

[Chem. Pharm. Bull.
34(11)4527—4532(1986)]

Novel Synthesis of Indan Derivatives

HIROSHI KASHIHARA, HIROSHI SHINOKI, HIROSHI SUEMUNE
and KIYOSHI SAKAI*

*Faculty of Pharmaceutical Sciences, Kyushu University,
3-1-1, Maidashi, Higashi-ku, Fukuoka 812, Japan*

(Received April 23, 1986)

During the course of synthetic studies on the 5,6-disubstituted 4-oxo-tetrahydro-2-pyrone skeleton in connection with biologically active compounds, we have found a convenient procedure for the regioselective introduction of a double bond in methyl alkyl ketones and a novel synthetic method for indan derivatives.

Keywords—1,2-disubstituted indan; methyl α,β -disubstituted vinyl ketone; 5,6-disubstituted 4-oxo-tetrahydro-2-pyrone; aldol condensation; 1-substituted 2-indanone

Pestalotin,¹⁾ which was isolated from culture broth of a fungal strain, is known to be a gibberellin synergist. This compound contains a 5,6-dihydro-4-hydroxy-2-pyrone skeleton. A certain similarity to this skeleton is also apparent in the structure²⁾ of thromboxane B₂. The biological activity profiles of these compounds prompted us to synthesize 5,6-dihydro-4-hydroxy-2-pyrone derivatives. In the course of synthetic studies on dihydro-2-pyrone derivatives, we have found a novel synthetic method for methyl α,β -disubstituted vinyl ketones and indan derivatives.

According to Huckin and Weiler,³⁾ aldol condensation of the dianion generated from methyl acetoacetate with carbonyl compounds afforded the δ -hydroxy- β -keto esters (II), which, on exposure to anhydrous hydrogen chloride in CHCl₃, were converted into the γ,δ -unsaturated keto esters (I) without yielding the dihydro-2-pyrone (III). However, in a similar aldol condensation using the dianion of methyl acetoacetate, Seebach and Meyer⁴⁾ obtained III (oxolactone). This result clearly differs from that of Huckin and Weiler (Chart 1).

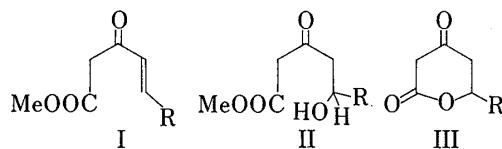


Chart 1

We have extensively investigated the aldol condensation of the dianion of the β -keto esters (IV)⁵⁾ with the aldehydes, and found that the 5,6-disubstituted 4-oxo-tetrahydro-2-pyrones (V) can be obtained by adjustment of the reaction mixture to pH 6 with 1 N HCl. As shown in Table I, the 4-oxo-tetrahydro-2-pyrones (V) were obtained in good yields except for Vg and Vh. Compounds Ve, Vf, Vi, and Vk were each obtained as a mixture of *cis* and *trans* isomers which showed two adjacent spots on thin-layer chromatography (TLC) and which could be separated by careful column chromatography on silica gel. On the basis of the spin-spin coupling constant⁶⁾ between C₅- and C₆-H, the 4-oxo-tetrahydro-2-pyrones with smaller coupling constant ($J=4$ Hz) were assigned the 5,6-*cis* configuration; these compounds were obtained from the less polar fraction. The isomers with larger coupling constant ($J=7$ —

10 Hz) were assigned the 5,6-*trans* configuration. The formation of the *trans* isomer as the main product may be rationalized on the assumption that this aldol condensation proceeded in such a way that the alkoxy function generated by nucleophilic attack of the dianion on the aldehyde is located at the least hindered site, and the substituent R_2 occupies a less hindered site (Chart 2).⁷⁾

