1862 *Chem. Pharm. Bull.* **38**(7) 1862—1871 (1990) Vol. 38, No. 7

Z–E Isomerization of *β*-Methoxychalcones: Preferred Existence of *E*-Isomers in Naturally Occurring *β*-Methoxychalcones

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Methylation of dibenzoylmethanes with diazomethane always gave *Z-β*-methoxychalcones, which are the products of kinetically controlled methylation of chelated enol forms of *β*-hydroxychalcones. *Z-β*-Methoxychalcones were thermodynamically unstable and readily isomerized into more stable *E*-isomers on contact with silica gel, on keeping in polar solvents, or on exposure to light. The structures of both isomers of the simplest *β*-methoxychalcone were determined by X-ray crystal structure analysis. All *β*-methoxychalcones prepared were fully characterized by spectroscopic methods, revealing that the *E*- and *Z*-isomers are distinguishable in terms of ultraviolet and ^{13}C-nuclear magnetic resonance spectra, and nuclear Overhauser effect between the *β*-methoxyl group and H-8 proton. The spectral data reported for natural *β*-methoxychalcones, methylpongamol and praecansone A, are attributable to the *E*-isomers.

Keywords *β*-methoxychalcone; *E,Z*-isomer; isomerization; dibenzoylmethane; methylation; methylpongamol; praecansone A; X-ray analysis; nuclear Overhauser effect; ^{13}C-NMR

In the course of our investigation of the constituents of *Tephrosia purpurea* (Leguminosae), we found that methylpongamol showed two spots in silica gel thin-layer chromatography (TLC), after it had been kept in a solvent for a while.[1] Since these spots were interconvertible, we thought that this phenomenon must be due to *Z–E* isomerization of the compound and that this could be an inherent property of *β*-methoxychalcones. However, the naturally occurring *β*-methoxychalcones so far reported, methylpongamol[2] and praecansone A,[3] have been described as being in *Z*-form, no isomerization having been reported.

On the other hand, the crystal polymorphism of *β*-alkoxychalcones was extensively studied by German (Eistert, *et al.*)[4a] and Japanese (Ikeda, *et al.*)[4b—g] groups in the 1950's in connection with *E–Z* isomerization of these molecules. They considered that the easy isomerization of the double bond configuration was one of the reasons for the polymorphism, and recognized that the unstable form readily changed into the stable one, to which they assigned *Z* and *E* configurations by the use of ultraviolet (UV) spectroscopy as a major tool. However, since the reported data are confusing and sometimes conflicting,[5] those results should be reinvestigated by the application of modern physico-chemical techniques.

In this paper we describe full characterization of the *E*- and *Z*-isomers of some *β*-methoxychalcones including methylpongamol by modern spectroscopic methods, showing that the *E*-configuration of the double bond is the preferred form, and demonstrate that the reported physical and spectral data for methylpongamol and praecansone A are those of the *E*-isomers.

Results and Discussion

Firstly, we prepared four dibenzoylmethanes **1**, **2**, **3**, and **14**, as precursors of *β*-methoxychalcones. They exist in chelated enol forms. This is exemplified by the results of X-ray crystallographic analyses of the simplest dibenzoylmethane **1**, which takes the symmetrical structure **1a**[6] (Chart 1), and also of pongamol **14**.[7] Analogous structures were also indicated to be present in solutions, because, in the nuclear magnetic resonance (NMR) spectra, they showed clear signals of an olefinic proton (as well as an olefinic carbon) at δ_H 6.8—7.3 (δ_C 92—99) and a strongly chelated hydroxyl proton at δ_H 15.6—17.3. These findings imply the *Z*-configuration of *β*-hydroxychalcone structures.[8]

***Z–E* Isomerization of *β*-Methoxychalcone (4)** Methylation of dibenzoylmethane **1** with diazomethane in an ether–methanol mixture afforded a single *O*-methylated product **4a** as pale yellow prisms, mp 83—84 °C. This compound was unambiguously proved to be the *Z*-isomer of *β*-methoxychalcone by X-ray crystal analysis (Fig. 1a).

Z-β-Methoxychalcone **4a** was rather unstable and changed into the isomer **4b** when kept in solution or even in a crystalline state. This change was particularly remarkable on silica gel. Although **4a** gave a single spot on silica gel TLC when it was developed immediately after

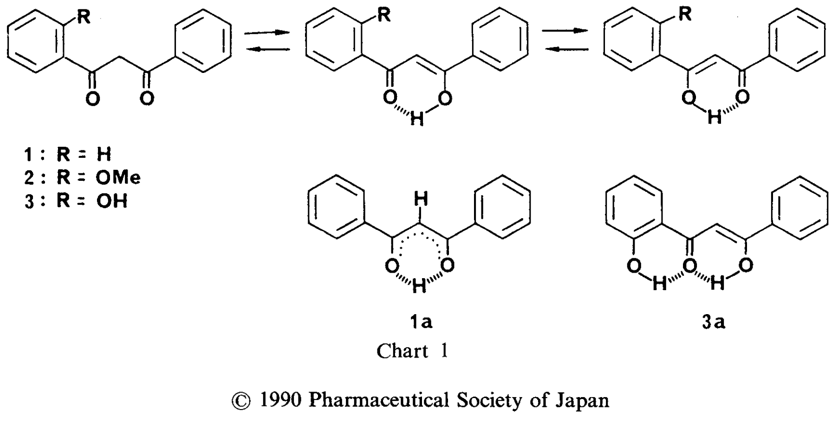

Chart 1

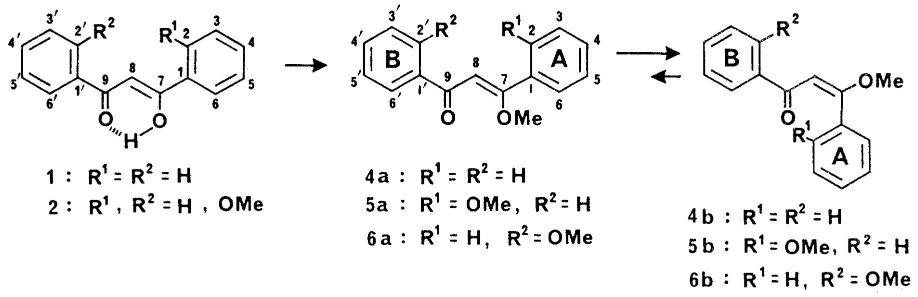

Chart 2

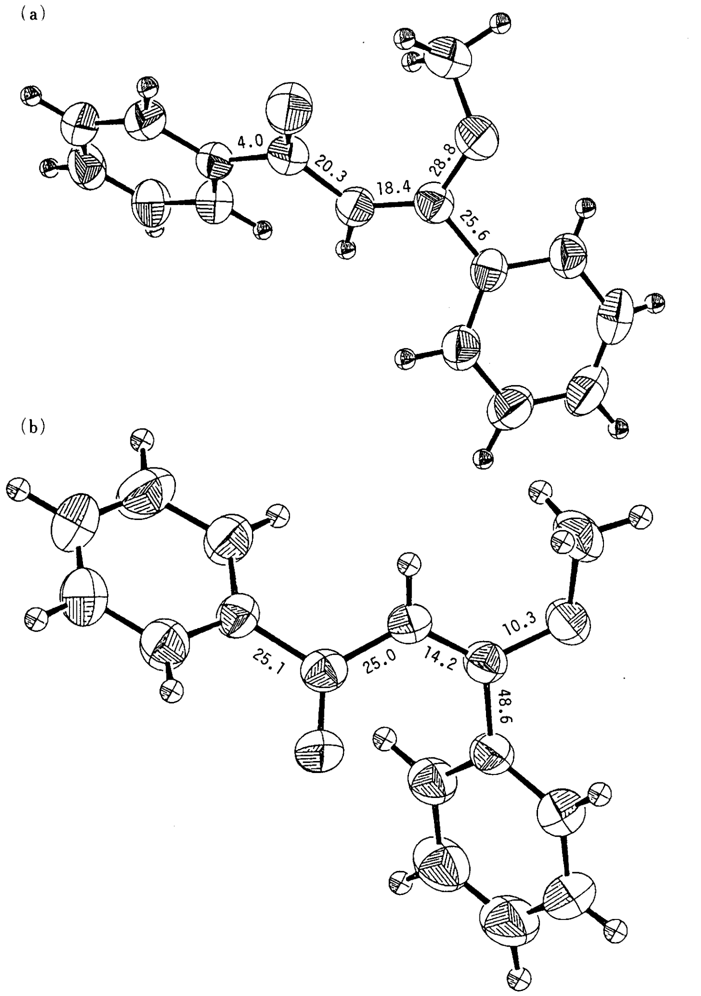

Fig. 1. ORTEP Drawing of (a) *Z*-*β*-Methoxychalcone **4a** and (b) *E*-*β*-Methoxychalcone **4b**

The value given along the bond shows the dihedral angle (°).

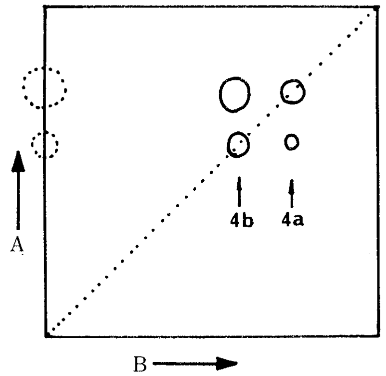

Fig. 2. Two-Dimensional TLC of *β*-Methoxychalcones

A mixture of **4a** and **4b** was spotted on a TLC plate and developed with ether : hexane = 1 : 1. After the first development (A), the plate was dried and left for 3 h at room temperature and developed with the same solvent at right angles to the first development (B).

