[Chem. Pharm. Bull. 28(8)2460—2467(1980)]

New Synthetic Routes to β-Polyketone Derivatives: Reactions of 3-Acetyl-2-hydroxy-6-methyl-4H-4-pyranone and 7-Chloro-2,2-dimethyl-2H,4H,5H-pyrano[4,3-*d*]-1,3-dioxin-4,5-dione with an Enamine (Studies on the β-Carbonyl Compounds connected with the β-Polyketides. III)[1]

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(Received March 19, 1980)

The reaction of 1-morpholino-1-cyclohexene **2** with 3-acetyl-2-hydroxy-6-methyl-4H-4-pyranone **1** gave a condensation product **3**, which was subsequently transformed into the 4-pyrone **4**, the β-triketone **10** and the phenol **12**. The reaction of **2** with 7-chloro-2,2-dimethyl-2H,4H,5H-pyrano[4,3-*d*]-1,3-dioxin-4,5-dione **13** gave three condensation products, **14**, **15** and **16**.

Keywords——β-polyketones; biogenetic-type synthesis; condensation reaction; pyrones; enamines; base-catalyzed cyclization

Various studies on synthetic methods for and reactions of β-polyketones have been reported, focusing on biogenetic-type syntheses of β-polyketones derived from natural sources,[3] either in protected or unprotected forms. We have investigated the condensation reactions of an enamine, 1-morpholino-1-cyclohexene **2**, with pyrones, *viz.*, 3-acetyl-2-hydroxy-6-methyl-4H-4-pyranone (dehydroacetic acid **1**) and 7-chloro-2,2-dimethyl-2H,4H,5H-pyrano-[4,3-*d*]-1,3-dioxin-4,5-dione **13** and subsequent transformations of the products into β-polyketones; this is a new method for the introduction of β-polyketone groups.

(A) Reaction of the Enamine 2 with Dehydroacetic Acid 1

First, the reaction of the enamine **2** with dehydroacetic acid **1** was undertaken. Although the reactions of dehydroacetic acid with primary amines,[4] secondary amines,[5] bromine,[6] hydrazines,[7] and benzaldehydes,[8] and photochemical reactions[9] have been reported, the reaction with enamines has not been described. We were particularly interested to determine whether the enamine shows a preference for one or more of the reaction sites of the polyfuctional molecule.

The reaction of the enamine **2** with dehydroacetic acid **1** in toluene at 60—70° for 3 hr gave a condensation product **3** (50%), mp 168—170°, $C_{14}H_{16}O_4$, which was isomerized to **4**

1) For a preliminary communication of this work, see S. Tobinaga, N. Takeuchi, and H. Nakagawa, *Chem. Commun.*, **1972**, 890. (Studies on the β-Carbonyl Compounds connected with the β-Polyketides Part I; Part II, N. Takeuchi, M. Murase, K. Ochi, and S. Tobinaga, *Chem. Commun.*, **1976**, 820).
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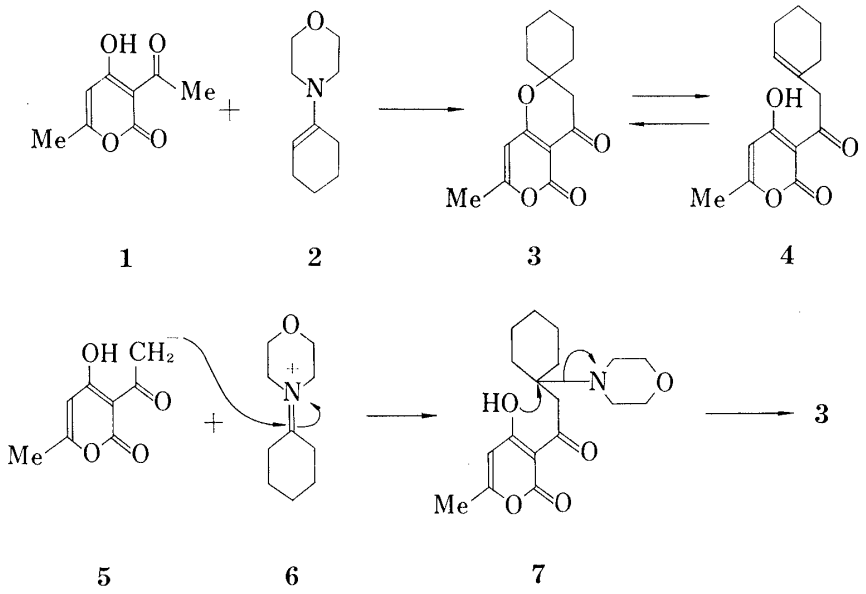


Chart 1

(80%), mp 108—109° upon treatment with 1 N KOH–MeOH at room temperature for 2 days. The isomer **4** reverted to **3** when treated with conc. HCl or H_2SO_4.

The structures of the condensation product **3** and the isomer **4** were supported by their physical data; infrared (IR) and ultraviolet (UV) spectra showed the presence of the 2-pyrone nucleus in both **3** and **4**, while the nuclear magnetic resonance (NMR) spectrum of **4** showed the presence of an acidic proton at δ 16.80 (1H, s) and an olefinic proton at δ 5.60 (1H, m) which were absent in **3**.

