Arch. Pharm. Res. Vol.19, No.6, pp. 581-585, 1996

# Studies on the Synthesis of Naphthoquinoids-1: Formal Total Synthesis of (+)-6-Oxo-3,4,4a,5-tetra hydro-3-hydroxy-2,2-dimethylnaphtho-1,2-pyran

**Oee Sook Park and Jae Gyeong Lim**

*Department of Chemistry, Chungbuk National University Cheongju, Chungbuk 361-763, Korea*

*(Received August 29, 1996)*

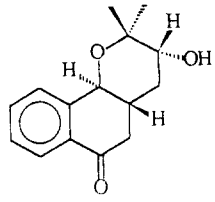
A new formal total synthesis of (+)-6-oxo-3,4,4a,5-tetrahydro-3-hydroxy-2,2-dimethylnaphtho-1,2-pyran (1) which has been known to have bactericidal, bacteriostatic, fungicidal, fungistatic activities against *Staphylococcus aureus* and other microorganism, is described. The key reaction involves enantioselective prenylation of α-tetralone via chiral lithioenamine.

**Key words :** (+)-6-Oxo-3,4,4a,5-tetrahydro-3-hydroxy-2,2-dimethylnaphtho-1,2-pyran, *Lippia sidoides* Cham (verbenaceae), Bactericidal, Fungicidal activity, *Staphylococcus aureus*, Formal total synthesis, Enantioselective prenylation of α-tetralone, Isocatalponol

## INTRODUCTION

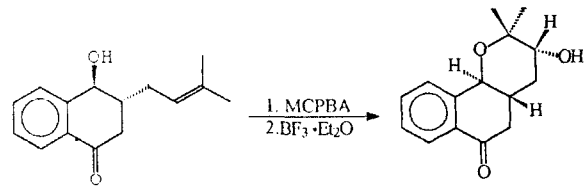
The essential oil of *Lippia sidoides* Cham (verbenaceae), which is an aromatic shrub widespread in Northeastern Brazil, has been known to show bactericidal, bacteriostatic, fungicidal and fungistatic activities against *Staphylococcus aureus* and other microorganisms.

(+)-6-Oxo-3,4,4a,5-tetrahydro-3-hydroxy-2,2-dimethylnaphtho-1,2-pyran (1) was first isolated from the essential oil of *Lippia sidoides* Cham (Macambira *et al.* 1986). Its structure was determined on the basis of spectroscopic method by the same authors.



1

During its structural determination, compound **1** was prepared from isocatalponol (2) (Macambira *et al.* 1986) (scheme 1) . Isocatalponol (2) was isolated from *Lippia origanoides* H. B. K. (Verbenaceae) and characterized in 1976 by Brieskorn and Pohlmann (Brieskorn and Pohlmann, 1976).



