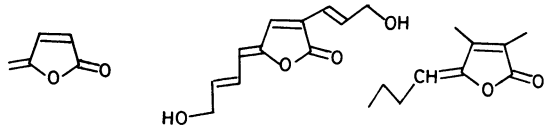
A Highly Stereoselective Synthesis of (*E*)-Enol Lactones by the Wittig Reaction of Cyclic Anhydrides with (α-Alkoxycarbonylethylidene)triphenylphosphorane

Sadao Tsuboi, Hirohumi Fukumoto, Hiroshi Wada, Akira Takeda,* and Keiichi Fukuyama†
Department of Synthetic Chemistry, School of Engineering, Okayama University, Tsushima, Okayama 700
†Department of Industrial Chemistry, Faculty of Engineering, Tottori University, Koyama-cho, Tottori 680
(Received August 11, 1986)

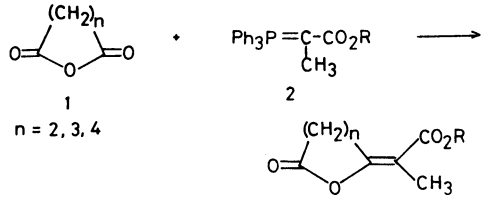
Reactions of glutaric anhydride and methyl- or phenyl-substituted ones with (α-alkoxycarbonylethylidene)-triphenylphosphorane (**2a**, ethoxy; **2b**, *t*-butoxy) gave the corresponding 6-alkoxycarbonyl-5-hepten-5-olides (**3**) and 6-alkoxycarbonyl-4-hepten-5-olides in good yields. The reaction proceeded highly stereoselectively to give (*E*)-**3**. The stereochemistry of **3** was determined by an X-ray crystallographic analysis. The reaction of adipic anhydride with **2a** afforded 7-ethoxycarbonyl-5-octen-6-olide, 7-ethoxycarbonyl-5,6-octadienoic acid, and (4*E*, 6*E*)-7-ethoxycarbonyl-4,6-octadienoic acid. A treatment of nonanedioic anhydride with **2a** gave 10-ethoxycarbonyl-8,9-undecadienoic acid, (7*E*,9*E*)-10-ethoxycarbonyl-7,9-undecadienoic acid, and diethyl 2-methyl-2,4-undecadienedioate in low yields.

Enol lactones as well as α-methylene lactones exhibit strong biological activities such as antibiotic activity, carcinogenic properties, and control activity of plant growth.[1] Many naturally occuring enol lactones have been isolated. For example, protoanemonin,[2] tetrenolin,[3] and bovolide[4] are well-known.



Protoanemonin Tetrenolin Bovolide

Recently, some synthetic methods of enol lactones have been developed.[5-8] We have also reported a facile, highly stereoselective synthesis of (*E*)-enol δ-lactones by the Wittig reaction of glutaric anhydrides (**1**, n=3) with (α-alkoxycarbonylethylidene)triphenylphosphorane (**2**).[9] Here, we report a full description of the previous communication[9] and its further extention to other cyclic anhydrides.

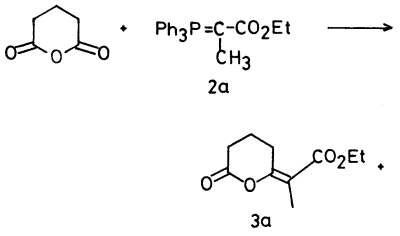


1
n = 2, 3, 4

2

A typical method for the synthesis of enol lactones is the Wittig reaction between stabilized phosphoranes and cyclic anhydrides.[1b] The Wittig reaction of stable phosphoranes with phthalic anhydride or succinic anhydride provides enol γ-lactones in good yield;[1b,10] it has been successfully applied to the syntheses of naturally occuring enol γ-lactones.[11-14] However, Wittig reactions of glutaric anhydrides and acid anhydrides of larger ring with phosphoranes have remained almost uninvestigated. Only Chopard et al. reported that an attempt to prepare enol δ-lactones by the Wittig reaction failed, but resulted in the formation of the ring-opened products.[15]

Recently, we found that a reaction of glutaric anhydride with (α-ethoxycarbonylethylidene)triphenylphosphorane (**2a**) gives 6-ethoxycarbonyl-5-hepten-5-olide (**3a**) (13%) and its *endo*-enol lactone (**4a**) (20%), in contrast to the above result.[15]



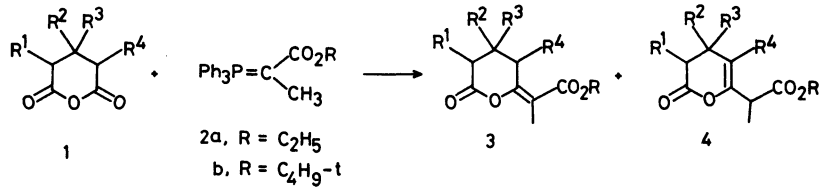
2a

3a **4a**

The generality of this Wittig reaction was examined by a reaction of various methyl- or phenyl-substituted glutaric anhydrides with phosphorane **2**; the results are shown in Table 1. Most of the reactions gave mixtures of *exo*-enol δ-lactone **3** and *endo*-enol δ-lactone **4**. The geometry of **3** was tentatively assigned as *E*-configuration by a ^{1}H NMR analysis.[9] Namely, the coupling constant between methylene protons of C_4 and methyl protons of the ethylidene group showed a small value (J=1.5 Hz).[16] The reaction of **2** with β-substituted glutaric anhydrides gave predominantly *exo*-enol δ-lactone **3** in good yields. Especially, the reaction of 3-methylglutaric anhydride (**1e**) with **2b** yielded *exo*-enol δ-lactone **3f** in a high yield (86%) along with *endo*-enol δ-lactone **4f** (6%). On the other hand, a reaction of **2** with glutaric anhydride and α-substituted ones afforded *exo*-enol δ-lactone **4** as the major product (except for the reaction of **1d** with **2b**). Treatments of 2-methylglutaric anhydride with **2** provided (*E*)-6-alkoxycarbonyl-2-methyl-5-hepten-5-olide regioselectively. All of the reactions proceeded highly stereoselectively to give only (*E*)-*exo*-enol δ-lactone **3**. A trace amount of the other stereoisomer, (*Z*)-enol δ-lactone, could not be detected.