The condensation reaction may take place *via* the anion **5**, which attacks the iminium structure of the enamine **6**, followed by elimination of morpholine by the attack of the hydroxy group to form **3** as shown in Chart 1.

The chemical transformation of the pyrone **3** was effected by refluxing in conc. HCl to give the 4-pyrone **8** (60%), bp 118—120° at 0.2 mmHg, and the phenol **9** (20%), mp 104—105°, MS *m/e* 162 (M^+). On treatment with $Ba(OH)_2$, the 4-pyrone **8** was converted into the triketone **10** (73.4%), which was identified as the pyrrolidine dienamine **11**, mp 104—106°. Further, the triketone **10** was converted to an Aldol condensation product **12** (75%). mp 103—105°, when treated with 20% aqueous KOH on a steam bath for 30 min.

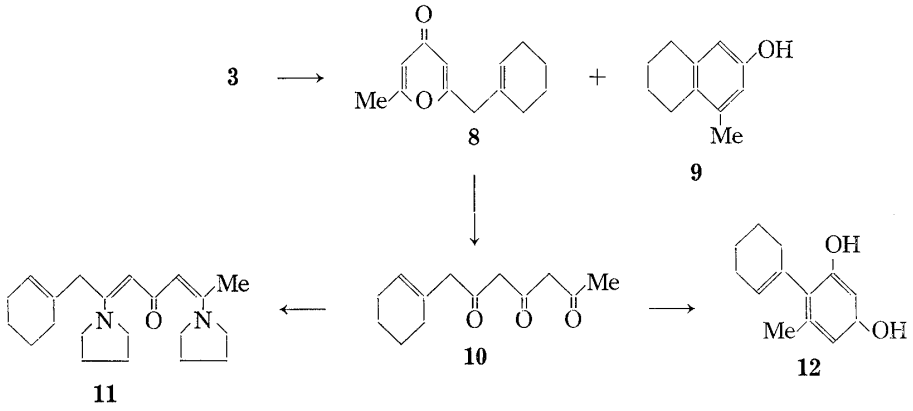


Chart 2

(B) Reaction of the Enamine 2 with 7-Chloro-2,2-dimethyl-2H,4H,5H-pyrano[4,3-*d*]-1,3-dioxin-4,5-dione 13

Although the reactions of a very reactive 2-pyrone, the 7-chloropyrano-1,3-dioxin **13** (which can be readily synthesized from malonyl dichloride and acetone), were studied extensively by Elvidge and his co-workers,[10] the reaction with enamines has not been reported. We studied the reaction of the enamine **2** with the reactive pyrone **13** to investigate whether the enamine shows a preference for reaction at one or several reaction sites, namely, the C_7, C_{8a}, C_4, and C_5 positions.

Reaction of the 7-chloropyrano-1,3-dioxin **13** with the enamine **2** in dry CCl_4 at 50—60° for 2 hr afforded four condensation products, namely, **14** (32.2%), $C_{15}H_{16}O_6$, mp 170—172.5°, **15** (42.8%), $C_{15}H_{16}O_6$, mp 118—120°, **16** (5%), $C_{18}H_{18}O_5$, mp 218—220° (dec.) and **17** (trace), mp 181—182° (dec.).

Structures were proposed for the condensation products **14** and **15** on the basis of their physical data; **14** and **15** have the same molecular formular, and the NMR spectra show that they retain the pyrano-1,3-dioxin nucleus and possess one cyclohexane moiety. Further, **14** has an olefinic proton at δ 5.67 (1H, s) and **15** has an olefinic proton at δ 5.98 (1H, s). The structure of the condensation product **16** was proposed on the basis of the following physical and chemical evidence; the NMR spectrum of **16** shows that it has eight additional methylenic protons of another cyclohexane moiety instead of the acetonide signal of **14** or **15**, and when the condensation reaction was carried out in the presence of excess **2** with respect to **13**, the ratio of the condensation products was changed (increase of **16** and decrease of **15**). Evidently, these results show that the product **16** is formed by the further reaction of **15** with the enamine **2**. Another condensation product **17** was identified by direct comparison with an authentic sample prepared from **13** and morpholine.

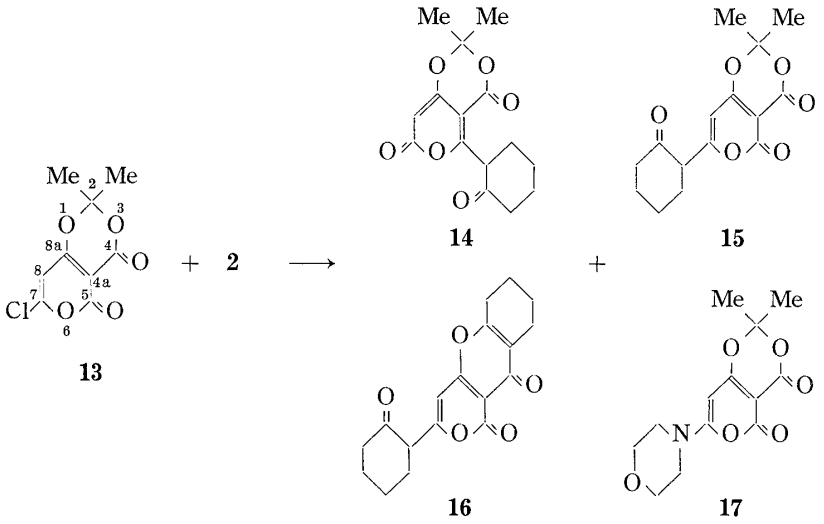
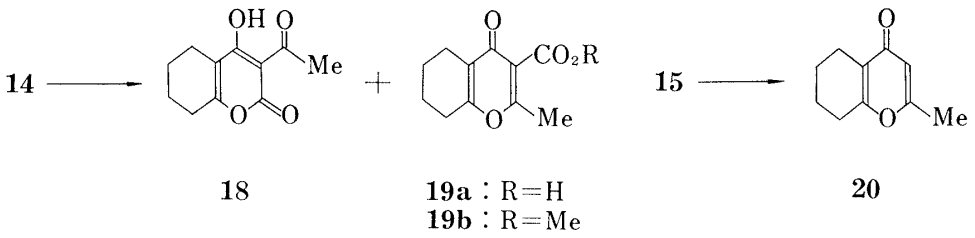


