Stereoselective Photo[4+2]cycloadditions of 2-Pyrone-5-carboxylates with Maleimides in the Solid State and in Solution

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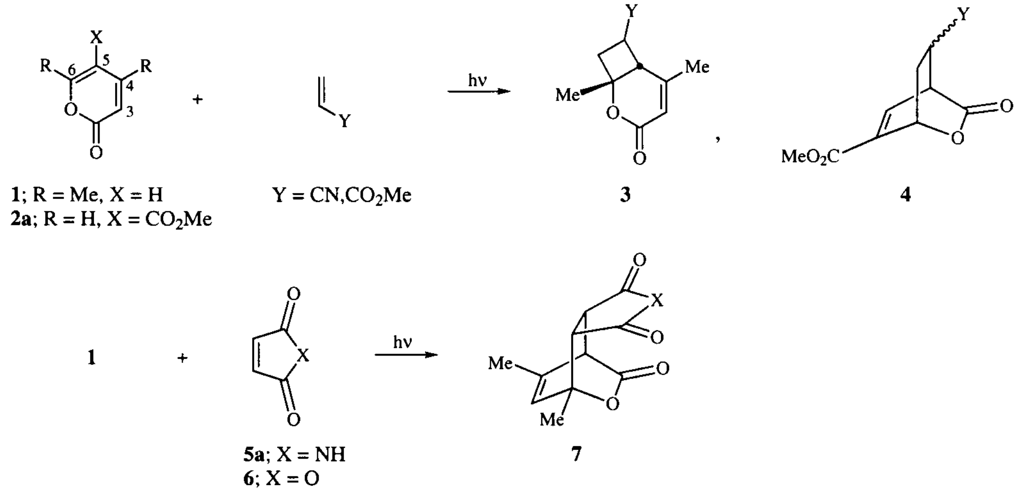
Received February 3, 1998

Solid state photoreactions and thermal reactions of 2-pyrone-5-carboxylates with maleimides gave endo-[4+2]cycloadducts, while the sensitized photoreactions gave exo-[4+2]cycloadducts stereo-selectively.

J. Heterocyclic Chem., **35**, 1361 (1998).

The photocycloaddition reactions of 2-pyrones with acyclic olefins were previously reported to give [2+2]- and/or [4+2]cycloadducts, peri-selectively, and the cycloaddition mechanism was also proposed [1]. Thus, sensitized photocycloadditions of 4,6-dimethyl-2-pyrone (**1**) with electron poor olefins afforded [2+2]cycloadducts **3** across the C_5-C_6 double bond in **1** while methyl 2-pyrone-5-carboxylate (**2a**) gave [4+2]cycloadducts **4** as major products, respectively (Scheme 1), and then the reaction mechanism was reasonably explained using molecular orbital method. On the other hand, **1** reacted with cyclic olefins **6** to give exo-[4+2]cycloadducts **7**, stereo-selectively [2]. The stereoselectivity of the photocycloaddition of 2-pyrones with cyclic olefins is also an interesting point.

