

tion of the molecular weight in the presence of sodium dodecyl sulfate,⁹⁾ it appears that this enzyme is composed of two identical subunits with a molecular weight of approximately 50000.

The purified acid phosphatase was active toward *p*-nitrophenyl phosphate (relative activity (R.A.): 100), α -glycerophosphate (R.A.: 55), β -glycerophosphate (R.A.: 67), pyridoxal phosphate (R.A.: 41), fructose 6-phosphate (R.A.: 28), fructose 1,6-diphosphate (R.A.: 34), glucose 6-phosphate (R.A.: 36), 2'-AMP (R.A.: 25), 3'-AMP (R.A.: 70), 5'-AMP (R.A.: 14), ADP (R.A.: 55), ATP (R.A.: 55), NADP⁺ (R.A.: 51), and inorganic pyrophosphate (R.A.: 98). No phosphodiesterase activity was detected toward NAD⁺ and diphenyl phosphate. The enzyme had pH optimum around pH 5.5 with the K_m value of $3.9 \times 10^{-4}M$ for *p*-nitrophenyl phosphate.

Acknowledgements Thanks are due to Prof. K. Uehara, Osaka University, for his encouragement. The authors express their thanks to Mr. Y. Sakamoto of the Faculty of Medicine, Osaka University for carrying out the ultracentrifugal analysis. They are also indebted to Nissei Sangyo Co., Ltd. for metal analysis. They wish to thank Mr. H. Nakamura and Mr. M. Nishihashi for the technical assistance in preparing the enzyme. This work was supported in part by a grant from the Ministry of Education, Science and Culture of Japan.

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[Chem. Pharm. Bull.]
25(6)1462-1468(1977)

UDC 547.567.3.04 : 581.192

Studies on Quinones and Related Compounds in Higher Plants. V.¹⁾
Model Experiments for the Preparation of Tritium-labeled
Precursors for the Biosynthetic Studies of
Prenyl-naphthoquinone Congeners²⁾

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(Received September 29, 1976)

Methods for the preparation of [³-³H]-4-(2'-carboxyphenyl)-4-oxobutanoic acid and [4,8-³H₂]-2-carboxy-4-hydroxy- α -tetralone (CHT) starting from 3-methoxyphthalic anhydride have been demonstrated as model experiments for the preparation of several ³H-labeled compounds necessary for the elucidation of the biosynthetic pathways of prenylnaphthoquinone congeners occurring in *Catalpa ovata*.

Keywords—prenyl-naphthoquinones; biosynthesis; precursors; 4-(2'-carboxyphenyl)-4-oxobutanoic acid; 2-carboxy-4-hydroxy- α -tetralone; labeling methods

Recently we reported studies on the biosynthesis of prenylnaphthoquinone congeners of *Catalpa ovata* G. Don such as catalpalactone (1), catalponol (2) and 4,9-dihydroxy- α -lapachone (3) which are biosynthesized *via* 4-(2'-carboxyphenyl)-4-oxobutanoic acid (4).^{1,4,5)} As part of continuing efforts to clarify the mechanism of prenylation on their biosynthetic

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pathway, the synthesis of labeled 2-carboxy-4-hydroxy- α -tetralone (CHT) and 2-carboxy-4-oxo- α -tetralone (COT) were required. This paper describes model experiments including deuterium labeling to establish methods for the preparation of keto diacid (4), CHT and its derivatives labeled with tritium, respectively.

We first attempted to prepare 4-(2'-carboxyphenyl)-4-oxobutanoic acid (4) labeled at an aromatic position. The synthetic plan included the preparation of 4 bearing a phenolic hydroxy group and the subsequent hydrogenolysis of its phenyltetrazolyl ether to introduce the isotope into an aromatic position.⁶⁾

Fusion of 3-methoxyphthalic anhydride (5)⁷⁾ with succinic acid gave two methoxydilactones,⁸⁾ colorless plates (6), mp 107—109° and colorless needles (7), mp 193—195°. The dilactone (6) was then subjected to alkali hydrolysis followed by esterification with diazomethane yielding a dimethyl ester, which was demethylated with boron tribromide to give a phenol. After treatment of this substance with 50% sulfuric acid, the reaction product was immediately treated with diazomethane to give the succinyl group-eliminated product, methyl *m*-hydroxybenzoate (8). On the other hand, the same work up of the dilactone (7) yielded a decarboxylation product, methyl 4-(3'-hydroxyphenyl)-4-oxobutyrate (9). Accordingly, it was concluded that the dilactones (6) and (7) are the 4-methoxy- and 7-methoxy compounds, respectively, and that 8 arises from 6 *via* the 6'-methoxy (10) and 6'-hydroxy compounds (11), while 9 arises from 7 *via* the 3'-methoxy (12) and 3'-hydroxy compounds (13).