Chart 3

The following chemical transformations were investigated to support the proposed structures of the condensation products **14**, **15** and **16**. Treatment of **14** with conc. HCl–AcOH (1: 1) gave two acidic compounds **18** (56%), mp 74—76°, $C_{11}H_{12}O_4$, λ_{max}^{EtOH} 315 nm (ε, 11400) and **19a** (14%), mp 133—133.5°, $C_{11}H_{12}O_4$, λ_{max}^{EtOH} 251 nm (ε, 3950); methylester **19b**, mp 70—72.5°. Similar treatment of **15** afforded a neutral compound **20** (40%), mp 95—96°, $C_{10}H_{12}O_2$, λ_{max}^{EtOH} 252 nm (ε, 5600). The above transformations of **14** into **18** and **19**, and of **15** into **20** can be assumed to occur as follows; the keto acids **21** and **22** may be intermediates in acid

10) J.M.A. Al-Rawi and J.A. Elvidge, *J. Chem. Soc.* (*C*), **1973**, 2432 and references cited therein.



18 **19a** : R=H **19b** : R=Me 20

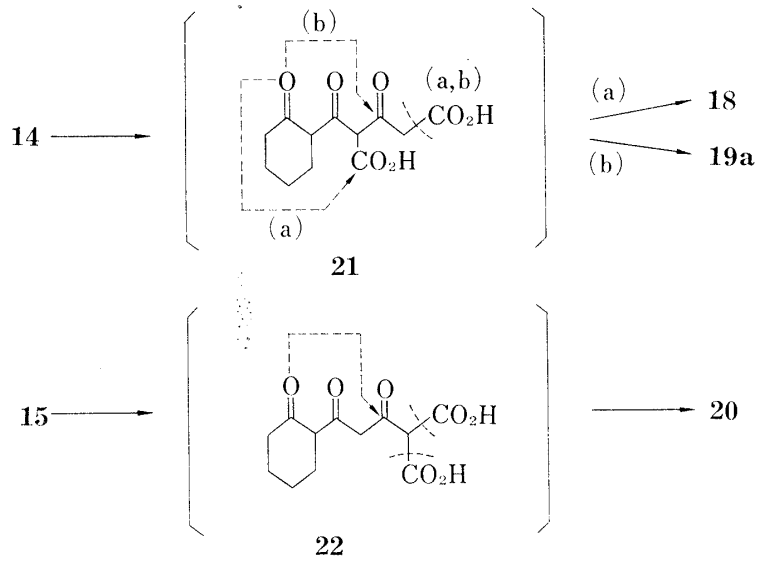
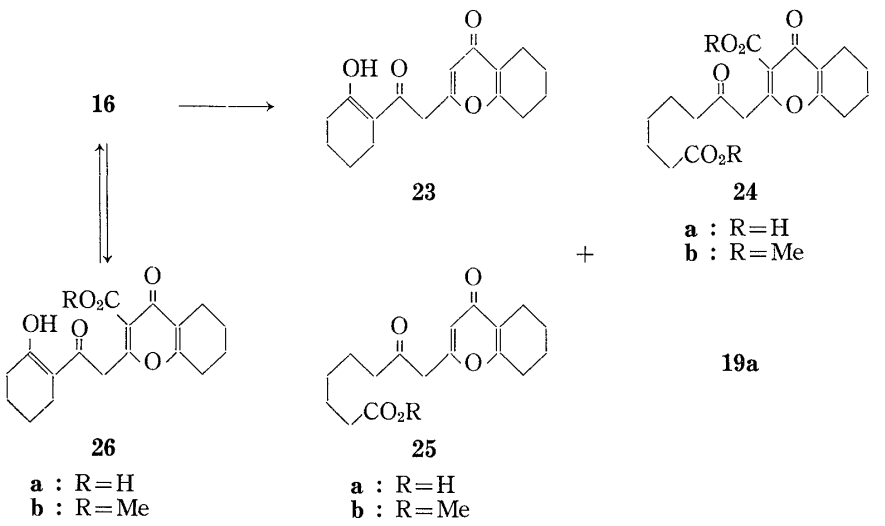