2 1

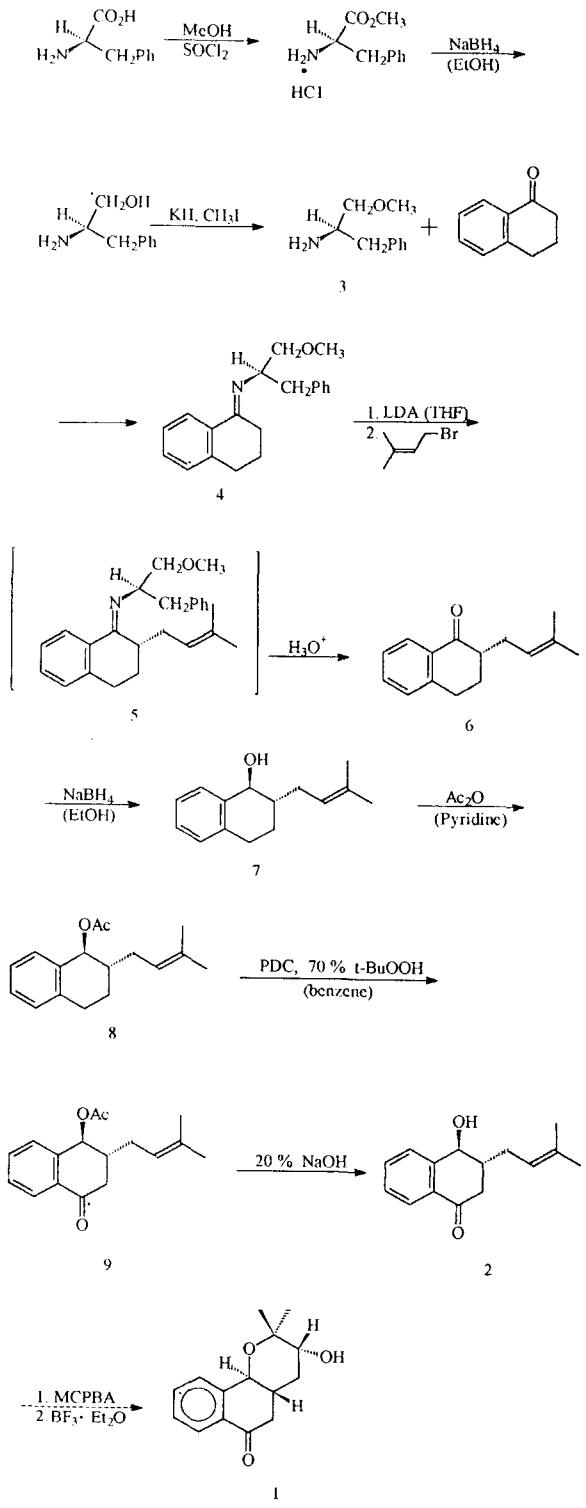
**Scheme 1.**

We report here a first synthesis of isocatalponol (2) and a new formal total synthesis of compound 1 from α-tetralone. Our synthetic route to compound 1 is outlined in scheme 2.

## MATERIALS AND METHODS

Reactions requiring anhydrous conditions were performed with the usual precautions for rigorous exclusion of air and moisture. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl prior to use. Thin layer chromatography (TLC) was performed on precoated silica gel 60 F 254 plates from EM reagents and visualized with 254-nm UV light or ceric sulfate-ammoniummolybdate-sulfuric acid spray. Flash chromatography was carried out on silica gel 60 (E. M. Merck, particle size 0.040~0.063 mm, 230~400 mesh ASTM). The $^{1}H$ and $^{13}C$ NMR spectra were recorded on a Brucker AC 80 (80 MHZ) and/or Varian Gemini 200 (200 MHZ) NMR spectrometer using $CDCl_3$ as a solvent except where noted. The chem-

*Correspondence to*: Oee Sook Park, Department of Chemistry, Chungbuk National University Cheongju, Chungbuk 361-763, Korea



**Scheme 2.**

ical shifts were reported in parts per million (ppm) downfield from tetramethylsilane, and J-values were in Hz. IR spectra were obtained on a Perkin-Elmer Model 782 spectrometer. Mass spectra were recorded on a Shimadzu-LKB 9000 GC/MS system. The optical rotations were measured with a JASCO DIP-1000 polarimeter at RT. All mps were uncorrected. When necessary, chemicals were purified according to the reported procedure (Perrin *et al.*, 1980).

### (*R*)-(+)-2-Amino-1-methoxy-3-phenylpropane (3)

The procedure reported by A. I. Meyers *et al.* (Meyers *et al.*, 1981) was employed. (*R*)-Phenylalanine (10.0 g, 60.5 mmol) was suspended in anhydrous methanol (22 ml). The solution was cooled to 0° and thionyl chloride (11 mL, 149.3 mmol) was added dropwise. The solution was allowed to warm to RT and stirred overnight. Concentration gave a yellow solid which was stirred with ether, filtered, and dried under high vacuum, to produce the white solid HCl salt of the methyl ester: mp 155~157°; $^1$H NMR (80 MHz, $CDCl_3$+$CD_3OD$) δ 7.39 (S, 5 H), 4.29 (br s, 4 H), 3.81 (s, 3 H), 3.32 (br s, 2 H); IR (KBr) 3475, 1745, 1585, 1495, 1240 cm$^{-1}$

The ester (10.0g, 46.4 mmol), without further purification, was dissoved in 50% aqueous EtOH (45 mL). This was slowly added to a cooled (0°) solution of $NaBH_4$ (8.4 g, 0.22 mol) in 50% aqueous EtOH (100 mL) over 1 h. The solution was stirred at RT for 4 h, then refluxed under nitrogen for 6 h, and allowed to stir at RT overnight. The top layer was decanted and the EtOH was removed in vacuo until a white solid appeared. The lower insoluble layer was extracted with EtOH and concentrated. The two concentrated aqueous layers were extracted with EtOAc. The combined EtOAc layers were dried over $MgSO_4$ and concentrated to yield a white solid. This was recrystallized in EtOAc-Hexane (2:1) to give the desired alcohol (5.78 g, 82.6%): mp 91~92.5°; $^1$H NMR (80 MHz) δ 7.30 (s, 5 H), 2.80-3.65 (m, 3 H), 2.65 (d, J= 6.0 Hz, 2 H), 2.25-2.50 (br s, 3 H); IR (KBr) 3345, 3290, 3100, 1575, 1485, 1060; $[\alpha]_D$+24.2° (c 1.5, EtOH).

