overnight. A small amount of H_2O was added to the residue and the solution, after filtration with an aid of filter cell, was treated with Amberlite CG-4B (acetate cycle, approximately 20 g). The resin was removed by filtration and the filtrate was lyophilized to give pale yellow powder; 0.91 g. From 10 g of the resin, totally 2.02 g of the crude peptide was obtained. Based on the weight of the initial resin started, yield of this cleavage step was 50%.

Partial Purification of the Product by Sephadex G-10——The product (200 mg) was dissolved in 3% acetic acid (5 ml) and the solution was applied to a column of Sephadex G-10 (3×31 cm), which was developed with 3% acetic acid. Individual fractions, 5 ml each, were collected and absorbancy at 280 mμ was determined in each fraction. The contents of the main peak (tube 20 to 29) were collected and the solvent was removed by lyophilization; yield 87 mg. *Rf* of the main spot, around 0.38 (*n*-BuOH–pyridine–AcOH–H_2O, 4:1:1:2), positive to ninhydrin, Pauly, Sakaguchi, methionine and Ehrlich tests.

Amino Acid Analysis of Acid Hydrolysates——During this operation, acid hydrolysis of peptide resin was performed at three points, heptapeptide stage (I), decapeptide stage (II) and pentadeca stage (III). Amino acid ratios in the acid hydrolysates of the eicosapeptide-resin (IV), the liberated peptide (V) and the partially purified peptide (VI) by Sephadex G-10 were listed in Table I. The recovery of alanine, which occured once near the C-terminus portion, was taken as a standard.

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Preparation of 6,10-Dimethylspiro[4,5]dec-6-en-2-one. Experiments directed towards the Synthesis of Spirovetivane Sesquiterpenes

Akira Ogiso, Masaaki Kurabayashi, Hitoshi Nagahori and Hiroshi Mishima

Central Research Laboratories, Sankyo Co., Ltd.[1]

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Since Ar_1-participation of a neighboring phenoxide group[2] is a suitable reaction for the synthesis of spirodienones, some applications for the construction of natural products have been reported.[3] We wish to report the preparation of 6,10-dimethylspiro[4,5]dec-6-en-2-one (**12**), a key intermediate for the synthesis of certain spirosesquiterpenoids[4] *e.g.* hinesol,[5] β-vetivone,[6] by using an Ar_1-5 participation reaction.

Reformatsky reaction of the benzyl ether (**1**) of 4-hydroxy-2,6-dimethylbenzaldehyde[7] underwent to form a *cis–trans* mixture of the corresponding ethyl cinnamate (**2**) in good yield, although attempts of aldol condensation reaction were unsuccessful. The ethyl cin-

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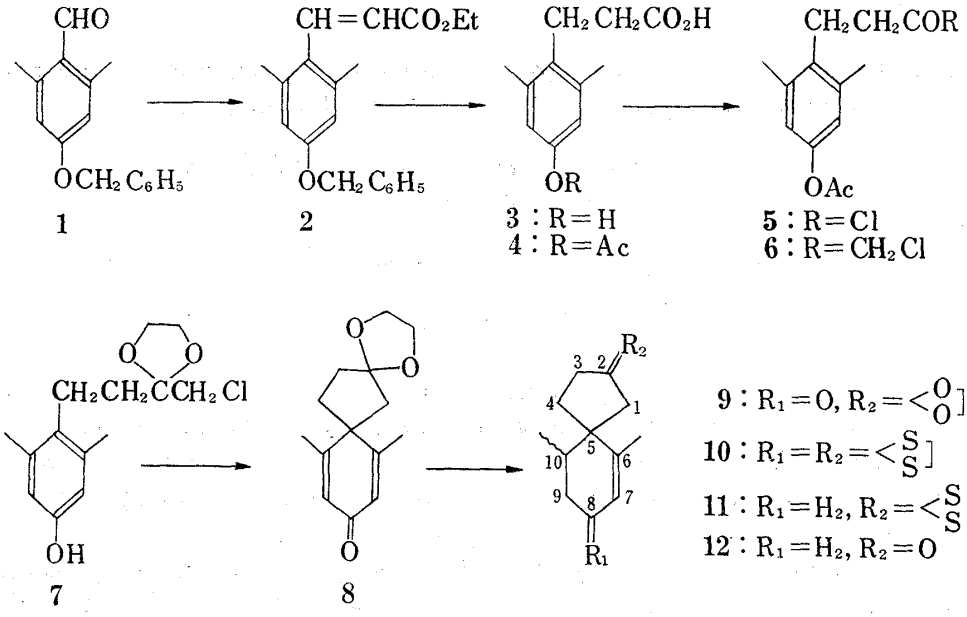
namate (**2**) was converted into the hydroxyphenylpropionic acid (**3**) by saponification followed by hydrogenation. The acetylation product (**4**) of **3** was treated with oxalyl chloride to give the corresponding acid chloride (**5**). Addition of an ether solution of **5** to ethereal diazomethane followed by treatment with hydrogen chloride yielded the chloromethylketone (**6**). Heating **6** in ethylene glycol and ethyl orthoformate in the presence of *p*-toluenesulfonic acid resulted in ketalization and removal of the acetyl group to furnish the ketal chloride (**7**). Cyclization of **7** was effected successfully by pyrolysis of its sodium salt[8] to give the spirodienone (**8**) in 80% yield. Evidence for the formation of the spirodienone (**8**) was provided by the spectral data, showing the maximum at 244 mμ (20000) in the ultraviolet and the absorption bands at 1665, 1620 cm^{-1} in the infrared (IR) spectrum due to the α,β-unsaturated ketone.[9] The high yield from this Ar_1-5 participation reaction may be attributed to the steric effect of the dimethyl group. Partial hydrogenation of **8** afforded an epimeric mixture of the enone (**9**) which yielded the bisethylenethioketal (**10**) upon thioketalization. Treatment of **10** with Raney nickel in dioxane–ethanol gave the monoethylenethioketal (**11**) showing the molecular peak at 254 in the mass spectrum. Hydrolysis of the thioketal function afforded the corresponding carbonyl compound and was achieved under mild conditions using mercuric chloride in aqueous acetonitrile in the presence of cadmium carbonate.[10] Gas chromatography of the resulting ketone (**12**) having the IR absorption band at 1745 cm^{-1} provided the fact that it was 1:1 epimeric mixture wherein one of the isomers showed the identical IR spectrum with that of an authentic sample.[6]



