

reported in Table I were obtained by dividing the pseudo-first-order rate constant by hydroxide ion concentration. It has previously been shown that rate constants obtained in this way for hydrolysis of diphenyl carbonate are independent of hydroxide ion concentration.<sup>1</sup>

**Rates in Neutral Solution.**—Rates in 1:1 dioxane-water at 100° were determined by bromometric titration of phenol, following the procedure previously described.<sup>1</sup> Reactions were followed to at least 85% of completion and the first-order rate constants were determined graphically in the usual manner.

### Catalyst Selectivity in Semihydrogenation of Some Conjugated Acetylenes<sup>1</sup>

ELLIOT N. MARVELL AND JOHN TASHIRO

Department of Chemistry, Oregon State University,  
Corvallis, Oregon

Received April 27, 1965

Semihydrogenation of an acetylene provides a classic route to the *cis* double bond. Both palladium<sup>2</sup> and Raney nickel<sup>3</sup> have been used with success. For isolated triple bonds the selectivity may approach 100%,<sup>4</sup> although it runs about 95% in general synthetic use.<sup>5</sup> It has been reported that selective reduction of a triple bond in a conjugated system proceeds with less success,<sup>6</sup> but no quantitative data have been provided. Faced with the need of some conjugated systems containing *cis* double bonds, we had occasion to examine quantitatively some examples of catalytic semihydrogenation of some enynes and dienyne.

The results of the semihydrogenation of three enynes and one dienyne over the Lindlar catalyst are shown in Table I. In no case does the rate of hydrogen uptake show a break after absorption of 1 mole of hydrogen, and the products shown in the table are obtained by arbitrary interruption of the reaction after addition of 1 mole of hydrogen. Analysis of the reaction mixtures was performed by gas chromatography. A second dienyne, 1,2-dicyclohexenylacetylene, was also submitted to the same reaction, but the products could not be analyzed successfully by gas chromatography. We were able to show by a combination of spectral and chemical methods that the reduction mixture contained unreduced starting material, over-reduction products in which the triple bond had been completely reduced and some in which one of the cyclohexene double bonds was reduced, and not more than 50% of *cis*-1,2-dicyclohexenylethylene. Schlatmann

(1) The authors are pleased to acknowledge partial financial support from the National Science Foundation under Grant G-23072.

(2) (a) O. Iser, W. Huber, A. Ronco, and M. Kofler, *Helv. Chim. Acta*, **30**, 1911 (1947); (b) H. Lindlar, *ibid.*, **35**, 446 (1952); (c) D. J. Cram and M. Cordin, *J. Am. Chem. Soc.*, **77**, 4090 (1955).

(3) (a) N. A. Khan, *ibid.*, **74**, 3018 (1952); (b) W. Oroshnik, G. Karmas, and A. D. Mebane, *ibid.*, **74**, 295 (1952), and subsequent papers.

(4) E. F. Meyer and R. L. Burwell, *ibid.*, **85**, 2877 (1963).

(5) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Academic Press Inc., New York, N. Y., 1955, pp. 22-27.

(6) (a) I. Heilbron, E. R. H. Jones, and F. Sondheimer, *J. Chem. Soc.*, 1586 (1947); (b) L. Crombie, S. H. Harper, and D. Thompson, *ibid.*, 2906 (1951); (c) L. Crombie, *ibid.*, 1007 (1955); (d) L. Crombie, S. H. Harper, and F. C. Newman, *ibid.*, 3063 (1956); (e) A. Butenandt, E. Hecker, and H. G. Zachau, *Chem. Ber.*, **88**, 1185 (1955); (f) W. Oroshnik and A. D. Mebane, *J. Am. Chem. Soc.*, **76**, 5719 (1954); (g) W. Oroshnik, *ibid.*, **78**, 2651 (1956).

(7) J. L. M. A. Schlatmann and E. Havinga, *Rec. trav. chim.*, **80**, 1101 (1961).