Chart 4



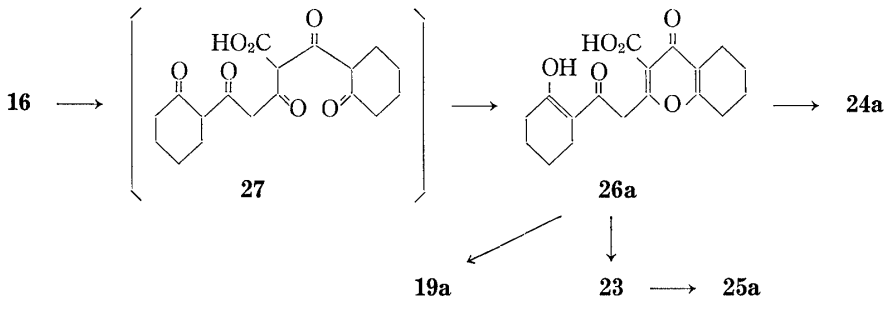


Chart 5

hydrolysis, and these intermediates are recyclized and decarboxylated to yield the corresponding pyrones by the routes shown in Chart 4, namely, **21** to **18** by route (a), **21** to **19a** by route (b) and **22** to **20**.

Treatment of **16** with conc. HCl–AcOH (1 : 1) for 6 hr gave a neutral compound **23** (5%), mp 124—126°, $C_{17}H_{20}O_4$, λ_{max}^{EtOH} 253 nm (ε, 14400) and 286 nm (ε, 7050), and three acidic compounds, **19a** (20%), **24a** (27.5%), mp 110—111°, $C_{18}H_{22}O_7$, λ_{max}^{EtOH} 252 nm (ε, 11200); methylester **24b**, liquid, and **25a** (39.7%), mp 63—65.5°, $C_{17}H_{22}O_5$, λ_{max}^{EtOH} 252 nm (ε, 13400); methylester, **25b**, liquid. Treatments of **16** under basic conditions were also investigated. Refluxing of **16** with 5% Na_2CO_3 gave **24a** and **19a** in yields of 30% and 36%, respectively. Treatment of **16** with $Ba(OH)_2$ at room temperature afforded an acid **26a** (46%), mp 151—153°, λ_{max}^{EtOH} 260 nm (ε, 7100) and 285 nm (ε, 7970); methylester **26b**, mp 115—116°, which was converted to **16** when treated with *p*-toluenesulfonic acid.

These transformations support the structure of the condensation product **16** and may take place *via* the β-pentaketone **27** and the 4-pyrone acid **26a** by hydrolysis of **16**, followed by decarboxylation to yield **23** and *retro*-Claisen condensation reaction to give the corresponding compounds **19a**, **24a** and **25a** as shown in Chart 5.

The condensation reaction of 7-chloropyrano-1,3-dioxin **13** with the enamine **2** may proceed as follows; the product **14** may form through the ketene intermediate **28** by attack of the enamino anion at C_5 of **13**. Compound **15** is a simple displacement product of the chlorine atom by the enamino anion, and **16** may be a further reaction product of **15** through the intermediate **29** by attack of the enamino anion at C_4 of **15** followed by elimination of morpholine by attack of the hydroxy group to form **16** as shown in Chart 6.

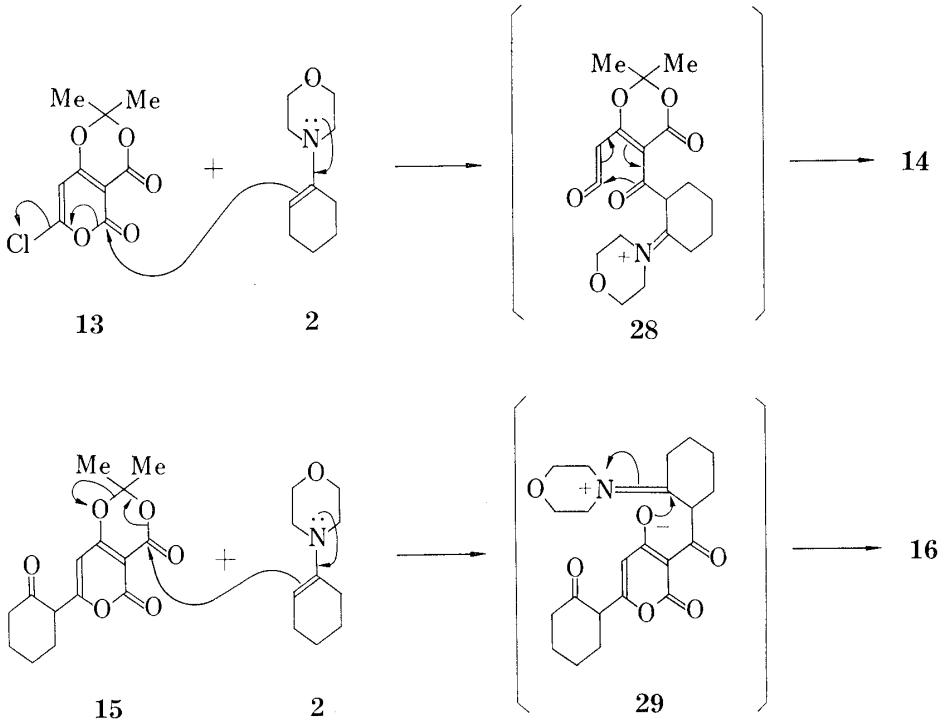


Chart 6

Summarizing the condensation reactions of the enamine **2** with dehydroacetic acid **1** and the 7-chloropyrano-1,3-dioxin **13**, the condensation products **3**, **14**, **15** and **16** are potentially equivalent to the β-triketone **10**, the β-triketo acids **21** and **22** and the β-pentaketo acid **27**, so these reactions provide new methods for the introduction of the β-polyketone group.

