A New Synthesis of β-Lactams *via* Photochemical γ-Hydrogen Abstraction of Monothioimides

Masami Sakamoto,* Shoji Watanabe, Tsutomu Fujita, and Masakazu Tohnishi
Department of Applied Chemistry, Faculty of Engineering, Chiba University, Yayoi-cho, Chiba, 260 Japan
Hiromu Aoyama and Yoshimori Omote
Department of Chemistry, University of Tsukuba, Sakura-mura, Ibaraki, 305 Japan

Photochemical reactions of acyclic and semicyclic monothioimides were studied. Photolysis of acyclic monothioimides gave β-lactams (Type II cyclization products) and thioamides (Type II cleavage products). 4-Mercapto-β-lactams were isolated as 4-acylthio-β-lactams by acylation with benzoyl chloride or acetyl chloride in the presence of triethylamine. Irradiation of six- or seven- membered semicyclic monothioimides gave bicyclic β-lactams, but five-membered semicyclic monothioimides gave only Type II cleavage products.

Considerable ingenuity has been demonstrated over many years in devising syntheses for the β-lactam system which forms the most salient feature of the penicillin and cephalosporin antibiotics. Much effort has also been put into the preparation of simple β-lactams for use as antibiotics, antidepressants, and antisedatives.[1] A number of preparative methods for the β-lactams, including photochemical routes, have been reported, most of them involving hydrogen abstraction,[2] ring contraction,[3] electrocyclization,[4] or the rearrangement of diazo compounds.[5] Other photochemical reactions[6] have also been used to synthesize a variety of β-lactam structures.

Recently the photochemistry of N-containing thiocarbonyl-compounds has received much attention, because it provides a route to the syntheses of some N-heterocycles,[7] and in particular, the Paterno-Büchi reactions have been investigated for this purpose. In relation to our study on the photochemical reactions of acyclic monothioimides[2i,6j,8] and *N*-acyltetrahydro-1,3-thiazine-2-thiones,[2j] we now report a synthesis of β-lactams involving photochemical γ-hydrogen abstraction (Type II reaction) of acyclic and semicyclic monothioimides.[9]

Results and Discussion

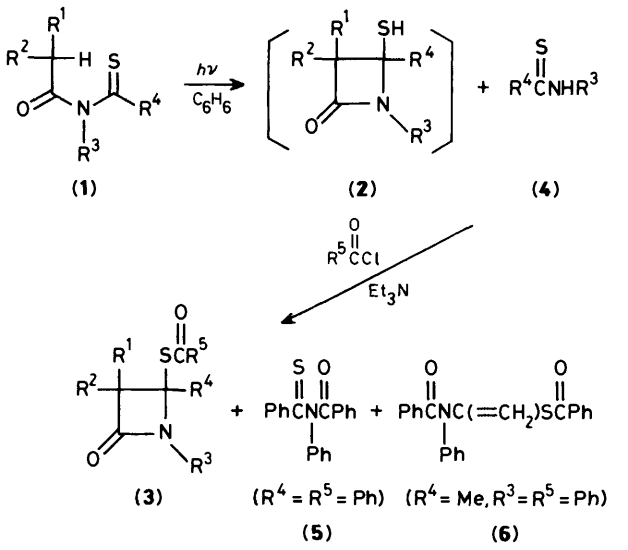
The monothioimides (**1a**—**h**) and (**7a**—**f**) were obtained almost quantitatively by acylation of the corresponding *N*-substituted thioamides. The visible spectrum of *N*-isobutyrylthiobenzanilide (**1a**) in cyclohexane showed a maximum at 490 nm (ε 170) assignable to the nπ* band of the thiocarbonyl group. When the monothioimide (**1a**) was irradiated with a 1000 W high pressure mercury lamp in benzene under argon until the disappearance of the starting materials, the i.r. spectrum of the reaction mixture exhibited absorption at 1 745 cm^{-1} derived from the β-lactam structure and the n.m.r. spectrum showed new signals at δ 0.79 (s, 3 H) and 1.55 (s, 3 H) instead of the peak at 1.15 (d, *J* 7 Hz, 6 H) derived from (**1a**). However, the β-lactam (**2a**) was too unstable to be isolated (Scheme 1). In order to prevent decomposition of compound (**2a**), benzoyl chloride and triethylamine were added to the reaction mixture, and 4-benzoylthio-3,3-dimethyl-1,4-diphenylazetidin-2-one (**3a**) (29%) and *N*-benzoylthiobenzanilide (**5**) (70%) were obtained as shown in Table 1. The formation of compound (**5**) was explained by benzoylation of the thione (**4**) which was produced by Type II cleavage of (**1a**).

Photolysis of the monothioimide (**1b**) gave the β-lactam (**3b**) (16%) which was benzoylated to the benzanilide (**6**) (39%). The formation of compound (**6**) from thioacetanilide (**4**) was confirmed by independent synthesis from (**4b**) by benzoylation. With compound (**1c**), under the same conditions, *S*-benzoyl-β-lactam (**3c**) (35%, *cis*:*trans* 49:51), *S*-phenylacetyl-β-lactam (**3c'**) (13%, *cis*-isomer), and the benzanilide (**6**) (17%) were obtained.[10] Photolysis of the methoxyacetyl derivative (**1d**) gave the β-lactam (**3d**) in high yield (76%) in the same manner, but only the *cis*-isomer was obtained. Photolysis of (**1e**) followed by acetylation with acetyl chloride and triethylamine gave *S*-acetyl-β-lactam (**3e**) as a mixture of two stereoisomers (*cis*:*trans* 63:27) in 90% yield.

Table 1. Photochemical reaction of acyclic monothioimides

						Yield (%)[a]		
(1)	R^1	R^2	R^3	R^4	R^5	(3)	(5)	(6)
a	Me	Me	Ph	Ph	Ph	29	70	—
b	Me	Me	Ph	Me	Ph	16	—	39
c	Ph	H	Ph	Me	Ph	35[b](13)[c]	—	17
d	MeO	H	Ph	Me	Ph	76[d]	0	—
e	MeO	H	Ph	Ph	Me	90[b]	0	—
f	Me	Me	Me	Ph	Me	52	29	—
g	Ph	Ph	Me	Ph	Me	54[d]	16	—
h	MeO	H	Me	Ph	Me	62	17	—

[a] Isolated yield, [b] Mixture of stereoisomers, [c] Yield of *S*-phenylacetyl-β-lactam (**3c'**), [d] Only *cis*-isomer was obtained.



Scheme 1.

