PHOTOCYCLIZATION OF ENAMIDES. 38[1,2]
REDUCTIVE PHOTOCYCLIZATION OF α-(METHYLTHIO)-
AND α-(ARYLTHIO)ENAMIDES

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Abstract--Reductive photocyclization of α-(methylthio)enamide (**2**) gave exclusively

six-membered lactams (**3**) and (**4**) while the same reaction of α-(arylthio)enamides

(**6**) and (**12**) was found to afford five-membered lactams (**7**) and (**13**) as major

products. A novel total synthesis of (±)-polyzonimine (**18b**) was accomplished by

applying the newly found reductive photocyclization of α-(naphthylthio)enamide

leading to the formation of five-membered lactams.

In connection with our interest in the evaluation of enamide photocyclizations[3] as an inherently useful synthetic

tool and also in the potentiality of the resulting lactams formed from the enamide as unique synthons, we have

undertaken the study of reductive photocyclization of α-(methylthio)- and α-(arylthio)enamides in the presence of

a hydride agent and found that reductive photocyclization of α-(arylthio)enamides gave five-membered lactams as

main products. This newly found reductive photocyclization of α-(arylthio)enamides has broadened the aspect of

the cyclizability of enamides and further evaluated usefulness of enamide photocyclization as a simple and useful

method for the construction of not only six-membered lactams (**3**), (**4**), (**8**), and (**14**) but also five-membered

lactams (**7**), (**13**), and (**17**), of which **17b** was effectively used as an intermediate for the total synthesis of (±)-

polyzonimine (**18b**).

Reductive Photocyclization of α-(Methylthio)- and α-(Phenylthio)enamides (2) and (6)

Acylation of the methylthioimidate (1)[4] with methacryloyl chloride in the presence of triethylamine gave an

unstable enamide (2) in quantitative yield which was characterized by the [1]H-nmr spectrum [δ 5.20-5.03 (3H, m)

and 4.79 (1H, m)]. Enamide (2) was subjected to irradiation with a high pressure mercury lamp through a Pyrex

filter in the presence of sodium borohydride in acetonitrile-methanol (9:1). Two photocyclized six-membered

lactams (3) and (4) were obtained in 41 and 7% yields respectively with 15% recovery of the starting enamide

(2). The mass spectra (ms) of two lactams (3) and (4) exhibited a quasi molecular ion peak at m/z 174 and the ir

spectra exhibited a peak at 1630-1632 cm^{-1} due to six-membered lactam carbonyl group. The stereochemistry of

the lactam (3) as having *cis*-configuration was deduced by the [1]H-nmr spectrum [δ: 2.37 (ddq, J=11, 8, 7 Hz, 3-

H) and 4.38 (ddd, J=4, 3, 1 Hz, 6-H) and a long-range W-shaped coupling (J=1 Hz) between two equatorial

hydrogens at the 4- and 6-positions]. Analogously the product (4) was also characterized as a stereoisomer of 3.

Upon treatment with tributyltin hydride and azobisisobutyronitrile (AIBN),[5] both lactams (3) and (4) were

converted into the known lactam (8b).[6] Thus, it was found that α-(methylthio)enamide (2) was reductively

photocyclized in the presence of hydride to give the six-membered lactams (3) and (4).
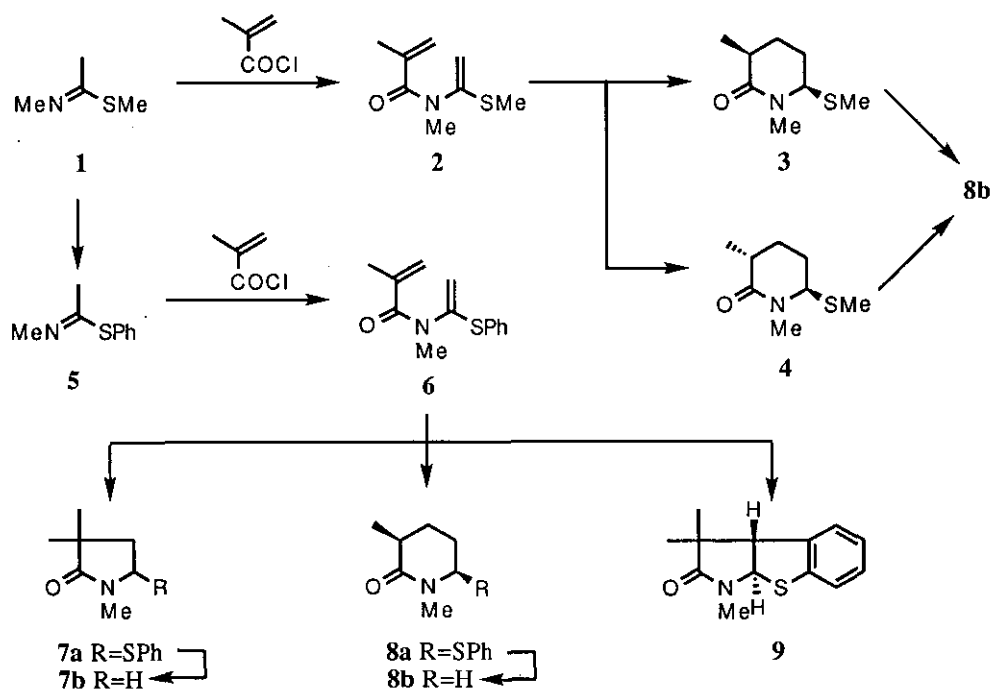
Scheme 1

Then, photocyclization of α -(phenylthio)enamide (6) was investigated.   Treatment of the methylthioimidate (1)

with thiophenol in the presence of p-toluenesulfonic acid gave the phenylthioimidate (5)[4b] in 55% yield which

was then acylated with methacryloyl chloride to give the unstable α-(phenylthio)enamide (6) in 81% yield.

Irradiation of 6 in the presence of hydride gave a mixture of three products (7a), (8a), and (9) in 20, 6, and 2 %

yields respectively, which were carefully separated by a medium-pressure column chromatography. The product

(8a) was a six-membered lactam and its structure was deduced upon spectral comparisons with those of the

lactams (3) and (4) obtained from α-(methylthio)enamide (2). The major product (7a) as being a five-membered

lactam was established from the following spectral data. The ms exhibited a molecular ion peak at m/z 235, two

mass units larger than that of the enamide (6). The ir absorption showed a peak at 1678 cm^{-1} due to a five-

membered lactam carbonyl group. The [1]H-nmr spectrum exhibited two singlet peaks at δ 0.98 and 1.14 due to

two methyl protons and signals at δ 2.02 (dd, J=14, 5 Hz, 4-H), 2.37 (dd, J=14, 8 Hz, 4-H), and 4.84 (dd,

J=8, 5 Hz, 5-H) as ABX system. The product (9) was found to have a tricyclic benzothienopyrrole derivative[7]

from the spectral data which also suggested its stereochemistry as shown. The [1]H-^{1}H NOESY spectra exhibited

two cross-peaks between the [1]H-nmr signals at δ 1.52 (s, 3-Me) and at 3.38 (br d, J=12 Hz, 3a-H) and also

signals at δ 1.18 (s, 3-Me) and at 4.87 (d, J=12 Hz, 8a-H). Furthermore, two lactams (7a) and (8a) were

readily desulfurized by treatment with tributyltin hydride and AIBN to give the known lactams (7b)[8] and (8b)[6]

respectively. In order to improve the yield for the formation of five-membered lactam (7a), we investigated the

solvent effect in the reductive photocyclization as shown in Table 1. Upon irradiation in methanol, the enamide

(6) was completely decomposed while in benzene-methanol (9:1), the cyclization reaction proceeded slowly to

give the lactams (7a) (15%) and (8a) (4%) with 54 % recovery of the starting enamide (6). Thus, we have

found a new photochemical cyclization of enamides leading to five-membered lactams in addition to the

established enamide photocyclization[3] which proceeds to form six-membered lactams exclusively.