Experimental[11]

7′-Methylspiro(cyclohexane-2′H,3′H,5′H-1,2′-pyrano[4,3-*b*]-1′-oxin-4′,5′-dione) (3)——1-Morpholino-1-cyclohexene **2** (9.8 g) was added dropwise to a solution of dehydroacetic acid **1** (13.5 g) in ab. toluene (30 ml) with stirring at 60—70°, and the mixture was stirred at 60—70° for 3 hr. The resulting mixture was washed with 5% HCl and H_2O, dried and concentrated. The residue was recrystallized from ether–*n*-hexane to yield 10 g (50%) of **3** as colorless crystals, mp 168—170°. *Anal.* Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.64; H, 6.49. MS *m/e*: 248 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1745, 1660 and 1638. UV λ_{max}^{EtOH} nm (ε): 310 (17400). NMR ($CDCl_3$) δ: 2.32 (3H, s, $-CH_3$), 2.72 (2H, s, $-COCH_2-$), and 6.02 (1H, s, olefinic H).

3-[2-(1-Cyclohexenyl)acetyl]-4-hydroxy-6-methyl-2H-2-pyranone (**4**)——A mixture of **3** (5 g) and 1 N KOH–MeOH (50 ml) was left for 2 days at room temperature. The solution was concentrated under a vacuum, acidified with 5% HCl and then extracted with ether. The ether layer was washed with H_2O, dried and concentrated. The residue was recrystallized from ether–*n*-hexane to yield 4 g (80%) of **4** as colorless crystals, mp 108—109°. *Anal.* Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.50; H, 6.55. IR ν_{max}^{KBr} cm^{-1}: 1710, 1650 and 1615. UV λ_{max}^{EtOH} nm (ε): 313 (28800). NMR ($CDCl_3$) δ: 2.29 (3H, s, $-CH_3$), 3.79 (2H, s, $-COCH_2-$), 5.60 (1H, s, olefinic H), 6.01 (1H, s, olefinic H) and 16.80 (1H, s –OH).

2-(1-Cyclohexenylmethyl)-6-methyl-4H-4-pyranone (**8**) **and 5,6,7,8-Tetrahydro-4-methyl-2-naphthalenol** (**9**)——A mixture of **3** (10 g) and conc. HCl (50 ml) was heated for 30 min at 105°. The reaction mixture was poured into ice-water and the mixture was extracted with ether. The aqueous layer (A) and the ether layer (B) were separated. A was made basic with sat. $NaHCO_3$ and then extracted with ether. The ether layer was washed with H_2O, dried and concentrated. The residue was distilled to give 5.6 g (60%) of **8** as a colorless oil, bp 118—129°/ 0.2 mmHg. IR $\nu_{max}^{liq.}$ cm^{-1}: 1665 and 1615. UV λ_{max}^{EtOH} nm (ε): 247 (16300). NMR ($CDCl_3$) δ: 2.26 (3H, s,$-CH_3$), 3.12 (2H, s, $-CH_2-$), 5.66 (1H, m, olefinic H) and 6.13 (2H, s, olefinic H).

B was extracted with 10% KOH. The aqueous layer was acidified with 5% HCl and then extracted with ether. The ether layer was washed with H_2O, dried and concentrated. The residue was recrystallized from ether–*n*-hexane to yield 1.8 g (20%) of **9** as colorless crystals, mp 104—105°. *Anal.* Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.25; H, 8.85. MS *m/e*: 162 (M^+), 147 (M^+-CH_3) and 134 ($M^+-C_2H_4$). IR ν_{max}^{KBr} cm^{-1}: 3220 and 1593. UV λ_{max}^{EtOH} nm (ε): 286 (2750). NMR ($CDCl_3$) δ: 2.18 (3H, s, $-CH_3$), 4.46 (1H, m, aromatic H), 6.46 (1H, d, J=2.2 Hz aromatic H) and 6.55 (1H, d, J=2.2 Hz, aromatic H).

1-(1-Cyclohexenyl)-2,4,6-heptanetrione (**10**)——A saturated aqueous solution of $Ba(OH)_2$ (1.4 g) was added to a solution of **8** (1 g) in methanol (7.5 ml) and H_2O (7.5 ml), and the whole was refluxed on a water bath for 30 min. The precipitated Ba salts were separated from the solution by filtration, and the filtrate was acidified with 5% HCl and then extracted with chloroform. The extract was washed with H_2O, dried and concentrated to give 0.8 g (73.4%) of **10** as an oil. IR $\nu_{max}^{liq.}$ cm^{-1}: 1720 and 1590.

