The Reaction of Trimethylsilyl Enol Ethers with Diols

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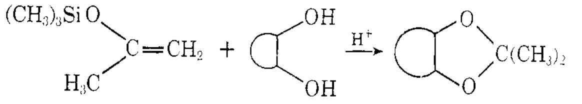
The acid-catalyzed reaction of 2-(trimethylsiloxy)propene (I) (TMSP) with cyclic diols, including the trans 1,2-diols of cyclohexane and cycloheptane and *cis*-1,2-cyclohexanediol, results in the formation of the corresponding acetonides in good yield. Similarly, the reaction of 1-(trimethylsiloxy)cyclohexene (II) with ethylene glycol, 1,3-propanediol, 1,4-butanediol, and 2-mercaptoethanol affords the corresponding ketals of cyclohexanone in good yield. The reactions are exothermic and offer a convenient alternative to other methods of preparing acetonides and ketals.

We wish to report that trimethylsilyl enol ethers react with a variety of diols with acid catalysis to give ketals in good yield. The reaction is general and has been used for the preparation of the heretofore unknown *trans*-1,2-cyclohexanediol acetonide.[1] The reactions are exothermic and require from 10 to 30 min for completion. They thus offer an attractive alternative to the more conventional preparations of ketals.[2]

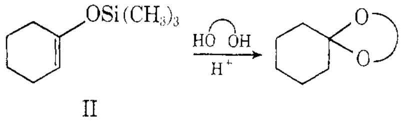
Results

Two systems were studied, the reaction of 2-(trimethylsiloxy)propene (I) (TMSP) with cyclic 1,2-diols (eq 1) and the reaction of 1-(trimethylsiloxy)cyclohexene (II) with acyclic diols and with 2-mercaptoethanol (eq 2).



(1)

I



(2)

II

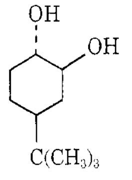
The first efforts were to form acetonides from the reaction of cyclic diols with TMSP using an acid catalyst. The reaction was catalyzed with either concentrated HCl or with trimethylchlorosilane.[3] A variety of solvents were employed, including ether, tetrahydrofuran, acetonitrile, carbon tetrachloride, chloroform, and benzene, with essentially the same results in all cases, although tetrahydrofuran has the advantage of being a better solvent for the diols. The synthesis of TMSP in quantities suitable for large-scale or repeated use presents somewhat of a problem. For this work the method of House and coworkers[4] was used, but there was always about 30% hexamethyldisiloxane present in the distilled product. Redistillation did not improve the product and it was determined that an azeotrope was formed. This problem was apparently also encountered by Krüger and Rochow in their preparation of TMSP.[5] The mixture, however, could be used with good results, since the hexamethyldisiloxane is inert to the reaction conditions and is volatile enough for easy removal under reduced pressure. The amount of TMSP present in the mixture was determined to be about 5 mmol/ml by using nmr spectroscopy with benzene as an internal standard. The exact amount of TMSP varied slightly from batch to batch.

The results of the reaction of TMSP with cyclic 1,2-diols are shown in Table I. The reaction is exothermic with reaction times of 5–10 min sufficient for complete reaction. Of particular interest is the formation of *trans*-1,2-cyclohexanediol acetonide in 80% yield. This compound was shown to be different from the corresponding cis isomer by comparison of their glpc retention times and nmr, ir, and mass spectra. Hydrolysis of this acetonide afforded the trans diol uncontaminated with the cis diol, thus ruling out the possibility of an isomerization occurring during the reaction. The spectral data are recorded in the Experimental Section. A trans acetonide was also formed with 4-*tert*-butyl-*trans*-1,*cis*-2-cyclohexanediol (III), but not from 4-*tert*-butyl-*cis*-1,*trans*-2-cyclohexanediol (IV), consistent with the results of Merkel and coworkers.[6] *trans*-1,2-Cyclopentanediol failed to give an acetonide. The use of a large excess of TMSP resulted in the formation of a considerable amount of 2,2-bis(trimethylsiloxy)propane from the reaction of trimethylsilanol with TMSP.

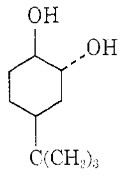
TABLE I
PRODUCTS FROM THE REACTION OF TMSP (I) WITH CYCLIC 1,2-DIOLS

Registry no. of diol	Diol	Registry no. of acetonide	Acetonide, yield, %	Bp, °C (mm)	$n^{20}D$
1792-81-0	*cis*-C_6	41564-26-5	80	92–96 (22)	1.4466[a]
1460-57-7	*trans*-C_6	24148-95-6	80	92–96 (22)	1.4450
13553-19-0	*trans*-C_7	41564-28-7	85	*b*	1.4536[c]
19793-88-5	4-*t*-Bu-*trans*-1,-*cis*-2-C_6	41564-29-8	85	*b*	1.4554[d]

[a] H. G. Derx, *Recl. Trav. Chim. Pays-Bas*, **41**, 331 (1922), gives $n^{17.5}D$ 1.4467. [b] Isolated by preparative glpc. [c] H. G. Derx, *Recl. Trav. Chim. Pays-Bas*, **41**, 312 (1922), gives $n^{15}D$ 1.45432. [d] See ref 6, which gives $n^{20}D$ 1.4572.