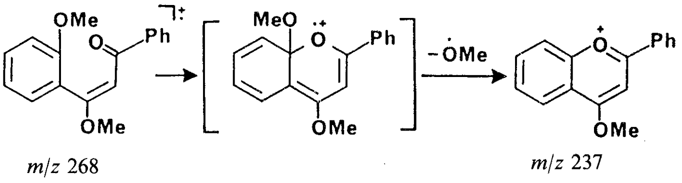

Chart 3

spotting, two spots (of **4a** and **4b**) were observed when the plate was left for a while before development. Thus **4b** was obtained as pale yellow prisms, mp 60—65 °C, by slow chromatography of **4a** through a long silica gel column. The *E*-configuration of the double bond in **4b** was unequivocally established by X-ray crystallography (Fig. 1b).

Equilibration of **4a** and **4b** on the surface of silica gel was clearly demonstrated by two-dimensional TLC (Fig. 2), which clearly indicated that each spot isomerized to the other, confirming **4a** and **4b** to be interconvertible.

The above results conclusively show that diazomethane methylation of **1** gives the *Z*-isomer **4a** (mp 83—84 °C, lit. mp 81 °C) as a kinetically controlled product which isomerizes to the thermodynamically more stable *E*-isomer **4b** (mp 60—65 °C, lit. mp 65 °C), and, although the results of methylation of **1** reported by the previous authors are confusing,[5] their conclusion that the *E*-isomer is more stable than the *Z*-isomer is correct (see also below).

***Z*–*E* Isomerization of 2,7-Dimethoxy- and 2′,7-Dimethoxychalcones (5 and 6)** Methylation of 2-methoxydibenzoylmethane **2** with diazomethane in ether–methanol produced two *O*-methylated compounds in a ratio of 2 : 1. They were assigned as 2,7-dimethoxychalcone **5a** and 2′,7-dimethoxychalcone **6a**, since they exhibited different ions, *m*/*z* 237 and 105, respectively, as the base peaks in their mass spectra (MS) (Table I). The former ion corresponds to the formation of a benzopyrilium cation by the loss of an OMe group (Chart 3), and is characteristic of 2-methoxychalcones.[2]

These assigned structures were confirmed by chemical means. On reduction of **5a** and **6a** with NaBH$_4$/CeCl$_3$ in methanol, the dimethylacetal **7** and **8a** were produced, respectively. When this reduction was carried out in ethanol for **6a**, the ethyl-methylacetal **8b** was obtained, thus indicating that the reaction proceeded as shown in Chart

TABLE I. MS Fragment Intensity (%) of β-Methoxychalcones

	2,7- and 2′,7-Dimethoxychalcones					*O*-Methylpongamols				
m/*z*	**5a**	**5b**	**6a**	**6b**	*m*/*z*	**15a**	**15b**	**16a**	**16b**	MP[a)]
268 M^+	0.1	0.5	43	23	308 M^+	0.9	0.6	63	72	23
267 M^+-1	0.5	2	82	44	307 M^+-1	0.8	0.6	47	54	19
237 M^+-31	100	100	26	15	277 M^+-31	100	100	48	35	18
161	1	3	96	65	175	11	6	71	78	100
135	6	13	99	65	161	8	5	95	100	70
105	20	44	100	100	105	37	16	100	72	92

a) Natural methylpongamol. See ref. 1.

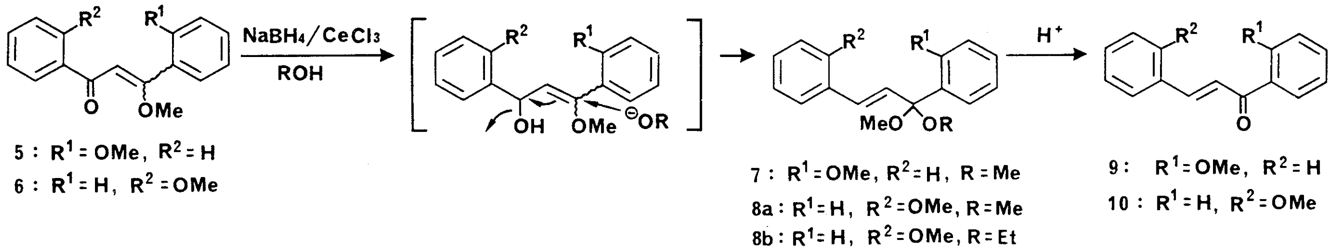

Chart 4

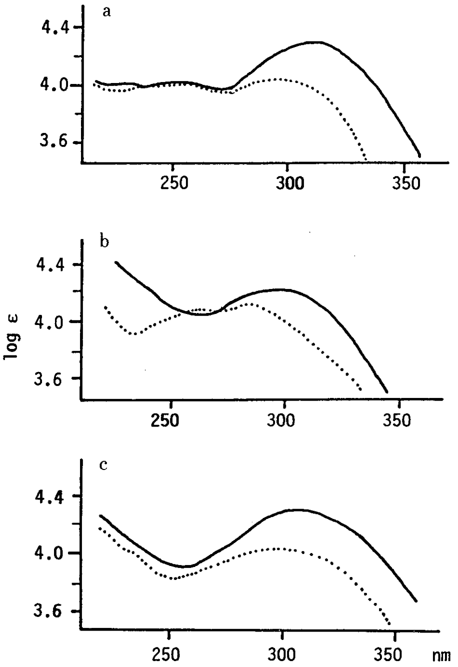

Fig. 3. UV Spectra of Isomers of β-Methoxychalcones

a: **4a** (——), **4b** (· · · ·). b: **5a** (——), **5b** (· · · ·). c: **6a** (——), **6b** (· · · ·).

4, in which the enol ether in the original compound was converted into the acetal. Such a reductive acetalization is presumably the result of the known catalytic action of a lanthanide ion on acetalization.[9)] Acid hydrolysis of **7** and **8** gave the chalcones **9** and **10** (identical with authentic specimens), respectively, in which the positions of the carbonyl and the double bond are interchanged from the original β-methoxychalcones. Thus the structures of **5a** and **6a** were established, except for the stereochemistry of the double bond.

Compounds **5a** and **6a** were also unstable and changed into the isomers, **5b** and **6b**, respectively, when chromatographed slowly over silica gel. However, these pairs behaved differently in chromatography. On silica gel TLC, **6a** was more mobile than **6b**, in agreement with the mobilities of **4a** and **4b**, whereas **5a** moved more slowly than **5b**. Although there were such discrepancies, we were able to assign the configurations as *Z* for **5a** and **6a** and *E* for **5b** and **6b** for the reasons described in the next section.

Spectroscopic Characterization of *E*- and *Z*-Isomers The intense UV absorption maximum at 310 nm of *Z*-β-methoxychalcone **4a** shifted to 292 nm with a decrease of the intensity on isomerization to the *E*-isomer **4b** (Fig. 3a). This agrees well with the reported UV change in *Z* to *E* isomerization of β-alkoxychalcones.[4)] A similar blue shift (10—15 nm) of the UV maximum was observed in the isomerization of **5a** to **5b** and **6a** to **6b** (Fig. 3b, c), suggesting that **5a** and **6a** are *Z*- and **5b** and **6b** are *E*-isomers.

In the ^{13}C-NMR spectra, the configurational change from *Z* to *E* resulted in a change of the C-8 (olefinic carbon) chemical shift from δ 102.8 (**4a**) to 98.6 (**4b**) (Table III). Similar upfield shifts (*ca.* 5 ppm) of $\delta_{\text{C-8}}$ were also observed in the isomerization of **5a** to **5b** and **6a** to **6b** (Table III), again indicating that **5a** and **6a** were *Z*- and **5b** and **6b** were *E*-isomers.

In contrast to the consistent UV and ^{13}C-NMR changes, the changes of $\delta_{\text{H-8}}$ (olefinic proton) in the ^{1}H-NMR spectra on *Z*–*E* isomerization are variable (Table II). The signal of H-8 shifted upfield by 0.3 ppm in the configurational change of **4a** to **4b** and **6a** to **6b**, whereas it shifted downfield by 0.3 ppm in the change of **5a** to **5b**. These opposite changes of H-8 in *Z* to *E* isomerization of β-methoxychalcones (see also the section on methylpongamol) may be summarized as follows[10)]: H-8 moves upfield by 0.2—0.3 ppm if there is no *ortho*-substituent on ring A, but it moves downfield by 0.2—0.3 ppm when the compound carries an *ortho*-substituent on ring A.

Although there were such irregular shifts in the ^{1}H-NMR spectra, observations of nuclear Overhauser effect (NOE) led to the correct assignment of the configurations. *E*-β-Methoxychalcone **4b** showed 7% NOE between the protons of OMe and H-8, whereas no NOE was observed

Table II. ^{1}H-NMR of β-Methoxychalcones[a]

	4a	**4b**	**5a**	**5b**	**6a**	**6b**	**15a**	**15b**	**16a**	**16b**	MP[b]
H-8	6.60	6.31	6.10	6.44	6.51	6.25	6.18	6.39	6.53	6.30	6.30
R-OMe	3.93	3.89	3.59	3.92	3.85	3.86	3.73	3.91	3.89	3.88	3.88
Ar-OMe	—	—	3.89	3.62	3.87	3.86	4.13	3.97	4.07	4.09	4.08

a) Chemical shifts (δ) in acetone-d_6 for **4**—**6** and in $CDCl_3$ for **15** and **16**, at 400 MHz. *b*) Natural methylpongamol (see ref. 1).