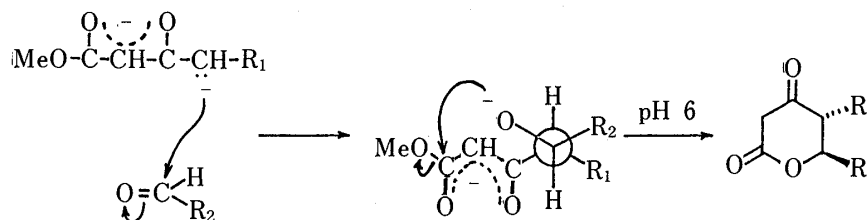
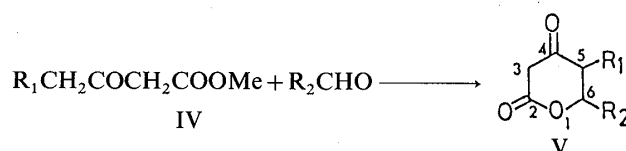


Chart 2

In the proton nuclear magnetic resonance ($^1\text{H-NMR}$) spectra of the *cis* and *trans* isomers, the signal of $\text{C}_3\text{-H}_2$ at δ 3.2—3.7 suggests that each compound exists mainly in the keto form. The enol content was estimated based on the signal of the $\text{C}_3\text{-olefinic}$ proton, observed as a singlet at δ 5.1—5.3 (see Experimental). The 5,6-disubstituted 4-oxo-tetrahydro-2-pyrones are not stable under acidic conditions, and even in column chromatography on silica gel, partial decomposition was observed. When the 4-oxo-tetrahydro-2-pyrones were heated under reflux in CH_3COOH in the presence of CH_3COOK , the methyl α,β -disubstituted vinyl ketones (VI) were obtained in moderate yields (Table II). The geometry of the double bond in the enones was determined to be *E*-form by the observation (13—21% enhancement) of nuclear Overhauser effect (NOE) between the vinylic proton ($\text{C}_4\text{-H}$) and the methyl protons ($\text{C}_1\text{-H}$) (Table II).

TABLE I. Synthesis of the 4-Oxo-tetrahydro-2-pyrones (V)



Compd. No.	R_1	R_2	R_3	Yield (%)	Ratio <i>trans/cis</i>	Config.	Appearance
Va	PhCH_2	Methyl		94	—	a)	Oil
Vb	PhCH_2	Propyl	H	96	—	a)	Oil
Vc	PhCH_2	Heptyl	H	82	100/ 0	<i>trans</i>	Oil
Vd	PhCH_2	Cyclohexyl	H	91	100/ 0	<i>trans</i>	Oil
Ve	PhCH_2	Cyclooctyl	H	85	89/11	<i>trans</i>	Oil
Ve						<i>cis</i>	Oil
Vf	PhCH_2	Phenyl		78	87/13	<i>trans</i>	Oil
Vf						<i>cis</i>	mp 156°C
Vg	<i>m</i> - $\text{CH}_3\text{OPhCH}_2$	Cyclohexyl		21	100/ 0	<i>trans</i>	Oil
Vh	<i>p</i> - CH_3PhCH_2	Propyl	CH_3	26	—	a)	Oil
Vi	$\text{CH}_2=\text{CHCH}_2$	Cyclohexyl		84	79/21	<i>trans</i>	Oil
Vi						<i>cis</i>	Oil
Vj	$\text{CH}_2=\text{CCH}_3\text{CH}_2$	Cyclohexyl		94	—	a)	Oil
Vk	Bu	Phenyl		83	63/37	<i>trans</i>	Oil
Vk						<i>cis</i>	mp 112°C

All substituents (R_1 , R_2 , R_3) are common to each table.

a) Although a single isomer was obtained, analysis of the $^1\text{H-NMR}$ spectrum was difficult.

TABLE I. (continued)