Table 1. Reductive Photocyclization of the Enamide (6)

solvent	6	7a	8a	9
MeCN-MeOH (9:1)	--	20	6	2
C$_6$H$_6$-MeOH (9:1)	54	15	4	--
MeOH	decomposition			

*Reductive Photocyclization of α-(2-Naphthylthio)enamide (12)*

Difference in the direction of cyclization in the cases of α-(methylthio)- and α-(phenylthio)enamides (2) and (6) has pushed us to investigate the cyclization of α-(2-naphthylthio)enamide (12) which was readily prepared by converting 10[9] to the unstable naphthylthioimidate (11) followed by acylation with methacryloyl chloride. The *N*-benzyl derivative (10) was employed as a substrate for uv monitoring of the formation of lactams (13a) and (14a). Upon irradiation under the same reaction condition, α-(naphthylthio)enamide (12) disappeared on tlc in 1h and two products (13a) and (14a)[10] were isolated in 43% and 7% yields. Both products (13a) and (14a) were found to be five- and six-membered lactams, respectively, both of which have surprisingly no naphthylthio group. Both lactams (13a) and (14a) showed the identical molecular ion peak at *m/z* 203 in the ms and a singlet signal at δ 1.18 (6H) in 13a and a doublet signal (*J*=7 Hz) at δ 1.33 in 14a in the [1]H-nmr spectra. Thus, it was established that reductive photocyclization of α-(naphthylthio)enamide (12) proceeded smoothly but with elimination of α -naphthylthio group to give five-membered lactam as a major product as in the case of α-(phenylthio)enamide (6).

Bn = CH$_2$Ph

Naph =

Scheme 2
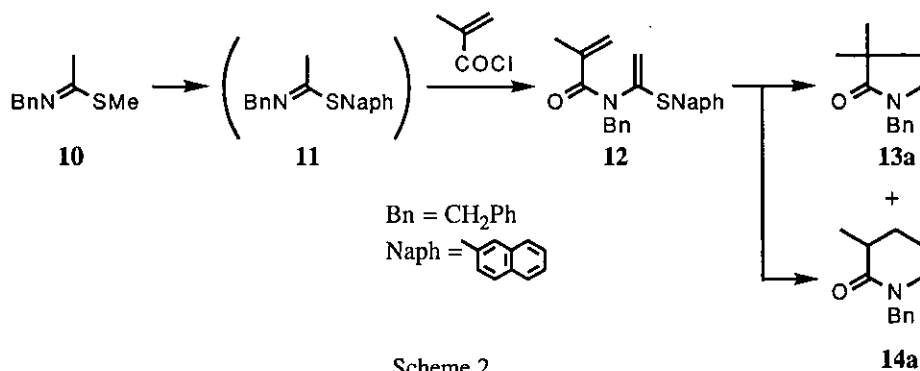
Reaction Pathway for Reductive Photocyclization of α–(Arylthio)enamides (6) and (12)

In order to disclose the reaction pathway of the photocyclization of α-(arylthio)enamides (6) and (12), we then investigated the reaction using deuteriated solvent and deuteriated reducing agent.

Irradiation of α-(phenylthio) enamide (6) in the absence of sodium borohydride gave the dehydrolactam (15), while treatment of 6 with sodium borohydride under non-photochemical condition yielded no cyclization product but only recovered the starting enamide (6). These two experiments showed that α-(phenylthio)enamide (6) undergoes smooth reductive photocyclization in the presence of hydride.

In order to shed light on the reaction pathway, we then carried out the reaction using sodium borodeuteride and deuteriated methanol. Deuterium incorporation in the products was detected by patterns and integral of signals in the [1]H-nmr spectra due to hydrogens around the deuteriated positions. Irradiation of α-(phenylthio)enamide (6) in the presence of sodium borodeuteride in acetonitrile-methanol gave two lactams (7c) and (8c) which were found to be incorporated by deuterium at the 5-position (62%) in (7c) and at the 6-position (90%) in (8c) respectively. On the other hand, irradiation of the enamide (6) in the presence of sodium borohydride in acetonitrile-CD3OD gave two lactams (7d) and (8d) which were incorporated by deuterium at the positions shown in Scheme 3.
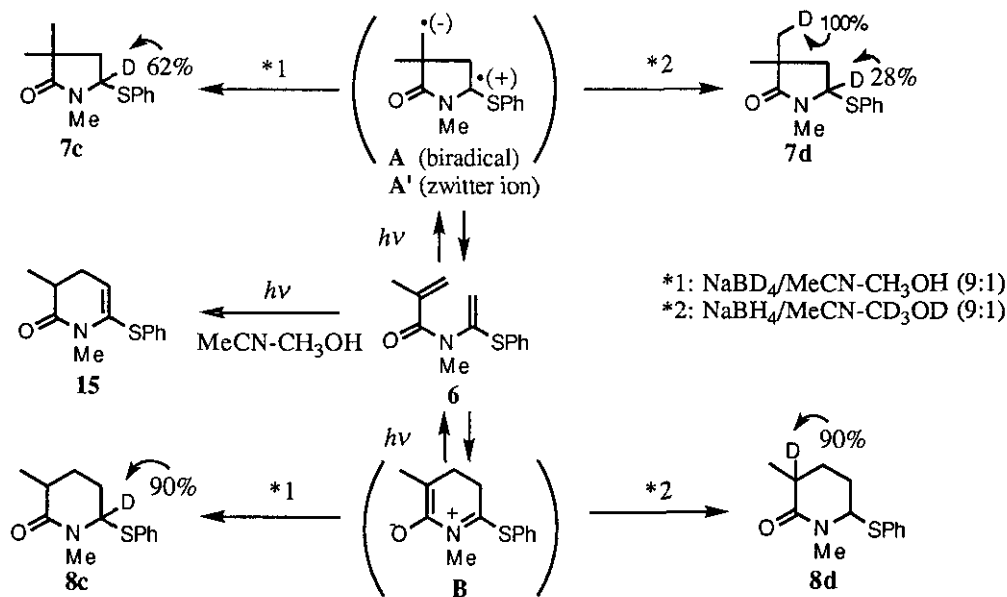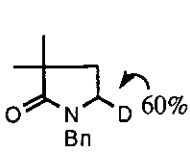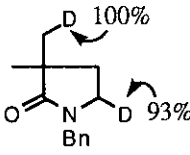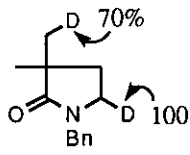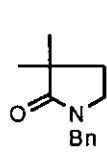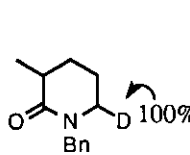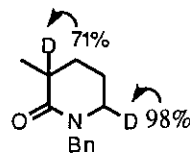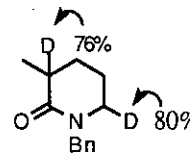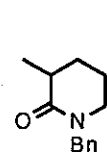

Scheme 3

In the cyclization of α-(phenylthio)enamide (6), five- and six-membered intermediates (A or A') and (B) are thought to be involved and the equilibrium between them would be shifted in favor of A or A'. The six-membered lactams (8cd) are formed *via* the established zwitter ion intermediate (B)[11] which constitutes from an enolate anion and iminium cation moieties, thus susceptible to be quenched by proton from the solvent methanol and hydride from the reducing agent present in the reaction mixture respectively, while the five-membered lactams (7cd) are formed *via* a route involving the intermediates of biradical (A) and zwitter ion (A') natures which would be suggested by the observed ratios of deuterium incorporation at the 5-position in the five-membered lactams (7cd).

Reductive photocyclization of α-(naphthylthio)enamide (**12**) was then investigated by employing various combination of deuteriated reagents and solvents (NaBD4, CD3OD, CH3OD, and CD3OH). The results obtained are summarized in Table 2. The structures of products and their ratios of deuterium incorporation were deduced by the comparison of the [1]H-nmr spectra with those of the corresponding non-deuteriated products. A similar reaction pathway for the reductive photocyclization of α-(naphthylthio)enamide (**12**) is suggested as shown in Scheme 4. The formation of the six-membered lactams (**14a-d**) would proceed *via* the route involving a zwitter ion intermediate (**D**) which is quenched also by proton from the solvent and hydride from the reducing agent to form **G** and **H**. Then, a naphthylsulfenium moiety is eliminated to form an α-acylamino carbanion which is then protonated by the solvent methanol to give the lactams (**14a-d**). On the other hand, in the formation of five-membered lactams (**13a-d**) from the (naphthylthio)enamide (**12**), the intermediacy of a biradical species is excluded because the deuteriated five-membered lactam was not obtained when CD3OH was used as solvent. Therefore, the five-membered lactams (**13a-d**) are formed *via* a route involving the ionic intermediates of **C**, **E**, and **F**, from which subsequent cleavage of a naphthylsulfenyl moiety would give the deuteriated lactams (**13a-d**) upon final protonation.

