

**17 $\beta$ -Hydroxyandrosta-4,7-dien-3-one (4).**—To 1.0 g of 17 $\beta$ -hydroxyandrosta-4,6-dien-3-one,<sup>7</sup> dissolved in 10 ml of dimethyl sulfoxide, was added 1.5 g of sodium methoxide. The mixture was stirred under nitrogen at room temperature for 1 hr and then added to 66 ml of ice-cold, aqueous 2 *N* hydrochloric acid with stirring. The precipitate was filtered, dissolved in methylene chloride, and then, after drying with sodium sulfate, chromatographed on Davidson silica gel, which had previously been deactivated by treatment with wet ether for 2 hr. Elution with methylene chloride-methanol 50:1 gave 400 mg of a yellow crystalline material which, after treatment with charcoal and recrystallization from methanol-ethyl acetate (1:1), gave 280 mg of white crystalline material: mp 162–164° (mp lit.<sup>3</sup> 161–163°);  $\lambda_{\text{max}}^{\text{OH}}$  239 m $\mu$  ( $\epsilon$  15,400); and  $\nu_{\text{max}}^{\text{CHCl}_3}$  3638 (OH), 3465 (OH) and 1662 (3 ketone) cm<sup>-1</sup>. The nmr spectrum showed maxima for 1 olefinic proton as a doublet ( $J = 2$  Hz) centered at 5.79 (4 position), 1 olefinic proton as a multiplet between 5.1 and 5.3 (7 position), 1 proton as a broad triplet between 3.6 and 4.0 (17 position), 1 proton as a broad triplet between 3.6 and 4.0 (17 position), 2 allylic protons as a multiplet between 2.6 and 3.5 (6 position), 3 protons as a singlet at 1.19 (19 position), and 3 protons as a singlet at 0.68 ppm (18 position).

**Registry No.**—1, 14532-68-4; 2, 24099-37-4; 3, 13209-46-6; 4, 13386-25-9.

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(7) Prepared from testosterone acetate by the method of S. K. Pradhan and H. J. Ringold, *J. Org. Chem.*, **29**, 601 (1964).

## Reaction of $\alpha$ Olefins with Aqueous Formaldehyde

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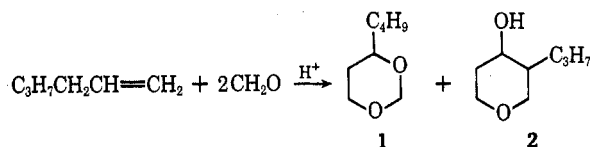
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The mineral acid catalyzed condensation of formaldehyde with olefins is commonly known as the Prins reaction.<sup>1</sup> It is well established that straight-chain 1-olefins are much less reactive than are substituted R(R')C=CHR'' types;<sup>2</sup> 1-olefins require either elevated temperatures with high catalyst concentrations<sup>2a</sup> or the use of acetic acid solvent<sup>3</sup> with substantial quantities of strong acid catalysts. This reaction generally leads to a rather complex mixture of products, mainly composed of 1,3-dioxanes, 1,3-glycols, and tetrahydropyranols,<sup>2,3</sup> along with minor amounts of tetrahydrofuran derivatives<sup>2b,3,4</sup> and the alcohol derived from hydration of the starting olefin.<sup>3</sup>

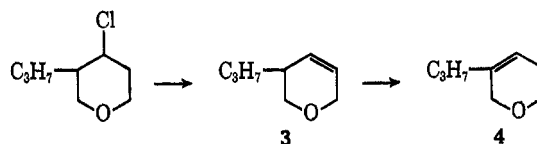
During the course of an investigation of modifications of the Prins reaction,<sup>5</sup> we have also studied the

condensation of 1-olefins with aqueous formaldehyde (formalin) solutions at elevated temperatures and have developed useful synthetic procedures for the preparation of 4-alkyl-1,3-dioxanes and 3-alkyltetrahydropyran-4-ols from representative olefins from 1-pentene through 1-dodecene.

Initial studies were carried out by heating 2.0 mol of 1-hexene with 4.9 mol of 37% formalin and 8 ml of sulfuric acid at 175° in an autoclave for 5 hr. Complete conversion of the starting olefin was attained at these conditions; after distillation from a small amount of heavy residue the resulting product was analyzed by glpc and found to contain 5% of 2-hexanol, 44% of 4-butyl-1,3-dioxane (1), 45% of *cis,trans*-3-propyltetrahydropyran-4-ol (2), 6% of a mixture of dihydropyrans, and traces of other materials.