Compd. No.	IR (neat) (cm ⁻¹)	¹ H-NMR (CDCl ₃)	MS (<i>m/z</i>)
Va	3400, 1644, 1250	—	—
Vb	3400, 1735, 1720	3.23 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.57 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 4.40 (1H, m, OCH)	246 (M ⁺) 202
Vc	3400, 1750, 1720	3.22 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.58 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 4.40 (1H, m, OCH; on irradiation at 1.72, d, <i>J</i> =7 Hz)	302 (M ⁺) 258
Vd	3400, 1720, 1655	3.36 (2H, s, COCH ₂ CO), 4.14 (1H, dd, <i>J</i> =4, 7 Hz, OCH; on irradiation at 1.68, d, <i>J</i> =7 Hz)	286 (M ⁺) 242
Ve (<i>trans</i>)	3400, 1755, 1720	3.37 (1H, s, COCH ₂ CO), 4.20 (1H, dd, <i>J</i> =4, 8 Hz, OCH; on irradiation at 1.92, d, <i>J</i> =8 Hz), 5.29 (0.5H, s, CH=C)	314 (M ⁺) 270
Ve (<i>cis</i>)	3400, 1755, 1720	3.36 (0.86H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.52 (0.86H, d, <i>J</i> =20 Hz, COCH ₂), 4.26 (1H, dd, <i>J</i> =2.5, 9 Hz, OCH), 5.29 (0.14H, s, CH=C)	314 (M ⁺) 270 223
Vf (<i>trans</i>)	3450, 1660, 1270	3.43 (1.62H, s, COCH ₂ CO), 5.28 (0.19H, s, CH=C), 5.34 (1H, d, <i>J</i> =8 Hz, OCH)	236 193
Vf (<i>cis</i>) ^b	3420, 1660, 1280	2.82 (1.42H, br s, COCH ₂ CO), 5.11 (0.29H, s, CH=C), 5.72 (1H, d, <i>J</i> =4 Hz, OCH) <i>Anal.</i> Calcd for C ₁₈ H ₁₆ O ₃ : C, 77.12; H, 5.75. Found: C, 77.35; H, 5.61.	280 (M ⁺) 236
Vg	3400, 1720, 1655	3.37 (1.26H, s, COCH ₂ CO), 4.16 (1H, dd, <i>J</i> =4, 8 Hz, OCH; on irradiation at 1.72, d, <i>J</i> =8 Hz), 5.28 (0.37H, s, CH=C)	316 (M ⁺) 272
Vh	3350, 1720, 1650	3.21 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.57 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 4.40 (1H, m, OCH)	260 (M ⁺) 216
Vi (<i>trans</i>)	3400, 1750, 1720	3.43 (1.76H, s, COCH ₂ CO), 4.29 (1H, dd, <i>J</i> =3, 9 Hz, OCH; on irradiation at 1.66, d, <i>J</i> =9 Hz), 5.29 (0.12H, s, CH=C)	236 (M ⁺) 192
Vi (<i>cis</i>)	3400, 1750, 1720	3.27 (0.92H, d, <i>J</i> =19 Hz, COCH ₂ CO), 3.59 (0.92H, d, <i>J</i> =19 Hz, OCH), 4.25 (1H, dd, <i>J</i> =3, 9 Hz, OCH), 5.24 (0.08H, s, CH=C)	236 (M ⁺) 192
Vj	3400, 1750, 1620	3.28 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.56 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 4.20 (1H, m, OCH)	250 (M ⁺) 206
Vk (<i>trans</i>)	3400, 1760, 1730	3.37 (1H, d, <i>J</i> =19 Hz, COCH ₂ CO), 3.67 (1H, d, <i>J</i> =19 Hz, COCH ₂ CO), 5.44 (1H, d, <i>J</i> =10 Hz, OCH)	246 (M ⁺) 202
Vk (<i>cis</i>) ^b	3400, 1650, 1280	3.41 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 3.72 (1H, d, <i>J</i> =20 Hz, COCH ₂ CO), 5.78 (1H, d, <i>J</i> =4 Hz, OCH) <i>Anal.</i> Calcd for C ₁₅ H ₁₈ O ₃ : C, 73.14; H, 7.37. Found: C, 73.01; H, 7.30.	246 (M ⁺) 202

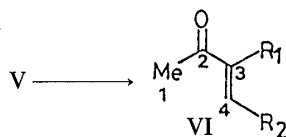
^b) Crystalline compounds were recrystallized from hexane and AcOEt, and IR spectra were taken in Nujol on an NaCl plate.

This sequence provides a convenient procedure for the regioselective introduction of a double bond in methyl alkyl ketones. The independent decarboxylation of the *cis* and *trans* isomers under the same reaction conditions yielded the identical enone (*E*-form). This may be rationalized by the assumption of the *E1* mechanism accompanied with decarboxylation. Thus, the C₆-carbonium ion formed as the intermediate may be transformed into the thermodynamically stable *E*-form.

