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

Grignard Reagents and Unsaturated Ethers. IV.[1] The Synthesis and Reaction of Several Vinyl Ethers with Grignard Reagents[2]

BY CARL M. HILL, RUBY M. PRIGMORE AND GEORGE J. MOORE

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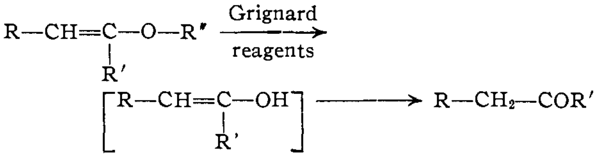
The reaction of α,β-unsaturated ethers of the type R—CH=C(R′)OR″, where R is H, n-C_3H_7, n-C_5H_{11} and n-C_6H_{13}, R′ is H, n-C_4H_9, n-C_5H_{11} and n-C_6H_{13}, and R″ is C_2H_5 and n-C_4H_9, with alkyl and aryl Grignard reagents has been investigated. The reaction products isolated indicate that the Grignard reagents cleave the unsaturated ethers at the carbon–oxygen bond to yield ketones. Seven substituted vinyl ethers have been synthesized and characterized.

Results from a study of the reaction of aryl substituted vinyl ethers with aryl Grignard reagents were reported in an earlier paper.[3] In an effort to characterize further the behavior of vinyl ethers toward Grignard reagents, our investigation has been extended to include the reaction of unsubstituted and alkyl substituted vinyl ethers with alkyl and aryl Grignard reagents.

The reaction of 5-butoxy-5-hendecene with n-butylmagnesium bromide yielded 5-hendecanone (76%) and butane. From the reaction of 5-ethoxy-4-hendecene with ethylmagnesium bromide, 5-hendecanone (55%) and ethane were isolated; from 6-ethoxy-6-tridecene with n-hexylmagnesium bromide, 6-tridecanone (65%), n-hexane and ethane.



$$R{-}CH{=}\underset{R'}{\underset{|}{C}}{-}O{-}R'' \xrightarrow[\text{reagents}]{\text{Grignard}} \left[R{-}CH{=}\underset{R'}{\underset{|}{C}}{-}OH\right] \longrightarrow R{-}CH_2{-}COR'$$

Differing from the results described above were those obtained when n-butyl vinyl ether reacted with phenylmagnesium bromide. This reaction produced n-butyl alcohol (60%) and vinylbenzene (35%). Worthy of note is the similarity between the products isolated from this reaction and those obtained from our investigation of α-styryl ethers and aryl Grignard reagents.[3] Also, the mode of cleavage of n-butyl vinyl ether by phenylmagnesium bromide is similar to that we observed for allyl ethers by alkyl and aryl Grignard reagents.[4]

All reactions of unsaturated ethers with Grignard reagents were carried out in absolute ether and in an excess (50–100%) of the reagents. A quantity of unreacted vinyl ether was recovered from each experiment.

The gaseous hydrocarbon products were analyzed on a vacuum line using the method of fractional condensation and vapor pressure measurement. Molecular weights observed for ethane and butane were 29 to 30 and 58, respectively.

The substituted vinyl ethers were characterized by measurement of physical constants, carbon and hydrogen analysis and ozonization.

Experimental studies designed to supply more information on the mechanism of these reactions and to give a more reliable basis for estimation of yields of the saturated hydrocarbon products are in progress. It is anticipated, for example, that the reaction between α,β-unsaturated ethers and Grignard reagents in which the alkyl groups are dissimilar would help to identify the source of each of the saturated hydrocarbon products.

Experimental[5]

Synthesis of Vinyl Ethers.—The alkyl substituted vinyl ethers were synthesized by the procedure of Lauer and Spielman.[6] The n-butyl vinyl ether was purchased from Matheson, Coleman and Bell, Inc. Yields and physical constants of the vinyl ethers are described in Table I.

Ozonization of Vinyl Ethers.—Two to seven-g. samples of the unsaturated ethers were dissolved in 75–200 ml. of petroleum ether and treated with a mixture of ozone–oxygen 12 to 30 hours. The ozonides were decomposed with 3% hydrogen peroxide or zinc dust. The ozonization products were separated by distillation and identified (see Table II).