III



IV

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(1) J. Böeseken, *Recl. Trav. Chim. Pays-Bas*, **40**, 553 (1921).

(2) See, for example, O. T. Schmidt in "Methods in Carbohydrate Chemistry," Vol. II, R. L. Whistler and H. L. Wolfram, Ed., Academic Press, New York, N. Y., 1963, p 318.

(3) Other acids were not tried. The trimethylchlorosilane may catalyze the reaction through the generation of HCl by reaction with an OH group or from the HCl present in the chlorosilane.

(4) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

(5) C. R. Krüger and E. G. Rochow, *J. Organometal. Chem.*, **1**, 476 (1964).

(6) D. Merkel, F. Wolf, and M. Lück, *Z. Chem.*, **8**, 225 (1968).

The results of the reaction of acyclic diols with II are summarized in Table II. It can be seen that the reaction results in the formation of the corresponding ketals of cyclohexanone in good yield. The reactions are exothermic and are complete in 10–30 min. Reaction with 2-mercaptoethanol went cleanly to give 1-oxa-4-thiaspiro[4.5]decane.

TABLE II
PRODUCTS OF THE REACTION OF ACYCLIC DIOLS WITH 1-(TRIMETHYLSILOXY)CYCLOHEXENE (II)

Registry no. of diol	Diol	Registry no. of ketal	Yield of ketal, %	Bp, °C (mm)	$n^{20}\text{D}$
107-21-1	Ethylene glycol	177-10-6	75	88–90 (28)[a]	1.4584
504-63-2	Trimethylene glycol	180-93-8	75	90–95 (18)	1.4699[b]
110-63-4	1,4-Butanediol	181-28-2	70	90–95 (10)[c]	1.4721[c]
60-24-2	2-Mercaptoethanol	177-15-1	75	119–120 (25)[d]	1.5150[d]

[a] J. Böeseken and F. Telleger, *Recl. Trav. Chim. Pays-Bas*, **57**, 133 (1938), give bp 67–74° (20 mm). [b] E. J. Salmi, *Ber.*, **71**, 1803 (1938), gives $n^{20}\text{D}$ 1.4692. [c] E. D. Bergamnn and A. Kaluszyner, *Recl. Trav. Chim. Pays-Bas*, **78**, 337 (1959), give bp 117–118° (40 mm), $n^{30}\text{D}$ 1.4681. [d] C. Djerassi and M. Gorman, *J. Amer. Chem. Soc.*, **75**, 3704 (1953), give bp 47° (0.6 mm), $n^{24}\text{D}$ 1.5155.

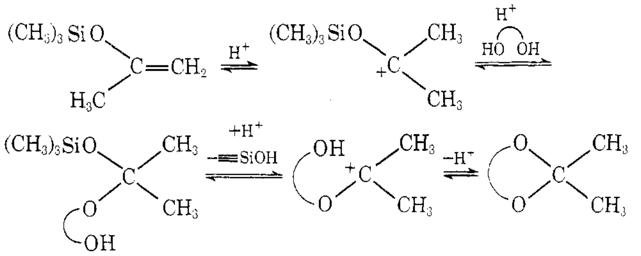
Discussion

Trimethylsilyl enol ethers are very active reagents with diols under acid catalysis. The advantages of forming ketals using trimethylsilyl enol ethers are found in the short reaction times, the high yields, and the formation of ketals that are not easily realized by other methods (*viz. trans*-1,2-cyclohexanediol acetonide and 4-*tert*-butyl-*trans*-1,*cis*-2-cyclohexanediol acetonide).

We have found that the reaction of alcohols with TMSP gives rise to silylation of the alcohol with the elimination of acetone (eq 3).[7] To rule out the possibility that the ketals are being formed by the reaction of silylated diols with the acetone formed, a mixture of *cis*-1,2-cyclohexanediol, acetone, and trimethylchlorosilane was shaken for 10 min and an nmr spectrum was taken. This showed no formation of a peak at about δ 1.3 for the isopropyl methyl groups of the acetonide, these protons being clearly evident in the spectrum of the reaction mixture of the diol with TMSP. A mechanism analogous to that for ketal formation from ketones and diols with acid catalysis is proposed. This is illustrated in Scheme I.

$$\text{I} + \text{ROH} \xrightarrow{\text{H}^+} \text{ROSi(CH}_3)_3 + (\text{CH}_3)_2\text{CO} \qquad (3)$$

