Pergamon

Tetrahedron 54 (1998) 14437–14454

TETRAHEDRON

Novel Heterocyclic Ring-Expansion and/or Dehydration-Hydration Reactions of Propargylic and Allenylic Hydroxy γ-Lactams in the Presence of Strong Base or Lewis Acid

Ill-Yun Jeong, Woo Song Lee, Satoru Goto, Shigeki Sano, Motoo Shiro†, and Yoshimitsu Nagao*

Faculty of Pharmaceutical Sciences, The University of Tokushima, Sho-machi, Tokushima 770-8505, Japan

†Rigaku Corporation, 3-9-2 Matsubara-cho, Akishima-shi, Tokyo 196-8666, Japan

Received 27 July 1998; accepted 24 September 1998

Abstract: Dehydration-hydration products were obtained in good yields by the treatment of propargylic hydroxy γ-lactams with some Lewis acids. Several propargylic and allenylic hydroxy γ-lactams were successfully converted to the corresponding ring-expanded benzazepines in various yields *via* a tandem decyclization-cyclization process in the presence of $(TMS)_2NLi$, $(TMS)_2NNa$, or *n*-BuLi under reflux conditions in THF.

Keywords: alkynes; allenes; benzazepines; Grignard reactions; X-Ray crystal structures

Introduction

Ring expansion reactions have become useful methods for the construction of medium- and large-sized ring systems which appear in a variety of biologically active natural products.[1] With an inimitable means of overcoming the entropy factor[1a, 2] related to the ring formations, these reactions have clearly displayed their worth by producing two-carbon ring expansions which involve the [2+2] cycloaddition of the enamines of cyclic ketones with electron-deficient alkynes followed by thermal rearrangment[3] and [2+2] cyclization-decyclization by photoreaction.[4] In the construction of a seven-membered ring for the benzazepine derivatives which exhibit pharmacological activities,[5] photochemical two-carbon expansion reactions must be remarkable.[6] Thus, a Lewis acid (LA) -promoted two-carbon atom ring expansion of propargylic hydroxy γ-lactams **1** to seven-membered lactams **3** *via* an endo-mode cyclization of the resulting allenyl ketone intermediate **2** was desinged and performed as a part of an application of this lab's allenyl ketone chemistry using Lewis acids (Figure 1).[7] In an earlier communication paper, we reported the Lewis acid-promoted two-carbon ring expansion reactions (**1**→**3**).[8] However, on the basis of an X-ray analysis of one of the reaction products (*vide infla*), we have recently realized that the ring expansion reactions were unsuccessfull. We now wish to revise our report of the earlier results of the

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00897-7

Lewis acid-catalyzed reactions and describe novel two-carbon atom ring expansion reactions based on tandem decyclization-cyclization under basic conditions.

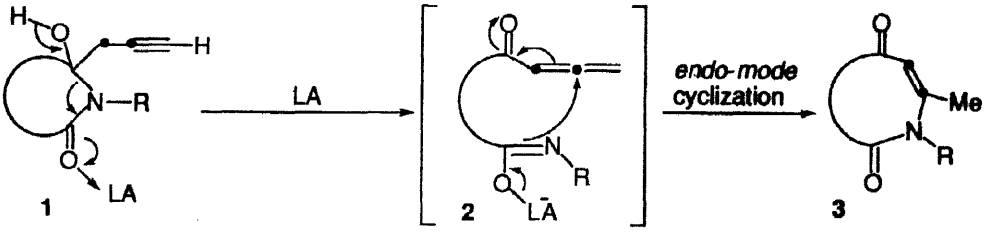
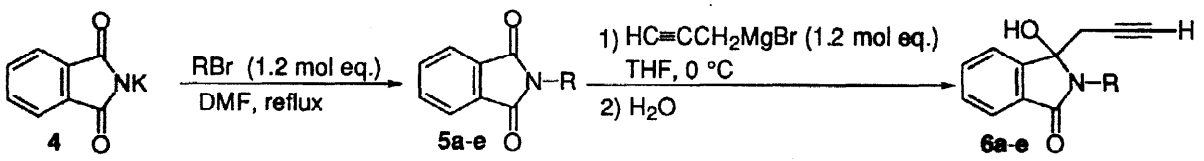


Figure 1. Two-carbon atom ring expansion mode in the presence of a Lewis acid.

Results and Discussion

Our synthesis commenced with commercially available phthalimide **5a** and *N*-alkylated phthalimides **5b-e**, readily available from the Gabriel reaction[9] of potassium phthalimide **4** with alkyl bromides (Scheme 1). Treatment of these compounds **5a-e** with propargylmagnesium bromide followed by quenching with water afforded in good yields the corresponding propargylic alcohols **6a-e** (Scheme 1), which possess the requisite two-carbon ring expansion moiety. The structures of compounds **6a-e** were deduced from their various spectroscopic analyses. Especially, the IR absorption spectra of **6a-e** showed characteristic CO-stretching peaks due to the amide moiety at 1713-1669 cm^{-1} and OH-stretching peaks at 3138-2922 cm^{-1}.



5a: commercial reagent,
5b: 88%, **5c**: 96%,
5d: 80%, **5e**: 72%

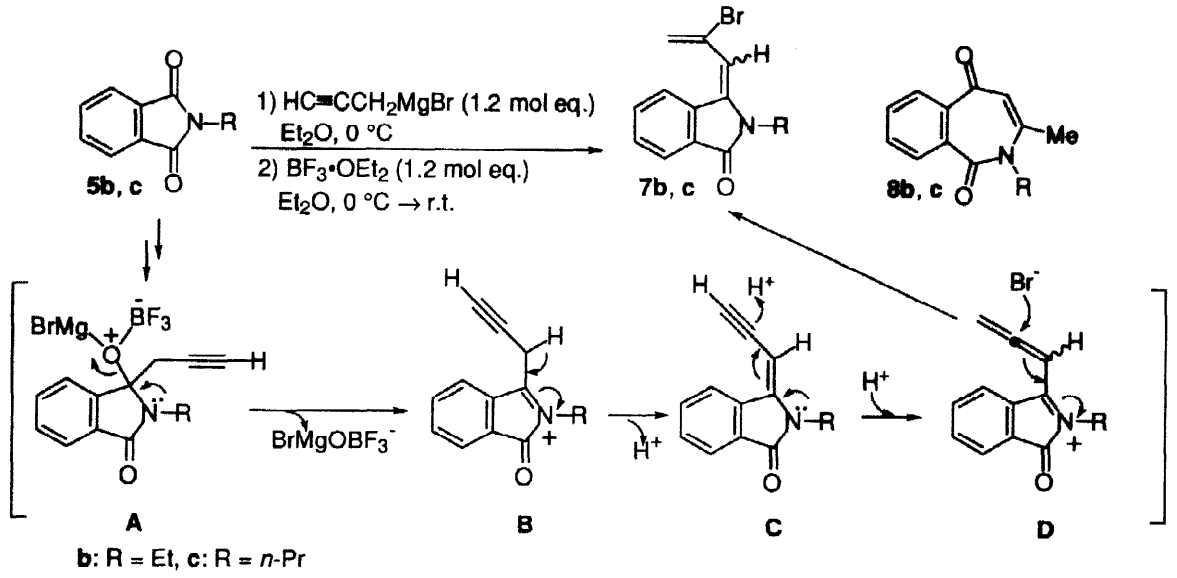
6a: 69%, **6b**: 83%, **6c**: 90%,
6d: 94%, **6e**: 85%

a: R = H, **b**: R = Et, **c**: R = *n*-Pr, **d**: R = *i*-Pr, **e**: R = Bn

Scheme 1

Tentatively, the Gabriel adducts **5b,c** without the isolation of the following **6b,c** were subjected to a direct ring expansion (**5**→**8**) (Scheme 2). Specifically, after the treatment of **5b,c** with propargylmagnesium bromide in Et_2O at 0 ℃ for 5 min, BF_3•OEt_2 was promptly added at 0 ℃, and the mixture was then stirred at room temperature for 5 min. However, the phthalimide **5b,c** were not converted into the desired ring-expanded benzazepine derivatives **8b,c**, and unexpected bromodienes **7b,c** were obtained in 65% and 79% yields as a single product, respectively. The structure of **7b,c** was confirmed based upon reasonable spectroscopic data. Their stereochemistry (*E* or *Z*) could not be determined by the ^1H NOE experiment because of difficulty in assignment of the three olefinic proton signals. We assumed that the formation of **7b,c** might occur *via* bromination onto allenyl acyliminium species **D** generated *in situ* from the corresponding ene-ynes **C**, which

would be derived from **A** by the BF_3-promoted elimination of BrMgO$^-$ followed by deprotonation of the resultant propargylic acyliminium species **B** as shown in Scheme 2.