Next, methyl 4-(2'-carbomethoxy-3'-hydroxyphenyl)-4-oxobutyrate (13) was treated with 1-phenyl-5-tetrazolyl chloride in acetone in the presence of anhydrous potassium carbonate to give tetrazolyl ether (14). Catalytic hydrogenation of 14 over 10% Pd-C gave phthalide (15), which was formed by the hydrogenolysis of the tetrazolyloxy group accompanied by reduction of the C-4 carbonyl group, together with a further reduced compound (16). A solution of 15 in carbon tetrachloride was treated with N-bromosuccinimide under ultraviolet (UV) irradiation to give a bromide, which was hydrolyzed with 1N HCl followed by esterification with diazomethane to give methyl 4-(2'-carbomethoxyphenyl)-4-oxobutyrate (17).

The tetrazolyl ether (14) was then deuterated over 10% Pd-C to give [3,7-²H₂]-phthalide (15-d₂) and methyl [3',4,4-²H₃]-4-(2'-carbomethoxyphenyl)-butyrate (16-d₃). In the nuclear magnetic resonance (NMR) spectrum of 15-d₂, most of proton signals on C-3 (dd, δ 5.58) and C-7 (m, δ 7.81—8.01) of 15 disappeared. Bromination of 15-d₂ with N-bromosuccinimide followed by hydrolysis with 1N HCl and esterification of the product in the same way as in the case of 15 provided methyl [3'-²H]-4-(2'-carbomethoxyphenyl)-4-oxobutyrate (17-d₁). Also in the NMR spectrum of this product, most of the signals assignable to the C-3' proton disappeared. As we have already reported the mild hydrolysis of 17 to give 4,¹⁾ it may be safely concluded that the method to label C-3' position of 4 with tritium has been established.

Subsequently, CHT and its derivatives have been prepared starting from keto diester (17). This synthetic route would almost parallel the biosynthetic pathway. However, as the direct Dieckmann condensation of 17 gave the indandione compound (18),⁹⁾ the phthalide

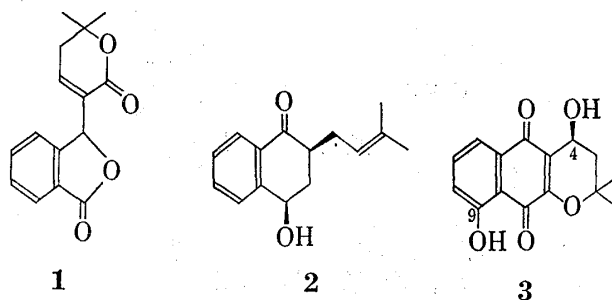


Fig. 1

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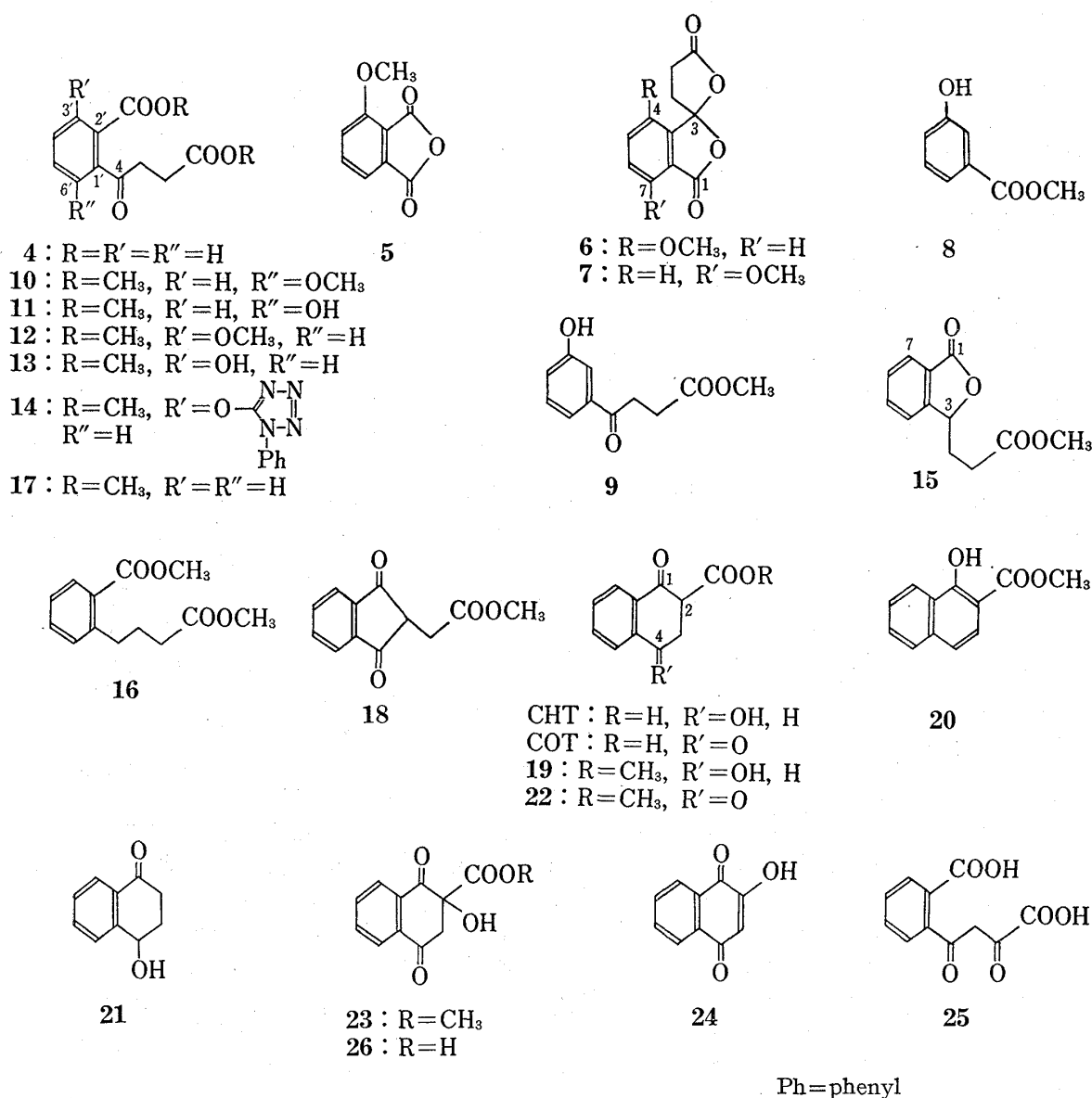


