8025, $n^{20}\text{D}$ 1.4367, *MR*D calcd. 60.03, found 59.39. Ozonolysis products were: enanthaldehyde and caproaldehyde, b.p. 129–131° (747 mm.), d^{20}_4 0.8729, $n^{20}\text{D}$ 1.4195, *MR*D calcd. 29.92, found 28.92; 2,4-dinitrophenylhydrazones of the aldehydes melted at 105–106° and 106°; reported are 108° and 107° by footnote *b*, p. 207. [n] Ozonolysis products were benzaldehyde and caproaldehyde whose 2,4-dinitrophenylhydrazones melted at 236–237° and 104–105°, respectively; reported melting points are 237° and 107° by footnote *b*, p. 207.

analogous, in regions where correlations are expected, to the spectra of the four vinyl ethers.

Physical constants and analytical data of the ethers are given in Table I.

Ozonization of Vinyl Ethers.—The position of the double bond in the vinyl ether molecule was determined by ozonization. A 3-g. sample of each ether was treated with an oxygen–ozone stream for 12 to 16 hours. Decomposition of the ozonide with hydrogen peroxide (30%) gave an acid, which was identified by comparison of its infrared spectrum with that of an authentic sample of the acid predicted.

The ester isolated from each ozonization produced an infrared spectrum analogous to the spectrum of an authentic formate. A slight dissimilarity was observed, probably due to the formation of an azeotrope with hexane which was used as solvent during ozonization of the vinyl ether sample.

Reaction of Vinyl Ethers with Grignard Reagents.—The procedure employed for study of the behavior of the vinyl ethers toward the Grignard reagents was similar for each experiment. *n*-Hexylmagnesium bromide (0.12 mole) was placed into a flamed flask. The apparatus was flushed with dry nitrogen and protected against atmospheric moisture by calcium chloride drying tubes. Stirring was started and 0.06 mole (7.7 g.) of freshly distilled *n*-butyl ethylvinyl ether diluted with an equal volume of dry diethyl ether was added dropwise. The reaction mixture then was heated 44 hours at reflux temperature of the mixture, cooled, and hydrolyzed with saturated ammonium chloride. The ether layer was separated and the aqueous layer extracted continuously. The extracts were combined, dried, and the solvent removed by distillation over a steam-bath. Distillation of the residue through a Todd assembly gave 1-butanol (46%), b.p. 117–120° (749 mm.), and 3-decene (66%), b.p. 167–170° (749 mm.).

Physical constants and yields of the reaction products are described in Table II.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Allylic Rearrangements. XLI. The Reaction of Thionyl Chloride with Steroid Allylic Alcohols[1]

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The reactions of thionyl chloride with 4β-hydroxycholest-5-ene and 6β-hydroxycholest-4-ene have been studied and the structures and rates of solvolysis of the resulting allylic chlorides have been determined. Both reactions provide examples of an SNi′ mechanism across a bridgehead position.

Introduction

An allylic alcohol, upon reaction with thionyl chloride, may conceivably yield allylic chlorides as a result of at least four different processes: SN1, SN2, SNi and SNi′. It is generally accepted that the initial step in all these mechanisms is the formation of the chlorosulfinate ester of the alcohol

$$ROH + SOCl_2 \longrightarrow ROSOCl + HCl$$

Unless suitable control of the reaction conditions is achieved the simultaneous occurrence of more than one of these mechanisms may result, leading to the formation of mixtures of isomeric allylic chlorides. Recently it has been shown[3] that competition by the SN1 and SN2 reactions may be eliminated by the use of dilute ether solutions which render inactive the liberated hydrogen chloride and ensure the absence of soluble chloride ion. By employing this simple technique Goering and coworkers[4] were able to convert (−)-*cis*-5-methyl-2-cyclohexenyl alcohol into (−)-*cis*-5-methyl-2-cyclohexenyl chloride with little loss of optical purity. The complete absence of that product which would result from an SNi mechanism demonstrates the total inability of this process to compete with the SNi′ process under these conditions.

If the thionyl chloride reaction is conducted in the presence of soluble chloride ion, then a comparison of the relative importances of the SN2 and SNi′ reactions can be made. Thus Young and coworkers have demonstrated[5] that in the presence of tri-*n*-butylamine, which forms an ether-soluble hydrochloride, γ-methylallyl alcohol reacts exclusively by way of a bimolecular displacement reaction giving only a chloride with preserved allylic structure.

It was considered of interest to ascertain whether similar product control could be achieved in the reaction of thionyl chloride with various steroid allylic alcohols. Here the concept of axial and equatorial bonds is all important. In the SNi′ process a cyclic transition state of the chlorosulfinate ester was envisioned,[6] chlorine attacking the γ-carbon atom of the allylic system with a simultaneous shift of the double bond and the elimination of sulfur dioxide. Later[3] it was recognized that highly oriented ion pairs might give the same result. Often in the steroid series the geometry of the molecule of necessity precludes this. One such example[7] is with 3β-hydroxycholest-1-ene, reaction with thionyl chloride affording 3β-chlorocholest-1-ene as the chlorine of the quasiequatorial chlorosulfinate group is too far removed from $C_{(1)}$ to enable the formation of a cyclic transition state. On the other hand, occurrence of the SNi′ mechanism is allowed in the reaction of thionyl chloride with 3β-acetoxy-5α-hydroxy-cholest-6-ene, the chlorine of the quasiaxial chlorosulfinate group being afforded relatively unhindered approach to the axial $C_{(7)}$ configuration.[8]

Results and Discussion

The reaction of thionyl chloride with 4β-hydroxycholest-5-ene (I) and 6β-hydroxycholest-4-ene (II) appeared worthy of study, as in both these cases the occurrence of the SNi′ mechanism should not be precluded on account of configurational factors. The

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[2] National Science Foundation Postdoctorate Fellow at U.C.L.A., 1954–1955.

[3] F. F. Caserio, G. E. Dennis, R. H. DeWolfe and W. G. Young, THIS JOURNAL, **77**, 4182 (1955).

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[7] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 3289 (1956).

[8] A. F. Bide, H. B. Henbest, F. R. H. Jones and P. A. Wilkinson, *ibid.*, 1788 (1948).