Stereospecific Synthesis of Bicyclic β-Lactams via Metal-Catalyzed Carbonylative Coupling and Cyclization Reactions

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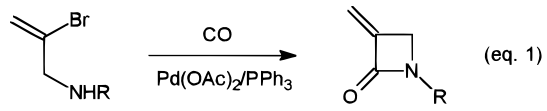
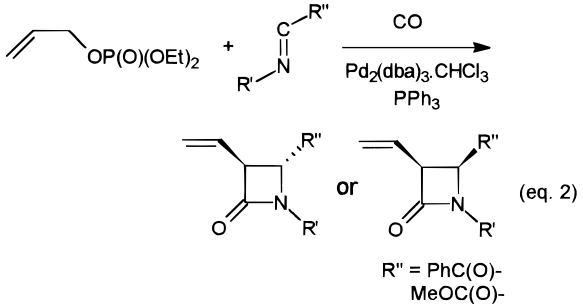
Bicyclic β-lactams were synthesized by the carbonylative coupling and cyclization reaction of 2-aryl-1,3-thiazines with allyl phosphates, catalyzed by bis(benzonitrile)palladium dichloride, using *N*,*N*-diisopropylethylamine as a base in tetrahydrofuran. Several rhodium complexes were also effective for this process. These transformations are stereospecific, with the aryl and vinyl groups on the β-lactam ring being *cis* to each other. This methodology provides a novel route for the preparation of the cepham analogs, *cis*-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-ones.

The synthesis of β-lactams has attracted widespread interest for many years.[1,2] In addition to conventional organic methodology,[1−8] transition metal complex-mediated synthesis of β-lactams has been the subject of a large number of investigations.[9,10] Although chromiumcarbonyl carbene complexes,[11−13] iron acyl complexes,[14−19] and iron vinylidenes[20,21] are elegant templates for the synthesis of a variety of β-lactams, they suffer the same disadvantage in that stoichiometric quantities of the metal complexes are required in all cases. Transition metal-catalyzed carbonylation[22] has proven to be a versatile method for the construction of the β-lactam skeleton.[9,10,23−34] Palladium acetate catalyzed carbonylation of amino vinyl halides (cf. eq 1)[23−25] provides a



(eq. 1)

convenient synthesis of the β-lactam ring. A recently reported route to monocyclic β-lactams involves Pd-catalyzed incorporation of carbon monoxide and an allylic moiety into imines with high stereoselectivity dependent on the nature of imines used (cf. eq 2).[33,34] Imines



(eq. 2)

conjugated with a carbonyl such as a ketone selectively give *cis*-β-lactams, whereas imines unconjugated with a carbonyl group specifically afford *trans*-β-lactams. The novel carbonylative ring expansion of aziridines catalyzed by rhodium (e.g. $[Rh(COD)Cl]_2$ or $[Rh(CO)_2Cl]_2$),[27,35] palladium (e.g. $Pd(PPh_3)_4$, $Pd(OAc)_2/PPh_3$, and $Pd(dba)_2{\cdot}CH_2Cl_2$),[26,28] and cobalt (e.g. $Co_2(CO)_8$)[29] complexes is a useful method for the synthesis of both monocyclic and bicyclic β-lactams. All of these processes are regiospecific and/or stereoselective. The reaction stereochemistry is strongly dependent on the catalyst used in the reaction (cf. eq 3), with retention of configuration occurring at the aziridine ring substituents when rhodium complexes were employed as the catalyst,[27,35] and inversion of configuration