Potassium hydride (1.14 g, 28.3 mmol) was suspended in anhydrous THF (22 mL). To this suspension, anhydrous THF (55 mL) solution of (*R*)-phenylalaninol (4.0 g, 26.4 mmol) was added dropwise with a syringe under nitrogen. The solution was stirred overnight under nitrogen. The anhydrous THF (32 mL) solution of methyl iodide (3.75 g, 26.5 mmol) was added slowly with a syringe and stirred for 3 h. The reaction mixture was extracted with ether three times after addition of a cold saturated solution of NaCl. The organic layer was dried over $MgSO_4$ and concenturated under vacuum to afford the crude product. The crude product was distilled under reduced pressure (90-93°/2 mmHg) to yield the desired product as a colorless oil (3.20 g, 73.3%): $^1$H NMR (80 MHz) δ 7.24 (s, 5 H), 3.35 (br s, 6 H), 2.63 (m, 2 H), 1.75 (br s, 2 H); MS m/z (relative intensity) 165 ($M^+$, 0.4), 120 (51.4), 91 (22.5), 77 (8.8), 74 (100), 51 (7.8);

IR (neat) 3380, 3290, 1600, 1120 $cm^{-1}$; $[\alpha]_D$ +13.8° (c 5.6 benzene). The product was kept tightly sealed under nitrogen immediately after distillation.

### α-Tetralone Imine of (*R*)-(+)-2-Amino-1-methoxy-3-phenylpropane (4)

In a system containing a Dean-Stark trap arranged for azeotropic removal of water, the methoxy amine 3 (4.0 g, 24.2 mmol) and α-tetralone (3.54g, 24.2 mmol) were dissolved in benzene (15 mL) and heated to reflux for 4 h. Removal of benzene in vacuo and distillation of the oily residue in Kugelrohr (155-160°/ 0.08 mmHg) gave the desired product as a clear viscous oil (4.33 g, 62.1%); $^1H$ NMR (60 MHz) δ 8.28 (m, 1 H), 7.20 (m, 8 H), 3.85-4.30 (m, 1 H), 3.55 (deformed d, J=7.2 Hz, 2 H), 3.35 (s, 3 H), 2.94 (deformed t, J=3.96 Hz, 2 H), 2.69 (t, J=6.0 Hz, 2 H), 1.85-2.35 (m, 2 H), 1.48-1.75 (m, 2 H); MS m/z (relative intensity) 293 ($M^+$, 3.9), 248 (100), 202 (96. 1), 157 (72.6), 129 (47.1), 91 (98.1), 45 (70.6); IR (neat) 1680, 1600, 1200 $cm^{-1}$.

