Tetrahedron Vol. 41, No. 12, pp. 2361 to 2368, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00

A SYNTHETIC APPROACH TO (+)-ALDOSTERONE AND ITS RELATIVES (2)- A STEREOSELECTIVE SYNTHESIS OF (+)-TRANS-4,5-(4-METHOXYBENZO)-1β,7aβ-(2α-METHOXYMETHYL-5-OXOFURO)HYDRINDANE

HIDEO NEMOTO, MITSUO NAGAI, and KEIICHIRO FUKUMOTO*

Pharmaceutical Institute, Tohoku University,
Aobayama, Sendai 980, Japan

and

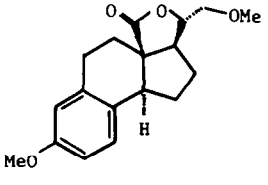
TETSUJI KAMETANI

Institute of Medicinal Chemistry, Hoshi University,
Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

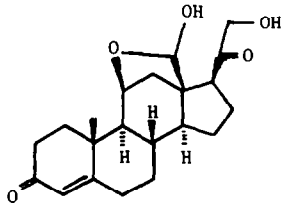
(*Received in Japan* 6 *February* 1985)

Abstract - A stereoselectivity in an intramolecular cycloaddition of the olefinic o-quinodimethanes **13** and **23** generated in situ from the thermolysis of optically active 4β-[2-(4-methoxybenzocyclobutenyl)ethyl]-5α-methoxymethyl-3-phenylthio-methylenefuran-2-ones **12** and **22**, respectively, is studied and a stereoselective synthesis of (+)-trans-4,5-(4-methoxybenzo)-1β,7aβ-(2α-methoxymethyl-5-oxofuro)hydrindane **1** is also described.

In a previous paper,[1] we have disclosed a new route for the construction of des-A B-aromatic steroid **1** as an optically pure form which could be a potential intermediate for the synthesis of aldosterone **2** and its relatives.



(**1**)

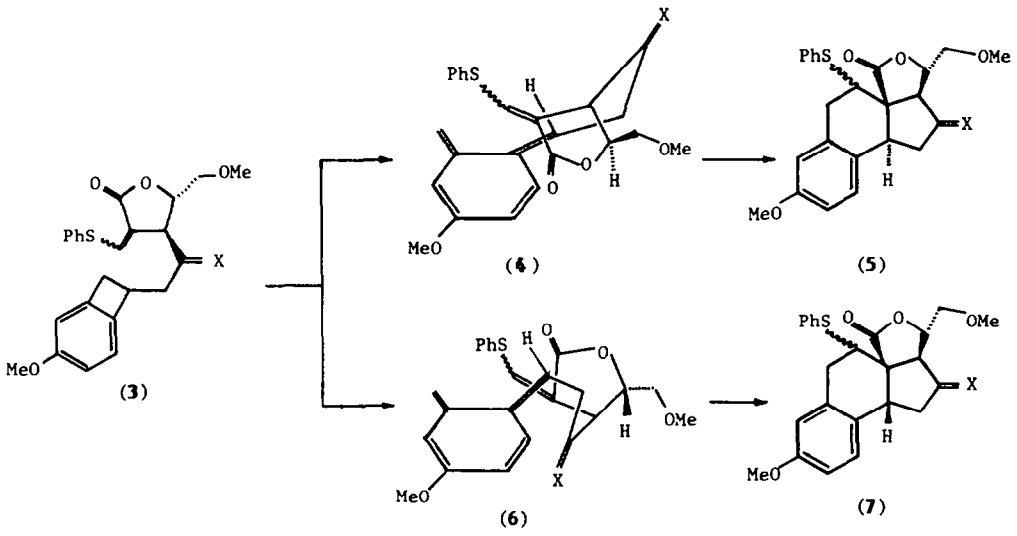


(**2**)

Scheme 1

Although an intramolecular cycloaddition[2] of an olefinic o-quinodimethane generated in situ from the thermolysis of an olefinic benzocyclobutene, which is a key step in this approach, has proceeded in a fairly good yield, the lack of stereoselectivity has made this approach unsatisfactory. The observed stereochemical course of this cycloaddition giving mainly the C D-cis fused compound **7** ($X = H_2$) could be reasonably explained by an intervention of the sterically favored transition state **6** ($X = H_2$) rather than **4** ($X = H_2$), which has a steric repulsion between the o-quinodimethane moiety and the lactone rings leading to the