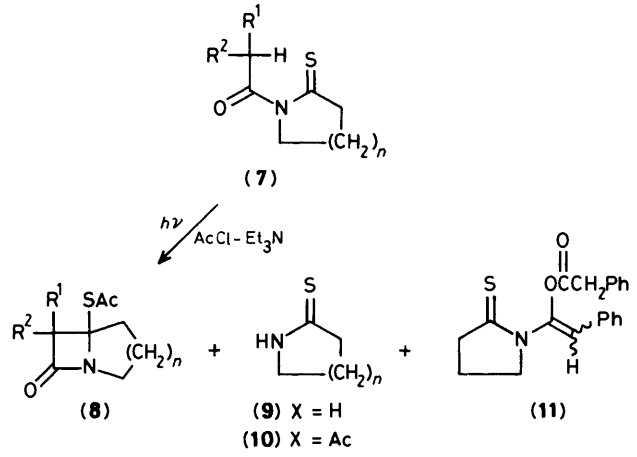
Table 2. Photochemical reaction of semicyclic monothioimides

				Yield (%)[a]		
(7)	*n*	R^1	R^2	(8)	(9)	(10)
a[c]	1	Me	Me	0	71	—
b[c]	1	Ph	H	0	47(51)[b]	—
c	2	Me	Me	21	—	39
d	2	MeO	H	49[d]	—	Trace
e	3	Me	Me	38	—	22
f	3	MeO	H	82[d]	—	9

[a] Isolated yield. [b] Yield of (**11**). [c] This photoreaction was not followed by acetylation. [d] Only *cis*-isomer.

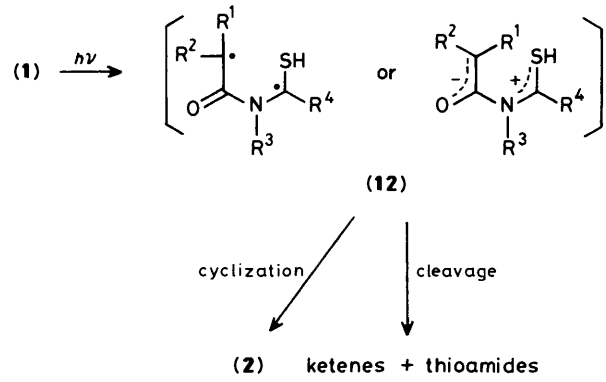
Photolysis of *N*-acyl-*N*-methylthiobenzamides (**1f**—**h**) followed by acetylation with acetyl chloride and triethylamine gave the *S*-acetyl-β-lactams (**3f**—**h**) in good yields as shown in Table 1. In the case of the photoreaction of (**1h**), only the *cis*-isomer (**3h**) was obtained.

The synthesis of bicyclic β-lactams *via* the photochemical reaction of semicyclic monothioimides was next attempted (Scheme 2). On photolysis, five-membered semicyclic monothioimides (**7a**) and (**7b**) mainly undergo Type II cleavage to produce pyrrolidine-2- thione (**9**) although compound (**7b**) gave (**9**) (51%) accompanied by the substituted derivative (**11**) (47%). Compound (**11**) was obtained as only one isomer, the stereochemistry of which was not ascertained. When *N*-isobutyrylpiperidine-2-thione (**7c**) was irradiated in benzene and the photoproducts were acetylated, a bicyclic β-lactam, 6-acetylthio-7,7-dimethyl-1-azabicyclo[4.2.0]octan-8-one (**8c**), was obtained (21%) along with a Type II cleavage product, *N*-acetylpiperidine-2-thione (**10c**) (39%). Photolysis of other semicyclic monothioimides (**7d**—**f**) under the same conditions gave the corresponding bicyclic β-lactams (Table 2). In the case of methoxyacetyl derivatives (**7d**) and (**7f**), only the *cis*-isomers (**8d**) and (**8f**) were obtained.

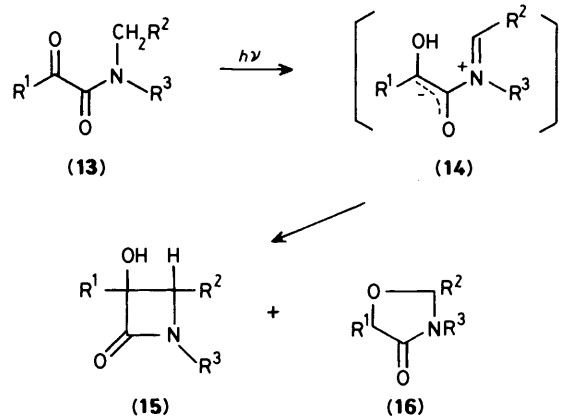


Scheme 2.

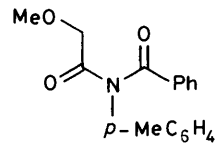
The photoreaction of monothioimides (**1a**—**h**) and (**7a**—**f**) can be explained in terms of the Type II process as shown in Scheme 3. The intermediacy of the zwitterion (**12**) was postulated for the following reason. Previously we have reported photochemical reactions of α-oxo amides (**13**) which gave the β-lactams (**15**) and the oxazolidines (**16**) *via* a zwitterionic intermediate (**14**)[2g] (Scheme 4). The zwitterion (**12**) resembles (**14**) very closely, however it may be more stable due to the sulphur atom at the cation centre and the absence of a hydroxy group at the anion centre. The formation of the ketenes (Type II cleavage products) was supported by the fact that *S*-phenylacetyl-β-lactam (**3c'**) was obtained on photolysis of (**1c**), and (**11**) on photolysis of (**7b**). The formation of (**11**) can be explained in terms of either the reaction of (**7b**) with phenylketene or that of piperidinethione with 2 equiv. of phenylketene. As for the formation of the thiones (**4**) and (**9**), direct homolysis of the C–N bond of the monothioimide could not be excluded as a minor process since *N*-benzoyl thiobenzanilide (**5**) which had no abstractable hydrogen underwent photocleavage to produce thiobenzanilide under prolonged irradiation.



Scheme 3.



Scheme 4.



(**18**) (36%) + (**19**) (12%)

Scheme 5.

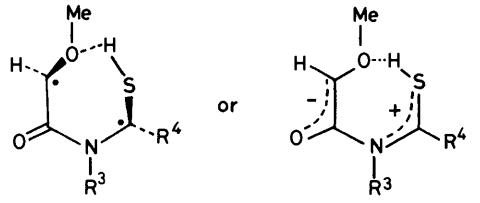


Figure 1.