1-(1-Cyclohexenyl)-2,6-dipyrrolidino-2,5-heptadien-4-one (**11**)——Pyrrolidine (1.67 g) was added dropwise to a solution of **10** (1.1 g) in ethanol (2 ml). The reaction mixture was refluxed on a water bath for 30 min and then allowed to stand overnight at room temperature. The separated crystals were collected and recrystallized from methanol to yield 2.2 g (80%) of **11** as yellow crystals, mp 104—106°. IR ν_{max}^{KBr} cm^{-1}: 1620 and 1590. UV λ_{max}^{EtOH} nm (ε): 378 (10200). NMR ($CDCl_3$) δ: 2.58 (3H, s, $-CH_3$), 3.33 (8H, t, J=7 Hz, $N-CH_2-$), 3.93 (2H, m, $-CH_2-$), 4.98 (1H, d, J=2 Hz, CO–CH=C), 5.03 (1H, d, J=2 Hz, CO–CH=C) and 5.45 (1H, m, olefinic H).

4-(1-Cyclohexenyl)-5-methyl-1,3-benzenediol (**12**)——A mixture of **10** (0.8 g) and 20% KOH (10 ml) was refluxed on a water bath for 30 min. The reaction mixture was washed with ether, acidified with 10% HCl and then extracted with ether. The ether layer was washed with sat. $NaHCO_3$ and H_2O, dried and concentrated. The residue was recrystallized from ether–*n*-hexane to yield 0.6 g (75%) of **12** as colorless crystals, mp 103—104.5°. *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.21; H, 7.81. IR ν_{max}^{KBr} cm^{-1}: 3380, 1625 and 1595. UV λ_{max}^{EtOH} nm (ε): 283 (5300). NMR ($CDCl_3$) δ: 2.16 (3H, s, $-CH_3$), 4.89 (1H, m, aromatic OH), 5.47 (1H, m, aromatic OH), 5.81 (1H, m, olefinic H) and 6.23 (2H, s, aromatic H×2).

Reactions of 7-Chloro-2,2-dimethyl-2H,4H,5H-pyrano[4,3-*d*]-1,3-dioxin-4,5-dione (**13**) **with 1-Morpholino-1-cyclohexene** (**2**)——Method A: Compound **2** (6.7 g) was added dropwise to a solution of **13** (4.6 g) in dry carbon tetrachloride (200 ml) with stirring at 60°, and then the mixture was stirred at 60° for 2 hr. The solution was concentrated under a vacuum, taken up into chloroform and then washed with 5% HCl and H_2O. The organic layer was dried and concentrated, and the residue was subjected to silica gel chromatography. The first chloroform elution gave 2 g (32.2%) of 2,2-dimethyl-5-(2-oxocyclohexyl)-2H,4H,7H-pyrano[4,3-*d*]-1,3-dioxin-4,7-dione (**14**) as colorless crystals (benzene), mp 170—172.5°. *Anal.* Calcd for

11) All melting points are uncorrected. IR spectra were recorded with a Hitachi 215 spectrometer, UV spectra with a Hitachi 124 spectrometer, NMR spectra with a Varian T-60 spectrometer with tetramethylsilane as an internal standard ($CDCl_3$ soln.), and MS spectra with a Hitachi RMS-4 spectrometer at 70 eV using the direct insertion technique. Elementary analyses were done by Mrs. K. Sasaki, Kissei Pharmaceutical Company, Matsumoto, Japan. Mallinckrodt silica gel (100 mesh) and Merck Kieselgel G nach Stahl were used for column chromatography and TLC, respectively.

$C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.67; H, 5.45. MS *m/e*: 292 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1733, 1710 and 1635. NMR ($CDCl_3$) δ: 1.87 (6H, s, $-CH_3\times2$), 4.90 (1H, t, $J=8$ Hz, ≡C–H) and 5.67 (1H, s, olefinic H). The second chloroform elution gave 2.5 g (43%) of 2,2-dimethyl-7-(2-oxocyclohexyl)-2H,4H,5H pyrano[4,3-*d*]-1,3-dioxin-4,5-dione (**15**) as colorless crystals ($CHCl_3$–ether), mp 118—120°. *Anal.* Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.66; H, 5.48. MS *m/e*: 292 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1780, 1710 and 1630. NMR ($CDCl_3$) δ: 1.79 (6H, s, $-CH_3\times2$), 3.51 (1H, m, ≡C–H) and 5.98 (1H, s, olefinic H). The third chloroform elution gave 0.314 g (5%) of 6,7,8,9-tetrahydro-3-(2-oxocyclohexyl)-1H,10H-pyrano[4,3-*b*]-chromone-1,10-dione (**16**) as colorless crystals ($CHCl_3$–ether), mp 218—220° (dec.). *Anal.* Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 69.01; H, 5.73. MS *m/e*: 314 (M^+). IR ν_{max}^{Nujol} cm^{-1}- 1755, 1715, 1660 and 1620. NMR ($CDCl_3$) δ: 3.55 (1H, m, ≡C–H) and 6.23 (1H, s, olefinic H). The fourth elution, with 20% ethyl acetate in chloroform, gave a trace of 2,2-dimethyl-7-morpholino-2H,4H,5H-pyrano[4,3-*d*]-1,3-dioxin-4,5-dione (**17**) as colorless crystals (ethanol), mp 181—182° (dec.). The compound **17** was identical with an independently sythesized authentic sample.

Method B: Compound **2** (8.01 g) was added dropwise to a solution of **13** (1.84 g) in dry carbon tetrachloride (100 ml) with stirring at 60°, and the mixture was refluxed for 6 hr. The reaction mixture was worked up as described in method A and gave 500 mg (21%) of **14**, a trace of **15** and 500 mg (20%) of **16**.