Table 2. Deuterium Incorporation in the Reductive Photocyclization of **12**

NaBD4-CH3OH	NaBH4-CD3OD	NaBH4-CH3OD	NaBH4-CD3OH
60% **13b**	D 100% / 93% **13c**	D 70% / 100% **13d**	**13a**
100% **14b**	D 71% / 98% **14c**	D 76% / 80% **14d**	**14a**

Scheme 4

Application of Reductive Photocyclization of α-(Naphthylthio)enamide to Construction of 2-Azaspiro[4.4]-

nonane Skeleton: Total Synthesis of (±)-Polyzonimine

Reductive photocyclization of α-(naphthylthio)enamide leading to the formation of five-membered lactam has

provided a new synthetic method for the pyrrolidinone with quaternary carbon by applying the reaction to the

synthesis of the spiro compound, 2-azaspiro[4.4]nonan-1-one. The spiro structure constitutes natural

polyzonimine (18b)[12a] which was isolated as a highly volatile substance from millipede *Polyzonium rosalbum* .

Our synthetic strategy is shown in Scheme 5.
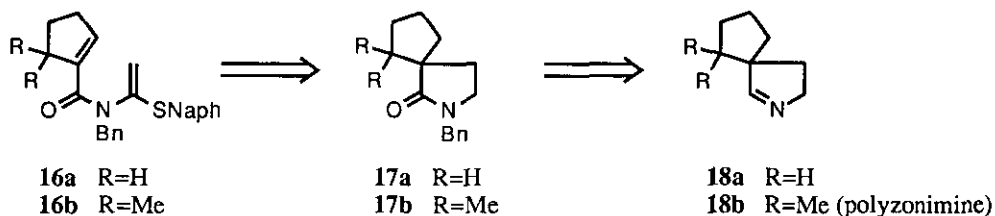
Scheme 5

As a preliminary experiment, the spiro compound (**18a**) was prepared *via* the spiro lactam (**17a**) from the starting

enamide (**16a**). Cyclopentenecarbonyl chloride (**20a**) was prepared in four steps[13] from the commercially

available keto ester (**19**) *via* reduction of the ketone, dehydration of the alcohol, hydrolysis of the ester, and

chlorination. The naphthylthioimidate (**11**) was acylated with the acid chloride (**20a**) to give the desired enamide

(**16a**) which was subjected to reductive photocyclization to afford two lactams (**17a**) and (**19a**) in 26 and 3%

yields respectively. Both lactams exhibited the identical molecular ion peak at *m/z* 229 in their ms. The lactams

(**17a**) and (**19a**) exhibited ir absorptions at 1670 (five-membered NCO) cm^{-1} and 1620 (six-membered NCO)

cm^{-1} respectively.

The spiro lactam (**17a**) was reduced by lithium aluminum hydride to give the amine (**21a**) in 92% yield which

was then hydrogenetically debenzylated in the presence of Pearlman's catalyst to afford the secondary amine

(**21b**). Oxidation of the amine (**21b**) with iodosobenzene[14] gave the very volatile imine (**18a**) which was

carefully isolated by chromatography in 44% yield. The structure of the imine (**18a**)[15] was deduced from the

spectral data [*m/z* 123 (M$^+$); 1660 (C=N) cm^{-1}; 7.37 (t, *J*= 2 Hz, 1-H) and 3.90 (td, *J*= 7, 2 Hz, 3-H$_2$)].

The synthetic route from the enamide (**16a**) to 2-azaspiro[4.4]non-1-ene (**18a**) was then successfully applied to

the total synthesis of (±)-polyzonimine (**18b**).[12] According to the procedure decribed in the literature,[16] 2,2-

dimethylcyclopentanone (**22**) was converted into the desired acid chloride (**20b**) in overall 47% yield from **22**.
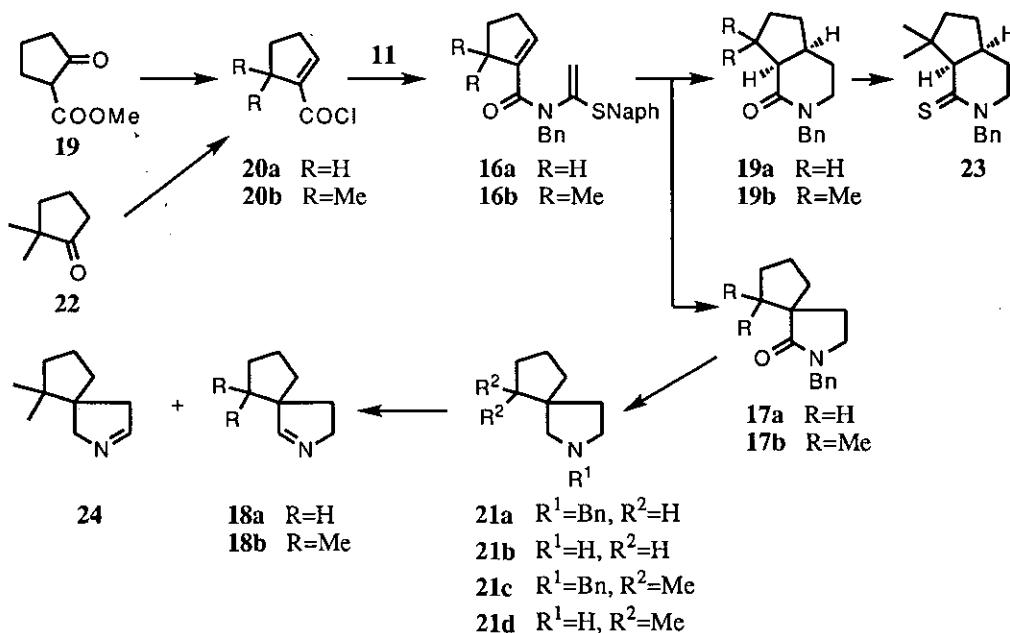
Scheme 6

Acylation of the imidate (11) with the acid chloride (20b) gave the enamide (16b) in 89% yield, which was subjected to reductive photocyclization to afford the lactams (17b) and (19b) in 25 and 24 % yields respectively. The stereochemistry of the lactam (19b) was indirectly deduced by the [1]H-^{1}H NOESY spectra between signals due to the hydrogens at the 4a- and 7a-positions in the corresponding thiolactam (23) which was readily prepared by treatment of 19b with Lawesson's reagent since the [1]H-nmr signals due to hydrogens at the same positions of the lactams (19b) are overlapped even in 500 MHz spectra. Reduction of the lactam (17b) to the amine (21c) and hydrogenolytic debenzylation to 21d (92%), and oxidation of the hydrochloride of the amine (21d) with iodosobenzene in the presence of potassium carbonate gave a 2:1 mixture of two imines (18b) and (24) in 55% yield, which were carefully separated by preparative tlc. The imine (18b) was identical with polyzonimine upon comparisons of the spectral data with those[12] of the reported natural product.

EXPERIMENTAL SECTION

[1]H-Nmr spectra were measured with JEOL PMX-60 (60 MHz), Varian XL-200 (200 MHz), and VXR-500 (500 MHz) instruments for solutions in deuteriochloroform (tetramethylsilane as internal reference), and ir spectra were measured with a Hitachi 215 spectrophotometer for solutions in chloroform. Ms were taken with Hitachi M-80 and M-4100 instruments. Mps were determined with Kofler-type hot-stage apparatus. Photochemical reactions were carried out by irradiation with a high-pressure (100 or 300 W) mercury lamp through a Pyrex filter (Eikosha, Osaka, Japan, PIH-100 or PIH-300); during irradiation the solutions were kept at 5-10 °C whilst being stirred and bubbled with nitrogen. All other reactions were carried out in a nitrogen stream. The extracts from the reaction mixtures were dried over anhydrous sodium sulfate and evaporated under reduced pressure. Thin layer chromatography (tlc) was performed on precoated silica gel 60F-254 (0.25 mm thick, Merck) and preparative tlc (p-tlc) on precoated silica gel 60F-254 (0.5 mm thick, Merck), with uv detection at 254 and 300 nm. Medium-pressure column chromatography (mcc) was undertaken on a 530-4-10V apparatus (Yamazen) with Lobar grosse B (310-25, Lichroprep Si60, Merck) as column adsorbent. For flash column chromatography (fcc), Merck Kieselgel 60 (230-400 mesh) was used. Short column chromatography (scc) was undertaken on a short glass filter using Merck Kieselgel 60 (230-400 mesh). Ether refers to diethyl ether.