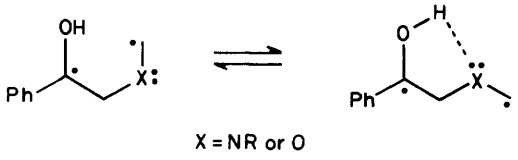


Figure 2.

In the present reaction, Type II cyclization occurred as the main process. However, Mazzocchi *et al.* reported photochemistry of acyclic imides [11] in which the imides undergo only Type II eliminations across the imide moiety in addition to those on the C-alkyl chain and α-cleavage reactions. The substituents in the photoreaction were limited to alkyl groups. In order to explain the differences between acyclic imides and acyclic monothioimides, we examined the photoreaction of *N*-methoxyacetyl-*N*-(*p*-tolyl)benzanilides (**17**) and found that anilides (**18**) (36%) and (**19**) (12%) were obtained. Only Type I and Type II cleavage reactions occurred; no β-lactams or ring opening products of (**17**) were obtained (Scheme 5). There is no satisfactory hypothesis to explain the differences in the photochemical behaviour between acyclic imides and acyclic monothioimides at present.

The fact that reaction proceeds stereoselectively in the case of the *N*-methoxyacetyl derivatives (**1d**), (**1e**), (**7d**), and (**7f**) can be explained in terms of the hydrogen bond between the methoxy oxygen and the mercapto group (Figure 1) and steric effects. The hydrogen bond of the resulting 1,4-diradical has been reported in the photochemical reaction of aryl alkyl ketones which possessed heteroatoms at the β-carbon. It has been concluded that this hydrogen bond makes Type II cyclization more favourable [12] (Figure 2).

Experimental

M.p.s were measured on a Yanagimoto micro melting point apparatus, and were uncorrected. I.r. spectra were measured on a Jasco IRA-1 spectrophotometer. ^{1}H- and ^{13}C-N.m.r. spectra were recorded on Hitachi R-24 and JEOL-100 spectrometers using tetramethylsilane as an internal standard. The chemical shifts are in δ-units (p.p.m.) with coupling constants in Hz, and $CDCl_3$ was used as a solvent unless otherwise stated. U.v. spectra were measured on a Shimadzu UV-365 UV-VIS-NIR recording spectrophotometer. An Eikohsya 1000-W high pressure mercury lamp was used as an irradiation source. Silica gel (Merck, Kieselgel 60, 230—400 mesh) was used for flash column chromatography.

Preparation of Monothioimides.—All monothioimides were prepared by the reaction of N-substituted thioamides with acid chlorides. The preparation of *N*-isobutyrylthiobenzanilide (**1a**) is given as an example. Triethylamine (300 mg, 3.0 mmol) was added dropwise to a solution of thiobenzanilide (600 mg, 2.8 mmol) and isobutyryl chloride (320 mg, 3.0 mmol) in dry benzene (30 ml) at room temperature under nitrogen and the reaction mixture was then stirred for 2 h. The precipitated triethylamine hydrochloride was removed by filtration through Celite, the benzene was evaporated off, and the residual mixture was subjected to chromatography on silica gel (eluant: benzene–ethyl acetate). Crystalline *N*-isobutyrylthiobenzanilide (**1a**), (720 mg, 90%) was isolated and recrystallized from chloroform–hexane. Since some of the monothioimides (**1c—e**), (**1g—h**), (**7b**), (**7d**), and (**7f**) were unstable liquids and decomposed by distillation, they were used immediately after isolation by flash column chromatography.

N-*Isobutyrylthiobenzanilide* (**1a**). M.p. 81—82 °C; $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 229 (ε 13 400 dm^3 mol^{-1} cm^{-1}), 310 (8 700), and 490 nm (170); δ_H 1.15 (d, *J* 7 Hz, 6 H, Me × 2), 2.81 (sept, *J* 7 Hz, 1 H, $CHMe_2$), 7.1—7.5 (m, 8 H, ArH), and 7.5—7.7 (m, 2 H, ArH); δ_C 19.6 (q, Me), 36.0 (d, CH), 127.3 (d, Ph), 128.2 (d, Ph), 128.3 (d, Ph), 128.5 (d, Ph), 129.7 (d, Ph), 131.2 (d, Ph), 143.6 (s, Ph), 145.1 (s, Ph), 180.7 (s, C=O), and 212.2 (s, C=S) (Found: C, 72.1; H, 6.05; N, 4.9. $C_{17}H_{17}NOS$ requires C, 72.05; H, 6.04; N, 4.94%).

N-*Isobutyrylthioacetanilide* (**1b**). B.p. 70 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 290 (ε 11 300 dm^3 mol^{-1} cm^{-1}) and 450 nm (20); δ_H 1.13 (d, *J* 7 Hz, 6 H, Me × 2), 2.75 (sept, *J* 7 Hz, 1 H, $CHMe_2$), 2.97 (s, 3 H, MeC=S), and 7.1—7.6 (m, 5 H, ArH) (Found: C, 63.85; H, 6.9; N, 5.95. $C_{12}H_{15}NOS$ requires C, 65.12; H, 6.83; N, 6.32%).

N-Phenylacetylthioacetanilide (**1c**). $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 287(ε 12 900 dm^3 mol^{-1} cm^{-1}) and 460 nm (30); δ_H 3.03 (s, 3 H, MeC=S), 3.63 (s, 2 H, CH_2), and 6.9—7.5 (m, 10 H, ArH).

N-Methoxyacetylthioacetanilide (**1d**). $\nu_{max.}(CHCl_3)$ 1 705 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 284 (ε 11 700 dm^3 mol^{-1} cm^{-1}) and 455 nm (30); δ_H 3.07 (s, 3 H, MeC=S), 3.31 (s, 3 H, OMe), 3.82 (s, 2 H, CH_2), and 7.0—7.5 (m, 5 H, ArH).

N-Methoxyacetylthiobenzanilide (**1e**). $\nu_{max.}(CHCl_3)$ 1 705 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 230 (ε 11 900 dm^3 mol^{-1} cm^{-1}), 313 (8 700), and 500 nm (170); δ_H 3.30 (s, 3 H, OMe), 4.07 (s, 2 H, CH_2), and 7.2—7.9 (m, 10 H, ArH).

