Pergamon

Tetrahedron 56 (2000) 1299–1307

TETRAHEDRON

Thermal Ene Reactions of 3-(Alk-2-enyl)benzylamino-2-(methoxycarbonyl)acrolein Derivatives Leading to 4,5-Dihydro-1*H*-azepines

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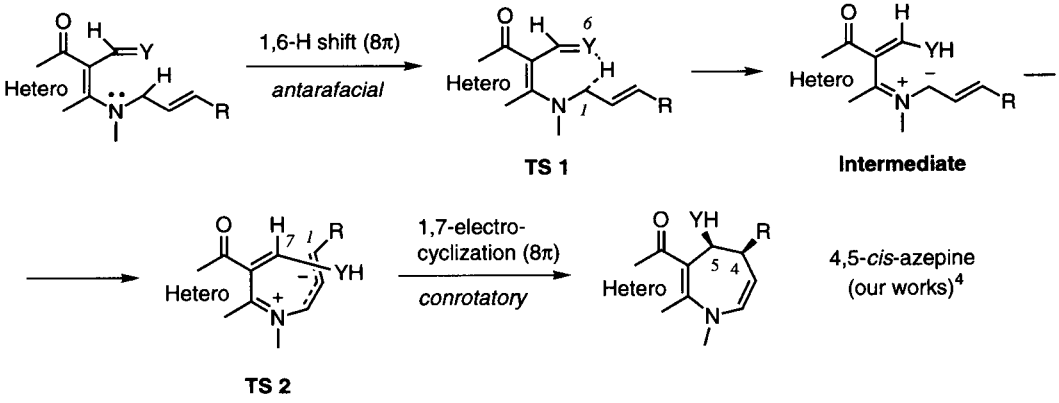
Received 11 November 1999; accepted 6 January 2000

Abstract—Thermal reaction of 3-(alk-2-enyl)benzylamino-2-(methoxycarbonyl)acrolein derivatives **3** gave 4,5-dihydro-1*H*-azepines **4** stereoselectively in good yields via an intramolecular carbonyl-ene reaction. Conjugated diene compounds **10** from acroleins **3** also underwent olefin-ene reaction to give azepine derivatives **11**. In these azepine-ring formation, the methoxycarbonyl group at the 2-position in **3** facilitated the progress of the reaction more effectively than the cyano group previously reported by us.

Introduction

Among the methodologies for the stereoselective synthesis of azepine derivatives from acyclic systems, much attention has been focused on the 1,7-cyclization of conjugated azomethine ylides totally bearing 8π electrons. The most popular access to the conjugated azomethine ylide substrates is concerned with the combination of an azomethine ylide (4π) and conjugated diene systems (4π), i.e. α,β,γ,δ-unsaturated azomethine ylides.[1–3] In previous papers,[4] we also reported the stereoselective azepine-ring formation by the cyclization of heterocyclic aldehydes and their imines bearing (alk-2-enyl)amino moieties at the neighboring position. Although the cyclization could be formally considered as 7 (1,4)-intramolecular carbonyl-[5] and imine-ene reactions,[6] the investigation on the mechanisms revealed that the azepine-ring formation consisted of two consecutive orbital-allowed reactions. Firstly, the [1,6] sigmatropic shift of the allylic hydrogen (**TS 1**) generates a conjugated azomethine ylide (**Intermediate**), which bears two 2π electron systems on the both carbon-termini of the parent azomethine ylide. Secondly, its [1,7] electrocyclic ring-closure (**TS 2**) gives the fused 4,5-*cis*-azepine stereoselectively (Scheme 1).[4d–f]



Scheme 1.

Keywords: azepines; ene reactions; cyclization; aldehydes.
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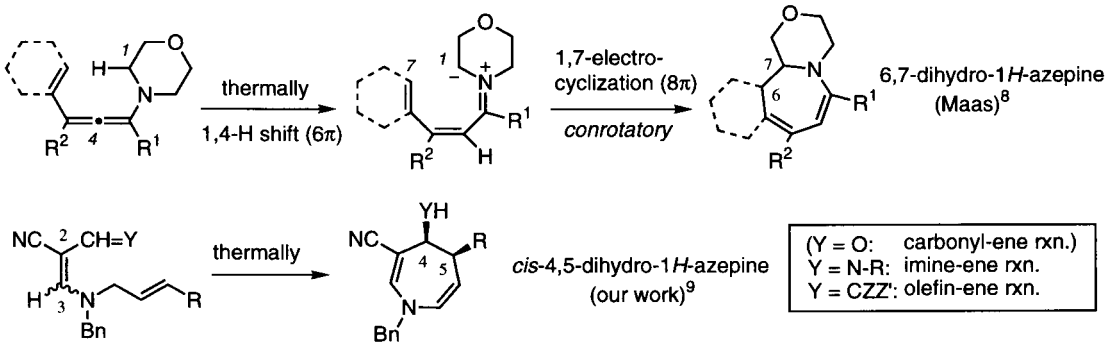


Scheme 2.