Reaction of Grignard Reagents with Vinyl Ethers.—The procedure employed for study of the behavior of the Grignard reagents toward the vinyl ethers was similar for each experiment. A description of this procedure is given for 5-butoxy-5-hendecene with n-butylmagnesium bromide: Thirty-six hundredths mole of n-butylmagnesium bromide was placed into a flask equipped with a condenser, mechanical stirrer and dropping funnel. The first of three tubes connected in series was attached to the condenser. The first tube was surrounded by an ice–water-bath; the second by a Dry Ice–acetone-bath; and the third contained 5% bromine–carbon tetrachloride. The apparatus was flushed with nitrogen and 39.8 g. (0.18 mole) of 5-butoxy-5-hendecene (b.p. 98–101° (2 mm.)) dissolved in 200 ml. of absolute ether added dropwise. The reaction mixture was heated 24 hours and then hydrolyzed with saturated ammonium chloride. The ether layer was separated and the aqueous layer extracted continuously with ether. Extracts were combined, dried and the solvent removed. Distillation[7] of the residue through a Todd column gave 21.2 g. (76%) of 5-hendecanone, b.p. 104–106° (11 mm.).

Diethyl ether collected in the first tube. No evidence of olefins was found in the third tube. The second tube was connected to a vacuum line and its contents identified as butane.

Molecular weights of the gaseous hydrocarbons were determined by measuring their vapor pressures and weighing 110.8 ml. of each gas at room temperature. For n-butane, vapor pressure was 11 mm. at −80° (literature value[8] −77.8° at 10 mm.); for ethane, vapor pressure, 188 mm at −112° (literature value[9] −111° at 188 mm). Molecular weights observed for n-butane and ethane were 58 and 30, respectively.

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[1] For the third paper of series, see C. M. Hill, G. W. Senter, L. Haynes and M. E. Hill, THIS JOURNAL, **76**, 4538 (1954).

[2] This investigation was supported by a research grant from the National Science Foundation, Contract G-60.

[3] C. M. Hill, R. A. Walker and M. E. Hill, THIS JOURNAL, **73**, 1663 (1951).

[4] C. M. Hill, L. Haynes, D. E. Simmons and M. E. Hill, *ibid.*, **75**, 5408 (1953).

(5) Melting points are corrected.

(6) W. M. Lauer and M. A. Spielman, THIS JOURNAL, **53**, 1533 (1931).

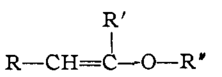
(7) To effect separation of ketone from unreacted vinyl ether several distillations were necessary.

(8) "Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 1952.

(9) Obtained from vapor pressure curve plotted from data found in reference 8 and "International Critical Tables of Numerical Data—Physics, Chemistry and Technology," Vol. III, McGraw-Hill Book Co., Inc., New York, N. Y., 1928, p. 217.

TABLE I

YIELDS AND PHYSICAL CONSTANTS OF VINYL ETHERS OF TYPE:



$R{-}CH{=}\overset{R'}{\overset{|}{C}}{-}O{-}R''$

R	R'	R″	B.p., °C.	B.p., Mm.	Yield, %	d^{20}_4	n^{20}_D	Formula	MRD Calcd.	MRD Found
n-C_6H_{13}	n-C_5H_{11}	C_2H_5	132–135	11	66	0.7995	1.4397	$C_{15}H_{30}O$	72.65	71.19
n-C_3H_7	n-C_6H_{13}	C_2H_5	107–111	19	52	.8117	1.4346	$C_{13}H_{26}O$	63.41	63.60
CH_3[a]	n-C_5H_{13}	C_2H_5	89–92	11	77	.8111	1.4256	$C_{12}H_{24}O$	58.79	58.01
H	n-C_7H_{15}	n-C_4H_9	109–112	17	24	.8301	1.4433	$C_{13}H_{26}O$	63.41	62.03
n-C_5H_{11}	n-C_5H_{11}	n-C_4H_9	126–129	6	45	.8328	1.4438	$C_{16}H_{32}O$	77.27	76.55
H	n-C_5H_{11}	n-C_8H_{17}	89–92	1	40	.8341	1.4440	$C_{15}H_{30}O$	72.65	71.97
n-C_5H_{11}	n-C_4H_9	n-C_4H_9	98–101	2	30	.8310	1.4400	$C_{15}H_{30}O$	72.65	71.65

[a] Formula for this ether is $(CH_3)_2C{=}C(C_6H_{13})OC_2H_5$.