Scheme 1

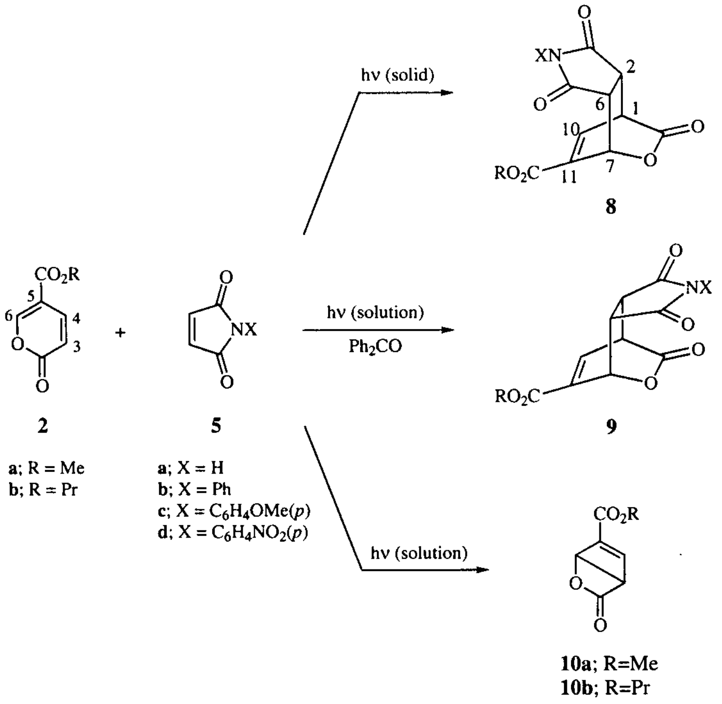


We describe herein the photoreactions of 2-pyrone-5-carboxylates **2** with maleimides **5** in the solid state and in solution to clarify the stereo-selectivity more in detail.

Equimolar mixed crystal of propyl 2-pyrone-5-carboxylate (**2b**) and maleimide (**5a**) was irradiated in the solid state with 400W high-pressure mercury lamp through a Pyrex filter at 40°. The irradiated sample was chromatographed on silica gel to afford endo-[4+2]cycloadduct **8c** in 52% yield. Similar solid state photoreactions of **2a** with **5a**, **2a** with **5b**, **2b** with **5b** and **2b** with **5c** gave **8a** [3] (48%), **8b** [3] (46%), **8d** (68%), and **8e** (47%), respectively. The solid state photoreaction of **2b** with *N*-(*p*-nitrophenyl)maleimide (**5d**) did not afford **8f** which was obtained by the thermal reaction. Although, compounds **8a**-**8e** were also obtained by the thermal reactions at 40°, photocycloadditions occurred in preference to the thermal ones. For example, the product ratio of **8d** in the photoreaction versus in the thermal one in the dark at 40° for 24 hours became to 2.6:1.0. In addition, low-temperature solid state photoreaction at -20° whose temperature did not afford thermal product, gave **8d** from the ^{1}H nmr spectroscopic analysis.

A solution of **2b** and *N*-phenylmaleimide (**5b**) in acetonitrile in the presence of benzophenone as a sensitizer was irradiated at room temperature. After removal of the solvent, the residue was chromatographed to give exo-[4+2]cycloadduct **9c** in 26% yield. Similar photosensitized reactions of **2a** with **5a** and **2a** with **5b** gave exo-[4+2]cycloadducts **9a** and **9b** in 21% and 33% yields, respectively. On the other hand, direct photoreactions of

Scheme 2



	R	X	Yield (%)
a;	Me	H	48
b;	Me	Ph	46
c;	Pr	H	52
d;	Pr	Ph	68
e;	Pr	$C_6H_4OMe(p)$	47
f;	Pr	$C_6H_4NO_2(p)$	11 (thermal)

