little effect on the CD. For compounds with one hydroxyl group vicinal to the chromophore (**4, 5,** and **8–10**), the attachment bond of the hydroxyl group is nearly antiparallel to the chromophore attachment bond and has an insignificant effect on the CD. In **6** the vicinal C(5)–O bond is also antiparallel to the chromophore attachment bond, but the vicinal C(3)–O bond has a dihedral angle of about −60°. Nevertheless, the CD for both bands I and II is positive as a result of the positive chirality of the C(5)–C(6) bond.

As is also shown in Table I for **14–19,** the sign of the CD for bands I and II is determined also by the chirality of the attachment bond of the salicylidenimino group and a carbon attachment bond to the cyclohexane ring bearing the chromophore. This carbon–carbon bond and the chromophore attachment bond are separated from each other by two σ bonds and have a dihedral angle close to ±120°, again assuming chair conformations for all cyclohexane rings. The one exception is **17,** for which negative CD bands I and II are predicted. Since the C(2)–O bond in **17** is antiparallel to the chromophore attachment bond, and **16,** with an A/B ring system the same as that of **17,** shows the predicted negative CD for bands I and II, the CD of band II of **17** should be reexamined. In **14,** the vicinal C(1)–O bond is antiparallel to the chromophore attachment bond, but the vicinal C(3)–O bond has a dihedral angle of about +60°. The CD of bands I and II for **14,** however, is negative as a result of the negative chirality of the chromophore attachment bond and the C(9)–C(10) bond. In **14** and **15** the C(10)–C(19) bond is parallel with the chromophore attachment bond and will have little effect on the CD.

For **20–25,** the chromophore is 3α on a 5β ring system (**20**), 3β on a 5α ring system (**21–24**), or 5α (**25**), and in each there is no obvious single carbon–carbon bond as a coupled oscillator. Hence, no straightforward prediction as to the CD of bands I and II is possible. Also, the chromophore in **26–30** is attached to a cyclopentane ring which is not symmetrically disposed with respect to the chromophore attachment bond, and no simple interpretation of these CD spectra in terms of the coupled oscillator mechanism can be made.

Registry No.—**4,** 57525-86-7; **4** quinoid form, 57484-06-7; **5,** 57525-87-8; **6,** 57525-88-9; **7,** 57525-89-0; **7** quinoid form, 57474-17-6; **8,** 57525-90-3; **8** quinoid form, 57474-18-7; **9,** 57525-91-4; **10,** 57525-92-5; **11,** 57525-93-6; **11** quinoid form, 57474-19-8; **12,** 57525-94-7; **13,** 57526-20-2; **14,** 57572-73-3; **15,** 57525-95-8; **16,** 57525-96-9; **16** quinoid form, 57474-20-1; **17,** 57525-97-0; **17** quinoid form, 57474-21-2; **18,** 57474-22-3; **19,** 57525-98-1; **19** quinoid form, 57484-00-1; **20,** 57525-99-2; **20** quinoid form, 57474-23-4; **21,** 57526-00-8; **21** quinoid form, 57474-24-5; **22,** 57526-01-9; **23,** 57526-21-3; **23** quinoid form, 57484-08-9; **24,** 57526-02-0; **24** quinoid form, 57474-25-6; **25,** 57474-26-7; **26,** 57572-74-4; **26** quinoid form, 57474-27-8; **27,** 57526-03-1; **28,** 57526-04-2; **29,** 57526-05-3; **30,** 57474-28-9.

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A Novel Transformation of Chromone-3-carboxaldehyde to an *o*-Hydroxybenzophenone

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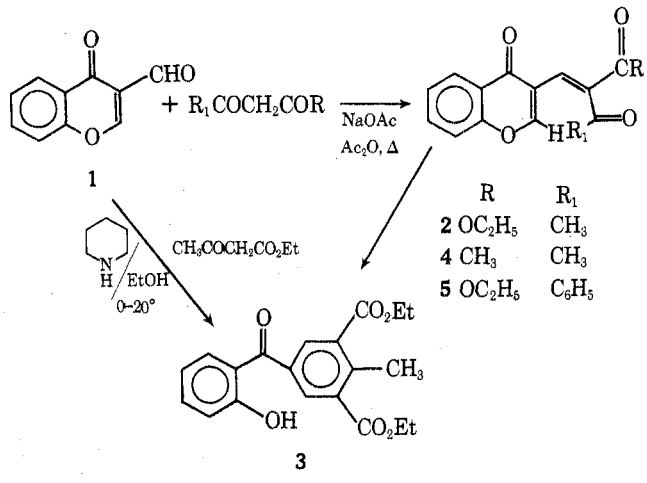
Recent publications[1–4] describing condensation reactions of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde (**1**) have prompted us to report a novel one-step transformation of **1** into an *o*-hydroxybenzophenone **3**.