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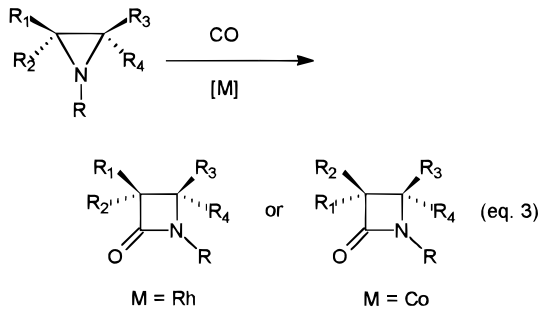
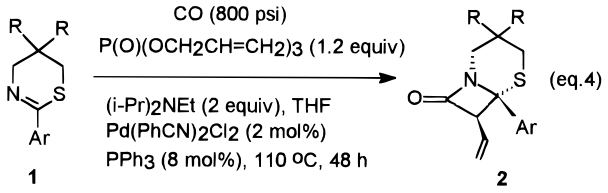


found when $Co_2(CO)_8$ was used as the catalyst.[29] These stereochemical features enables one to prepare a wide range of β-lactams in a completely stereospecific manner. Herein we report the stereospecific synthesis of bicyclic β-lactams by the palladium complex catalyzed carbonylative coupling and cyclization reaction of 2-aryl-1,3-thiazines with allyl phosphates. Several rhodium complexes are also effective for this transformation.

Results and Discussion

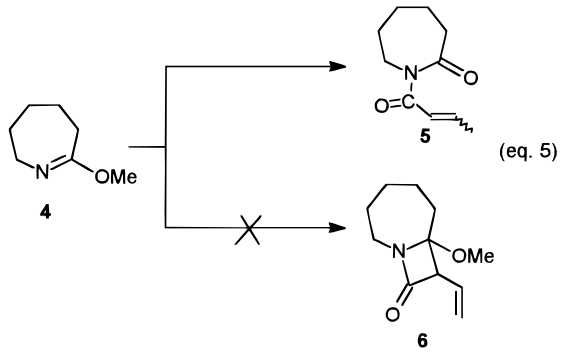
Treatment of 5,6-dihydro-5,5-dimethyl-2-phenyl-4*H*-1,3-thiazine, **1a** (cf. eq 4, Ar = Ph, R = CH_3), with 1.2 equiv of triallyl phosphate and 2 equiv of $(i\text{-}Pr)_2NEt$ in 10 mL of THF under 800 psi of CO at 110 °C for 48 h, with a catalytic amount of $Pd(PhCN)_2Cl_2$ (50/1 ratio of **1a**/Pd) and PPh_3 (4 equiv relative to Pd), afforded the bicylic β-lactam, **2a**, in 61% isolated yield. The reaction



proceeded with high selectivity giving *cis*-**2a** as the only product (Table 1, entry 3). Starting material was recovered when the reaction was effected in the absence of either the catalyst (entry 1) or $(i\text{-}Pr)_2NEt$ (entry 2). Prolonged heating did not increase the reaction yield (76 h versus 48 h) as illustrated in Table 1, entry 4, while decreasing (to 75 °C) or increasing (to 150 °C) the reaction temperature resulted in a reduction of the yield of **2a** (entries 5 and 6). Using allyl diethyl phosphate instead of triallyl phosphate as the allylic souce afforded the bicyclic β-lactam **2a** in comparable yield (entry 7), while allyl ethyl carbonate (entry 8) or allyl phenyl sulfone (entry 9) did not react with **1a**. Under the same conditions, $Pd(PPh_3)_2Cl_2$, $[Pd(2\text{-methylallyl})Cl]_2$, $[Rh(COD)Cl]_2$, and zwitterionic $(\eta^6\text{-}PhBPh_3)^-Rh^+(1,5\text{-}COD)$[36,37] were effective catalysts giving **2a**, in 60−64% yield (entries 10−13).

