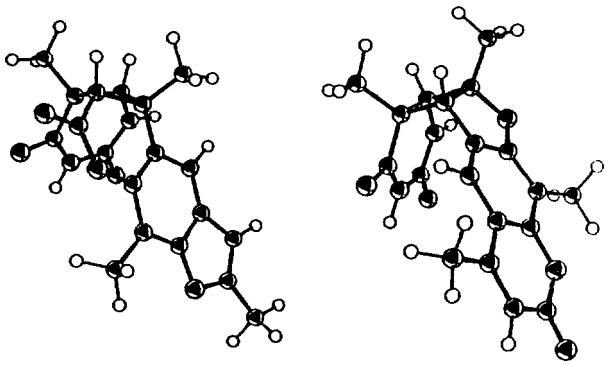

(a) TMP(3,4)< >Thy, cis-syn (b) TMP(4',5')< >Thy, cis-anti

Figure 8. Stereo ORTEP drawing of molecular conformation of photocyclo adducts of TMP< >Thymine.

field than their energies.

In Table 4 compare eight photocycloadducts, *cis-syn* conformation for 4,5',8-TMP's pyrone ring and *cis-anti* conformation for 4,5',8-TMP's furan ring with thymine are most profitable to formation, stereo ORTEP drawing for thes two conformers are given in Figure 6. The *cis* conformation found for the model adduct is that which might be expected from the position of intercalation of 4,5',8-TMP with thymine which is often assumed.[4]

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Transformation of Bicyclic Ketal Compound to 1,2-Cyclopentanediol *via* 1,5-Diketone

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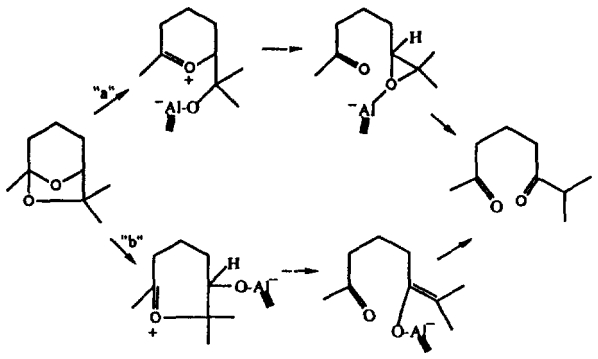
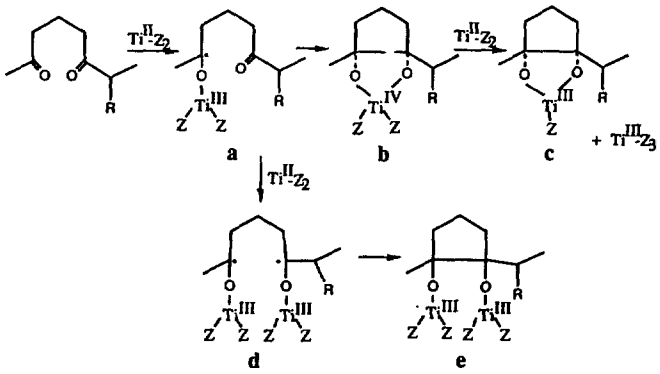
New method for preparing cyclopentanediol from bicyclic ketal is described. Bicyclic ketal is cleaved to give 1,5-diketone, which is then reductively coupled intramolecularly to yield 1,2-cyclopentanediol. A solution of bicyclic ketal (**1a**) in methylene chloride was treated with aluminum chloride(2 eq.)-sodium iodide(1.5 eq.) at ambient temperature for 3 h to give the 1,5-diketone (**2a**) in 71% yield after basic work-up followed by short path column chromatography. A solution of the 1,5-diketone (**2a**) in THF was reacted with titanium tetrachloride(6 eq.)-Mg(Hg)(0.3 eq.) at 0℃ for 4 h to give the 1,2-cyclopentanediol (**3a**) in 75% yield after basic work-up followed by short path column chromatography.