On the other hand, only a few precedents of the thermally induced cyclization of dialkylaminopolyenes such as 1-dimethylamino-1,3,4-pentatrienes[7] and 1-morpholino-3-vinylallenes[8] leading to azepine derivatives were found in the literatures, in which α,β,γ,δ-unsaturated azomethine ylides were postulated as intermediates generated by the sigmatropic shift of the hydrogen adjacent to the amino-nitrogen. More recently, we successfully extended our azepine-ring formation methodology to the imine and conjugated diene derivatives of 3-(alk-2-enyl)amino-2-cyanoacrolein, in which poly-functionalized 4,5-dihydro-1*H*-azepine derivatives were obtained efficiently and stereoselectively (Scheme 2).[9]

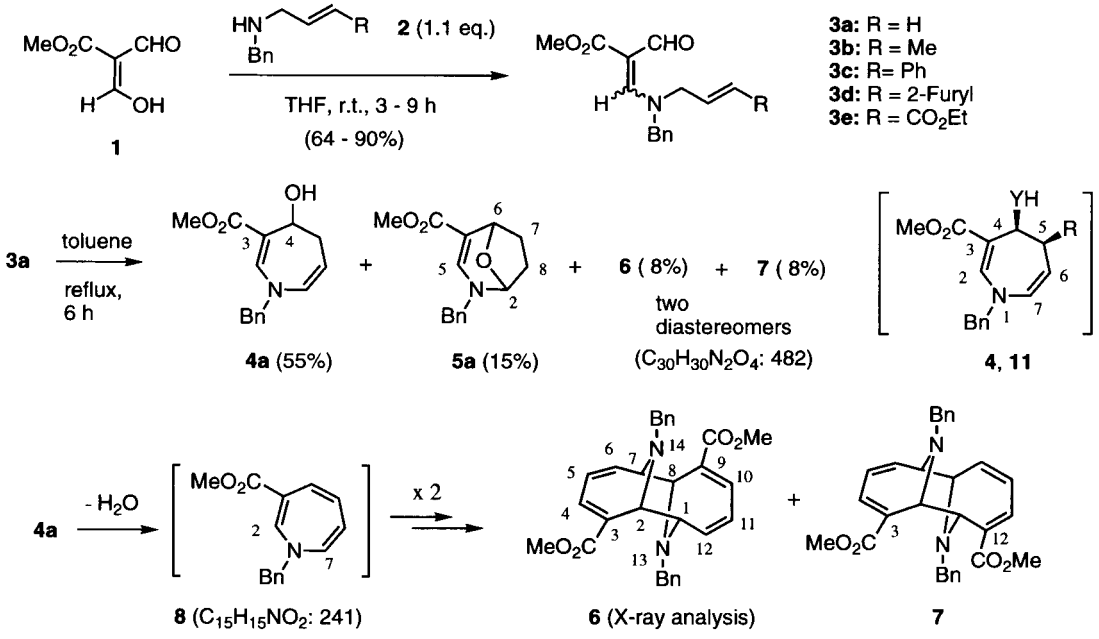
In this paper, we describe the thermal reaction of 3-[*N*-(alk-2-enyl)benzylamino]-2-(methoxycarbonyl)acrolein derivatives in order to examine the effects of the substituent at the 2-position of the acrolein derivatives on the azepine-ring formation.

Results and Discussion

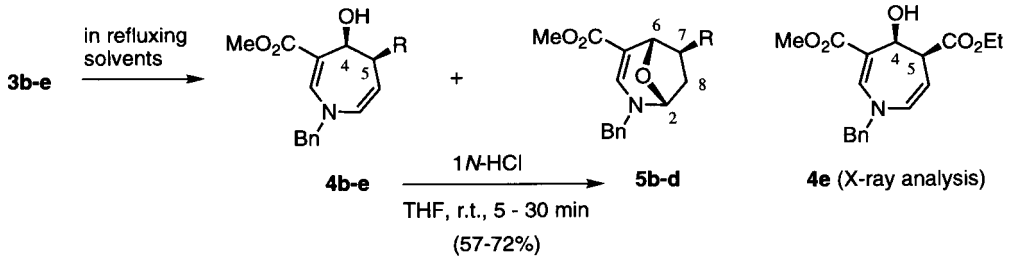
Carbonyl-ene reaction of 3-(alk-2-enyl)amino-2-(methoxycarbonyl)acrolein derivatives 3