The carbonylative coupling and cyclization reaction of a series of 2-aryl-1,3-thiazine derivatives (**1a**−**d**) was effected using 1.2 equiv of $P(O)(OCH_2CH{=}CH_2)_3$, 2 equiv of $(i\text{-}Pr)_2NEt$, 2 mol % of $Pd(PhCN)_2Cl_2$, and 8 mol % of PPh_3, in THF at 800 psi CO for 48 h at 110 °C. The bicyclic β-lactams, in which the aryl and vinyl substituents are *cis* to each other, were isolated in 47−78% yield (Table 2). An electron-withdrawing group on the arene ring favors the formation of the bicyclic β-lactam in higher yield. Specifically, introducing a NO_2 group at the *para* position of the 2-aryl substituent resulted in an increase of the isolated yield (78% for **2b** versus 61% for **2a**, entries 1 and 2). In contrast, reaction of 5,6-dihydro-2-(4-methoxyphenyl)-4*H*-1,3-thiazine (**1d**) with CO and $P(O)(OCH_2CH{=}CH_2)_3$ under the same conditions afforded the bicyclic β-lactam (**2d**) in 47% isolated yield, which is lower when compared with 5,6-dihydro-2-phenyl-4*H*-1,3-thiazine (**1c**) (64% isolated yield, entries 3 and 4). Introducing a methyl group at the 2-position of the allyl unit afforded the corresponding β-lactams in lower yield, i.e. reaction of 2-methylallyl diethyl phosphate with **1a** and **1c** gave **2e** and **2f** in 32% and 40% isolated yield, respectively (entries 5 and 6). The methyl group on the terminal carbon of the allyl moiety, however, has less effect on the yield of the reaction. Treatment of **1c** with CO and $(EtO)_2P(O)(OCH_2CH{=}CH(Me))$ (E/Z = 9/1) resulted in the formation of the β-lactam (*cis*-**2g**) in 69% isolated yield with E/Z = 2/1 (entry 7). This suggests that the reaction may occur by the formation of the allyl−metal complex, along with double bond isomerization. Note that reaction of 5,6-dihydro-2-benzyl-4*H*-1,3-thiazine (**1e**) with CO and $P(O)(OCH_2CH{=}CH_2)_3$ gave numerous unidentified carbonylation products.

Only starting materials were recovered when 2-phenylthiazoline (**3**) was treated under the usual conditions. Reaction of 1-aza-2-methoxy-1-cycloheptene (**4**) with triallyl phosphate and carbon monoxide under otherwise identical conditions resulted in the formation of *N*-(1-propenylcarbonyl)azepinone (**5**), instead of the expected bicyclic β-lactam, 7-methoxy-8-vinyl-1-azabicyclo[5.2.0]-nonan-9-one (**6**, cf. eq 5). It is conceivable that **5** is formed via **6**, by S_N2 reaction on the methyl group, the phosphate possibly acting as a nucleophile.



The structures of **2a**−**g** were assigned on the basis of analytical and spectral data (cf. Experimental Section). Let us consider the characterization of **2a** as an example. A molecular ion peak was observed in the mass spectrum at *m*/*e* 273, and the occurrence of an intense infrared carbonyl stretching band at 1762 cm^{-1} suggested the presence of a β-lactam unit. The two chiral centers in the bicyclic β-lactam **2a** render all protons and carbons nonequivalent (except several of the phenyl protons and carbons). The two methyl groups of reactant **1a**, which appeared as a singlet in the ^1H NMR spectrum, became two singlets in **2a** (cf. Scheme 1). Meanwhile the two singlets assigned to the CH_2N and CH_2S protons in the substrate **1a** became two sets of AB doublets, and the equatorial-*H*'s were further split by coupling to each other (ABX). The doublet for the CH proton of the β-lactam ring was split into triplets by coupling to the vinyl protons. The ^{13}C spectrum of **2a** displayed a signal for the carbonyl carbon at 166.45 ppm which, along with

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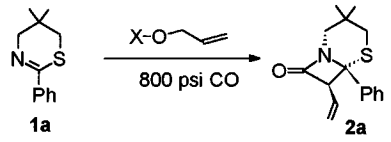
Table 1. Carbonylative Coupling and Cyclization of 1a to the Bicyclic β-Lactam 2a under Different Conditions[a]