Pure 1 and 2 were obtained by fractional distillation. Structures were confirmed by elemental and spectral analysis, and in the case of 2 (a *cis-trans* mixture) by comparison with an authentic sample.<sup>5</sup> 2-Hexanol and other minor products were separated by preparative glpc and identified by comparison with authentic samples (ir spectra, glpc retention times). 3,6-Dihydro-3-propyl-2H-pyran (3) and 5,6-dihydro-3-propyl-2H-pyran (4) were identified in approximately 2:1 proportions by glpc comparison with a 3:2 mixture synthesized by dehydrochlorination of *cis,trans*-4-chloro-3-propyltetrahydropyran<sup>5</sup> with potassium hydroxide in ethylene glycol.



A study of variations in reaction parameters was carried out in an attempt to define optimum conditions for more selective production of either 1 or 2 from 1-hexene. A number of experiments were conducted in which the sulfuric acid concentration was varied between 0.24 and 0.40 *M*. In general, the higher acid concentrations provided increased reaction rates but also increased by-product formation. Replacement of the sulfuric acid by phosphoric acid decreased the reaction rate considerably; in addition, autoclave corrosion was markedly accelerated. Substitution of paraformaldehyde-water mixtures for the commercial formalin (stabilized with ca. 12% methanol) did not appreciably affect either the yield or product distribution nor did rather substantial variation in the olefin/formaldehyde ratio. A recycle of coproduct 4-butyl-1,3-dioxane did not affect the selectivity; the same relative distribution of products was obtained. Variation in temperature between 125 and 225° gave the expected results. At the lower end of the range reactions were slower and often incomplete while the higher temperatures gave faster reaction rates and more by-products (principally dihydropyrans). Indeed, at 225° the condensation proceeded slowly in the absence of added

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(2) (a) F. Arundale and L. A. Mikeska, *Chem. Rev.*, **51**, 505 (1952); (b) M. Hellin, M. Davidson, D. Lumbroso, P. Guilian, and F. Coussement, *Bull. Soc. Chim. Fr.*, 2974 (1964); (c) Y. Nishimura and T. Tanaka, *Kogyo Kagaku Zasshi*, **70**, 466 (1967).

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TABLE I  
 CONDENSATION OF 1-OLEFINS WITH FORMALIN<sup>a</sup>

R	Conversion, %	Yield, <sup>b</sup> %	
		1	2
C <sub>2</sub> H <sub>5</sub>	100	46	42
C <sub>3</sub> H <sub>7</sub>	100	41	46
C <sub>5</sub> H <sub>11</sub>	85	43	45
C <sub>7</sub> H <sub>15</sub>	53	40	47
C <sub>9</sub> H <sub>19</sub>	39	42	46

<sup>a</sup> Reactions were carried out for 6 hr at 150° using 2 mol of olefin to 4.9 mol of 37% formalin 0.24 M in H<sub>2</sub>SO<sub>4</sub>. <sup>b</sup> Based on reacted olefin.

with nitrogen, and heated with stirring at 150° for 6 hr. After cooling, the product was extracted into ether and the ether extracts were washed with sodium carbonate solution and dried (MgSO<sub>4</sub>); the ether was then removed. A portion of the residue was analyzed by glpc using the 5-ft column for the 1-decene and 1-dodecene reactions and the 10-ft column for the remainder. The order of elution is 2-alkanol, 4-alkyl-1,3-dioxane, dihydro-pyran, and 3-alkyltetrahydropyran-4-ol. The product 4-alkyl-1,3-dioxanes (Table II) and 3-alkyltetrahydropyran-4-ols (Table III) were isolated by fractionation through a 4 ft × 0.75 in. helices packed column.

**Registry No.**—1 (R = C<sub>2</sub>H<sub>5</sub>), 15601-78-2; 1 (R = C<sub>3</sub>H<sub>7</sub>), 2244-87-3; 1 (R = C<sub>5</sub>H<sub>11</sub>), 2244-85-1; (R = C<sub>7</sub>H<sub>15</sub>), 23433-02-5; 1 (R = C<sub>9</sub>H<sub>19</sub>), 24647-61-8; *2-cis* (R = C<sub>2</sub>H<sub>5</sub>), 24647-33-4; *2-cis* (R = C<sub>3</sub>H<sub>7</sub>), 24647-34-5; *2-cis* (R = C<sub>5</sub>H<sub>11</sub>), 24647-35-6; *2-cis* (R = C<sub>7</sub>H<sub>15</sub>), 24647-36-7; *2-cis* (R = C<sub>9</sub>H<sub>19</sub>), 24647-37-8; *2-trans* (R = C<sub>2</sub>H<sub>5</sub>), 24646-96-6; *2-trans* (R = C<sub>3</sub>H<sub>7</sub>), 24646-97-7;