Introduction

There has been an increased interest in methods for forming cyclopentane ring systems, reflecting the increasing number of natural products known to incorporate such ring systems as a major structural entity.[1]



Scheme 1



Scheme 2

In our continuous program of bicyclic ketal chemistry,[2] we developed a new fragmentation reaction to 1,5-diketone which is a useful intermediate for natural product synthesis.[3] We used this 1,5-diketone to the cyclopentanediol synthesis by using low valent titanium as a reductive coupling reagent developed by McMurry *et al.*[4] We report herein the utility of bicyclic ketal which is easily prepared from methyl vinyl ketone[5] transforming to the other important structures.

Results and Discussion

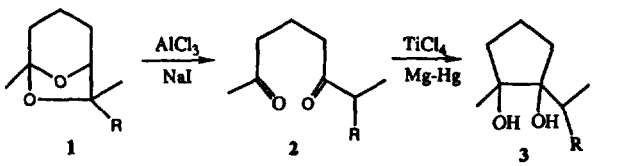
Synthesis of 1,5-diketone. 6,8-Dioxabicyclo[3.2.1]octane skeletal system has a very unique and interesting feature. The fragmentation of this bicyclic ketal could derive a variety of structures. Although Lewis acid induced rearrangements of bicyclic ketals are an attractive method for the synthesis of natural products,[6] they have been little investigated. In our studies of rearrangement reaction of bicyclic ketal systems,[7] we have found a new synthetic route from bicyclic ketals to 1,5-diketone derivatives.[3]

A solution of 5,7,7-trimethyl-6,8-dioxabicyclo[3.2.1]octane (**1a**)[2a] in methylene chloride was treated with aluminum chloride(2 eq.)-sodium iodide(1.5 eq.) at ambient temperature for 3 h to give the 1,5-diketone (**2a**) in 71% yield after basic work-up followed by short path column chromatography. There are two possible mechanisms to explain this transformation reaction; (1) C(5)-O(6) bond cleavage followed by a 1,2-hydride shift via an epoxide intermediate (Path "a" in Scheme 1), (2) C(5)-O(8) bond cleavage followed by a deprotonation (Path "b" in Scheme 1). All of our previous experience[7,8] had been specifically directed towards the O(6)-C(5) bond cleavage as a way to prepare pyran rings from the bicyclic ketals. The specificity of this cleavage can be seen in the reductive cleavage of **1a** with acetyl iodide,[7] and with Et_3SiH-$TiCl_4$ or DIBAH.[8] It also has been established that O-6 is the preferred site of lanthanide interaction during lanthanide-induced shift studies.[9]

Synthesis of 1,2-cyclopentanediol. Reductive coupling reactions of dicarbonyl compounds have been intensively investigated within past 20 years.[4] Intramolecular coupling reaction of 1,5-diketone by using low valent Ti should give cyclopentane derivatives. We used $TiCl_4$/Zn,[10] $TiCl_3$/LAH,[4a] $TiCl_3$/Zn-Cu,[11] $TiCl_3$/K,[12] $TiCl_3$/Li,[13] and $TiCl_4$/Mg(Hg)[4b] in known reducing systems for the coupling reaction, and found that the 1,2-cyclopentanediol (**3**) was obtained in good yield by using $TiCl_4$/Mg(Hg). Although the reductive coupling of carbonyl compounds to form pinacols can be carried out by using a variety of reduction conditions,[4b] two procedures are most often used: the classical [Al-Hg] method[14] and the more recent [Mg-Hg]/$TiCl_4$ method.[4b] The latter has been suggested as the method of choice for routine coupling reaction because of the ease of reaction and the relatively good yields. Both Corey[4b] and McMurry[13] have agreed that a reduced state of titanium is intimately involved in the coupling reaction. It has been reported that Ti(II) complexes of known structure are capable of effecting the reductive coupling of carbonyl compounds.[4a,b] The plausible mechanism for intramolecular coupling reaction could be explained as reported by Corey[4b] (Scheme 2). Reduction of the carbonyl group by the Ti(II) reagent gives a Ti(III)-radical intermediate (**a**). The Ti(III)-radical with internal carbonyl participates in a cycloaddition process to form a cyclic Ti(IV) derivative (**b**) which is reduced to Ti(III) species (**c**) and should favors cis-1,2-diol. Whereas a pinacol bis-Ti(III) complex (**e**) in altanative pathway could produce either *cis* or *trans* diols. Even though Corey's[4b] report that *cis* diols were formed exclusively in the case of intramolecular processes forming four- to six membered carbocyclic systems, we have obtained *cis-trans* mixture in our systems except **3a** which shows single isomer.