No	Catalyst	X–O	Temp (°C)	Conv. (yield %)[b]
1	-	$(CH_2=CHCH_2O)_2P(O)$-	110	0
2	$Pd(PhCN)_2Cl_2$ + 4PPh_3[c]	$(CH_2=CHCH_2O)_2P(O)$-	110	0
3	$Pd(PhCN)_2Cl_2$ + 4PPh_3	$(CH_2=CHCH_2O)_2P(O)$-	110	72 (61)
4	$Pd(PhCN)_2Cl_2$ + 4PPh_3[d]	$(CH_2=CHCH_2O)_2P(O)$-	110	74 (62)
5	$Pd(PhCN)_2Cl_2$ + 4PPh_3	$(CH_2=CHCH_2O)_2P(O)$-	75	59 (49)
6	$Pd(PhCN)_2Cl_2$ + 4PPh_3	$(CH_2=CHCH_2O)_2P(O)$-	150	44 (36)
7	$Pd(PhCN)_2Cl_2$ + 4PPh_3	$(EtO)_2P(O)$-	110	73 (63)
8	$Pd(PhCN)_2Cl_2$ + 4PPh_3	EtO-C(O)-	110	0
9	$Pd(PhCN)_2Cl_2$ + 4PPh_3	$PhSO_2$-($CH_2CH=CH_2$)	110	0
10	$Pd(PPh_3)_2Cl_2$ + 2PPh_3	$(CH_2=CHCH_2O)_2P(O)$-	110	72 (60)
11	[ClPd–  –]$_2$ + 4PPh_3	$(CH_2=CHCH_2O)_2P(O)$-	110	74 (64)
12	$[Rh(COD)Cl]_2$	$(CH_2=CHCH_2O)_2P(O)$-	110	68 (60)
13	Rh(COD)(η^6-$PhBPh_3$)	$(CH_2=CHCH_2O)_2P(O)$-	110	66 (62)

[a] Reaction conditions: **1a**, 2 mmol; Catalyst, 2 mol% of M (M = Pd or Rh); $(i\text{-}Pr)_2NEt$, 4 mmol; allylic reagent, 2.4 mmol; Solvent, 10 mL THF; P_{CO} = 800 psi; 48h. [b] Determined by ^1H NMR with *cis*-**2a** as the only detectable product; yields are isolated yield; unreacted **1a** was recovered in all cases. [c] No $(i\text{-}Pr)_2NEt$. [d] 76 h.

other well separated resonances, is consistent with the bicyclic β-lactam structure.

The ^1H NMR resonances for the vinyl protons are diagnostic of the stereochemistry of **2a**–**g**. Normally, the C*H*=CH_2 unit shows two sets of well-separated multiplets with the methyne proton in the region of 6.0–7.0 ppm, and the methylene protons at 4.5–5.5 ppm, respectively.[28,34] However, the C*H*=CH_2 resonances in **2a**–**g** were shifted by about 1 ppm to higher field in all cases. This suggests that the vinyl group in these bicyclic β-lactams is *cis* to the aryl group with the C*H*=CH_2 proton situated under the aromatic ring. The structure and the stereochemistry of **2a**–**g** were confirmed by an X-ray crystallographic determination of **2c**.[38]

In conclusion, a useful method has been developed for the synthesis of bicyclic β-lactams by palladium and rhodium complex-catalyzed carbonylative coupling and cyclization of 2-aryl-1,3-thiazines and allylphosphates. These reactions proceed in a stereospecific manner affording *cis*-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-ones in good yield.

(38) Bensimon, C. Unpublished results.

Experimental Section

General. Column chromatography was performed with Merck Silica gel 60 (70–230 or 230–400 mesh) using solvent combinations determined via initial TLC analysis with Merck Silica gel 60 F_{254} plates (precoated). Analytically pure samples were obtained by JAI LC-908 preparative HPLC (column JAIGEL 2H). 1-Aza-2-methoxy-1-cycloheptene (**4**), triallyl phosphate, allyl ethyl carbonate, allyl phenyl sulfone, and *N*,*N*-diisopropylethylamine and all other chemicals for making allyl diethyl phosphate analogs and 2-aryl-1,3-thiazines were purchased from Aldrich, Lancaster, or Strem chemical companies and used as received. The metal complexes, $Pd(PhCN)_2Cl_2$,[22,39] $Pd(PPh_3)_2Cl_2$,[22] $[Pd(2\text{-methylallyl})Cl]_2$,[40,41] $[Rh(COD)Cl]_2$,[42] and (η^6-$PhBPh_3$)$^-$Rh$^+$(1,5-COD),[43] as well as allyl diethyl phosphate derivatives,[44–46] 2-aryl-1,3-thiazines,[47–49] and thiazolines[47,48]