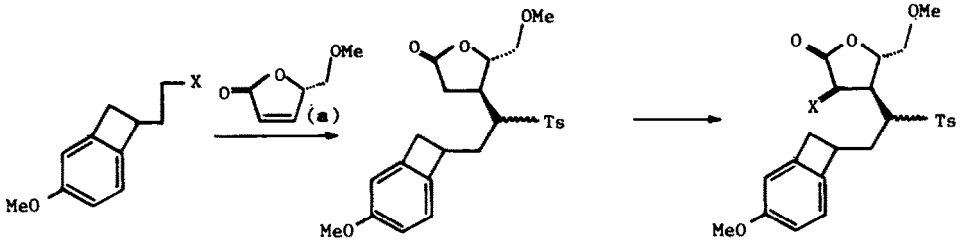
C D-trans fused compound **5** (X = H_2). On the basis of this consideration, the presence of a bulky substituent X in **3** could enforce the reaction course to be through the transition state **4** rather than **6** because of the enhancement of the steric repulsion between X and o-quinodimethane ring.



Scheme 2

Herein, we report the stereochemical results of a cycloaddition reaction of **13** and **23** and the stereoselective synthesis of des-A B-aromatic steroid **1**.

First, the key intermediate **12** required for the generation of **13** was prepared as follows. The p-tolyl sulfone **9** [m/z 316 (M^+)], obtained in 97 % yield by the substitution (p-Tol-SO_2Na, NaI, DMF, 80°C) of the p-toluenesulfonate **8**[3], was subjected to the Michael reaction (LDA, THF-HMPA, -78°C) with the butenolide **a**[1,4] to give the adduct **10** [m/z 444 (M^+)] in 71 % yield. Next, the hydroxymethylene **11** [m/z 472 (M^+)], prepared in 73 % yield by the formylation (HCO_2Et, NaH, benzene, room temperature) of **10**, was converted in 97 % yield into the phenylthiomethylene **12** [m/z 564 (M^+)] by the successive treatment ($MeSO_2Cl$, pyridine, room temperature; PhSH, pyridine, room temperature). The thermolysis of the olefinic benzocyclobutene **12** thus obtained was conducted in o-dichlorobenzene at 180°C for 4 h to furnish the cyclized products **14** [m/z 564 (M^+); IR 1760 cm^{-1} (C=O)] and **15** [m/z 564 (M^+); IR 1764 cm^{-1} (C=O)] in 61 % and 23 % yields, respectively, after the careful purification of the resulting products. Finally, the acetals **16** [m/z 580 (M^+)] and **18** [m/z 580 (M^+)], obtained in 90 % and 77 % yields respectively by the successive treatment (DIBAL, THF, -78 °C; BF_3 Et_2O, MeOH, room temperature) of **14** and **15**, were transformed (Li, liq. NH_3, THF, EtOH, -78 °C; benzoquinone, benzene, room temperature) into the desulfurylated acetals **17** [m/z 318 (M^+)] and **19** [m/z 318 (M^+)] in 41 % and 40 % yields respectively. These acetals **17** and **19** thus obtained were oxidized (Jones reagent, acetone, 0 °C) to furnish the des-A B-aromatic steroids **1** and **7** in 23 % and 58 % yields respectively which were identical with the authentic samples synthesized previously[1] in all aspects including optical rotations. Thus, although the stereochemical course of the cycloaddition of the o-quinodimethane **13** generated by the thermolysis of **12** was improved by introducing p-toluenesulfonyl group into X of **3** to afford mainly C D-trans fused compound **14**, the stereoselectivity was still not satisfactory and the reason for



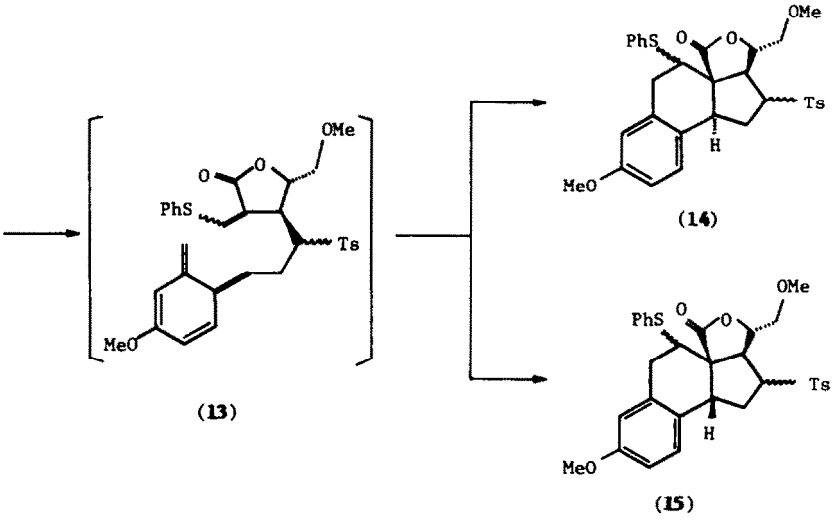
(8): X = OTs

(9): X = Ts

(10)