3-Acetyl-5,6,7,8-tetrahydro-4-hydroxycoumarin (18) and 5,6,7,8-Tetrahydro-2-methyl-3-chromonecarboxylic Acid (19a)——A mixture of **14** (500 mg), conc. HCl (10 ml) and acetic acid (10 ml) was refluxed for 2 hr. The solution was concentrated under a vacuum, poured into water and extracted with chloroform. The organic layer was washed with sat. $NaHCO_3$ and H_2O, dried and concentrated. The residue was crystallized from ether–*n*-hexane to yield 200 mg (56%) of **18** as colorless crystals, mp 74—76°. *Anal.* Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.49; H, 5.75. MS *m/e*: 208 (M^+), 193 (M^+-CH_3), 180 ($M^+-C_2H_4$) and 165 ($M^+-C_2H_3O$). IR ν_{max}^{Nujol} cm^{-1}: 1730, 1640, 1600 and 1560. UV λ_{max}^{EtOH} nm (ε): 315 (11400). NMR ($CDCl_3$) δ: 2.65 (1H, s, $-COCH_3$) and 17.15 (1H, s, –OH). The sat. $NaHCO_3$ layer was acidified with 10% HCl and extracted with chloroform. The organic layer was washed with H_2O, dried and concentrated. The residue was crystallized from ether–*n*-hexane to yield 50 mg (14%) of **19a** as colorless crystals, mp 133—133.5°. *Anal.* Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.31; H, 5.88. MS *m/e*: 208 (M^+), 190 (M^+-H_2O) and 164 (M^+-CO_2). IR ν_{max}^{Nujol} cm^{-1}: 1738, 1650 and 1580. UV λ_{max}^{EtOH} nm (ε): 251 (3950). NMR ($CDCl_3$) δ: 2.87 (3H, s, $-CH_3$) and 15.12 (1H, m, –COOH).

Methyl 5,6,7,8-Tetrahydro-2-methyl-3-chromonecarboxylate (19b)——A large excess of an ether solution of diazomethane was added to a solution of **19a** (100 mg) in ether (2 ml) and the mixture was kept at room temperature for 15 min. The solution was concentrated and the residue was recrystallized from ether–*n*-hexane to yield 100 mg (93%) of **19b** as colorless crystals, mp 70—72.5°. IR ν_{max}^{Nujol} cm^{-1}: 1730, 1672 and 1635. NMR ($CDCl_3$) δ: 2.37 (3H, s, $-CH_3$) and 3.93 (3H, s, $-COOCH_3$).

5,6,7,8-Tetrahydro-2-methylchromone (20)——A mixture of **15** (1.5 g), conc. HCl (50 ml) and acetic acid (50 ml) was refluxed for 2 hr. The solution was concentrated under a vacuum, poured into water and extracted with chloroform. The organic layer was washed with sat. $NaHCO_3$ and H_2O, dried and concentrated. The residue was crystallized from ether to yield 365 mg (40%) of **20** as colorless crystals, mp 95—96.5°. *Anal.* Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.08; H, 7.45. IR ν_{max}^{Nujol} cm^{-1}: 1665, 1620 and 1600. UV λ_{max}^{EtOH} nm (ε): 252 (5600). NMR ($CDCl_3$) δ: 2.22 (3H, s, $-CH_3$) and 5.99 (1H, s, olefinic H).

Treatment of 16 with conc. HCl in Acetic Acid——A mixture of **16** (570 mg), conc. HCl (15 ml) and acetic acid (15 ml) was refluxed for 6 hr. The solution was concentrated under a vacuum, poured into water and extracted with chloroform. The organic layer was washed with sat. $NaHCO_3$ and H_2O, dried and concentrated. The residue was subjected to silica gel chromatography. Chloroform elution gave 26 mg (5%) of 2-[2-(5,6,7,8-tetrahydro-2-chromonyl)acetyl]-1-cyclohexenol (**23**) as colorless crystals (ether–*n*-hexane) mp 124—126°. *Anal.* Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.89; H, 6.87. IR ν_{max}^{Nujol} cm^{-1}: 1665, 1610 and 1605. UV λ_{max}^{EtOH} nm (ε): 253 (14400) and 286 (7050). NMR ($CDCl_3$) δ: 3.61 (2H, s, $-CH_2-$), 6.10 (1H, s, olefinic H) and 15.40 (1H, s, –OH). The sat. $NaHCO_3$ layer was acidified with 10% HCl and extracted with chloroform. The organic layer was washed with H_2O, dried and concentrated. The residue was subjected to silica gel chromatography. Chloroform elution gave 76 mg (20%) of **19a** as colorless crystals (ether–*n*-hexane), mp 133—133.5°. Elution with 20% ethyl acetate in chloroform gave 175 mg (27.5%) of 8-(3-carboxyl-5,6,7,8-tetrahydro-2-chromonyl)-7-oxooctanoic acid (**24a**) as colorless crystals (ether), mp 110—111°. *Anal.* Calcd for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found: C, 61.52; H, 6.33. MS *m/e*: 350 (M^+), 332 (M^+-H_2O) and 306 (M^+-CO_2). IR ν_{max}^{Nujol} cm^{-1}: 1730, 1700, 1640 and 1565. UV λ_{max}^{EtOH}nm (ε): 252 (11200). NMR ($CDCl_3$) δ: 4.33 (2H, s, $-CH_2-$) and 12.37 (2H, broad, $-COOH\times2$). Elution with 50% ethyl acetate in chloroform gave 219 mg (39.7%) of 8-(5,6,7,8-tetrahydro-2-chromonyl)-7-oxooctanoic acid (**25a**) as colorless crystals ($CHCl_3$–ether), mp 63—65.5°. *Anal.* Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.61; H, 7.19. MS *m/e*: 306 (M^+) and 288 (M^+-H_2O). IR ν_{max}^{Nujol} cm^{-1}: 1730, 1715, 1660 and 1580. UV λ_{max}^{EtOH} nm (ε): 252 (13400). NMR ($CDCl_3$) δ: 3.59 (2H, s, $-CH_2-$), 6.20 (1H, s, olefinic H) and 8.55 (1H, broad, –COOH).