Table III. ^{13}C-NMR Chemical Shifts of β-Methoxychalcones[a]

No.[b]	**4a**[c]	**4b**[c]	**5a**[b]	**5b**[b]	**6a**	**6b**	**15a**	**15b**	**16a**	**16b**	7-MP[d]	9-MP[d]	Praecansone A[e]
1	136.7	136.4	141.4 (1′)	141.1 (1′)	137.4	137.1	139.9	139.7	135.8	135.4	135.5	139.8	140.0[h]
2,6	128.8	128.8	129.2 (2′,6′)	129.0 (2′,6′)	128.8	130.4	128.0	128.0	127.6	128.9	129.0	128.0[g]	127.8[h]
3,5	129.0	128.6	129.5 (3′,5′)	129.3 (3′,5′)	129.9	128.5	128.2	128.2	128.5	127.6	127.6	128.2[g]	127.9[h]
4	132.7	132.4	132.9 (4′)	132.8 (4′)	131.7	130.9	131.7	131.8	130.3	129.6	129.6	131.8	131.4
7	168.6	171.1	189.5 (9)	190.0 (9)	167.6	170.8	189.1	189.9	167.3	170.5	170.6	190.0	190.1
8	102.8	98.6	105.9 (8)	100.8 (8)	109.5	104.5	104.7	99.7	108.4	103.2	103.2	99.7	101.5
9	189.0	189.5	168.1 (7)	168.8 (7)	190.7	191.2	168.0	169.3	190.0	191.0	191.0	169.3	165.9
1′	140.1	140.4	125.4 (1)	127.2 (1)	132.7	132.6	119.7	121.1	127.6	127.6	—[f]	121.1[g]	107.7
2′	128.1	128.0	158.7 (2)	158.2 (2)	159.1	158.7	151.5	151.2	153.0	152.8	152.8[g]	151.2[g]	157.9
3′	129.1	126.6	112.6 (3)	112.3 (3)	113.1	112.9	118.4	118.5	119.3	119.2	119.1[g]	118.5[g]	111.6
4′	131.1	129.9	132.8 (4)	131.5 (4)	133.4	133.2	157.7	157.4	158.3	158.2	158.2[g]	157.4[g]	154.7
5′	129.1	126.6	121.9 (5)	121.1 (5)	121.7	121.4	106.1	106.0	106.6	106.5	106.5[g]	106.0[g]	96.1
6′	128.1	128.0	131.8 (6)	131.1 (6)	130.9	130.5	126.5	126.0	126.6	126.8	126.8	126.1	155.7
7′							105.0	105.1	105.2	105.1	105.1[g]	105.1[g]	166.9
8′							144.8	144.1	144.7	144.6	144.6	144.1	126.8
R-OMe	61.9	56.8	58.8	57.1	62.2	57.3	58.3	56.3	61.2	56.4	56.1[g]	56.4[g]	55.8[i]
Ar-OMe			56.5	56.2	56.6	56.4	60.1	60.2	61.3	61.4	61.3[g]	60.2[g]	62.0 55.9[i]

a) Chemical shifts (δ) in acetone-d_6 at 25 MHz for **4**—**6** and in $CDCl_3$ at 100 MHz for **15** and **16**. The data were confirmed by the ^1J and $^{2,3}J$ values in C–H COSY spectra. *b*) For comparisons of the data, pongamol numbering is adopted for **5a** and **5b**. The real numbering (according to Chart 2) is indicated in parentheses. *c*) The assignment of signals was done with reference to the data for **5** and **6**. *d*) Data from Pelter *et al.* (ref. 2). 7-MP, 7-*O*-methylpongamol; 9-MP, 9-*O*-methylpongamol. *e*) Data from ref. 3*b*. *f*) Chemical shift is not given in ref. 2. *g*) The original assignments were revised with reference to our data (see ref. 11). *h*, *i*) Attributions having the same superscript may be interchanged.

between these protons in **4a**. This is consistent with the fact that β-OMe and H-8 are on the same side of the double bond in **4b** and they are on opposite sides in **4a**. For **5** and **6**, two OMe signals have to be identified before the NOE experiment. Thus, firstly, all proton and carbon signals of **5a, b** and **6a, b**, including those of methoxyls, were assigned on the basis of H–H chemical shift correlation spectroscopy (COSY), C–H COSY [$J=150$ Hz; ^1J(C–H)] and long-range C–H COSY [$J=10$ Hz; $^{2,3}J$(C–H)] spectra.[11] In a $^{2,3}J$(C–H) spectrum of **5a**, correlation peaks were observed between the OMe at δ 3.59 and C-9 (δ 168.1), and between OMe at δ 3.89 and C-2 (δ 158.7). These findings indicate that the OMe signals at δ 3.59 and 3.89 are due to the β-methoxy and aromatic methoxy groups, respectively. By similar procedures, the two OMe signals of **5b** at δ 3.92 and 3.62, were assigned to the β-methoxy and aromatic methoxy groups, respectively. Next, when β-OMe (δ 3.92) in **5b** was irradiated, appreciable NOE (18%) was observed at H-8, whereas no NOE at H-8 was observed on irradiation of the β-OMe signal at δ 3.59 in **5a** (Fig. 4), thus confirming our stereochemical assignment of **5a** and **5b** (**5a** is *Z* and **5b** is *E*).

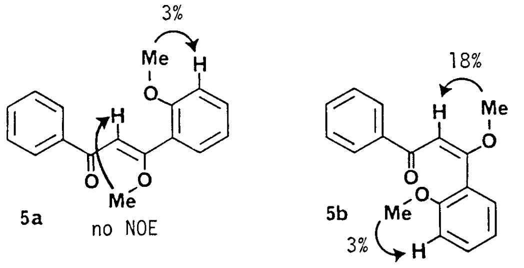

Fig. 4. Observed NOE on Irradiation of the Methoxyl Groups in **5a** and **5b**

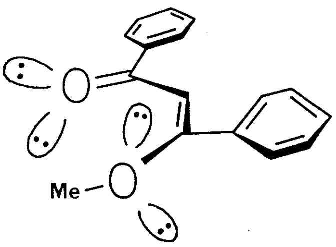

Fig. 5. Orientation of Lone Pairs in **4a**

The results of X-ray analyses of **4a** and **4b** can account for the spectroscopic behavior of the *E*- and *Z*-isomers. In the crystalline state, the benzoyl group of the *Z*-isomer **4a** is almost in one plane and the double bond makes a dihedral angle of 20 °C to that plane. Ring A is twisted by *ca.* 26° from the plane of the double bond (Fig. 1a). On the other hand, coplanarity of the molecule **4b** is almost lost. The planes of ring B and C=O make an angle of 25°, and those of C=O and C=C make an angle of 25°. Ring A is twisted by *ca.* 50° from the C=C plane (Fig. 1b). This loss of coplanarity in the *E*-isomer explains the blue shift of the UV absorption on *Z* to *E* isomerization.

The methyl group in **4a** is twisted by 29° from the enol plane and is facing the carbonyl group. This structure must

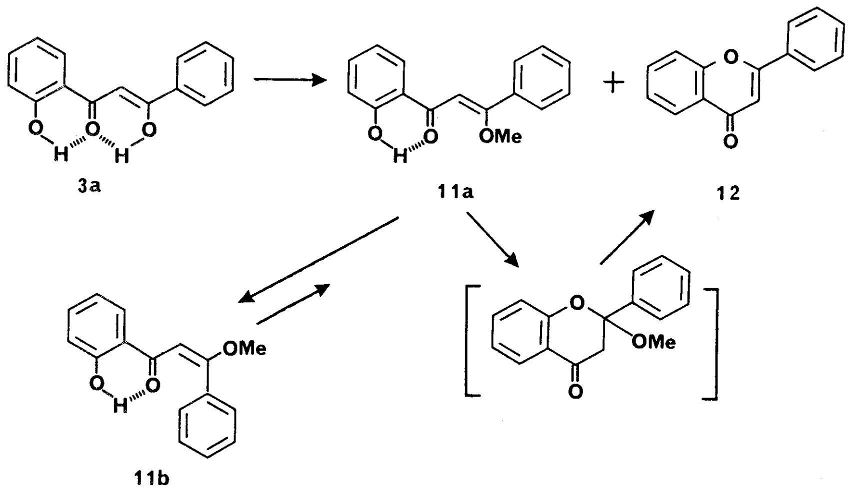

Chart 5

suffer severe steric repulsion between these groups compared to the structure with the methyl group in the opposed orientation. In fact, the methyl group in **4b** is facing the olefinic proton, where the steric repulsion is smaller than in the structure in which it is facing ring A. Why is the methyl group of OMe in **4a** at the more repulsive carbonyl side? It may be because the methoxy group takes the position that minimizes the repulsion between the lone pairs of the oxygen atoms (Fig. 5). This lone pair repulsion, together with the dipole repulsion of the two oxygen functions, may be the driving force of the *Z* to *E* isomerization.

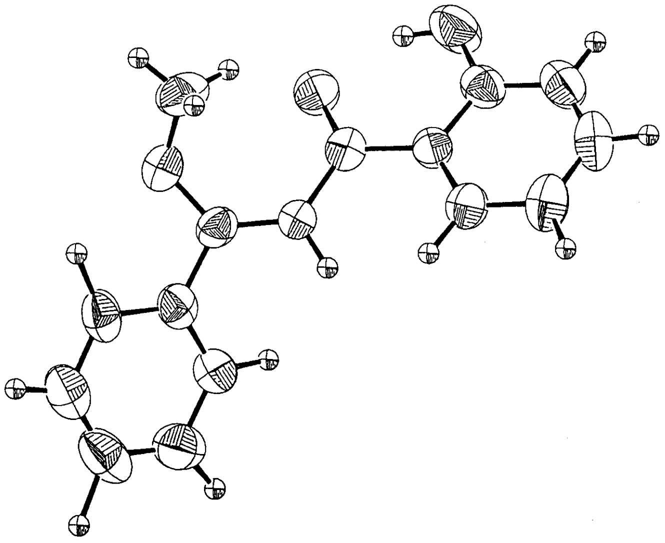

Fig. 6. ORTEP Drawing of **11a**

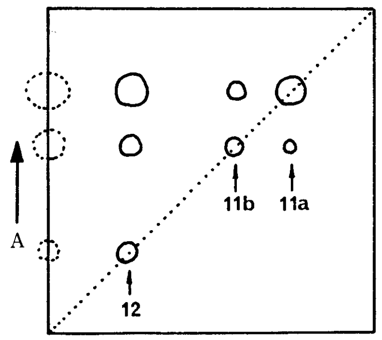

Fig. 7. Two-Dimensional TLC of **11a**

Compound **11a** (contaminated with **11b** and **12**) was spotted on a TLC plate and developed with hexane : ether = 1 : 1. After the first development (A), the plate was dried and kept in the dark at room temperature for 30 min and then developed with the same solvent at right angles to the first development (B).