TABLE II

ANALYTICAL DATA OF VINYL ETHERS

Vinyl ether			Analyses, %				Ozonization products					
			Carbon		Hydrogen		Acid			Ester		
								Neut. equiv.			Sapn. equiv.	
R	R'	R″	Calcd.	Found	Calcd.	Found		Calcd.	Found		Calcd.	Found
n-C_6H_{13}	n-C_5H_{11}	C_2H_5	79.65	80.30	13.27	13.14	Enanthic[a]	130	129	Ethyl caproate[b]	144	144
n-C_3H_7	n-C_6H_{13}	C_2H_5	78.79	78.57	13.13	13.21	Butyric[c]	81	82	Ethyl enanthate[d]	158	155
CH_3[e]	n-C_6H_{13}	C_2H_5	78.26	78.08	13.04	12.85	Acetone[f]			[g]		
H	n-C_7H_{15}	n-C_4H_9	78.79	78.01	13.13	12.96						
n-C_5H_{11}	n-C_5H_{11}	n-C_4H_9	80.00	80.53	13.33	13.71	Caproic[h]	116	117	Butyl caproate[i]	172	176
H	n-C_5H_{11}	n-C_8H_{17}	79.65	79.00	13.27	13.90						
n-C_5H_{11}	n-C_4H_9	n-C_4H_9[j]	79.65	78.99	13.27	13.13	Caproaldehyde[k]			Butyl valerate	158	149

[a] Observed n^{20}_D 1.4170, d^{20}_4 0.9411; *MR*D (calcd.) 36.06, (found) 35.00. [b] Observed n^{20}_D 1.4286, d^{20}_4 0.9507; *MR*D (calcd.) 40.80, (found) 39.03. [c] Observed n^{20}_D 1.4062, d^{20}_4 0.9694; *MR*D (calcd.) 22.22, (found) 22.33. [d] Observed n^{20}_D 1.4225, d^{20}_4 0.7775; *MR*D (calcd.) 45.43., (found) 51.69. [e] Formula for this ether is $(CH_3)_2C{=}C(C_6H_{13}){-}O{-}C_2H_5$. [f] B.p. 58° (756 mm.); m.p. of 2,4-dinitrophenylhydrazone, 125°; reported m.p. of hydrazone of acetone is 128° by S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1953, p. 256. [g] Product's physical constants: d^{20}_4 0.8817, n^{20}_D 1.4100; *MR*D (calcd.) for ethyl heptanoate, 45.42; (found) 44.00; reported d^{20}_4 and n^{20}_D for ethyl heptanoate are 0.8685 and 1.41296, respectively, by "Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 1952. [h] B.p. 189–192° (756 mm.), n^{20}_D 1.4167, d^{20}_4 0.9471. [i] B.p. 196–199° (756 mm.), n^{20}_D 1.4011, d^{20}_4 0.9072. [j] Monobromo ether from which unsaturated ether was prepared was analyzed for bromine. *Anal.* Calcd. for $C_{15}H_{31}OBr$: Br, 26.06. Found: Br, 25.97. [k] B.p. 130° (750 mm.); m.p. of 2,4-dinitrophenylhydrazone, 104–105°; reported m.p. of hydrazone of caproaldehyde is 107°; footnote *f*, p. 207.

TABLE III

PHYSICAL CONSTANTS AND YIELDS OF REACTION PRODUCTS

Vinylether $R{-}CH{=}C(R'){-}O{-}R''$			Grignard reagents	Product, $R{-}CH_2{-}CO{-}R$						
						B.p.,				
R	R'	R″		R	R'	°C.	Mm.	Yield,[a] %	d^{20}_4	n^{20}_D
n-C_5H_{11}	n-C_4H_9	n-C_4H_9	n-C_4H_9	n-C_5H_{11}	n-C_4H_9[b]	104–106	11	76	0.8338	1.4359
H	H	n-C_4H_9	C_6H_5	[c]						
n-C_3H_7	n-C_6H_{13}	C_2H_5	C_2H_5	n-C_3H_7	n-C_6H_{13}[d]	85–88	4	55	.8100	1.4291
n-C_6H_{13}	n-C_5H_{11}	C_2H_5	n-C_6H_{13}	n-C_6H_{13}	n-C_5H_{11}[e]	110–113 M.p. 17	4	65	.8200	1.4352