A starting material 3-(*N*-allylbenzylamino)-2-(methoxycarbonyl)acrolein (**3a**) was prepared in a good yield in the reaction of 2-(methoxycarbonyl)malonaldehyde (**1**)[10] with *N*-allylbenzylamine (**2a**) in THF at room temperature. Similarly, reaction with *N*-[(*E*)-but-2-enyl]-(**2b**), *N*-[(*E*)-cinnamyl]- (**2c**), *N*-[(*E*)-3-(2-furyl)prop-2-enyl]-(**2d**), and *N*-[(*E*)-3-(ethoxycarbonyl)prop-2-enyl]-benzylamine (**2e**) gave also 3-(alk-2-enyl)benzylamino-2-(methoxycarbonyl)-acroleins **3b**–**e** as shown in Scheme 3. Acrolein derivatives **3** were obtained as ca (3:7) to (4:5) inseparable mixtures of two geometric isomers and the mixtures were utilized for the ene reaction without further purification.

A reaction of acrolein derivative **3a** in toluene heated under



Scheme 3.



Scheme 4.

Table 1. Carbonyl-ene reaction of 3-(alk-2-enyl)benzylamino-2-(methoxycarbonyl)acroleins **3b**–**e**

Run	Substrate	*R*	Solvent	Time (h)	Products (Yield %)[a]	
1	**3b**	Me	Toluene	24	**4b** (62)	**5b** (12)
2	**3c**	Ph	Benzene	20	**4c** (66)	**5c** (9)
3	**3d**	2-Furyl	Benzene	12	**4d** (71)	**5d** (19)
4	**3e**	CO_2Et	Benzene	6	**4e** (88)	–
5[b]	**3e**	CO_2Et	Toluene	2	**4e** (72)	–

[a] Based on isolated product.
[b] A mixture of unidentified products was also obtained.

reflux for 6 h gave the desired azepine **4a**, [1,3]oxazine **5a** and two diastereomeric products **6** and **7** in 55, 15, 8, and 8% yields, respectively. Under more harsh conditions (in refluxing xylene for 2 h), the corresponding yields of the products were shifted to 28, 26, 15, and 12%. The structure of **4a** was deduced to be 1-benzyl-3-(methoxycarbonyl)-4-hydroxy-4,5-dihydro-1*H*-azepine from its spectroscopic data in comparison with those of related azepine derivatives reported previously.[4] In the IR spectrum of **4a** the absorption at 3480 cm^{-1} was attributed to hydroxyl group and its ^1H NMR spectrum showed three vinyl protons, 2-, 6-H, and 7-H, characteristic to the enamine moieties and individual methylene and methine protons apart from methoxycarbonyl and benzyl groups. On the other hand, the structure of **5a** was deduced to be 3-benzyl-5-(methoxycarbonyl)-3,6-dihydro-2,6-ethano-2*H*-[1,3]oxazine, a secondary product from azepine **4a**, also on the basis of its spectroscopic data.

The molecular formula ($C_{30}H_{30}N_2O_4$: M_w 482) of products **6** and **7** corresponds to that of dimeric products of the fully conjugated azepine **8**, which is formed by dehydration of **4a**. The ^{13}C NMR spectra of **6** and **7** were almost identical with each other over the whole region. The signal patterns in the ^1H NMR spectra of both products **6** and **7** and their 2D-NOESY spectra exhibited one set of alignment of protons; olefin (δ=7.39)-olefin (ca 6.2)-olefin (ca 6.2)-methine (3.41)-methine proton (4.02) for **6** and olefin (δ=7.32)-olefin (6.25)-olefin (5.93)-methine (3.28)-methine proton (4.20) for **7**. The simple signal patterns in the ^1H and ^{13}C NMR spectra of **6** implied a symmetrical structure; the benzylic methylene protons were observed as singlet. On the other hand, the benzylic methylene protons of **7** were AB quartet. The structure of crystalline **6** was speculated to be the dimer coupled between the 2- and 7′-carbons (7- and 2′-carbons) of two moles of azepine **8** and confirmed unambiguously to be 13,14-dibenzyl-3,9-bis(methoxycarbonyl)-13,14-diazatricyclo[6.4.1.$1^{2,7}$]tetradecan-3,5,9,11-tetraene by the X-ray crystallographic analysis.[11] Consequently, the structure of **7** was deduced to be the corresponding 3,12-bis(methoxycarbonyl) derivative due to the dimerization by coupling between the 2- and 2′-carbons (7- and 7′-carbons) of two moles of **8**. The formation of products **6** and **7** is explained by the dimerization and its mechanism of *N*-substituted 1*H*-azepine proposed by Paquette and other groups.[12]