Fig. 2

(15) in which the ketone group of 17 has been reduced to the hydroxy group was used as a starting material to obtain a six-membered condensation product. Substance (15) was also obtainable by reduction of 17 with sodium borohydride. Dieckmann condensation of 15 in the presence of potassium *t*-butoxide in hot toluene produced the desired 2-carbomethoxy-4-hydroxy- α -tetralone (19) in 67% yield together with small amounts of methyl 1-hydroxy-2-naphthoate (20) and 4-hydroxy- α -tetralone (21). CHT methyl ester (19) in chloroform mostly assumes the enol form as exhibited by the NMR (in δ CDCl₃, 2.80 (d, $J=6.0$ Hz, C-3 methylene) and δ 4.80 (t, $J=6.0$ Hz, C-4 methine)) and the infrared (IR) (in CHCl₃, 1640 (strong, COOCH₃ of the enol form) and 1730 cm⁻¹ (weak, COOCH₃ of the keto form)). CHT methyl ester (19) was hydrolyzed with dil. NaOH at room temperature to give CHT, which was also found to assume the enol form on the basis of the NMR spectrum in acetone-*d*₆. This substance was so labile that even the crystalline form gradually underwent decarboxylation on standing at room temperature to yield 4-hydroxy- α -tetralone (21) which is also obtainable as a minor product on Dieckmann condensation of 15. Immediately after the hydrolysis of CHT methyl ester (19), the prompt treatment of the resultant CHT with diazomethane regenerated the methyl ester (19).

All attempts to convert CHT methyl ester (19) to COT methyl ester (22) with various oxidizing agents were unsuccessful. But oxidation of 19 with manganese dioxide gave 2-carbomethoxy-2-hydroxy-4-oxo- α -tetralone (23). Treatment of 23 with dil. NaOH gave lawsone (24). Although Campbell, *et al.*¹⁰ assumed keto acid (25) as a biogenetic intermediate of lawsone (24), the free carboxylic acid (26) corresponding to 23 seems to be a more probable precursor of 24 than 25. The possibility should be examined in the near future.

So far we have demonstrated the synthetic methods and chemical properties of CHT and related compounds. We next carried out the reduction of keto diester (17) with sodium borodeuteride yielding [3-²H]-phthalide (15-d₁) which was then subjected to the Dieckmann condensation as described above to give [4-²H]-CHT methyl ester (19-d₁). Comparison of the NMR spectra of both substances revealed that the C-3 proton of 15-d₁ was completely replaced by deuterium, while in the Dieckmann condensation product (19-d₁), 40% of the deuterium on C-4 was retained. Hydrolysis of 19-d₁ with dil. NaOH gave [4-²H]-CHT (CHT-d₁), the NMR spectrum of which indicated that most of the deuterium of 19-d₁ was retained in this compound. Accordingly, it has been demonstrated that [4,8-³H₂]-CHT methyl ester (19-t₂) and [4,8-³H₂]-CHT (CHT-t₂) are obtainable by the synthesis starting with [3,7-³H₂]-phthalide (15-t₂) which can be derived through the hydrogenolysis of 14 under tritium gas. Details of the synthesis of these tritium-labeled compounds and their administration to *Catalpa ovata* will be reported elsewhere.