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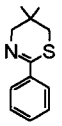
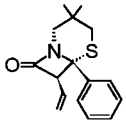
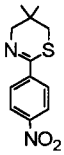
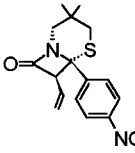
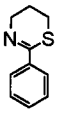
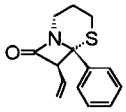
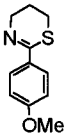
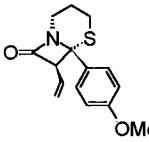
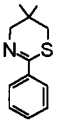
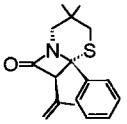
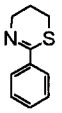
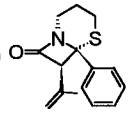
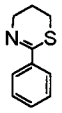
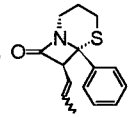
Table 2. Carbonylative Coupling and Cyclization of Different 1,3-Thiazines to Bicyclic β-Lactams[a]

No	Substrate	X–O	Product	Conv. (yield %)[b]
1	 **1a**	$(CH_2{=}CHCH_2O)_2P(O)$-	 **2a**	72 (61)
2	 **1b**	$(CH_2{=}CHCH_2O)_2P(O)$-	 **2b**	84 (78)
3	 **1c**	$(CH_2{=}CHCH_2O)_2P(O)$-	 **2c**	70 (64)
4	 **1d**	$(CH_2{=}CHCH_2O)_2P(O)$-	 **2d**	55 (47)
5	 **1a**	$(EtO)_2P(O)$-$(OCH_2C(Me){=}CH_2)$	 **2e**	(32)
6	 **1c**	$(EtO)_2P(O)$-$(OCH_2C(Me){=}CH_2)$	 **2f**	(40)
7	 **1c**	$(EtO)_2P(O)$-$(OCH_2CH{=}CHMe)$ *E*/*Z* = 9/1	 **2g** *E*/*Z* = 2/1	(69)

[a] Reaction conditions: Substrate, 2.0 mmol; Catalyst, $Pd(PhCN)_2Cl_2$, 2 mol%; PPh_3 = 8 mol%; $(i\text{-}Pr)_2NEt$, 4 mmol; $P(O)(OCH_2CH{=}CH_2)_3$, 2.4 mmol; Solvent, THF, 10 mL; P_{CO} = 800 psi; Temp, 110 °C; Time, 48 h. [b] Determined by ^1H NMR with *cis*-isomer as the only detectable product; yields are isolated yield; unreacted starting materials were recovered in all cases.

were prepared by following literature procedures and characterized by spectral methods.

5,6-Dihydro-5,5-dimethyl-2-phenyl-4*H*-1,3-thiazine (1a): mp, 47−48 °C; IR (neat) ν(C=N) 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78 (m, 2H), 7.39 (m, 3H), 3.61 (s, 2H), 2.86 (s, 2H), 1.10 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 157.18, 139.14, 130.15, 128.21, 126.16, 59.75, 38.23, 26.03, 23.96; MS (*m*/*e*) 205 [M^+]. Anal. Calcd for $C_{12}H_{15}NS$: C, 70.20, H, 7.36, N, 6.82. Found: C, 70.64, H, 7.40, N, 6.83.

