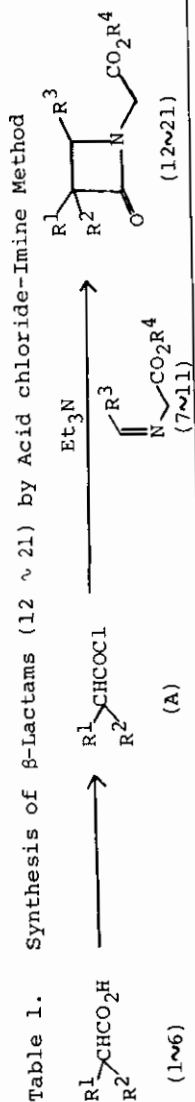


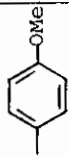
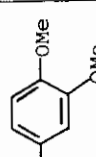
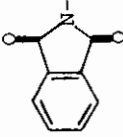
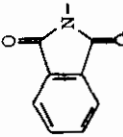
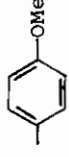
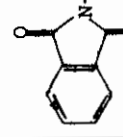
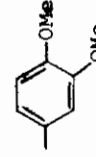
(A) Acid chloride-Imine Method

Commercially available carboxylic acids (1 ~ 4) were firstly converted into the corresponding acid chlorides (A) with thionyl chloride or oxalyl chloride as usual. Diphenylacetyl chloride was treated with triethylamine according to Bachi's procedure¹⁰ to give the ketene¹¹, which was added to a solution of N-benzyl-ideneglycinates (7 ~ 9) in dry benzene. The reaction was carried out overnight at room temperature. In the case of the other acid chlorides from the carboxylic acids (2 ~ 4), the acid chlorides were directly added to a mixture of the imines (7 ~ 11) and triethylamine in dry methylene chloride and the resulting mixture was stirred for 1 h at room temperature. The results are summarised in Tables 1 and 2.

(B) Phosphate Anhydride-Imine Method

After stirring an equimolecular mixture of the carboxylic acids (4 ~ 6) and diethyl-phosphorochloridate in dry methylene chloride at room temperature for 20 min, the resulting solution was added dropwise to a stirred mixture of the imines (7,10) and triethylamine in dry methylene chloride and the resulting mixture was stirred overnight at the same temperature. The results are shown in Tables 3 and 4. It was varified from the nmr analysis based on the coupling constant due to the protons on the azetidinone ring that only trans-isomers (21 ~ 25) were obtained by this method.



Compound	R ¹	R ²	R ³	R ⁴	yield (%)	mp (°C)	Formula	MS m/e (M ⁺)	Anal. Calcd. (Found) C H N
12	Ph	Ph	Ph	Et	79.0	100.5 ~ 101	C ₂₅ H ₂₃ NO ₃	385	77.90 (77.40) 6.01 (6.31) 3.63 (3.55)
13	Ph	Ph		Et	69.0	87 ~ 88	C ₂₆ H ₂₅ NO ₄	415	75.16 (75.16) 6.07 (6.11) 3.37 (3.34)
14	Ph	Ph		Et	66.0	130	C ₂₇ H ₂₇ NO ₅	445	72.79 (72.72) 6.11 (6.32) 3.14 (3.02)
<u>cis</u> 15 <u>trans</u>		H	Ph	Et	27.6	192 ~ 193	C ₂₁ H ₁₈ N ₂ O ₅	378	66.66 (66.38) 4.80 (4.75) 7.40 (7.36)
<u>cis</u> 16 <u>trans</u>		H		Et	10.2	133	C ₂₂ H ₂₀ N ₂ O ₆	408	64.70 (64.46) 4.94 (5.06) 6.86 (6.75)
<u>cis</u> 17 <u>trans</u>		H		Et	12.5	170 ~ 171	C ₂₃ H ₂₂ N ₂ O ₇	438	63.01 (63.00) 5.06 (5.17) 6.39 (6.49)
					43.7	oil	C ₂₃ H ₂₂ N ₂ O ₇ ·0.25 H ₂ O	438	62.36 (62.47) 5.12 (5.44) 6.33 (6.07)