Scheme 2

Subsequently, propargylic alcohols **6a-e** were treated with several Lewis acids to take place desired ring expansion reactions, as summarized in Table 1. The corresponding dehydration-hydration products **9a-e**, however, were formed in good yields in place of the desired ring-expanded products **8a-e**. Moreover, in the case of **6a**, when the reaction was undergone in the presence of some Lewis acids, the ene-yne compound **10a** was always obtained in various yields (entries 1-4 in Table 1). The characteristic spectroscopic data of the compounds

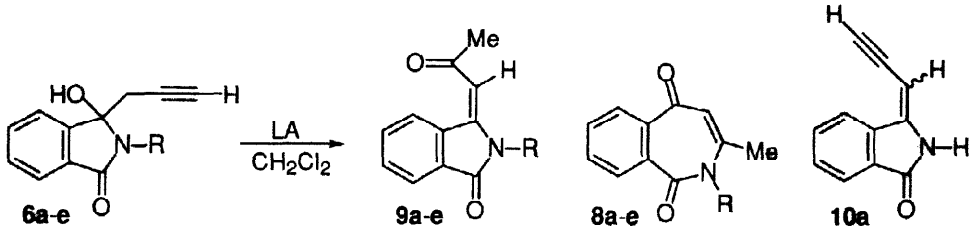


Table 1. Conversion of propargylic alcohols **6a-e** to **9a-e**.

entry	compd 6	reaction conditions			product 9	yield (%) [b]
		LA[a]	temp (°C)	time (h)		
1	**6a** [c]	B	-78 - r.t.	6.5	**9a**	27 [d]
2	"	AT	-78 - 0	2.5	"	40 [e]
3	"	BT	-78 - 10	2.6	"	81 [f]
4	"	HBT	"	1.8	"	30 [g]
5	**6b**	HBT	"	3	**9b**	80
6	**6c**	HBT	"	3	**9c**	98
7	**6d**	HBT	"	2.8	**9d**	94
8	**6e**	HBT	"	3.5	**9e**	85

a) LA : Lewis acids (15 mol %), B = BF_3•OEt_2, AT = $Al(CF_3SO_3)_3$, BT = $B(CF_3SO_3)_3$, HBT = $HB(CF_3SO_3)_2$. b) Isolation yield. c) A solution (CH_2Cl_2 : THF = 2 : 1) was employed. d-g) Ene-yne compound **10a** was also obtained in various yields [d) 25 %, e) 9 %, f) trace, and g) 42 %].

9a-e bearing two carbonyl groups, one vinyl proton, and one methyl group misled us into incorrectly identifying the products as benzazepine structures **8a-e**.[8] The X-ray analysis of one of the products proved to be the dehydration-hydration structure **9b** as shown in Figure 2. Therefore, the correct structures for all the products obtained from the Lewis acid-promoted reactions of **6a-e** should be the dehydration-isomerization-hydration stru-

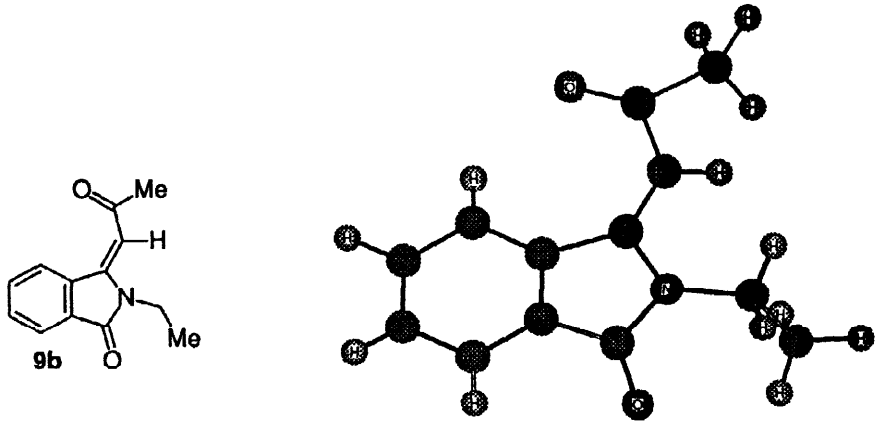
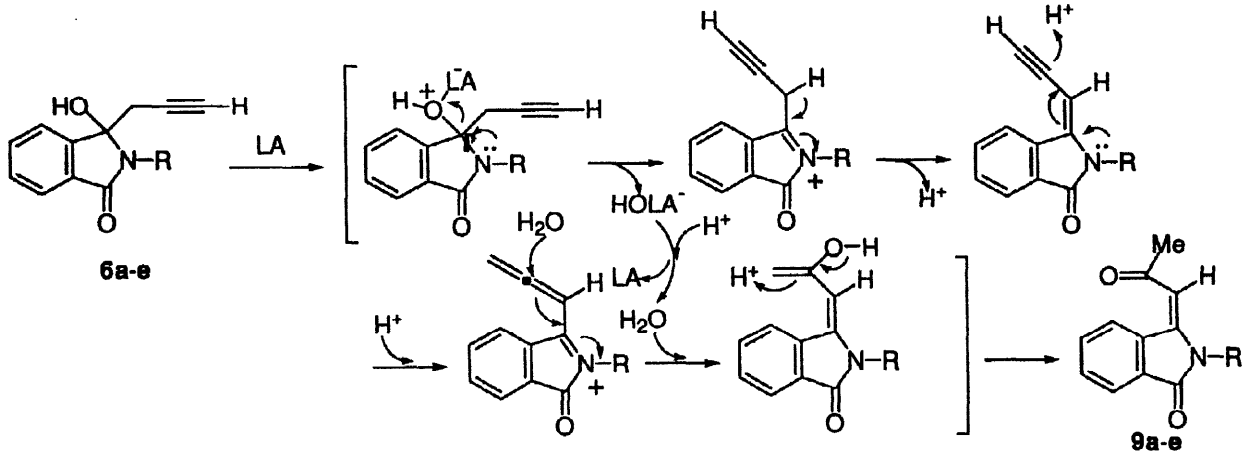


Figure 2. Computer-generated drawing of the compound **9b** derived from the X-ray coordinates

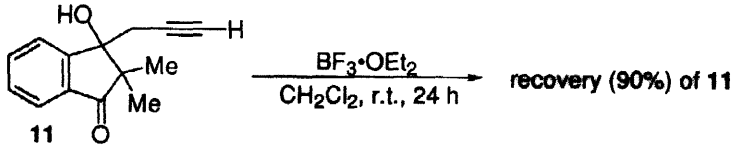
ctures **9a-e**. Instead of the ring expansion, unexpected tandem reactions occurred as shown in Scheme 3, namely, the elimination of the hydroxy group followed by hydration onto the resultant allenyl acyliminium species in a similar process to the derivatization of **5b,c** into the bromodienes **7b,c**. The generally accepted mechanism for hydration onto the alkynes is the Ad_E2 process,[10] which begins with a rate-limiting protonation to the ethyne moiety to form a vinyl cation intermediate followed by attack with H_2O and isomerization of the resultant enol to the more stable ketone. On the other hand, initiation of the hydration onto the propargylic alcohols **6a-e** seems to be a Lewis acid-promoted β-elimination of the hydroxy group assisted by an electron-donation of the alkylated lactam nitrogen atom to form the conjugated acyliminium system, which can be followed by the tandem reactions



Scheme 3

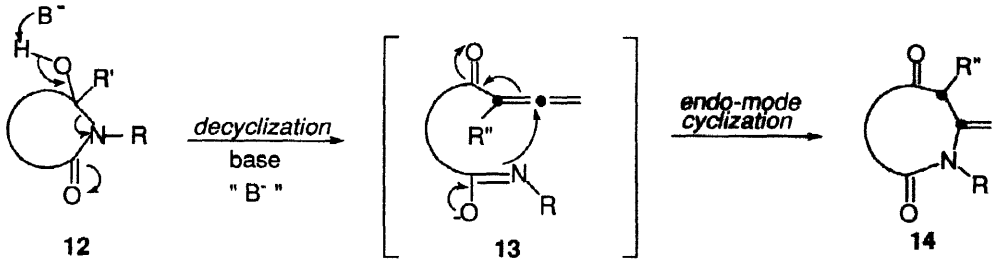
via conjugated yne-enamine and then allenyl acyliminium intermediates as represented in Scheme 3. This proposed mechanism must be supported by the following experimental results. Namely, a similar reaction of the propargylic alcohol **6a**, with its somewhat less electron-donating effect on the formation of the acyliminium intermediate than that of **6b-e**, always afforded a significant amount of ene-yne **10a** with the dehydration-hydration product **9a**. The similar treatment of propargylic alcohol **11** without the electron-donating nitrogen

atom resulted in a recovery of the starting compound as shown in Scheme 4.