 TABLE II  
 4-ALKYL-1,3-DIOXANES

R	Bp, °C	Pressure, mm	n <sub>D</sub> <sup>20</sup>	Formula	Calcd, %		Found, %	
					C	H	C	H
C <sub>2</sub> H <sub>5</sub>	60-61	16.0	1.4278	C <sub>7</sub> H <sub>14</sub> O <sub>2</sub>	64.6	10.8	64.7	10.9
C <sub>3</sub> H <sub>7</sub>	62-63	8.0	1.4355	C <sub>8</sub> H <sub>16</sub> O <sub>2</sub>	66.6	11.1	66.7	11.1
C <sub>5</sub> H <sub>11</sub>	105-107	12.0	1.4397	C <sub>10</sub> H <sub>20</sub> O <sub>2</sub>	69.8	11.6	70.0	11.8
C <sub>7</sub> H <sub>15</sub>	132-134	12.0	1.4462	C <sub>12</sub> H <sub>24</sub> O <sub>2</sub>	72.0	12.0	72.0	12.1
C <sub>9</sub> H <sub>19</sub>	128-130	1.5	... <sup>a</sup>	C <sub>14</sub> H <sub>28</sub> O <sub>2</sub>	73.6	12.3	73.7	12.4

<sup>a</sup> Solidified, mp 41-42° from pentane, lit.<sup>3</sup> mp 41.5-42.5°.

 TABLE III  
 3-ALKYLTETRAHYDROPYRAN-4-OLS

R	Bp, °C	Pressure, mm	n <sub>D</sub> <sup>20</sup>	Formula	Calcd, %		Found, %	
					C	H	C	H
C <sub>2</sub> H <sub>5</sub>	112-114	16.0	1.4598	C <sub>7</sub> H <sub>14</sub> O <sub>2</sub>	64.6	10.8	64.5	10.6
C <sub>3</sub> H <sub>7</sub>	105-106	8.0	1.4591	C <sub>8</sub> H <sub>16</sub> O <sub>2</sub>	66.6	11.1	66.4	11.0
C <sub>5</sub> H <sub>11</sub>	95-99	0.5	1.4585	C <sub>10</sub> H <sub>20</sub> O <sub>2</sub>	69.8	11.6	69.8	11.8
C <sub>7</sub> H <sub>15</sub>	168-170	12.0	1.4588	C <sub>12</sub> H <sub>24</sub> O <sub>2</sub>	72.0	12.0	71.9	12.0
C <sub>9</sub> H <sub>19</sub>	150-154	1.5	1.4590	C <sub>14</sub> H <sub>28</sub> O <sub>2</sub>	73.6	12.3	73.6	12.3

acid catalyst to produce the expected spectrum of products with a rather considerable increase in dihydropyran formation.

Although attempts to improve the selectivity of the Prins reaction under these conditions to either major product were unsuccessful, this procedure does represent a most convenient and useful synthesis of 4-alkyl-1,3-dioxanes and *cis,trans*-3-alkyltetrahydropyran-4-ols. A minimum of by-products is produced and the boiling point difference between the dioxane and tetrahydropyranol is sufficiently great that separation by fractionation is easily accomplished. Table I summarizes product yields from the condensation of a number of typical 1-olefins from 1-pentene through 1-dodecene using standard conditions. It is apparent that reaction rates are slower for the higher molecular weight olefins, probably because of decreased solubility, and more nearly optimum conditions would require longer reaction times, higher temperatures, more catalyst, or some combination thereof for complete conversion.

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

**Condensation of 1-Olefins with Formalin.**—A 1-l. Magnedrive autoclave constructed of Hastelloy C<sup>7</sup> was charged with 2 mol of olefin (4.9 mol) of 37% formalin, and 5 ml of concentrated sulfuric acid. (One-half quantities were used for the 1-decene and 1-dodecene reactions.) The autoclave was sealed, flushed

*2-trans* (R = C<sub>5</sub>H<sub>11</sub>), 24646-98-8; *2-trans* (R = C<sub>7</sub>H<sub>15</sub>), 24646-99-9; *2-trans* (R = C<sub>9</sub>H<sub>19</sub>), 24647-00-5; formaldehyde, 50-00-0.

(6) All melting and boiling points are uncorrected. Olefins used were Phillips Petroleum Co. Pure Grade materials. Gas chromatographic analyses were carried out on a Perkin-Elmer Model 720 gas chromatograph using 5 ft and 10 ft × 0.25 in. columns of 20% Ucon LB-550-X on Chromosorb P.

(7) Autoclave Engineers, Inc., Erie, Pa.

### Chemotaxonomy of the Rutaceae. VII.<sup>1</sup> Alkaloids in *Evodia zanthoxyloides* F. Muell.

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The alkaloids occurring in *Evodia zanthoxyloides* F. Muell. (Rutaceae) have been the subject of an extended investigation by Ritchie and coworkers.<sup>2</sup>

(1) Part VI: D. L. Dreyer and A. Lee, *Phytochemistry*, **8**, 1499 (1969).

(2) R. H. Prager, E. Ritchie, A. V. Robertson, and W. C. Taylor, *Aust. J. Chem.*, **15**, 301 (1962), and previous papers in this series.