N,2-Dimethyl-*N*-[1-(methylthio)ethenyl]-2-propenamide (2). A solution of methacryloyl chloride (1.36 g,
0.013 mol) in benzene (50 ml) was added to a solution of the methylthioimidate (1)[4] (1.08 g, 0.01 mol) and
triethylamine (1.52 g, 0.015 mol) in benzene (50 ml) with stirring at room temperature. After being refluxed
for 3.5 h, the reaction mixture was filtered to remove triethylamine hydrochloride. The filtrate was evaporated
to give the crude product which was purified by fcc (AcOEt-*n*-hexane=1:2) to give the unstable enamide (2)
(1.71 g, 99%) as a pale yellow oil. This enamide (2) was used for the following photocyclization without
further purification. Ir: 1678 (NCO) cm^{-1}. ^{1}H-Nmr (60 MHz) δ: 5.17 (1H, m, olefinic H), 5.20-5.03 (2H, m,
olefinic H), 4.79 (1H, m, olefinic H), 3.10 (3H, s, NMe), 2.23 (3H, s, SMe), 2.00 (3H, br s, CMe).

Reductive Photocyclization of the Enamide (2). Sodium borohydride (3.04 g, 0.08 mol) and methanol (125
ml) were added successively to a stirred solution of the enamide (2) (1.87 g, 0.011 mol) in acetonitrile (1125
ml) at room temperature. When the added sodium borohydride had dissolved, the resulting solution was
cooled at 0-5 °C and irradiated for 10.5 h. The reaction mixture was then evaporated. Water was added to the
residue and the mixture was extracted with methylene dichloride. The extract was washed, dried, and
evaporated to give a residue which was purified by fcc (AcOEt-*n*-hexane=1:2) to give *cis*-1,3-dimethyl-6-
(methylthio)-2-piperidinone (3) (0.77 g, 41%) and *trans*-1,3-dimethyl-6-(methylthio)-2-piperidinone (4) (0.13
g, 7%), and the starting enamide (2)(0.28 g, 15%). The lactam (3): a colorless oil. Ir: 1630 (NCO) cm^{-1}. ^{1}H-
Nmr (500 MHz) δ: 4.38 (1H, ddd, *J*=4, 3 ,1 Hz, 6-H), 3.03 (3H, s, NMe), 2.37 (1H, ddq, *J*=11, 8, 7 Hz, 3-H),
2.20-2.06 (2H, m, 5-H$_2$), 2.11 (3H, s, SMe), 1.96 (1H, tdd, *J*=13, 11, 4 Hz, 4-Hax), 1.87 (1H, m, 4-Heq), 1.24
(3H, d, *J*=7 Hz, 3-Me). High resolution ms (CI, isobutane) *m/z*: Calcd for C$_8$H$_{15}$NOS+H (QM$^+$) 174.0951 .
Found: 174.0932. The lactam (4): a colorless oil. Ir: 1632 (NCO) cm^{-1}. ^{1}H-Nmr (500 MHz) δ: 4.38 (1H, t,
J=5.5 Hz, 6-H), 3.02 (3H, s, NMe), 2.45 (1H, br sextet, *J*=7 Hz, 3-H), 2.28 (1H, dddd, *J*=11, 9, 5.5, 3 Hz, 5-H),
2.17 (1H. dddd, *J*=14, 9, 7, 3 Hz, 4-H), 2.06 (3H, s, SMe), 1.99 (1H, dddd, *J*=14, 9, 5.5, 3 Hz, 5-H), 1.51 (1H,
m, 4-H), 1.24 (3H, d, *J*=7 Hz, 3-Me). High resolution ms (CI, isobutane) *m/z*: Calcd for C$_8$H$_{15}$NOS+H
(QM$^+$) 174.0951. Found: 174.0952.

Phenyl *N*-Methylethanimidothioate (5). A solution of the methylthioimidate (1) (4.12 g, 0.04 mol) in
tetrahydrofuran (THF) (120 ml) was refluxed for 5 min with bubbling nitrogen to remove the dissolved
oxygen, and then thiophenol (9.9 g, 0.09 mol) and *p*-toluenesulfonic acid (10 mg) were added to the cooled

solution. After being heated under reflux for 3 h, the reaction mixture was cooled to room temperature, poured to a 5% NaOH solution, and extracted with methylene dichloride. The extract was washed, dried, and evaporated to give a residue which was distilled to afford the thioimidate (5) (3.64g, 55%) as a pale yellow oil. This thioimidate (5) was used for the following reaction without further purification. bp 98-99 °C / 8 mmHg (lit.,[4b] bp 65.5 °C / 0.1 mmHg). ^{1}H-Nmr (60 MHz) δ: 7.68-7.08 (5H, m, aromatic H), 3.25 (3H, s, NMe), 1.91 (3H, br s, CMe).

N,2-Dimethyl-N-[1-(phenylthio)ethenyl]-2-propenamide (6). According to the procedure described for **2**, acylation of the phenylthioimidate (5) (1.65g, 0.01 mol) with methacryloyl chloride (1.57g, 0.015 mol) gave the unstable enamide (6) (1.89 g, 81 %) as a pale yellow oil which was used for the photocyclization without purification. Ir: 1652 (NCO) cm^{-1}. ^{1}H-Nmr (60 MHz) δ: 7.69-7.01 (5H, m, aromatic H), 5.20-5.07 (3H, m, olefinic H), 4.97 (1H, m, olefinic H), 3.15 (3H, s, NMe), 1.97 (3H, br s, CMe). High resolution ms (CI, isobutane) m/z: Calcd for $C_{13}H_{15}NOS+H$ (QM$^+$) 234.0950 . Found: 234.0933.

Reductive Photocyclization of the Enamide (6). [1] Irradiation in acetonitrile-methanol=9:1. According to the procedure described for **2**, a solution of the enamide (6), which was prepared from phenylthioimidate (5) (0.4 g, 2.4 mmol) and methacryloyl chloride (0.38 g, 3.6 mmol), in acetonitrile-methanol (9:1, 300 ml) in the presence of sodium borohydride (0.73 g, 19.2 mmol) was irradiated for 3.5 h. The crude product was repeatedly purified with mcc (AcOEt-n-hexane=1:3 and then methylene dichloride-acetonitrile=3:1) to give 1,3,3-trimethyl-5-(phenylthio)-2-pyrrolidinone (7a) (110 mg, 20%), cis-1,3-dimethyl-6-(phenylthio)-2-piperidinone (8a) (33.8 mg, 6%), and trans-2,3,3a,8a-tetrahydro-1,3,3-trimethyl-1H-[1]benzothieno[2,3-b]pyrrol-2-one (9) (10 mg, 2%). The lactam (7a): a pale yellow oil. Ir: 1678 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.52-7.24 (5H, m, aromatic H), 4.84 (1H, dd, J=8, 5 Hz, 5-H), 2.93 (3H, s, NMe), 2.37 (1H, dd, J=14, 8 Hz, 4-H), 2.02 (1H, dd, J=14, 5 Hz, 4-H), 1.14 and 0.98 (each 3H, s, 3-Me×2). High resolution ms m/z: Calcd for $C_{13}H_{17}NOS$ (M$^+$) 235.1030. Found: 235.1001. The lactam (8a): a pale yellow oil. Ir: 1632 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.58-7.34 (5H, m, aromatic H), 4.75 (1H, t-like, J=3.5 Hz, 6-H), 3.09 (3H, s, NMe), 2.37 (1H, ddq, J=10, 8, 7 Hz, 3-H), 2.20-1.80 (4H, m, 5- and 4-H$_2$), 1.22 (3H, d, J=7 Hz, 3-Me). High resolution ms m/z: Calcd for $C_{13}H_{17}NOS$ (M$^+$) 235.1030. Found: 235.1004 . The lactam (9): a pale yellow oil. Ir: 1702 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.43 (1H), 7.34-7.18 (3H)(each m, aromatic H), 4.87 (1H, d,

J=12 Hz, 8a-H), 3.38 (1H, br d, J=12 Hz, 3a-H), 2.98 (3H, s, NMe), 1.52 and 1.18 (each 3H, s, 3-Me×2).
The cross peaks were observed in ^{1}H-^{1}H NOESY spectrum between signals due to 8a-H (δ 4.87) and 3-Me (δ 1.18) and due to 3a-H (δ 3.38) and 3-Me (δ 1.52). High resolution ms m/z: Calcd for $C_{13}H_{15}NOS$ (M$^+$) 233.0873. Found: 233.0876.