TABLE I

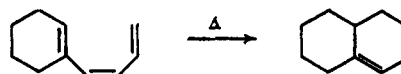
PRODUCTS OF SEMIHYDROGENATION OF ENYNES AND DIENYNES<sup>a</sup>

Substrate	Product composition (%)
$C_6H_9C\equiv CH$	$C_6H_9CH=CH_2$ (86) $C_6H_9CH_2-CH_2$ (8) $C_6H_9C\equiv CH$ (6)
$C_6H_9C\equiv C-CH_2$	$C_6H_9CH=CH-CH_2$ , <i>cis</i> (76), <i>trans</i> (2) $C_6H_9CH_2-CH_2-CH_2$ (8) $C_6H_9C\equiv C-CH_2$ (14)
$C_6H_9C\equiv C-Et$	$C_6H_9CH=CH-Et$ , <i>cis</i> (85), <i>trans</i> (5) $C_6H_9CH_2-CH_2-Et$ (5) $C_6H_9C\equiv C-Et$ (5)
$C_6H_9C\equiv C-CH=CH_2$	$C_6H_9CH=CH-CH=CH_2$ , <i>cis</i> (47), <i>trans</i> (7) $C_6H_9CH=CH-Et$ , <i>cis</i> (13), <i>trans</i> (8) $C_6H_9C\equiv C-Et$ (8) $C_6H_9CH_2CH_2Et$ (4) $C_6H_9C\equiv C-CH=CH_2$ (8) Unidentified (5)

<sup>a</sup>  $C_6H_9$  = 1-cyclohexenyl.

and Havinga<sup>7</sup> have reported similar results for the semihydrogenation of 1-(2-methylcyclohexenyl)-2-cyclohexenylacetylene.

In the course of this work two new *cis*-dienes and a *cis*-triene were obtained. The two dienes were isolated by preparative chromatography and identified by their ultraviolet and n.m.r. spectra as compared with the spectra of the products obtained from them by treatment with iodine in diffuse sunlight. Both *cis*-dienes undergo a thermal 1,5 hydrogen shift, a reaction which Wolinsky, Chollar, and Baird have shown to be diagnostic of *cis*-dienes.<sup>8</sup> The *cis*-triene was identified by comparison with a synthetic sample.<sup>9</sup> The *cis* configuration of the double bond was confirmed by the valence isomerization<sup>10</sup> occurring on the gas chromatographic column. The cyclized product was obtained *via* preparative chromatography and identified by its spectral properties and dehydrogenation to naphthalene.



The data of Table I provide several interesting conclusions. For the three enynes studied, addition occurs exclusively at the triple bond, and the stereoselectivity is not greatly different from that generally observed with isolated triple bonds. Unlike the situation with isolated triple bonds,<sup>11</sup> further hydrogenation of the product proceeds to an appreciable extent while the enyne is still present. For the examples studied here, this overreduction problem is not serious and the reaction is synthetically useful. Since it has been shown<sup>12</sup> that the order of bond selectivity is

(8) J. Wolinsky, B. Chollar, and M. D. Baird, *J. Am. Chem. Soc.*, **84**, 1775 (1962).

(9) J. Tashiro, Ph.D. Thesis, Oregon State University, 1964.

(10) See, for example, E. N. Marvell, G. Caple, and B. Schatz, *Tetrahedron Letters*, 385 (1965); E. Vogel, W. Grimme, and E. Dinne, *ibid.*, 391 (1965); D. W. Glass, J. W. H. Watthey, and S. Winstein, *ibid.*, 377 (1965).

(11) For an excellent review of this subject, see G. C. Bond and P. B. Wells, *Advan. Catalysis*, **15**, 91 (1964).

(12) N. A. Dobson, G. Eglinton, M. Krishnamurti, R. A. Raphael, and R. G. Willis, *Tetrahedron*, **16**, 16 (1961).