SCHEME I



Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 237 spectrometer, nmr spectra on a Varian T60, and mass spectra on a Hitachi RMS-4 spectrometer. Melting points are uncorrected. Glpc analyses were carried out using a 12 ft × 0.125 in., 10% Carbowax on Chromosorb W HMDS treated column. All reactions were carried out under an atmosphere of dry nitrogen. Tetrahydrofuran, ether, and benzene were distilled from benzophenone ketyl, acetonitrile from P_2O_5. Ethylene glycol (Eastman), 1,3-propanediol (Shell), 1,4-butanediol (Aldrich), and 2-mercaptoethanol (Union Carbide) were used without further purification. Trimethylchlorosilane, generously supplied by Union Carbide, was distilled prior to use. *cis*-1,2-Cyclohexanediol was prepared according to Fieser and Fieser.[8] The trans 1,2-diols of cyclopentane, mp 45–47° (lit.[9] mp 50°), cyclohexane, mp 101–103° (lit.[10] mp 104°), and cycloheptane, mp 56–58° (lit.[11] mp 57–58°), were prepared *via* the hydroboration–oxidation of the trimethylsilyl enol ethers of cyclopentanone, cyclohexanone, and cycloheptanone, respectively.[12] The 4-*tert*-butyl-*trans*-1,*cis*-2-cyclohexanediol (III), mp 101–104° (lit.[6] mp 104–104.5°), and 4-*tert*-butyl-*cis*-1,*trans*-2-cyclohexanediol (IV, mp 139–141° (lit.[6] mp 142–142.5°), were prepared analogously and separated by careful crystallization from ether–pentane.

Preparation of Cyclic Ketals of Cyclohexanone. A General Procedure.—Into a 25-ml flask was placed 20 mmol of II, 20 mmol of diol (or mercaptoethanol), and about 10–15 ml of solvent. To this was added 2 drops of concentrated HCl (or about 20 μl of trimethylchlorosilane). After the exothermic reaction subsided the reaction mixture was stirred for an additional 10–30 min (longer times for the longer chain length of the diol), dried, filtered, and distilled under reduced pressure.

Preparation of *trans*-1,2-Cyclohexanediol Acetonide.—Into a 25-ml flask was placed 1.16 g (10 mmol) of *trans*-1,2-cyclohexanediol, 4 ml of CCl_4, and 12 mmol of TMSP. Two drops of concentrated HCl were added. An exothermic reaction occurred immediately. The reaction mixture was stirred for 10 min, dried, filtered, and distilled through a short-path distillation apparatus to yield 1.25 g (80%) of the acetonide (*ca.* 96% pure by glpc, bp 92–96° (22 mm). A sample purified by preparative glpc gave $n^{20}\text{D}$ 1.4450; nmr (CCl_4, TMS) 1.30 (s), 1.67 (m), and 3.14 ppm (m); ir (neat) 2950 (s), 1360 (s, doublet), 1210 (s), 1110 (s), 1055 (s), and 835 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel intensity) 155 (4), 141 (100), 99 (67), 81 (95), 59 (88), 43 (95), and 41 (77).

Hydrolysis of *trans*-1,2-Cyclohexanediol Acetonide.—About 10 drops of the acetonide was placed in a vial with 2 ml of ether and 1 ml of 10% HCl. The two-phase system was shaken for 5 min, and the ether layer was removed dried, and evaporated. The resulting solid was sublimed to give a solid, mp 99–101°, whose infrared and nmr spectra were identical with those of an authentic sample of *trans*-1,2-cyclohexanediol.

Preparation of 4-*tert*-Butyl-*trans*-1,*cis*-2-cyclohexanediol Acetonide.—A 15-ml flask was charged with 0.43 g (2.5 mmol) of the diol III, 2 ml of CCl_4, and 2.8 mmol of TMSP. One drop of concentrated HCl was added. After 10 min the reaction mixture was dried, filtered, and concentrated to give 0.48 g of residue. Glpc analysis of this residue showed the acetonide to be present in about 85% yield. The acetonide was purified by preparative glpc to afford a sample with $n^{20}\text{D}$ 1.4554; nmr (CCl_4, TMS) 0.90 (s), 1.30 (s), 2.00 (m), 3.18 (m), and 3.51 ppm (m); ir (neat) 2950 (s), 1265 (s, doublet), 1230 (s), 1080 (s), and 830 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel intensity) 197 (60), 137 (83), 81 (57), 59 (91), 55 (40), 43 (100), and 41 (42).

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Registry No.—I, 1833-53-0; II, 6651-36-1.

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(7) Unpublished work with Antonio Hernandez. It was felt that this reaction involved attack of the alcohol at silicon, but this is now being investigated in view of the present findings.

(8) L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Wiley-Interscience, New York, N. Y., 1961, p 191.

(9) L. N. Owen and P. N. Smith, *J. Chem. Soc.*, 4026 (1952).

(10) "Dictionary of Organic Compounds," Vol. II, Eyre and Spottiswoode, London, 1965, p 783.

(11) A. C. Cope, J. C. Heeren, and V. Seeman, *J. Org. Chem.*, **28**, 516 (1963).

(12) J. Klein, R. Levene, and E. Dunkelblum, *Tetrahedron Lett.*, 2845 (1972); G. Larson and D. Hernandez, unpublished work.