[2] Irradiation in benzene-methanol=9:1. According to the procedure described for 2, the enamide (6), which was prepared from phenylthioimidate (5) (0.4 g, 2.4 mmol) and methacryloyl chloride (0.38 g, 3.6 mmol), in benzene-methanol (9:1, 300 ml) in the presence of sodium borohydride (0.73 g, 19.2 mmol) was irradiated for 7 h and purification of the crude product by mcc (same solvents in [1]) gave two lactams (7a) (84 mg, 15%) and (8a) (27 mg, 4%) and the starting enamide (6) (306 mg, 54%), of which 7a and 8a were identical with the samples obtained in [1] based on comparisons of their Rf values, ir and nmr spectra respectively.

[3] Irradiation in methanol. According to the procedure described for 2, irradiation of the methanolic solution of the enamide (6) (0.2 g, 0.86 mmol) in the presence of sodium borohydride (260 mg, 6.8 mmol) for 3.5 h gave a unidentifiable complex mixture.

1,3,3-Trimethyl-2-pyrrolidinone (7b). Tributyltin hydride (350 mg, 1.2 mmol) and AIBN (10 mg) were added to a solution of the lactam (7a) (149 mg, 0.6 mmol) in benzene (20 ml). After being refluxed for 2 h, the solution was subjected to scc (benzene) to remove the stannyl compounds. The fraction eluted with AcOEt was further purified with mcc (AcOEt-n-hexane=1:1) to afford the volatile lactam (7b) (91.7 mg, quant.) as a colorless oil. The lactam (7b) was identical with the authentic sample upon comparisons for their spectral data.[8] Ir: 1674 (NCO) cm^{-1}. ^{1}H-Nmr (60 MHz) δ: 3.25 (2H, t, J=7 Hz, 5-H$_2$), 2.82 (3H, s, NMe), 1.85 (2H, t, J=7 Hz, 4-H$_2$), 1.13 (6H, s, 3-Me×2). High resolution ms m/z: Calcd for $C_7H_{13}NO$ (M$^+$) 127.0996 . Found: 127.0996.

1,3-Dimethyl-2-piperidinone (8b). [1] From 8a. According to the procedure described in the preparation of 7b, the lactam (8a) (48.9 mg, 0.2 mmol) was treated with tributyltin hydride (121 mg, 0.4 mmol) in the presence of AIBN (10 mg) in benzene (15 ml), and the following purification of the crude product with scc (AcOEt-n-hexane=1:1) gave the lactam (8b) (14.2 mg, 54%) as a colorless oil. The lactam (8b) was identical with the authentic sample upon comparisons for their spectral data.[6] Ir: 1620 (NCO) cm^{-1}. ^{1}H-Nmr (200

MHz) δ: 3.28-3.25 (2H, m, 6-H$_2$), 2.94 (3H, s, NMe), 2.42 (1H, br sextet, J=7 Hz, 3-H), 2.10-1.68 (4H, m, 5- and 4-H$_2$), 1.24 (3H, d, J=7 Hz, 3-Me). High Resolution ms m/z : Calcd for C$_7$H$_{13}$NO (M$^+$) 127.0996. Found: 127.0998.

[2] From **3** and **4** . According to the procedure as described above, the lactam (**3**)(60 mg, 0.35 mmol) gave **8b** (22.5 mg, 51%), while the lactam (**4**)(100 mg, 0.58 mmol) gave **8b** (50 mg, 68%), which was identical with the sample obtained in [1] based on comparisons of their R$_f$ values, ir and nmr data.

2-Naphthyl N-(Phenylmethyl)ethanimidothioate (11). A mixture of the N-benzylmethylthioimidate (**10**) (2.99 g, 16.7 mmol) and 2-naphthalenethiol (3.47 g, 21.7 mmol) was stirred at 120 °C for 7 h. The mixture was cooled to room temperature and the resulting solid was triturated with ether and recrystallized from n-hexane to give the thioimidate (**11**) (1.25 g, 26 %) which included small amount of 2-naphthalenethiol and the corresponding disulfide. The imidate (**11**) was used for the next reaction without further purification. ^{1}H-Nmr (60 MHz) δ 8.10-7.07 (12H, m, aromatic H), 4.66 (2H, br s, NCH_2Ph), 2.00 (3H, br s, CMe).

2-Methyl-N-[1-(2-naphthylthio)ethenyl]-N-(phenylmethyl)-2-propenamide (12). A solution of methacryloyl chloride (1.6 g, 15.4 mmol) in benzene (30 ml) was added to a solution of the thioimidate (**11**) (1.7 g, 5.5 mmol) and triethylamine (2.12g, 21 mmol) in benzene (30 ml) with stirring at room temperature. The solution was stirred under reflux for 1 h. Then, methacryloyl chloride (1.29 g, 12.3 mmol) and triethylamine (1.7g, 16.8 mmol) were added to the reaction mixture by monitoring the reaction by tlc. After being refluxed for further 1.5 h, the reaction mixture was filtered to remove triethylamine hydrochloride. The filtrate was evaporated to give the crude product which was purified by fcc (AcOEt-n-hexane=1:4) to give the unstable enamide (**12**) (1.57 g, 78%) as a pale yellow oil. Ir: 1656 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 8.01-7.24 (12H, m, aromatic H), 5.42-4.80 (4H, m, olefinic H), 4.95 (2H, s, NCH_2Ph), 2.03(3H,br s, CMe). High resolution ms m/z: Calcd for C$_{23}$H$_{21}$NOS (M$^+$) 359.1342. Found: 359.1343.

Reductive Photocyclization of the Enamide (12). According to the procedure described for **2**, a solution of the enamide (**12**) (500 mg, 1.39 mmol) in acetonitrile-methanol (9:1, 162 ml) was irradiated for 1 h in the presence of sodium borohydride (423 mg, 11.1 mmol). The crude product was purified with mcc (AcOEt-n-

hexane=1:4) to give 3,3-dimethyl-1-(phenylmethyl)-2-pyrrolidinone (**13a**) (120 mg, 43%) and 3-methyl-1-(phenylmethyl)-2-piperidinone (**14a**) (19.8 mg, 7%). The lactam (**14a**) is identical with the authentic sample[10] upon comparisons of the spectral data. The lactam (**13a**): a colorless oil. Ir: 1674 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.40-7.20 (5H, m, aromatic H), 4.47 (2H, s, NCH_2Ph), 3.14 (2H, t, J=7 Hz, 5-H_2), 1.84 (2H, t, J=7 Hz, 4-H_2), 1.18 (6H, s, 3-Me×2). High resolution ms m/z : Calcd for $C_{13}H_{17}NO$ (M$^+$) 203.1309. Found: 203.1301. The lactam (**14a**): a colorless oil. Ir: 1622 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.46-7.25 (5H, m, aromatic H), 4.70 and 4.56 (2H, ABq, J=14 Hz, NCH_2Ph), 3.24 (2H, br t, J=7 Hz, 6-H_2), 2.52 (1H, br sextet, J=7 Hz, 3-H), 2.08-1.44 (4H, m, 4- and 5-H_2), 1.33 (3H, d, J=7 Hz, 3-Me). High resolution ms m/z: Calcd for $C_{13}H_{17}NO$ (M$^+$) 203.1309. Found: 203.1314.

