[CONTRIBUTION FROM THE ORGANIC BASIC RESEARCH LABORATORY, THE DOW CHEMICAL COMPANY, TEXAS DIVISION]

Preparation of Ketone Acetals from Linear Ketones and Alcohols

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Simple ketone acetals were prepared by reaction of alcohols with ketones. The composition of several ketone-alcohol reaction systems at equilibrium was determined at 24° and −28° and in each case the formation of the acetal was favored at the low temperature.

In the past most ketone acetals were prepared by one of two general methods. One of these methods was the reaction of an ortho ester with a ketone to give the desired ketone acetal.[1-4] The alkyl orthosilicates were also reacted in a similar manner.[5] The second general method was the reaction of a substituted acetylene with two moles of alcohol to give a ketone acetal.[6,7] A related preparation utilized the reaction of isopropenyl acetate with an alcohol.[8,9] While both of these general methods give satisfactory to good yields of ketone acetals, they are limited by the availability of the *ortho* esters and substituted acetylenes.

A large number of aldehyde acetals have been prepared by the reaction of an alcohol with an aldehyde, but until recently the status of the analogous reaction between an alcohol and a ketone was characterized by the following statement of Carswell and Adkins:[10] "The reaction of ketones with alcohols to form acetals analogous to the reaction of aldehydes with alcohols proceeds to so slight an extent, if at all, that the reaction is of no importance." The first successful published experiment that was found on this reaction was in a paper presented at the Southwide Chemical Conference in 1956 by Suter and Guedin.[11] They reported that when acidic solutions of simple aliphatic ketones and methanol were introduced into the mass spectrometer, the resulting mass peaks indicated that some ketals had been formed. It was also reported that "no new ketals were prepared by this new method."

Independently and at about the same time as our work,[12] McCoy, Baker, and Gohlke[13] reported the preparation of cyclohexanone dimethyl acetal from cyclohexanone and methanol. Their work was limited to cyclohexanone, which is much more reactive than the linear ketones with methanol. Although our interest was primarily in the linear ketones, some work with cyclohexanone is included for comparative purposes.

We have found that linear ketones react directly with simple alcohols to give ketone acetals and that the ketone acetals can be readily recovered. The success of the reaction depends on shifting the equilibrium in favor of the ketone acetal by conducting the reaction at low temperature. Strong acids, including the sulfonic acid ion exchange resins, are good catalysts for the reaction. The isolation of the lower ketone acetals was based largely on washing with strong aqueous sodium hydroxide, as described by Bond and Klar,[14] to separate the alcohols from the ketals and thus avoid the troublesome alcohol-acetal azeotropes.

The use of Dowex 50 (a sulfonic acid cation exchange resin) in conjunction with Dowex 2 (a quaternary ammonium anion exchange resin) made possible a reaction system that resulted in good temperature control and a crude reaction product that was neutral. The use of the acid ion exchange resin also provides the means of conveniently achieving a very high concentration of acid catalyst which is necessary for producing reasonably large reaction rates at the low temperatures employed. In experiments with soluble acids at practicable concentrations, the reactions were impracticably slow. The catalyst is exceedingly long lived; after three months of continuous use no detectable decrease in activity was observed.

Stock solutions of alcohols and ketones were slowly passed successively through a bed of the cation exchange resin in the acid form and a bed of the anion exchange resin in the hydroxyl form, both maintained at the desired temperature. The rate of flow was low enough that equilibrium was approached at the low temperature in the acid resin bed. Passage through the basic resin then removed any dissolved acid and effectively prevented any reversal of the reaction due to the effect of any sub-

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sequent temperature changes on the position of the equilibrium. The acid-free reaction solution which passed from the reactor could be stored at room temperature and even distilled without further treament; however, a small amount of sodium hydroxide or sodium methylate was usually added prior to distillation to insure the maintenance of alkalinity. The presence of any acid would not only cause a change in the composition of the products but would also cause pyrolytic cracking of the ketone acetal to an unsaturated ether during the distillation. It was advantageous to wash the reaction solution with the strong sodium hydroxide solution to remove the water-soluble reactants from the ketone acetal. This was necessary in three cases where it was found that the alcohol and the ketone acetal formed an azeotrope. No binary azeotropes composed of the ketone and the ketone acetal were noted. Good conversion of acetone was obtained with methanol, but conversions were lower with ethanol, propanol, and butanol.

In the reaction of several alcohols with acetone, methanol gave the largest conversions to acetal. For this reason it was selected for reaction with three other linear ketones. For the three ketones chosen, conversions were smaller and decreased with increase in molecular weight.

All of the ketone acetals described in the experimental section were prepared directly from ketone and alcohol; however, except for the dimethyl acetals of acetone and butanone, the conversions were low. Thus, although they can be made directly, ketone acetals other than these two are more easily prepared by ketone and/or alkoxyl moiety interchange reactions, and since acetone dimethyl acetal is now commercially available these interchanges provide an excellent method of obtaining a large number of ketone acetals. A paper now in preparation will describe these interchange reactions in detail.