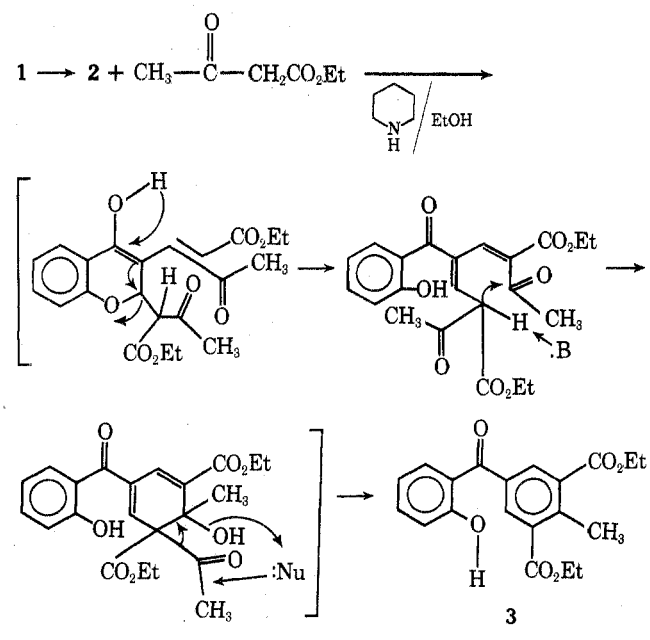
Condensation of **1** with ethyl acetoacetate afforded **2** or **3** depending on reaction conditions. For example, reaction of



1 with ethyl acetoacetate in the presence of NaOAc–Ac_2O gave **2** in 62% crude yield. Similar condensations of **1** with 2,4-pentanedione and ethyl benzoylacetate gave **4** and **5** in 60 and 30% yield, respectively.

Reaction of **1** with excess ethyl acetoacetate in NaOAc–Ac_2O or pyridine–EtOH also gave **2**.

When the reaction was carried out in the presence of piperidine–EtOH the benzophenone **3** and a red oil were formed. This oil showed no trace of **3** on TLC (Et_2O–hexane, 1:1 silica gel). Upon prolonged standing it solidified. Examination of the solid by GC showed two components,



compound 3, which comprised 80% of the mixture, and a second unidentified component, which was neither 1 nor 2.

A plausible mechanism for the formation of 3 involves initial condensation of 1 with ethyl acetoacetate followed by Michael addition of another molecule of ethyl acetoacetate and subsequent rearrangement. Evidence supporting this mechanism was the conversion of 2 with excess ethyl acetoacetate in piperidine–EtOH to 3 in 70% yield (NMR).

While 3 represents only one example of this synthesis, in principle it should be applicable to the preparation of other similarly substituted *o*-hydroxybenzophenones.

Experimental Section

General. Melting points were determined in open capillaries on a Thomas-Hoover melting point apparatus and are uncorrected. The infrared and ultraviolet spectra were obtained on Perkin-Elmer 521 and Perkin-Elmer 350 recording spectrometers, respectively. Nuclear magnetic resonance spectra were obtained on a Varian A-60A spectrometer. Mass spectra were obtained on a Finnigan 1015 quadrupole mass spectrometer. All compounds were analyzed for C and H and were within ±0.4% of the theoretical value.

3-(4-Oxo-4*H*-1-benzopyran-3-yl)-2-(1-oxoethyl)-2-propenoic Acid Ethyl Ester (2). Ethyl acetoacetate (13.0 g, 0.1 mol), NaOAc (8.2 g, 0.1 mol), and 1 (17.4 g, 0.1 mol) were heated and stirred in Ac_2O (50 ml) on the steam bath for 2 hr and diluted with H_2O (300 ml); the resulting tan solid was recrystallized from Et_2O to give 10.00 g of 2, mp 120–122°. Further concentration gave an additional 8.0 g, mp 95–100°. The first crop when recrystallized ($EtOH–H_2O$) gave tan needles of 2: mp 120–122°; ir (KBr) 1705, 1680, and 1650 cm^{-1} (ester, α,β-unsaturated ketone, and chromone carbonyl); NMR[3,5] ($CDCl_3$) δ 8.35 (s, 1 H, C_2 H), 8.18 (dd, 1, J = 7.0 Hz, benzene H_5), 7.28–8.05 (m, 4 H, benzene and olefinic), 4.3 (q, 2 H, J = 7.0 Hz, CH_2), 2 5 (s, 3 H, CH_3), 1.35 (t, 3 H, J = 7.0 Hz, CH_3); uv max (95% EtOH) 220 nm (ϵ 17 900). Anal. C, H.

5-(2-Hydroxybenzoyl)-2-methylbenzene-1,3-dicarboxylic Acid Diethyl Ester (3). To a stirred solution of 1 (26.2 g, 0.15 mol) and ethyl acetoacetate (35.4 g, 0.25 mol) in EtOH at 0–20° was added piperidine (10.0 ml). The resulting red solution was allowed to warm to room temperature over several hours, neutralized with HOAc, poured onto ice–H_2O (1 l.), and extracted with Et_2O (1 l.). The Et_2O layer was then washed with H_2O, 5% $NaHCO_3$, and brine and dried ($MgSO_4$). Concentration in vacuo gave a red oil. Boiling the oil with hexane followed by decantation gave, after cooling, 4.0 g of 3: mp 55–55.5°; ir (KBr) 1730 and 1630 cm^{-1} (ester and ketone carbonyl); NMR ($CDCl_3$) δ 8.3 (s, 2 H, H_4 and H_6), 7.8–6.8 (m, 4 H, aromatic) 4.5 (q, 4 H, J = 7.0 Hz, 2-CH_2), 2.8 (s, 3 H, CH_3), 1.35 (t, 6 H, J = 7.0 Hz, 2-CH_3); uv max 258 nm (ϵ 12 100); mass spectrum (70 eV) *m/e* 356 (P^+). Anal. C, H.