Experimental¹¹⁾

Preparation of Methoxy-dilactones (6) and (7) from 3-Methoxyphthalic Anhydride (5)—3-Methoxyphthalic anhydride (5) (3.0 g), succinic acid (3.5 g) and anhyd. AcONa (1.5 g) were mixed well and heated at 230° for 14 min. After cooling to room temperature, the resulting solid mass was broken up and taken into CHCl₃ (40 ml) and H₂O (30 ml). After removal of the insoluble material by filtration, the aqueous layer was further extracted with CHCl₃ (2 × 20 ml). The combined CHCl₃ extracts were washed successively with sat. aq. NaHCO₃ and sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo*. The crystalline residue (1.82 g) was purified by chromatography on silica gel with C₆H₆ and C₆H₆-ether as eluent. The first eluted compound was recrystallized from EtOH to give 6 (391 mg) as colorless prisms, mp 107–109°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1790, 1618, 762, 725; NMR (CDCl₃) δ : 2.40–3.25 (m, -CH₂CH₂-), 3.95 (s, OCH₃), 7.21 (dd, $J=7.0$ and 2.0 Hz, 5-H), 7.45 (dd, $J=7.0$ and 2.0 Hz, 7-H), 7.65 (t, $J=7.0$ Hz, 6-H). Anal. Calcd. for C₁₂H₁₀O₅: C, 61.54; H, 4.30. Found: C, 61.29; H, 4.10. The second eluted compound was recrystallized from MeOH to give 7 (389 mg) as colorless needles, mp 193–195°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1790, 1772, 1607, 800, 699; NMR (CDCl₃) δ : 2.45–3.20 (m, -CH₂CH₂-), 4.01 (s, OCH₃), 7.10 and 7.15 (each dd, $J=8.0$ and 1.0 Hz, 4-H and 6-H), 7.75 (t, $J=8.0$ Hz, 5-H). Anal. Calcd. for C₁₂H₁₀O₅: C, 61.54; H, 4.30. Found: C, 61.79; H, 4.24.

Methyl 4-(2'-Carbomethoxy-6'-methoxyphenyl)-4-oxobutyrate (10)—A suspension of dilactone (6) (475 mg) in 2N NaOH (10 ml) was stirred for 1 hr at 60°. The cooled reaction mixture was acidified with 10% sulfuric acid and extracted with AcOEt (4 × 25 ml). The combined extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo* to give a crystalline residue (502 mg). After treatment of this substance with CH₂N₂, the product (504 mg) was purified by distillation to yield 10 as a colorless oil, bp 160° (bath temp.)/1 mmHg. TLC: C₆H₆-ether (7: 3), R_f 0.40; IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 1720, 1590, 1580; NMR (CDCl₃) δ : 2.62–2.90 (m, 2-H₂), 3.03–3.32 (m, 3-H₂), 3.70 (s, 1-COOCH₃), 3.81 and 3.84 (each s, 6'-OCH₃ and 2'-COOCH₃), 7.10 (dd, $J=8.0$ and 2.0 Hz, 5'-H), 7.38 (t, $J=8.0$ Hz, 4'-H), 7.58 (dd, $J=8.0$ and 2.0 Hz, 3'-H). Anal. Calcd. for C₁₄H₁₆O₆: C, 59.99; H, 5.75. Found: C, 59.80; H, 5.53.

Methyl 4-(2'-Carbomethoxy-6'-hydroxyphenyl)-4-oxobutyrate (11)—A 20 w/v % solution (2.8 ml) of BBr₃ in anhyd. CH₂Cl₂ was added dropwise to a solution of 10 (463 mg) in anhyd. CH₂Cl₂ (6.7 ml) at -74°. After standing at the same temperature for an additional 1 hr, the reaction mixture was brought to room temperature and kept for a further 2.5 hr. The reaction mixture was cooled again to -74° and H₂O (35 ml) was carefully added. After warming to room temperature, the CH₂Cl₂ layer was separated and the aqueous layer was extracted with CHCl₃ (3 × 25 ml). The combined organic extracts were washed successively with sat. aq. NaHCO₃ and sat. aq. NaCl, dried over anhyd. MgSO₄ and the solvent was removed *in vacuo* to give a crystalline residue (430 mg) which was recrystallized from CHCl₃-pet. ether to afford 11 as colorless plates, mp 86–87°. TLC: C₆H₆-ether (7: 3), R_f 0.20; IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3300, 1715, 1600, 1585, 920, 770; NMR (CDCl₃)

10) E. Grotzinger and I.M. Campbell, *Phytochemistry*, **11**, 675 (1972).

11) For general procedures, see reference 1.

δ : 2.68—2.95 (m, 2-H₂), 3.02—3.30 (m, 3-H₂), 3.71 (s, 1-COOCH₃), 3.87 (s, 2'-COOCH₃), 7.00—7.45 (m, 3 aromatic protons and phenolic OH; one proton signal disappeared upon treatment with D₂O). *Anal.* Calcd. for C₁₃H₁₄O₆: C, 58.65; H, 5.30. Found: C, 58.59; H, 5.36.