EXPERIMENTAL

Preparation of the catalyst and reactor. Dowex 50 was converted to the hydrogen form with 3*N* hydrochloric acid and thoroughly washed successively with distilled water and methanol. Dowex 2 was converted to the hydroxyl form with 5% sodium hydroxide solution and then washed similarly. A straight tube Pyrex condenser 90 cm. long, 19 mm. ID was mounted vertically and an 18-cm. layer of the Dowex 2 was put at the bottom followed by a 55-cm. layer of the Dowex 50. The acid resin catalyst occupied a total volume of 155 ml. of which 120 ml. was resin and 35 ml. was void volume. The temperature of the catalyst bed was controlled by passing a coolant with the desired temperature through the jacket of the condenser.

Preparation of acetone dimethyl acetal. A stock solution of methanol and acetone in a 4 to 1 mole ratio was passed over the resin bed at −27° at a rate of 10 to 15 ml./min. The refractive index of the reaction solution changed from n_D^{24} 1.3380 to n_D^{24} 1.3455. After a steady state had been obtained, a 1500-ml. sample of the effluent solution was combined with 200 ml. of a 160–170° fraction of Stoddard solvent. The combined solution was washed 3 times with a 15% sodium hydroxide water solution, first with a volume 1.5 times and then twice with volumes equal to that of the reaction solution. The insoluble organic layer was dried with potassium carbonate and distilled. At 56°, 10 ml. of a ternary azeotrope consisting of 75% (vol.) acetone, 20% methanol, and 5% acetone dimethyl acetal was collected. A second 10-ml. fraction at 61–62° was a binary azeotrope consisting of 55% acetone dimethyl acetal and 45% methanol. Finally 175 ml. of acetone dimethyl acetal was collected, b.p. 80° (760 mm.) and 43° (205 mm.), d_{24} 0.835 g./ml., n_D^{25} 1.3748 (lit.[6] b.p. 78–80° (747 mm.), d_{20} 0.8448, n_D^{20} 1.3746).

Preparation of butanone dimethyl acetal. A stock solution of methanol and butanone (4 to 1 mole ratio) was passed through the reactor at −26° at a rate of 5 to 10 ml./min. The refractive index of the reaction solution changed from n_D^{24} 1.3470 to n_D^{24} 1.3520. Two liters of the steady-state effluent solution was added to 200 ml. of Stoddard solvent (b.p. 160–170°) and the combined solution was washed 3 times with 15% aqueous sodium hydroxide, each time with a volume of wash solution equal to that of the organic phase. The organic portion was dried with potassium carbonate and distilled at 200 mm., giving 260 ml. of butanone and 180 ml. of butanone dimethyl acetal, b.p. 66° (200 mm.), 50° (100 mm.), n_D^{24} 1.3915, d_{24} 0.8505 (lit.[6] b.p. 48–50° (100 mm.), d_4^{28} 0.8535, n_D^{28} 1.3899).

Mixtures of methanol and butanone dimethyl acetal distill as an azeotrope which boils at 64.5°, n_D^{25} 1.3385, and is 18.5% acetal by weight.

Preparation of cyclohexanone dimethyl acetal. A solution of methanol and cyclohexanone (4 to 1 mole ratio) was passed over the resin catalyst at −26° at 5 to 10 ml./min. An 800-ml. portion of the effluent was washed 3 times with 15% aqueous sodium hydroxide. The organic layer was dried with potassium carbonate and distilled, giving 168 ml. of cyclohexanone, b.p. 74° (50 mm.), and 179 ml. of cyclohexanone dimethyl acetal, b.p. 83° (50 mm.), n_D^{24} 1.4373, d_{24} 0.9484 (lit.[13] n_D^{25} 1.4372).

Other ketone acetals. The following ketone acetals were prepared in a similar manner and used as infrared standards to obtain the data in Table I.

TABLE I

EQUILIBRIUM CONVERSION OF KETONES

Ketone[a]	Alcohol[a]	Conversion, % 24°	Conversion, % −28°
Acetone	Methanol	11	32
Acetone	Ethanol	2	17
Acetone	Propanol	2	19
Acetone	Butanol	<1	17
2-Butanone	Methanol	7	24
3-Pentanone	Methanol	3	13
4-Methyl-2-pentanone	Methanol	4	9
Cyclohexanone	Methanol	46	86

[a] Mole ratio of alcohol to ketone was 4 to 1.

Acetone diethyl acetal. b.p. 45° (60 mm.), n_D^{25} 1.3851, d_{25} 0.824, (lit.[15] n_D^{20} 1.3861). This acetal forms an azeotrope (b.p. 76°, n_D^{25} 1.3660, 20% by vol. acetone diethyl acetal) with ethanol.