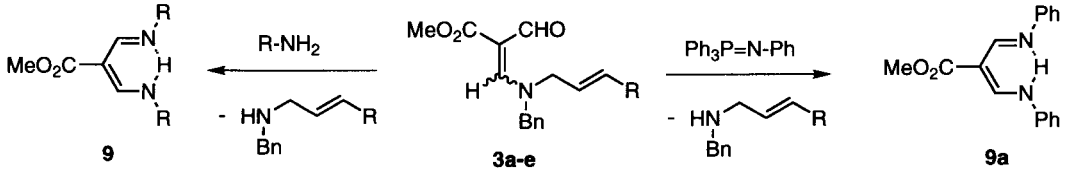
Similar thermal reaction of acrolein derivatives **3b**–**e** gave azepines **4b**–**e** and [1,3]oxazines **5b**–**d** in good to excellent total yields (Scheme 4 and Table 1). 4,5-*Cis* relationship of azepines **4b**–**e** was supported by the small vicinal coupling constants (ca 0 Hz) between the 4- and 5-H in comparison with that of the azepine obtained by the ene reaction of 3-{*N*-benzyl[(*E*)-3-(ethoxycarbonyl)prop-2-enyl]amino}-2-cyanoacrolein (ca 0 Hz).[9] The structure of azepine **4e** was also confirmed unambiguously by its X-ray crystallographic analysis.[11] The treatment of azepines **4** with 1N hydrochloric acid in THF gave [1,3]oxazines **5** in moderate to good yields. The stereochemistry of the substituents at the 7-position of **5b**–**d** was deduced to be *exo* also from small vicinal coupling constants between the bridge-head proton 6-H and 7-H (ca 0 Hz; 7-H: *endo*).[4,9]

As mentioned above, 2-(methoxycarbonyl)acrolein derivatives **3** underwent an intramolecular carbonyl-ene reaction to afford 4-hydroxy-4,5-dihydro-1*H*-azepines stereoselectively, while some 2-cyanoacrolein analogs except for 3-{*N*-benzyl[(*E*)-3-(ethoxycarbonyl)prop-2-enyl]amino}-2-cyanoacrolein, the most reactive one in the runs, did not give any azepine derivatives under similar or more harsh conditions. The methoxycarbonyl group at the 2-position of acrolein derivatives **3**, therefore, should facilitate the carbonyl-ene reaction more effectively than the cyano group.

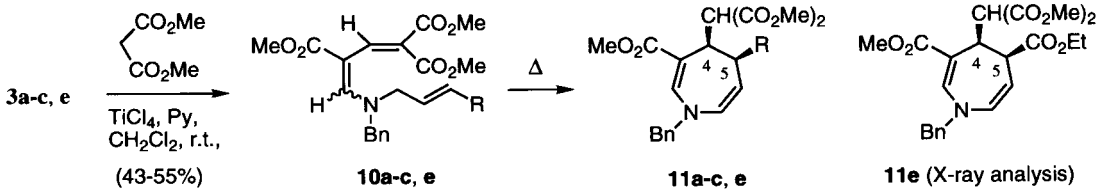
Stimulated by the above findings, we examine the reaction of acrolein derivatives **3** with primary amines to form the corresponding imines. Many efforts were made, yet products obtained in good to excellent yields were vinamidine derivatives **9**[13] in which acrolein derivatives **3** predominantly reacted with two moles of the amines. Utilizing *N*-(triphenylphosphoranylidene)aniline instead of aniline for the imine preparation also gave a disappointing result (Scheme 5). Therefore, our concern was turned toward the thermal reaction of conjugated diene compounds from acroleins **3**.

Olefin-ene reaction of conjugated diene compounds 10 from acroleins 3

Starting materials, methyl 5-*N*-(alk-2-enyl)benzylamino-



Scheme 5.



Scheme 6.

Table 2. Olefin-ene reaction of conjugated diene compounds **10** from acroleins **3**

Run	Substrate	*R*	Solvent	Temp (°C)	Time (h)	Product (Yield %)[a]
1	**10a**	H	Toluene	Reflux	12	**11a** (90)
2	**10b**	Me	Toluene	Reflux	20	**11b** (96)
3	**10c**	Ph	Toluene	Reflux	12	**11c** (92)
4[b]	**10e**	CO_2Et	Toluene	90	6	**11e** (72)
5	**10e**	CO_2Et	Benzene	70	12	**11e** (95)

[a] Based on isolated product.
[b] A mixture of unidentified products was also obtained.