Photocyclization of the Enamide (6). According to the procedure described for the irradiation of **6**, a solution of the enamide (**6**), prepared from the phenylthioimidate (0.4 g, 2.4 mmol) and methacryloyl chloride (0.3 g, 2.9 mmol), in acetonitrile-methanol (9:1, 300 ml) was irradiated in the absence of sodium borohydride for 6 h. Evaporation of the solvent gave the viscous oil which was purified by mcc (AcOEt-n-hexane=1:5) to give 3,4-dihydro-3-methyl-6-(phenylthio)-2(1H)-pyridinone (**15**) (60 mg, 11%) and the starting enamide (**6**) (240 mg, 43%). The lactam (**15**): ^{1}H-Nmr (60 MHz) δ: 7.15 (5H, br s, aromatic H), 5.83 (1H, t, J=7 Hz, 5-H), 3.07 (3H, s, NMe), 2.43-2.17 (3H, m, 3-H and 4-H_2), 1.23 (3H, d, J=7 Hz, 3-Me).

Attempted Thermal Cyclization of the Enamide (6). A solution of the enamide (**6**) (90 mg, 0.39 mmol) and sodium borohydride (117 mg, 3.08 mmol) in acetonitrile-methanol (9:1, 50 ml) was stirred at room temperature for 4.5 h. Work-up described for reductive photocyclization of the enamide (**6**) gave exclusively the starting enamide (**6**) (85 mg, quant.).

Reductive Photocyclization of the α-(Phenylthio)enamide (6) Using the Deuteriated Solvents and/or Reagents (General Procedure). According to the procedure given for reductive photocyclization of **6**, a solution of the enamide (**6**) in the solvents shown in Table 3 was irradiated in the presence of the reducing agents shown in Table 3. Work-up described for reductive photocyclization of the enamide (**6**) afforded five- and six-membered lactams (**7cd**) and (**8cd**) in the chemical yields and deuteriated ratios shown in Table 3 and Scheme 3.

Table 3. The [1]H-Nmr Data and Yields of the Lactams (7cd) and (8cd) (200 MHz)

[five-membered lactams (7cd)]

Conditions	NaBD$_4$ / MeCN-MeOH(9:1)	NaBH$_4$ / MeCN-CD$_3$OD(9:1)
Protons	7c (17%)	7d (12%)
aromatic H	7.50-7.30 (5H, m)	7.54-7.32 (5H, m)
5-H	4.84 (0.38H, dd, J=8, 5 Hz)	4.83 (0.72H, dd, J=8, 5 Hz)
NMe	2.93 (3H, s)	2.93 (3H, s)
4-H$_2$	2.36 (1H, m)[*1]	2.36 (1H, dd, J=14, 8 Hz)
	2.00 (1H, m)[*2]	2.00 (1H, dd, J=14, 5 Hz)
3-Me	1.13 (3H, s)	1.14 (2.5H, s)
3-Me	0.97 (3H, s)	0.98 (2.5H, s)

[*1] Two peaks [(dd, J=14, 8 Hz) and (d, J=14 Hz)] were overlapped.

[*2] Two peaks [(dd, J=14, 5 Hz) and (d, J=14 Hz)] were overlapped.

[six-membered lactams (8cd)]

Conditions	NaBD$_4$ / MeCN-MeOH(9:1)	NaBH$_4$ / MeCN-CD$_3$OD(9:1)
Protons	8c (3%)	8d (5%)
aromatic H	7.56-7.28 (5H, m)	7.58-7.30 (5H, m)
6-Heq	4.73 (0.1H, t-like, J=3.5 Hz)	4.76 (1H, t-like, J=3.5 Hz)
NMe	3.08 (3H, s)	3.12 (3H, s)
3-Hax	2.36 (1H, ddq, J=10, 8, 7 Hz)	2.38 (0.1H, m)
4- and 5-H$_2$	2.16-1.80 (4H, m)[*3]	2.18-1.76 (4H, m)
3-Me	1.20 (3H, d, J=7 Hz)	1.20 (3H, s)

[*3] Signal pattern was slightly different from that of 8a.

Reductive Photocyclization of the α-(Naphthylthio)enamide (12) Using the Deuteriated Solvent and/or

Reagents (General Procedure). According to the procedure described above, a solution of the enamide (12) in

the solvents shown in Table 4. was irradiated in the presence of the reducing agents shown in Table 4. Work-

up described for reductive photocyclization of the enamide (12) gave the five- and six-membered lactams

(13a-d) and (14a-d) in the chemical yields and deuterated ratios shown in Tables 2 and 4. Photocyclization

of 12 in MeCN-CD3OH (9:1) in the presence of NaBH4 gave non-deuteriated products (13a) (16%) and (14a)

(5%).

Table 4. The [1]H-Nmr Data and Yields of the Lactams (13bcd) and (14bcd) (200 MHz)

[five-membered lactams (13bcd)]

Conditions	NaBD4 / MeCN-MeOH(9:1)	NaBH4 / MeCN-CD3OD(9:1)	NaBH4 / MeCN-CH3OD(9:1)
Protons	13b (15%)	13c (16%)	13d (12%)
aromatic H	7.40-7.20 (5H, m)	7.44-7.22 (5H, m)	7.38-7.24 (5H, m)
NCH2Ph	4.48 (2H, s)	4.50 (2H, s)	4.48 (2H, s)
5-H2	3.16 (1.4H, t, J=7 Hz)	3.15 (1.07H, t, J=7 Hz)	3.16 (1.0H, t, J=7 Hz)
4-H2	1.86 (1.4H, t, J=7 Hz)	1.86 (1.07H, t, J=7 Hz)	1.86 (1.0H, t, J=7 Hz)
	1.84 (0.6H, d, J=7 Hz)	1.84 (0.93H, d, J=7 Hz)	1.84 (1.0H, d, J=7 Hz)
3-Me×2	1.20 (6H, s)	1.20 (5.0H, s)	1.20 (5.3H, s)

[six-membered lactams (14bcd)]

Conditions	NaBD4 / MeCN-MeOH(9:1)	NaBH4 / MeCN-CD3OD(9:1)	NaBH4 / MeCN-CH3OD(9:1)
Protons	14b (9%)	14c (8%)	14d (8%)
aromatic H	7.44-7.22 (5H, m)	7.46-7.10 (5H, m)	7.42-7.22 (5H, m)
NCH2Ph	4.70 and 4.54	4.68 and 4.54	4.68 and 4.54
	(2H, ABq, J=14 Hz)	(2H, ABq, J=14 Hz)	(2H, ABq, J=14 Hz)
6-H2	3.23 (1H, br s)	3.22 (1.02H, br t, J=7 Hz)	3.21 (1.2H, br t, J=7 Hz)
3-H	2.50 (1H, br sextet, J=7 Hz)	2.50 (0.29H, m, J=7 Hz)	2.49 (0.24H, m)
4- and 5-H2	2.09-1.48 (4H, m)	2.10-1.50 (4H, m)	2.04-1.44 (4H, m)
3-Me	1.30 (3H, d, J=7 Hz)	1.30 (3H, br s)	1.30 (3H, s and d, J=7 Hz)

1-Cyclopentene-1-carbonyl Chloride (20a).   Reduction of the keto ester (19) (7.0 g, 0.05 mol) with sodium borohydride (1.25 g, 0.033 mol), dehydration of the resulting hydroxy ester by treatment with *p*-toluene-sulfonyl chloride (11 g, 0.058 mol) in pyridine (18 ml) , and hydrolysis of the unsaturated ester with 10% KOH solution (25 ml) gave the carboxylic acid as colorless crystals (2.8 g, 53%), mp 115-117 °C (lit.,[13] mp 119 °C). [1]H-Nmr (60 MHz) δ: 9.21 (1H, br s, COOH), 6.86 (1H, br s, 2-H), 2.54 (4H, br t, J=7 Hz, 3- and 5-H$_2$), 2.01 (2H, br quintet, J=7 Hz, 4-H$_2$).   Treatment of the acid (3 g, 8 mmol) with thionyl chloride (18 ml) gave the acid chloride (20a) (1.9 g, 54%) as a colorless oil (bp 73-75 °C / 20 mmHg) which was directly used for the following reaction.