N-*Isobutyryl*-N-*methylthiobenzamide* (**1f**). B.p. 70 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 695 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 256 (ε 8 800 dm^3 mol^{-1} cm^{-1}), 313 (12 000), and 470 nm (100); δ_H 0.93 (d, *J* 7 Hz, 6 H, Me × 2), 2.50 (sept, *J* 7 Hz, 1 H, $CHMe_2$), 3.67 (s, 3 H, NMe), and 7.1—7.6 (m, 5 H, ArH) (Found: C, 64.9; H, 6.8; N, 6.35. $C_{12}H_{15}NOS$ requires C, 65.12; H, 6.83; N, 6.32%).

N-Diphenylacetyl-*N*-methylthiobenzamide (**1g**). $\nu_{max.}(CHCl_3)$ 1 695 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 286 (ε 7 400 dm^3 mol^{-1} cm^{-1}), 295 (7 600), 317 (9 100), and 480 nm (70); δ_H 3.57 (s, 3 H, NMe), 5.15 (s, 1 H, Ph_2), and 6.9—7.7 (m, 15 H, ArH).

N-Methoxyacetyl-*N*-methylthiobenzamide (**1h**). $\lambda_{max.}(CHCl_3)$ 1 695 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 312 (ε 9 200 dm^3 mol^{-1} cm^{-1}) and 480 nm (80); δ_H 3.31 (s, 3 H, OMe), 3.65 (s, 3 H, NMe), 3.68 (s, 2 H, CH_2), and 7.2—7.8 (m, 5 H, ArH).

N-*Isobutyrylpyrrolidine*-2-*thione* (**7a**). B.p. 55 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 690 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 290 (ε 15 000 dm^3 mol^{-1} cm^{-1}) and 410 nm (20); δ_H 1.18 (d, *J* 7 Hz, 6 H, Me × 2), 2.03 (quint, *J* 7 Hz, 2 H, 4-CH_2), 3.18 (t, *J* 7 Hz, 2 H, 3-CH_2), 4.13 (t, *J* 7 Hz, 2 H, 5-CH_2), and 4.57 (sept, *J* 7 Hz, 1 H, $CHMe_2$) (Found: C, 56.05; H, 7.6; N, 8.15. $C_8H_{13}NOS$ requires C, 56.1; H, 7.65; N, 8.17%).

N-Phenylacetylpyrrolidine-2-thione (**7b**). $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 288 (ε 12 800 dm^3 mol^{-1} cm^{-1}) and 415 nm (30); δ_H 1.98 (quint, *J* 7 Hz, 2 H, 4-CH_2), 3.17 (t, *J* 7 Hz, 2 H, 3-CH_2), 4.12 (t, *J* 7 Hz, 2 H, 5-CH_2), 4.62 (s, 2 H, CH_2Ph), and 7.22 (s, 5 H, ArH).

N-*Isobutyrylpiperidine*-2-*thione* (**7c**). B.p. 60 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 303 (ε 9 100 dm^3 mol^{-1} cm^{-1}) and 410 nm (40); δ_H 1.21 (d, *J* 7 Hz, 6 H, Me × 2), 1.6—2.1 (br, 4 H, 4- and 5-CH_2), 2.7—3.1 (br, 2 H, 3-CH_2), and 3.4—3.9 (br, 3 H, 6-CH_2 and $CHMe_2$) (Found: C, 58.1; H, 8.1; N, 7.25. $C_9H_{15}NOS$ requires C, 58.34; H, 8.15; N, 7.55%).

N-Methoxyacetylpiperidine-2-thione (**7d**). $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 295 (ε 10 100 dm^3 mol^{-1} cm^{-1}) and 420 nm (20); δ_H 1.7—2.0 (br, 4 H, 4- and 5-CH_2), 2.8—3.2 (br, 2 H, 3-CH_2), 3.50 (s, 3 H, OMe), 3.7—4.0 (br, 2 H, 6-CH_2), and 4.65 (s, 2 H, CH_2OMe).

N-*Isobutyryl*-ε-*thiocaprolactam* (**7e**). B.p. 65 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 303 (ε 10 100 dm^3 mol^{-1} cm^{-1}) and 410 nm (45); δ_H 1.20 (d, *J* 7 Hz, 6 H, Me × 2), 1.4—2.0 (br, 6 H, 4-, 5-, and 6-CH_2), and 2.9—3.3 (br, 2 H, 3-CH_2), 3.61 (sept, *J* 7 Hz, 1 H, $CHMe_2$), and 3.7—3.9 (br, 2 H, 7-CH_2) (Found: C, 60.0; H, 8.4; N, 6.95. $C_{10}H_{17}NOS$ requires C, 60.26; H, 8.59; N, 7.02%).

N-*Methoxyacetyl*-ε-*thiocaprolactam* (**7f**). $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 300 (ε 9 600 dm^3 mol^{-1} cm^{-1}) and 400 nm (20); δ_H 1.5—2.0 (br, 6 H, 4-, 5-, and 6-CH_2), 3.0—3.3 (br, 2 H, 3-CH_2), 3.40 (s, 3 H, OMe), 3.8—4.1 (br, 2 H, 7-CH_2), and 4.63 (s, 2 H, CH_2OMe).

General Procedure for the Photochemical Reaction of Monothioimides (**1a**—**h**) *and* (**7a**—**f**).—A benzene solution of the monothioimide was irradiated with a 1000-W high pressure mercury lamp under argon at 10—15 °C until the starting material had disappeared. Acid chloride (3 equiv.; 1M) and triethylamine were added to the reaction mixture and the mixture was left overnight. The precipitated triethylamine hydrochloride was filtered off through Celite. After evaporation of the solvent, the filtrate was subjected to chromatography on silica gel, using benzene–ethyl acetate as eluant. The crystalline products were recrystallized from chloroform–hexane.

4-*Benzoylthio*-3,3-*dimethyl*-1,4-*diphenylazetidin*-2-*one* (**3a**). M.p. 152.5—153 °C; $\nu_{max.}(CHCl_3)$ 1 665 (SC=O) and 1 755 cm^{-1} (C=O); δ_H 0.95 (s, 3 H, Me), 1.61 (s, 3 H, Me), 6.9—7.6 (m, 13 H, ArH), and 7.7—7.9 (m, 2 H, ArH); δ_C 19.4 (q, Me), 22.2 (q, Me), 62.4 (s, C-3), 82.7 (s, C-4), 117.9 (d, Ph), 123.9 (d, Ph), 126.2 (d, Ph), 127.3 (d, Ph), 128.6 (d, Ph), 133.6 (d, Ph), 136.9 (s, Ph), 137.5 (s, Ph), 170.6 (s, C=O), and 190.0 (s, SC=O) (Found: C, 74.35; H, 5.45; N, 3.60. $C_{24}H_{21}NO_2S$ requires C, 74.39; H, 5.46; N, 3.61%).