### (*S*)-(+)-2-Prenyl-1-tetralone (6)

An oven-dried 50 mL flask equipped with a magnetic bar, a pressure-equalized addition funnel, and a rubber septum cap was charged with anhydrous THF (10 mL) under a nitrogen atmosphere. Freshly distilled diisopropylamine (1.51 g, 15.0 mmol) was added via syringe and the solution cooled to 0°. n-Butyllithium (13.6 mL of a 1.1 M solution in hexane, 15. 0 mmol) was added. The solution was stirred at 0° for 15 min and then cooled -30°. α-Tetralone imine of (*R*)-(+)-2-amino-1-methoxy-3-phenylpropane (3.13 g, 10.7 mmol) in anhydrous THF (10 mL) was added over 10 min and allowed to stir for 1.5 h at -15°. The solution was then cooled to -78° and prenyl bromide (3.50 g, 21.4 mmol) was added in a solution of anhydrous THF (5 mL) over a period of 10 min. The mixture was allowed to stir at -78° for 3 h and then warmed to RT and stirred overnight. A cold saturated NaCl solution was poured into the reaction mixture. The resulting solution was extracted with ether 3 times. The combined ether extracts were washed with brine, then dried ($MgSO_4$), and concentrated in vacuo to give an amber oil. This crude imine was subjected to hydrolysis immediately. A buffer solution comprised of sodium acetate (2.6 g), acetic acid (6.0 mL) and water (28 mL) was added to the crude imine in hexane (39 mL) and shaken for 30 min and the aqueous layer removed and saved to recover **2**. The aqueous layer was extraced with hexane, and the combined hexane layers were washed with 1 N HCl, water, 5% sodium bicarbonate, water and brine. The hexane solution was then dried ($MgSO_4$), filtered, concentrated in vacuo to afford the crude product. Chromatography of the crude product on silica gel (1:40 EtOAC/hexane) gave the desired product (1.20 g, 52. 4%); 1H NMR (200 MHz) δ 7.90-8.20 (m, 1 H), 7.10-7.55 (m, 3 H), 5.18 (deformed t, J=6.6 Hz, 1 H), 2.87-3.08 (m, 2 H), 2.40-2.79 (m, 2 H), 2.12-2.38 (m, 2 H), 1.79-1.95 (m, 1 H), 1.72 (s, 3 H), 1.64 (s, 3 H); MS m/ z (relative intensity) 214 ($M^+$, 17.2), 199 (4.1), 159 (25.1), 146 (100), 115 (25.4), 90 (33.3); $^{13}C$ NMR (50. 29 MHz) δ 144.10, 133.48, 133.08, 32.59, 128.74, 127.40, 126.48, 121.78, 48.06, 28.66, 28.10, 28.00, 25.83, 17.85; IR (neat) 1675, 1595, 1210 $cm^{-1}$; $[\alpha]_D$ + 8.20° (*c* 0.5, $CHCl_3$).

### Recovery of (*R*)-(+)-2-Amino-1-methoxy-3-phenylpropane (3)

The acidic aqueous layer from the above which was saved for the recovery of **2** was neutralized with solid KOH to pH 14 and then saturated with NaCl. This aqueous solution was extracted with ether four times , and the combined ether layers were washed with brine. Drying ($K_2CO_3$) and concentration gave an oil which was distilled: bp 90-93° (2 mmHg); $[\alpha]_D$ +13.7° (*c* 5.8, benzene).

### (*1S,2S*)-2-Prenyl-1-tetralol (7a)

To a solution of (*S*)-(+)-2-prenyl-1-tetralone (226 mg, 1.06 mmol) in ethanol (8 mL) was added sodium borohydride (80 mg, 2.12 mmol) portionwise. After stirring at RT for 5 h, the reaction mixture was diluted with water, acidified with 10% HCl solution and extracted with dichloromethane (three times). The combined extracts were washed successively with water, $NaHCO_3$ solution and water, dried over $MgSO_4$, and then concentrated under reduced pressure. Chromatography of the crude product on silica gel (1:60 ethyl acetate/hexane) gave the desired product 7a (119 mg, 52.2%): $^1H$ NMR (80 MHz) δ 7.01-7.53 (m, 4 H), 5.25 (deformed t, J=6.9 Hz, 1 H), 4.49 (br d, J= 7.5 Hz, 1 H), 2.71 (deformed t, J=6.1 Hz, 2 H), 1.45-2.59 (m, 6 H), 1.72 (s, 3 H), 1.64 (s, 3 H); MS m/z (relative intensity) 216 ($M^+$, 23.2), 198 ($M^+$-$H_2O$, 4.3), 159 (80.3), 131 (42.1), 129 (23.3), 91 (61.8), 41 (100); IR (neat) 3320, 1490, 1220 $cm^{-1}$.

### (*1R,2S*)-2-Prenyl-1-tetralol (7b)

An oven-dried 100-mL flask equipped with a magnetic bar and a rubber septum cap was charged with L-selectride (8.7 mL of a 1.0 M solution in THF, 8.7 mmol) under a nitrogen atmosphere. The solution was cooled to -15°. (*S*)-(+)-2-prenyl-1-tetralone (930 mg, 4.35 mmol) was added dropwise in a solution of THF (9.5 mL) via a syringe. The solution was stirred for 2 h at this temperature. NaOH (9.5 mL of a 3.0 M solution in water) was poured into the reaction mix-