$\text{HC}\equiv\text{CR} > \text{R}-\text{C}\equiv\text{C}-\text{R} > \text{CH}_2=\text{CHR} > \text{RCH}=\text{CHR}$ , there is no certainty that these conclusions will apply to systems where an acetylenic bond is conjugated to a di- or monosubstituted double bond. Crombie<sup>6d</sup> has used this method for the reduction of  $-\text{C}\equiv\text{C}-\text{CH}=\text{CH}_2$  to  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$ , but his data do not permit even a semiquantitative measure of the selectivity in that case.

The prognosis for synthetic use of semihydrogenation to prepare trienes with a central *cis* double bond is clearly unsatisfactory. Unless adequate separation procedures are available, isolation of the desired *cis*-triene from the complex reduction mixture will be impossible. In the case studied here, reduction of the vinyl group proceeds in competition with that of the triple bond, the stereoselectivity is markedly reduced, and overreduction occurs to a considerable degree even in the presence of unreduced starting material. Orshnik and Mebane<sup>6f</sup> reported that no *cis*-triene could be isolated on semihydrogenation of 3,7-dimethyl-3,7-nonadien-5-yn-2-ol. Schlattmann and Havinga<sup>7</sup> have noted a similar finding and Vogel<sup>13</sup> has had a similar experience with dicyclohexenylacetylene. Oddly, however, this drastic loss of selectivity does not always appear to pertain in long conjugated systems.<sup>14</sup>

### Experimental Section

**1-Ethynylcyclohexene.**—This was prepared from 1-ethynylcyclohexanol by the method of Hamlett, Henbest, and Jones.<sup>15</sup> The product, b.p. 52–55° (27 mm.),  $n_D^{20}$  1.4962,  $\lambda_{\text{max}}$  222 m $\mu$  ( $\epsilon$  12,400),  $\bar{\nu}$  3325 and 1628 cm.<sup>-1</sup>, was obtained in 80% yield. The previous authors<sup>15</sup> reported b.p. 53–56 (43 mm.),  $n_D^{17}$  1.4978,  $\lambda_{\text{max}}$  223.5 m $\mu$  ( $\epsilon$  10,500).

**1-Cyclohexenyl-1-propyne.**—A solution of lithium amide in liquid ammonia was prepared from 1.95 g. (0.28 g.-atom) of lithium. To this was added dropwise 30.1 g. (0.28 mole) of 1-ethynylcyclohexene, followed by 46.8 g. (0.33 mole) of methyl iodide. The mixture was stirred for 24 hr. and the ammonia was allowed to evaporate. The residue was hydrolyzed with saturated ammonium chloride solution, and the product was taken up in petroleum ether (b.p. 40–60°). The solution was washed successively with water, dilute phosphoric acid, dilute sodium bicarbonate, and again with water. The solution was dried over calcium chloride, the solvent was evaporated, and the product was distilled, b.p. 54–55° (4.5 mm.),  $n_D^{20}$  1.5097,  $\lambda_{\text{max}}$  224 m $\mu$  ( $\epsilon$  11,600),  $\bar{\nu}$  2070 and 1628 cm.<sup>-1</sup>, 13.6 g. (40%). The hydrocarbon gave a single peak on a 6 ft.  $\times$  0.25 in. Replex 400 column.

*Anal.* Calcd. for C<sub>9</sub>H<sub>12</sub>: C, 89.94; H, 10.06. Found: C, 89.90; H, 10.52.

**1-Cyclohexenyl-1-butyne.**—This substance was prepared in 63% yield from 2.0 g. (0.288 g.-atom) of lithium, 38.7 g. (0.365 mole) of 1-ethynylcyclohexene, and 38.5 g. (0.354 mole) of ethyl bromide using the procedure described under the preparation of 1-cyclohexenyl-1-propyne. The clear liquid boiled at 55–58° (2.7 mm.),  $n_D^{20}$  1.5025,  $\lambda_{\text{max}}$  225 m $\mu$  ( $\epsilon$  12,700),  $\bar{\nu}$  1637 cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>11</sub>H<sub>14</sub>: C, 89.49; H, 10.51. Found<sup>16</sup>: C, 88.50; H, 10.36. C, 86.59; H, 10.22. C, 84.89; H, 9.86.