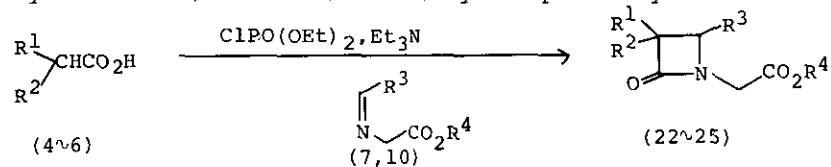
18	Cl	Cl	Ph	Et	26.8	oil	$C_{13}H_{13}NO_3Cl_2$	300, 302, 304
19	Cl	Cl		Et	8.0	oil	$C_{15}H_{15}NO_3Cl_2$	326, 328, 330
20	Cl	Cl		CH_2Ph	7.7	oil	$C_{20}H_{17}NO_3Cl_2$	289, 301, 303
21	SPh	H		CH_2Ph	30.0	oil	$C_{26}H_{23}NO_3S$	429

Table 2 Spectral Data of the β -Lactams (12 ~ 21)

Compound	IR(CHCl ₃) cm ⁻¹	NMR (δ)
12	1760, 1740	(CCl ₄): 1.20 (3H, t, J = 7 Hz, CH ₂ CH ₃), 3.45 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.16 (2H, q, J = 7 Hz, CH ₂ CH ₃), 4.45 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.55 (1H, s, 4-H), 7.00 ~ 7.66 (15H, m, 3 x Ph)
13	1760, 1740	(CCl ₄): 1.20 (3H, t, J = 7 Hz, CH ₂ CH ₃), 3.36 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 3.69 (3H, s, OMe), 4.15 (2H, q, J = 7 Hz, CH ₂ CH ₃), 4.40 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.46 (1H, s, 4-H), 6.60 (2H, d, J = 8 Hz, 2 x ArH), 6.83 ~ 7.83 (12H, m, 12 x ArH)
14	1760, 1740	(CCl ₄): 1.20 (3H, t, J = 7 Hz, CH ₂ CH ₃), 3.46 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 3.48 (3H, s, OMe), 3.73 (3H, s, OMe), 4.13 (2H, q, J = 7 Hz, CH ₂ CH ₃), 4.32 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.40 (1H, s, 4-H), 6.26 (1H, s, ArH), 6.65 (2H, s, 2 x ArH), 7.03 ~ 7.70 (10H, m, 2 x Ph)
<u>cis</u>	1770, 1740, 1720	(CDCl ₃): 1.33 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.80 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.26 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.70 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.33 (1H, d, J = 5 Hz, 3 or 4-H), 5.66 (1H, d, J = 5 Hz, 3 or 4-H), 7.26 (5H, s, Ph), 7.63 (4H, s, 4 x ArH)
15 <u>trans</u>		(CDCl ₃): 1.33 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.60 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.03 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.43 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.10 (1H, s, 3 or 4-H), 5.20 (1H, s, 3 or 4-H), 7.40 (5H, s, Ph), 7.76 (4H, s, 4 x ArH)
<u>cis</u>	1770, 1740, 1720	(CDCl ₃): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.66 (3H, s, OMe), 3.73 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.26 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.66 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.30 (1H, d, J = 5 Hz, 3 or 4-H), 7.20 (2H, d, J = 8 Hz, 2 x ArH), 7.63 (4H, s, 4 x ArH)
16 <u>trans</u>	1770, 1730, 1720	(CDCl ₃): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.53 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.26 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.66 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.26 (1H, s, 3 or 4-H), 5.33 (1H, s, 3 or 4-H), 6.96 (2H, J = 8 Hz, 2 x ArH), 7.33 (2H, d, J = 8 Hz, 2 x ArH), 7.56 ~ 8.00 (4H, m, 4 x ArH)