Methyl 8-(5,6,7,8-Tetrahydro-3-methoxycarbonyl-2-chromonyl)-7-oxooctanoate (24b)——A large excess of an ether solution of diazomethane was added to a solution of **24a** (117 mg) in chloroform (2 ml), and the mixture was kept at room temperature for 10 min. The solution was concentrated and the residue was subjected to silica gel chromatography. Chloroform elution gave 114.7 mg (91%) of **24b** as a colorless oil.

IR $\nu_{max}^{liq.}$ cm^{-1}: 1740, 1670 and 1635. NMR ($CDCl_3$) δ: 3.70 (3H, s, $-COOCH_3$), 3.77 (2H, s, $-CH_2-$) and 3.90 (3H, s, $-COOCH_3$).

Methyl 8-(5,6,7,8-Tetrahydro-2-chromonyl)-7-oxooctanoate (25b)——Methylation of **25a** with diazomethane by the method described above afforded **25b** (93%) as a colorless oil. IR $\nu_{max}^{liq.}$ cm^{-1}: 1740, 1670, 1660 and 1630. NMR ($CDCl_3$) δ: 3.56 (2H, s, $-CH_2-$), 3.68 (3H, s, $-COOCH_3$) and 6.07 (1H, s, olefinic H).

Treatment of 16 with 10% Na_2CO_3——A mixture of **16** (500 mg), 10% Na_2CO_3 (20 ml) and methanol (20 ml) was refluxed for 3 hr. The solution was concentrated under a vacuum and the residue was poured into water, and washed with chloroform. The aqueous solution was acidified with 10% HCl and then extracted with chloroform. The organic layer was washed with water, dried and concentrated. The residue was subjected to silica gel chromatography. Chloroform elution gave 100 mg (30%) of **19a** as colorless crystals (ether–*n*-hexane), mp 133—133.5°. Elution with 20% ethyl acetate in chloroform gave 200 mg (36%) of **24a** as colorless crystals (ether), mp 110—111°.

2-[2-(2-Hydroxycyclohexenyl)-2-oxoethyl]-3-chromonecarboxylic Acid (26a)——A solution of $Ba(OH)_2$ (320 mg) in water (10 ml) was added to a solution of **16** (100 mg) in methanol (10 ml), and the mixture was stirred at room temperature for 24 hr. The solution was acidified with 10% HCl and extracted with chloroform. The organic layer was extracted with sat. $NaHCO_3$, then the aqueous layer was acidified with 10% HCl and extracted with chloroform. The organic layer was washed with water, dried and concentrated. The residue was crystallized from chloroform–ether to yield 50 mg (47%) of **26a** as colorless crystals, mp 151—153°. *Anal.* Calcd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07. Found: C, 64.81; H, 6.07. MS *m/e*: 332 (M^+), 314 (M^+-H_2O). IR ν_{max}^{Nujol} cm^{-1}: 1740, 1650, 1630 and 1575. UV λ_{max}^{EtOH} nm (ε): 260 (7100) and 285 (7970). NMR ($CDCl_3$) δ: 4.47 (2H, s, $-CH_2-$), 14.70 (1H, s, –OH) and 15.10 (1H, broad, –COOH).

Methyl 2-[2-(2-Hydroxycyclohexenyl)-2-oxoethyl]-3-chromonecarboxylate (26b)——Methylation of **26a** with diazomethane by the method described above afforded **26b** (86%) as colorless crystals (ether–*n*-hexane), mp 115—116°. IR ν_{max}^{Nujol} cm^{-1}: 1725, 1670, 1625 and 1580. NMR ($CDCl_3$) δ: 3.87 (3H, s, $-COOCH_3$), 3.93 (2H, s, $-CH_2-$) and 14.98 (1H, s, –OH).

Treatment of 26a with *p*-Toluenesulfonic Acid (16)——A catalytic amount of *p*-toluenesulfonic acid was added to a solution of **26a** (50 mg) in ab. toluene (5 ml), and the mixture was refluxed for 5 hr. The solution was concentrated under a vacuum, and the residue was taken up into chloroform. The organic layer was washed with sat. $NaHCO_3$ and water, dried and concentrated. The residue was recrystallized from chloroform–ether to yield 32 mg (60.5%) of **16** as colorless crystals, mp 218—220° (dec.).