[a] Based on the amount of vinyl ether not recovered. [b] *MR*D (calcd.) 53.01, (found) 53.31; m.p. of semicarbazone, 72–73°. *Anal.* Calcd. for $C_{12}H_{25}ON_3$: N, 18.51. Found: N, 18.55; reported m.p. of semicarbazone of n-butyl hexyl ketone, 75° by J. v. Braun, H. Kraper and H. Wienhaus, *Ber.*, **62**B, 2880 (1929); mixed m.p. of semicarbazones of isolated ketone and authentic n-butyl hexyl ketone was 73–74°. The authentic n-butyl hexyl ketone was prepared by heating mixture of calcium salts of valeric and enanthic acids; observed b.p. 103–106° (12 mm.), d^{20}_4 0.8315, n^{20}_D 1.4287, n^{18}_D 1.4290; reported b.p. 105–106° (12 mm.), d^{19}_4 0.8278, n^{18}_D 1.4275. [c] Products were: (1) n-butyl alcohol (60%), b.p. 114–117° (756 mm.), d^{20}_4 0.8115, n^{20}_D 1.4065, *MR*D (calcd.) 22.20, (found) 22.42; m.p. of p-nitrobenzoate, 33–34° and 3,5-dinitrobenzoate, 61–62°; reported m.p. of benzoates, 36 and 64°, respectively, by S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1953, p. 201; mixed m.p. with authentic specimens of the benzoates showed no depression; and (2) vinylbenzene (35%), b.p. 143–147° (752 mm.), d^{20}_4 1.0442, n^{20}_D 1.5333; *MR*D (calcd.) 29.88, (found) 30.93; ozonization prducts were formaldehyde and benzaldehyde, whose 2,4-dinitrophenylhydrazones melted at 161–163° (reported value 166°; footnote *c*, p. 207) and 154–155°, respectively. The 2,4-dinitrophenylhydrazone of benzaldehyde was analyzed for nitrogen. *Anal.* Calcd. for $C_{13}H_{10}O_4N_4$: N, 19.58. Found: N, 18.96 [d] The hydantoin, prepared by procedure reported by: H. R. Henze and R. J. Speer, THIS JOURNAL, **64**, 522 (1942), melted at 105–107°; m.p. of hydantoin prepared from authentic n-butyl hexyl ketone, 103–105°; mixed m.p. 103–105°. *Anal.* (authentic hydantoin) Calcd. for $C_{13}H_{24}O_2N_2$: N, 11.66. Found: N, 11.51. *Anal.* (hydantoin of isolated ketone). Found: N, 11.54. [e] *MR*D (calcd.) 62.25, (found) 63.00; reported d^{25}_4 0.8244, n^{20}_D 1.4320, b.p. 128–129° (11 mm.) and m.p. 18.5° by J. v. Braun and G. Manz, *Ber.*, **67**B, 1696 (1934). Physical constants of authentic n-heptyl amyl ketone prepared from calcium salts of caproic and caprylic acids: b.p. 124–127° (11 mm.), d^{25}_4 0.8319, n^{20}_D 1.4356; *MR*D (calcd.) 62.25, (found) 62.14; m.p. 17.5°; m.p. of semicarbazone of ketone isolated from reaction mixture, 163–164°; m.p. of semicarbazone of authentic n-heptyl amyl ketone, 162°; mixed m.p. was not lowered; m.p. of hydantoin, 97–98°. *Anal.* Calcd. for $C_{15}H_{28}O_2N_2$: N, 10.45. Found: N, 10.79.

By removing the collecting tubes before hydrolysis of the reaction mixtures, the quantities obtained of the saturated hydrocarbons were roughly equivalent to the amount of the unsaturated ethers which reacted. In the experiment in which 27.0 g. (0.12 mole) of 6-ethoxy-6-tridecene and 0.20 mole of n-hexylmagnesium bromide were allowed to react, the collecting tubes were removed after hydrolysis. From this reaction 4.3 g. of *n*-hexane and approximately 0.08 mole of ethane were isolated.

Physical constants, yields and identification data for the ketones are shown in Table III.

NASHVILLE, TENNESSEE

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

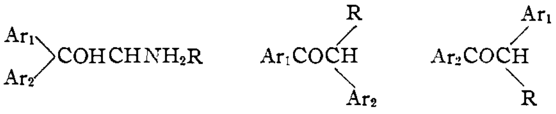
Rearrangement with Nitrous Acid of the Diastereoisomeric 1-*p*-Anisyl-1-phenyl-2-aminopropanols. The *cis* Effect of Methyl and Phenyl Groups[1]

BY DAVID Y. CURTIN[2] AND MALCOLM C. CREW

RECEIVED JULY 1, 1954

The rearrangement with nitrous acid of *erythro*- and *threo*-1-*p*-anisyl-1-phenyl-2-aminoethanol has been shown to give mixtures of the two possible ketones, *p*-anisyl α-phenylethyl ketone and phenyl α-*p*-anisylethyl ketone. Ultraviolet analysis was used to determine the relative amounts of the two products. The results have been interpreted in terms of a steric factor (the *cis* effect of the phenyl and methyl groups) and an electronic effect (the *p*-anisyl/phenyl migration ratio in the absence of the steric effect). The magnitudes of these quantities (11 and 1.5, respectively) are in agreement with values suggested by other work.