In order to definitely determine the stereochemistry of *exo*-enol δ-lactone **3**, an X-ray crystallographic analysis of **3d** was carried out representatively; this

Table 1. Reaction of Glutaric Anhydride **1** with (α-Alkoxycarbonylethylidene)triphenylphosphorane **2**



No.	R_1	R_2	R_3	R_4	R	Products (yield/%)[a]	
						3	**4**
a	H	H	H	H	C_2H_5	13[b]	20[b]
b	H	H	H	H	C_4H_9-*t*	0	35
c	CH_3	H	H	H	C_2H_5	12	27
d	CH_3	H	H	H	C_4H_9-*t*	38	33
e	H	CH_3	H	H	C_2H_5	55	12
f	H	CH_3	H	H	C_4H_9-*t*	86	6
g	H	C_6H_5	H	H	C_2H_5	58	13
h	H	CH_3	CH_3	H	C_2H_5	30	0
i	H	CH_3	CH_3	H	C_4H_9-*t*	57	0
j	CH_3	H	H	CH_3	C_2H_5	21[c]	0

a) Isolated yield unless otherwise indicated. b) Estimated by GLC. Analytical sample was purified by preparative GLC (column, 200 °C carrier gas, He, 25 ml min^{-1}): **3a**, R_t 2.6 min; **4a**, R_t 1.6 min. c) Produced together with **5**.

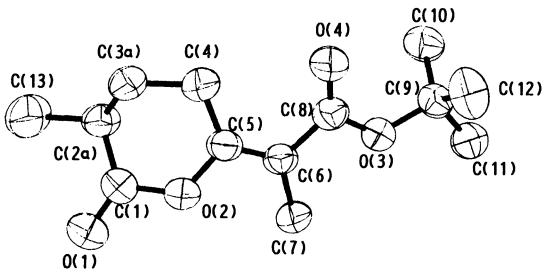
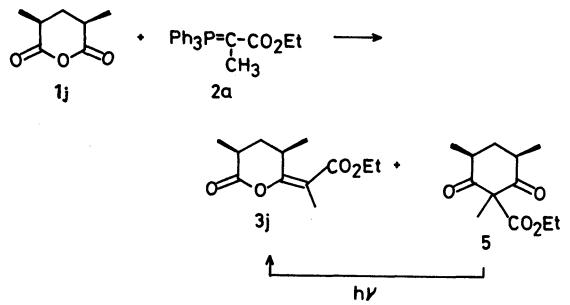


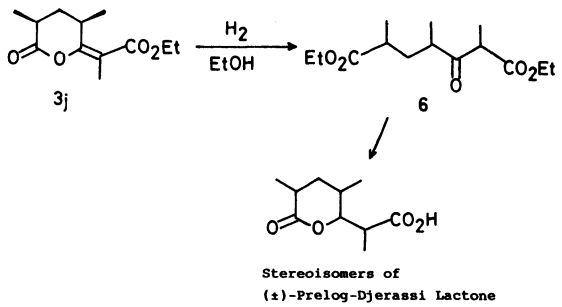
Fig. 1. Perspective view of **3d** drawn by DCMS-3.[17] Only one of the two conformations is shown for the sake of clarity.

revealed that it has an (*E*)-configuration. A perspective view of **3d** drawn by DCMS-3[17] is shown in Fig. 1.

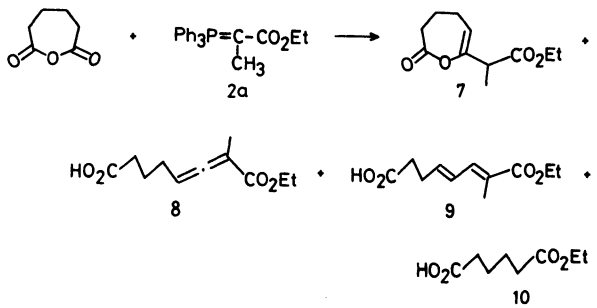
The reaction of *meso*-2,4-dimethylglutaric anhydride (**1j**) with **2a** also afforded a mixture of *exo*-enol δ-lactone **3j** (21%) and 2,6-dioxocyclohexanecarboxylate **5** (7%). The photochemical rearrangement of 1,3-cyclohexanedione to enol δ-lactone is well-known.[18] Irradiation of **5** with a high-pressure Hg lamp in benzene provided **3j** although in a low yield (10%).



Attempted conversion of **3j** to Prelog-Djerassi lactone or its stereoisomers by hydrogenation resulted in the formation of ring-opened product **6** in 91% yield. ^{13}C NMR analysis revealed that it consists of three stereoisomers. It has been reported that the reduction of β-keto ester **6** affords stereoisomers of the racemic Prelog-Djerassi lactone although the stereochemistry could not be evaluated.[19]

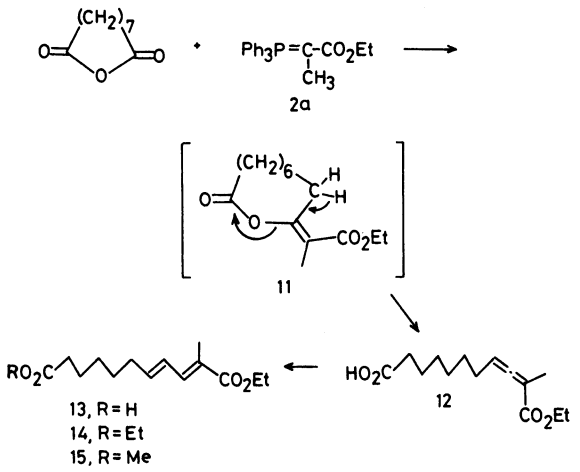


A further extention of the present reaction to other cyclic anhydrides was attempted. The reaction of adipic anhydride with **2a** gave *endo*-enol ε-lactone **7** in 13% yield, accompanied by the formation of ring-opened products, α-allenic ester **8** (4.2% yield) and its isomer **9** (6.3% yield), and ethyl hydrogen adipate (**10**). The structural elucidation of half esters **8** and

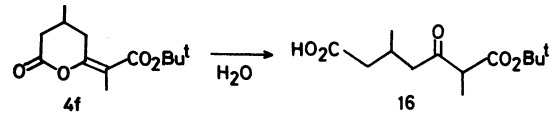


9 was carried out by an analysis of the spectral data of the corresponding methyl ethyl esters. The stereochemistry of **9** was determined by ^{1}H NMR spectral data. Namely, the signal due to C_β H which appeared considerably down field (7.25 ppm) showed α,β-trans geometry.[20] A large coupling constant (J=15.3 Hz) between C_γ H and C_δ H revealed the γ,δ-trans geometry.