**1-Cyclohexenyl-1-butyne-4-ol.**—A solution of lithium amide in liquid ammonia was prepared from 2.0 g. (0.29 g.-atom) of lithium. To this was added 42 g. (0.40 mole) of 1-ethynylcyclohexene followed by 20 ml. (0.40 mole) of ethylene oxide. After the solution had stirred for 24 hr., the ammonia was allowed to evaporate, and the residue was treated with saturated ammonium

chloride. The alcohol was isolated by distillation, b.p. 70–72° (0.1 mm.),  $n_D^{20}$  1.5264,  $\lambda_{\text{max}}$  226 m $\mu$  ( $\epsilon$  13,400),  $\bar{\nu}$  3300 and 1050 cm.<sup>-1</sup>, 34.9 g. (59%).

The *p*-nitrobenzoate melted at 72–73°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>17</sub>NO<sub>4</sub>: C, 68.23; H, 5.73; N, 4.68. Found: C, 68.16; H, 5.78; N, 4.72.

The phenylurethan of the above alcohol melted at 84.4–85.2°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>2</sub>: C, 75.85; H, 7.11; N, 5.20. Found: C, 75.76; H, 7.16; N, 5.03.

**1-Cyclohexenyl-3-buten-1-yne.**—A solution containing 24 g. (0.126 mole) of *p*-toluenesulfonyl chloride in 12 ml. (0.15 mole) of pyridine was cooled in an ice-salt bath under an atmosphere of dry nitrogen. To this was added dropwise 16.6 g. (0.11 mole) of 1-cyclohexenyl-1-butyne-4-ol, and the reaction mixture was stirred for 24 hr. After 25 ml. of water had been added, the product was taken up in ether. The ether solution was washed with water, dilute phosphoric acid, dilute sodium bicarbonate, and again with water. The ether solution was dried over anhydrous potassium carbonate and the ether was removed by evaporation. The crude tosylate was used directly in the next step. The yield was 33 g. (98%).

A solution of the above tosylate in 14 ml. of anhydrous dimethyl sulfoxide was cooled in an ice bath under dry nitrogen. To this was added a mixture of 8.27 g. (0.082 mole) of potassium *t*-butoxide and 55 ml. of anhydrous dimethyl sulfoxide. The reaction mixture was taken up in petroleum ether, and the solution was washed thoroughly with water. The petroleum ether solution was dried over anhydrous potassium carbonate, and the solvent was removed by evaporation. The product was obtained as a clear liquid: b.p. 62–65° (4 mm.);  $n_D^{20}$  1.5477;  $\lambda_{\text{max}}$  259 m $\mu$  ( $\epsilon$  14,900) and 269 m $\mu$  sh ( $\epsilon$  12,300);  $\bar{\nu}$  3020, 2200, 1605, and 971 cm.<sup>-1</sup>; 2.43 g. (17%). The n.m.r. spectrum showed a complex series of peaks between 5.07 and 5.93 p.p.m., a multiplet centered at 2.04 p.p.m., and another at 1.58 p.p.m.

*Anal.* Calcd. for C<sub>10</sub>H<sub>12</sub>: C, 90.85; H, 9.15. Found: C, 90.70; H, 9.28.

**Semihydrogenations.**—A mixture of Lindlar catalyst (0.50 g.) and 0.04 ml. of quinoline in 60 ml. of petroleum ether (b.p. 60–80°) was stirred at room temperature under 1 atm. of hydrogen until the catalyst no longer absorbed hydrogen. The sample of unsaturate (normally 0.015 mole, but samples as large as 0.075 mole were run with no large deviation from the results reported) was introduced *via* a serum cap and syringe. The reaction mixture was stirred vigorously at room temperature (water bath) and under 1 atm. of hydrogen until 1 mole of hydrogen had been absorbed. The catalyst was removed by filtration, and the solvent was removed by evaporation. The product was analyzed directly or was distilled first and then analyzed.