Acetone dipropyl acetal. b.p. 86° (83 mm.), n_D^{25} 1.3995, d_{24} 0.827, (lit.[16] b.p. 91° (95 mm.), n_D^{20} 1.4026).

Acetone dibutyl acetal. b.p. 66° (5 mm.), n_D^{26} 1.4103, d_{26} 0.831, (lit.[16] n_D^{22} 1.4084).

3-Pentanone dimethyl acetal. b.p. 59° (63 mm.), n_D^{26} 1.4013, d_{25} 0.863.

Anal. Calcd. for $C_7H_{16}O_2$: C, 63.59; H, 12.20. Found: C, 63.65; H, 12.18.

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4-Methyl-2-pentanone dimethyl acetal. b.p. 58° (35 mm.), n_D^{25} 1.4042, d_{26} 0.850.

Anal. Calcd. for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 66.07; H, 12.35.

Yields. The acetone-methanol reaction system was the only case where attempts were made to account for all of the starting materials. It was possible to distill the unreacted acetone and methanol from the alkaline wash solution with recovery of more than 90% of the unreacted acetone and methanol. Therefore, for this system the conversion of acetone was 25–30% and the yield based on unrecovered acetone and methanol was consistently over 90%. No effort was made to account for all of the materials used in the other reaction systems, but it is believed that most of the unreacted materials could be recovered because no appreciable discoloration of the solutions was observed and no high boiling distillation residues or other by-products were obtained.

Effect of temperature on the reaction of ketones with alcohols. Stock solutions of 4 moles of alcohol per mole of ketone were passed slowly through the reactor at the desired temperature to ensure thorough displacement of all foreign fluids by the reaction solution. The flow was then stopped and the stock solution was kept in contact with the catalyst for a period of time. When the flow was again started, the effluent was collected in increments of 10 ml. each and the refractive index of each increment was measured. This procedure was repeated with successively longer contact times until there was no further increase in the maximum index observed in each set of effluent increments. Since the refractive index increases with conversion, the sample with the highest refractive index was taken as the one most nearly approaching equilibrium. The amount of ketone acetal present was then determined from its absorbance in the infrared. Methanol and ethanol were at equilibrium after 1 hr. in their reactions with every ketone except cyclohexanone. In the methanol-cyclohexanone system, the conversion of the cyclohexanone increased from 79% after 5 hr. to 86% after an 8-hr. contact period. Both propanol and butanol were at equilibrium in the reaction with acetone after a 5-hr. contact period. The values in Table I give the conversion of the ketones at equilibrium as determined in this manner.

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FREEPORT, TEX.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

An Improved Synthesis of Dichlorocarbene from Ethyl Trichloroacetate[1]

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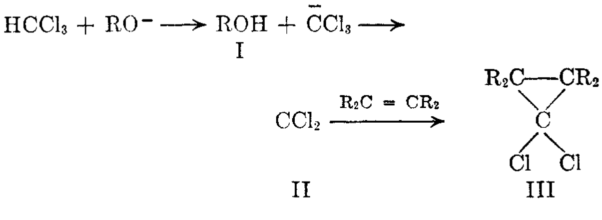
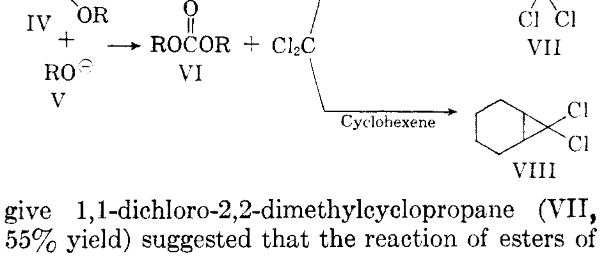
The reaction of ethyl trichloroacetate(IV) with sodium methoxide (commercial), sodium ethoxide, or potassium *t*-butylate in the presence of the olefins cyclohexene and isobutylene were studied both in the presence and absence of solvent (pentane). Similar results were obtained with all bases used, and yields of 72–88% of the derived cyclopropanes resulted. This reaction affords significantly higher yields of cyclopropanes than analogous reactions in which chloroform is used as the carbene precursor.

The reaction of chloroform, potassium *t*-butylate, and olefin constitutes an excellent synthesis of certain cyclopropane derivatives.[2] The yield of cyclopropane(III), obtained from such reactions, is generally 55–65%[2] and is unquestionably lowered by a side reaction occurring between dichlorocarbene and the alcohol (I) formed in the reaction.[2a,3] The superiority of *t*-butylate[2b] over other alkoxides in this reaction may be related, at least in part, to decreased reactivity of the more highly hindered *t*-alcohol with the derived carbene.



The formation of dichlorocarbene,[4] in the absence of alcohol, from *t*-butyl trichloroacetate (IV. R = *t*-butyl) and potassium *t*-butylate (V. R = *t*-butyl), and its further reaction with isobutylene to give 1,1-dichloro-2,2-dimethylcyclopropane (VII, 55% yield) suggested that the reaction of esters of



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