A treatment of nonanedioic anhydride with **2a** gave 10-ethoxycarbonyl-8,9-undecadienoic acid (**12**) unexpectedly, although in a low yield. Allene **12** is produced by a prototropic rearrangement of the initially formed *exo*-enol η-lactone **11**. The prolonged reaction gave (7*E*,9*E*)-10-ethoxycarbonyl-7,9-undecadienoic acid (**13**) (20% yield) and its diethyl ester **14** (23% yield), both of which can be produced by a prototropic rearrangement of **12**. The structural assignment of **13** was carried out after a conversion to its methyl ester **15** with diazomethane.



Enol lactones **3** and **4** prepared in this study gradually decomposed with moisture to yield an acid ester. For example, compound **4f** produced 6-*t*-butoxycarbonyl-3,6-dimethyl-5-oxoheptanoic acid (**16**) as a 1 : 1 diastereomeric mixture after 40 days at room temperature.



The structural assignment of the products obtained in the present study was made on the basis of IR and NMR data (Tables 2—5). IR absorptions of *exo*-enol δ-lactone **3** at 1770, 1705, and 1640 cm^{-1} indicate the presence of a δ-lactone ring and a α,β-unsaturated ester group. The *exo*-enol lactone skeleton is also supported by the ^{1}H NMR spectra in which a singlet or a triplet (J=1.5 Hz) at 1.80—1.92 ppm due to methyl group attached to the double bond was exhibited. IR absorptions of *endo*-enol δ-lactone **4** at 1770 and 1740 cm^{-1} indicate the presence of a δ-lactone ring and an isolated ester carbonyl group. The structure of **4** was also supported by ^{1}H NMR data, which exhibited a doublet at δ=1.38 due to the methyl group attached to α-carbon of the ester group and a signal at δ=5.23 due to a olefinic proton of endo enol structure. As a part of a continuing ^{13}C NMR study of organic compounds, the ^{13}C NMR spectra of enol δ-lactones **3** and **4** were measured and assigned with the aid of an off-resonance decoupling technique. For the assignment of ^{13}C NMR spectra of **3h**, two peaks due to secondary

Table 2. Spectral and Analytical Data of *exo*-Enol δ-Lactones **3**

Compd	bp[a] (mp) (°C)	IR cm^{-1}	^{1}H NMR (δ)[b]	Found (%) (Calcd) C	H
3a		1770, 1705, 1640	1.21 (3H, t, J=7 Hz), 1.90 (3H, t, J=1.5 Hz), 1.59—2.14 (2H, m), 2.63 (2H, t, J=6 Hz), 3.07 (2H, t, J=6 Hz), 4.17 (2H, q, J=7 Hz)	60.39 (60.59)	7.04 (6.97)
3c		1770, 1700, 1640	1.25 (3H, d, J=7 Hz), 1.33 (3H,t, J=7 Hz), 1.83 (3H, t, J=1.5 Hz), 2.0—3.4 (4H, m), 4.08 (2H, q, J=7 Hz)	62.10 (62.25)	7.67 (7.60)
3d	(71—72)	1770, 1700, 1630	1.24 (3H, d, J=7 Hz), 1.45 (9H, s), 1.80 (3H, t, J=1.5 Hz), 2.0—3.5 (4H, m)	64.92 (64.98)	8.34 (8.39)
3e		1770, 1705, 1640	1.08 (3H, d, J=6 Hz), 1.28 (3H, t, J=7 Hz), 1.86 (3H, s), 1.97—3.00 (4H, m), 3.34, 3.59 (1H, 2br. s), 4.14 (2H, q, J=7 Hz)	62.41 (62.25)	7.51 (7.60)
3f		1770, 1700, 1640	1.11 (3H, d, J=6 Hz), 1.48 (9H, s), 1.84 (3H, s), 1.94—2.84 (4H, m), 3.14—3.36 (1H, m)	64.89 (64.98)	8.38 (8.39)
3g	(65—65.5)	1780, 1705, 1640	1.23 (3H, t, J=7 Hz), 1.90 (3H, br. s), 2.21—3.50 (4H, m), 3.63 (1H, br. s), 4.06 (2H, q, J=7 Hz), 7.16 (5H, s)	70.12 (70.06)	6.52 (6.61)
3h		1770, 1710, 1640	1.07 (6H, s), 1.92 (3H, t, J=1.5 Hz), 2.49 (2H, br. s), 2.95 (2H, s), 4.20 (2H, q, J=7 Hz)	63.71 (63.70)	8.18 (8.02)
3i	160/0.25[c]	1770, 1700, 1640	1.24 (6H, s), 1.47 (9H, s), 1.86 (3H, t, J=1.5 Hz), 2.37 (2H, s), 2.87 (2H, s)	66.22 (66.12)	8.75 (8.72)
3j		1780, 1710, 1640	1.15 (3H, d, J=7 Hz), 1.21 (3H, d, J=7 Hz), 1.31 (3H, t, J=7 Hz), 1.86 (3H, s), 2.0—3.0 (3H, m), 4.15 (2H, q, J=7 Hz)	63.72 (63.70)	7.97 (8.02)

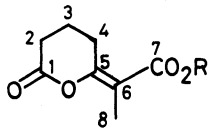
a) If not indicated, the boiling point was not measured although the material was an oil. b) Compds **3a**, **3c**, **3d**, **3e**, **3f**, and **3g** were measured in CCl_4 and others in $CDCl_3$. c) Bath temperature on bulb-to-bulb distillation.