**1-Vinylcyclohexene.**—The main product of the semihydrogenation of 1-ethynylcyclohexene was isolated by preparative gas chromatography. The hydrocarbon showed  $\bar{\nu}$  1645, 1605, and 990 cm.<sup>-1</sup>; b.p. 52–54°;  $n_D^{20}$  1.4982.

*Anal.* Calcd. for C<sub>8</sub>H<sub>12</sub>: C, 88.82; H, 11.18. Found: C, 88.93; H, 11.03.

***cis*-1-Cyclohexenyl-1-propene** was isolated from the semihydrogenation of 1-cyclohexenyl-1-propyne by preparative gas chromatography. It showed  $n_D^{20}$  1.4956,  $\lambda_{\text{max}}$  229 m $\mu$  ( $\epsilon$  12,600), and its n.m.r. spectrum had a series of peaks in the olefinic region between 5.42 and 6.27 p.p.m. which included the AB portion of an ABX<sub>2</sub> spectrum with  $J_{AB} = 13$  c.p.s.,  $J_{AX} = 0$  c.p.s.,  $J_{BX} = 6$  c.p.s., and two multiplets, one centered at 2.25, the second at 1.84 p.p.m. Treatment of a sample of this alkene with a small amount of iodine in petroleum ether under exposure to diffuse light for 24 hr. under nitrogen gave a new isomer:  $n_D^{20}$  1.5013;  $\lambda_{\text{max}}$  230 m $\mu$  ( $\epsilon$  26,800); n.m.r., AB portion in olefinic region having  $J_{AB} = 17$  c.p.s.

An analytical sample of the *cis* isomer was prepared by preparative gas chromatography followed by distillation.

*Anal.* Calcd. for C<sub>8</sub>H<sub>14</sub>: C, 88.46; H, 11.54. Found: C, 88.54; H, 11.26.

***cis*-1-Cyclohexenyl-1-butene.**—This olefin was isolated by preparative gas chromatography from the semihydrogenation of 1-cyclohexenyl-1-butyne. The hydrocarbon had b.p. 48–49° (3 mm.),  $n_D^{20}$  1.4910,  $\lambda_{\text{max}}$  230 m $\mu$  ( $\epsilon$  12,800). Its n.m.r. spectrum showed a complex series of peaks in the olefinic region between 5.00 and 5.84 p.p.m. including the AB part of an ABX<sub>2</sub> spectrum with  $J_{AB} = 12$  c.p.s.,  $J_{AX} = 0$  c.p.s.,  $J_{BX} = 7$  c.p.s., a near quintet at 2.24 superimposed on an unresolved multiplet, a multiplet at 1.62, and a triplet ( $J = 7.5$  c.p.s.) at 0.97 p.p.m.

(13) E. Vogel, private communication.

(14) For some syntheses involving semihydrogenation of an interior triple bond in a long conjugated system, where excellent selectivity is reported, see M. Akhtar and B. C. L. Weedon, *J. Chem. Soc.*, 4058 (1959); O. Isler, H. Lindlar, M. Montavon, R. Rügge, and P. Zeller, *Helv. Chim. Acta*, **39**, 249 (1956).

(15) J. C. Hamlett, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 2652 (1951).

(16) Successive analyses on the same sample showing peroxide formation.

Isomerization as described under *cis*-1-cyclohexenyl-1-propene gave the *trans* isomer,  $n_D^{20}$  1.5021,  $\lambda_{\max}$  233  $m\mu$  ( $\epsilon$  23,000),  $J_{AB} = 16$  c.p.s. A value of  $n_D^{20}$  1.5028,  $\lambda_{\max}$  234  $m\mu$  ( $\epsilon$  23,700), has been reported for this isomer.<sup>17</sup> An analytical sample of the *cis* isomer was prepared by gas chromatography.

Anal. Calcd. for  $C_{10}H_{16}$ : C, 88.18; H, 11.82. Found: C, 88.24; H, 11.41.