Treatment of Methyl 4-(2'-Carbomethoxy-6'-hydroxyphenyl)-4-oxobutyrate (11) with 50% Sulfuric Acid

—A mixture of **11** (60 mg) in 50% H₂SO₄ (20 ml) was refluxed gently for 2 hr. The mixture was diluted with H₂O (20 ml) and extracted with ether (3 × 20 ml). The combined ether extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo*. The resulting crystalline residue (35 mg) was methylated with CH₂N₂. Purification of the product by preparative TLC (C₆H₆-ether 7:3, *Rf* 0.40) followed by recrystallization from C₆H₆-pet. ether yielded colorless needles, mp 69—71°, which was identical in mixed mp, IR and NMR spectra with an authentic sample of methyl 3-hydroxybenzoate (**8**).

Methyl 4-(2'-Carbomethoxy-3'-methoxyphenyl)-4-oxobutyrate (12)—Dilactone (**7**) (527 mg) was hydrolyzed with 2N NaOH (15 ml) and subsequently methylated with CH₂N₂ to give **12** as a colorless oil, bp 140° (bath temp.)/0.8 mmHg. TLC: C₆H₆-ether (7:3), *Rf* 0.30; IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 1730, 1690, 1590, 790; NMR (CDCl₃) δ : 2.57—2.87 (m, 2-H₂), 3.13—3.40 (m, 3-H₂), 3.68 (s, 1-COOCH₃), 3.85 (s, OCH₃), 3.90 (s, 2'-COOCH₃), 7.14 (t, *J* = 5.0 Hz, 5'-H), 7.48 and 7.49 (each d, *J* = 5.0 Hz, 4'-H and 6'-H). *Anal.* Calcd. for C₁₄H₁₆O₆: C, 59.99; H, 5.75. Found: C, 59.94; H, 5.65.

Methyl 4-(2'-Carbomethoxy-3'-hydroxyphenyl)-4-oxobutyrate (13)—A 20 w/v % solution (8.4 ml) of BBr₃ in anhyd. CH₂Cl₂ was added dropwise to a solution of **12** (1.35 g) in anhyd. CH₂Cl₂ at -74°. Work up of the mixture as described above for **11** yielded a residue (1.13 g) which was chromatographed on silica gel (30 g) with increasing percentage of ether in C₆H₆ as eluent to give **13** (776 mg) as a colorless oil, bp 160° (bath temp.)/1 mmHg. TLC: C₆H₆-ether (7:3), *Rf* 0.40; IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3100, 1730, 1705, 1680, 1605, 1580, 810; NMR (CDCl₃) δ : 2.57—2.85 (m, 2-H₂), 2.96—3.25 (m, 3-H₂), 3.72 (s, 1-COOCH₃), 3.90 (s, 2'-COOCH₃), 6.76 (dd, *J* = 7.0 and 1.0 Hz, 4'-H), 7.05 (dd, *J* = 9.0 and 1.0 Hz, 6'-H), 7.48 (dd, *J* = 9.0 and 7.0 Hz, 5'-H), 10.80 (broad s, phenolic OH, disappeared upon treatment with D₂O). *Anal.* Calcd. for C₁₃H₁₄O₆: C, 58.65; H, 5.30. Found: C, 58.41; H, 5.09.

Treatment of Methyl 4-(2'-Carbomethoxy-3'-hydroxyphenyl)-4-oxobutyrate (13) with 50% Sulfuric Acid

—**13** (77 mg) was treated with 50% H₂SO₄ (20 ml) and subsequently methylated with CH₂N₂ by the same procedure as described for the preparation of **8**. The product was purified by preparative TLC (C₆H₆-ether 7:3, *Rf* 0.30) to give a crystalline residue (28 mg) which was recrystallized from ether-pet. ether to yield **9** as colorless leaflets, mp 104—105°. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3300, 1735, 1708, 1678, 1600, 880, 785; NMR (CDCl₃) δ : 2.60—2.88 (m, 2-H₂), 3.15—3.44 (m, 3-H₂), 3.69 (s, COOCH₃), 6.50 (broad s, phenolic OH; disappeared upon treatment with D₂O), 6.90—7.60 (m, 4 aromatic protons). *Anal.* Calcd. for C₁₁H₁₂O₄: C, 63.45; H, 5.81. Found: C, 63.60; H, 5.77.