Scheme 4

Next, an alternative promising method under basic conditions in the conversion of **12** to **14**, as represented in Figure 3, was envisioned by considering the oxazole formation of acetylamino allenyl ester.[11] Accordingly, it

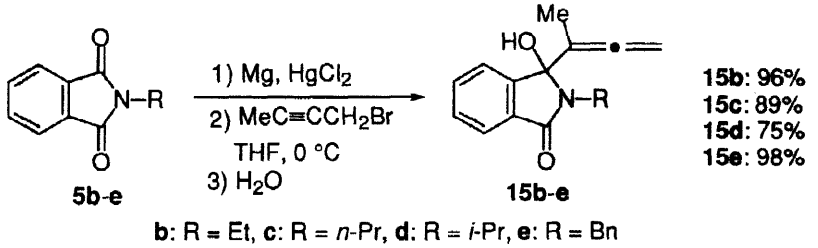


R = alkyl or benzyl, R' = $CH_2C{\equiv}CH$ or $MeC{=}C{=}CH_2$, R" = H or Me

Figure 3. Two-carbon atom ring expansion mode in the presence of a base

was decided that the ring-opening of the hydroxylactam **12** without the elimination of the hydroxyl group would be essential in the first step toward generation of the conjugated allenylketone intermediate **13** *in situ*. Eventually, the tandem reaction (**12**→**13**→**14**) involving an intramolecular Michael-type addition ("endo-mode cyclization") of the resultant imidiate anion to the conjugated allenylketone moiety will furnish the desired two-carbon atom ring-expanded lactam **14**.

Before embark upon an investigation of the conversion of **12** to **14**, preparation of allenic alcohols **15b-e** as additional precursors possessing the two-carbon atom ring expansion moiety to extend range of the reaction was examined and a successful convenient one-pot procedure was found, as follows (Scheme 5). A solution of 1-bromo-2-butyne in anhydrous THF was added very slowly to a mixture of *N*-benzylphthalimide **5e**, magnesium



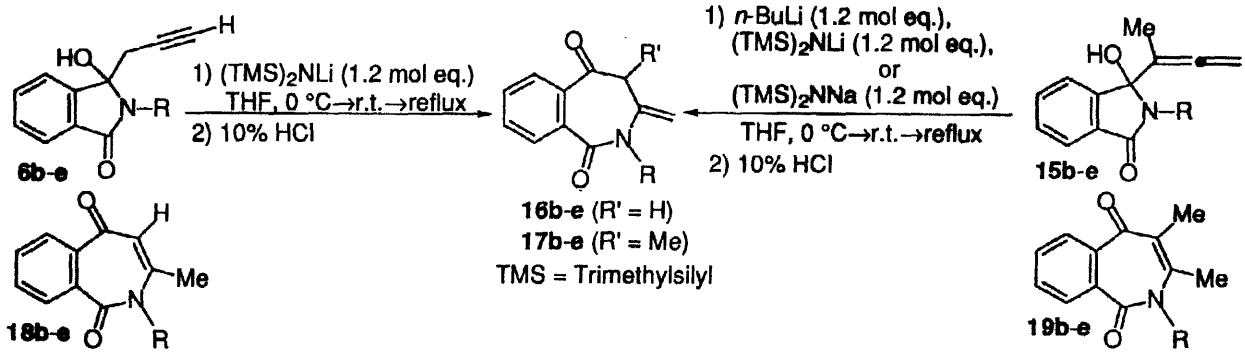
b: R = Et, **c**: R = *n*-Pr, **d**: R = *i*-Pr, **e**: R = Bn

Scheme 5

flakes, and catalytic $HgCl_2$ in anhydrous THF with vigorous stirring at 0 °C under N_2, and stirred for 2 h. The reaction afforded the allenic alcohol **15e** exclusively in 98% yield. The same treatment of **5b-d** as described above gave the corresponding allenic alcohols **15b-d** in excellent yields, respectively. The structures of **15b-e** bearing the allenic moiety were readily determined by their characteristic spectroscopic data [IR ($CHCl_3$) 3350-3300 (OH), 1958-1950 (allenyl), and 1697-1688 cm^{-1}(amide carbonyl); ^1H NMR (200 MHz, $CDCl_3$) δ 1.03-1.30 (s, 3 H, Me) and 5.17-5.20 ppm (s, 2 H, allenyl); high resolution MS (M^+ ion)] and/or elemental analyses. Interestingly, each Grignard reagent prepared from 1-bromo-2-propyne or 1-bromo-2-butyne exhibited highly

propargylic or allenic selectivity, as shown in Schemes 1 and 5.[12] Because the structures (or the equilibrium ratios) of both Grignard reagents have never been determined, it has not been clarified whether their exclusive nucleophilic addition reactions are controlled in a direct addition manner or in a conjugate addition manner.

Subsequently, we investigated the ring expansion reactions as shown in Scheme 6, and the results are summarized in Table 2. The propargylic alcohol **6d** was treated with 1M lithium bis(trimethylsilyl)amide [$(TMS)_2NLi$] in anhydrous THF with stirring at -78 ℃ for 10 min, and the mixture was warmed to room temperature. After being refluxed for 1 h, the reaction furnished the desired ring-expanded benzazepine **16d** in 70% yield, as anticipated (entry 3 in Table 2). The same treatment of **6b,c,e**, and **15c** with 1M $(TMS)_2NLi$ in THF as described above gave the corresponding 3-methylenebenz[c]azepines **16b,c,e**, and **17c** in poor yields (32-36%) (entries 1, 2, 4, and 6 in Table 2). These unsatisfactory results led us to improve the poor chemical yields by employing other bases [*e.g.*, Et_3N, *n*-BuLi, and $(TMS)_2NNa$]. However, our efforts resulted in the decomposition of the starting compounds except for the case of **15c**. The thermal ring expansion of the allenic de-



Scheme 6

Table 2. Conversion of propargylic alcohols **6** and allenic alcohols **15** to benzazepines **16** and **17**

entry	compd 6 and 15	reaction conditions[a] base	time (h)	product 16 or 17	yield (%)[b]
1	**6b**	$(TMS)_2NLi$	6	**16b**	34
2	**6c**	"	4	**16c**	35
3	**6d**	"	1	**16d**	70
4	**6e**	"	10	**16e**	36
5	**15b**	*n*-BuLi	4.5	**17b**	73
6	**15c**	$(TMS)_2NLi$	5	**17c**	32
7	"	*n*-BuLi	3.5	"	67
8	**15d**	"	0.5	**17d**	73
9	**15e**	"	1	**17e**	33
10	"	$(TMS)_2NNa$	0.5	"	80

[a] All reactions were carried out in the presence of 1.2 mol eq. of base under reflux in THF. [b] Isolation yield.

rivatives **15b-e** with *n*-BuLi in anhydrous THF utilizing the same procedure as the cases of $(TMS)_2NLi$

proceeded smoothly to give the corresponding 3-methylenebenz[c]azepines **17b-d** in moderate yields (67-73%) (entries 5, 7, and 8) and **17e** in 33% yield (entry 9), respectively. When **15e** was treated with sodium bis(trimethylsilyl)amide [$(TMS)_2NNa$], however, the product **17e** was obtained in 80% yield (entry 10). In the case of *N*-nonalkylated propargylic alcohol **6a**, we did not attempt the ring expansion reaction, since it was estimated to be an unsuitable substrate under the basic conditions. The structures of 3-methylenebenzazepines-1,5-diones **16d** and **17d** were clarified by X-ray crystallographic analyses, as shown in Figure 4. The structures

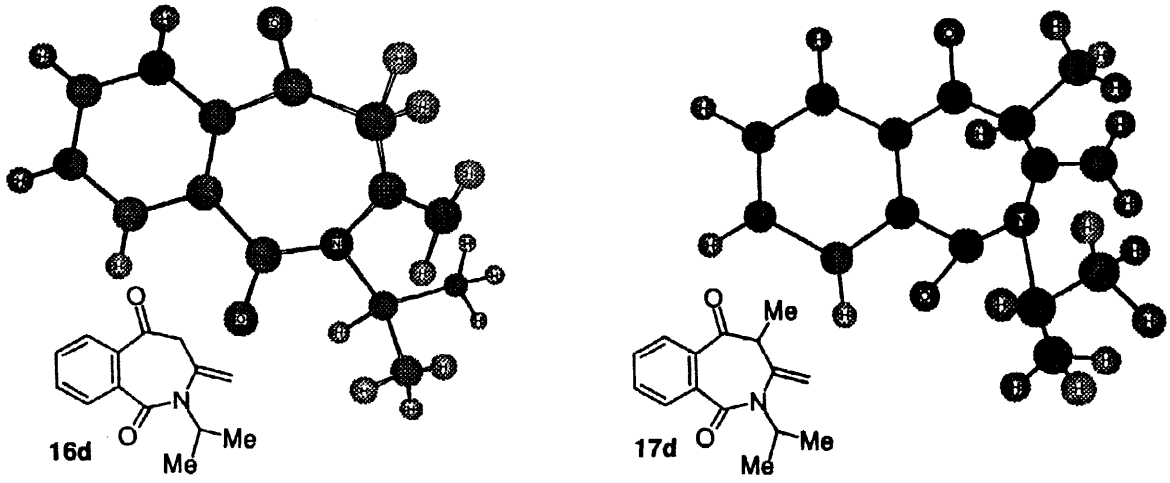


Figure 4. Computer-generated drawing of the compounds **16d** and **17d** derived from their X-ray coordinates