	R	X	Yield (%)
a;	Me	H	21
b;	Me	Ph	33
c;	Pr	Ph	26

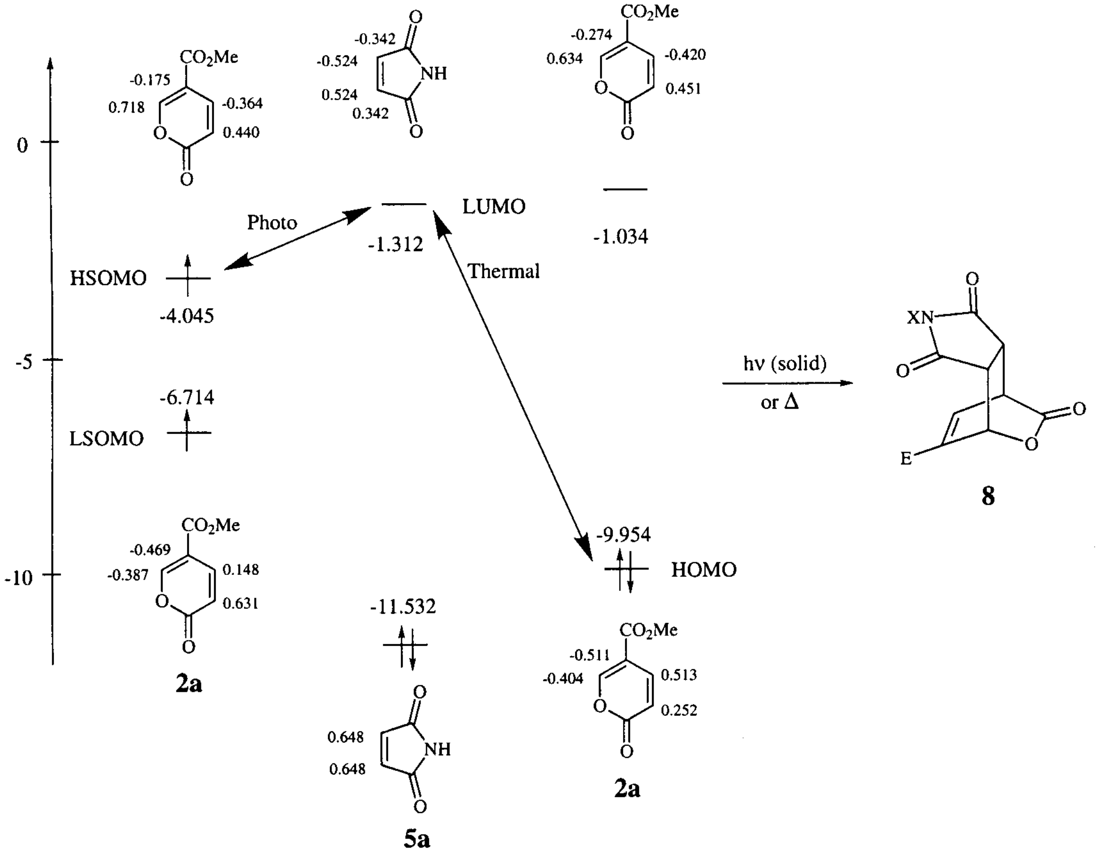
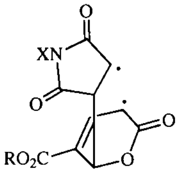


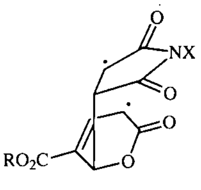
Figure 1. Estimated energies and coefficients for triplet and ground states of **2a** and ground state of **5a** using PM3-CI method.

2a with **5a** and **2b** with **5b** gave no cycloadducts but gave valence isomers **10a**,**10b**, respectively. The exo configurations of **9a-c** were assigned on the basis of the comparison of chemical shifts at 2-H and 6-H with those of **8a**,**b**,**d**, respectively, considering the shielding effect of the C_{10}-C_{11} double bonds.

On the basis of these results as shown in Scheme 2, photocycloaddition reactions of 2-pyrone-5-carboxylates with maleimides in the solid state and in solutions were confirmed to be peri- and stereo-selective. Figure 1 shows the estimated orbital energies and coefficients for triplet and ground states of **2a** and ground state of **5a** using PM3-CI method [4]. The reaction mechanism *via* biradical A or B was theoretically predicted from the HSOMO(2-pyrone)-LUMO(maleimide) interaction since 2-pyrones have been known to undergo triplet photocycloadditions [5]. It is inferred that intermediate **A** is favored in the tightly arranged solid state photoreactions to give **8** because of the endo-type packing between the ground state substrates. On the other hand, intermediate **B** is estimated to form in the unrestricted solution photoreactions because of the small steric hindrance between the alkoxy carbonyl group and imide ring in **A**.



A



B

Since the solid state photocycloadditions of **2a** with **5** proceeded in preference to the thermal cycloadditions, it is suggested that HSOMO(2-pyrone)-LUMO(maleimide) interaction is larger than HOMO(2-pyrone)-LUMO-(maleimide) interaction in this system.

EXPERIMENTAL

All the melting points were measured on a Yanagimoto Meltemp apparatus and are uncorrected. The ir and mass spectra were recorded on JASCO A-3 and JEOL JMSOISG spectrometers, respectively. ^{1}H nmr spectra were measured on JEOL JNM-GSX 400 spectrometer.