(11): X = CHOH

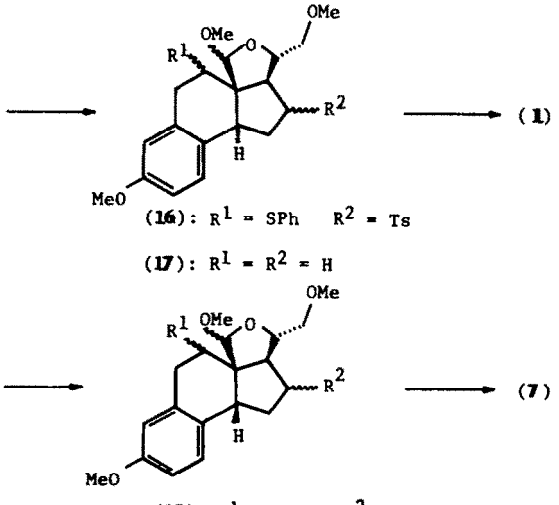
(12): X = CHSPh



(13)

(14)

(15)



(16): R^1 = SPh R^2 = Ts

(17): R^1 = R^2 = H

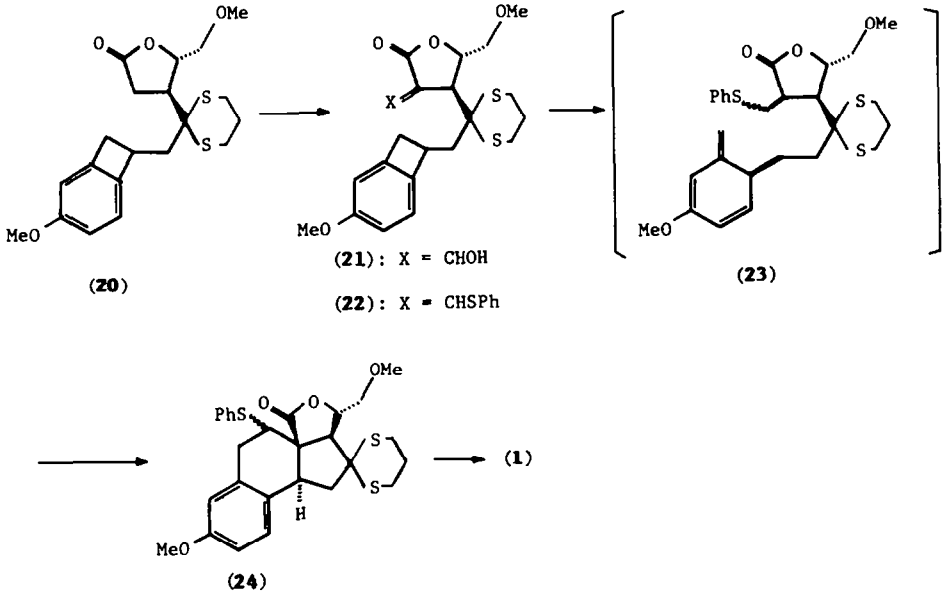
(18): R^1 = SPh R^2 = Ts

(19): R^1 = R^2 = H

Scheme 3

this result remained unclear because of the of p-toluenesulfonyl group of **12** is obscure. So, our attention was turned into the thermolysis of **22** which has no chiral center at the position substituted by X of **3**.

The thermolysis of the phenylthiomethylene **22**, which was prepared in 34 % yield from the thioketal **20**[1] via the hydroxymethylene derivative **21** [m/z 422 (M^+)] by the successive treatment (HCO_2Et, NaH, benzene, room temperature; $MeSO_2Cl$, pyridine, room temperature; PhSH, pyridine, room temperature), was heated in o-dichlorobenzene at 180 °C for 14 h to give the cyclized compound **24** in 76 % yield as a sole isolated product and then the product **24** was converted (Raney-Ni, EtOH, reflux) into the des-A B-aromatic steroid **1** in 65 % yield which was identical with the authentic sample prepared previously[1] in all aspects including optical rotation.