Methyl 4-(2'-Carbomethoxy-3'-(1"-phenyl-5"-tetrazolyloxy)phenyl)-4-oxobutyrate (14)—A mixture of **13** (100 mg), 1-chloro-5-phenyltetrazole (102 mg) and anhyd. K₂CO₃ (206 mg) in anhyd. acetone (4 ml) was refluxed with stirring under N₂ for 8 hr. Water (20 ml) was added to the mixture cooled on an ice bath. The resulting mixture was adjusted to pH 2 with 1N HCl and was extracted with AcOEt (3 × 20 ml). The combined extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo* to give a residue which was purified by preparative TLC (C₆H₆-ether 7:3, *Rf* 0.35). The crystalline product (70 mg) was recrystallized from MeOH to give **14** as colorless prisms, mp 134—135°. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1730, 1688, 1605, 1545, 1510, 800, 760; NMR (CDCl₃) δ : 2.75 (t, *J* = 6.5 Hz, 2-H₂), 3.30 (t, *J* = 6.5 Hz, 3-H₂), 3.67 and 3.68 (each s, 2 × COOCH₃), 7.45—8.06 (m, 8 aromatic protons). *Anal.* Calcd. for C₂₀H₁₈O₆N₄: C, 58.53; H, 4.42; N, 13.65. Found: C, 58.65; H, 4.30; N, 13.68.

Hydrogenolysis of Tetrazolyloxy-ether (14)—A solution of tetrazolyloxy-ether (**14**) (85 mg) in MeOH (15 ml) was stirred under H₂ over a 10% Pd-C (prepared from 10% PdCl₂-HCl solution (1.10 ml) and activated charcoal (90 mg)) at room temperature. After 14 hr, the catalyst was filtered off and washed with MeOH. The combined filtrate and washings were evaporated *in vacuo* to give a crystalline residue (73 mg) which was purified by preparative TLC (C₆H₆-ether 7:3). The crystalline residue (30 mg) obtained from the zone around *Rf* 0.52 was recrystallized from ether-pet. ether to give **15** as colorless pillars, mp 36—37°. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1775, 1720, 1615, 1600, 760, 750; NMR (CDCl₃) δ : 1.86—2.67 (m, 1'-H₂ and 2'-H₂), 3.68 (s, COOCH₃), 5.58 (dd, *J* = 8.0 and 3.0 Hz, 3-H), 7.36—7.78 (m, 4, 5, 6-H₃), 7.81—8.01 (m, 7-H). Mass Spectrum *m/e*: 220 (M⁺). *Anal.* Calcd. for C₁₂H₁₂O₄: C, 65.44; H, 5.49. Found: C, 65.35; H, 5.52. A colorless oil (**16**) (12 mg) was obtained from the zone around *Rf* 0.75. IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 1720, 1600; NMR (CDCl₃) δ : 1.75—2.10 (m, 3-H₂), 2.13—2.56 (dd, *J* = 13.0 and 8.0 Hz, 2-H₂), 2.87—3.18 (t, *J* = 7.0 Hz, 4-H₂), 3.66 (s, 1-COOCH₃), 3.88 (s, 2'-COOCH₃), 7.07—7.50 (m, 4', 5', 6'-H₃), 7.77—8.00 (m, 3'-H). Mol. wt. Calcd. for C₁₃H₁₆O₄: 236.105. Found: 236.105.

Methyl 4-(2'-Carbomethoxyphenyl)-4-oxobutyrate (17)—A mixture of phthalide (**15**) (100 mg) and N-bromosuccinimide (70 mg) in anhyd. CCl₄ (2 ml) was irradiated with a UV lamp under N₂ for 30 min while it was stirred and warmed with an IR lamp. The precipitate was filtered off and washed with CCl₄. The combined filtrate and washings were evaporated *in vacuo* and the residue (104 mg) was stirred with 1N HCl (8 ml) for 30 min. The reaction mixture was extracted with AcOEt (4 × 20 ml). The combined AcOEt extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo*. The crude product was methylated with CH₂N₂ and purified by preparative TLC (C₆H₆-ether, *Rf* 0.58) to give **17** (65 mg)

as an oil, bp 145° (bath temp.)/1 mmHg. IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 1725, 1598, 1575, 800; NMR δ : 2.62—2.93 (m, 2-H₂), 3.05—3.30 (m, 3-H₂), 3.70 (s, 1-COOCH₃), 3.87 (s, 2'-COOCH₃), 7.35—8.01 (m, 4 aromatic protons); Mass Spectrum m/e : 250 (M⁺). Anal. Calcd. for C₁₃H₁₄O₅: C, 62.40; H, 5.64. Found: C, 62.31; H, 5.79.

Hydrogenolysis of Tetrazolyloxy-ether (14) with Deuterium—A solution of 14 (200 mg) in MeOH (30 ml) was stirred under deuterium over 10% Pd-C (prepared from 10% PdCl₂-HCl (1.10 ml) and activated charcoal (90 mg) under deuterium) at room temperature. Work up in the same manner as described above gave 15-d₂ (33 mg) as colorless crystals and 16-d₃ (25 mg) as a colorless oil. Mass Spectra: 15-d₂, m/e 222 (M⁺); 16-d₃, m/e 239 (M⁺).