Methylation of 2-Hydroxydibenzoylmethane (3) When 2-hydroxydibenzoylmethane **3** was treated with diazomethane in ether, 2′-hydroxy-*β*-methoxychalcone **11a** was obtained together with small amounts of flavone **12** and the dimethyl derivatives (**5a** and **6a**). The product **11a** was the *Z*-isomer as definitively determined by X-ray crystal analysis (Fig. 6). 2-Methoxydibenzoylmethane **2** was not isolated in this methylation.[12] This result can be explained if we consider the dichelated enol form **3a**, which is supported by the ^{1}H-NMR spectrum of **3** (two chelated hydroxyls at δ 12.0 and 15.4). The more acidic enolic hydroxy group in this structure was methylated.

On treatment of **11a** in methanol with a catalytic amount of acid (*p*-TsOH) or base (KOH), it readily changed into the flavone **12**. Unexpectedly, treatment of **11a** with diazomethane in methanol exclusively gave the flavone **12**.

When **11a** was kept in a refrigerator, it slowly changed into a mixture of compounds including **12**. Although the two-dimensional TLC of the resulting mixture suggested the formation of the *E*-isomer **11b** (Fig. 7), it could not be isolated.

Configurations of Methylpongamol and Praecansone A Pongamol **14** was synthesized by condensation of 5-acetyl-4-methoxybenzofuran **13** with ethyl benzoate.[13] The recent X-ray analysis[7] showed that it has the *trans*-enol form. In solution, it also took an enol form as shown by a chelated hydroxyl signal at δ 16.87 and an olefinic proton signal at δ 7.16 (and also an olefinic carbon signal at δ 97.9).

Methylation of pongamol **14** with diazomethane in ether–methanol gave two *O*-methylated products, **15a** and **16a**, with a slight excess of the former. They were identified as the 9-*O*-methyl and 7-*O*-methyl derivatives, respectively, on the basis of their MS: *i.e.*, **15a** gave a base peak at *m*/*z* 277 ($M^+ - OMe$), whereas **16a** gave one at *m*/*z* 105 (Table I).

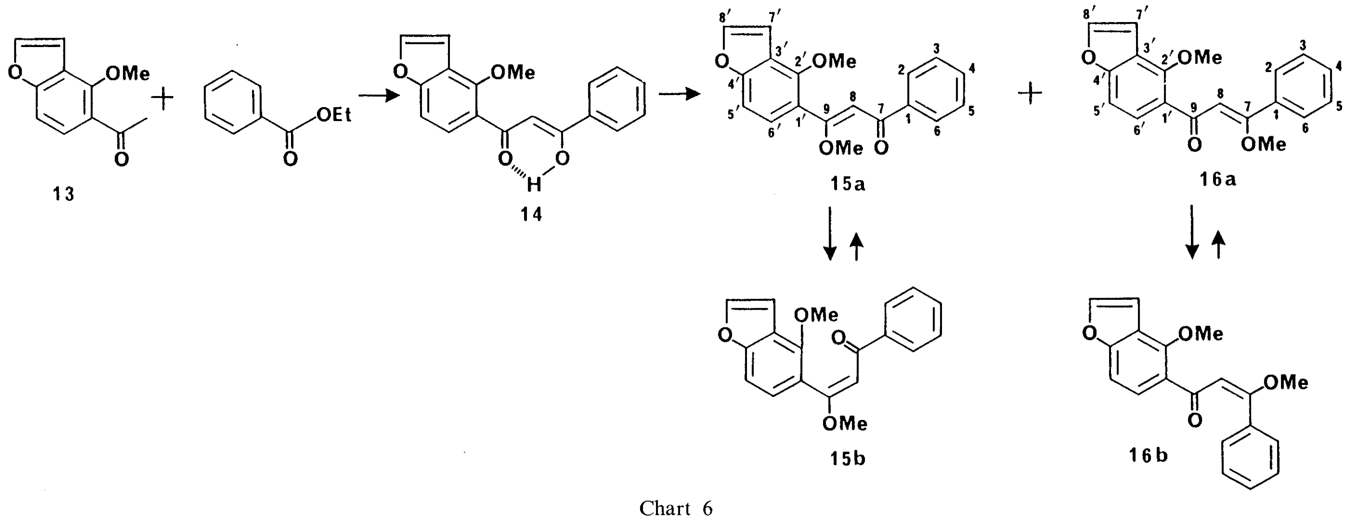

Chart 6

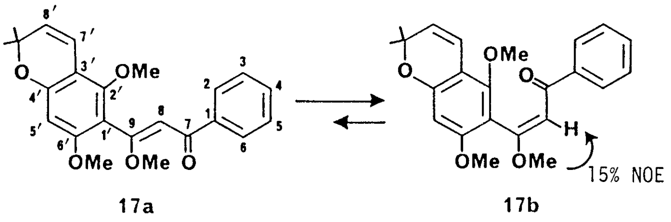

Chart 7

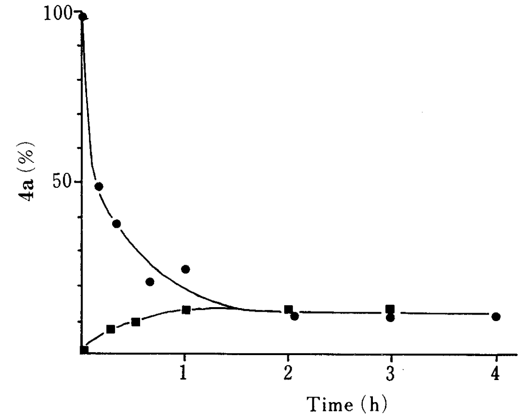

Fig. 8. Isomerization of β-Methoxychalcone (**4**) on the Surface of Silica Gel

●—●: from **4a**. ■—■: from **4b**.

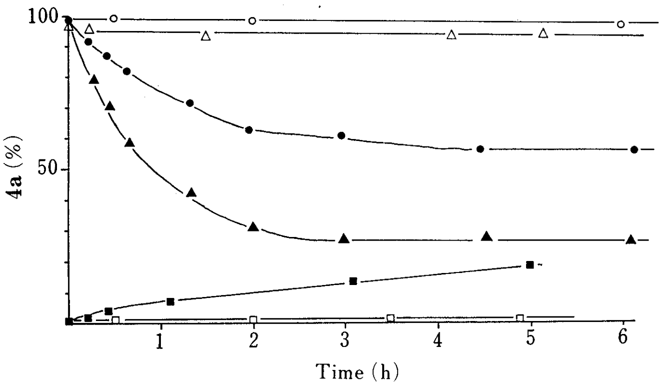

Fig. 9. Isomerization of β-Methoxychalcone (**4**) in Various Solvents

Compound **4a** or **4b** was dissolved in a solvent and heated in the dark at 55 °C. ○—○: **4a** in dry hexane. △—△: **4a** in dry acetone. ●—●: **4a** in dry methanol. ▲—▲: **4a** in 10% water in methanol. ■—■: **4b** in dry methanol. □—□: **4b** in dry acetone.

Compounds **15a** and **16a** readily isomerized on contact with silica gel. As in the cases of **5** and **6**, isomerization of **15a** to **15b** increased and that of **16a** to **16b** decreased the mobility of the compounds on TLC. Comparisons of the UV maxima of **15a** (302 nm) and **15b** (279 nm) and those of **16a** (307 nm) and **16b** (293 nm) revealed that **15a** and **16a** are *Z*-isomers and **15b** and **16b** are *E*-isomers. The ^{13}C-NMR spectra supported these assignements: the C-8 signals shifted upfield by *ca.* 5 ppm on isomerization of **15a** and **16a** to **15b** and **16b**, respectively (Table III).

The H-8 signal in the ^{1}H-NMR also showed expected movement: it shifted upfield by 0.23 ppm on isomerization from **16a** to **16b** and downfield by 0.18 ppm from **15a** to **15b** (Table II).

Finally, all the spectral data of **16b** were in good agreement with those reported for natural methylpongamol,[1,2] indicating that natural methylpongamol so far reported is the *E*-7-*O*-methyl isomer. However, it should be mentioned that the *E*- and *Z*-isomers of methylpongamol are interconvertible: either isomer gave spots of the *E*- and *Z*-isomers on TLC when a spotted sample was kept for a while on the plate before development. In reversed-phase high-performance liquid chromatography (HPLC), 7-*O*-methylpongamols (**16a** and **16b**) were well separated [relative retention times (rt_R), 1.56 and 1.29, respectively], whereas the isomers of 9-*O*-methylpongamol (**15a** and **15b**) were not separable (rt_R, 1.27). The reported two peaks of methylpongamol in the extract of *T. purpurea*[1] were identical with those of *Z*- and *E*-7-*O*-methylpongamol.

Pelter *et al.*[2] also reported methylation of pongamol and observed two products, the 9-*O*-methyl and 7-*O*-methyl derivatives. However, the reported data (^{1}H- and ^{13}C-NMR) for their *O*-methylpongamols are those of the *E*-isomers (see Table III). It seems that they had observed only the isomerized products and missed the formation of the *Z*-isomers.

Praecansone A is a β-methoxychalcone isolated from some *Tephrosia* spp.[3] The proposed structure **17a** is mainly based on the fact that it gave a base peak due to $M^+ - OMe$ in the MS and also on ^{13}C-NMR data, though the configuration of the double bond remains to be determined.