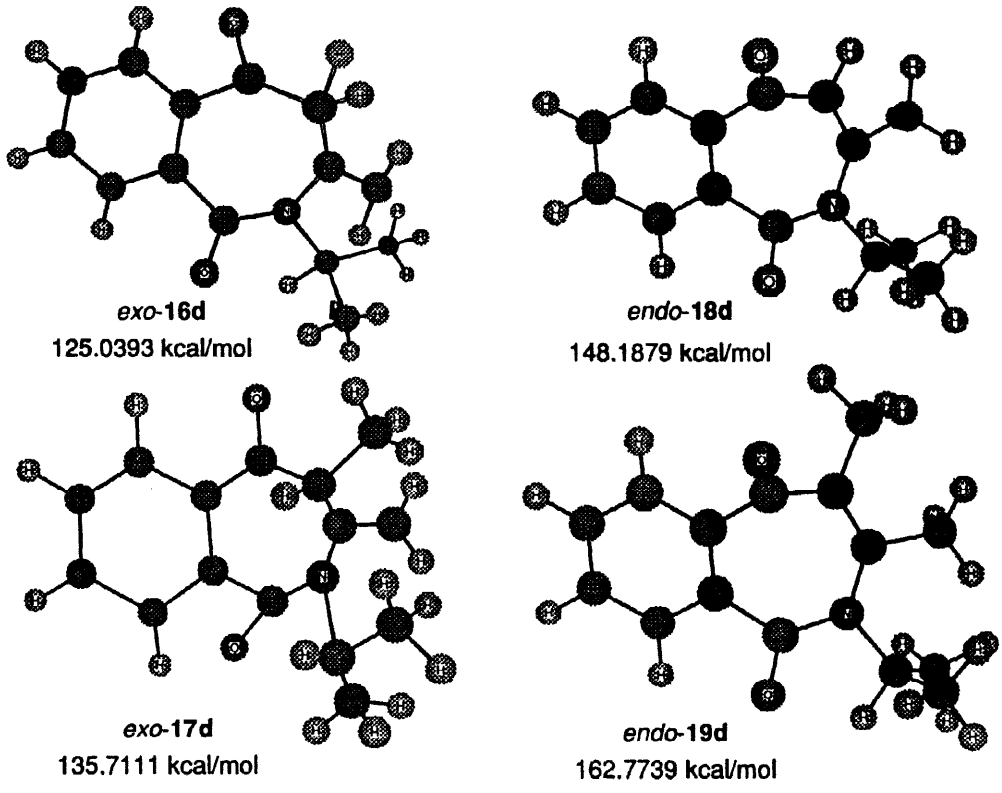
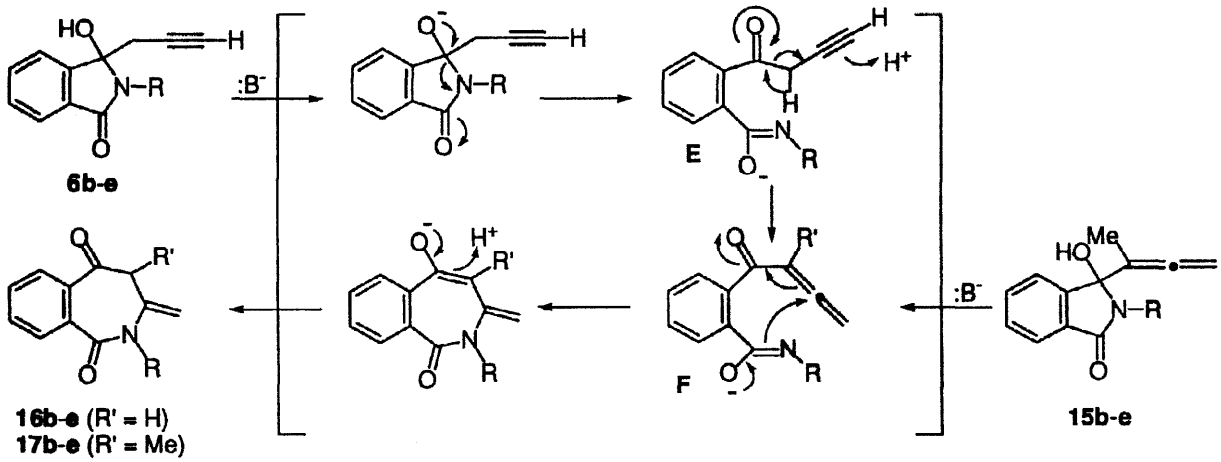


Figure 5. Molecular mechanics calculations for *exo*-**16d**, **17d** and *endo* -**18d**, **19d**.

of **16b,c,e**, **17b,c**, and **17e** were determined by their similar characteristic spectroscopic data to those of **16d**

and **17d**. The *endo*-olefinic (α,β-unsaturated ketone) products **18b-e** and **19b-e** have never been obtained in thermal ring expansion reactions under basic conditions, unlike reactions involving benzcycloheptanones.[7b] Thus, the molecular mechanics (MM2) calculation, in examining the energy of some *exo*- and *endo*-olefinic products, shows that *exo*-**16d** and **17d** are more stable than the corresponding *endo*-**18d** and **19d** by 23 kcal/mol and 27 kcal/mol, respectively, as shown in Figure 5. The lesser stability of these *endo*-olefinic products compared to the corresponding *exo*-olefinic ones may be due to the severe steric repulsion between the methyl group and the *N*-alkyl group or among the two methyl groups and the *N*-alkyl group on the azepine lactam ring.

Finally, we propose plausible reaction mechanisms by which the 3-methylenebenzazepines **16b-e** and **17b-e** can be produced *via* intramolecular *endo*-mode cyclization in the common intermediates **F**. These intermediates are derived by the decyclization of the propargylic hydroxy γ-lactams **6b-e** followed by rapid isomerization of the resultant propargylic ketones **E** or directly by the decyclization of the allenic hydroxy γ-lactams **15b-e**, as shown in Scheme 7.



Scheme 7

Experimental Section

General

All melting points were measured using a Yanagimoto apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1720 infrared Fourier transform spectrophotometer. ^{1}H NMR (200 MHz) and ^{13}C NMR (100 MHz) spectra were taken on a JEOL JNM-FX 200 or JEOL JNM-GSX 400 spectrometer with tetramethylsilane as an internal standard, and chemical shifts are recorded in δ values. EI-MS and HR-EI-MS were measured on a JEOL JMS SX-102A mass spectrometer using a direct inlet system. Combustion analyses were performed by a Yanagimoto CHN corder. Molecular mechanics calculations were performed using the molecular modeling system Insight II/Discover 95.0 (Biosym/MSI, San Diego) on the Silicon Graphics workstation computer. Molecular geometries were generated based on the crystal, optimizing with the CVFF

forcefield under the general conditions. Column chromatography was performed using Katayama silica gel 60K070 (70-230 mesh).

Synthesis of N-Alkyl- and N-Benzylphthalimides 5b-e

***N*-ethylphthalimide 5b**. 88% yield, colorless needles (Et_2O-hexane-CH_2Cl_2), mp 71-72 ℃.[13] Anal. Calcd for $C_{10}H_9NO_2$: C, 5.18; H, 68.56; N, 8.00. Found: C, 5.31; H, 68.57; N, 7.98.

***N*-(*n*-propyl)phthalimide 5c**. 96% yield, colorless plates (Et_2O-hexane-CH_2Cl_2), mp 64 ℃ (lit.[14] mp 63.5-64.5 ℃). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 5.86; H, 69.83; N, 7.40. Found: C, 5.92; H, 69.78; N, 7.38.

***N*-isopropylphthalimide 5d**. 80% yield, colorless needles (Et_2O-hexane-CH_2Cl_2), mp 84-86 ℃ (lit.[15] mp 85 ℃). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 5.86; H, 69.83; N, 7.40. Found: C, 5.83; H, 69.72; N, 7.34.