**Gas Chromatographic Analyses.**—Analyses were performed on a Perkin-Elmer 154B gas chromatograph. The analysis of the products from reduction of 1-ethynylcyclohexene was made on a 6 ft.  $\times$  0.25 in. column containing 20% Reoplex 400 on Chromosorb W at 110°. The studies on reduction of 1-cyclohexenyl-1-propyne and 1-cyclohexenyl-1-butyne were made on the same column at 140°. Analysis of the mixture from 1-cyclohexenyl-3-buten-1-yne was carried out on a 6 ft.  $\times$  0.25 in. column containing 5% Ucon Polar on firebrick at 164°. All components were identified by comparison with internal standards prepared by synthesis. Helium was used as carrier gas.

**1-Alkylcyclohexenes.**—A series of 1-alkylcyclohexenes was prepared for internal standards. In each case the necessary Grignard reagent prepared from an alkyl halide and magnesium in ether was allowed to react with cyclohexanone. The distilled alkylcyclohexanols were distilled from anhydrous potassium acid sulfate using the general procedure of Ohloff.<sup>18</sup> The following were prepared in this way.

**1-Ethylcyclohexene.**—The product was obtained in 42% overall yield: b.p. 54–56° (47 mm.),  $n_D^{20}$  1.4564; lit.<sup>19</sup> b.p. 136°.

**1-Propylcyclohexene.**—This hydrocarbon was obtained in 15% over-all yield as a light oil: b.p. 70–73° (53 mm.),  $n_D^{20}$  1.4565; lit.<sup>20</sup> b.p. 154.7–157.7°,  $n_D^{20}$  1.4578.

**1-Butylcyclohexene.**—This olefin was prepared in 34% over-all yield: b.p. 65–68° (28 mm.),  $n_D^{20}$  1.4606; lit.<sup>20</sup> b.p. 178–179°,  $n_D^{20}$  1.4568.

**N.m.r. Spectra.**—The n.m.r. spectra were run on a Varian A-60 n.m.r. spectrometer<sup>22</sup> in carbon tetrachloride solution using tetramethylsilane as an internal standard.

(17) O. Grummitt and Z. Mandel, *J. Am. Chem. Soc.*, **78**, 1054 (1956).

(18) G. Ohloff, *Ann.*, **627**, 79 (1959).

(19) R. A. Benkeser and J. J. Hazdra, *J. Am. Chem. Soc.*, **81**, 228 (1959).  $n_D^{20}$  1.4562.

(20) F. K. Signaigo and P. L. Cramer, *ibid.*, **55**, 3326 (1933).

(21) R. A. Benkeser, C. Arnold, Jr., R. F. Lambert, and O. H. Thomas, *ibid.*, **77**, 6042 (1955).

(22) We are indebted to the National Science Foundation for a grant which provided part of the funds for purchase of this instrument.

## Chloromethylation of Estrone Methyl Ether

WILLIAM F. JOHNS

Division of Chemical Research, G. D. Searle and Company,  
Skokie, Illinois

Received May 17, 1965

The chloromethylation reaction represents a classical method for the introduction of a functional group into an aromatic system.<sup>1</sup> Its application to the activated A ring of estrone derivatives was explored as a potential route to C-2 and C-4 substituted steroids.<sup>2,3</sup>

The title reaction was seen to proceed smoothly with aqueous formaldehyde and hydrogen chloride, no additional catalyst being necessary. The resultant mixture of chloromethyl compounds was best utilized by displacement of the halogen by acetate ion. Subsequent hydrolysis provided, by direct crystallization, 40% of the 2-hydroxymethyl derivative 1a. Structural

(1) R. C. Fuson and C. H. McKeever, *Org. Reactions*, **1**, 63 (1942).

(2) See W. M. Hoehn and W. F. Johns [U. S. Patent 2,853,501 (1958)] for the initial disclosure of a portion of this work.