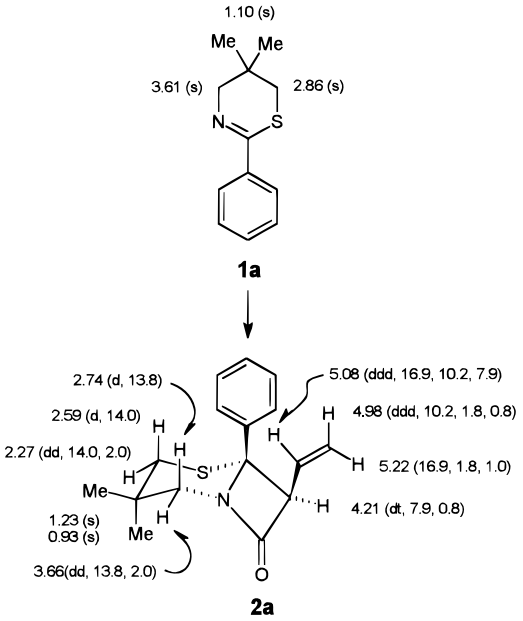
5,6-Dihydro-5,5-dimethyl-2-(4-nitrophenyl)-4*H*-1,3-thiazine (1b): mp, 78−80 °C; IR (neat) ν(C=N) 1594 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.23 (d, J = 9.0 Hz, 2H), 7.95 (d, J = 9.0 Hz, 2H), 3.66 (s, 2H), 2.90 (s, 2H), 1.10 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 155.39, 144.44, 127.19, 123.48, 60.03, 38.20, 26.01, 23.97; MS (*m*/*e*) 250 [M^+]. Anal. Calcd for $C_{12}H_{14}N_2O_2S$: C, 57.58, H, 5.64, N, 11.19. Found: C, 57.63, H, 5.30, N, 10.84.

5,6-Dihydro-2-phenyl-4*H*-1,3-thiazine (1c):[48,50] IR (neat) ν(C=N) 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (m, 2H), 7.37 (m, 3H), 3.92 (t, J = 5.8 Hz, 2H), 3.16 (t, J = 5.8 Hz, 2H), 1.91 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 157.88, 139.74, 130.16, 128.18, 126.15, 47.99, 26.47, 19.06; MS (*m*/*e*) 177 [M^+].

5,6-Dihydro-2-(4-methoxyphenyl)-4*H*-1,3-thiazine (1d): mp, 43−44 °C; IR (neat) ν(C=N) 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.73 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 3.89 (t, J = 5.5 Hz, 2H), 3.82 (s, 3H), 3.14 (t, J = 5.5 Hz, 2H), 1.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 161.27, 157.08, 132.30, 127.63, 113.45, 55.29, 47.95, 26.53, 19.28; MS (*m*/*e*) 207 [M^+]. Anal. Calcd for $C_{11}H_{13}NSO$: C, 63.74, H, 6.32, N, 6.76. Found: C, 63.82, H, 6.35, N, 6.63.

5,6-Dihydro-2-benzyl-4*H*-1,3-thiazine (1e):[49] IR (neat) ν(C=N) 1632 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (m, 5H), 3.70 (t, J

Scheme 1



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= 5.8 Hz, 2H), 3.62 (s, 2H), 2.98 (t, J = 5.8 Hz, 2H), 1.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 160.08, 136.84, 129.12, 128.41, 126.81, 48.56, 47.49, 26.44, 19.00; MS (*m/e*) 191 [M^+].

2-Phenyl-1,3-thiazoline (3):[47,48] IR (neat) ν(C=N) 1607 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 784 (m, 2H), 7.42 (m, 3H), 4.46 (t, J = 8.3 Hz, 2H), 3.41 (t, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 168.35, 133.16, 131.04, 128.71, 128.27, 65.16, 33.59; MS (*m/e*) 163 [M^+].

General Procedure for the Synthesis of Bicyclic β-Lactams by Carbonylative Coupling and Cyclization. To a 45-mL Parr autoclave fitted with a glass liner and stirring bar was added $Pd(PhCN)_2Cl_2$ (0.04 mmol), substrate (2.0 mmol), triphenylphosphine (0.16 mmol), *N*,*N*-diisopropylethylamine (4.0 mmol), allyl phosphate (2.4 mmol), and dry THF (10 mL). The CO line was flushed three times with CO and the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 800 psi with CO. The mixture was stirred in the autoclave at 110 °C (oil bath temperature) for 48−76 h. The excess CO was released, the system disassembled, and the solvent removed from the reaction mixture by rotary evaporation. The residue (analyzed by ^{1}H NMR) was separated by silica gel column chromatography using 3/1 (v/v) *n*-pentane/ether as the eluant followed by ether. The product was purified further by preparative HPLC. All products were fully characterized analytically and spectroscopically, as shown below. The structure assignment was obtained on the basis of a combination of COSY, HETCOR, and DEPT experiments.