2,4-bis(methoxycarbonyl)penta-2,4-dienates (**10a**–**c** and **10e**), were prepared in moderate yields by the condensation of acroleins **3a**–**c** and **3e** and dimethyl malonate in the presence of titanium tetrachloride and pyridine according to the method reported by Lehnert.[14] Conjugated diene compounds **10** existed as almost single isomers in the $CDCl_3$ solutions, while the 4-cyano analogs did as mixtures of *E*/*Z* isomers. The configuration of dienes **10**, however, could not be determined. Thermal reaction of diene compounds **10a**–**c** and **10e** in toluene or benzene gave the desired azepine derivatives **11a**–**c** and **11e** in almost quantitative yields (Scheme 6 and Table 2).

Fortunately, the structure of **11e** was confirmed to be 1-benzyl-5-(ethoxycarbonyl)-3-(methoxycarbonyl)-4-bis(methoxycarbonyl)methyl-4,5-dihydro-1*H*-azepine by its X-ray crystallographic analysis.[11] The structures of **11a**–**c** were also determined on the basis of their spectroscopic data in comparison with those of azepine **11e**. The results in Table 2 showed that the olefin-ene reaction of dienes **10** proceeded under milder conditions than that of the corresponding 2-cyano analogs.[9]

In order to obtain further understanding of the reaction features, the solvent effect on the reaction rates of diene **10c** was examined. Replacement of dioxane by more polar solvents such as DMF, propionitrile, and butan-1-ol resulted in reduced reaction rates [relative rates: dioxane (1.00), DMF (0.65), propionitrile (0.51), and butan-1-ol (0.41); see experimental section]. The same propensity for the rate-decreasing in polar solvents was observed in the carbonyl- and imine-ene reactions of 2-(*N*-allylbenzylamino)-3-formylpyrido[1,2-*a*]pyrimidine system.[4e]

Conclusion

We have described the stereoselective azepine-ring formation via intramolecular ene reactions of 3-(alk-2-enyl)-benzylamino-2-(methoxycarbonyl)acrolein derivatives **3** and **10**. The methoxycarbonyl substituent at the 2-position of **3** induced the reactivity with a nucleophile such as primary amines; acroleins **3** reacted with two moles of the amines to afford vinamidine derivatives. The substituent of **3** and **10** enhanced the reactivity toward the carbonyl- and olefin-ene reaction in comparison with the corresponding 2-cyano analogs. Although the exact reason remains unclear, we suggest that the electronic nature of the methoxycarbonyl group does not so much influence the rate of the thermal reaction, but its steric restriction may align the *N*-attached olefinic configuration more favorably toward the intramolecular ene reactions. Further details on the mechanistic aspects and investigations on the effect of the 2-position are in progress and will be reported elsewhere.

Experimental

General

Melting points were measured on a Yanagimoto micro

melting point apparatus and are uncorrected. IR spectra were measured on a JASCO IR-Report-100 spectrophotometer from samples as KBr pellets or NaCl discs. NMR spectra were measured on a JEOL EX-270 and/or EX-400 spectrometers (270 and 400 MHz of ^{1}H and 67.8 and for ^{13}C) in deuteriochloroform solutions unless otherwise stated. Tetramethylsilane was used as internal standard and *J* values are given in Hz. Splitting patterns are indicated as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal; and ov, overlapping signals. Mass spectra were determined on a JEOL JMS-SX102A spectrometer. Elemental analyses were performed on a Yanagimoto MT-5 CHN analyzer. All non-aqueous reactions were run under positive pressure of argon or nitrogen. All solvents were dried by standard methods before use. The progress of reactions was monitored by TLC (silica gel 60F-254, Merck). Chromatographic purification was performed with Wakogel C-200 (100–200 mesh, Wako Pure Chemical Industries) and/or silica-gel 60 (230–400 mesh, Merck).

Starting materials

Preparation of 3-(*N*-allylbenzylamino)-2-(methoxycarbonyl)acrolein (3a). Typical procedures. To a solution of 2-(methoxycarbonyl)malonaldehyde (**1**;[10] 0.81 g, 6.2 mmol) in THF (10 ml) added *N*-allylbenzylamine (**2a**; 1.00 g, 6.8 mmol) and the mixture was stirred at room temperature for 9 h. The solvent was evaporated and the residue was subjected to column chromatography on silica-gel to afford 3-(*N*-allylbenzylamino)-2-(methoxycarbonyl)acrolein (**3a**; 1.44 g, 90%) with hexane/ethyl acetate (5/1).