Methyl 3,5,9-Trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate(endo adduct) (**8a**), Methyl 4-Phenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate(endo adduct) (**8b**), Propyl 3,5,9-Trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate(endo adduct) (**8c**), Propyl 4-Phenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]-undec-10-ene-11-carboxylate(endo adduct) (**8d**), Propyl 4-*p*-Methoxyphenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]-undec-10-ene-11-carboxylate(endo adduct) (**8e**) and Propyl 4-*p*-Nitrophenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate(endo adduct) (**8f**).

A mixture of methyl 2-pyrone-5-carboxylate (**2a**) (62.5 mg, 0.41 mmole) and maleimide (**5a**) (40.0 mg, 0.41 mmole) was dissolved in acetone (5 ml) in a Pyrex tube then the solvent was removed by rotary evaporator *in vacuo* to give a mixed crystal to the Pyrex tube wall. After irradiation to the crystal under nitrogen for 24 hours at 40°, the reaction mixture was chromatographed using ethyl acetate-hexane 1:2 v/v mixture to give **8a** [3] (120 mg, 48%). Similar solid state photoreactions of **2a** with *N*-phenylmaleimide (**5b**), propyl 2-pyrone-5-carboxylate (**2b**) with **5a**, **2b** with **5b**, **2b** with *N*-(*p*-methoxyphenyl)maleimide (**5c**) gave **8b**, **8c**, **8d** and **8e** in 46%, 52%, 68% and 47% yields, respectively. But the solid state photoreaction of **2b** with *N*-(*p*-nitrophenyl)maleimide (**5d**) gave no product. Thermal reactions of **2a** with **5a** and **5b**, and **2b** with **5a-5d** at 40-50° for 24 hours in the dark gave **8a**, **8b**, **8c**, **8d**, **8e** and **8f** in 45%, 37%, 43%, 60%, 32% and 11% yields, respectively.

Compound **8c** had mp 196-198°; ir (potassium bromide): 1790, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 0.90, 1.62, 4.10 (CO_2Pr), 3.63 (dd, 1H, 2-H, $J_{1,2}$ = 3.4, $J_{2,6}$ = 7.7 Hz), 3.86 (dd, 1H, 6-H, $J_{2,6}$ = 7.7, $J_{6,7}$ = 4.9 Hz), 4.05 (dd, 1H, 1-H, $J_{1,2}$ = 3.4, $J_{1,10}$ = 6.3 Hz), 5.86 (dd, 1H, 7-H, $J_{6,7}$ = 4.9, $J_{7,10}$ = 2.1 Hz), 7.50 (dd, 1H, 10-H, $J_{1,10}$ = 6.3, $J_{7,10}$ = 2.1 Hz), 11.64 (s, 1H, NH); ms: m/z 279 (M^+).

Anal. Calcd. for $C_{13}H_{13}NO_6$: C, 55.91; H, 4.69; N, 5.02. Found: C, 56.23; H, 4.71%; N, 4.82.

Compound **8d** had mp 84-86°; ir (potassium bromide): 1780, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 0.87, 1.60, 4.12 (CO_2Pr), 3.89 (dd, 1H, 2-H, $J_{1,2}$ = 3.4, $J_{2,6}$ = 7.8 Hz), 4.08 (dd, 1H, 6-H, $J_{2,6}$ = 7.8, $J_{6,7}$ = 4.6 Hz), 4.19 (dd, 1H, 1-H, $J_{1,2}$ = 3.4, $J_{1,10}$ = 6.0 Hz), 5.98 (dd, 1H, 7-H, $J_{6,7}$ = 4.6, $J_{7,10}$ = 2.4 Hz), 7.0-7.5 (m, 5H, Ph), 7.58 (dd, 1H, 10-H, $J_{1,10}$ = 6.0, $J_{7,10}$ = 2.4 Hz); ms: m/z 355 (M^+).

Anal. Calcd. for $C_{19}H_{17}NO_6$: C, 64.22; H, 4.82; N, 3.94. Found: C, 64.10; H, 4.91; N, 3.79.