3,3-Dimethyl-6-phenyl-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-one (2a): mp, 73−75 °C; IR (neat) ν(C=O) 1762 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.45 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 5.22 (ddd, J = 16.9, 1.8, 1.0 Hz, 1H), 5.08 (ddd, J = 16.9, 10.2, 7.9 Hz, 1H), 4.98 (ddd, J = 10.2, 1.8, 0.8 Hz, 1H), 4.21 (dt, J = 7.9, 0.8 Hz, 1H), 3.66 (dd, J = 13.8, 2.0 Hz, 1H), 2.74 (d, J = 13.8 Hz, 1H), 2.59 (d, J = 14.0 Hz, 1H), 2.27 (dd, J = 14.0, 2.0 Hz, 1H), 1.23 (s, 3H), 0.93 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.45, 137.44, 128.35, 128.68, 128.13, 127.68, 120.76, 69.10, 66.80, 49.18, 39.02, 28.21, 27.96, 23.75; MS (*m/e*) 273 [M^+]. Anal. Calcd for $C_{16}H_{19}NOS$: C, 70.29, H, 7.00, N, 5.12. Found: C, 69.98, H, 6.85, N, 5.29.

3,3-Dimethyl-6-(4-nitrophenyl)-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-one (2b): mp, 155−157 °C; IR (neat) ν(C=O) 1765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 9.1 Hz, 2H), 7.66 (d, J = 9.1 Hz, 2H), 5.29 (m, 1H), 5.06 (m, 1H), 4.32 (d, J = 6.0 Hz, 1H), 3.74 (dd, J = 14.2, 2.0 Hz, 1H), 2.72 (d, J = 14.2 Hz, 1H), 2.57 (d, J = 14.2 Hz, 1H), 2.34 (dd, J = 14.2, 2.0 Hz, 1H), 1.27 (s, 3H), 0.99 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.95, 147.66, 145.37, 128.68, 127.83, 123.57, 121.86, 69.36, 66.00, 49.37, 38.95, 28.09, 27.92, 23.60; MS (*m/e*) 318 [M^+]. Anal. Calcd for $C_{16}H_{18}N_2O_3S$: C, 60.36, H, 5.70, N, 8.80. Found: C, 60.37, H, 5.58, N, 8.83.

6-Phenyl-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-one (2c): mp, 80−81 °C; IR (neat) ν(C=O) 1761 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51−7.28 (m, 5H), 5.31−4.97 (m, 3H), 4.18 (d, J = 6.7 Hz, 1H), 4.16 (m, 1H), 3.08 (m, 1H), 2.65 (m, 2H), 1.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 166.00, 137.62, 128.35, 128.63, 128.06, 127.70, 120.73, 69.72, 67.39, 37.79, 25.68, 23.83; MS (*m/e*) 245 [M^+]. Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54, H, 6.16, N, 5.71. Found: C, 68.27, H, 6.07, N, 5.51.

6-(4-Methoxyphenyl)-7-vinyl-5-thia-1-azabicyclo[4.2.0]octan-8-one (2d): mp, 75−76 °C; IR (neat) ν(C=O) 1759 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40 (d, J = 9.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 5.31−4.99 (m, 3H), 4.14 (d, J = 6.5 Hz, 1H), 4.12 (m, 1H), 3.83 (s, 3H), 3.05 (m, 1H), 2.64 (m, 2H), 1.84 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 166.02, 159.21, 129.13, 129.04, 128.75, 120.53, 113.60, 69.64, 67.19, 55.21, 37.57, 25.65, 23.86; MS (*m/e*) 275 [M^+]. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43, H, 6.22, N, 5.09. Found: C, 65.06, H, 6.13, N, 4.98.