***N*-benzylphthalimide 5e**. 72% yield, colorless needles (Et_2O-hexane-CH_2Cl_2), mp 113-114 ℃ (lit.[16] mp 114-115 ℃). Anal. Calcd for $C_{15}H_{11}NO_2$: C, 4.67; H, 75.94; N, 5.90. Found: C, 4.77; H, 75.96; N, 5.83.

A General Procedure for the Synthesis of Propargylic Alcohols 6a-d

Preparation of an ethereal solution of the Grignard reagent (1M solution) from 1-bromopropyne and magnesium flakes

A mixture of magnesium flakes (0.24 g, 10.10 atm) and mercury (II) chloride (0.14 g, 5 mol %) was placed in a two-necked 30 mL flask equipped with a cooling condenser and then anhydrous Et_2O (5 mL) was added under N_2 atmosphere. After 3-bromo-1-propyne (1.20 g, 10.10 mmol) was added, the mixture was stirred at room temperature for 5 min. Finally, the reaction mixture was diluted with anhydrous Et_2O (5 mL).

***N*-isopropyl-3-hydroxy-3-propargylisoindolin-1(3H)-one 6d**. To a solution of *N*-isopropyl phthalimide **5d** (1.0 g, 4.29 mmol) in THF (20 mL) was added a solution of the above Grignard reagent (5.10 mL, 5.10 mmol) at 0 ℃ under N_2 atmosphere. After being stirred at 0 ℃ for 5 min, the reaction mixture was treated with water and then extracted with Et_2O. The ethereal extract was washed with water, dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **6d**, which was purified by flash column chromatography on silica gel with Et_2O-hexane (1 : 1) to give the pure product **6d** (1.14 g, 94% yield) as white powder: mp 160-161 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3577, 3309, 1689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (d, J = 7.3 Hz, 3H), 1.57 (d, J = 7.3 Hz, 3H), 1.81 (t, J = 2.7 Hz, 1H), 2.90 (dd, $J_{AB,\,AX}$ = 16.9, 2.7 Hz, 1H), 3.03 (dd, $J_{AB,BX}$ = 16.9, 2.7 Hz, 1H), 3.05-3.92 (m, 1H), 6.01 (s, 1H), 7.39-7.71 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 20.06, 20.81, 28.37, 43.76, 71.27, 78.36, 89.70, 121.78, 122.37, 129.35, 131.69, 132.81, 146.25, 166.90; HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1098 (M^+); Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H 6.59; N, 6.11. Found: C, 73.37; H, 6.74; N, 5.99.

3-hydroxy-3-propargylisoindolin-1(3H)-one 6a. 69% yield, white powder, mp 158-159 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3294, 3138, 1713 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (t, J = 2.7 Hz, 1H), 2.94 (d, J = 2.7 Hz, 1H), 2.96 (d, J = 2.7 Hz, 1H), 6.14 (s, 1H), 7.39 (brs, 1H), 7.49-7.75 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 30.32, 71.10, 79.11, 86.00, 122.18, 122.75, 129.28, 131.60, 132.24, 148.10, 168.69; HRMS calcd for $C_{11}H_9NO_2$ 187.0633, found *m/z* 187.0627 (M^+).

***N*-ethyl-3-hydroxy-3-propargylisoindolin-1(3H)-one 6b.** 83% yield, white powder, mp 111-112 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3280, 3137, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (t, J = 7.1 Hz, 3H), 1.83 (t, J = 1.5 Hz, 1H), 2.92 (dd, $J_{AB,\ AX}$ = 16.9, 1.5 Hz, 1H), 3.08 (dd, $J_{AB,\ BX}$ = 16.9, 1.5 Hz, 1H), 3.23-3.30 (m, 1H), 3.38-3.89 (m, 1H), 3.88 (s, 1H), 7.23-7.67 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.23, 28.16, 33.23, 71.49, 77.70, 89.50, 121.78, 122.79, 129.50, 131.20, 132.19, 146.09, 167.50; HRMS calcd for $C_{13}H_{13}NO_2$ MW 215.0946, found *m/z* 215.0953 (M^+); Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.39; H, 6.10; N, 6.18.

***N*-(*n*-propyl)-3-hydroxy-3-propargylisoindolin-1(3H)-one 6c.** 90% yield, colorless needles, mp 132 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3295, 3138, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 7.6 Hz, 3H), 1.66-1.73 (m, 2H), 1.82 (t, J = 2.7 Hz, 1H), 2.90 (dd, $J_{AB,\ AX}$ = 16.8, 2.7 Hz, 1H), 3.07 (dd, $J_{AB,\ BX}$ = 16.8, 2.7 Hz, 1H), 3.31-3.46 (m, 2H), 3.38 (s, 1H), 7.40-7.70 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 11.76, 22.22, 28.20, 40.42, 71.51, 77.63, 89.45, 121.80, 123.00, 129.66, 131.20, 132.22, 146.01, 167.70; HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1110 (M^+); Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.59; N, 6.11. Found: C, 73.15; H, 6.70; N, 6.18.

***N*-benzyl-3-hydroxy-3-propargylisoindolin-1(3H)-one 6e.** 85% yield, white powder, mp 156 °C (Et_2O-hexane-CH_2Cl_2) ; IR ($CHCl_3$) 3582, 3308, 1697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83 (t, J = 2.4 Hz, 1H), 2.69 (dd, $J_{AB,AX}$ = 16.9, 2.4 Hz, 1H), 2.93 (dd, $J_{AB,BX}$ = 16.9, 2.4 Hz, 1H), 4.60 (d, J = 15.6 Hz, 1H), 4.80 (d, J = 15.6 Hz, 1H), 6.54 (s, 1H), 7.21-7.79 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 29.02, 41.97, 71.27, 78.20, 89.34, 122.29, 122.84, 127.05, 128.27, 128.38, 129.46, 131.49, 132.11, 138.15, 146.82, 167.61; HRMS calcd for $C_{18}H_{15}NO_2$ MW 277.1102, found *m/z* 277.1103 (M^+); Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.95; H, 5.46; N, 5.05. Found: C, 77.80; H, 5.64; N, 5.01.

A General Procedure for the Formation of Bromodienes 7b and 7c

***N*-(*n*-propyl)-3-(2-bromo-2-propenylidene)isoindolin-1(3H)-one 7c.** To a solution of *N*-propyl phthalimide **5c** (0.19 g, 1.0 mmol) in anhydrous Et_2O (20 mL) was added propargylmagnesium bromide (1.2 mL 1.2 mmol) at 0 °C under N_2 atmosphere, and then BF_3•OEt_2 was added to the solution. After being stirred at 0 °C for 5 min, the reaction mixture was allowed to warm to room temperature over 5 min. The reaction was quenched

with sat. $NaHCO_3$ and extracted with Et_2O. The ethereal extract was dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **7c**, which was purified by flash column chromatography on silica gel with Et_2O-hexane (1 : 3) to give the pure product **7c** (0.23 g, 79% yield) as colorless oil: IR ($CHCl_3$) 3019, 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (t, J = 7.3 Hz, 3H), 1.65-1.76 (m, 2H), 3.73 (t, J = 7.3 Hz, 2H), 5.95 (dd, J = 2.0, 1.5 Hz, 2H), 6.06 (t, J = 1.5 Hz, 1H), 7.48-7.56 (m, 2H), 7.83-7.85 (m, 1H), 8.23 (d, J = 6.84 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.38, 21.49, 40.04, 104.67, 108.33, 119.49, 122.45, 124.12, 129.88, 131.87, 133.80, 134.41, 137.55, 168.45; HRMS calcd for $C_{14}H_{14}BrNO$ MW 291.0259, found *m/z* 293.0291 [$(M+2)^+$].

***N*-ethyl-3-(2-bromo-2-propenylidene)isoindolin-1(3H)-one 7b.** 65% yield, colorless oil: IR ($CHCl_3$) 3019, 1701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 3H), 3.83 (q, J = 7.1 Hz, 2H), 5.95 (dd, J = 2.4, 1.2 Hz, 2H), 6.10 (t, J = 1.2 Hz, 1H), 7.47-7.58 (m, 2H), 7.69-7.87 (m, 1H), 8.22-8.26 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.46, 34.11, 108.25, 122.49, 123.26, 124.18, 129.94, 130.41, 131.91, 133.83, 134.49, 137.12, 166.07; HRMS calcd for $C_{13}H_{12}BrNO$ MW 277.0102, found *m/z* 279.0081 [$(M+2)^+$].