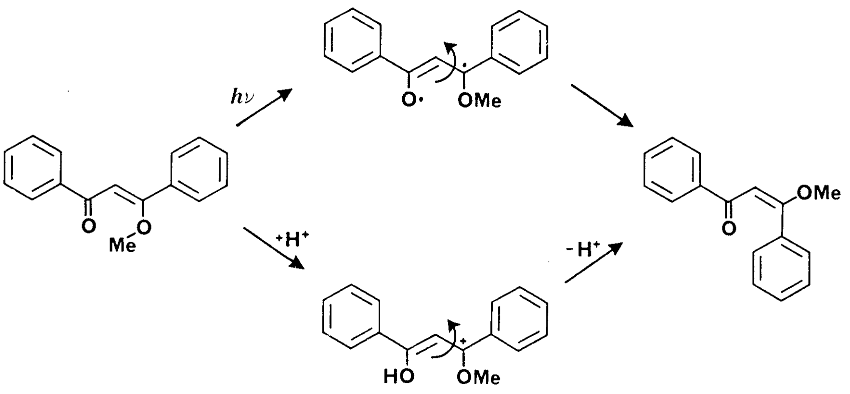

Chart 8

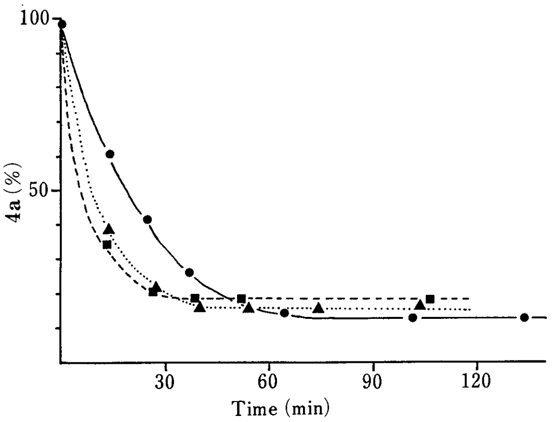

Fig. 10. Light-Induced Isomerization of β-Methoxychalcone (4)

Compound **4a** was dissolved in a solvent and irradiated with a xenon lamp at 0 °C. ●—●: dry hexane. ▲···▲: dry acetone. ■---■: dry methanol.

The reported data for praecansone A [UV: 284 nm[3a]; $\delta_{\text{H-8}}$: 6.43; $\delta_{\text{C-8}}$: 101.5[3b]] suggest its configuration to be *E* rather than *Z*. The NOE (15%) observed between H-8 and 9-OMe[3b] supports our conclusion that the reported data for praecansone A can be ascribed to the *E*-isomer **17b**.

Preliminary Kinetic Studies Interconversion of **4a** and **4b** on a silica gel plate at room temperature reached equilibrium within 2 h to give a 1 : 7 mixture of **4a** and **4b** from both isomers (Fig. 8).

The isomerization of **4a** to **4b** in solution has been reported. Ikeda[4g] reported that equilibration of **4a** and **4b** occurs either in heptane or methanol to give, after two weeks, the same equilibrium mixture of $E:Z=72:28$, and thus he assumed that this isomerization was little affected by the solvent polarity. However, we have observed that the isomerization rate was markedly affected by the solvent polarity, as shown in Fig. 9. The isomerization was obviously accelerated by increase of the solvent polarity from hexane to 10% water in methanol solution. In the former solvent, the isomerization of **4a** in the dark was practically negligible.

As reported already,[4b] light also induced and/or accelerated the isomerization. Thus, on irradiation with visible light, **4a** isomerized in hexane solution, giving rise to a 15 : 85 mixture of **4a** and **4b** within 70 min. The isomerization by light was accelerated by increase of the solvent polarity: the same equilibrium mixture was obtained within 40 min in methanol or in acetone (Fig. 10).

The above evidence suggests that the *Z*–*E* isomerization of β-methoxychalcones occurs through either or both of the routes, ionic and/or radical, as illustrated in Chart 8. Details of kinetic studies in connection with the reaction mechanisms will be presented in a future publication.

Conclusion

Methylation of dibenzoylmethanes (β-hydroxychalcones) with diazomethane in ether–methanol always gives *Z*-β-methoxychalcones, which are produced by the kinetically controlled methylation of chelated enol forms of β-hydroxychalcones. The *Z*-isomers are thermodynamically unstable and isomerize, either on contact with silica gel, on keeping in polar solvents, or on exposure to light, to the more stable *E*-isomers. Natural β-methoxychalcones so far isolated should therefore have preferred *E*-configuration, since they have been treated with organic solvents (extraction, partition, *etc.*) and/or chromatographed (sometimes repeatedly) during isolation. This was the case for methylpongamol and praecansone A.

The *E*- and *Z*-isomers were well characterized by UV, ^{13}C-NMR, and/or NOE between β-OMe and H-8, and could be definitively determined by X-ray crystal structure analysis (if the product was crystalline).

Experimental

General Melting points were determined on a Yanagimoto micro hot-stage melting point apparatus and are uncorrected. UV spectra were measured on a Hitachi 323 spectrophotometer in ethanol and are given as λ_{max} nm ($\log \varepsilon$). Infrared (IR) spectra were taken as $CHCl_3$ solutions on a JASCO A-202 and/or Shimadzu IR-460 spectrometer and are given in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra were measured on a JEOL JNM FX-100 and/or JNM GX-400 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard, and chemical shifts are given in δ. MS and high-resolution mass spectra (HRMS) were measured on a Hitachi M-80 machine. HPLC was carried out on a Tosoh apparatus (CCPD and CO-8000) equipped with a UV-8000 UV detector (set at 254 nm). Fuji Davison BW-820MH (silica gel) was used for column chromatography. For normal and reversed-phase TLC, Macherey-Nagel precoated TLC plates SIL G-25 UV254 and Merck HPTLC precoated plates RP-8 F254 were used, respectively.

Dibenzoylmethanes (1) Dibenzoylmethane **1** was prepared by the condensation of acetophenone and ethyl benzoate as colorless needles from ether–hexane, mp 69—71 °C, changing to pale yellow crystals of mp 78—79 °C (lit. mp 77—78 °C)[14] on standing at room temperature. IR: 1600. ^{1}H-NMR (acetone-d_6): 7.23 (1H, s), 7.36—7.65 (6H, m), 8.00—8.20 (4H, m), 17.22 (1H, br s). ^{13}C-NMR (acetone-d_6): 93.7, 128.0, 129.5, 133.4, 136.1, 186.5. MS *m*/*z*: (%): 224 (M^+, 84), 223 (87), 147 (50), 105 (100), 77 (62).

(2) 2-Methoxydibenzoylmethane **2** was prepared by the condensation of acetophenone and methyl *o*-anisate as yellow prisms from ether–hexane, mp 66—67 °C (lit. mp 65 °C).[15] UV: 250 (3.74), 355 (4.34). IR: 1600. ^{1}H-NMR: 3.94 (3H, s), 6.88—7.12 (2H, m), 7.13 (1H, s), 7.32—7.52 (4H,

m), 7.80—8.00 (3H, m), 16.84 (1H, brs). ^{13}C-NMR: 55.9, 98.5, 111.8, 120.9, 125.0, 127.3, 128.6, 130.4, 132.2, 133.2, 136.1, 158.5, 184.2, 185.8. MS *m/z* (%): 254 (M$^+$, 12), 236 (15), 223 (100), 135 (95), 105 (48).

(3) 2-Hydroxydibenzoylmethane **3** was prepared from *o*-hydroxyacetophenone and benzoyl chloride according to the method in Organic Syntheses[16] as yellow needles, mp 121—124 °C (lit. mp 117—120 °C).[16] UV: 253 (4.05), 364 (4.41). IR: 1605, 1564, 1490. ^{1}H-NMR: 6.84 (1H, s), 6.9—7.04 (2H, m), 7.36—7.6 (4H, m), 7.72 (1H, dd, $J=8$, 1.5 Hz), 7.88—8.02 (2H, m), 12.0 (1H, s), 15.4 (1H, s). ^{13}C-NMR: 92.3, 118.9, 119.1, 126.9, 128.5, 128.8, 131.0, 132.5, 133.7, 135.9, 162.6, 177.5, 195.7. MS *m/z* (%): 240 (M$^+$, 87), 223 (14), 163 (11), 121 (74), 105 (100), 77 (61).

Methylation of Dibenzoylmethane 1 Compound **1** (0.8 g) was dissolved in ether : methanol = 2 : 1 (10 ml) and treated with an excess of diazomethane at 0 °C. The mixture was concentrated to dryness and the residue was crystallized from hexane to give the *Z*-isomer **4a** (0.5 g) as pale yellow prisms, mp 83—84 °C (lit. mp 81 °C).[4b] UV: 227 (4.00), 252 (4.00), 310 (4.27). IR: 1638, 1563. ^{1}H-NMR (acetone-d_6): 3.93 (3H, s), 6.60 (1H, s), 7.36—7.58 (6H, m), 7.68—7.84 (2H, m), 7.90—8.08 (2H, m). MS *m/z* (%): 238 (M$^+$, 48), 237 (100), 221 (44), 161 (84), 105 (75), 77 (47).

Methylation of 2-Methoxydibenzoylmethane 2 Compound **2** (1.5 g) in ether : methanol = 2 : 1 (50 ml) was treated with an excess of diazomethane as described above at 0 °C. The mixture was concentrated to dryness and the residue was chromatographed over silica gel. Rapid elution with hexane : ether = 1 : 1 gave the *Z*-isomers, **5a** (1 g) and **6a** (0.5 g).

5a: Pale yellow oil. UV: 295 (4.16). IR: 1641, 1605, 1570. ^{1}H-NMR (400 MHz, acetone-d_6): 3.59 (3H, s, R-OMe), 3.89 (3H, s, Ar-OMe), 6.10 (1H, s, H-8), 7.05 (1H, td, $J=7.5$, 1 Hz, H-5), 7.12 (1H, d, $J=8$ Hz, H-3), 7.42 (1H, dd, $J=7.5$, 1 Hz, H-6), 7.43—7.54 (4H, m, H-4, 3′, 4′, 5′), 7.92—7.95 (2H, m, H-2′, 6′). HRMS (*m/z*) Calcd for $C_{16}H_{13}O_2$ (M$^+$ − OMe): 237.0914. Found: 237.0893.