3-(*N*-Allylbenzylamino)-2-(methoxycarbonyl)acrolein (3a). Pale yellow oil. $C_{15}H_{17}NO_3$ (259.3): calcd C, 69.48; H, 6.61; N, 5.40%; found C, 69.18; H, 6.77; N, 5.61%. This compound was a (4:5) mixture of two geometric isomers in $CDCl_3$. Major isomer: ^{1}H NMR ($CDCl_3$) δ=3.77 (3H, s, OMe), 3.93 (2H, br d, *J*=5.3 Hz, >NC*H*$_2$CH=), 4.61 (2H, s, C*H*$_2$Ph), 5.09–5.35 (2H, ov, =C*H*$_2$), 5.75 (1H, m, –C*H*=CH$_2$), 7.16–7.39 (5H, ov, Ph), 7.90 (1H, br s, 3-H), 9.75 (1H, s, 1-H). Assigned signals for minor isomer: ^{1}H NMR ($CDCl_3$) δ=4.26 (2H, br d, *J*=5.7 Hz, >NC*H*$_2$CH=), 4.97 (2H, s, C*H*$_2$Ph).

Similarly, acrolein derivatives **3b**–**e** were obtained.

3-{*N*-Benzyl[(*E*)-but-2-enyl]amino}-2-(methoxycarbonyl)-acrolein (3b). Yield: 76%; pale yellow oil. $C_{16}H_{19}NO_3$ (273.3): calcd C, 70.31; H, 7.01; N, 5.12%; found C, 70.56; H, 7.16; N, 5.12%. This compound was a (4:5) mixture of two geometric isomers in $CDCl_3$. Major isomer: ^{1}H NMR ($CDCl_3$) δ=1.71 (3H, d, *J*=6.3 Hz, =CH*Me*), 3.76 (3H, s, OMe), 3.86 (2H, d, *J*=6.0 Hz, >NC*H*$_2$CH=), 4.59 (2H, s, C*H*$_2$Ph), 5.43, 5.63 (each 1H, each m, –C*H*=C*H*–), 7.15–7.38 (5H, ov, Ph), 7.88 (1H, br s, 3-H), 9.74 (1H, s, 1-H). Assigned signals for minor isomer: ^{1}H NMR ($CDCl_3$) δ=4.15 (2H, br d, *J*=5.7 Hz, >NC*H*$_2$CH=), 4.99 (2H, s, C*H*$_2$Ph).

3-{*N*-Benzyl[(*E*)-cinnamyl]amino}-2-(methoxycarbonyl)-acrolein (3c). Yield: 72%; pale yellow oil. $C_{21}H_{21}NO_3$ (335.4): calcd C, 75.20; H, 6.31; N, 4.18%; found C, 75.07; H, 6.43; N, 4.08%. This compound was a (2:3) mixture of two geometric isomers in $CDCl_3$. Major isomer: ^{1}H NMR ($CDCl_3$) δ=3.75 (3H, s, OMe), 4.12 (2H, d, *J*=6.6 Hz, >NC*H*$_2$CH=), 4.65 (2H, s, C*H*$_2$Ph), 6.30 (1H, td, *J*=6.6 and 15.8 Hz, –C*H*=CH–Ph), 6.42 (1H, br d, *J*=15.8 Hz, =C*H*–Ph), 7.22–7.37 (10H, ov, Ph), 7.94 (1H, s, 3-H), 9.77 (1H, s, 1-H). Assigned signals for minor isomer: ^{1}H NMR ($CDCl_3$) δ=3.74 (3H, s, OMe), 4.41 (2H, d, *J*=6.0 Hz, >NC*H*$_2$CH=), 5.05 (2H, s, C*H*$_2$Ph), 6.51 (1H, br d, *J*=15.8 Hz, =C*H*–Ph).