When the enones (VI) were submitted to more drastic reaction conditions (150 °C in H₃PO₄ for 7—15 h), the indan derivatives (VII) were obtained in 41—52% yields (Table III). Lewis acids such as SnCl₄, BF₃-etherate, and FeCl₃ were not effective for this cyclization reaction.

Next, we undertook the direct conversion of the 4-oxo-tetrahydro-2-pyrones (V) to indan

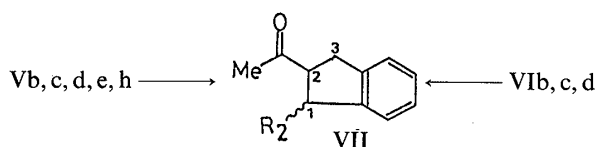
TABLE II. Synthesis of the Enones (VI)



Compd. No.	Yield (%)	IR (neat) (cm ⁻¹)	MS (m/z)	¹ H-NMR and NOE (CDCl ₃)
VIa	20	1670, 1600	174 (M ⁺) 159	1.93 (3H, d, <i>J</i> = 7 Hz, =CHCH ₃), 2.30 (3H, s, COCH ₃), 7.10—7.30 (5H, m, Ar-H), + 6.9%
VIb	49	1660, 1600	202 (M ⁺) 159	0.92 (3H, t, <i>J</i> = 8 Hz, CH ₃), 2.30 (3H, s, COCH ₃), 6.75 (1H, t, <i>J</i> = 7 Hz, -CH=) ^{a)}
VIc	51	1660, 1600	258 (M ⁺) 159	0.92 (3H, t, <i>J</i> = 8 Hz, CH ₃), 2.30 (3H, s, COCH ₃), 6.70 (1H, t, <i>J</i> = 8 Hz, -CH=) ^{a)}
VI d	80	1670, 1600	242 (M ⁺) 159	2.30 (3H, s, COCH ₃), 6.55 (1H, d, <i>J</i> = 10 Hz, -CH=), 7.10—7.30 (5H, m, Ar-H), + 21.3%
VI f	74 (from Vf- <i>cis</i>) ^{b)} 99 (from Vf- <i>trans</i>)	1660, 1600	236 (M ⁺) 193	2.44 (3H, s, COCH ₃), 7.73 (1H, s, -CH=), + 15.2%
VI g	57	1670, 1600	272 (M ⁺) 189	2.29 (3H, s, COCH ₃), 3.75 (3H, s, OCH ₃), 6.55 (1H, d, <i>J</i> = 10 Hz, -CH=), + 14.3%
VI j ⁸⁾	23	1670, 1630	206 (M ⁺) 163	2.31 (3H, s, COCH ₃), 4.52 (1H, m, =CH ₂), 4.68 (1H, m, =CH ₂), 6.52 (1H, d, <i>J</i> = 10 Hz, -CH=), + 13.4%
VI k	75 (from Vk- <i>cis</i>) 76 (from Vk- <i>trans</i>)	1670, 1600	202 (M ⁺) 187	2.44 (3H, s, COCH ₃), 7.34—7.42 (5H, m, Ar-H), 7.44 (1H, s, -CH=) ^{a)}

^{a)} NOE was not measured. ^{b)} mp 65°C (recrystallized from hexane and AcOEt); the IR spectrum was taken in Nujol on an NaCl plate.

TABLE III. Synthesis of the Indan Derivatives (VII)