ture. The resulting solution was stirred for 10 min and then $H_2O_2$ solution (9.5 mL of 30% solution) was added. After stirring for 10 min, the reaction mixture was saturated with potassium carbonate and then extracted with dichloromethane. The combined dichloromethane extracts were washed with water, then dried ($MgSO_4$), and concentrated in vacuo to afford the crude product. The crude product was chromatographed on silica gel (1:60 ethyl acetate/hexane) to give the desired product (885 mg, 94.3%): $^1$H NMR (80 MHz) δ 7.08-7.32 (m, 4 H), 5.25 (deformed t, J=7.2 Hz, 1 H), 4.61 (br s, 1 H), 2.80 (deformed t, J =6.4 Hz, 2 H), 2.24 (dd, J=16, 5.6 Hz 2 H), 1.9-1.56 (m, 3 H), 1.74 (s, 3 H), 1.67 (s, 3 H) 1.55 (s, 1 H); MS m/z (relative intensity) 216 ($M^+$, 25.9), 198 ($M^+$-$H_2O$, 3.9), 159 (84.3), 131 (45.1), 129 (33.3), 91 (58.8), 41 (100); IR (neat) 3280, 1490, 1220 $cm^{-1}$.

### (*1S,2S*)-2-Prenyl-1-tetralol acetate (8)

A solution of (*1S,2S*)-2-prenyl-1-tetralol (9600 mg, 4. 44 mmol) in anhydrous pyridine (3.4 mL) was treated with acetic anhydride (1.81 g, 17.8 mmol). The resulting solution was stirred at RT overnight. The solution was poured into ice-$H_2O$ and extracted with dichloromethane 3 times. The organic extracts were washed with cold 5% aq. HCl, water, saturated $NaHCO_3$ solution, water and brine two times, respectively. The organic layer was dried over anhydrous $MgSO_4$ and condensed at reduced pressure. The residue was chromatographed on the silica gel column. Elution with hexane : EtOAc (20:1) gave (*1S,2S*)-2-prenyl-1-tetralol acetate (1.07 g, 94%); $^1$H NMR (80 MHz) δ 7.14-7.36 (m, 4 H), 6.05 (br d, J=7.2 Hz, 1 H), 5.18 (deformed t, J=6.6 Hz, 1 H), 2.85 (t, J=6.0 Hz, 2 H), 2.03 (s, 3 H), 1.73 (s, 3 H), 1.71 -2.27 (m, 5 H), 1. 61 (s, 3 H); MS m/z (relative intensity) 258 ($M^+$, 0.3), 198 ($M^+$-HAc), 183 (70.6), 129 (66.7), 115 (29.1),91 (25.5), 43 (100); IR (neat) 1720, 1590, 1225 $cm^{-1}$.

### (*1S,2R*)-4-Oxo-2-prenyl-1-tetralol acetate (9)

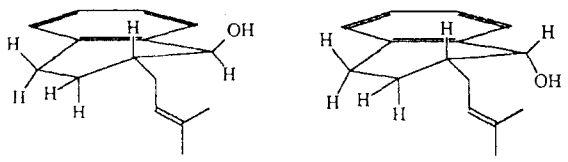
To a stirred solution of (*1S,2S*)-2-prenyl-1-tetralol acetate (170 mg, 0.66 mmol) in benzene (7.9 mL) and celite (0.8 g) was added pyridinium dichromate (620 mg, 1.65 mmol) followed by the addition of 70% *tert*-butylhydroperoxide (192 mg, 1.65 mmol) at 10°. After 20 min at 10°, the reaction mixture was stirred for 5 h at 25°. Dichloromethane (25 mL) was added, and the reaction mixture was filtered through a pad of Celite and washed twice with 18 mL portions of dichloromethane. Combined filtrate was washed with water, dried with $MgSO_4$ and concentrated in vacuo to afford the crude product. It was purified by flash chromatography (1:15 ether/hexane) to give unreacted starting material (50 mg) and the desired product (54 mg, 30%) as a colorless liquid: $^1$H NMR (200 MHz) δ 8.03 (d, J=7.8 Hz, 1 H), 7.44-7.60 (m, 3 H), 6.09 (br d, J=7.2 Hz, 1 H), 5.14 (deformed t, J=7.3 Hz, 1 H), 1.95-3.04 (m, 5 H), 2.05 (s, 3 H), 1.73 (s, 3 H), 1.61 (s, 3 H); MS m/z (relative intensity) 272 ($M^+$, 0.4), 212 ($M^+$-HAc, 100), 197 (38.3), 144 (40.6), 115 (26.9), 77 (11.0); $^{13}$C NMR (50.29 MHz) δ 196.67, 170.48, 139.82, 134.57, 133.95, 131.85, 128.79, 128.60, 126.76, 120.19, 72.56, 40.06, 30.26, 25.75, 21.14, 21.08, 17.79; IR (neat) 1730, 1685, 1595, 1225 $cm^{-1}$.