3-{*N*-Benzyl[(*E*)-3-(2-furyl)prop-2-enyl]amino}-2-(methoxycarbonyl)acrolein (3d). Yield: 83%; yellow oil. $C_{19}H_{19}NO_4$ (325.4): calcd C, 70.14; H, 5.89; N, 4.31%; found C, 70.11; H, 5.92; N, 4.29%. This compound was a (4:5) mixture of two geometric isomers in $CDCl_3$. Major isomer: ^{1}H NMR ($CDCl_3$) δ=3.75 (3H, s, OMe), 4.05 (2H, d, *J*=6.3 Hz, >NC*H*$_2$CH=), 4.65 (2H, s, C*H*$_2$Ph), 6.04 (1H, m, furyl 3-H), 6.34 (3H, ov, –C*H*=C*H*– and furyl 4-H), 7.22–7.37 (6H, ov, Ph and furyl 5-H), 7.92 (1H, s, 3-H), 9.77 (1H, s, 1-H). Assigned signals for minor isomer: ^{1}H NMR ($CDCl_3$) δ=3.77 (3H, s, OMe), 4.38 (2H, d, *J*=6.7 Hz, >NC*H*$_2$CH=), 5.02 (2H, s, C*H*$_2$Ph).

3-{*N*-Benzyl[(*E*)-3-(ethoxycarbonyl)prop-2-enyl]-amino}-2-(methoxycarbonyl)acrolein (3e). Yield: 64%; yellow oil. $C_{18}H_{21}NO_5$ (331.4): calcd C, 65.24; H, 6.39; N, 4.23%; found C, 65.33; H, 6.42; N, 4.28%. This compound was a (2:3) mixture of two geometric isomers in $CDCl_3$. Major isomer: ^{1}H NMR ($CDCl_3$) δ=1.26 (3H, t, *J*=7.3 Hz, CH$_2$C*H*$_3$), 3.75 (3H, s, OMe), 4.07 (2H, d, *J*=6.7 Hz, >NC*H*$_2$CH=), 4.11–4.23 (2H, ov, C*H*$_2$CH$_3$), 4.60 (2H, s, C*H*$_2$Ph), 5.77 (1H, ov, =C*H*–Es), 6.70–6.88 (1H, ov, –C*H*=CH–Es), 7.21–7.37 (5H, ov, Ph), 7.95 (1H, br s, 3-H), 9.77 (1H, br s, 1-H). Assigned signals for minor isomer: ^{1}H NMR ($CDCl_3$) δ=3.78 (3H, s, OMe), 4.62 (2H, s, C*H*$_2$Ph), 7.79 (1H, br s, 3-H).

Preparation of Methyl 5-(*N*-allylbenzylamino)-2,4-bis(methoxycarbonyl)penta-2,4-penta-2,4-dienate (10a). Typical procedures. To a solution of $TiCl_4$ (0.22 ml, 2 mmol) in THF (7 ml) cooled at 0°C added acrolein **3a** (0.267 g, 1 mmol) and dimethyl malonate (0.198 g, 1.5 mmol) in THF (1 ml), and the mixture was stirred at the same temperature for 1 h. Pyridine (0.32 ml, 4.0 mmol) was added to the mixture and the reaction mixture was allowed to stand at room temperature for 8 h. After quenching the reaction with water, the mixture was extracted with ethyl acetate (3×10 ml) and the organic layer was evaporated to give a residue. The residue was subjected with column chromatography on silica-gel to afford conjugated diene **10a** (0.177 g, 47%) with hexane/ethyl acetate (2/1).

Methyl 5-(*N*-allylbenzylamino)-2,4-bis(methoxycarbonyl)-penta-2,4-dienate (10a). Pale yellow prisms from hexane-ethyl acetate; mp 64–65°C; ^{1}H NMR ($CDCl_3$) δ=3.63, 3.68, 3.74 (each 3H, each s, OMe), 3.93 (2H, dd, *J*=0.7 and 5.7 Hz, >NC*H*$_2$CH=), 4.55 (2H, s, C*H*$_2$Ph), 5.25 (1H, br dd, *J*=1.0 and 17.2 Hz, =C*H*H), 5.35 (1H, br d, *J*=9.2 Hz, =CH*H*), 5.86 (1H, m, –C*H*=CH$_2$), 7.21–7.43 (5H, ov, Ph), 7.71 (1H, s, 3-H), 7.81 (1H, s, 5-H); ^{13}C NMR ($CDCl_3$) δ=51.2, 51.6, 52.0 (OMe), 55.3 (*C*H$_2$Ph), 58.6

(>N*C*H$_2$CH=), 95.8 (2-C), 119.2 (4-C), 120.6 (=*C*H$_2$), 127.4, 128.3, 129.0, 135.4 (Ph–C), 132.1 (–*C*H=CH$_2$), 140.6 (3-C), 154.3 (5-C), 165.7, 166.6, 167.7 (CO_2). $C_{20}H_{23}NO_6$ (373.3): calcd C, 64.33; H, 6.28; N, 3.75%; found C, 64.16; H, 6.33; N, 3.79%.