Methyl [3'-²H]-4-(2'-Carbomethoxyphenyl)-4-oxobutyrate (17-d₁)—Treatment of 15-d₂ (29 mg) in the same way as described for the conversion of 15 to 17 gave 17-d₁ (18 mg) as a colorless oil, which showed the same *Rf* as that of 17. Mass Spectrum m/e : 251 (M⁺).

3-(2'-Carbomethoxyethyl)-phthalide (15)—NaBH₄ (38 mg) was added to an ice-cooled solution of 17 (220 mg) in MeOH (3 ml) with stirring and the mixture was stirred at room temperature for an additional hour, diluted with H₂O (30 ml), adjusted to pH 4.0 with 1N HCl and extracted with CHCl₃ (3 × 15 ml). The combined CHCl₃ extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo*. The crystalline residue (215 mg) was recrystallized from ether-pet. ether to yield colorless pillars, mp 36—37°, which were identified with 15 obtained by hydrogenolysis of 14 by mixed mp and IR comparison.

Dieckmann Condensation of 3-(2'-Carbomethoxyethyl)-phthalide (15)—A solution of phthalide (15) (180 mg) in anhyd. toluene (1 ml) was added dropwise to a suspension of potassium *t*-butoxide (300 mg) in anhyd. toluene (3 ml) at 110—115° (bath temp.) under N₂ over a period of 45 min and the resulting mixture was heated under gentle reflux for an additional hour. The ice-cooled reaction mixture was diluted with H₂O (20 ml), adjusted to pH 2 with 1N HCl and extracted with ether (3 × 20 ml). The extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and concentrated to 20 ml, to which excess CH₂N₂-ether was added and immediately evaporated *in vacuo*. The oily residue (158 mg) was purified by preparative TLC (C₆H₆-ether 7:3). The crystalline residue (15.0 mg) obtained from the zone around *Rf* 0.64 was recrystallized from EtOH to give 20 as colorless needles, mp 77—78°. IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3050, 1660, 1635, 1600, 1580; NMR (CDCl₃) δ : 3.90 (s, COOCH₃), 7.13—7.80 (m, 3, 4, 5, 6, 7-H₂), 8.30—8.50 (m, 8-H), 11.98 (s, phenolic OH, disappeared upon treatment with D₂O). Anal. Calcd. for C₁₂H₁₀O₃: C, 71.28; H, 4.98. Found: C, 71.23; H, 5.19. The crystalline residue (120 mg) obtained from the zone around *Rf* 0.28 was recrystallized from C₆H₆-*n*-hexane to give 19 as colorless needles, mp 67—68°. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3300—3200, 1755 (sh.), 1735, 1715 (sh.), 1670 (sh.), 1642, 1615, 1590, 1560; IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3600—3400, 1730, 1715 (sh.), 1680, 1640, 1610, 1595, 1560; NMR (CDCl₃) δ : 2.35 (broad s, 4-OH, disappeared upon treatment with D₂O), 2.80 (d, *J*=6.0 Hz, 3-H₂), 3.82 (s, COOCH₃), 4.81 (t, *J*=6.0 Hz, 4-H), 7.38—8.10 (m, 4 aromatic protons), 12.43 (s, 1-OH, disappeared upon treatment with D₂O). Anal. Calcd. for C₁₂H₁₂O₄: C, 65.45; H, 5.49. Found: C, 65.53; H, 5.70. From the zone around *Rf* 0.15, 21 was obtained as a colorless oil (7 mg). IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3400, 1680, 1600, 930; NMR (CDCl₃) δ : 1.97—2.45 (m, 3-H₂), 2.50—3.04 (m, 2-H₂), 2.90 (broad s, 4-OH, disappeared upon treatment with D₂O), 4.93 (dd, *J*=4.5 and 7.0 Hz, 4-H), 7.16—7.66 (m, 5, 6, 7-H₂), 7.87—8.09 (m, 8-H).

2-Carboxy-4-hydroxy- α -tetralone (CHT)—A mixture of CHT methyl ester (19) (96 mg) in 0.5N NaOH (4 ml) was stirred at room temperature for 2 hr. The ice-cooled reaction mixture was adjusted to pH 2 with 1N HCl and extracted with ether (4 × 7 ml). The combined ether extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo* to give a crystalline residue (82 mg) which was recrystallized from ether to give CHT as colorless prisms, mp 107—109° (decomp.). IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3300—3200, 2700—2300, 1640, 1605, 1585, 1560; NMR (acetone-*d*₆) δ : 2.73 (dd, *J*=15.5 and 9.0 Hz, 3-H_{ax}), 2.83 (dd, *J*=15.5 and 6.0 Hz, 3-H_{eq}), 4.87 (dd, *J*=9.0 and 6.0 Hz, 4-H), 5.50—7.30 (broad s, 4-OH and COOH, disappeared on addition of D₂O), 7.25—8.10 (m, 4 aromatic protons), 13.0 (broad s, 1-OH, disappeared on addition of D₂O). An ice-cooled methanolic solution of CHT thus obtained was mixed with CH₂N₂-ether and the mixture was immediately concentrated to give CHT methyl ester (19).