A solution of the 1,5-diketone (**2a**) in THF was reacted with titanium tetrachloride(6 eq.)-Mg(Hg)(0.3 eq.) at 0℃ for 4 h to give the 1,2-cyclopentanediol (**3a**) in 75% yield after

Table 1. Transformation of Bicyclic Ketal to 1,2-Cyclopentanediol(**3**) *via* 1,5-Diketone(**2**)



Entry(R)	% yield of **2**	% yield of **3**
a(Me)	71	75
b(Et)	75	72
c(Pr)	91	70
d(i-Pr)	86	82
e(n-Bu)	70	75
f(t-Bu)	70	70
g(Ph)	43	72

basic work-up followed by short path column chromatography. The table shows the generality of this method in terms of substitution pattern.

Experimental

NMR spectra were recorded on a Varian EM-360L or Varian Jemini-200 by using TMS as an internal standard. IR spectra were taken on a Shimadzu IR-435 spectrometer. GLC analysis were performed using a Shimadzu GC-7A gas chromatography equipped with 7′×1/8″, 10% SE-30 column. Reported melting points were uncorrected.

General procedure for 1,5-diketone (2a-2g). To a dried NaI(1.5 eq.) was slowly added a solution of bicyclic ketal(1 eq.) in CH_2Cl_2(5 m*l*) followed by $AlCl_3$(2 eq.) at 0℃ and stirred for 3 h at room temperature. After addition of aqueous 10% NaOH solution at 0℃, the reaction mixture was extracted with ether and dried with $MgSO_4$. Evaporation of the solvent gave an oily residue, which was chromatographed on silica gel with ether/hexane=2/8 as an eluent to give corresponding 1,5-diketone.

7-Methyl-2,6-octanedione (2a). yield: 71%; IR (neat): 2964, 1709 (br, C=O), 1467, 1379 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.58 (1H, m, CH), 2.49 (2H, t, *J*=7.0 Hz, $COCH_2$), 2.46 (2H, t, *J*=7.0 Hz, $COCH_2$), 2.13 (3H, s, COMe), 1.83 (2H, p, *J*=7.0 Hz, CH_2), 1.09 (6H, d, *J*=7.2 Hz, 2×Me); ^{13}C-NMR ($CDCl_3$): δ 214.2(s), 208.4(s), 42.6(t), 40.8(d), 39.0(t), 29.8(q), 18.2 (q, 2×Me), 17.8(t).

7-Methyl-2,6-nonanedione (2b). yield: 75%; IR (neat): 2960, 1707, 1458, 1431 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.70-2.40 (5H, m), 2.13 (3H, s), 1.83 (2H, m), 1.60-1.45 (2H, m), 1.12 (3H, d), 1.10(3H, t).

7-Methyl-2,6-decanedione (2c). yield: 91%; IR (neat): 2954, 1707, 1454, 1424 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.48 (1H, m), 2.46-2.41 (4H, m), 2.12 (3H, s), 1.81 (2H, p, *J*=7.0 Hz), 1.4-1.2 (4H, m), 1.03 (3H, d, *J*=7.0 Hz), 0.88 (3H, t, *J*=7.0 Hz); ^{13}C-NMR ($CDCl_3$): δ 214.3(s), 208.5(s), 46.1(d), 42.6(t), 39.7(t), 35.1(t), 29.8(q), 20.5(t), 17.6(t), 16.3(q), 14.1(q).

7,8-Dimethyl-2,6-nonanedione (2d). yield: 85%; IR (neat): 2958, 1709, 1459, 1369 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.58-2.39 (5H, m), 2.13 (3H, s), 1.90-1.39 (3H, m), 0.90 (3H, s), 0.80 (3H, d).