Table 3. Spectral and Analytical Data of *endo*-Enol δ-Lactones **4**

Compd[a]	IR (neat) cm^{-1}	^1H NMR (CCl_4, δ)	Found (%) (Calcd) C	H
4a	1770, 1740, 1700	1.21 (3H, t, J=7 Hz), 1.30 (3H, d, J=7 Hz), 2.04—2.86 (4H, m), 3.24 (1H, q, J=7 Hz), 4.10 (2H, q, J=7 Hz), 5.23 (1H, t, J=4 Hz)	60.54 (60.59)	6.97 (7.12)
4b	1770, 1740, 1690, 1640	1.28 (3H, d, J=7 Hz), 1.42 (9H, s), 2.42 (2H, J=4 Hz), 2.02—2.72 (2H, m), 2.08 (1H, q, J=7 Hz), 5.10 (1H, t, J=4 Hz)	63.80 (63.70)	8.06 (8.02)
4c	1770, 1740, 1700, 1640	1.23 (6H, d, J=7 Hz), 1.25 (3H, t, J=7 Hz), 1.80—2.90 (3H, m), 3.17 (1H, q, J=7 Hz), 4.09 (2H, q, J=7 Hz), 5.10 (1H, t, J=4 Hz)	62.16 (62.25)	7.54 (7.60)
4d	1770, 1740, 1700, 1640	1.26 (3H, d, J=7 Hz), 1.31 (3H, d, J=7 Hz), 1.40 (9H, s), 1.8—2.9 (2H, m), 3.04 (1H, q, J=7 Hz), 5.03 (1H, t, J=4 Hz)	64.89 (64.98)	8.33 (8.39)
4e	1770, 1740, 1696	1.16 (3H, t, J=7 Hz), 1.32 (6H, 2d, J=7 Hz), 1.84—2.89 (3H, m), 3.14 (2H, q, J=7 Hz), 5.01 (1H, d, J=4 Hz)	62.41 (62.25)	7.51 (7.60)
4f	1770, 1740, 1700	1.12 (3H, d, J=6.5 Hz), 1.30 (3H, d, J=7 Hz), 1.45 (9H, s), 1.77—2.80 (3H,m), 3.05 (1H, q, J=6.5 Hz), 4.98 (1H, d, J=4 Hz)	64.79 (64.98)	8.25 (8.39)
4g	1770, 1740, 1690	1.23 (3H, t, J=7 Hz), 1.35 (3H, d, J=7 Hz), 2.23—2.97 (2H, m), 3.21 (1H, q, J=7 Hz), 3.48—3.88 (1H,m), 4.08 (2H, q, J=7 Hz), 5.17 (1H, d, J=4 Hz), 7.13 (5H, s)	70.08 (70.06)	6.45 (6.61)

a) All compounds are liquid.

Table 4. ^{13}C NMR Data ($CDCl_3$, δ) of *exo*-Enol δ-Lactone **3**

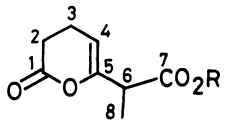


3

Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	Others
3a	168.2	30.8	25.4	18.0	158.8	110.0	167.4	11.8	14.3(q), 60.6 (t)
3c	170.9	36.2[a]	26.0	25.7[a]	158.9	109.0	168.2	11.8	14.3(q), 16.0(q), 60.4(t)
3d	170.9	36.0	26.0	25.7	157.9	111.1	167.4	12.2	28.2(q), 16.0(q), 80.5(s)
3e	167.9	38.3	25.3	33.2	158.7	109.3	166.7	11.8	14.3(q), 20.5(q), 60.4(t)
3f	167.6	38.5	25.2	33.2	156.7	111.6	167.4	12.2	20.6(q), 28.2(q), 80.8(s)
3g	168.0	37.7	35.5	32.8	157.5	110.4	166.8	11.9	14.2(q), 60.5 (t), 126.5(d), 127.4(d), 129.0(d), 141.3 (s)
3h	168.0	44.1[b]	29.5	38.6[b]	157.8	110.4	166.6	11.7	14.2(q), 27.7(q), 60.3(t)
3i	167.5	44.3	29.6	38.6	156.3	112.2	167.1	12.2	28.2(q), 27.9(q), 60.3(t)
3j	172.8	34.9	30.9	34.1	162.3	112.5	167.7	12.3	14.2(q), 15.0(q), 60.6(t)

a), b) Distinguished by selective decoupling technique.

Table 5. ^{13}C NMR Data of *endo*-Enol δ-Lactone **4**



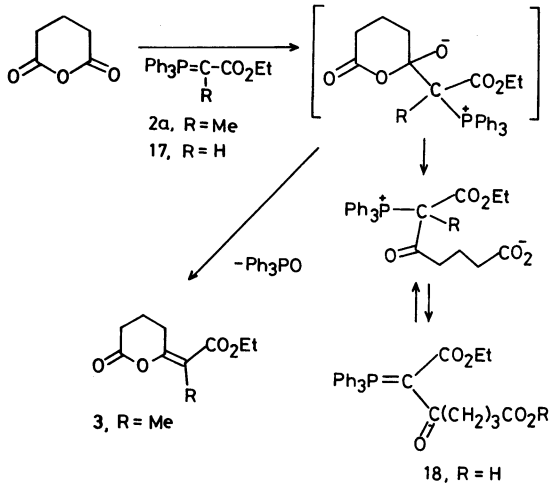
4

Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	Others
4a	172.0	28.3	18.7	101.6	151.4	43.2	168.5	14.5	14.1(q), 61.1 (t)
4b	171.0	28.3	18.6	101.2	151.9	44.0	168.1	14.5	14.5(q), 27.8(q), 80.7(s)
4c	172.7[b]	33.5	26.8	101.2	152.1	43.0	172.3[b]	14.5	14.1(q), 15.4(q), 61.1(t)
						43.2		14.7	
4d[a]	171.0[b]	33.5	26.8	100.8	152.5	43.9	171.1[b]	14.4	15.4(q), 27.9(q), 80.8(s)
	171.4[b]			101.0		44.1			
4e	172.5	36.9	26.1	108.4	151.2	43.5	169.0	14.6	15.1(q), 20.6(q), 61.7(t)
4g	171.8	36.8	36.7	105.5	152.0	43.3	167.4	14.5	14.1(q), 61.3 (t),
								14.7	126.9(d), 127.4(d),
									129.1(d), 141.4 (s)

a) Diastereomeric mixture. b) May be interchangeable.

carbon could be assigned using a selective-decoupling technique. The ^{13}C NMR data summarized in Tables 4 and 5 are apparently the first reported for substituted enol δ-lactones, making structural assignments unambiguous.