A General Procedure for the Formation of Dehydration-Hydration Compounds 9a-e

***N*-(*n*-propyl)-3-(2-oxopropylidene)isoindolin-1(3H)-one 9c.** To a solution of BH_3•THF (1M solution in THF) (32.70 μL, 0.03 mmol) in anhydrous CH_2Cl_2 (2 mL) was added CF_3SO_3H (8.70 μL, 0.10 mmol) at 0 ℃ under N_2 atmosphere. The mixture was stirred at 0 ℃ for 10 min and then compound **6c** (0.05g, 0.20 mmol) was added at -78 ℃. After being stirred at -78 - 10 ℃ for 2.8 h, the reaction was quenched with sat. $NaHCO_3$ and then extracted with Et_2O. The ethereal extract was dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **9c**, which was purified by preparative thin-layer chromatography on a silica gel plate with Et_2O-hexane (1 : 2) to give the pure product **9c** (49 mg, 98% yield) as colorless needles: mp 73-74 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3080, 1718, 1683 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (t, 3H, J = 7.3 Hz), 1.71 (m, 2H), 2.42 (s, 3H), 3.77 (t, 2H, J = 7.3 Hz), 6.06 (s, 1H), 7.58-7.68 (m, 2H), 7.83 (d, J = 8.1 Hz, 1H), 9.00 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.37, 21.21, 32.68, 41.07, 105.87, 123.08, 127.61, 129.88, 131.55, 133.39, 134.94, 146.94, 167.79, 196.34; HRMS cacld for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1100 (M^+). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.21; H, 6.71; N, 6.13.

3-(2-oxopropylidene)isoindolin-1(3H)-one 9a. 81% yield, colorless prisms, mp 120-122 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3333, 1724, 1674 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12-0.40 (brs, 1H), 2.36 (s, 3H), 6.15 (s, 1H), 7.60-7.90 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 31.10, 98.37, 121.05, 124.12, 129.44, 131.89, 132.88, 136.94, 146.40, 169.02, 199.06; HRMS cacld for $C_{11}H_9NO_2$ MW 187.0633, found *m/z* 187.0623 (M^+).

***N*-ethyl-3-(2-oxopropylidene)isoindolin-1(3H)-one 9b.** 80% yield, colorless prisms, mp 92-94 ℃

(Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3110, 1713, 1678 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, 3H, J = 7.1 Hz), 2.43 (s, 3H), 3.86 (q, 2H, J = 7.1 Hz), 6.08 (s, 1H), 7.54-7.70 (m, 2H), 7.82-7.86 (m, 1H), 9.02 (dd, J = 1.22, 7.81 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.17, 32.68, 34.31, 105.69, 123.06, 127.69, 130.03, 131.55, 133.41, 134.03, 146.62, 167.45, 196.32; HRMS cacld for $C_{13}H_{13}NO_2$ MW 215.0946, found *m/z* 215.0953 (M^+). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.25; H, 6.22; N, 6.44.

***N*-isopropyl-3-(2-oxopropylidene)isoindolin-1(3H)-one 9d.** 94% yield, colorless needles, mp 83-84 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3016, 1719, 1577 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (d, 6H, J = 7.0 Hz), 2.4 (s, 3H), 4.53-4.56 (m, 1H), 6.22 (s, 1H), 7.52-7.67 (m, 2H), 7.78-7.81 (m, 1H), 8.93 (dd, J = 1.46, 6.78 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.01, 20.15, 32.79, 44.53, 106.33, 123.01, 127.32, 130.00, 131.45, 133.28, 133.78, 146.73, 167.94, 196.61; HRMS cacld for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1115 (M^+).

***N*-benzyl-3-(2-oxopropylidene)isoindolin-1(3H)-one 9e.** 85% yield, colorless needles, mp 125-126 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3068, 1718, 1686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 (s, 3H), 5.02 (s, 2H), 6.01 (s, 1H), 7.30-7.34 (m, 5H), 7.57-7.70 (m, 2H), 7.89-7.93 (m, 2H), 9.00 (dd, J = 1.46, 6.34 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 32.57, 43.31, 107.28, 123.41, 126.77, 127.69, 127.74, 128.91, 129.70, 131.65, 133.67, 134.00, 135.75, 146.40, 167.88, 196.28; HRMS cacld for $C_{18}H_{15}NO_2$ MW 277.1103, found *m/z* 77.1101 (M^+). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.95; H, 5.46; N, 5.05. Found: C, 77.85; H, 5.64; N, 5.04.

3-propenylideneisoindolin-1(3H)-one 10a. 9-42% yields, colorless powder, mp 138-140 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3176, 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.49 (d, J = 2.4 Hz, 1H), 5.52 (d, J = 2.4 Hz, 1H), 7.50-7.69 (m, 3H), 7.86 (dd, J = 1.5, 6.2 Hz, 1H), 8.00-8.20 (brs, 1H); ^{13}C NMR ($CDCl_3$) δ 83.54, 86.34, 120.01, 123.87, 129.61, 130.30, 132.55, 135.79, 144.73, 167.46; HRMS cacld for $C_{11}H_7NO$ MW 169.0528, found *m/z* 169.0519 (M^+).

Synthesis of 2,2-Dimethyl-3-hydroxy-3-propargylindan-1-one 11 and Its Treatment with BF_3•OEt_2

2,2-dimethyl-3-hydroxy-3-propargylindan-1-one 11. To a solution of 1,3-indandione (3.0 g, 20.50 mmol) in THF (40 mL) was added NaH (1.50 g, 61.50 mmol) at -78 °C. After being stirred for 5 min, methyl iodide (3.86 mL, 61.50 mmol) was added and then the mixture was stirred at room temperature for 15h. The reaction mixture was quenched with 10% HCl, extracted with Et_2O, and washed with brine. The extract was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by silica gel column chromatography with Et_2O-hexane (1:9) to afford 2,2-dimethyl-1,3-indandione (3.0 g, 84% yield) as colorless needles: mp 140-142 °C (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 1747, 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (s, 6H), 7.77-8.02 (m, 4H); MS calcd for $C_{11}H_{10}O_2$ 174, found *m/z* 174 (M^+). To a solution of 2,2-dimethyl-1,3-indandione (0.50 g, 2.87 mmol) in anhydrous THF (30 mL) at -78 °C was added propargylmagnesium bromide (3.45 mL, 3.45 mmol) under N_2

atmosphere. After being stirred for 5 min, the reaction mixture was quenched with H_2O, extracted with Et_2O, and washed with brine. The extract was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by silica gel column chromatography with Et_2O-hexane (1 : 2) to afford **2,2-dimethyl-3-hydroxy-3-propargylindan-1-one 11** (0.37 g, 60% yield) as white powder: mp 135-137 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3583, 3300, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (s, 3H), 1.31 (s, 3H), 2.07 (s, 1H), 2.68 (s, 1H), 2.73 (s, 2H), 7.46-7.82 (m, 4H); MS calcd for $C_{14}H_{14}O_2$ 214, found *m/z* 214 (M^+).

Treatment of compound 11 with BF_3•OEt_2

To a solution of 2,2-dimethyl-3-hydroxy-3-propargylindan-1-one **11** (0.15 g, 0.70 mmol) in anhydrous CH_2Cl_2 (5 mL) was added BF_3•OEt_2 (0.11 mL, 0.84 mmol) at room temperature under N_2 atmosphere. After being stirred at room temperature for 24 h, the reaction mixture was quenched with 10% HCl and then extracted with Et_2O. The extract was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by preparative thin-layer chromatography on a silica gel plate with Et_2O-hexane (1 : 1) to recover the starting compound **11** in 90% yield.

A General Procedure for the Synthesis of Allenic Alcohols 15b-e

***N*-benzyl-3-hydroxy-3-allenylisoindolin-1(3H)-one 15e.** To a mixture of *N*-benzylphthalimide **5e** (1.0 g, 4.22 mmol), magnesium flakes (0.15 g, 6.17 atm), and mercury (II) chloride (0.086 g, 5 mol %) in anhydrous THF (20 mL) was added slowly a solution of 1-bromo-2-butyne (0.82 g, 6.33 mmol) in anhydrous THF (3 mL) using a dropping funnel under N_2 atmosphere, and then the mixture was vigorously stirred at 0 ℃ for 2 h. The reaction mixture was quenched with excess water and then extracted with Et_2O. The ethereal extract was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **15e**, which was purified by flash column chromatography on silica gel with Et_2O-hexane (1 : 1) to give the pure product **15e** (1.20 g, 98% yield) as colorless needles: mp 155-156 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3330, 1958, 1697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3H), 3.56 (s, 1H), 4.44 (d, J = 15.1 Hz, 1H), 4.64 (d, J = 15.1 Hz, 1H), 5.19 (s, 2H), 7.30-7.60 (m, 8H), 7.74 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.92, 42.45, 80.19, 100.35, 122.09, 123.41, 127.27, 128.25, 128.77, 129.75, 131.40, 132.55, 137.76, 146.14, 167.65, 206.23; HRMS calcd for $C_{19}H_{17}NO_2$ MW 291.1259, found *m/z* 291.1269 (M^+); Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.32; H 5.89; N, 4.81. Found: C, 78.11; H, 5.97; N, 4.76.