Compound **8e** had mp 182-184°; ir (potassium bromide): 1780, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 0.88, 1.61, 4.12 (CO_2Pr), 3.77 (s, 3H, Me), 3.85 (dd, 1H, 2-H, $J_{1,2}$ = 3.6, $J_{2,6}$ = 8.0 Hz), 4.05 (dd, 1H, 6-H, $J_{2,6}$ = 8.0, $J_{6,7}$ = 4.9 Hz), 4.17 (dd, 1H, 1-H, $J_{1,2}$ = 3.6, $J_{1,10}$ = 6.1 Hz), 5.97 (dd, 1H, 7-H, $J_{6,7}$ = 4.9, $J_{7,10}$ = 2.5 Hz), 6.9-7.3 (m, 4H, C_6H_4), 7.58 (dd, 1H, 10-H, $J_{1,10}$ = 6.1, $J_{7,10}$ = 2.5 Hz); ms: m/z 385 (M^+).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.63. Found: C, 62.51; H, 4.77; N, 3.92.

Compound **8f** had mp 130-132°; ir (potassium bromide): 1780, 1765, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 0.85, 1.59, 4.13 (CO_2Pr), 3.95 (dd, 1H, 2-H, $J_{1,2}$ = 3.6, $J_{2,6}$ = 8.2 Hz), 4.12 (dd, 1H, 6-H, $J_{2,6}$ = 8.2, $J_{6,7}$ = 4.8 Hz), 4.21 (dd, 1H, 1-H, $J_{1,2}$ = 3.6, $J_{1,10}$ = 6.6 Hz), 6.00 (dd, 1H, 7-H, $J_{6,7}$ = 4.8, $J_{7,10}$ = 2.4 Hz), 7.2-7.8 (m, 4H,C_6H_4), 7.59 (dd, 1H, 10-H, $J_{1,10}$ = 6.6, $J_{7,10}$ = 2.4 Hz); ms: m/z 400 (M^+).

Anal. Calcd. for $C_{19}H_{16}N_2O_8$: C, 57.00; H, 4.03; N, 7.00. Found: C, 57.00; H, 4.02; N, 7.50.

Methyl 3,5,9-Trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate (exo adduct) (**9a**), Methyl 4-Phenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate (exo adduct) (**9b**), and Propyl 4-Phenyl-3,5,9-trioxo-4-aza-8-oxatricyclo[5.2.2.0^{2,6}]undec-10-ene-11-carboxylate (exo adduct) (**9c**).

A solution of **2a** (63.2 mg, 0.41 mmole), **5a** (40.1 mg, 0.41 mmole) and benzophenone (34.7 mg, 0.19 mmole) in a acetonitrile (10 ml) was irradiated at room temperature for 3 hours. After evaporation of the solvent, the resulting residue was chromatographed using ethyl acetate-hexane 1:2 v/v mixture to afford **9a** (21.6 mg, 21%). Similar sensitized photoreactions of **2a** with **5b** and **2b** with **5b** afforded **9b** and **9c** in 33% and 26% yields, respectively.

Compound **9a** had mp 168-171°; ir (potassium bromide): 1780, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 3.47 (dd, 1H, 2-H, $J_{1,2} = 2.0$, $J_{2,6} = 8.0$ Hz), 3.56 (dd, 1H, 6-H, $J_{2,6} = 8.0$, $J_{6,7} = 4.8$ Hz), 3.69 (s, 3H, Me), 4.00 (dd, 1H, 1-H, $J_{1,2} = 2.0$, $J_{1,10} = 6.6$ Hz), 5.73 (dd, 1H, 7-H, $J_{6,7} = 4.8$, $J_{7,10} = 2.2$ Hz), 7.49 (dd, 1H, 10-H, $J_{1,10} = 6.6$, $J_{7,10} = 2.2$ Hz), 11.63 (s, 1H, NH); ms: m/z 251 (M$^+$).

Anal. Calcd. for $C_{11}H_9NO_6$: C, 52.60; H, 3.61; N, 5.58. Found: C, 52.38; H, 3.63; N, 5.86.