Scheme 4

Thus, the stereochemical course of the cycloaddition of the olefinic o-quinodimethane generated by the thermolysis of **3** was shown to be controlled largely by the bulkiness of X and we succeeded in the stereoselective synthesis of des-A B-aromatic steroid **1** in optically pure form which could be a potential intermediate for the synthesis of aldosterone and its relatives.

Experimental Section

General M.p.s were determined on a Yanagimoto MP-22 apparatus and are uncorrected. IR spectra were recorded on a Hitachi 260-10 spectrophotometer. NMR spectra were obtained on a JEOL JNM-PMX-60 and JEOL PS-100 spectrometers. Chemical shifts are reported as δ values relative to internal $SiMe_4$. Mass spectra were taken on a Hitachi M-52G and JEOL-TMS-01SG 2 spectrometers. Optical rotations were measured in a Nihonbunko DIP-4 polarimeter. All reactions were carried out under dry nitrogen. Column chromatography was carried out with silica gel (Wako-gel C-200). The phrase 'residue upon work-up' refers to the residue obtained when the organic layer was separated, dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. All new compounds described in this Experimental sections were homogeneous on t.l.c..

2-(4-Methoxybenzocyclobutenyl)ethyl p-tolyl sulfone (9). To a stirred soln of 2-(4-methoxybenzocyclobutenyl)ethyl p-toluenesulfonate (8) (4.1 g, 12.3 mmol) in anhydrous dimethylformamide (60 mL) was added sodium p-toluenesulfinate (4.3 g, 17.2 mmol) and sodium iodide (2.4 g, 16.0 mmol) at room temp. After being stirred for 2 h at 80°C, the reaction mixture was diluted with water and extracted with benzene, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using methylene dichloride to give the sulfone (9) (3.8 g, 97 %) as a oil: ^{1}H NMR (CCl_4) δ 2.41 (3H, s, Me), 3.69 (3H, s, OMe), 6.50-6.92 (3H, m, ArH), 7.26 (2H, d, J = 8 Hz, ArH), 7.70 (2H, d, J = 8 Hz, ArH); MS m/z 316 (M^+). Found: C, 68.17; H, 6.30. Calc for $C_{18}H_{20}O_3S$: C, 68.32; H, 6.37 %.

4β-[2-(4-Methoxybenzocyclobutenyl)-1-p-toluenesulfinyl]-ethyl-5α-methoxymethyl-furan-2-one (10). To a soln of lithium diisopropylamide [8.86 mmol prepared from diisopropylamine (942 mg, 9.31 mmol) and n-buthyllithium (1.56 M n-hexane solution 5.68 mL, 8.86 mmol)] in anhydrous tetrahydrofuran (50 mL) was added a soln of the sulfone (9) (765 mg, 2.42 mmol) in anhydrous tetrahydrofuran (5 mL) at -78°C. After being stirred for 1 h at the same temp., hexamethylphosphoramide (787 mg, 3.17 mmol) and the butenolide (a) (568 mg, 4.43 mmol) in anhydrous tetrahydrofuran (7 mL) was added to the mixture at -78°C and the reaction mixture was stirred for 2 h at the same temp. After being quenched with saturated aqueous ammonium chloride (10 mL), the mixture was extracted with ether and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using n-hexane-ethyl acetate (5 : 1, v/v) to afford the adduct (10) (760 mg, 71 %) as an oil: IR ν max ($CHCl_3$) 1780 (C=O) cm^{-1}, ^{1}H NMR (CCl_4) δ 2.49 (3H, s, Me), 3.41 (3H, s, OMe), 3.72 (3H, s, OMe), 4.97 (1H, br s, O=CH-CH_2), 6.60-6.92 (3H, m, ArH), 7.35 (2H, d, J = 8 Hz, ArH), 7.88 (2H, d, J = 8 Hz, ArH); MS m/z 444 (M^+). Found: C, 63.41; H, 6.05. Calc for $C_{22}H_{28}O_6S$ 0.5H_2O: C, 63.55; H, 6.44 %.