Experimental[11]

4-Benzyloxy-2,6-dimethylbenzaldehyde (1)——A mixture of 71 g of 4-hydroxy-2,6-dimethylbenzaldehyde, 78 g of benzyl chloride and 75 g of potassium carbonate in 420 ml of dimethylformamide was heated

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11) The melting points were determined in capillary tubes and uncorrected. The ultraviolet absorption spectra were measured in 95% ethanol using a Beckman DK-2A spectrometer. The infrared spectra were determined on an Infracord and the mass spectra on a JMS-OISG spectrometer. The nuclear magnetic resonance (NMR) spectra were determined with a Varian A-60 spectrometer using tetramethylsilane as an internal reference in deuterochloroform.

at 140° for 3 hr. The reaction mixture was poured into ice–water and the resulting crystalline mass was collected by filtration. The benzene solution of the crystals was washed with 5% sodium hydroxide and evaporated. Distillation of the residue gave 107 g of the benzyl ether (**1**), bp 175° (1 mmHg), mp 59°. *Anal.* Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.00; H, 6.78.

4-Benzyloxy-2,6-dimethylcinnamic Acid——To a mixture of 80 g of 4-benzyloxy-2,6-dimethylbenzaldehyde (**1**), 65 g of granular zinc and 3 g of mercuric chloride in 400 ml of benzene was added 112 g of ethyl bromoacetate at room temperature. After refluxing for 1 hr, 16 g of granular zinc were added and the mixture was refluxed further for 2.5 hr. The reaction mixture was poured into ice-cooled 10% sulfuric acid and extracted with benzene. Evaporation of the solvent gave a brown oil which was treated with 20 g of phosphorous pentoxide in 400 ml of benzene under reflux. The crude ethyl cinnamate (**2**) was dissolved in 300 ml of methanol containing 20 g of sodium hydroxide and 100 ml of water. After refluxing for 1 hr, the solution was concentrated and extracted with ether. The aqueous layer was acidified with hydrochloric acid to give 80 g of a *cis–trans* mixture of the cinnamic acid. IR ν_{max}^{Nujol} cm^{-1}: 2700, 1675, 1615, 1585.

Hydrogenation of the Cinnamic Acid——A solution of 3.6 g of the cinnamic acid in 30 ml of ethyl acetate containing 1.0 g of 10% palladiumcharcoal was shaken under hydrogen atmosphere. The resulting hydrogenated product was recrystallized from benzene to give 2.3 g of prisms, mp 126—127°. *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.34; H, 7.30. IR ν_{max}^{Nujol} cm^{-1}: 3470, 2700, 1690, 1610, 1600.

Acetylation of the Hydroxyphenylpropionic Acid (**3**)——To a solution of 19.4 g of the phenol (**2**) in 10% sodium hydroxide solution was added 15 g of acetic anhydride at −5° and the mixture was shaken vigorously for few minutes. The reaction mixture was made acidic by addition of dilute sulfuric acid and extracted with ether. The ether layer was extracted with aqueous sodium bicarbonate. Acidification of the aqueous fraction gave the acetate (**4**) which was recrystallized from methanol yielding 15.5 g of prisms, mp 95—96°. *Anal.* Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 65.90; H, 7.07. IR ν_{max}^{Nujol} cm^{-1}: 2700, 1750, 1700, 1200.