Compd. No.	Yield (%)	IR (neat) (cm ⁻¹)	MS (m/z)	¹ H-NMR (CDCl ₃)
VII b	45 (47) ^{a)}	1715, 1500	202 (M ⁺) 129	0.90, 1.03 (1.5H each, t, <i>J</i> = 7 Hz, CH ₃), 2.24 (3H, s, COCH ₃), 7.05—7.30 (4H, m, Ar-H)
VII c	34 (52) ^{a)}	1710, 1500	258 (M ⁺) 129	0.88, 0.90 (1.5H each, t, <i>J</i> = 7 Hz, CH ₃), 2.24 (3H, s, COCH ₃), 7.06—7.24 (4H, m, Ar-H)
VII d	50 (41) ^{a)}	1715, 1450	242 (M ⁺) 199	2.27 (3H, s, COCH ₃), 7.05—7.45 (3H, m, Ar-H) ^{b)} <i>Anal.</i> Calcd for C ₁₇ H ₂₂ O: C, 84.25; H, 9.15. Found: C, 84.49; H, 9.28.
VII e	42	1715, 1490	270 (M ⁺) 227	2.16, 2.27 (1H, 2H, respectively, s, COCH ₃), 7.05—7.45 (4H, m, Ar-H)
VII h ⁹⁾	42	1710, 1500	216 (M ⁺) 143	0.92, 1.03 (1.5H each, t, <i>J</i> = 7.0 Hz, CH ₃), 2.24 (3H, s, COCH ₃), 2.31 (3H, s, Ar-CH ₃), 7.00—7.45 (4H, m, Ar-H)

^{a)} Numbers in parenthesis indicate yields from VI. ^{b)} mp 51°C (recrystallized from hexane and AcOEt); the IR spectrum was taken in Nujol on an NaCl plate.

derivatives (VII) (Table III). When the tetrahydro-2-pyrones were heated at 150 °C in H_3PO_4 , similar cyclization was observed, although the reaction proceeded in unsatisfactory yields. The facile formation of the enones (VI) from the tetrahydro-2-pyrones (V) under acidic conditions suggests that this direct conversion to the indan derivatives also proceeded *via* the enones (VI). Each indan derivative gave a single spot on TLC, and was an inseparable mixture of stereoisomers. In the $^1\text{H-NMR}$ spectra of VIIb, VIIc and VIIh, the acetyl function was observed as a singlet at δ 2.24, while the ω -methyl function in each compound was observed as a pair of triplets ($J = 7$ Hz) in the same ratio at δ 0.90 and 1.03, δ 0.88 and 0.90, and δ 0.92 and 1.03. The acetyl signal of VIIe was observed as two peaks (δ 2.16 and 2.27) in the ratio of 1 to 2. In the $^1\text{H-NMR}$ spectrum of VIId, there is no signal to suggest the presence of a stereoisomeric mixture. However, the signal of $\text{C}_1\text{-H}$ in the 2-acetoxyindan (**1**) obtained by Baeyer–Villiger oxidation of VIId was observed as a pair of double doublets ($J = 2, 5$ Hz) at δ 3.06 and 3.21. To confirm the indan skeleton, the acetoxyindan (**1**) was further converted into the 2-indanone (**3**). By treatment with K_2CO_3 in MeOH, **1** was hydrolyzed to the 2-indanol (**2**), and subsequent Jones oxidation yielded the indanone (**3**) (Chart 3). The $^1\text{H-NMR}$ spectrum of **3** showed that this compound exhibits keto-enol tautomerism, because the signals of $\text{C}_1\text{-H}$ and $\text{C}_3\text{-H}_2$ in the keto form were observed as a broad singlet at δ 3.32, and those of the $\text{C}_3\text{-olefinic H}$ and the $\text{C}_2\text{-OH}$ in the enol form were also observed as broad singlets at δ 6.81 and 8.75, respectively. The signal due to the enol at δ 8.75 disappeared rapidly on addition of D_2O . The infrared (IR) spectrum also indicated the existence of enol, carbonyl, and the double bond moieties (absorption bands of 3350, 1715 and 1640 cm^{-1}).