***N*-ethyl-3-hydroxy-3-allenylisoindolin-1(3H)-one 15b.** 96% yield, white powder, mp 89-90 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3350, 1950, 1692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, J = 7.6 Hz, 3H), 1.29 (s, 3H), 3.21-3.35 (m, 1H), 3.56 (s, 1H), 3.48-3.66 (m, 1H), 5.20 (s, 2H), 7.40-7.59 (m, 3H), 7.66 (d, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.16, 14.27, 33.78, 80.25, 89.90, 100.31, 121.91, 123.12, 129.53, 131.84 132.30, 146.16, 167.34, 206.03; HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1102, found *m/z* 229.1106 (M^+).

***N*-(*n*-propyl)-3-hydroxy-3-allenylisoindolin-1(3H)-one 15c.** 89% yield, white powder, mp 80 ℃

(Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3300, 1950, 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, J = 7.3 Hz, 3H), 1.27 (s, 3H), 1.61-1.83 (m, 2H), 3.02-3.17 (m, 1H), 3.41-3.52 (m, 1H), 3.56 (s, 1H), 5.17 (s, 2H), 7.42-7.59 (m, 3H), 7.70 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.85, 14.12, 22.15, 40.93, 80.12, 89.96, 100.31, 121.94. 123.13, 129.64, 131.73, 132.28, 146.18, 167.54, 206.11; HRMS calcd for $C_{15}H_{17}NO_2$ MW 243.1259, found *m/z* 243.1262 (M^+).

***N*-isopropyl-3-hydroxy-3-allenylisoindolin-1(3H)-one 15d.** 75% yield, white powder, mp 34-35 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 3350, 1958, 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.46 (d, J = 6.8 Hz, 6H), 3.66-3.79 (m, 1H), 4.50 (s, 1H), 5.17 (s, 2H), 7.38-7.53 (m, 3H), 7.60 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 41.52, 19.99, 20.87, 44.26, 80.08, 90.31, 100.24, 121.82, 122.82, 129.53, 132.06, 132.61, 145.94, 167.28, 206.29; HRMS calcd for $C_{15}H_{17}NO_2$ MW 243.1259, found *m/z* 243.1254 (M^+); Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.05; N, 5.76. Found: C, 73.70; H, 7.04; N, 5.65.

A General Procedure for the Conversion of 6b-e to 16b-e

***N*-isopropylbenzazepine-1,5-dione 16d.** To a solution of compound **6d** (0.50 g, 2.18 mmol) in anhydrous THF (20 mL) was added 1.0 M $(TMS)_2NLi$ (2.61 mL, 2.61 mmol) in hexane at -78 ℃ under N_2 atmosphere. After being stirred for 10 min at -78 ℃, the reaction mixture was allowed to warm to room temperature, and refluxed for 1 h. After cooling to 0 ℃, the reaction mixture was quenched with 10% HCl and then extracted with Et_2O. The ethereal extract was washed with sat. aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **16d**, which was purified by flash column chromatography on silica gel with Et_2O-hexane (1 : 2) to give the pure product **16d** (0.35 g, 70% yield) as colorless prisms: mp 70 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 1692, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (d, J = 7.3 Hz, 6H), 3.61 (s, 2H), 4.92-5.05 (m, 1H), 5.17 (s, 1H), 5.29 (s, 1H), 7.49-7.66 (m, 3H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.89, 47.33, 54.11, 119.51, 127.65, 130.49, 130.96, 132.75, 134.18, 134.84, 138.31, 166.33, 199.63; HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1101 (M^+); Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.6; N, 6.11. Found: C, 72.88; H, 6.72; N, 6.15.

***N*-ethylbenzazepine-1,5-dione 16b.** 34% yield, white powder, mp 91-92 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 1691, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 3.66 (s, 2H), 3.87 (q, J = 7.1 Hz, 2H), 5.21 (s, 1H), 5.29 (s, 1H), 7.51-7.80 (m, 3H), 7.86 (d, J = 7.3 Hz, 1H); HRMS calcd for $C_{13}H_{13}NO_2$ MW 215.0946, found *m/z* 215.0940 (M^+); Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.73; H, 6.19; N, 6.27.

***N*-(*n*-propyl)benzazepine-1,5-dione 16c.** 35% yield, white powder, mp 44-45 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 1690, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (t, J = 7.3 Hz, 3H), 1.65-1.80 (m, 2H), 3.66 (s, 2H), 3.76 (t, J = 7.3 Hz, 2H), 5.20 (s, 1H), 5.30 (s, 1H), 7.50-7.87 (m, 3H), 7.95 (d, J = 7.8 Hz, 1H);

HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1103, found *m/z* 229.1104 (M^+); Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H 6.6; N, 6.11. Found: C, 73.24; H, 6.64; N, 6.04.

***N*-benzylbenzazepine-1,5-dione 16e.** 36% yield, pale yellow oil; IR ($CHCl_3$) 1691, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.38 (s, 2H), 5.00 (s, 2H), 5.15 (s, 1H), 5.17 (s, 1H), 7.32-7.36 (brs, 5H), 7.51-7.77 (m, 3H), 8.00 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.78, 52.63, 52.91, 116.62, 117.65, 126.11, 127.91, 128.77, 131.22, 133.08, 134.45, 137.11, 141.13, 145.57, 166.77, 198.19; Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.95; H, 5.46; N, 5.05. Found: C, 77.50; H, 5.55; N, 5.06.

A General Procedure for the Conversion of 15b-e to 17b-e

***N*-ethylbenzazepine-1,5-dione 17b.** To a solution of compound **15b** (0.50 g, 2.18 mmol) in anhydrous THF (20 mL) was added 1.68 M *n*-BuLi (1.56 mL, 2.62 mmol) in hexane at -78 ℃ under N_2 atmosphere. After being stirred at -78 ℃ for 10 min, the reaction mixture was allowed to warm to room temperature, and refluxed for 4.5 h. After cooling to 0 ℃, the reaction mixture was quenched with 10% HCl and extracted with Et_2O. The ethereal extract was washed with sat. aqueous $NaHCO_3$, brine, dried over $MgSO_4$, and filtered. The filtrate was evaporated *in vacuo* to afford the crude **17b**, which was purified by flash column chromatography on silica gel with Et_2O-hexane (1 : 2) to give the pure product **17b** (0.37 g, 73 %) as colorless oil: IR ($CHCl_3$) 1691, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (t, *J* = 7.1 Hz, 3H), 1.46 (d, *J* = 7.3 Hz, 3H), 3.55 (q, *J* = 7.3 Hz, 1H), 3.65-3.72 (m, 1H), 3.92-4.10 (m, 1H), 5.20 (s, 2H), 7.48-7.67 (m, 3H), 7.92 (d, *J* = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.81, 15.49, 44.97, 55.52, 114.48, 127.82, 130.30, 131.03, 132.53, 134.18, 134.91, 146.87, 166.46, 201.86; HRMS calcd for $C_{14}H_{15}NO_2$ MW 229.1102, found *m/z* 229.1109 (M^+).

***N*-(*n*-propyl)benzazepine-1,5-dione 17c.** 67% yield, colorless oil; IR ($CHCl_3$) 1693, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (t, *J* = 7.3 Hz, 3H), 1.46 (d, *J* = 7.3 Hz, 3H), 1.52-1.85 (m, 2H), 3.41-3.49 (m, 1H), 3.57 (q, *J* = 7.3 Hz, 1H), 3.86-4.00 (m, 1H), 5.20 (s, 2H), 7.48-7.67 (m, 3H), 7.92 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 11.43, 15.49, 21.80, 51.83, 55.34, 114.45, 127.80, 130.34, 131.02, 132.55, 134.25, 134.84, 147.09, 166.68, 201.86; HRMS calcd for $C_{15}H_{17}NO_2$ MW 243.1259, found *m/z* 243.1258 (M^+).

***N*-isopropylbenzazepine-1,5-dione 17d.** 73% yield, colorless prisms, mp 73 ℃ (Et_2O-hexane-CH_2Cl_2); IR ($CHCl_3$) 1693, 1631 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (d, *J* = 6.8 Hz, 3H), 1.33 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* = 7.3 Hz, 3H), 3.50 (q, *J* = 6.8 Hz, 1H), 4.80-4.93 (m, 1H), 5.20 (s, 1H), 5.28 (s, 1H), 7.46-7.63 (m, 3H), 7.88 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.38. 20.30. 21.45. 47.90. 56.24. 116.57. 127.56. 130.00. 130.89. 132.33. 134.60. 135.00. 143.85. 166.44. 203.14; HRMS calcd for $C_{15}H_{17}NO_2$ MW 243.1259, found *m/z* 243.1268 (M^+); Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.05; N, 5.76. Found: C, 73.93; H, 7.09; N, 5.69.