N-*Benzoylthiobenzanilide* (**5**). M.p. 100—101.5 °C; $\nu_{max.}(CHCl_3)$ 1 680 cm^{-1} (C=O); $\lambda_{max.}(C_6H_{12})$ 242 (ε 22 000 dm^3 mol^{-1} cm^{-1}) and 488 nm (160); δ_H 6.8—8.2 (m, ArH) (Found: C, 75.5; H, 4.75; N, 4.4. $C_{20}H_{15}NOS$ requires C, 75.68; H, 4.76; N, 4.41%).

4-*Benzoylthio*-3,3,4-*trimethyl*-1-*phenylazetidin*-2-*one* (**3b**). B.p. 120 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 660 (SC=O) and 1 750 cm^{-1} (C=O); δ_H 1.52 (s, 3 H, 3-Me), 1.56 (s, 3 H, 3-Me), 2.18 (s, 3 H, 4-Me), 7.0—7.8 (m, 8 H, ArH), and 7.8—8.0 (m, 2 H, ArH); δ_C 18.6 (q, Me), 20.2 (q, Me), 22.8 (q, Me), 60.5 (s, C-3), 76.7 (s, C-4), 118.1 (d, Ph), 124.2 (d, Ph), 127.0 (d, Ph), 128.5 (d, Ph), 128.9 (d, Ph), 133.6 (d, Ph), 136.4 (s, Ph), 169.9 (s, C=O), and 190.4 (s, SC=O) (Found: C, 69.95; H, 5.75; N, 4.2. $C_{19}H_{19}NO_2S$ requires C, 70.12; H, 5.88; N, 4.30%).

N-(1-Benzoylthiovinyl)benzanilide (**6**). $\nu_{max.}(CHCl_3)$ 1 665 cm^{-1} (C=O); δ_H 5.55 and 5.67 (ABq, *J* 2 Hz, 2 H, CH_2) and 7.0—8.2 (m, 15 H, ArH); δ_C 125.7 (t, CH_2=C), 127.0 (d, Ph), 127.5 (d, Ph), 127.8 (d, Ph), 127.9 (d, Ph), 128.3 (d, Ph), 128.7 (d, Ph), 129.1 (d, Ph), 129.3 (d, Ph), 130.7 (d, Ph), 133.7 (d, Ph), 135.2 (s, Ph), 136.5 (s, Ph), 138.3 (s, Ph), 142.5 (s, CH_2=*C*), 170.4 (s, C=O), and 189.2 (s, SC=O). This material was an unstable liquid and decomposed on distillation.

4-Benzoylthio-4-methyl-1,3-diphenylazetidin-2-one (**3c**). *cis*-Isomer (17%), $\nu_{max.}(CHCl_3)$ 1 660 (SC=O) and 1 750 cm^{-1} (C=O); δ_H 2.22 (s, 3 H, 4-Me), 4.75 (s, 1 H, 3-H), and 6.9—7.8 (m, 15 H, ArH); δ_C 25.8 (q, Me), 69.2 (d, C-3), 74.6 (s, C-4), 118.2 (d, Ph), 124.6 (d, Ph), 126.6 (d, Ph), 127.3 (d, Ph), 127.7 (d, Ph), 128.2 (d, Ph), 129.0 (d, Ph), 130.4 (d, Ph), 132.1 (s, Ph), 133.1 (d, Ph), 136.2 (s, Ph), 136.5 (s, Ph), 164.2 (s, C=O), and 188.6 (s, SC=O).

trans-Isomer (18%), $\nu_{max.}(CHCl_3)$ 1 660 (SC=O) and 1 750 cm^{-1} (C=O); δ_H 1.73 (s, 3 H, 4-Me), 5.06 (s, 1 H, H-3), and 7.0—8.0 (m, 15 H ArH); δ_C 22.5 (q, Me), 69.0 (d, C-3), 72.6 (s, C-4), 118.1 (d, Ph), 124.7 (d, Ph), 127.2 (d, Ph), 128.2 (d, Ph), 128.7 (d, Ph), 129.7 (d, Ph), 129.8 (d, Ph), 132.3 (s, Ph), 133.9 (d, Ph), 136.4 (s, Ph), 136.6 (s, Ph), 164.4 (s, C=O), and 190.1 (s, SC=O).

4-Methyl-1,3-diphenyl-4-phenylacetylthioazetidin-2-one (**3c′**). *cis*-Isomer, $\nu_{max.}(CHCl_3)$ 1 670 (SC=O) and 1 750 cm^{-1} (C=O); δ_H 2.24 (s, 3 H, 4-Me), 3.30 (s, 2 H, CH_2), 4.63 (s, 1 H, 3-CH), 6.7—6.9 (m, 2 H, ArH), and 7.0—7.9 (m, 13 H, ArH); δ_C 25.7 (q, Me), 50.3 (t, CH_2), 69.0 (d, C-3), 74.4 (s, C-4), 118.2 (d, Ph), 124.6 (d, Ph), 127.2 (d, Ph), 127.5 (d, Ph), 127.8 (d, Ph), 128.4 (d, Ph), 129.1 (d, Ph), 129.3 (d, Ph), 130.5 (d, Ph), 132.2 (s, Ph), 132.3 (s, Ph), 136.2 (s, Ph), 164.1 (s, C=O), and 194.0 (s, SC=O).

4-*Benzoylthio*-3-*methoxy*-4-*methyl*-1-*phenylazetidin*-2-*one* (**3d**). *cis*-Isomer, b.p. 130 °C/10^{-3} mmHg; $\nu_{max.}(CHCl_3)$ 1 670 (SC=O) and 1 760 cm^{-1} (C=O); δ_H 2.15 (s, 3 H, 4-Me), 3.58 (s, 3 H, OMe), 4.54 (s, 1 H, 3-H), 7.0—7.7 (m, 8 H, ArH), and 7.8—8.0 (m, 2 H, ArH); δ_C 24.1 (q, 4-Me), 60.5 (q, OMe), 75.6 (s, C-4), 91.5 (d, C-3), 118.3 (d, Ph), 124.7 (d, Ph), 127.0 (d, Ph), 128.4 (d, Ph), 129.0 (d, Ph), 133.4 (d, Ph), 135.6 (s, Ph), 136.6 (s, Ph), 162.9 (s, C=O), and 189.0 (s, SC=O) (Found: C, 65.9; H, 5.2; N, 4.0. $C_{18}H_{17}NO_3S$ requires C, 66.03; H, 5.23; N, 4.27%) Only the *cis*-isomer was obtained and the configuration was determined on the basis of n.O.e. effects.