Oxidation of CHT Methyl Ester (19) with MnO₂—Activated MnO₂ (200 mg, prepared acc. to the method of Attenburrow, *et al.*¹²) was added to a stirred solution of 19 (50 mg) in CHCl₃ (3 ml) and stirring was continued at room temperature for 15 hr. The precipitate was filtered off and washed with hot CHCl₃. The filtrate and washings were combined and evaporated *in vacuo* to give a residue which was purified by preparative TLC (CHCl₃, *Rf* 0.40). Recrystallization of the crystalline product (25 mg) from ether-pet. ether to afford 23 as colorless needles, mp 95—98°. IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3500, 1740, 1695, 1595, 955, 930; NMR (CDCl₃) δ : 3.11 and 3.65 (each d, *J*=17.0 Hz, 3-H₂), 3.70 (s, COOCH₃), 4.55 (broad s, 2-OH, disappeared on addition of D₂O), 7.70—7.95 (m, 6, 7-H₂), 7.95—8.23 (m, 5, 8-H₂). Mol wt. Calcd. for C₁₂H₁₀O₅: 234.053. Found: 234.049.

Alkali Treatment of 2-Hydroxy-CHT Methyl Ester (23)—A mixture of 23 (20 mg) in 1N NaOH (1 ml) was stirred at room temperature for 2 hr. The resulting solution was adjusted to pH 2 with 1N HCl and extracted with AcOEt (3 × 5 ml). The combined AcOEt extracts were washed with sat. aq. NaCl, dried over anhyd. MgSO₄ and evaporated *in vacuo*. The yellow crystalline residue (14.4 mg) was recrystallized

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from acetic acid to give yellow needles, mp 193—195°, which were identified with an authentic sample of lawsone (24) by mixed mp and comparisons of IR and NMR spectra.

[3-²H]-3-(2'-Carbomethoxyethyl)-phthalide (15-d₁)—Reduction of 17 (250 mg) with NaBD₄ in the same manner as described above for the conversion of 17 to 15 gave 15-d₁ as crystals (215 mg), the NMR spectrum of which was identical with that of 15 except for the absence of a signal at δ 5.58 assignable to a proton on C-3 of 15. Mass Spectrum *m/e*: 221 (M⁺).

[4-²H]-2-Carbomethoxy-4-hydroxy-α-tetralone (19-d₁)—Dieckmann condensation of 15-d₁ (120 mg) was carried out using the same procedure as described for the preparation of 19. The crude product (108 mg) was purified by preparative TLC (C₆H₆-ether 7:3). From the zone corresponding to that of 19, 19-d₁ (35 mg) was obtained as crystals.

[4-²H]-2-Carboxy-4-hydroxy-α-tetralone (CHT-d₁)—Hydrolysis of CHT-d₁ methyl ester (19-d₁) in the same manner as described for 19 gave CHT-d₁ (20 mg) as colorless prisms. The NMR spectrum of this substance showed the deuteration of 40% of the proton on C-4.

Acknowledgement This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture to which the authors express their gratitude. Thanks are also due to the members of the Microanalytical Center of this University for elemental analyses, to Dr. A. Kato and Mrs. M. Uobe of this Faculty for measurements of MS and NMR spectra, and to Mrs. J. Tanaka of the Institute for Chemical Research of this University for determinations of high resolution mass spectra.

[Chem. Pharm. Bull.]
25(6)1468—1470(1977)

UDC 547.384.04 : 547.245.04 : 546.824.04

Selective Reduction of Conjugated Enones and Dienones with Trialkylsilane and Titanium Tetrachloride

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(Received October 2, 1976)

The reaction of conjugated enones and dienones with trimethyl- or triethyl-silane in the presence of titanium tetrachloride followed aqueous workup produced the corresponding α,β-saturated ketones. This particular Lewis acid catalysis has advantage over Rh(I) complex catalysis which fails for sterically hindered substrates.

Keywords—hydrogenation enone; hydrogenation dienone; hydrosilylation titanium catalyst; hydrosilylation trialkylsilane; silane trialkyl

Catalytic hydrosilylation of α,β-unsaturated carbonyl compounds has been employed as a synthetic tool for obtaining silyl enol ethers²⁾ (or ketene alkyl silyl acetals³⁾) or saturated carbonyl compounds which are readily formed on hydrolytic workup.^{3a,4)} Among a variety of catalysts,⁵⁾ classical Speier catalyst (chloroplatinic acid in isopropanol)⁶⁾ and tris(triphenyl-

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