6a: Pale yellow oil. UV: 305 (4.30). IR: 1635, 1600, 1565. ^{1}H-NMR (400 MHz, acetone-d_6): 3.85 (3H, s, R-OMe), 3.87 (3H, s, Ar-OMe), 6.51 (1H, s, H-8), 7.01 (1H, td, $J=7.5$, 1 Hz, H-5′), 7.09 (1H, d, $J=8.5$ Hz, H-3′), 7.40—7.47 (4H, m, H-3, 4, 5, 4′), 7.56 (1H, dd, $J=7.5$, 1 Hz, H-6′), 7.70 (2H, m, H-2, 6). HRMS (*m/z*) Calcd for $C_{17}H_{16}O_3$ (M$^+$): 268.1097. Found: 268.1057.

Methylation of 2-Hydroxydibenzoylmethane 3 Compound **3** (3 g) in ether was treated with an excess of diazomethane for 2 h. The mixture was concentrated to dryness and the residue was crystallized from ether–hexane to give **11a** (1.63 g) as pale yellow prisms, mp 104—105 °C. UV: 245 (4.08), 257sh (4.04), 310 (4.04). IR: 1625, 1565, 1490. ^{1}H-NMR: 4.05 (3H, s), 6.78 (1H, s), 6.90 (1H, td, $J=8$, 1.5 Hz), 6.96 (1H, d, $J=8$ Hz), 7.42—7.60 (4H, m), 7.76—7.90 (2H, m), 8.00 (1H, dd, $J=8$, 1.5 Hz). MS *m/z* (%): 254 (M$^+$, 4), 223 (100), 177 (21), 133 (38), 105 (15), 104 (17). *Anal.* Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.71; H, 5.20.

Chromatography of the mother liquor from **11a** with hexane–ether gave the flavone **12**[16] (200 mg, colorless needles from ether, mp 100—101 °C), **5a** (12 mg), and **5b** (120 mg).

Conversion of the *β*-Methoxychalcone (5a) to the Chalcone (9) A solution of *Z*-*β*-methoxychalcone **5a** (107 mg) and $CeCl_3 \cdot 7H_2O$ (0.8 g) in methanol (25 ml) was stirred at 0 °C for 10 min, then $NaBH_4$ (41 mg) was added. Stirring was continued for 1 h at 0 °C, then the reagent was decomposed by addition of water, and the mixture was extracted with ether. The ether extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness, and the residue was purified by chromatography (hexane : ether = 9 : 1) to give the dimethylacetal **7** (35 mg) as a colorless oil. IR: 1600, 1495, 1465. ^{1}H-NMR (acetone-d_6): 3.13 (6H, s), 3.74 (3H, s), 6.29 (1H, d, $J=16$ Hz), 6.68 (1H, d, $J=16$ Hz), 6.80—7.00 (2H, m), 7.10—7.44 (6H, m), 7.74 (1H, dd, $J=8$, 1.5 Hz). MS *m/z* (%): 284 (M$^+$, 22), 253 (68), 237 (37), 210 (33), 135 (94), 121 (78), 91 (100), 77 (59).

A methanol solution (20 ml) of **7** (35 mg) and *p*-toluenesulfonic acid (2 mg) was heated at 80 °C for 10 min. The reaction mixture was diluted with water and extracted with ether. The ethereal layer was washed with brine, dried, and concentrated, and the residue was purified by chromatography (hexane : ether = 4 : 1) to give 2′-methoxychalcone **9** (23 mg) as a pale yellow oil.[17] IR: 1650. ^{1}H-NMR (acetone-d_6): 3.93 (3H, s), 7.41 (1H, d, $J=13$ Hz), 7.60 (1H, d, $J=13$ Hz), 6.95—7.85 (9H, m). ^{13}C-NMR (acetone-d_6): 56.7, 113.4, 122.0, 128.6, 129.7, 130.3, 130.9, 131.2, 131.5, 134.2, 136.6, 143.4, 159.6, 193.0.

Conversion of the *β*-Methoxychalcones (6a and 6b) to the Chalcone (10) *Z*-*β*-Methoxychalcone **6a** (30 mg) in methanol was reduced as described above with $NaBH_4$ (20 mg) and $CeCl_3 \cdot 7H_2O$ (160 mg) to give the dimethylacetal **8a** (25 mg) as a colorless oil. IR: 1595, 1485, 1458. ^{1}H-NMR (acetone-d_6): 3.18 (6H, s), 3.85 (3H, s), 6.14 (1H, d, $J=16$ Hz), 6.76—7.01 (2H, m), 7.22 (1H, d, $J=16$ Hz), 7.14—7.60 (7H, m). MS *m/z* (%): 284 (M$^+$, 64), 253 (100), 237 (30), 210 (49), 207 (59), 161 (15), 151 (16), 145 (27), 121 (27), 105 (31), 91 (22). HRMS (*m/z*) Calcd for $C_{18}H_{20}O_3$ (M$^+$): 284.1411. Found: 284.1414.

Similar reduction of **6b** (20 mg) with $NaBH_4/CeCl_3$ in methanol gave the same dimethylacetal **8a** (19 mg).

Treatment of **6a** (35 mg) with $NaBH_4/CeCl_3$ in ethanol as described above gave the ethyl-methylacetal **8b** (34 mg) as a colorless oil. IR: 1594, 1485, 1457. ^{1}H-NMR (acetone-d_6): 1.23 (3H, t, $J=5$ Hz), 3.18 (3H, s), 3.45 (2H, m), 3.84 (3H, s), 6.17 (1H, d, $J=16$ Hz), 6.87—6.99 (2H, m), 7.22 (1H, d, $J=16$ Hz), 7.10—7.60 (7H, m). MS *m/z* (%): 298 (M$^+$, 34), 267 (34), 253 (54), 237 (46), 210 (23), 207 (57), 197 (12), 194 (15), 161 (31), 151 (23), 135 (31), 121 (60), 105 (100), 91 (58). HRMS (*m/z*) Calcd for $C_{19}H_{22}O_3$ (M$^+$): 298.1567. Found: 298.1558.

The dimethylacetal **8a** (19 mg) in methanol was hydrolyzed with *p*-toluenesulfonic acid and worked up as described above to give 2-methoxychalcone **10** (15 mg) as pale yellow prisms (from ether–hexane), mp 59—61 °C (lit. 58—59 °C).[18]

Acid hydrolysis of **8b** (20 mg) in a similar manner gave **10** (14 mg).

Isomerization of *Z*-*β*-Methoxychalcones to *E*-*β*-Methoxychalcones (1) *Z*-*β*-Methoxychalcone **4a** (200 mg) was applied to a silica gel column (2 × 30 cm) and eluted with hexane : ether = 1 : 1 over a period of 3 h. Crystallization of the eluate from hexane gave the *E*-isomer **4b** (111 mg) as pale yellow prisms, mp 60—65 °C (lit. mp 65 °C).[4b] UV: 236 (3.98), 255 (4.00), 292 (4.03). IR: 1660, 1563. ^{1}H-NMR (acetone-d_6): 3.89 (3H, s), 6.31 (1H, s), 7.16—7.48 (8H, m), 7.80—7.94 (2H, m). MS *m/z* (%): 238 (M$^+$, 41), 237 (100), 221 (36), 161 (77), 105 (67), 77 (43). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.86; H, 5.94.

(2) *Z*-2,7-Dimethoxychalcone **5a** (260 mg) was applied to a silica gel column (2 × 30 cm) and eluted with hexane : ether = 1 : 1 over a period of 3 h to give the *E*-isomer **5b** (130 mg), and a mixture of **5a** and **5b** (86 mg). **5b**: Pale yellow oil. UV: 263 (4.17), 283 (4.19). IR ($CHCl_3$): 1660, 1610, 1570. ^{1}H-NMR (400 MHz, acetone-d_6): 3.62 (3H, s, Ar-OMe), 3.92 (3H, s, R-OMe), 6.44 (1H, s, H-8), 6.91 (1H, br t, $J=8$ Hz, H-4), 6.94 (1H, br d, $J=8$ Hz, H-3), 7.20 (1H, dd, $J=7.5$, 1 Hz, H-6), 7.31 (1H, td, $J=7.5$, 1 Hz, H-5), 7.39—7.43 (2H, m, H-3′, 5′), 7.50 (1H, m, H-4′), 7.87—7.90 (2H, m, H-2′, 6′). HRMS (*m/z*) Calcd for $C_{16}H_{13}O_2$ (M$^+$ − OMe): 237.0914. Found: 237.0902.

(3) *Z*-2′,7-Dimethoxychalcone **6a** (180 mg) was similarly isomerized by slow chromatography over silica gel to the *E*-isomer **6b** (130 mg). **6b**: Pale yellow oil. UV: 217sh (4.49), 236sh (4.30), 297 (4.34). IR: 1640, 1600, 1560. ^{1}H-NMR (400 MHz, acetone-d_6): 3.86 (6H, s, OMe × 2), 6.25 (1H, s, H-8), 6.89 (1H, td, $J=7.5$, 1 Hz, H-5′), 6.95 (1H, d, $J=8$ Hz, H-3′), 7.24—7.35 (4H, m, H-3, 4, 5, 4′), 7.38—7.41 (3H, m, H-2, 6, 6′). HRMS (*m/z*) Calcd for $C_{17}H_{16}O_3$ (M$^+$): 268.1097. Found: 268.1070.