	<u>cis</u>	1775, 1740, 1730	(CDCl ₃): 1.35 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.78 (3H, s, OMe), 3.83 (3H, s, OMe), 4.36 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.70 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.33 (1H, d, J = 6 Hz, 3 or 4-H), 5.69 (1H, d, J = 6 Hz, 3 or 4-H), 6.86 (3H, br s, 3 x ArH), 7.70 (4H, s, 4 x ArH),
17			
	<u>trans</u>	1775, 1730, 1720	(CDCl ₃): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.86 (3H, s, OMe), 3.90 (3H, s, OMe), 4.36 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.66 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.26 (1H, s, 3 or 4-H), 5.33 (1H, s, 3 or 4-H), 6.73 ~ 7.06 (3H, m, 3 x ArH), 7.56 ~ 7.99 (4H, m, 4 x ArH)
18		1790, 1740	(CCl ₄): 1.25 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.52 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.18 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.43 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 5.33 (1H, s, 4-H), 7.23 ~ 7.60 (5H, m, 5 x ArH)
19		1790, 1745	(CCl ₄): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃), 3.67 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.20 (2H, q, J = 7 Hz, OCH ₂ CH ₃), 4.22 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.82 (1H, d, J = 8 Hz, 4-H), 6.11 (1H, dd, J = 8 and 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 6.83 (1H, d, J = 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 7.07 ~ 7.63 (5H, m, 5 x ArH)
20		1795, 1750	(CCl ₄): 3.72 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.28 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.73 (1H, d, J = 9 Hz, 4-H), 5.20 (2H, s, CH ₂ Ph), 6.07 (1H, dd, J = 9 and 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 6.75 (1H, d, J = 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 7.35 (10H, br s, 10 x ArH)
21	<u>trans</u>	1765, 1750	(CCl ₄): 3.73 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.12 (1H, d, J = 18 Hz, >C< $\frac{H}{H}$), 4.37 (1H, dd, J = 2.2 and 9 Hz, 4-H), 5.07 (2H, s, CH ₂ Ph), 6.22 (1H, dd, J = 9 and 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 6.68 (1H, d, J = 16 Hz, $\frac{H}{H}$ >= < $\frac{H}{Ph}$), 7.07 ~ 7.63 (15H, m, 15 x ArH)

Table 3 Synthesis of β -Lactams (22 ~ 25) by Phosphate Anhydride-Imine Method





Compound	R ¹	R ²	R ³	R ⁴	yield (%)	mp (°C)	Formula	MS m/e (M ⁺)	Anal. Calcd.		
									C	H	N
22 <u>trans</u>	Ph	H	Ph	Et	48.9	61 ~ 62°	C ₁₉ H ₁₉ NO ₃	264 (M ⁺ -45)	73.76 (74.11)	6.19 (6.25)	4.53 (4.50)
23 <u>trans</u>	Ph	H		Et	69.2	oil	C ₂₁ H ₂₁ NO ₃	335			
24 <u>trans</u>	Cl	H	Ph	Et	3.8	oil	C ₁₃ H ₁₄ NO ₃ Cl	267, 269			
25 <u>trans</u>	SPh	H		Et	4.5	oil	C ₂₁ H ₂₁ NO ₃ S	367			

Table 4 Spectral data of the β -Lactams (22 ~ 25)

Compound	IR (CHCl ₃) cm ⁻¹	NMR (δ)
22	1760, 1735	(CCL ₄ ^d): 1.27 (3H, t, J = 7 Hz, OCH ₂ CH ₃ ⁻³), 3.40 (1H, d, J = 18 Hz, >C< ^H), 4.06 (1H, d, J = 2 Hz, 3-H), 4.25 (2H, q, J = 7 Hz, OCH ₂ CH ₃ ⁻²), 4.46 (1H, d, J = 18 Hz, >C< ^H), 4.76 (1H, d, J = 2 Hz, 4-H), 7.30 (10H, s, 10 x ArH)
23	1750, 1735	(CCL ₄ ^d): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃ ⁻³), 3.66 (1H, d, J = 18 Hz, >C< ^H), 4.12 (1H, d, J = 2 Hz, 3-H), 4.23 (2H, q, J = 7 Hz, OCH ₂ CH ₃ ⁻²), 4.26 (1H, d, J = 18 Hz, >C< ^H), 6.20 (1H, dd, J = 15 and 8 Hz, \bar{H}), 6.67 (1H, d, J = 15 Hz, H) => < ^H Ph), 7.30 (10H, s, 10 x ArH)
24	1780, 1750	(CCL ₄ ^d): 1.30 (3H, t, J = 7 Hz, OCH ₂ CH ₃ ⁻³), 3.43 (1H, d, J = 18 Hz, >C< ^H), 4.16 (2H, q, J = 7 Hz, OCH ₂ CH ₃ ⁻²), 4.30 (1H, d, J = 18 Hz, >C< ^H), 4.50 (1H, d, J = 2 Hz, 4-H), 4.83 (1H, d, J = 2 Hz, 3-H), 7.36 (5H, s, 5 x ArH)
25	1760, 1740	(CDCl ₃): 1.23 (3H, t, J = 7 Hz, OCH ₂ CH ₃ ⁻³), 3.72 (1H, d, J = 18 Hz, >C< ^H), 4.15 (1H, d, J = 18 Hz, >C< ^H), 4.18 (2H, q, J = 7 Hz, OCH ₂ CH ₃ ⁻²), 4.41 (1H, dd, J = 2 and 9 Hz, 4-H), 6.22 (1H, dd, J = 9 and 16 Hz, \bar{H}), 6.76 (1H, d, J = 16 Hz, H) => < ^H Ph), 7.20 ~ 7.80 (10H, m, 10 x ArH)