We briefly discuss the reaction mechanism regarding the present reaction. In contrast to our results, the reaction of (ethoxycarbonylmethylene)triphenylphosphorane (**17**) with glutaric anhydride gave a ring-opened product **18**,[15] which would be stabilized by prototropic rearrangement. Therefore, it would be



necessary for the formation of the desired enol δ-lactones that an alkylidenephosphorane has no hydrogen atom on the α-position. The present reaction is the first synthesis of enol δ- and ε-lactones, and 2,3- or 2,4-dienedioic esters by the Wittig reaction. It will be useful for the synthesis of these derivatives.

Experimental

The melting and boiling points are uncorrected. Elemental analyses were carried out by Eiichiro Amano of our laboratory. IR spectra were obtained with a JASCO Model A-102 infrared spectrophotometer. ^1H NMR spectra (60 MHz) were recorded with a JEOL JNM-PMX60SI apparatus. ^1H NMR (100 MHz) and ^{13}C NMR spectra (25 MHz) were obtained with a JEOL JNM-FX100 apparatus, with $CDCl_3$ as a solvent. All chemical shifts are reported in δ units downfield from the internal Me_4Si; J values are given in hertz. Analytical determinations by GLC were performed on a Hitachi Model 163 gas chromatograph fitted with 10% Apiezone Grease L on Chromosorb W column (3 mm o.d.×1 m). Preparative GLC was performed on a Yanagimoto Model G-80 gas chromatograph fitted with 10% Apiezone Grease L on Chromosorb W column (3 mm o.d.×1 m). Column chromatography was accomplished with a 100—200 mesh Wakogel C-200. Chloroform was dried over $CaCl_2$ and distilled prier to use. The Wittig reaction was carried out under dry conditions.

(α-Ethoxycarbonylethylidene)triphenylphosphorane (**2a**) and (α-*t*-buthoxycarbonylethylidene)triphenylphosphorane (**2b**) were prepared by the method described in the literature.[21] Glutaric anhydride was purchased from Tokyo Kasei Kogyo Co., LTD. Substituted glutaric anhydrides were obtained by the known methods:[22-27] 2-methylglutaric anhydride, bp 130 °C/10 Torr (1 Torr=133.322 Pa) (lit,[24] 180—182 °C/25 Torr); 3,3-dimethylglutaric anhydride, bp 122 °C/12 Torr (lit,[25] 181 °C/25 Torr); 2,4-dimethylglutaric anhydride, bp 117—119 °C/4.5 Torr (lit,[26] 154—158 °C/20 Torr); mp 91—92 °C (lit,[26] 91.5 °C); ^{13}C NMR ($CDCl_3$) δ=15.8 (q), 33.0 (t), 36.8 (d), 170.4 (s); 3-phenylglutaric anhydride, mp 104—105 °C (lit,[27] 105 °C).

Some Wittig reactions were shown representatively.

6-*t*-Butoxycarbonyl-4-hepten-5-olide (4b). To a mixture of glutaric anhydride (0.50 g, 4.39 mmol) and **2b** (2.1 g, 5.49 mmol) was added 4 ml of dry $CHCl_3$ under N_2 and the solution was heated at the reflux temperature for 21 h. After removing the solvent, 30 ml of petroleum ether was added and the mixture was stirred at 40 °C for 3 h and then cooled. After filtration, concentration of the filtrate gave 0.962 g of crude **4b**, which was distilled to give 0.342 g (35%) of **4b**: Bp 135—155 °C/0.22 Torr. Spectral and analytical data are shown in Tables 3 and 5.

(5*E*)-6-*t*-Butoxycarbonyl-2-methyl-5-hepten-5-olide (3c) and 6-*t*-Butoxycarbonyl-2-methyl-4-hepten-5-olide (4c). A solution of 2-methylglutaric anhydride (0.50 g, 3.91 mmol) and **2b** (1.50 g, 3.92 mmol) in 7 ml of dry $CHCl_3$ was heated at the reflux temperatere for 12 h. After concentration, the residue was mixed with petroleum ether. After filtration, the filtrate was concentrated to give 0.938 g of crude product; this was chromatographed on SiO_2 (hexane/ether (20:1—1:1)) to give 0.355 g (38%) of **3c** as crystals (mp 71—72 °C) from the early fraction and 0.307 g (33%) of **4c** as a clean oil from the later fraction. Spectral and analytical data are shown in Tables 2, 3, 4, and 5.

(5*E*)-6-*t*-Butoxycarbonyl-2-methyl-5-hepten-5-olide (3f) and 6-*t*-Butoxycarbonyl-2-methyl-4-hepten-5-olide (4f). A solution of 3-methylglutaric anhydride (0.22 g, 1.72 mmol) and **2b** (0.85 g, 2.18 mmol) in 2 ml of dry $CHCl_3$ was heated at the reflux temperature for 12 h. After concentration, the residue was mixed with petroleum ether and then filtered. After filtration, the filtrate was concentrated and the residue was chromatographed on SiO_2 (hexane/ether (20:1—2:1)) to give 0.354 g (86%) of **3f** from the early fraction and 25 mg (6%) of **4f** from the later fraction. Spectral and analytical data are shown in Tables 2, 3, 4, and 5.

(5*E*)-2,4-Dimethyl-6-ethoxycarbonyl-5-hepten-5-olide (3j) and Ethyl 1,3,5-Trimethyl-2,6-dioxocyclohexanecarboxylate (5). A solution of 2,4-dimethylglutaric anhydride (0.50 g, 3.52 mmol) and **2a** (1.30 g, 3.59 mmol) in 4 ml of $CHCl_3$ was heated at the reflux temperature for 13 h. After removing the solvent, the residue was mixed with petroleum ether and filtered. The filtrate was concentrated to give 0.434 g of the residue. Preparative TLC (SiO_2, hexane/ether (3:1)) gave 0.169 g (21%) of **3j** as an oil at R_f value 0.31. Spectral and analytical data are shown in Tables 2 and 4. The component of R_f value 0.18 gave 53 mg (7%) of **5** as an oil: IR (neat)1760, 1740, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.16 (6H, d, J=7 Hz), 1.24 (3H, t, J=7 Hz), 1.47 (3H, s), 1.62—2.50 (2H, m), 2.5—3.28 (2H, m), and 4.22 (2H, q, J=7 Hz); ^{13}C NMR ($CDCl_3$) δ=13.7 (q), 14.2 (q), 14.5 (q), 20.1 (q), 35.1 (t), 43.1 (d), 62.4 (t), 71.0 (s), 168.9 (s), 202.4 (s). Found: C, 63.41; H, 7.78%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