4-*Acetylthio*-3-*methoxy*-1,4-*diphenylazetidin*-2-*one* (**3e**). *cis*-Isomer, m.p. 111.5—113 °C; $\nu_{max.}(CHCl_3)$ 1 700 (SC=O) and 1 760 cm^{-1} (C=O); δ_H 2.30 (s, 3 H, MeC=O), 3.58 (s, 3 H, OMe), 4.42 (s, 1 H, 3-CH), and 7.0—7.6 (m, 10 H, ArH); δ_C 31.3 (q, MeC=O), 60.3 (q, OMe), 80.1 (s, C-4), 94.3 (d, C-3), 118.3 (d, Ph), 124.5 (d, Ph), 125.0 (d, Ph), 128.9 (d, Ph), 129.3 (s, Ph), 136.4 (s, Ph), 138.1 (s, Ph), 162.9 (s, C=O), and 191.8 (s, SC=O) (Found: C, 66.0; H, 5.3; N, 4.25. $C_{18}H_{17}NO_3S$ requires C, 66.03; H, 5.23; N, 4.27%).

trans-Isomer, m.p. 130.5—132 °C; $\nu_{max.}(CHCl_3)$ 1 690 (SC=O) and 1 760 cm^{-1} (C=O); δ_H 2.32 (s, 3 H, MeC=O), 3.32 (s, 3 H, OMe), 5.28 (s, 1 H, 3-Me), and 7.0—7.8 (m, 10 H, ArH); δ_C 31.2 (q, MeC=O), 59.1 (q, OMe), 78.4 (s, C-4), 92.9 (d, C-3), 118.5 (d, Ph), 124.9 (d, Ph), 127.4 (d, Ph), 128.5 (d, Ph), 129.0 (d, Ph), 129.1 (d, Ph), 133.9 (s, Ph), 136.0 (s, Ph), 162.9 (s, C=O), and 193.7 (s, SC=O) (Found: C, 65.95; H, 5.25; N, 4.2).

4-*Acetylthio*-1,3,3-*trimethyl*-4-*phenylazetidin*-2-*one* (**3f**). M.p. 108—109 °C; $\nu_{max.}(CHCl_3)$ 1 690 (SC=O) and 1750 cm^{-1} (C=O); δ_H(C=O) 0.71 (s, 3 H, 3-Me), 1.40 (s, 3 H, 3 × Me), 2.23 (s, 3 H, MeC=O), 2.97 (s, 3 H, NMe), and 7.1—7.4 (m, 5 H, ArH); δ_C 19.2 (q, 3-Me), 20.6 (q, 3-Me), 27.1 (q, NMe), 31.2 (q, MeC=O), 62.5 (s, C-3), 81.3 (s, C-4), 128.3 (d, Ph), 127.7 (d, Ph), 125.9 (d, Ph), 139.9 (s, Ph), 172.4 (s, C=O), and 193.2 (s, SC=O) (Found: C, 63.85; H, 6.5; N, 5.25. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.50; N, 5.31%).

4-*Acetylthio*-1-*methyl*-3,3,4-*triphenylazetidin*-2-*one* (**3g**). M.p. 128—129 °C; $\nu_{max.}(CHCl_3)$ 1 695 (SC=O) and 1 750 cm^{-1} (C=O); δ_H 2.11 (s, 3 H, MeC=O), 3.02 (s, 3 H, NMe), and 6.8—7.8 (m, 15 H, ArH); δ_C 27.0 (q, NMe), 31.0 (q, MeC=O), 79.4 (s, C-4), 84.8 (s, C-3), 126.7 (d, Ph), 127.1 (d, Ph), 127.6 (d, Ph), 127.7 (d, Ph), 127.9 (d, Ph), 128.0 (d, Ph), 128.2 (d, Ph), 128.4 (d, Ph), 128.6 (d, Ph), 136.8 (s, Ph), 137.3 (s, Ph), 137.4 (s, Ph), 168.7 (s, C=O), and 192.7 (s, SC=O) (Found: C, 74.1; H, 5.55; N, 3.55. $C_{24}H_{21}NO_2S$ requires C, 74.39; H, 5.46; N, 3.61%).

4-*Acetylthio*-3-*methoxy*-1-*methyl*-4-*phenylazetidin*-2-*one* (**3h**). *cis*-Isomer, m.p. 128—129 °C; $\nu_{max.}(CHCl_3)$ 1 695 (SC=O) and 1 760 cm^{-1} (C=O); δ_H 2.36 (s, 3 H, MeC=O), 2.98 (s, 3 H, NMe), 3.56 (s, 3 H, OMe), 4.31 (s, 1 H, 3-CH), and 7.15—7.25 (m, 5 H, ArH); δ_C 32.0 (q, MeC=O), 35.4 (q, NMe), 59.9 (q, OMe), 80.4 (s, C-4), 95.3 (d, C-3), 124.8 (d, Ph), 128.2 (d, Ph), 129.0 (d, Ph), 139.4 (s, Ph), 165.6 (s, C=O), and 193.5 (s, SC=O) (Found: C, 58.65; H, 5.65; N, 5.26. $C_{13}H_{15}NO_3S$ requires C, 58.84; H, 5.69; N, 5.27%).

1-(β-*Phenyl*-α-*phenylacetoxyvinyl*)*pyrrolidine*-2-*thione* (**11**). M.p. 64—65 °C; $\nu_{max.}$($CHCl_3$) 1 665 (C=C) and 1 750 cm^{-1} (C=O); δ_H 1.98 (quint, *J* 7.5 Hz, 2 H, 4-CH_2), 2.96 (t, *J* 7.5 Hz, 2 H, 3-CH_2), 3.71 (t, *J* 7.5 Hz, 2 H, 5-CH_2), 3.80 (s, 2 H, $PhCH_2$), 6.40 (s, 1 H, C=C), and 7.2—7.3 (m, 10 H, ArH); δ_C 21.9 (t, C-4), 40.4 (t, C-3), 45.0 (t, C-5), 55.3 (t, $PhCH_2$), 116.9 (d, C=*C*HPh), 127.4 (d, Ph), 127.7 (d, Ph), 128.4 (d, Ph), 128.7 (d, Ph), 129.4 (d, Ph), 131.8 (s, Ph), 132.9 (s, Ph), 139.6 (s, *C*=CHPh), 169.7 (s, C=O), and 206.1 (s, C=S) (Found: C, 71.05; H, 5.6; N, 4.15. $C_{20}H_{19}NO_2S$ requires C, 71.18; H, 5.67; N, 4.15%).