### (*1S,2R*)-4-Oxo-2-prenyl-1-tetralol (2)

A solution of (*1S,2R*)-4-oxo-2-prenyl-1-tetralol acetate (166 mg, 0.62 mmol) in methanol (3 mL) in 95% EtOH was stirred with $K_2CO_3$ (179 mg, 1.30 mmol) for 30 min at RT before addition of ether (60 mL) and a saturated $NH_4Cl$ solution (20 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane. The combined organic layers were washed with water and saturated $Na_2CO_3$ solution and dried over anhydrous $MgSO_4$. Solvent was removed at reduced pressure to give the crude product. It was purified by flash chromatography (1:5 ethyl acetate/hexane) to afford (*1S,2R*)-4-oxo-2-prenyl-1-tetralol (100 mg, 71.4%): mp 79-80°; $^1$H NMR (200 MHz) δ 7.96 (dd, J=8.2, 1.0 Hz, 1 H), 7.54-7.69 (m, 2 H), 7.32-7.45 (m, 1 H), 5.16 (deformed t, J=6.5 Hz, 1 H), 4.67 (br d, J=7.0 Hz, 1 H), 2.06-3.05 (m, 5 H), 2. 58 (br s, 1 H), 1.72 (s, 3 H), 1.60 (s, 3 H); MS m/z (relative intensity) 230 ($M^+$, 66.5), 212 ($M^+$-$H_2O$, 4.8), 173 (72.1), 161 (100), 160 (88.5), 105 (50.7), 77 (34. 0); $^{13}$C NMR (50.29 MHz) δ 197.48, 145.24, 134.57, 134.10, 131.07, 127.96, 126.99, 126.62, 120.65, 72. 08, 43.54, 41.33, 30.57, 25.86, 17.91; IR (KBr) 3200, 1680, 1600, 1300 $cm^{-1}$; $[\alpha]^D$ +4.8° (*c* 1.3, MeOH).

## RESULTS AND DISCUSSION

The key compound in this synthesis was isocapalponol (2). To prepare this compound, enantioselective prenylation of α-tetralone was achieved by using the known method (Meyers *et al.*, 1981) via chiral lithioenamines. α-Tetralone imine of (*R*)-(+)-2-amino-1-methoxy-3-phenylpropane (4) was readily prepared from α-tetralone and (*R*)-(+)-2-amino-1-methoxy-3-phenylpropane (3). Compound **3** was obtained as follows: (*R*)-Phenylalanine was first esterified with thionyl chloride and methanol to give the corresponding ester. This ester was reduced with $NaBH_4$ to afford (*R*)-phenylalaninol. This alcohol was methylated with KH-MeI to yield compound **3**. The compound **4** was transformed into its lithioenamine by using lithium diisopropylamide (LDA) and followed by prenylation. This prenylation led to **5** by predominant entry from the *Re* face (backside) of the



7a 7b

**Fig. 1.**

naphthenyl moiety producing, after hydrolysis, the (*S*)-(+)-2-prenyl-1-tetralone (6). The establishment of the *trans* relationship between the prenyl group and hydroxyl group in isocatalponol was achieved by stereoselective reduction of carbonyl group (Park and Jang, 1995). Reduction of compound **6** with sodium borohydride afforded *trans*-2-prenyl-1-tetralol (7a). This apparently exclusive formation of the *trans* isomer is somewhat surprising, even though a prenyl group on C-2 is at equatorial position. In 2-prenyl-1-tetralol (7), the alicyclic ring is assumed to be held in a half chair conformation with the 2-substituent occupying an equatorial position (Fig. 1) (Shadbolt *et al.*, 1976), based an $^1$H NMR study.

In the $^1$H NMR spectrum of compound **7a**, the 1-H signal which occurs as broad doublet at (=4.49 with a coupling constant J=7.5 Hz indicates the *trans* configuration of the two protons at C-1 and C-2 as in **7a** in Fig. 1. For comparision, compound **6** was reduced with L-selectride (Brown and Krishnamurthy, 1972) to give *cis*-2-prenyl-1-tetralol (7b). The 1-H signal of this compound (7b) occurs at δ=4.61 as a broad singlet in the $^1$H NMR spectrum.