7-Methyl-2,6-undecanedione (2e). yield: 70%; IR (neat): 2953, 1709, 1458, 1408 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.70-2.30 (5H, m), 2.13 (3H, s), 1.90-1.70 (3H, m), 1.50-0.90 (9H, m), 1.20 (3H, d).

7,8,8-Trimethyl-2,6-nonanedione (2f). yield: 70%; IR (neat): 2945, 1710, 1458, 1364 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.60-2.30 (5H, m), 2.13 (3H, s), 1.80-1.20 (5H, m), 1.00 (9H, s).

7-Phenyl-2,6-octanedione (2g). yield: 43%; IR (neat): 2928, 1710, 1598, 1492 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 7.10 (5H, s), 3.80 (1H, q), 2.60-2.20 (4H, m), 2.10 (3H, s), 2.00-1.80 (2H, m), 1.50 (3H, d).

General procedure for 1,2-cyclopentanediol (3a-3g). To a dried Mg(12 eq.) was added a solution of $HgCl_2$(0.3 eq.) in THF (10 m*l*) and stirred for 1 h at room temperature. After removal of THF by syringe, the reagents were washed with portions of THF (3×5 m*l*) and cooled down to −10℃ in THF (10 m*l*). To the resulting amalgam, $TiCl_4$(6 eq.) and 1,5-diketone(1 eq.) were added sequentially and the temperature was raised to 0℃ and stirred for 4 h. The reaction mixture was quenched with saturated K_2CO_3 solution (5 m*l*) at the same temperature and stirred for 0.5 h. Filtration, evaporation, and column chromatography (ether/hexane=15/85) gave the product.

1-Isopropyl-2-methyl-1,2-cyclopentanediol (3a). yield: 75%; mp. 42-43℃; IR (KBr): 3414, 2950, 1460, 1374 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.15 (1H, br s), 2.07 (1H, br s), 2.03 (1H, m), 1.90-1.40 (6H, m), 1.25 (3H, s), 0.98 (3H, d, *J*=7 Hz), 0.94 (3H, d, *J*=7 Hz); ^{13}C-NMR ($CDCl_3$): δ 83.2, 82.3, 40.9, 36.5, 33.1, 24.1, 18.9, 18.0, 17.1.

1-sec-Butyl-2-methyl-1,2-cyclopentanediol (3b). yield: 72%; IR (neat): 3420, 2926, 1465, 1370 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.23 (2H, br s), 2.01 (1H, m), 1.90-1.35 (8H, m), 1.24 (3H, s), 0.98-0.85 (6H, m).

1-Methyl-2-(1-methylbutyl)-1,2-cyclopentanediol (3c). yield: 70%; IR (neat): 3414, 2970, 1462, 1375 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.28 (2H, br s), 2.00 (1H, m), 1.90-1.30 (10H, m), 1.23 (3H, s), 0.98-0.84 (6H, m).

1-(1,2-Dimethylpropyl)-2-methyl-1,2-cyclopentanediol (3d). yield: 82%; IR (neat): 3440, 2970, 1460, 1370 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.40 (2H, br s), 2.00-1.40 (8H, m), 1.23 (3H, s), 0.91 (3H, d, *J*=7 Hz), 0.89 (6H, d, *J*=7 Hz).

1-Methyl-2-(1-methylpentyl)-1,2-cyclopentanediol (3e). yield: 75%; IR (neat): 3441, 2974, 1465, 1370 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.22 (2H, br s), 2.00 (1H, m), 1.90-1.25 (12H, m), 1.23 (3H, s), 0.98-0.85 (6H, m).

1-Methyl-2-(1,2,2-trimethylpropyl)-1,2-cyclopentanediol (3f). yield: 70%; IR (neat): 3430, 2945, 1455, 1370 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 2.23 (2H, br s), 2.01 (1H, m), 1.90-1.30 (6H, m), 1.24-0.91 (15H, m).