X-Ray Crystallographic Analysis of 3d. The unit-cell constants and intensities were measured at room temperature using Ni-filtered Cu $K\alpha$ radiation on a Rigaku four-circle diffractometer. Crystal data are as follows: $C_{13}H_{20}O_4$, M=

240.3, monoclinic, space group $P2_1/a$, a=24.452(5), b=6.089(2), c=9.206(3) Å, β=99.72(3)°, V=1351.0 Å^3, Z=4, D_c=1.18 g cm^{-3}. Due to broad diffraction profiles ω-scan technique was applied with a scan width of 2.0°+0.15°tanθ. The backgrounds were counted for 4 s at the start and end points of the scan. Of the 2001 independent reflections measured up to 2θ=120°, 1579 reflections with $F>3\sigma$ were used for the structure analysis. The intensities were corrected for the Lorentz and polarization factors. The structure was solved by the direct method,[28] and refined by the block-diagonal least-squares method.[29] Each of the two carbon atoms (C(2) and C(3)) has two sites, and their occupancies were fixed to be 0.5 during the refinement. Most of the hydrogen atoms were located in the difference Fourier synthesis calculated after the refinement with anisotropic temperature factors for the non-hydrogen atoms; the electron density distribution around C(13) was too broad to locate hydrogen atoms. The two positions were calculated for each hydrogen atom bonded to C(2), C(3), and C(4), and their occupancies given 0.5. The contribution of these hydrogen atoms were included in the refinement with their parameters being fixed. The other hydrogen atoms were refined with isotropic temperature factors. The unit weight was given for all reflections. The final R value was 0.066 for 1579 reflections. The atomic-scattering factors were taken from the International Tables for X-ray Crystallography.[30] The final atomic parameters are given in Table 6.[31]

Table 6. Final Atomic Coordinates and Equivalent Temperature Factors

	x	y	z	B_{eq}
C(1)	0.1252(2)	0.2566(8)	0.2937(6)	5.8
C(2a)	0.1130(4)	0.5003(15)	0.2970(10)	5.1
C(2b)	0.1145(4)	0.4735(17)	0.3692(12)	6.6
C(3a)	0.1579(4)	0.5694(15)	0.4402(9)	4.9
C(3b)	0.1558(4)	0.6298(18)	0.3677(13)	7.0
C(4)	0.2146(2)	0.5553(8)	0.3913(6)	5.9
C(5)	0.2212(2)	0.3610(7)	0.2964(5)	4.6
C(6)	0.2640(2)	0.3080(7)	0.2302(5)	4.5
C(7)	0.2635(2)	0.1083(8)	0.1338(6)	5.9
C(8)	0.3147(2)	0.4469(7)	0.2551(5)	5.0
C(9)	0.4071(2)	0.4760(8)	0.1847(5)	5.5
C(10)	0.4026(2)	0.7186(9)	0.1400(7)	7.4
C(11)	0.4321(2)	0.3441(9)	0.0714(6)	7.1
C(12)	0.4395(2)	0.4402(11)	0.3375(6)	7.7
C(13)	0.0533(2)	0.5343(11)	0.3288(8)	8.8
O(1)	0.0924(1)	0.1089(6)	0.2783(4)	7.5
O(2)	0.1782(1)	0.2084(5)	0.2756(4)	5.6
O(3)	0.3515(1)	0.3769(5)	0.1723(3)	5.3
O(4)	0.3230(1)	0.6004(6)	0.3386(4)	6.8

$B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij} a_i a_j$.

Photochemical Rearrangement of 5 to 3j. Following a procedure described in the literature,[18] a solution of **5** (0.20 g, 0.83 mmol) in 10 ml of benzene was irradiated with a 200-W high-pressure Hg lamp (quartz jacket) from a distance of 4 cm under an N_2 atmosphere at room temperature for 65 h. After evaporating the solvent, the residual oil was purified with preparative TLC (SiO_2, hexane/ether (3 : 1)) to give 21 mg (10%) of **3j**: R_f value 0.31. Spectral data were identical with those of an authentic sample. The fraction of R_f value 0—0.2 gave a mixture of unidentified materials.

Preparation of Diethyl 3-Oxo-2,4,6-trimethylheptanedioate (6)[19] by the Hydrogenation of 3j. A mixture of **3j** (0.10 g, 0.42 mmol), dry ethanol (3 ml), Pd/$BaSO_4$ (14 mg),[32] and $FeCl_3$ (60 mg) was stirred under H_2 atmosphere for 8 h at room temperature. After filtration, the organic materials were extracted with ether. The combined extracts were washed with water, and dried over $MgSO_4$. Removal of the solvent gave a pale brown oil, which was purified by preparative TLC (SiO_2, hexane/ethyl acetate (4 : 1), R_f value 0.47) to give 74 mg of **6**:[19] IR (neat) 1740, 1720, 1182, 760 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.1 (9H, m), 1.20 (6H, t, J=7 Hz), 1.5—3.0 (4H, m), 3.6 (1H, q, J=7 Hz), 4.07 (2H, q, J=7 Hz), 4.12 (2H, q, J=7 Hz); ^{13}C NMR ($CDCl_3$) δ=12.8 (q), 13.0 (q), 14.0 (q), 14.2 (q), 15.9 (q), 16.4 (q), 17.2 (q), 17.5 (q), 17.6 (q), 17.8 (q), 17.9 (q), 35.9 (t), 36.1 (t), 36.5 (t), 36.9 (d), 37.1 (d), 37.3 (d), 43.2 (d), 43.5 (d), 43.7 (d), 51.0 (d), 51.3 (d), 52.0 (d), 60.3 (q), 60.4 (q), 170.3 (s), 175.9 (s), 176.1 (s), 176.2 (s). Found: C, 61.47; H, 8.91%. Calcd for $C_{14}H_{24}O_5$: C, 61.74: H, 8.88%.