3,3-Dimethyl-6-phenyl-7-(1-methylvinyl)-5-thia-1-azabicyclo[4.2.0]octan-8-one (2e): mp, 134−135 °C; IR (neat) ν(C=O) 1760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.54 (m, 2H), 7.39 (m, 3H), 4.98 (m, J = ∼1.0 Hz, 1H), 4.77 (m, J = ∼1.5 Hz, 1H), 4.24 (s, 1H), 3.67 (dd, J = 13.8, 2.0 Hz, 1H), 2.67 (d, J = 13.8 Hz, 1H), 2.59 (d, J = 14.0 Hz, 1H), 2.30 (dd, J = 14.0, 2.0 Hz, 1H), 1.26 (s, 3H), 1.12 (s, 3H), 0.94 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.23, 136.33, 136.25, 128.19, 128.06, 127.82, 116.39, 72.66, 67.25, 48.74, 39.08, 28.08, 27.84, 23.75, 21.39; MS (*m/e*) 287 [M^+]. Anal. Calcd for $C_{17}H_{21}NOS$: C, 71.04, H, 7.36, N, 4.87. Found: C, 70.66, H, 7.33, N, 4.78.

6-Phenyl-7-(1-methylvinyl)-5-thia-1-azabicyclo[4.2.0]octan-8-one (2f): mp, 133−135 °C; IR (neat) ν(C=O) 1753 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.54 (m, 2H), 7.34 (m, 3H), 4.98 (m, J = ∼1.0 Hz, 1H), 4.78 (m, J = ∼1.5 Hz, 1H), 4.18 (s, 1H), 4.14 (m, 1H), 3.00 (m, 1H), 2.65 (m, 2H), 1.84 (m, 2H); 1.20 (s, 2H) ^{13}C NMR ($CDCl_3$) δ 165.96, 136.72, 136.35, 128.33, 128.08, 127.93, 116.57, 73.51, 67.97, 37.48, 25.86, 23.79, 21.42; MS (*m/e*) 259 [M^+]. Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46, H, 6.61, N, 5.40. Found: C, 69.78, H, 6.39, N, 5.52.

6-Phenyl-7-(1-propenyl)-5-thia-1-azabicyclo[4.2.0]octan-8-one (2g): oil; IR (neat) ν(C=O) 1756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.48−7.28 (m, 5H), 5.65 (m, 1H), 4.77 (m, 1H), 4.13 (d, J = 8.6 Hz, 1H), 4.14 (m, 1H), 3.06 (m, 1H), 2.65 (m, 2H), 1.84 (m, 2H), 1.65 (dd, J = 6.5, 1.7 Hz, minor isomer, CH_3), 1.47 (dm, J = 6.5, ∼0.8 Hz, major isomer, CH_3); ^{13}C NMR ($CDCl_3$) δ (major isomer) 166.81, 137.85, 132.27, 128.21, 127.87, 127.66, 121.36, 69.35, 64.35, 37.73, 25.67, 23.88, 17.85; ^{13}C NMR ($CDCl_3$) δ (minor isomer) 166.84, 130.75, 128.50, 127.93, 127.58, 120.36, 67.67, 37.87, 25.76, 24.01, 13.59, other signals are obscured by those of the major isomer; MS (*m/e*) 259 [M^+]; HRMS calcd for $C_{15}H_{17}NOS$: 259.1031, found: 259.1033.

***N*-(1-Propenylcarbonyl)azepinone (5):** oil; IR (neat) ν(C=O) 1699, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.99 (dqd, J = 15.1, 6.8, 0.5 Hz, 1H), 6.73 (dqd, J = 15.1, 1.5, 0.5 Hz, 1H), 3.89 (m, 2H), 2.72 (m, 2H), 1.91 (ddd, J = 6.8, 1.5, 0.5 Hz, 3H), 1.75 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 177.98, 168.76, 143.08, 126.24, 43.60, 39.52, 29.27, 28.62, 23.68, 18.23; MS (*m/e*) 181 [M^+]; HRMS calcd for $C_{10}H_{15}NO_2$ 181.1103, found 181.1095.

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