6-*Acetylthio*-7,7-*dimethyl*-1-*azabicyclo*[4.2.0]*octan*-8-*one* (**8c**). B.p. 110 °C/10^{-1} mmHg; $\nu_{max.}$($CHCl_3$) 1 680 (SC=O) and 1 740 cm^{-1} (C=O); δ_H 0.9—3.0 (m, 6 H, 3-, 4-, and 5-CH_2), 1.40 (s, 3 H, 7-Me), 1.45 (s, 3 H, 7-Me), 2.35 (s, 3 H, MeC=O), and 3.5—4.0 (m, 2 H, 2-CH_2); δ_C 18.3 (q, 7-Me), 20.4 (q, 7-Me), 20.6 (t, CH_2), 24.4 (t, CH_2), 31.0 (q, MeC=O), 32.2 (t, CH_2), 37.3 (t, CH_2), 62.2 (s, C-7), 75.3 (s, C-6), 171.3 (s, C=O), and 195.3 (s, MeC=O) (Found: C, 65.9; H, 5.15; N, 4.2. $C_{18}H_{17}NO_2S$ requires C, 66.03; H, 5.23; N, 4.27%).

6-*Acetylthio*-7-*methoxy*-1-*azabicyclo*[4.2.0]*octan*-8-*one* (**8d**). M.p. 78—79 °C; $\nu_{max.}$($CHCl_3$) 1 690 (SC=O) and 1 760 cm^{-1} (C=O); δ_H 1.2—1.9 (br, 4 H, 3- and 4-CH_2), 2.3—2.9 (br, 2 H, 5-CH_2), 2.35 (s, 3 H, MeC=O), 3.53 (s, 3 H, OMe), 3.6—3.9 (m, 2 H 2-CH_2), and 4.44 (s, 1 H, 7-H); δ_C 20.3 (t, CH_2), 24.0 (t, CH_2), 31.2 (q, MeC=O), 34.2 (t, CH_2), 37.5 (t, CH_2), 60.6 (q, OMe), 74.4 (s, C-6), 93.6 (d, C-7), 163.5 (s, C=O), and 194.3 (s, SC=O) (Found: C, 52.4; H, 6.65; N, 6.1. $C_{10}H_{15}NO_3S$ requires C, 52.38; H, 6.59; N, 6.10%).

7-*Acetylthio*-8,8-*dimethyl*-1-*azabicyclo*[5.2.0]*nonan*-9-*one* (**8e**). B.p. 115 °C/10^{-3} mmHg; $\nu_{max.}$($CHCl_3$) 1 680 (SC=O) and 1 740 cm^{-1} (C=O); δ_H 1.0—2.6 (br, 6 H, CH_2 × 3), 1.37 (s, 6 H, Me × 2), 2.33 (s, 3 H, MeC=O), 2.8—3.2 (br, 2 H, CH_2), and 3.3—3.8 (br, 2 H, CH_2); δ_C 18.2 (q, 8-Me), 20.8 (q, 8-Me), 26.5 (t, CH_2), 29.1 (t, CH_2), 31.0 (q, MeC=O), 36.7 (t, CH_2), 42.3 (t, CH_2), 60.4 (s, C-8), 80.5 (s, C-7), 172.1 (s, C=O), and 194.7 (s, SC=O) (Found: C, 60.0; H, 8.15; N, 5.95. $C_{12}H_{19}NO_2S$ requires C, 59.71; H, 7.93; N, 5.80%).

7-*Acetylthio*-8-*methoxy*-1-*azabicyclo*[5.2.0]*nonan*-9-*one* (**8f**). B.p. 120 °C/10^{-3} mmHg; $\nu_{max.}$($CHCl_3$) 1 680 (SC=O) and 1 755 cm^{-1} (C=O); δ_H 1.2—1.9 (br, 6 H, CH_2 × 3), 2.0—2.6 (br, 2 H, CH_2), 2.35 (s, 3 H, MeC=O), 2.8—3.8 (br, 4 H, CH_2 × 2), 3.53 (s, 3 H, OMe), and 4.34 (s, 1 H, 8-CH); δ_C 25.0 (t, CH_2), 28.0 (t, CH_2), 29.2 (t, CH_2), 31.4 (q, MeC=O), 38.6 (t, CH_2), 42.2 (t, CH_2), 60.1 (q, OMe), 79.5 (s, C-7), 89.9 (d, C-8), 165.2 (s, C=O), and 194.5 (s, SC=O). (Found: C, 54.1; H, 7.0; N, 5.75. $C_{11}H_{17}NO_3S$ requires C, 54.29; H, 7.04; N, 5.75%).

N-*Methoxyacetyl*-N-(*p-tolyl*)*benzanilide* (**17**).—Methoxyacetyl chloride (390 mg, 3.6 mmol) and triethylamine (360 mg, 3.6 mmol) were added to a benzene solution of *N*-(*p*-tolyl)benzanilide (630 mg, 3 mmol) and the reaction mixture was refluxed for 6 h. The benzene solution was washed with water, aqueous $NaHCO_3$, and saturated NaCl and dried (Na_2SO_4). The benzene was evaporated and the residual mixture was subjected to chromatography on silica gel (eluant: benzene–ethyl acetate). The title compound was isolated (560 mg) in 66% yield, b.p. 95 °C/10^{-3} mmHg; $\nu_{max.}$($CHCl_3$) 1 680 (C=O) cm^{-1}; δ_H 2.23 (s, 3 H, Me), 3.37 (s, 3 H, OMe), 4.40 (s, 2 H, CH_2), and 6.9—7.7 (m, 9 H, ArH) (Found: C, 72.15; H, 6.1; N, 5.0. $C_{17}H_{17}NO_3$ requires C, 72.06; H, 6.04; N, 4.94%).

Photochemical Reaction of (**17**).—Compound (**17**) (200 mg) in benzene (40 ml) was irradiated according to the method of photolysis of monothioimides. The photolysate was subjected to chromatography on silica gel. Anilides (**18**), (46 mg, 36%) and (**19**) (18 mg, 12%) were obtained and the structures confirmed by direct comparison with authentic samples.

References

1 (*a*) N. S. Isaacs, *Chem. Soc. Rev.*, 1976, **5**, 181 and references cited therein; (*b*) D. H. Davies and R. C. Storr, 'Comprehensive Heterocyclic Chemistry,' Pergamon Press, 1984, vol. 7, p. 237—362.