***N*-benzylbenzazepine-1,5-dione 17e.** 33% yield, colorless oil; IR ($CHCl_3$) 1692, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (d, J = 7.1 Hz, 3H), 3.28 (q, J = 7.1 Hz, 1H), 4.64 (d, J = 14.2 Hz, 1H), 5.05 (s, 1H), 5.14 (s. 1H), 5.30 (d, J = 14.2 Hz, 1H), 7.31-7.37 (brs, 5H), 7.50-7.69 (m, 3H), 8.00 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.17, 53.13, 55.16, 114.97, 127.79, 127.88, 128.59, 128.79, 130.49, 131.13, 132.56, 133.78, 134.74, 137.13, 146.31, 166.78, 201.47; HRMS calcd for $C_{19}H_{17}NO_2$ MW 291.1259, found *m/z* 291.1270 (M^+); Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.32; H, 5.89; N, 4.81. Found: C, 78.04; H, 5.93; N, 4.68.

X-Ray Crystallographic Analyses of the Compounds 9b, 16d, and 17d

Table 3. Summary of Crystal Data and Structure Refinement for Compounds 9b, 16d, and 17d

	9b	16d	17d
formular	$C_{13}H_{13}NO_2$	$C_{14}H_{15}NO_2$	$C_{15}H_{17}NO_2$
formular weight	215.25	229.28	243.30
crystal description	colorless prism	colorless prism	colorless prism
crystal system	orthorhombic	orthorhombic	monoclinic
space group	pb_{ca} (#61)	pb_{ca} (#61)	C2/c (#15)
lattice type	primitive	primitive	C-centered
lattice constants			
a, Å	18.07 (3)	13.264 (3)	15.42 (1)
b, Å	14.120 (2)	16.267 (2)	9.547 (8)
c, Å	8.6076 (7)	11.35 (7)	19.049 (10)
ß, deg	—	—	110.13 (6)
volume, $Å^3$	2196.3 (4)	2448 (4)	2633 (3)
Z	8	8	8
density (calcd), g/cm^3	1.302	1.244	1.227
F_{000}	912.00	976.00	1040.00
residual R, R_w	0.039, 0.053	0.037, 0.058	0.054, 0.082
GOF	1.19	1.14	1.14
P	0.0470	0.0820	0.1270

The experiments have been performed by employing the Rigaku RAXIS-IV (for compounds **9b** and **17d**) and Rigaku AFC 7R (for compound **16d**) diffractmeters. Three standard reflections monitored every 150 reflections, showed no significant changes during data collection. The structures were solved by directed methods (SIR-92)[17] and refined anisotropically by full-matrix least-squares technique to minimize Σ ($w|\Delta F|^2$). The weighting scheme was based on counting statistics and included a factor, p, to downweight the intense reflections: $w = [s^2_c\ (Fo) + p^2/4Fo^2]^{-1}$. All calculations were performed using the teXsan[18] crystallographic software package. The crystallographic data are summarized in Table 3.

Acknowledgment

This work was supported by the Grant-in-Aid for Scientific Research on Priority Areas (No. 8245101) and for Scientific Research (B) (No. 8457585) from the Ministry of Education, Science, Sports, and Culture of

Japanese Government.

References and Notes

1. (a) Hesse M. "Ring Enlargement in Organic Chemistry", VCH Publishers, Inc., New York, 1991. (b) Lin M-S, Snieckus V. J. Org. Chem. 1971;36:645-650. (c) Reinhoudt DN, Kouwenhoven CG. Tetrahedron 1974;30:2093-2098. (d) Stork G, Macdonald TL. J. Am. Chem. Soc. 1975;97:1264-1265.
2. Dowd P, Zhang W. Chem. Rev. 1993;93:2091-2115.
3. (a) Fuks R, Viehe HG. In "Chemistry of the Acetylenes"; Viehe HG, Ed. New York: Marcel Dekker, 1969;435-439. (b) Cook AG. In "Enamines: Synthesis, Structure and Reactions"; Cook AG. Ed. New York: Marcel Dekker, 1969;230-232. (c) Reinhoudt DN, Verboom W, Visser GW, Trompenaars WP, Harkema S, Van Hummel GJ. J. Am. Chem. Soc. 1984;106:1341-1350.
4. (a) Schreiber SL. Science. 1985;227:857. (b) Crimmins MT. Chem. Rev. 1988;88:1453-1473. (c) Schuster DI, Lem G, Kaprinidis NA. Chem. Rev. 1993;93:3-22. (d) De Keukeleire D, He SL. Chem. Rev. 1993;93:359-380. (e) Winkler JD, Bowen CM, Liotta F. Chem. Rev. 1995;95:2003-2020.
5. (a) Busacca CA, Johnson RE. Tetrahedron Lett. 1992;33:165-168 and references cited therein. (b) Robl JAR, Karanewsky DS, Asaad MM. Tetrahedron Lett. 1995;36:1593-1596. (c) Ehrlich PP, Campbell JR. Tetrahedron Lett. 1996;37:7345-7348.
6. (a) Kanaoka Y, Migita Y, Koyama K, Sato Y, Nakai H, Mizoguchi T. Tetrahedron Lett. 1973;14:1193-1196. (b) Kanaoka Y, Koyama K, Flippen JL, Karle IL, Witkop B. J. Am. Chem. Soc. 1974;96:4719-4721. (c) Maruyama K, Kubo Y. Chem. Lett. 1978;851-854. (d) Machida M, Nakamura M, Oda K, Takechi H, Ohno K, Nakai H, Sato Y, Kanaoka Y. Heterocycles 1987;26:2683-2690. (e) Griesbeck AG, Mauder H. Angew. Chem. Int. Ed. Engl. 1992;31:73-75. (f) Paleo MR, Dominguez D, Castedo L. Tetrahedron Lett. 1993;34:2369-2370. (g) Lee YJ, Ling R, Mariano PS, Yoon UC, Kim DU, Oh SW. J. Org. Chem. 1996;61:3304-3314.
7. (a) Nagao Y, Lee WS, Kim K. Chem. Lett. 1994;389-392. (b) Nagao Y, Lee WS, Komaki Y, Sano S, Shiro M. Chem. Lett. 1994;597-600. (c) Nagao Y, Lee WS, Jeong I-Y, Shiro M. Tetrahedron Lett. 1995;36:2799-2802. (d) Lee WS, Nakazawa N, Shiro M, Nagao Y. Heterocycles 1996;43:1859-1862. (e) Lee WS, Jeong I-Y, Shiro M, Sano S, Nagao Y. Tetrahedron Lett. 1997;38:611-614.
8. Nagao Y, Jeong I-Y, Lee W S. Tetrahedron Lett. 1996;37:393-396.
9. Gibson MS, Bradshaw RW. Angew. Chem. Int. Ed. Engl. 1968;7:919-930.
10. Carey FA, Sundberg RJ. "Advanced Organic Chemistry 3rd ed.", Plenum Press, New York, 1990;361-365.
11. Nagao Y, Kim K, Sano S, Kakegawa H, Lee WS, Shimizu H, Shiro M, Katunuma N. Tetrahedron Lett. 1996;37:861-864.
12. (a) Daniels RG, Paquette LA. Tetrahedron Lett. 1981;22:1579-1582. (b) Suzuki M, Morita Y, Noyori R. J. Org. Chem. 1990;55:441-449. (c) Zhang L-J, Mo X-S, Huang J-L, Huang Y-Z. Tetrahedron Lett. 1993;34:1621-1624.
13. Yoon CY, Kim DK, Lee CH, Choi YS, Lee YJ, Ammon HL, and Mariano PS. J. Am. Chem. Soc. 1995;117:2968-2710.
14. Gibian MJ, Russo S. J. Org. Chem. 1984;49:4304-4306.
15. Gabriel S. Ber. dtsch. chem. Ges. 1891;24:3104-3107.
16. Rastetter WH, Spero DM, Adams J, Harpp DN, and Ash DK. J. Org. Chem. 1982;47:2785-2787.
17. (a) MITHRIL84: Gilmore CJ. J. Appl. Crystallogr. 1984;17:42-46. (b) SHELXS86: Sheldrick GM, Program for the solution of

crystal structures, University of Göttingen, Germany, 1985. (c) SIR92: Altomare A, Burla MC, Camalli M, Cascarano M, Giacovazzo C, Guagliardi A, Polidori G. J. Appl. Crystallogr. 1994;27:435.

18. teXsan: Crystal structure analysis package, Molecular Structure Corporation, 1996.