Formation of the Chloromethylketone (**6**)——The acid (**4**) (10 g) was dissolved in 11 g of oxalyl chloride at room temperature. After the gas evolution was ceased, the solution was heated under gentle reflux for 3 hr. Excess reagent was evaporated under reduced pressure to give 11 g of the crystalline acid chloride (**5**). A solution of the chloride in 30 ml of absolute ether was added at 5—10° to a solution of diazomethane prepared from 22 g of *p*-tolylsulfonylmethylnitrosamide in 150 ml of ether. After several hours, dry hydrogen chloride was passed onto the resulting solution of the diazoketone under ice-cooling until the evolution of nitrogen ceased. The precipitated product was recrystallized from methanol affording 8.5 g of the chloromethylketone (**6**), mp 113—114°. *Anal.* Calcd. for $C_{14}H_{17}O_3Cl$: C, 62.51; H, 6.37; Cl, 13.18. Found: C, 62.51; H, 6.35; Cl, 13.13. IR ν_{max}^{Nujol} cm^{-1}: 1760, 1740, 1200, 770.

Ketalization of the Chloromethylketone (**6**)——A solution of 2.5 g of the chloromethylketone (**6**), 1.5 g of ethyl orthoformate and a catalytic amount of *p*-toluenesulfonic acid in 50 ml of ethylene glycol was heated at 120° for 1 hr. The reaction mixture was poured into aqueous sodium bicarbonate solution and extracted with ether. Evaporation of the solvent and recrystallization from *n*-hexane–ether gave 2.9 g of the ketal (**7**), mp 96—97°. *Anal.* Calcd. for $C_{14}H_{19}O_3Cl$: C, 62.04; H, 7.07; Cl, 13.08. Found: C, 62.25; H, 7.30; Cl, 13.00. IR ν_{max}^{Nujol} cm^{-1}: 3450, 1590.

Cyclization of the Ketal Chloride (**7**)——The sodium salt, prepared from 3.0 g of the ketal chloride (**7**) and an equimolecular amount of sodium hydroxide, was heated at 220° at 0.01 mmHg. Pyrolysis took place with distillation of the crystalline dienone (**8**), which was recrystallized from *n*-hexane–acetone yielding 1.7 g of prisms, mp 99—100°. *Anal.* Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.50; H, 7.73. IR ν_{max}^{Nujol} cm^{-1}: 1665, 1620. UV λ_{max} mμ (ε): 244 (20000). NMR ppm: 2.12 (3H, s), 2.14 (3H, s), 3.96 (4H, s), 6.05 (2H, s).

Hydrogenation of the Spirodienone (**8**)——A solution of 3.5 g of the spirodienone (**8**) in 30 ml of ethyl acetate containing 300 mg of 5% palladiumcalcium carbonate was hydrogenated. The hydrogenation was stopped when one mole equivalent of hydrogen was absorbed. The product was chromatographed on silica gel (100 g), elution with benzene–ethyl acetate (5%) gave 700 mg of the saturated ketone, IR ν_{max}^{Neat} cm^{-1}: 1720. Further elution with the same solvent gave 2.0 g of the enone (**9**), IR ν_{max}^{Neat} cm^{-1}: 1670, 1615. Benzene–ethyl acetate (20%) eluted 500 mg of the recovered starting materials.

Thioketalization of the Enone (**9**)——To a solution of 1.8 g of the enone (**9**) in 3 ml of ethanedithiol was added 0.1 ml of boron trifluoride etherate. After standing overnight at room temperature, the reaction mixture was dissolved in ether and washed with 5% sodium hydroxide. Column chromatography using alumina was eluted with benzene gave 1.6 g of the bisethylenethioketal (**10**). Mass Spectrum (M^+): 344.

Dethioketalization of the Bisethylenethioketal (**10**)——A mixture of 1.6 g of the crude bisethylenethioketal (**10**) and 15 g of Raney nickel (W-2) in 5 ml of dioxane and 20 ml of ethanol was refluxed for 4 hr. The reaction mixture was filtered and evaporated to dryness. The residual oil was dissolved in 5 ml of dioxane and 20 ml of ethanol and 10 g of Raney nickel was added again. After refluxing for 30 min, the resulting product was chromatographed on alumina. Elution with *n*-hexane gave 520 mg of the monoethylenethioketal (**11**). Mass Spectrum (M^+): 254.

6,10-Dimethylspiro[4,5]dec-6-en-2-one (12)——A mixture of 480 mg of the monoethylenethioketal (**11**), 1.2 g of mercuric chloride and 650 mg of cadmium carbonate in 25 ml of acetonitrile and 1.0 ml of water was stirred at 50° for 2 hr under nitrogen. The reaction mixture was evaporated and extracted with *n*-hexane. Evaporation of the solvent and purification using preparative thin-layer chromatography gave 240 mg of epimeric mixture of the ketone (**12**). IR ν_{max}^{Neat} cm^{-1}: 1745, 1410, 1160, 845, 805.