1-Methyl-2-(1-methylphenyl)-1,2-dicyclopentanediol (3g). yield: 72%; mp. 52-54℃; IR (KBr): 3441, 2974, 1465, 1370 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.30 (5H, m), 2.85 (1H, m), 2.10 (2H, br s), 1.80-1.30 (6H, m), 1.38 (3H, s), 1.30 (3H, d, *J*=7 Hz).

Acknowledgement. This work was supported by the Research Center for New Bio-Materials in Agriculture sponsored by the Korea Science and Engineering Foundation.

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14. A rapid survey of organic chemistry teaching manuals shows this to be the method of choice for carrying out the experiment at the undergraduate level.

Inclusion Complex of Permethylated-β-Cyclodextrin with Benzaldehyde

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A stable solid new inclusion complex with benzaldehyde and permethyl-β-cyclodextrin was obtained by recrystallization method. The structure of the benzaldehyde-permethyl-β-cyclodextrin inclusion complex in the solid and solution state have been studied by UV, IR, ^{1}H-NMR, ^{13}C-NMR and FAB-mass spectroscopy.

Introduction

In the past decade, cyclodextrins (CDX) have received considerable attention in biological and pharmaceutical research[1-3]. Because of their unique physical and chemical properties, these compounds serve as complexing agents for drugs in controlled drug delivery formulation and as enzyme models, etc. Microencapsulation of drugs can lead to desirable modification of the physical and chemical properties and improvements in stability of air- or light- sensitive substances, water solubility, suppression of unpleasant taste or odor and *in vivo* bioavailability. Cyclodextrins therefore have been extensively applied to improve the physicochemical properties of various drugs[4,5].

Cyclodextrins are cyclic oligosaccharides composed of at least six α-1,4 linked α-D-glucosyl residues, which have the shape of a hollow, truncated cone with primary and secondary hydroxyl groups crowning the narrower and the wider ends, respectively. In the solid state and in solution state, they can form inclusion complexes with a variety of guest molecules. Methylated cyclodextrins can form inclusion complexs with several guest molecules, some of which are more stable than the corresponding unmodified cyclodextrin complexes.

The pharmaceutical use of benzaldehyde was first attempted in the use of fig fruit (Ficus carica L.) as a traditional carcinostatic drug. Kochi *et al.*[6] have been interested in the clinical use of fig and they had observed suppression of Ehrlich carcinoma in mice by its extracts. The active component in the fig was benzaldehyde as revealed by GC-MS, UV and IR methods. To determine the carcinostatic activity of the purified authentic benzaldehyde, 100 mg/kg dose was injected daily intraperitoneally to seven BDF mice which had been implanted with adenocarcinoma 755 (AC755) subcutaneously 24 hours prior to administration with the benzaldehyde. A 40% inhibition of the tumor cell growth compared to the untreated mice was reported.

However, benzaldehyde (BAL) is an oily liquid and has some unfavorable properties, such as instability in air and light, low water solubility, and unpleasant odor. The pharmaceutical use of benzaldehyde is therefore limited. Thus, some modification is required in order to use benzaldehyde as an orally acceptable drug. Upon complexation with cyclodextrins, benzaldehyde become powdered and can be conveniently manufactured as tablets[7].

Benzaldehyde was first used in inclusion complexation with α, β, and γ-cyclodextrin by Takeuchi *et al.*[7]. The X-ray crystal structure of the α-cyclodextrin-benzaldehyde (1 : 1) complex hexahydrate was determined[8]. The crystal structure of the hexakis (2,3,6-tri-o-methyl) α-cyclodextrin-benzaldehyde (1 : 1) complex was also investigated by X-ray method[9]. Studies of the benzaldehyde inclusion complexes with α-, β-, and permethylated-α-cyclodextrin by solid state ^{13}C-NMR spectroscopy provide further solid state information. The molecular dynamics and mobility of benzaldehyde inclusion complexes with cyclodextrins was studied by observing chemical shift changes and line-widths in solid state ^{13}C-NMR spectra of these complexes. These spectral studies were also applied to propose the benzaldehyde and cyclodextrins com-

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