Reaction of Adipic Anhydride with 2a. Synthesis of 7-Ethoxycarbonyl-5-octen-6-olide (7), 7-Ethoxycarbonyl-5,6-octadienoic Acid (8), and (4*E*,6*E*)-7-Ethoxycarbonyl-4,6-octadienoic Acid (9). A solution of adipic anhydride (0.90 g, 7 mmol) and **2a** (2.69 g, 7.4 mmol) in 7 ml of dry $CHCl_3$ was heated at the reflux temperature for 13 h. After concentration, the residue was chromatographed on SiO_2 (hexane/ethyl acetate (10 : 1–1 : 1)). Concentration of the early fraction gave 0.187 g (13%) of **7**: IR (neat) 1760, 1735, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.23 (3H, t, J=7 Hz), 1.38 (3H, d, J=6 Hz), 1.6—3.0 (6H, m), 3.25 (1H, q, J=5 Hz), 4.12 (2H, q, J=7 Hz), 5.42 (1H, t, J=6 Hz). Found: C, 62.42; H, 7.46%. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60%. Concentration of the second fraction gave 0.246 g of carboxylic acids which were treated with diazomethane. HPLC analysis [SA-I, 6ϕ×250; hexane/ethyl acetate (2 : 1)] of the methylated products showed 4 peaks. The peaks, retention times (min), and integrated percentages are as follow: 1, 12.6, 25%; 2, 13.7, 38%; 3, 15.2, 19%; 4, 16.6, 16%. Each component was collected by preparative HPLC and identified.

1-Ethyl 8-Methyl 2-Methyl-2,3-octadienedioate (Methyl Ester of 8): Peak 1; 4.2% yield; IR (neat) 1961, 1740, 1710, 1270, 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.28 (3H, t, J=7 Hz), 1.86 (3H, d, J=3.5 Hz), 1.60—1.92 (2H, m), 2.12 (2H, t, J=7 Hz), 2.36 (2H, t, J=7 Hz), 3.67 (3H, s), 4.18 (2H, q, J=7 Hz), and 5.40 (1H, m). Found: C, 63.55; H, 7.78%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

(2*E*,4*E*)-1-Ethyl 8-Methyl 2-Methyl-2,4-octadienedioate (Methyl Ester of 9): Peak 2; 6.3% yield; IR (neat) 1740, 1710, 1640, 1240, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.29 (3H, t, J=7 Hz), 1.92 (3H, s), 2.46 (4H, s), 3.67 (3H, s), 4.18 (2H, q, J=7 Hz), 6.0 (1H, m), 6.39 (1H, dd, J=10.6 and 15 Hz), 7.25 (1H, d, J=10.6 Hz). Found: C, 63.64; H, 8.11%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

Peak 3: *N*-Methyl-*N*-nitroso-*p*-toluenesulfonamide (diazomethane source). IR and ^{1}H NMR spectra were identical with those of an authentic sample.

Ethyl Methyl Adipate (Methyl Ester of 10):[33] Peak 4: 3.2% yield: IR and ^{1}H NMR spectra were identical with those of an authentic sample.

10-Ethoxycarbonyl-8,9-undecadienoic Acid (12). A solution of azelaic anhydride (2.26 g, 0.0133 mol) and **2a** (4.88 g, 0.0133 mol) in 14 ml of dry $CHCl_3$ was heated at the reflux temperature for 12 h. After removing the solvent, 40 ml of petroleum ether was added and the mixture was stirred for 3 h and then filtered. The concentration of the filtrate gave an

oil (0.706 g) which was chromatographed on SiO_2 (hexane/ether (20 : 1-1 : 1)). Concentration of the early fraction gave 0.255 g of a mixture of unidentified products. The later fraction gave 0.338 g (10%) of **12** as an oil: IR (neat) 3700—2200, 1960, 1740, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.6—1.8 (10H, m), 1.83 (3H, d, J=3 Hz), 2.02—2.60 (4H, m), 4.19 (2H, q, J=7 Hz), 5.40 (1H, m), 10.2 (1H, s); ^{13}C NMR ($CDCl_3$) δ=14.3 (q), 15.2 (q), 24.6 (t), 24.9 (t), 27.9 (t), 28.6 (t), 28.9 (t), 34.0 (t), 60.8 (t), 93.7 (d), 95.7 (s). Found: C, 65.98; H, 8.68%. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72%.

(7*E*,9*E*)-10-Ethoxycarbonyl-7,9-undecadienoic Acid (13) and 1-Ethyl 11-Methyl (2*E*,4*E*)-2-Methyl-2,4-undecadienedioate (14). A solution of azelaic anhydride (0.172 g, 1.01 mmol) and **2a** (0.366 g, 1.01 mmol) in 2 ml of dry $CHCl_3$ was heated at the reflux temperature for 21 h. After removing the solvent, 30 ml of petroleum ether was added and the mixture was stirred for 1 h and then filtered. Concentration of the filtrate gave a semisolid (0.445 g) which was separated by preparative TLC [SiO_2, hexane/ethyl acetate (1 : 1)]. **14**: 64 mg (23% yield); R_f 0.90; IR (neat) 1730, 1702, 1640, 1235, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.23 (3H, t, J=6 Hz), 1.30 (3H, t, J=6 Hz), 1.2—1.8 (6H, m), 1.92 (3H, s), 2.0—2.5 (4H, m), 4.13 (4H, m), 5.9—6.6 (2H, m), 7.10 (1H, d, J=11 Hz). The component of the carboxylic acid (R_f 0.37—0.63) was treated with diazomethane to give 172 mg of a clean oil which was chromatographed on preparative HPLC [column, SA-I, 6ϕ×250 mm; eluent, hexane/ethyl acetate (5 : 1), 1.3 ml min^{-1}].

(2*E*,4*E*)-1-Ethyl 11-Methyl 2-Methylundeca-2,4-dienedioate (15) (Methyl Ester of 13): R_t 10.0 min; 52 mg (19% yield); IR (neat) 1740, 1703, 1640, 1235, 1102, 970, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.30 (3H, t, J=7 Hz), 1.58 (6H, s), 2.24 (4H, m), 3.66 (3H, s), 4.18 (2H, q, J=7 Hz), 6.33 (1H, dd, J=11 and 14.7 Hz). Found: C, 67.15; H, 8.81%. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01%.

Ethyl Methyl Nonanedioate:[34] R_t 10.5 min; 43 mg; IR (neat) 1740, 1175, 1100, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.24 (3H, t, J=6 Hz), 1.60 (10H, m), 2.32 (4H, m), 3.67 (3H, s), 4.12 (2H, q, J=6 Hz). The other component (55 mg, R_t 15 min) was identified as *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide by a comparison of the spectral data with that of an authentic sample.