2 (*a*) K. R. Henry-Logan and C. G. Chen, *Tetrahedron Lett.*, 1973, 1103; (*b*) N. G. Johnson, B. Akermark, and B. Sjonberg, *Acta Chem. Scand., Ser. B.*, 1976, **30**, 383 and references cited therein; (*c*) U. Zehavi, *J. Org. Chem.*, 1977, **42**, 2821; (*d*) H. Aoyama, M. Okazaki, and Y. Omote, *J. Chem. Soc., Perkin Trans. 1*, 1979, 263 and references cited therein; (*e*) M. Shiozaki and T. Hirooka, *Synth. Commun.*, 1979, **9**, 179; (*f*) H. Wehlri, *Helv. Chim. Acta*, 1980, **63**, 1915; (*g*) H. Aoyama, M. Sakamoto, K. Kuwabara, K. Yoshida, and Y. Omote, *J. Am. Chem. Soc.*, 1983, **105**, 1958 and references cited therein; (*h*) M. Ikeda, T. Uchino, H. Ishibashi, Y. Tamura, and M. Kido, *J. Chem. Soc., Chem. Commun.*, 1984, 758; (*i*) M. Sakamoto, H. Aoyama, and Y. Omote, *Tetrahedron Lett.*, 1985, **26**, 4475; (*j*) M. Satamoto, H. Aoyama, and Y. Omote, *ibid.*, 1986, **27**, 1335.

3 (*a*) S. N. Ege, *J. Chem. Soc. C*, 1969, 2624 and references cited therein; (*b*) N. Bashir and T. L. Gilchist, *J. Chem. Soc., Perkin Trans. 1*, 1973, 868; (*c*) G. Stork and R. P. Szajewski, *J. Am. Chem. Soc.*, 1974, **96**, 5787; (*d*) P. Y. Johnson and C. E. Hatch, III, *J. Org. Chem.*, 1975, **40**, 3502 and references cited therein; (*e*) J. E. T. Corrie, J. R. Hlubucek, and G. Lowe, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1412 and references cited therein; (*f*) M. R. Johnson, M. J. Fazio, D. L. Ward, and L. R. Sousa, *J. Org. Chem.*, 1983, **48**, 494.

4 (*a*) R. C. Salems and W. R. Schleigh, *Tetrahedron Lett.*, 1972, 3563; (*b*) H. Furrer, *Chem. Ber.*, 1972, **105**, 2780; (*c*) W. L. Dilling, N. B. Tefertiller, and A. B. Mitchel, *Mol. Photochem.*, 1973, **5**, 371; (*d*) E. Ager, G. E. Chivers, and H. Suschitzky, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1125; (*e*) S. Hirokami, Y. Hirai, M. Nagata, T. Yamazaki, and T. Date, *J. Org. Chem.*, 1979, **44**, 2083; (*f*) N. Katagiri, M. Sata, N. Yoneda, S. Saikawa, T. Sakamoto, M. Muto, and C. Kaneko, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1289 and references cited therein.

5 (*a*) E. G. Corey and A. Felix, *J. Am. Chem. Soc.*, 1965, **87**, 2518; (*b*) R. H. Earle, D. T. Hurst, and M. Viney, *J. Chem. Soc. C*, 1969, 2093; (*c*) R. R. Rando, *J. Am. Chem. Soc.*, 1970, **92**, 1629 and references cited therein; (*d*) B. D. Golding and D. R. Hall, *J. Chem. Soc., Chem. Commun.*, 1973, 293; (*e*) D. M. Brunwin and G. Lowe, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1321 and references cited therein.

6 (*a*) O. L. Chapman and W. R. Adams, *J. Am. Chem. Soc.*, 1968, **90**, 2333; (*b*) T. Kubota and H. Sakurai, *J. Chem. Soc., Chem. Commun.*, 1972, 362; (*c*) G. Kretsmer and R. N. Warrener, *Tetrahedron Lett.*, 1975, 1335; (*d*) D. H. R. Barton, E. Buschmann, J. Hausler, C. W. Holzapfel, T. Sheradsky, and D. A. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1107; (*e*) S. St. C. Black and A. B. Boscacci, *Aust. J. Chem.*, 1977, **30**, 1109; (*f*) P. K. Sen, C. J. Veal, and D. W. Young, *J. Chem. Soc., Chem. Commun.*, 1977, 678; (*g*) K. Ogino, S. Yamashina, T. Matsumoto, and S. Kozuka, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1552; (*h*) A. Padwa, K. F. Koehler, and A. Rogriguez, *J. Am. Chem. Soc.*, 1981, **103**, 4974; (*i*) M. Sakamoto, Y. Omote, and H. Aoyama, *J. Org. Chem.*, 1984, **49**, 396.

7 (*a*) J. D. Coyle, *Tetrahedron*, 1985, **41**, 5393 and references cited therein ; (*b*) K. Oda, M. Machida, and Y. Kanaoka, *Synthesis*, 1986, 768 and references cited therein; (*c*) M. Machida, K. Oda, and Y. Kanaoka, *Tetrahedron Lett.*, 1986, **26**, 5137; (*d*) K. Oda, M. Machida, and Y. Kanaoka, *Chem. Pharm. Bull.*, 1986, **34**, 4406.

8 (*a*) H. Aoyama, M. Sakamoto, and Y. Omote, *Chem. Lett.*, 1983, 1397; (*b*) M. Sakamoto, H. Aoyama, and Y. Omote, *J. Org. Chem.*, 1984, **49**, 1837.

9 Part of this reaction has been reported in preliminary form, see reference 2*i*.

10 The configurations of the β-lactams (**3c**) and (**3c'**) were determined on the basis of n.m.r. spectra, see T. J. Batterham, 'NMR Spectra of Simple Heterocycles,' Wiley, Chichester, 1973.

11 (*a*) D. H. Mazzocchi, 'Organic Photochemistry,' Marcel Dekker, inc., New York, 1973, vol. 5, p. 421—471; (*b*) D. H. Mazzocchi, J. Tomas, and F. Danisi, *J. Org. Chem.*, 1979, **44**, and references cited therein.

12 (*a*) M. C. Caserio, W. Lauer, and T. Novinson, *J. Am. Chem. Soc.*, 1970, **92**, 6082; (*b*) A. Padwa, W. Eisenhardt, R. Gruber, and D. Pashayan, *J. Am. Chem. Soc.*, 1971, **93**, 6998.

Received 3*rd August* 1987; *Paper* 7/1416