Compound **9b** had mp 184-186°; ir (potassium bromide): 1780, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 3.30 (dd, 1H, 2-H, $J_{1,2} = 3.0$, $J_{2,6} = 9.0$ Hz), 3.36 (dd, 1H, 6-H, $J_{2,6} = 9.0$, $J_{6,7} = 2.2$ Hz), 3.88 (s, 3H, Me), 4.26 (dd, 1H, 1-H, $J_{1,2} = 3.0$, $J_{1,10} = 6.6$ Hz), 6.18 (dd, 1H, 7-H, $J_{6,7} = 2.2$, $J_{7,10} = 2.0$ Hz), 7.2-7.5 (m, 5H, Ph), 7.53 (dd, 1H, 10-H, $J_{1,10} = 6.6$, $J_{7,10} = 2.0$ Hz); ms: m/z 327 (M$^+$).

Anal. Calcd. for $C_{17}H_{13}NO_6$: C, 62.39; H, 4.00; N, 4.28. Found: C, 62.09; H, 4.50; N, 3.82.

Compound **9c** had mp 144-147°; ir (potassium bromide): 1790, 1770, 1720 cm^{-1}; ^{1}H nmr (dimethyl-d$_6$ sulfoxide): δ 0.95, 1.69, 4.16 (CO$_2$Pr), 3.58 (dd, 1H, 1-H, $J_{1,2} = 3.2$, $J_{2,6} = 9.0$ Hz), 3.72 (dd, 1H, 6-H, $J_{2,6} = 9.0$, $J_{6,7} = 2.4$ Hz), 4.13 (dd, 1H, 1-H, $J_{1,2} = 3.2$, $J_{1,10} = 7.0$ Hz), 5.85 (dd, 1H, 7-H, $J_{6,7} = 2.4$, $J_{7,10} = 3.2$ Hz), 7.0-7.8 (m, 5H, Ph), 7.48 (dd, 1H, 10-H, $J_{1,10} = 7.0$, $J_{7,10} = 3.2$ Hz); ms: m/z 355 (M$^+$).

Anal. Calcd. for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.63. Found: C, 62.21; H, 5.13; N, 3.57.

Methyl 3-Oxo-2-oxabicyclo[2.2.0]hept-5-ene-6-carboxylate (**10a**) and Propyl 3-Oxo-2-oxabicyclo[2.2.0]hept-5-ene-6-carboxylate (**10b**).

A solution of **2a** (7.7 mg, 0.05 mmole) with **5b** (8.6 mg, 0.05 mmole) in deuteriochloroform (1.0 ml) without benzophenone was irraidiated for 24 hours gave only **10a** which was identified by ^{1}H nmr spectral data [6]. Similar direct photoreaction of **2b** with **5b** gave only **10b** which was detected by ^{1}H nmr.

Compound **10b** had ^{1}H nmr (deuteriochloroform): δ 0.97, 1.72, 4.18 (CO$_2$Pr), 4.48 (dd, 1H, 4-H, $J_{1,4} = 2.0$, $J_{4,5} = 0.8$ Hz), 5.52 (dd, 1H, 1-H, $J_{1,4} = 2.0$, $J_{1,5} = 4.4$ Hz), 7.31 (dd, 1H, 5-H, $J_{1,5} = 4.4$, $J_{4,5} = 0.8$ Hz).

REFERENCES AND NOTES

[1] T. Shimo, S. Yamasaki, K. Date, H. Uemura and K. Somekawa, *J. Heterocyclic Chem.*, **30**, 419 (1993), and references cited therein.

[2] T. Shimo, H. Yoshimura, H. Uemura, K. Somekawa and O. Tsuge, *Heterocycles*, **24**, 303 (1986).

[3] T. Shimo, H. Yoshimura, T. Suishu and K. Somekawa, *Nippon Kagaku Kaishi*, 1984 (1988); *Chem. Abstr.*, **111**, 23339s (1989).

[4] K. Somekawa, T. Shimo and T. Suishu, *Bull. Chem. Soc. Japan*, **65**, 354 (1992).

[5] K. Somekawa, T. Shimo, H. Yoshimura and T. Suishu, *Bull. Chem. Soc. Japan*, **63**, 3456 (1990).

[6] H. Javaheripour and D. C. Neckers, *J. Org. Chem.*, **42**, 1844 (1977).