Synthesis of Pongamol 14 5-Acetyl-4-methoxybenzofuran **13** (900 mg), ethyl benzoate (782 mg), and NaH (60% oil dispersion, 417 mg) in tetrahydrofuran (THF, 60 ml) were heated under reflux for 4 h. The reaction mixture was quenched with acetic acid, diluted with water, and extracted with ether. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. Chromatography of the residue over silica gel (benzene : hexane = 1 : 1) gave pongamol **14** (734 mg) and the unchanged starting material **13** (333 mg). Pongamol crystallized in yellow prisms from methanol, mp 130—131 °C (lit. 127—129 °C).[2] UV: 240 (3.97), 352 (3.96). IR (KBr): 1595, 1552, 1537, 1470. ^{1}H-NMR (400 MHz): 4.13 (3H, s, OMe), 6.98 (1H, dd, $J=2.4$, 1 Hz, H-7′), 7.16 (1H, s, H-8), 7.29 (1H, dd, $J=8.5$, 1 Hz, H-5′), 7.45—7.57 (3H, m, H-3, 4, 5), 7.61 (1H, d, $J=2.5$ Hz, H-8′), 7.86 (1H, d, $J=8.5$ Hz, H-6′), 7.96—7.99 (2H, m, H-2, 6), 16.87 (1H, br s). ^{13}C-NMR (100 MHz): 61.1 (OMe), 97.9 (C-8), 105.3 (C-7′), 107.0 (C-5′), 119.6 (C-3′), 122.3 (C-1′), 126.5 (C-6′), 127.1 (C-2, 6), 128.6 (C-3, 5), 132.1 (C-4), 135.7 (C-1), 144.8 (C-8′), 153.8 (C-2′), 158.7 (C-4′), 184.3, 186.1 (C-7 and C-9). MS *m/z* (%): 294 (M$^+$, 25), 263 (100), 175 (73), 160 (19), 105 (27). *Anal.* Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80. Found: C, 73.42; H, 4.78. Spectral data of **14** were identical with those of an authentic sample of pongamol.[1]

Methylation of Pongamol 14 Pongamol **14** (300 mg) was dissolved in ether : methanol = 2 : 1 (60 ml) and treated with an excess of diazomethane at room temperature for 3 h. The reaction mixture was concentrated to dryness and the residue was rapidly chromatographed over a silica gel column (hexane : ether = 1 : 1) to give 7-*O*-methylpongamol **16a** (105 mg), 9-*O*-methylpongamol **15a** (108 mg), a mixture of **16a** : **16b** : **15b** = 7 : 2 : 4 (40 mg), and a mixture of **15a** and **15b** (54 mg).

15a: Pale yellow oil. UV: 253 (4.17), 302 (4.14). IR ($CHCl_3$): 1645, 1595, 1580, 1567. ^{1}H-NMR (400 MHz): 3.73 (3H, s, 9-OMe), 4.13 (3H, s, 2′-OMe), 6.18 (1H, s, H-8), 6.99 (1H, dd, $J=2.1$, 1 Hz, H-7′), 7.26 (1H, dd, $J=8.5$, 1 Hz, H-5′), 7.27 (1H, d, $J=8.5$ Hz, H-6′), 7.41 (2H, t with fine splittings, J=8.5 Hz, H-3, 5), 7.47 (1H, m, H-4), 7.63 (1H, d, J=2.1 Hz, H-8′), 7.94 (2H, m, H-2, 6). HRMS (m/z) Calcd for $C_{19}H_{16}O_4$ (M^+): 308.1047. Found: 308.1041. Calcd for $C_{18}H_{13}O_3$ (M^+ − OMe): 277.0863. Found: 277.0858.

16a: Pale yellow oil. UV: 245 (4.38), 307 (4.31). IR ($CHCl_3$): 1635, 1598, 1585, 1560. ^{1}H-NMR (400 MHz): 3.89 (3H, s, 7-OMe), 4.07 (3H, s, 2′-OMe), 6.53 (1H, s, H-8), 6.95 (1H, dd, J=2.4, 1 Hz, H-7′), 7.25 (1H, dd, J=8.5, 1 Hz, H-5′), 7.38—7.45 (3H, m, H-3, 4, 5), 7.59 (1H, d, J=2.4 Hz, H-8′), 7.63—7.67 (2H, m, H-2, 6), 7.65 (1H, d, J=8.5 Hz, H-6′). HRMS (m/z) Calcd for $C_{19}H_{16}O_4$ (M^+): 308.1047. Found: 308.1053.

Isomerization of *O*-Methylpongamols (1) *Z*-7-*O*-Methylpongamol **16a** (30 mg) was dissolved in ether : hexane = 1 : 1, applied to a silica gel column and left for 3 h, then the column was eluted with ether : hexane = 1 : 1 to give the *Z*-isomer **16a** (5 mg) and the *E*-isomer **16b** (23 mg). **16b**: Pale yellow oil. UV: 244 (4.41), 293 (4.19). IR: 1645, 1600, 1584, 1558. MS m/z (%): 308 (M^+, 72), 307 (54), 293 (21), 292 (23), 291 (87), 277 (35), 175 (78), 161 (100), 160 (30), 145 (27), 133 (21), 105 (73), 91 (21). ^{1}H-NMR (400 MHz): 3.88 (3H, s, 7-OMe), 4.09 (3H, s, 2′-OMe), 6.30 (1H, s, H-8), 6.90 (1H, dd, J=2.1, 1 Hz, H-7′), 7.14 (1H, dd, J=8.5, 1 Hz, H-5′), 7.27—7.30 (3H, m, H-3, 4, 5), 7.44 (2H, m, H-2, 6), 7.48 (1H, d, J=8.5 Hz, H-6′), 7.56 (1H, d, J=2.1 Hz, H-8′). HRMS (m/z) Calcd for $C_{19}H_{16}O_4$ (M^+): 308.1047. Found: 308.1033.

(2) *Z*-9-*O*-Methylpongamol **15a** (60 mg) was similarly treated with silica gel to give the *E*-isomer **15b** (47 mg) and the *Z*-isomer **15a** (12 mg). **15b**: Pale yellow oil. UV: 248 (4.22), 279sh (4.04). IR: 1660, 1595, 1574, 1536. ^{1}H-NMR (400 MHz): 3.91 (3H, s, 9-OMe), 3.97 (3H, s, 2′-OMe), 6.39 (1H, s, H-8), 6.88 (1H, dd, J=8.5, 1 Hz, H-7′), 7.15 (1H, d, J=8.5 Hz, H-6′), 7.19 (1H, dd, J=8.5, 1 Hz, H-5′), 7.36 (2H, t with fine splittings, J=8.5 Hz, H-3, 5), 7.42 (1H, m, H-4), 7.53 (1H, d, J=2.4 Hz, H-8′), 7.87 (2H, m, H-2, 6). HRMS (m/z) Calcd for $C_{19}H_{16}O_4$ (M^+): 308.1047. Found: 308.1056. Calcd for $C_{18}H_{13}O_3$ (M^+ − OMe): 277.0863. Found: 277.0859.

Time Course Experiment on *Z*-*E* Isomerization (1) Isomerization on a Silica Gel TLC Plate: Compound **4a** or **4b** was spotted on a TLC plate and left for an appropriate period at room temperature in the dark, then the plate was developed with hexane : ether = 1 : 1. The absorption intensity of each spot at 254 nm was determined with a Shimadzu CS-920 high-speed TLC scanner.

(2) Light-Induced Isomerization: Compound **4a** was dissolved in an appropriate solvent at a concentraton of 1 mg/ml, placed in a water-jacketed Pyrex test tube, and cooled with ice-water at 0 °C. The solution was irradiated with a UXL-500D xenon lamp (500 W, Ushio Electric Inc.). Aliquots of the solution were taken at appropriate intervals and the composition was analyzed by HPLC. HPLC conditions: column, TSK-gel Si-60 (4.6 i.d. × 250 mm); solvent, hexane : THF = 3 : 2; flow rate, 0.6 ml/min. t_R (min): **4a** = 8.5, **4b** = 10.8.

(3) Isomerization in Solvents: Compound **4a** or **4b** was dissolved in an appropriate solvent and heated in a sealed tube at 55 °C in the dark. Aliquots of the solution were taken at appropriate interval and the composition was analyzed by TLC using a Shimadzu CS-920 high-speed TLC scanner.

X-Ray Crystal Analyses Reflection data were collected on a Rigaku AFC-5R four-circle diffractometer controlled by the MSC/AFC program package, using MoK_α radiation monochromated by a graphite monochromator, in the 2θ–ω scan mode. Reflections with intensity above the 3σ(I) level were used for the structure determination. The structure

TABLE IV. Crystal Data for β-Methoxychalcones

Compound	**4a**	**4b**	**11a**
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic
Lattice parameters			
a (Å)	10.5934 (5)	16.977 (3)	10.4889 (6)
b (Å)	15.561 (1)	7.288 (1)	15.645 (2)
c (Å)	7.6888 (5)	21.454 (5)	7.963 (1)
V (Å^3)	1267.5 (2)	2654 (2)	1306.7 (2)
Space group	$P2_12_12_1$	$Pbcn$	$P2_12_12_1$
Z value	4	8	4
D_c (g/cm^3)	1.25	1.19	1.29
Number of reflections			
Collected	1711	2717	1768
Used for calculated (> $3\sigma(I)$)	1065	961	883
R value	0.035	0.038	0.032