A number of racemic amino alcohols of the general type (A) have been shown to rearrange stereospecifically to the ketone (B) or (C) (when treated with nitrous acid) in such a way that the non-migrating aryl and R groups are *trans* to each other in the transition state.[3]



$$(\mathrm{Ar_1})(\mathrm{Ar_2})\mathrm{COHCHNH_2R} \qquad \mathrm{Ar_1COCH(R)(Ar_2)} \qquad \mathrm{Ar_2COCH(Ar_1)(R)}$$

(A) (B) (C)

R = C_6H_5, CH_3, $C_6H_5CH_2-$

In each of the rearrangements above, a single racemic ketone was isolated from the rearrangement of any racemate and since none of the isomeric ketone which might have been formed in small amount was found, no estimate of the magnitude of the steric effect could be made.

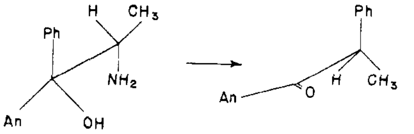
For this reason it was desired to carry out a careful study of the amounts of products obtained from such a rearrangement with the hope of estimating the magnitude of the steric effect.

dl-erythro- and *threo*-1-*p*-anisyl-1-phenyl-2-aminopropanol (*erythro*- and *threo*-I)[4] were chosen as suitable for this purpose.

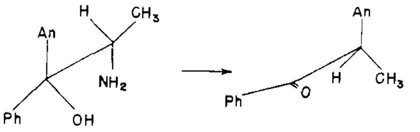
erythro-I was synthesized by the reaction previously employed by Tiffeneau, Levy and Ditz of α-aminopropiophenone hydrochloride with *p*-anisylmagnesium bromide[5] while *threo*-I was prepared by the reaction which had been carried out by the same workers of *p*-methoxy-α-aminopropiophenone hydrochloride with phenylmagnesium bromide.[5] The configurations are assigned by analogy with other such Grignard additions.[6]

The rearrangements of *erythro*- and *threo*-I were carried out at 0° in 50% glacial acetic acid to which was added aqueous sodium nitrite solution. The rearrangement of *erythro*-I was found to lead to *p*-anisyl α-phenylethyl ketone (II) (formed with phenyl migration) which could be isolated in a yield of 42% in agreement with the work of Tiffeneau, Levy and Ditz.[5] Rearrangement of *threo*-I gave phenyl α-*p*-anisylethyl ketone (III) (formed with *p*-anisyl migration) in a yield of 40%. The total neutral fraction from each rearrangement was subjected to ultraviolet analysis. Each amino alcohol (*erythro*- and *threo*-I) was then recrystallized four more times, rearranged and the products analyzed. The results of the ultraviolet analyses are given in Table I.

It is clear that the *erythro*-isomer rearranges with predominant phenyl migration and that the *threo*-



erythro-I II (+ III)



threo-I III (+ II)

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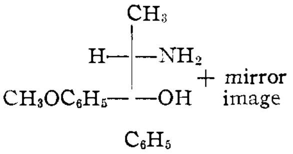
[1] From the Ph.D. Dissertation to be submitted to Columbia University by Malcolm C. Crew. Presented in part at the Thirteenth National Organic Chemistry Symposium of the American Chemical Society, Ann Arbor, Michigan, June, 1953.

[2] University of Illinois, Urbana, Illinois.

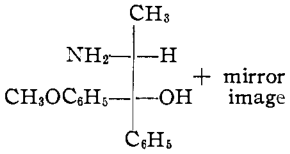
[3] (a) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950); (b) D. Y. Curtin and P. I. Pollak, *ibid.*, **73**, 992 (1951); D. Y. Curtin, E. E. Harris and P. I. Pollak, *ibid.*, **73**, 992 (1951); (c) A. McKenzie and A. K. Mills, *Ber.*, **62**, 284 (1929); (d) A. McKenzie and A. D. Wood, *Ber.*, **71**, 358 (1938); (e) A. K. Mills, private communication to C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 507.

[4] The designations *erythro*- and *threo*-I will be used as shown below.



$$\begin{array}{c} CH_3 \\ H-\!\!|\!\!-NH_2 \\ CH_3OC_6H_5-\!\!|\!\!-OH \\ C_6H_5 \end{array} + \text{mirror image}$$

erythro-I



$$\begin{array}{c} CH_3 \\ NH_2-\!\!|\!\!-H \\ CH_3OC_6H_5-\!\!|\!\!-OH \\ C_6H_5 \end{array} + \text{mirror image}$$

threo-I

[5] M. Tiffeneau, J. Levy and E. Ditz, *Bull. soc. chim.*, [5] **2**, 1848 (1935).

[6] (a) D. Y. Curtin, E. E. Harris and E. K. Meislich, THIS JOURNAL, **74**, 2901 (1952); (b) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952).