4β-[2-(4-Methoxybenzocyclobutenyl)-1-p-toluenesulfinyl]-ethyl-5α-methoxymethyl-3-phenylthiomethylenefuran-2-one (12). To a suspension of sodium hydride (60 % in oil; 107 mg, 2.67 mmol) in anhydrous benzene (10 mL) was added a soln of (10) (154 mg, 0.347 mmol) in anhydrous benzene (5 mL) at room temp. and the mixture was stirred for 30 min at the same temp. To the reaction mixture was then added dropwise ethyl formate (165 mg, 2.23 mmol) and after being stirred for 8 h at room temp., the mixture was diluted with water (3 mL), acidified with 10 % hydrochloric acid, extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using n-hexane-ethyl acetate (5 : 1, v/v) to afford the hydroxymethylene (11) (119 mg, 73 %) as a pale yellow oil: IR ν max ($CHCl_3$) 1738, 1720 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.49 (3H, s, Me), 3.40 (3H, s, OMe), 3.74 (3H, s, OMe), 5.00 (1H, br s, O=  CH-CH_2), 6.61-7.08 (3H, m, ArH), 7.40 (2H, d, J = 8 Hz, ArH), 7.85 (2H, d, J = 8 Hz, ArH); MS m/z 472 (M^+).

To a stirred soln of the hydroxymethylene (11) (37 mg, 0.078 mmol) in anhydrous pyridine (2 mL) was added methanesulfonyl chloride (14 mg, 0.122 mmol) at room temp. After being stirred for 1 h, the reaction mixture was treated with thiophenol (17 mg, 0.154 mmol) for 3 h at room temp. The resulting mixture was then diluted with 10 % hydrochloric acid, extracted with ether, and the extract was washed with aqueous potassium hydrogen sulfate and saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (19 : 1, v/v) to afford the phenylthiomethylene (12) (43 mg, 97 % from (11)) as a pale yellow oil: IR ν max ($CHCl_3$) 1750 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) δ 2.26 (3H, s, Me), 3.39 (3H, s, OMe), 3.69 (3H, s, OMe), 4.14 (1H, br s, O=  CH-CH_2), 6.43 - 6.82 (3H, m, ArH) 7.14 - 7.48 (7H, m, ArH) 7.76 (2H, d, J = 8 Hz, ArH); MS m/z 564 (M^+). Found: C, 61.05; H, 5.64. Calc for $C_{31}H_{32}O_6S_2$ 2.5 H_2O: C, 61.06; H, 6.11 %.

Thermolysis of (12). A soln of the benzocyclobutene (12) (43 mg, 0.076 mmol) in o-dichlorobenzene (8 mL) was heated at 180°for 4 h. After removal of the solvent, the residue was chromatographed using n-hexane-ethyl acetate (17 : 3, v/v) to give cis-4,5-(4-methoxybenzo)-1β,7aβ-(2α-methoxymethyl-5-oxofuro)-7-phenylthio-2-p-toluenesulfinylhydrindane (15) (10 mg, 23 %) as a pale yellow oil: IR ν max ($CHCl_3$) 1760 (C=O) cm^{-1}; NMR (CCl_4) δ 2.38 (3H, s, Me), 3.13 (3H, s, OMe), 3.66 (3H, s, OMe), 4.48 (1H, br s, O  CH-CH_2), 6.43 - 6.97 (3H, m, ArH), 7.08 - 7.47 (7H, m, ArH), 7.70 (2H, d, J = 8 Hz, ArH); MS m/z 564 (M^+). Found: C, 64.47; H, 5.68. Calc for $C_{31}H_{32}O_6S_2$ 0.5 H_2O: C, 64.90; H, 5.80 %. From the later fractions trans-4,5-(4-methoxybenzo)-1β,7aβ-(2α-methoxymethyl-5-oxofuro)-7-phenylthio-2-p-toluenesulfinylhydrindane (14) (26 mg, 61 %) was obtained as an oil: IR ν max ($CHCl_3$) 1764 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) δ 2.43 (3H, s, Me), 3.30 (3H, s, OMe), 3.66 (3H, s, OMe), 4.02 (1H, br s, O=CH-CH_2), 6.48 - 6.81 (3H, m, ArH), 7.18 - 7.60 (7H, m, ArH), 7.80 (2H, d, J = 8 Hz, ArH); MS m/z 564 (M^+). Found: C, 63.76; H, 5.93. Calc for $C_{31}H_{32}O_6S_2$ H_2O: C, 63.89; H, 5.88 %.

trans-4,5-(4-Methoxybenzo)-1β,7aβ-(5α-methoxy-2α-methoxymethylfuro)-7-phenylthio-2-p-toluenesulfinylhydrindane (16). To a stirred soln of (14) (155 mg, 0.275 mmol) in anhydrous tetrahydrofuran (10 mL) was added diisobutylaluminum

hydride (1.75M n-hexane solution 0.62 mL, 1.09 mmol) at -78 °C and the mixture was stirred for 3 h. After being quenched with saturated aqueous ammonium chloride, the mixture was extracted with ether and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (5 : 1, v/v) to afford the lactol (154 mg, 99 %) as an oil: IR ν max ($CHCl_3$) 3600 (OH) cm^{-1}; ^1H NMR (CCl_4) δ 2.41 (3H, s, Me), 2.88 (3H, s, OMe), 3.58 (3H, s, OMe), 3.90 (1H, br s, O=C(O)-CH-CH_2), 4.81 (1H, br s, O-CH<O), 6.32 - 6.99 (3H, m, ArH), 7.05 - 7.47 (7H, m, ArH), 7.73 (2H, d, J = 8 Hz, ArH); MS m/z 548 (M^+-H_2O).