The residual red oil showed no trace of 3 by TLC (silica gel, Et_2O–hexane, 1:1). Attempts to crystallize it were unsuccessful. After prolonged standing it solidified to a waxy yellow solid yielding 18.5 g. GC analysis (2-ft 1% OV-22, 190°) showed that 80% of 3 was present.

3-[(4-Oxo-4*H*-1-benzopyran-3-yl)-methylene]-2,4-pentanedione (4). 2,4-Pentanedione (10.05 g, 0.1 mol), 1 (17.4 g, 0.1 mol), and NaOAc (8.2 g, 0.1 mol) were heated and stirred in Ac_2O (65.0 ml) for 3 h on the steam bath. The mixture was cooled and diluted with a two-phase $CH_2Cl_2–H_2O$ mixture. The CH_2Cl_2 was separated, extracted with saturated $NaHCO_3$ and brine, and dried ($MgSO_4$). Filtration and concentration in vacuo yielded a tan semisolid, which when recrystallized (EtOH, 300 ml) gave 5, 15.7 g (60%), mp 168–170°. Anal. C, H.

β-(Oxo-α-[(4-oxo-4*H*-1-benzopyran-3-yl)-methylene]benzenepropanoic Acid Ethyl Ester (5). Ethyl benzoylacetate (9.7 g, 0.05 mol), 1 (8.7 g, 0.05 mol), and NaOAc (4.2 g, 0.05 mol) were heated and stirred in Ac_2O (50 ml) for 4 h on the steam bath. Dilution with a two-phase $CH_2Cl_2–H_2O$ solution and separation of the CH_2Cl_2 followed by drying ($MgSO_4$), filtration, and concentration in vacuo yielded an oily residue. Recrystallization (CH_2Cl_2–heptane) gave 5, 5.0 g (30%), mp 111–112°. Anal. C, H.

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Registry No.—1, 17422-74-1; 2, 57443-89-7; 3, 57443-90-0; 4, 57443-91-1; 5, 57443-92-2; ethyl acetoacetate, 141-97-9; 2,4-pentanedione, 123-54-6; ethyl benzoylacetate, 94-02-0.

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Total Synthesis of Steroids. XI.[1] Synthesis of Optically Active 11-Ketoestrane Derivatives

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In addition to our work on the total synthesis of racemic 11-oxidized estrogens published recently,[2,3] we would like to report the total synthesis of optically active new estrane derivatives, which was based on the method applied to the synthesis of *rac*-14α-hydroxy-3-methoxy-8α-estra-1,3,5(10)-triene-11,17-dione.[2]

The Torgovs secodione 1[4] can be transformed easily by microbial reduction[5] to the secolone **2a**. The latter has been used as the starting material in the present synthesis. The acetate of the secolone **2b** obtained by standard method was subjected to the action of *m*-chloroperbenzoic acid (MCPBA) under the same conditions as we described earlier[6] for the secodione 1. Surprisingly, the reaction resulted in so many products that their separation was not rewarding, although some of them have been isolated and identified (**5a,b**, **6**, and **7**). In order to avoid the undesirable reactions we tried to carry out the oxidation in the presence of weak alkali and to vary the reaction solvent. The best results were obtained with methanol as solvent and pyridine *N*-oxide as weak base. Although it was not possible to prevent oxirane ring cleavage, the number of reaction products under these conditions was limited to only two, i.e., the methoxy alcohols **4a** and **4b**, obtained in ca. 90% yield. They could be separated very easily owing to their different polarities and they were reasonable stable. We suppose that they are formed by the cleavage of epoxides **3a** and **3b** with methyl alcohol; however, we were not able to assign an absolute configuration on the basis of our spectroanalytical data. One can conclude from the model studies that there is no special steric preference in formation of either of them, which also explains the 1:1 ratio of formation. These two products (**4a,b**) (Scheme I) proved to be very useful for further synthesis. Each of them undergoes in the presence of weak acid (acetic acid) in chloroform solution a methanol elimination to yield the allylic alcohols **5a** and **5b**, respectively; the more polar **4b** looses methanol more easily and produces a small amount of **7**, as by-product; the elimination of methanol from the less polar **4a** is not accompanied by any side reaction. The elimination reaction can be also conducted on **4a,b** mixture; however, the separation of the allylic alcohols is very difficult. Also in the case of the alcohols **5a** and **5b** we were not able to ascribe an absolute configuration to either of them.

Under the influence of strong acids at elevated temperature in benzene solution **5a** and **5b** undergo a rearrange-