Acetylation of (*1S,2S*)-2-prenyl-1-tetralol (7a) with acetic anhydride in the presence of pyridine, produced (*1S,2S*)-2-prenyl-1-tetralol acetate (8) in 94% yield. In the IR spectrum, the band at 3320 cm$^{-1}$ disappeared, and instead a strong peak at 1720 cm$^{-1}$ came out, showing the formation of an ester. In the $^1$H NMR spectrum, a three-proton singlet at δ 2.03 was observed due to methyl group of acetoxy function.

For the benzylic oxidation of compound **8**, several oxidation agents were tried without success before tert-butylhydroperoxide-pyridinium dichromate was found to be effective. With this reagent, compound **8** was converted to (*1S,2R*)-4-oxo-2-prenyl-1-tetralol acetate (9) in 42.5% yield, based on the recovered starting material.

The saponification of compound **9** with 20% NaOH solution gave isocatalponol (2), in 71.4% yield, which was our key intermediate to compound **1**. The obtained isocatalponol (2) showed expected physical and spectral characteristics (Inoue *et al.*, 1980). To our knowledge, this work is the first synthesis of isocatalponol (2).

Compound **1** was synthesized from isocatalponol (2) during its structural determination as mentioned previously. Consequently our work also contributes a new formal total synthesis of (+) 6-oxo-3,4,4a,5-tetrahydro-3-hydroxy-2,2-dimethylnaphtho-1,2-pyran (1).

## ACKNOWLEDGEMENT

This work has been supported by the Basic Science Research Institute Program (BSRI-95-3433), Ministry of Education.

## REFERENCES CITED

Brieskorn, C. H. and Poehlmann, R., The occurrence of isomeric catalponol and tectol dimethyl ether in the root of *Lippia origanoides*. *Arch. Pharm.*, 309, 829-836 (1976).

Brown, H. C. and Krishnamurthy, S., Lithium Tri-*sec*-butylborohydride. A New Reagent for the Reduction of Cyclic and Bicyclic Ketones with Super Stereoselectivity. A Remarkably Simple and Practical Procedure for the Conversion of Ketones to Alcohols in Exceptionally High Stereochemical Purity. *J. Am. Chem. Soc.*, 94, 7159-7161 (1972).

Chidambaram, N. and Chandrasekaram, S., *tert*-Butyl Hydroperoxide-Pyridinium Dichromate: A Convenient Reagent System for Allylic and Benzylic Oxidations. *J. Org. Chem.*, 52, 5048-5051 (1987).

Inoue, K., Inouye, H., Taga, T., Fujita, R., Osaki, K. and Kuriyama, K., Quinones and Related Compounds in Higher Plants. IX. Absolute Structures of Catalponol and Its Congeners. *Chem. Pharm. Bull.*, 28(4), 1224-1229 (1980).

Macambira, L. M. A., Andrade, C. H. S., Matos, F. J. A. and Craveiro, A. A., Naphthoquinoids from *Lippia sidoides*. *J. Nat. Pro.*, 49 (2), 310-312 (1986).

Meyers, A. I., William, D. R., Erickson, G. W., White, S. and Druelinger, M., Enantioselective Alkylation of Ketones via Chiral, Nonracemic Lithioenamines. An Asymmetric Synthesis of α-Alkyl and α,α'-Dialkyl Cyclic Ketones. *J. Am. Chem. Soc.*, 103, 3081-3087 (1981).

Mitsui, S., Kasahara, A. and Hanaya, K., The stereochemistry of a tetralin-1-ols. *Bull. Chem. Soc. Jpn.*, 41, 2523-2528 (1968).

Park, O. S. and Jang, B. S., Synthesis of 4-Hydroxycoumarin Derivatives-1: An Efficient Synthsis of Flocoumafen. *Arch. Pharm. Res.*, 18, 277-281 (1995).

Perrin, D. D., Armarego, L. F. and Perrin, O. R., *Purification of laboratory chemicals*. 2nd ed., Pergamon Press, New York, 1980.

Shadbolt, R. S., Woodward, D. R. and Birchwood, P. J., Synthesis of Some Tetrahydronaphthyl- and Flavanylcoumarins. *J. Chem. Soc. Perkin.*, I, 1190-1194 (1976).