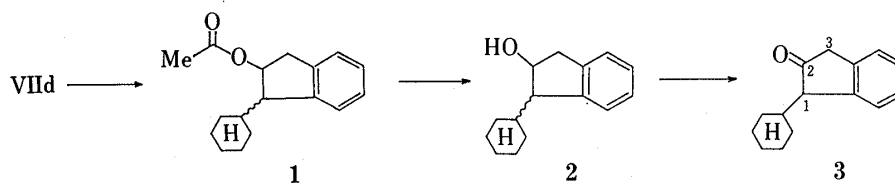


Chart 3

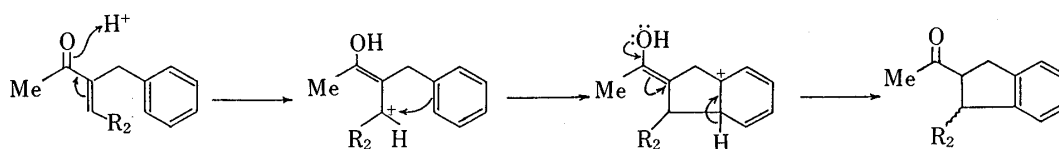


Chart 4

The reaction mechanism is tentatively proposed to be as shown in Chart 4. It is noteworthy that the ring closure reaction of the enone (VI) to the five-membered ring occurs *via* the disfavored 5-*endo*-trigonal process according to Baldwin's rule.¹⁰⁾ Thus, the above method may be useful for the synthesis of 1,2-disubstituted indan derivatives.

Experimental

IR spectra were measured with a JASCO A-202 spectrometer, and $^1\text{H-NMR}$ spectra were measured on a JEOL LNP-PS-100 spectrometer. Mass spectra (MS) were taken on a JEOL JMS-D 300 spectrometer. For column chromatography, silica gel (Merck, Kieselgel 60, 70–230 mesh) was used. TLC and preparative TLC were performed on silica gel plates (Merck, Kieselgel 60 F₂₅₄, 0.25 and 2 mm, respectively). All organic solvent extracts were washed with satd. brine and dried over anhydrous sodium sulfate. All compounds were obtained as colorless oils, unless otherwise stated.

General Procedure for the Synthesis of the 4-Oxo-tetrahydro-2-pyrones (V)—A solution of IV (10 mmol) in tetrahydrofuran (THF, 5 ml) was added dropwise with stirring to a suspension of NaH (60% content, 11 mmol) in THF (20 ml) under an Ar atmosphere at 5–10 °C. After 0.5 h, BuLi (15% (w/v), 10.5 mmol) was added dropwise over

0.5 h at less than 5 °C, and then an aldehyde (11 mmol) was added dropwise. After 2 h, the reaction mixture was diluted with H₂O (50 ml), adjusted to pH 6 with 1 N HCl, and extracted with AcOEt (50 ml × 4). The combined extracts were washed and dried. Removal of the solvent *in vacuo* afforded an oily residue, which was rapidly chromatographed on silica gel. Analytical samples of the *cis* and *trans* isomers were obtained by further chromatography on silica gel or by preparative TLC.

General Procedure for the Synthesis of the Enones (VI)—A mixture of V (5 mmol), CH₃COOK (15 mmol), and CH₃COOH (7 ml) was heated under reflux. After 1 h, CH₃COOH was removed *in vacuo* to leave an oily residue, which was diluted with H₂O, and then extracted with CH₂Cl₂ (50 ml × 3). The CH₂Cl₂ extract was washed and dried, then the solvent was removed *in vacuo* to leave an oily residue, which was subjected to column chromatography on silica gel.

General Procedure for the Synthesis of the Indan Derivatives (VII)—A) An enone (VI, 0.2–1 g) in 85% H₃PO₄ (5–7 ml) was heated at 140–150 °C under an N₂ atmosphere for 7–15 h. The reaction mixture was diluted with H₂O, and then extracted with CH₂Cl₂. The CH₂Cl₂ extract was washed and dried. Removal of the solvent *in vacuo* afforded an oily residue, which was purified by column chromatography on silica gel.

B) The 4-oxo-tetrahydro-2-pyrones (V) were converted to VII in a manner similar to that described above (A).

2-Acetoxy-1-cyclohexylindan (1)—The acetylindan VIId (0.549 g) in CH₂Cl₂ (20 ml) was added dropwise to a well-stirred solution of *m*-chloroperbenzoic acid (MCPBA) (purity 80%, 1.471 g) and NaHCO₃ (0.570 g) in CH₂Cl₂ (10 ml) at room temperature. After 24 h, the reaction mixture was subjected to usual work-up, and the oily compound was purified by column chromatography on silica gel (24 g). The fraction eluted with 2% AcOEt in hexane (v/v) afforded **1** (0.462 g, 79%) as a colorless oil. IR (neat): 1735, 1240, 1035 cm⁻¹. ¹H-NMR (CDCl₃) δ: 2.08 (3H, s, CH₃CO), 3.06 (dd, *J*=2, 6 Hz, C₁-H), 3.21 (dd, *J*=2, 6 Hz, C₁-H), 5.10 (1H, m, C₂-H), 7.01–7.68 (4H, m, Ar-H). MS *m/z*: 198 (M⁺ – CH₃COOH), 91.