To a stirred soln of the lactol (185 mg, 0.338 mmol) in methanol (13 mL) was added a catalytic amount of boron trifluoride-diethyl ether at room temp. After the mixture was stirred for 43 h at the same temp., sodium bicarbonate was added, and the solvent was then evaporated. The residue was diluted with water (20 mL), extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (19 : 1, v/v) to afford the (16) (170 mg, 90 %) as an oil: ^1H NMR (CCl_4) δ 2.42 (3H, s, OMe), 4.30 (1H, br s, O-CH<O), 6.40 - 6.96 (3H, m, ArH), 7.08 - 7.52 (7H, m, ArH), 7.76 (2H, d, J = 8 Hz, ArH); MS m/z 580 (M^+). Found: C, 63.99; H, 6.29. Calc for $C_{32}H_{36}O_6S_2$ H_2O: C, 64.18; H, 6.39 %.

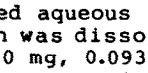
trans-4,5-(4-Methoxybenzo)-1β,7aβ-(5α-methoxy-2α-methoxymethylfuro)hydrindane (17) from (16). A soln of (16) (62 mg, 0.107 mmol) in anhydrous tetrahydrofuran (5 mL) and ethanol (5 mL) was added cautiously to liquid ammonia (20 mL). To this soln was added lithium (20 mg, 2.85 mmol) at -78°C. After the mixture was stirred for 30 min at -78°C, ethanol (10 mL) was added dropwise, and the solvent was then evaporated. The residue was diluted with water and the mixture was extracted with ether and the extract was washed with saturated aqueous sodium chloride. The extract was evaporated to give the residue which was dissolved in benzene (8 mL). This solution was treated with benzoquinone (20 mg, 0.185 mmol) for 13 h at room temp. The benzene layer was washed with 10 % potassium hydroxide soln and then saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (19 : 1, v/v) to afford (17) (14 mg, 41 % from (16)) as an oil: ^1H NMR (CCl_4) δ 2.83 (3H, s, OMe), 3.31 (3H, s, OMe), 3.69 (3H, s, OMe), 6.40 - 7.00 (3H, m, ArH); MS m/z 318 (M^+).

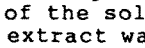
To a stirred soln of the methyl ether (17) (14 mg, 0.044 mmol) in acetone (3 mL) was added a Jones reagent (7 drops) at 0 °C and the mixture was stirred 5 h. After removal of the solvent, water was added to the residue, extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using n-hexane-ethyl acetate (10 : 1, v/v) to afford (1) (30 mg, 23 %) as needles after recrystalisation from ethanol, m.p. 91 - 92 °C; $[\alpha]_D^{20}$ +57.1 (c = 0.34, $CHCl_3$); IR ν max ($CHCl_3$) 1754 (C=O) cm^{-1}; ^1H NMR (CCl_4) δ 3.43 (3H, s, OMe), 3.80 (3H, s, OMe), 4.23 (1H, br s, O=C(O)-CH-CH_2), 6.51 - 6.98 (3H, m, ArH); MS m/z 302 (M^+). Found: C, 70.00; H, 7.32. Calc for $C_{18}H_{22}O_4$ 0.25 H_2O: C, 70.45; H, 7.39 %.

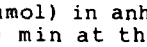
cis-4,5-(4-Methoxybenzo)-1β,7aβ-(5α-methoxy-2α-methoxymethylfuro)-7-phenylthio-2-p-toluenesulfinylhydrindane (18). To a stirred soln of (15) (236 mg, 0.42 mmol) in anhydrous tetrahydrofuran (15 mL) was added diisobutylaluminum hydride (1.75M n-hexane solution 2.38 mL, 4.17 mmol) at -78 °C and the mixture was stirred for 1 h. After being quenched with saturated aqueous ammonium chloride, the mixture was extracted with chloroform and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (5 : 1, v/v) to afford the lactol (209 mg, 88 %) as an oil: IR ν max ($CHCl_3$) 3600 (OH) cm^{-1}; ^1H NMR (CCl_4) δ 2.26 (3H, s, Me), 3.27 (3H, s, OMe), 3.70 (3H, s, OMe), 6.18 - 6.90 (3H, m, ArH), 6.99 - 7.50 (7H, m, ArH), 7.65 (2H, d, J = 8 Hz, ArH); MS m/z 566 (M^+).