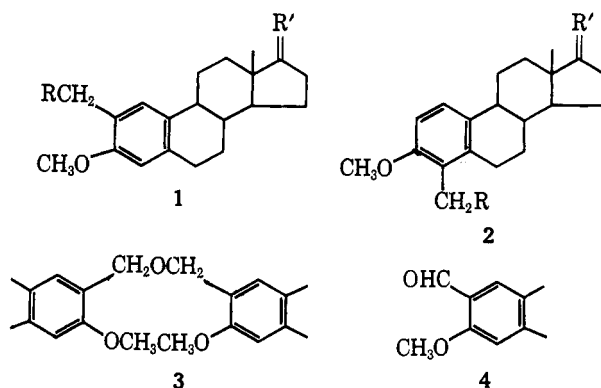
(3) More recent work of a similar nature includes the Mannich addition described by T. L. Patton [*J. Org. Chem.*, **25**, 2148 (1960)] and extended by H. Kaneko, M. Hashimoto, and A. Kobayashi [*Chem. Pharm. Bull. (Tokyo)*, **12**, 196 (1964)].

assignment was made on the basis of the infrared absorption (12.0  $\mu$ )<sup>4</sup> and the n.m.r. spectrum (two singlets in the aromatic region). The nature of the hydroxyl group was demonstrated by manganese dioxide oxidation to the corresponding aldehyde 4. In addition, a facile hydrogenolysis over palladium catalyst afforded the 2-methyl derivative 1d.

Investigation of the mother liquors revealed as a minor constituent the 4-hydroxymethyl derivative 2a. The n.m.r. spectrum of this compound showed the AB pattern expected for the vicinal aromatic protons, in accord with the assignment made from the infrared spectrum (12.3  $\mu$ ). Again, hydrogenolysis afforded the methyl derivative 2d.

Direct hydrolysis of the chloromethylation mixture in aqueous dioxane containing potassium hydroxide afforded a lower yield of the hydroxymethyl derivatives owing to a competitive formation of dimeric materials such as 3. When methanol was substituted as solvent the methoxymethyl derivative 1b was formed as demonstrated by the new methoxyl absorption in the n.m.r. spectrum. Hydrogenolysis of this compound afforded the 2-methyl derivative 1d, although the rate of reaction was much slower than that seen for hydrogenolysis of the hydroxy derivative 1a.

Hydride reduction of the 17-carbonyl groups in 1a, 1d, 2a, and 2d proceeded normally to furnish the corresponding alcohol derivatives. The derivatives 1d and 2d showed especially clearly the infrared distinction due to aromatic protons.<sup>4</sup>



a, R = OH; R' = O  
b, R = OCH<sub>3</sub>; R' = O  
c, R = R' = OH  
d, R = H; R' = O  
e, R = H; R' = OH

### Experimental Section<sup>5,6</sup>

**2-Hydroxymethyl estrone 3-Methyl Ether (1a).**—A stream of hydrogen chloride was passed through a stirred solution of 15 g. of estrone methyl ether in 150 ml. of ethylene dichloride and 10 ml. of 40% aqueous formaldehyde at 20°. After 2 hr. an additional 10 ml. of aqueous formaldehyde was added. After a total of 6 hr. the solution was diluted with aqueous sodium carbonate and extracted with chloroform. Chromatography of a portion of the resultant crude product failed to yield a crystalline com-

(4) Infrared distinction between isolated and adjacent hydrogens on an aromatic ring in steroids has been pointed out by A. S. Dreiding, W. J. Pummer, and A. J. Tomaszewski [*J. Am. Chem. Soc.*, **75**, 3159 (1953)].

(5) Infrared spectra were determined as KBr disks, ultraviolet spectra in methanol, rotations in chloroform (1%), and n.m.r. spectra in deuteriochloroform ( $\Delta\nu = 0$  from tetramethylsilane as an internal standard, with a Varian A-60 spectrometer). The spectral and analytical data reported were furnished by Dr. R. T. Dillon and staff.

(6) The chromatography described was carried out by Dr. E. G. Daskalakis and staff, using silica gel as adsorbent.