1-Cyclohexyl-2-indanol (2)—A mixture of **1** (0.236 g) and K₂CO₃ (0.040 g) in MeOH (4 ml) was stirred for 7 h at room temperature. The reaction mixture was diluted with brine (10 ml), and extracted with AcOEt (30 ml × 3). The AcOEt extract was washed and dried. Removal of the solvent *in vacuo* afforded an oily residue, which was chromatographed on silica gel. The fraction eluted with 3% AcOEt in hexane (v/v) afforded **2** (0.145 g, 74%) as a colorless oil. IR (neat): 3250, 1640, 1055 cm⁻¹. ¹H-NMR (CDCl₃) δ: 3.01 (dd, *J*=2, 5 Hz, C₁-H), 3.16 (dd, *J*=2, 5 Hz, C₁-H), 3.88–4.19 (1H, m, C₂-H), 7.02–7.42 (4H, m, Ar-H). MS *m/z*: 216 (M⁺), 198, 91.

1-Cyclohexyl-2-indanone (3)—Jones reagent (0.50 ml) was added to a stirred solution of **2** (0.106 g) in acetone (4 ml) under ice-water cooling. After 0.5 h, the excess reagent was decomposed by adding isopropanol (0.7 ml). The reaction mixture was diluted with H₂O and extracted with CH₂Cl₂ (30 ml × 2). The CH₂Cl₂ extract was washed and dried. Removal of the solvent *in vacuo* gave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 2% AcOEt in hexane (v/v) afforded **3** (0.063 g, 61%) as a colorless oil. IR (neat): 3350, 1715, 1640 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ: 1.34–2.18 (11H, m, cyclohexyl), 3.32 (br s, COCH₂–, COCH–), 6.81 (s, O–C=CH–), 7.16–8.08 (4H, m, Ar-H), 8.75 (s, OH). MS *m/z*: 214 (M⁺), 199. High-MS for C₁₅H₁₈O (M⁺): Calcd *m/z* 214.13567; Found 214.13501.

References and Notes

- 1) Y. Kimura and S. Tamura, *Agric. Biol. Chem.*, **36**, 1925 (1972).
- 2) S. M. Roberts and F. Scheinmann, "New Synthetic Routes to Prostaglandins and Thromboxanes," Academic Press, New York, 1982, pp. 181–190.
- 3) S. N. Huckin and L. Weiler, *Can. J. Chem.*, **52**, 2157 (1974).
- 4) D. Seebach and H. Meyer, *Angew. Chem.*, **86**, 40 (1974).
- 5) The β-keto esters (IV) were prepared by the reported method: S. N. Huckin and L. Weiler, *J. Am. Chem. Soc.*, **96**, 1082 (1974).
- 6) Coupling constant between C₅- and C₆-H was measured by the decoupling technique.
- 7) a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, 1971; b) Y. Izumi and A. Tai, "Stereodifferentiating Reactions," Academic Press, New York, 1977; c) J. Lucchetti and A. Krief, *Tetrahedron Lett.*, **1978**, 2693; d) J. I. Luengo and M. Koreeda, *ibid.*, **25**, 4881 (1984).
- 8) An attempt to cyclize VIj to the cyclopentene derivative was unsuccessful.
- 9) The nature of the substituent on the benzene ring had no apparent effect on the ring closure reaction.
- 10) a) J. E. Baldwin and L. I. Kruse, *J. Chem. Soc., Chem. Commun.*, **1977**, 233; b) J. E. Baldwin, *ibid.*, **1976**, 734; c) J. E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman, and R. C. Thomas, *ibid.*, **1976**, 736; d) J. E. Baldwin, *ibid.*, **1976**, 738.