6-*t*-Butoxycarbonyl-3,6-dimethyl-5-oxoheptanoic Acid (16). Compound **4f** (25 mg) was left at room temperature for 40 days to give 26 mg (97% yield) of **16** as a mixture of two diastereomers: IR (neat) 3500—2500, 1740, 1715 cm^{-1}; ^1H NMR (CCl_4) δ=0.95 (3H, d, J=6 Hz), 1.20 (3H, d, J=7 Hz), 1.42 (9H, s), 1.6—2.6 (5H, m), 3.25 (1H, q, J=6 Hz), 7.40 (1H, s); ^{13}C NMR ($CDCl_3$) δ=12.5 (q), 19.8 (q), 25.7 (d), 27.8 (q), 40.2 (t), 47.3 (t), 53.9 (d), 54.1 (d), 81.8 (s), 169.5 (s), 178.0 (s), 204.9 (s), 205.0 (s). Compound **16** was converted to its methyl ester with diazomethane, purified by preparative TLC [hexane/ethyl acetate (3 : 1), R_f 0.37], and analyzed.

1-*t*-Butyl 7-Methyl 2,5-Dimethyl-3-oxoheptanedioate: IR (neat) 1730, 1705, 1365, 1155, 1010, 845 cm^{-1}; ^1H NMR (CCl_4) δ=0.98 (3H, d, J=6 Hz), 1.19 (3H, d, J=6 Hz), 1.43 (9H, s), 2.06—2.78 (5H, m), 3.30 (1H, q, J=7 Hz), 3.59 (3H, s). Found: C, 61.83; H, 8.96%. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88%.

We thank the whole staff of the Crystallographic Research Center of Osaka University for permitting us to use the fourcircle diffractometer.

References

1) For example, see: a) M. Yamamoto, *Yuki Gosei Kagaku Kyokai Shi*, **39**, 25 (1981); b) C. F. Ingham, R. A. Massy-Westropp, G. D. Reynolds, and W. D. Thorpe, *Aust. J. Chem*, **28**, 2499 (1975). Literatures cited therein.

2) B. C. Seegal, M. Holden, *Science*, **101**, 413 (1945).

3) G. G. Gallo, C. Coronelli, A. Vigevani, G. C. Lancini, *Tetrahedron*, **25**, 5677 (1969).

4) G. Lardelli, G. Dijkstra, P. D. Harkes, J. Boldingh, *Rec. Trav. Chim.*, **85**, 43 (1966).

5) D. W. Knight and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 635, 641.

6) H. Tomioka, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **23**, 99 (1982).

7) J. Eriksen and P. E. Plith, *Tetrahedron Lett.*, **23**, 481 (1982).

8) N. Yanagihara, C. Lambert, K. Iritani, K. Utimoto, and H. Nozaki, *J. Am. Chem. Soc.*, **108**, 2753 (1986).

9) S. Tsuboi, H. Fukumoto, and A. Takeda, *Chem. Lett.*, **1983**, 1219.

10) P. A. Chopard, R. F. Hudson, and R. J. G. Searle, *Tetrahedron Lett.*, **1965**, 2357.

11) C. F. Ingham, R. A. Massy-Westropp, and G. D. Reynolds, *Aust. J. Chem.*, **27**, 1477 (1974).

12) C. F. Ingham and R. A. Massy-Westropp, *Aust. J. Chem.*, **27**, 1491 (1974).

13) M. J. Begley, D. R. Gedge, and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, **1978**, 60.

14) D. R. Gedge and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, **1978**, 880.

15) P. A. Chopard, R. J. G. Searle, and F. H. Devitt, *J. Org. Chem.*, **30**, 1015 (1965).

16) H. O. House and V. Kramas, *J. Org. Chem.*, **28**, 3362 (1963).

17) A. Takenaka, DCMS-3, Tokyo Institute of Technology (1977).

18) H. Nozaki, Z. Yamaguti, T. Okada, R. Noyori, and M. Kawanishi, *Tetrahedron*, **23**, 3993 (1967).

19) a) P. A. Bartlett, *Tetrahedron*, **36**, 54 (1980); b) L. D. Bergel'son and S. G. Batrakov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1963**, 1259.

20) a) K. C. Chan, R. A. Jewell, W. H. Nutling, and H. Rapoport, *J. Org. Chem.*, **33**, 3382 (1968); b) S. Tsuboi, T. Masuda, and A. Takeda, *J. Org. Chem.*, **47**, 4478 (1982).

21) O. Tsler and H. Gutmann, *Helv. Chim. Acta*, **40**, 1242 (1957).

22) A. Michael and J. Ross, *J. Am. Chem. Soc.*, **52**, 4598 (1930).

23) Fr.Fichter and A. Beisswenger, *Chem. Ber.*, **36**, 1205 (1903).

24) F. V. Darbishire and J. F. Thorpe, *J. Chem. Soc.*, **87**, 1717 (1905).

25) W. H. Perkin, Jr. and J. F. Thorpe, *J. Chem. Soc.*, **75**, 54 (1899).

26) C. R. Noller and C. E. Pannell, *J. Am. Chem. Soc.*, **77**, 1862 (1955).

27) D. Vorlander and P. Herrmann, *Ann. Chem.*, **320**, 85 (1902).

28) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect A*, **27**, 368 (1971).

29) T. Ashida, HBLS-V, The Universal Crystallographic

Computing System-Osaka, pp. 55—61. The Computation Center of Osaka University (1973).

30) International Tables for X-ray Crystallography, Vol. IV, Birmingham, Kynoch Press (1974).

31) The atomic parameters of hydrogen atoms, anisotropic temperature factors, bond lengths and angles, and the list of observed and calculated structure factors (×10) are deposited as Document No. 8710 at the Office of the Editor of Bull. Chem. Soc. Jpn.

32) R. Mozingo, *Org. Synth.*, Vol. 26, p. 77 (1964).

33) M. Tokuda, Y. Watanabe, and M. Ito, *Bull. Chem. Soc. Jpn.*, **51**, 905 (1978).

34) C. R. Strauss, *J. Chromatogr.*, **87**, 576 (1973).