TABLE Va. Positional Parameters and B_{eq} for **4a**

Atom	x	y	z	B_{eq}
O1	−0.1584 (2)	0.0445 (1)	0.1276 (3)	5.3 (1)
O2	0.0616 (2)	0.1389 (1)	−0.0584 (3)	5.2 (1)
C1	−0.1318 (2)	−0.1023 (2)	0.0828 (4)	3.6 (1)
C2	−0.0829 (3)	−0.1683 (2)	−0.0176 (5)	4.4 (1)
C3	−0.1330 (3)	−0.2505 (2)	−0.0079 (6)	5.5 (2)
C4	−0.2329 (3)	−0.2667 (2)	0.1030 (6)	5.8 (2)
C5	−0.2845 (3)	−0.2018 (3)	0.1971 (6)	5.5 (2)
C6	−0.2356 (3)	−0.1198 (2)	0.1883 (5)	4.3 (1)
C7	−0.0734 (2)	−0.0157 (2)	0.0809 (4)	3.7 (1)
C8	0.0484 (3)	−0.0036 (2)	0.0445 (5)	4.0 (1)
C9	0.1159 (3)	0.0749 (2)	−0.0041 (4)	4.0 (1)
C1′	0.2567 (2)	0.0743 (2)	0.0102 (4)	3.6 (1)
C2′	0.3234 (3)	0.0077 (2)	0.0853 (5)	4.4 (1)
C3′	0.4550 (3)	0.0100 (2)	0.0953 (5)	5.0 (2)
C4′	0.5171 (3)	0.0798 (2)	0.0295 (5)	5.1 (2)
C5′	0.4542 (3)	0.1466 (2)	−0.0438 (6)	5.3 (2)
C6′	0.3226 (3)	0.1442 (2)	−0.0541 (5)	4.7 (1)
C16	−0.1167 (5)	0.1203 (2)	0.2188 (7)	6.2 (2)
H1	−0.015 (3)	−0.154 (2)	−0.101 (4)	4.7 (7)
H2	−0.086 (4)	−0.294 (2)	−0.078 (6)	8 (1)
H3	−0.266 (3)	−0.322 (2)	0.113 (4)	5.3 (8)
H4	−0.336 (3)	−0.208 (2)	0.269 (5)	6 (1)
H5	−0.266 (3)	−0.079 (2)	0.252 (4)	3.6 (6)
H6	0.085 (3)	−0.052 (2)	0.035 (4)	3.6 (6)
H7	0.272 (4)	−0.045 (2)	0.129 (5)	6.5 (9)
H8	0.500 (3)	−0.037 (2)	0.153 (4)	4.1 (7)
H9	0.596 (3)	0.083 (2)	0.031 (4)	5.3 (8)
H10	0.494 (3)	0.196 (2)	−0.099 (5)	5.2 (7)
H11	0.269 (3)	0.190 (2)	−0.106 (4)	3.6 (6)
H12	−0.034 (3)	0.110 (2)	0.279 (5)	6 (1)
H13	−0.087 (4)	0.163 (3)	0.131 (6)	9 (1)
H14	−0.199 (4)	0.141 (3)	0.276 (6)	10 (1)

TABLE Vb. Positional Parameters and B_{eq} for **4b**

Atom	x	y	z	B_{eq}
O1	0.8736 (1)	−0.1215 (3)	0.4153 (1)	4.5 (1)
O2	0.8306 (1)	0.3534 (3)	0.5244 (1)	4.4 (1)
C1	0.9123 (2)	0.1825 (5)	0.4165 (2)	3.6 (2)
C2	0.9745 (2)	0.2809 (5)	0.4410 (2)	4.3 (2)
C3	1.0110 (3)	0.4160 (6)	0.4071 (2)	5.7 (3)
C4	0.9861 (3)	0.4549 (7)	0.3484 (2)	6.6 (3)
C5	0.9250 (4)	0.3602 (7)	0.3229 (2)	6.3 (3)
C6	0.8877 (3)	0.2231 (6)	0.3565 (2)	4.8 (2)
C7	0.8757 (2)	0.0297 (5)	0.4518 (2)	3.4 (2)
C8	0.8528 (2)	0.0359 (5)	0.5109 (2)	3.6 (2)
C9	0.8437 (2)	0.2032 (5)	0.5474 (2)	3.6 (2)
C1′	0.8480 (2)	0.1877 (5)	0.6169 (2)	3.5 (2)
C2′	0.8924 (2)	0.0554 (6)	0.6460 (2)	4.8 (2)
C3′	0.8978 (3)	0.0514 (7)	0.7106 (2)	6.2 (3)
C4′	0.8583 (3)	0.1764 (7)	0.7453 (2)	6.6 (3)
C5′	0.8133 (3)	0.3061 (7)	0.7176 (2)	6.2 (3)
C6′	0.8090 (3)	0.3133 (6)	0.6532 (2)	4.8 (2)
C16	0.8327 (2)	−0.2795 (5)	0.4384 (2)	5.6 (2)
H1	0.992 (2)	0.250 (4)	0.483 (1)	3.8 (8)
H2	1.054 (3)	0.484 (6)	0.424 (2)	8 (1)
H3	1.011 (3)	0.546 (6)	0.323 (2)	8 (1)
H4	0.902 (2)	0.381 (5)	0.285 (2)	6 (1)
H5	0.842 (2)	0.159 (4)	0.341 (1)	3.7 (8)
H6	0.835 (2)	−0.067 (4)	0.531 (1)	3.0 (7)
H7	0.917 (2)	−0.037 (5)	0.623 (2)	5 (1)
H8	0.930 (2)	−0.044 (6)	0.729 (2)	7 (1)
H9	0.861 (2)	0.170 (5)	0.790 (2)	7 (1)
H10	0.783 (3)	0.394 (6)	0.740 (2)	9 (1)
H11	0.777 (2)	0.393 (4)	0.635 (1)	4 (1)
H12	0.7800	−0.2477	0.4480	6.9
H13	0.8329	−0.3727	0.4071	6.9
H14	0.8584	−0.3242	0.4745	6.9

TABLE Vc. Positional Parameters and B_{eq} for **11a**

Atom	x	y	z	B_{eq}
O1	0.6582 (2)	0.0359 (2)	0.3474 (4)	5.7 (1)
O2	0.4443 (2)	0.1271 (2)	0.5350 (4)	5.5 (1)
O3	0.2393 (4)	0.2016 (2)	0.6203 (5)	6.5 (2)
C1	0.6312 (3)	−0.1098 (2)	0.3907 (5)	4.0 (2)
C2	0.5821 (4)	−0.1746 (3)	0.4859 (6)	5.0 (2)
C3	0.6332 (5)	−0.2566 (3)	0.4773 (8)	6.0 (2)
C4	0.7348 (5)	−0.2724 (3)	0.3740 (7)	6.6 (3)
C5	0.7862 (5)	−0.2082 (4)	0.2818 (7)	6.2 (3)
C6	0.7367 (4)	−0.1269 (3)	0.2888 (6)	4.9 (2)
C7	0.5733 (3)	−0.0239 (2)	0.3910 (5)	4.0 (2)
C8	0.4495 (3)	−0.0118 (2)	0.4262 (5)	4.1 (2)
C9	0.3844 (4)	0.0655 (2)	0.4762 (5)	4.3 (2)
C1′	0.2439 (3)	0.0694 (2)	0.4666 (5)	3.7 (2)
C2′	0.1783 (4)	0.1384 (2)	0.5389 (5)	4.5 (2)
C3′	0.0471 (4)	0.1431 (3)	0.5269 (7)	5.4 (2)
C4′	−0.0196 (5)	0.0814 (4)	0.4474 (7)	5.8 (2)
C5′	0.0405 (4)	0.0125 (3)	0.3753 (6)	5.7 (2)
C6′	0.1714 (3)	0.0070 (3)	0.3856 (5)	4.5 (2)
C16	0.6173 (4)	0.1109 (3)	0.2602 (7)	6.6 (2)
H1	0.512 (4)	−0.166 (2)	0.556 (5)	3.7 (8)
H2	0.590 (3)	−0.299 (2)	0.545 (5)	5 (1)
H3	0.771 (4)	−0.333 (3)	0.367 (6)	7 (1)
H4	0.854 (5)	−0.217 (3)	0.212 (7)	8 (1)
H5	0.765 (4)	−0.085 (2)	0.223 (5)	5 (1)
H6	0.402 (3)	−0.062 (2)	0.426 (4)	3.0 (7)
H7	0.321 (4)	0.188 (2)	0.609 (5)	5 (1)
H8	0.008 (4)	0.186 (3)	0.568 (6)	5 (1)
H9	−0.108 (5)	0.085 (2)	0.440 (6)	6 (1)
H10	−0.004 (4)	−0.033 (2)	0.318 (5)	6 (1)
H11	0.217 (4)	−0.045 (2)	0.334 (5)	5 (1)
H12	0.6007	0.1575	0.3355	7.8
H13	0.6800	0.1300	0.1802	7.8
H14	0.5393	0.1006	0.1979	7.8

was solved by the direct method using MITHRIL[19] and refined by the full-matrix least-squares procedure with the assumption of positional anisotropic thermal parameters for all nonhydrogen atoms (see Tables IV and V).

References and Notes

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5) Ikeda *et al.*[4b,c] isolated, after diazomethane methylation of **1**, crystals of mp 81 °C and assigned *Z*-configuration to this compound which isomerized to crystals of mp 65 °C (*E*-isomer) on irradiation under a mercury lamp. On the other hand, on similar methylation, Eistert *et al.*[4a] obtained a mixture, from which they isolated crystals of mp 65 °C. They assigned *Z*-configuration to this compound and claimed that it isomerized to the isomer of mp 81 °C.

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10) Although the reason for this irregularity is obscure, one of the possible explanations is as follows. The H-8 of **4a** (and **6a**) is originally deshielded by the anisotropic effect of ring A, and may be nearly at the edge of the deshielding region, since ring A is twisted by *ca.* 26° to the enol plane. Isomerization of *Z* to *E* removes this deshielding effect, resulting in the upfield shift of H-8. On the other hand, introduction of an *ortho*-substituent into ring A will increase the twisting of ring A to bring H-8 into the shielding region. Therefore, H-8 in **5a** may appear at exceptionally high field (δ 6.10) compared to the corresponding proton of **4a** and **6a** (δ 6.5—6.6). Isomerization of *Z* to *E* removes this unusual situation, thus causing the downfield shift of this proton.

11) By use of these methods, the signal assignment of each compound was achieved independently, *i.e.*, without any comparison of the data with those of analogous compounds. Consequently, the previous carbon assignments of *O*-methylpongamols[2] were partially revised (Table III). For example, in **16b**, the signal at δ 158.2 showed correlation peaks with H-6′, H-7′, and H-8′, whereas the signal at δ 152.8 showed them with H-6′ and OMe. Thus they are the signals of C-4′ and C-2′, respectively.

12) Dewar and Sutherland [D. J. Dewar and R. G. Sutherland, *J. Chem. Soc., Perkin Trans. 2*, **1977**, 1522] reported that methylation of **3** with diazomethane gave the 2-*O*-methylated product **2**, without presenting any physical data of the product. Since their structure assignment was a tentative one, our present results suggested that the structure of their product must be revised to **11a**.

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