EXPERIMENTAL

Melting points were determined on a Yanagimoto hotstage apparatus. Ir and nmr spectra were measured with a Hitachi 215 spectrophotomer and a JNM-PMX-6 spectrometer (tetramethylsilane as an internal standard), respectively.

4-Substituted 1-Ethoxycarbonylmethyl-3,3-diphenyl-2-azetidiones (12 ~ 14).

— To a solution of ethyl *N*-benzylideneglycinates (7 ~ 9) (3.16 mmol) in dry benzene (50 ml) was added diphenyl ketene, which was prepared by stirring diphenylacetyl chloride (4.34 mmol) during 1 h under nitrogen atmosphere at room temperature and the mixture was further stirred overnight under the same conditions. After evaporation of the solvent, the residue was recrystallised from ethanol to give 12 - 14.

4-Substituted 1-Ethoxycarbonylmethyl-3-phthaloylimino-2-azetidiones (15 ~

17). — To a mixture of the *N*-benzylideneglycinates (7 ~ 9) (2 mmol) and triethylamine (6 mmol) in dry methylene chloride (150 ml) was added a solution of *N*-phthaloylglycyl chloride (2.4 mmol) in dry methylene chloride (50 ml) under stirring and nitrogen atmosphere at 0°C and the resulting mixture was stirred for 20 h at room temperature, then washed with water and dried (Na₂SO₄). After evaporation of the solvent, the residue was crystallised from ethanol to give the *cis*-isomers of 15 ~ 17 as crystals. The mother liquid was concentrated and subjected to chromatography on silica gel eluting with *n*-hexane-ethyl acetate (1 : 1 v/v) to afford the *trans*-isomers of 15 ~ 17 as a pale yellowish oil.

3,3-Dichloro-1-ethoxycarbonylmethyl-4-phenyl-2-azetidinone (18). — To a mixture of ethyl *N*-benzylideneglycinate (7) (298 mg, 1.56 mmol) and triethylamine (189 mg, 1.87 mmol) in dry methylene chloride (20 ml) was added a solution of dichloroacetyl chloride (276 mg, 1.87 mmol) in dry methylene chloride (10 ml) under ice-cooling and stirring. The mixture was further stirred for 1 h, then washed with a brine and dried (Na₂SO₄). Evaporation of the solvent gave a brownish oil, which was purified by chromatography on silica gel eluting with *n*-hexane-ethyl acetate to give 18 (105 mg, 26.8 %) as an oil.

3-Substituted 1-Alkoxycarbonylmethyl-4-styryl-2-azetidiones (19 ~ 21). — A

mixture of the esters of glycinates (2.03 mmol) and cinnamic aldehyde (2.03 mmol) in dry carbon tetrachloride (20 ml) was stirred for 1 h at room temperature. After drying (MgSO_4), the resulting solution of imines (10 ~ 11) was diluted with dry methylene chloride to 250 ml. After addition of triethylamine (2.84 mmol), a solution of the acid chlorides (2.44 mmol) in dry methylene chloride (50 ml) was added to the above mixture within 3 h under ice-cooling and the resulting mixture was stirred for 30 min, washed with a brine and dried (Na_2SO_4). Evaporation of the solvent, followed by purification with silica gel column chromatography gave 19 ~ 21.

General method using Diethylphosphorochloridate. — After stirring a mixture of the carboxylic acids (4 ~ 6) (8 mmol) and diethylphosphorochloridate (8 mmol) in dry methylene chloride (40 ml) for 20 min at room temperature, a solution of the imines (7, 10) (8 mmol) and triethylamine (1.6 mmol) in methylene chloride was added dropwise to the above mixture during 2 h at the same temperature under stirring. The mixture was further stirred for 15 ~ 20 h, washed with water and dried (Na_2SO_4). Evaporation of the solvent, followed by purification with silica gel column chromatography eluting with *n*-hexane-ethyl acetate (20 : 1 v/v) gave 22 ~ 25.

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