N-[1-(2-Naphthylthio)ethenyl]-N-(phenylmethyl)-1-cyclopentene-1-carboxamide (16a).   A solution of the acid chloride (20a) (0.217 g, 1.66 mmol) in benzene (7 ml) was added to a solution of the thioimidate (11) (0.373 g, 1.28 mmol) and triethylamine (0.182 g, 1.8 mmol) in benzene (5 ml) with stirring at room temperature. After being refluxed for 15.5 h, the reaction mixture was cooled and then filtered. The filtrate was evaporated to give the crude product which was purified by mcc (methylene chloride) to give the enamide (16a) (0.256 g, 52%) as a pale yellow oil. [1]H-Nmr (200 MHz) δ: 8.02 (1H, br s, aromatic H), 7.82-7.78 (3H, m, aromatic H), 7.64-7.28 (8H, m, aromatic H), 6.35 (1H, t, J=2 Hz, 2-H), 4.98 and 4.86 (each 1H, d, J=1 Hz, olefinic H), 4.96 (2H, s, NCH_2Ph), 2.68 (2H, m, 5-H$_2$), 2.48 (2H, m, 3-H$_2$), 1.94 (2H, quintet, J=7 Hz, 4-H$_2$).

Reductive Photocyclization of the Enamide (16a).   According to the procedure described for 2, a solution of the enamide (16a) (297 mg, 0.77 mmol) in acetonitrile-methanol (9:1, 81 ml) in the presence of sodium borohydride (234 mg, 6.16 mmol) was irradiated for 1 h. The crude product was purified by mcc (AcOEt-*n*-hexane=1:3) to give 2-(phenylmethyl)-2-azaspiro[4.4]nonan-1-one (17a) (46.2 mg, 26%) and octahydro-2-(phenylmethyl)-1H-2-pyrindin-1-one (19a) (4.5 mg, 3%). The lactam (17a): a pale yellow oil. Ir: 1670 (NCO) cm^{-1}. [1]H-Nmr (200 MHz) δ: 7.58-7.20 (5H, m, aromatic H), 4.50 (2H, s, NCH_2Ph), 3.17 (2H, t, J=7 Hz, 3-H$_2$), 1.89 (2H, t, J=7 Hz, 4-H$_2$), 2.10-1.46 (8H, m, 6-, 7-, 8- and 9-H$_2$). High resolution ms m/z: Calcd for C$_{15}$H$_{19}$NO (M$^+$) 229.1466. Found: 229.1485. The lactam (19a): a pale yellow oil. Ir: 1620 (NCO) cm^{-1}. [1]H-Nmr (200 MHz) δ: 7.62-7.04 (5H, m, aromatic H), 4.74 and 4.54 (2H, ABq, J=14 Hz, NCH_2Ph), 3.20 (2H, t-like, J=7 Hz, 3-H$_2$), 2.80 (1H, q, J=8 Hz, 7a-H), 2.48-1.39 (9H, m, 4a-H and 4-, 5-, 6- and 7-H$_2$). High resolution ms m/z: Calcd for C$_{15}$H$_{19}$NO (M$^+$) 229.1466. Found: 229.1464.

2-(Phenylmethyl)-2-azaspiro[4.4]nonane (21a). A suspension of lithium aluminum hydride (135 mg, 3.58 mmol) in anhydrous ether (10 ml) was added dropwise to a solution of the lactam (**17a**) (164 mg, 0.716 mmol) in anhydrous ether (20 ml) with stirring at room temperature. After being stirred at room temperature for 0.5 h, usual work-up gave the crude amine (**21a**) (142 mg, 92%) as a colorless oil, which was used for the following reaction without further purification. ^{1}H-Nmr (200 MHz) δ: 7.50-7.26 (5H, m, aromatic H), 3.74 (2H, s, NCH_2Ph), 2.78 (2H, t, J=7 Hz, 3-H$_2$), 2.56 (2H, s, 1-H$_2$), 1.78 (2H, t, J=7 Hz, 4-H$_2$), 1.56 (8H, br s, 6-, 7-, 8- and 9-H$_2$). High resolution ms m/z: Calcd for $C_{15}H_{21}N$ (M$^+$) 215.1673. Found: 215.1680.

2-Azaspiro[4.4]non-1-ene (18a). A solution of the amine (**21a**) (142 mg, 0.66 mmol) in methanol (25 ml) was catalytically hydrogenated over 20% palladium hydroxide on carbon (50 mg) under 1.8 atm at room temperature for 16 h. After filtration off of the catalyst, the filtrate was evaporated to give the amine (**21b**) (53 mg, 65%) as a colorless oil. To a stirred suspension of this amine (**21b**) in methylene dichloride (10 ml), iodosobenzene (93 mg, 0.424 mmol) was added under ice-cooling and the mixture was stirred at 7-8 °C for 1 h and then at room temperature for 1 h. The reaction mixture was filtered and the filtrate was evaporated to give the residue which was purified by scc (Aluminium oxid PF$_{254}$ (Type T), Merck, methylene dichloride) to afford the imine (**18a**) (22.9 mg, 44%), as a colorless oil. Ir: 1660 (C=N) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.37 (1H, t, J=2 Hz, 1-H), 3.90 (2H, td, J=7, 2 Hz, 3-H$_2$), 1.95-1.44 (10H, m, 4-, 6-, 7-, 8- and 9-H$_2$). High resolution ms m/z: Calcd $C_8H_{13}N$ (M$^+$) 123.1046. Found: 123.1037.

5,5-Dimethyl-1-cyclopentene-1-carbonyl Chloride (20b). A solution of 2,2-dimethylcyclopentanone (**22**) (10g, 0.089 mol), trimethylsilyl cyanide (11.49 g, 0.116 mol), and zinc iodide (0.712 g) in benzene (36 ml) was stirred at room temperature for 7.5 h. The resulting solution was distilled to give the cyanohydrin trimethylsilyl ether (17.9 g, 95%) as a colorless oil (bp 103 °C / 25 mmHg). ^{1}H-Nmr (60 MHz) δ: 2.40-1.38 (6H, m, 3-,4- and 5-H$_2$), 1.10 and 1.02 (each 3H, s, 2-Me×2), 0.23 (9H, s, SiMe×3). A mixture of the trimethylsilyl ether (17.9 g, 0.11 mol), phosphorus oxychloride (39 g, 0.267 mol), and pyridine (136 ml) was stirred at 110 °C for 30 h. The reaction mixture was poured into 10% HCl solution and extracted with ether. The organic layer was washed with brine, dried, and evaporated to give the residue which was distilled to afford 5,5-dimethyl-1-cyclopentene-1-carbonitrile (8.15g, 76%) as a colorless oil (bp 76 °C / 25 mmHg). Ir: 2216 (CN) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 6.54 (1H, t, J=2 Hz, 2-H), 2.54 (2H, td, J=7, 2 Hz, 3-H$_2$), 1.84 (2H,

t, $J=7$ Hz, 4-H$_2$), 1.20 (6H, s, 5-Me×2). High resolution ms m/z: Calcd for C$_8$H$_{11}$N (M$^+$) 121.0890. Found: 121.0883. A mixture of the unsaturated nitrile (2.0 g, 16.5 mmol), KOH (1.9 g, 33 mmol), and diethylene glycol (120 ml) was stirred at 120 °C for 72 h. The reaction mixture was washed with ether. The aqueous layer was acidified with concentrated HCl and extracted with ether. The organic layer was washed with brine, dried, and evaporated to give the residue which was purified by scc (methylene dichloride) to afford 5,5-dimethyl-1-cyclopentene-1-carboxylic acid (1.85 g, 80%) as pale yellow solids. Ir: 3400-2500, 1680 (COOH) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 10.0 (1H, br s, COOH), 6.91 (1H, t, $J=1.5$ Hz, 2-H), 2.45 (2H, td, $J=7$, 1.5 Hz, 3-H$_2$), 1.84 (2H, br t, $J=7$ Hz, 4-H$_2$), 1.24 (6H, s, 5-Me×2). High resolution ms m/z: Calcd for C$_8$H$_{12}$O$_2$ (M$^+$) 140.0837. Found: 140.0837. A solution of the acid (2.5 g, 0.018 mol) in thionyl chloride (12 ml, 0.17 mol) was heated under reflux for 1 h. The mixture was distilled to give the acid chloride (20b) (2.38 g, 81%) as a colorless oil (bp 94 °C / 43 mmHg), which was used for the following reaction.