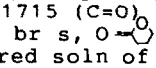
To a stirred soln of the lactol (209 mg, 0.37 mmol) in methanol (15 mL) was added a catalytic amount of boron trifluoride-diethyl ether at room temp. After the mixture was stirred 15 h at the same temp, sodium bicarbonate was added, and the solvent was then evaporated. The residue was diluted with water (20 mL), extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene-ethyl acetate (19 : 1, v/v) to afford the (18) (186 mg, 87 %) as an oil: ^1H NMR (CCl_4) δ 2.30 (3H, s, Me), 3.40 (3H, s, OMe), 3.53 (3H, s, OMe), 5.00 (1H, br s, O-CH<O), 6.21 - 6.82 (3H, m, ArH), 6.99 - 7.52 (7H, m, ArH), 7.53 (2H, d, J = 8 Hz, ArH); MS m/z 580 (M^+). Found: C, 64.46; H, 6.70. Calc for $C_{32}H_{36}O_6S_2$ H_2O: C, 64.18, H, 6.39.

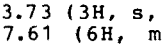
cis-4,5-(4-Methoxybenzo)-1β,7aβ-(5α-methoxy-2α-methoxymethylfuro)hydrindane (19) from (18). A soln of (18) (41 mg, 0.071 mmol) in anhydrous tetrahydrofuran (4 mL) and ethanol (4 mL) was added cautiously to liquid ammonia (16 mL). To this soln was added lithium (20 mg, 2.85 mmol) at -78 C. After the mixture was stirred for 30 min at -78 C, ethanol (10 mL) was added dropwise, and the solvent was then

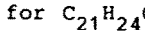
evaporated. The residue was diluted with water and the mixture was extracted with ether and the extract was washed saturated aqueous sodium chloride. The extract was evaporated to give the residue which was dissolved in benzene (8 mL). This solution was treated with benzoquinone (10 mg, 0.093 mmol) for 28 h at room temp. The benzene layer was washed with 10 % aqueous potassium hydroxide soln and then saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene to afford (**19**) (9 mg, 40 % from (**18**)) as an oil: ^{1}H NMR (CCl_4) δ 3.33 (6H, s, OMe), 3.73 (3H, s, OMe), 4.50 (2H, br s, ), 6.42 - 7.25 (3H, m, ArH); MS m/z 318 (M^+).

To a stirred soln of methyl ether (**19**) (9 mg, 0.028 mmol) in acetone (2 mL) was added a Jones reagent (5 drops) at 0 °C and the mixture was stirred for 2.5 h. After removal of the solvent, water was added to the residue, extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using n-hexane-ethyl acetate (19 : 1, v/v) to afford (**7**) (5 mg, 58 %) as an oil: IR ν max ($CHCl_3$) 1758 (C=O) cm^{-1}, ^{1}H NMR (CCl_4) δ 3.40 (3H, s, OMe), 3.70 (3H, s, OMe), 4.03 (1H, br s, ), 6.42 - 7.10 (3H, m, ArH); MS m/z 302.1526 (M^+). Calc for $C_{18}H_{22}O_4$ 302.1518.

4β-[2-(4-Methoxybenzocyclobutenyl)-1,1-trimethylenedithio]ethyl-5α-methoxymethyl-3-phenylthiomethylenefuran-2-one (22). To a suspension of sodium hydride (60 % in oil; 151 mg, 3.77 mmol) in anhydrous benzene (10 mL) was added a soln of (**20**) (310 mg, 0.79 mmol) in anhydrous benzene (2 mL) at room temp. and the mixture was stirred for 30 min at the same temp. To the reaction mixture was then added dropwise ethyl formate (233 mg, 3.15 mmol) and after being stirred for 2 h at room temp., the mixture was diluted with water, acidified with 10 % hydrochloric acid, extracted with ether, and the extract was washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed using methylene dichloride to afford the hydroxymethylene (**21**) (220 mg, 66 %) as a pale yellow oil: IR νmax ($CHCl_3$) 1770, 1715 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ3.38 (3H, s, OMe), 3.69 (3H, s, OMe), 4.72 (1H, br s, ), 6.57 - 7.00 (3H, m, ArH); MS m/z 422 (M^+).

To a stirred soln of the hydroxymethylene (**21**) (138 mg, 0.33 mmol) in anhydrous pyridine (1 mL) was added methanesulfonyl chloride (49 mg, 0.43 mmol) and a catalytic amount of 4-dimethylaminopyridine at room temp. After being stirred for 23 h, the reaction mixture was treated with thiophenol (64 mg, 0.58 mmol) for 4 h at room temp. The resulting mixture was then diluted with 10 % hydrochloric acid, extracted with ether, and the extract was washed with aqueous potassium hydrogen sulfate and saturated aqueous sodium chloride. The residue upon work-up was chromatographed using benzene to afford the phenylthiomethylene (**22**) (81 mg, 52 % from (**21**)) as an oil: IR ν max ($CHCl_3$) 1748 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) δ 3.44 (3H, s, OMe), 3.73 (3H, s, OMe), 4.87 (1H, br s, ), 6.52 - 7.18 (3H, m, ArH), 7.41 - 7.61 (6H, m, ArH, s-C<u>H</u>=C); MS m/z 404.1091 (M^+-SPh), Calc for $C_{21}H_{22}O_4S_2$: 404.1116.

trans-4,5-(4-Methoxybenzo)-1β,7aβ-(2α-methoxymethyl-5-oxofuro)-7-phenylthio-2,2-trimethylenedithiohydrindane (24). A soln of the benzocyclobetene (**22**) (81 mg, 0.20 mmol) in o-dichlorobenzene (7 mL) was heated at 180 °C for 14 h. After removal of the solvent, the residue was chromatographed using benzene-ethyl acetate (19 : 1, v/v) to give (**24**) (59 mg, 76 %) as an oil: IR ν max ($CHCl_3$) 1766 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) δ3.31 (3H, s, OMe), 3.72 (3H, s, OMe), 4.97 (1H, br s, ), 6.49 - 6.99 (3H, m, ArH), 7.19 - 7.60 (5H, m, ArH); MS m/z 404.1100 (M^+-SPh), Calc for $C_{21}H_{24}O_4S_2$ 404.1115.

trans-4,5-(4-Methoxybenzo)-1β,7aβ-(2α-methoxymethyl-5-oxofuro)hydrindane (1) from (24). To a suspension of Raney Ni (1.1 g) in ethanol (10 mL) was added a solution of (**24**) (49 mg, 0.12 mmol) in ethanol (2 mL). The reaction mixture was refluxed for 5 h. After cooling the mixture was filtered through Celite, evaporation of the solvent afforded a crude product wich was chromatographed using n-hexane-ethyl acetate (10 : 1, v/v) afforded (**1**) (33 mg, 65 %) as colorless needles after recrystallisation from ethanol, m.p. 91 - 92 °C; $[\alpha]_D^{20}$ +57.1° (C=0.34, $CHCl_3$); IR max ($CHCl_3$) 1754 (C=O) cm^{-1}; ^{1}H NMR (CCl_4) 3.43 (3H, s, OMe), 3.80 (3H, s, OMe), 4.23 (1H, br s, ), 6.51 - 6.98 (3H, m, ArH); MS m/z 302 (M^+). Found: C, 70.00; H, 7.32. Calc for $C_{18}H_{22}O_4$ 0.25 H_2O: C, 70.45; H, 7.39 %.

Acknowledgements
We thank Miss K. Mushiake, Miss K. Koike, Miss E. Kurosawa, and Mr. K. Kawamura, Pharmaceutical Institute, Tohoku University for microanalyses and spectral measurements.

References and Notes

(1) H. Nemoto, M. Nagai, K. Fukumoto, and T. Kametani, J. Org. Chem., in press.
(2) Reviews on cycloaddition of an olefinic o-quinodimethane: I. L. Klundt, Chem. Rev., **70**, 471 (1970); T. Kametani and K. Fukumoto, Heterocycles **3**, 29 (1975); Ibid., **8**, 465 (1977); W. Oppolzer, Angew. Chem. Int. Ed. Engl., **16**, 10 (1977); Synthesis 793 (1978); T. Kametani and H. Nemoto, Tetrahedron, **37**, 3 (1981).

(3) T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama, H. Matsumoto, and K. Fukumoto, J. Am. Chem. Soc., **99**, 3461 (1977).
(4) P. Camps, J. Font, and O. Ponsati, Tetrahedron Lett., **1981**, 1471.