5,5-Dimethyl-N-[1-(2-naphthylthio)ethenyl]-N-(phenylmethyl)-1-cyclopentene-1-carboxamide (16b).
A solution of the acid chloride (20b) (0.273 g, 3.65 mmol) in benzene (10 ml) was added to a solution of the thioimidate (11) (0.6 g, 1.95 mmol) and triethylamine (0.37 g, 3.65 mmol) in benzene (40 ml) with stirring at room temperature. After the solution was heated under reflux for 5 h, the acid chloride (20b) (0.273 g, 3.65 mmol) and triethylamine (0.37 g, 3.65 mmol) were added to the reaction mixture by monitoring the reaction by tlc. After being refluxed for further 5 h, the reaction mixture was cooled and then filtered. The filtrate was evaporated to give the crude product which was purified by mcc (AcOEt-n-hexane=1:9) to give the enamide (16b) (0.72 g, 89%) as a pale yellow oil. Ir: 1670 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.18 (5H, br s, aromatic H), 4.40 (2H, s, NCH_2Ph), 3.07 (2H, t, $J=7$ Hz, 3-H$_2$), 2.43-1.23 (8H, m, 4-, 7-, 8- and 9-H$_2$), 1.02 and 0.88 (each 3H, s, 6-Me×2). High resolution ms m/z: Calcd for C$_{17}$H$_{23}$NO (M$^+$) 257.1778. Found: 257.1774.

Reductive Photocyclization of the Enamide (16b).   According to the procedure described for 2, a solution of the enamide (16b) (884.5 mg, 2.1 mmol) in acetonitrile-methanol (9:1, 260 ml) in the presence of sodium borohydride (635 mg, 16.8 mmol) was irradiated for 1 h. The crude product was purified by mcc (AcOEt-n-hexane=1:3) to give 6,6-dimethyl-2-(phenylmethyl)-2-azaspiro[4.4]nonane (17b) (135.8 mg, 25%) and 7,7-

dimethyl-2-(phenylmethyl)-1*H*-pyrindin-1-one (**19b**) (130.7 mg, 24%). The lactam (**17b**): a colorless oil. Ir 1670 (NCO) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.18 (5H, br s, aromatic H), 4.40 (2H, s, NC*H*2Ph), 3.07 (2H, t, *J*=7 Hz, 3-H2), 2.43-1.23 (8H, m, 4-, 7-, 8- and 9-H2), 1.02 and 0.88 (each 3H, s, 6-Me×2). High resolution ms *m/z*: Calcd for C17H23NO (M$^+$) 257.1778. Found: 257.1774. The lactam (**19b**): a colorless oil. Ir: 1622 (NCO) cm^{-1}. ^{1}H-Nmr (500 MHz) δ: 7.31-7.26 (5H, m, aromatic H), 4.76 and 4.47 (2H, ABq, *J*=15 Hz, NC*H*2Ph), 3.22-3.12 (2H, m, 3-H2), 2.49 (1H, d, *J*=11 Hz, 7a-H), 2.45 (1H, m, 4a-H), 1.86 (1H, m, 5-H), 1.75 (1H, m, 4-H), 1.58-1.46 (4H, m, 4-H, 5-H and 6-H2), 1.34 and 1.00 (each 3H, s, 7-Me×2). High resolution ms *m/z*: Calcd for C17H23NO (M$^+$) 257.1778. Found: 257.1782.

7,7-Dimethyl-2-(phenylmethyl)-1*H*-2-pyrindinethione (23). A solution of the lactam (**19b**) (50 mg, 0.195 mmol) and Lawesson's reagent (150 mg, 0.37 mmol) in toluene (2 ml) was stirred at 105 °C for 25 h. Evaporation of the solvent gave the residue which was purified by mcc (AcOEt-*n*-hexane=15:85) to give the thiolactam (**23**) (34 mg, 63%) as a pale yellow oil. ^{1}H-Nmr (500 MHz) δ: 7.38-7.27 (5H, m, aromatic H), 5.42 and 5.33 (2H, ABq, *J*=15 Hz, NC*H*2Ph), 3.36 (1H, d, *J*=10 Hz, 7a-H), 3.32-3.28 (2H, m, 3-H2), 2.47 (1H, m, 4a-H), 1.77-1.68 (2H, m, 4-H2), 1.64-1.47(4H, m, 5- and 6-H2), 1.46 and 0.91 (each 3H, s, 7-Me×2). High resolution ms *m/z*: Calcd for C17H23NS (M$^+$) 273.1550. Found: 273.1558. The *cis*-ring juncture of the thiolactam (**23**) was established by the observation of cross peaks in ^{1}H-^{1}H NOESY spectrum between signals at δ 3.36 (7a-H) and at δ 2.47 (4a-H).

6,6-Dimethyl-2-(phenylmethyl)-2-azaspiro[4.4]nonane (21c). According to the procedure described for **17a**, reduction of the lactam (**17b**) (167 mg, 0.65 mmol) with lithium aluminum hydride (0.25 g, 6.5 mmol) and purification of the crude product with mcc (AcOEt-*n*-hexane=1:1) gave the amine (**21c**) (147 mg, 93%). The amine (**21c**) was used for the following reaction without further purification. Ms *m/z*: 243 (M$^+$). ^{1}H-Nmr (200 MHz) δ: 7.50-7.26 (5H, m, aromatic H), 3.82 (2H, s, NC*H*2Ph), 2.84 (1H, dt, *J*=9, 7 Hz, 3-H), 2.54 and 2.37 (2H, ABq, *J*=10 Hz, 1-H2), 2.57 (1H, m, 3-H), 1.96-1.32 (8H, m, 4-, 7-, 8-, and 9-H2), 0.88 and 0.85 (each 3H, s, 6-Me×2).

Conversion of the Amine (21c) into (±)-Polyzonimine (18b). A solution of the amine (**21c**) (206 mg, 0.85 mmol) in methanol (53 ml) was catalytically hydrogenated over 20% palladium hydroxide on carbon (84 mg)

under 1.8 atm at room temperature for 95 h. After filtration of the catalyst, concentrated HCl (0.02 ml) was added to the filtrate, and the solution was evaporated to give the hydrochloride of **21d** (148 mg, 92%). To a stirred suspension of the hydrochloride of **21d** (19 mg, 0.1 mmol) and potassium carbonate (21 mg, 0.15 mmol) in methylene dichloride (2 ml), iodosobenzene (22 mg, 0.1 mmol)[7] was added under ice-cooling and the solution was stirred at room temperature for 30 min. After being filtered, the filtrate was extracted with 10% HCl solution, and the aqueous layer was made alkaline by the addition of powdered potassium carbonate and extracted with methylene dichloride. The extract was directly subjected to p-tlc (AcOEt) to give the highly volatile polyzonimine (6,6-dimethyl-2-azaspiro[4.4]non-1-ene) (**18b**) and 6,6-dimethyl-2-azaspiro[4.4]non-2-ene (**24**). The yield (10 mg, 55%) was calculated from the amount of a mixture of the corresponding hydrochlorides due to the highly volatile nature of the free bases. The ratio (2:1) of two products (**18b**) and (**24**) was estimated from ^{1}H-nmr spectrum of the mixture. The imine (**18b**) was identical with polyzonimine upon comparisons of the spectral data with those of the reported natural product.[12] The imine (**18b**): a colorless oil. Ir: 1625 (C=N) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.42 (1H, t, J=2.5 Hz, 1-H), 3.80 (2H, m, 3-H$_2$), 1.98-1.44 (8H, m, 4-H$_2$ and 7~9-H$_2$), 0.90 and 0.88 (each 3H, s, 6-Me×2). High resolution ms m/z: Calcd for C$_{10}$H$_{17}$N (M$^+$) 151.1359. Found: 151.1359. The imine (**24**): a colorless oil; Ir 1619 (C=N) cm^{-1}. ^{1}H-Nmr (200 MHz) δ: 7.57 (1H, br s, 3-H), 3.74 and 3.56 (each 1H, br d, J=18 Hz, 1-H$_2$), 2.56 and 2.23 (each 1H, br d, J=18 Hz, 4-H$_2$), 1.78-0.96 (6H, m, 7~9-H$_2$), 0.88 (6H, s, 6-Me×2). High resolution ms m/z: Calcd for C$_{10}$H$_{17}$N (M$^+$) 151.1359. Found: 151.1359.

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