Similarly, diene compounds **10b**,**c**,**e** were obtained.

Methyl 5-{*N*-benzyl[(*E*)-but-2-enyl]amino}-2,4-bis-(methoxycarbonyl)penta-2,4-dienate (10b). Yield: 55%; pale yellow needles from hexane–benzene; mp 78–79°C; ^{1}H NMR ($CDCl_3$) δ=1.75 (3H, dd, *J*=1.3 and 6.3 Hz, =CH–*Me*), 2×3.66, 3.74 (total 9H, each s, OMe), 3.86 (2H, dd, *J*=0.7 and 5.7 Hz, >NC*H*$_2$CH=), 4.55 (2H, s, C*H*$_2$Ph), 5.48, 5.66 (each 1H, each m, –C*H*=C*H*–), 7.20–7.42 (5H, ov, Ph), 7.71 (1H, s, 3-H), 7.79 (1H, s, 5-H); ^{13}C NMR ($CDCl_3$) δ=17.7 (=CH–*Me*), 51.1, 51.6, 51.9 (OMe), 54–60 (br, *C*H$_2$Ph and >N*C*H$_2$CH=), 95.5 (2-C), 120.0 (4-C), 124.8 (=*C*H–Me), 127.2, 128.1, 128.9, 135.6 (Ph–C), 131.4 (–C*H*=CH–Me), 140.8 (3-C), 154.3 (5-C), 165.7, 166.6, 167.8 (CO_2). $C_{21}H_{25}NO_6$ (387.4): calcd C, 65.10; H, 6.50; N, 3.62%; found C, 65.10; H, 6.54; N, 3.65%.

Methyl 5-{*N*-benzyl[(*E*)-cinnamyl]amino}-2,4-bis-(methoxycarbonyl)penta-2,4-dienate (10c). Yield: 43%; pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=3.63, 3.66, 3.74 (each 3H, each s, OMe), 4.09 (2H, d, *J*=5.3 Hz, >NC*H*$_2$CH=), 4.61 (2H, s, C*H*$_2$Ph), 6.17 (1H, td, *J*=5.3 and 15.8 Hz, –C*H*=CH–Ph), 6.51 (1H, d, *J*=15.8 Hz, =C*H*–Ph), 7.24–7.44 (10H, ov, Ph), 7.74 (1H, s, 3-H), 7.86 (1H, s, 5-H); ^{13}C NMR ($CDCl_3$) δ=51.2, 51.6, 52.0 (OMe), 54–60 (br, *C*H$_2$Ph and >N*C*H$_2$CH=), 95.9 (2-C), 120.7 (4-C), 123.1 (=C*H*–Ph), 126.5, 127.3, 128.2, 128.6, 129.0, 134.5, 135.5, 135.7 (Ph–C and –*C*H=CH–Ph), 140.7 (3-C), 154.2 (5-C), 165.6, 166.5, 167.7 (CO_2). $C_{26}H_{27}NO_6$ (449.5): calcd C, 69.47; H, 6.05; N, 3.12%; found C, 69.99; H, 6.24; N, 3.25%. $C_{26}H_{27}NO_6$: calcd 449.1839; observed *m/z* (EI) 449.1826.

Methyl 5-{*N*-benzyl[(*E*)-3-(ethoxycarbonyl)prop-2-enyl]-amino}-2,4-bis(methoxycarbonyl)penta-2,4-dienate (10e). Yield: 53%; yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.31 (3H, t, *J*=7.3 Hz, CH$_2$C*H*$_3$), 3.66, 3.68, 3.75 (each 3H, each s, OMe), 4.06 (2H, dd, *J*=1.7 and 5.0 Hz, >NC*H*$_2$CH=), 4.22 (2H, q, *J*=7.3 Hz, C*H*$_2$CH$_3$), 4.55 (2H, s, C*H*$_2$Ph), 5.95 (1H, td, *J*=1.7 and 15.8 Hz, =C*H*–Es), 6.87 (1H, td, *J*=5.0 and 15.8, >NCH$_2$C*H*=), 7.21–7.43 (5H, ov, Ph), 7.63 (1H, s, 3-H), 7.63 (1H, s, 5-H); ^{13}C NMR ($CDCl_3$) δ=14.1 (*C*H$_2$CH$_3$), 51.3, 52.1, 52.4 (OMe), 54.5 (br, *C*H$_2$Ph), 56–59 (br, >N*C*H$_2$CH=), 60.8 (*C*H$_2$CH$_3$), 96.5 (2-C), 122.0 (4-C), 124.2 (=*C*H–Es), 127.4, 128.5, 129.1, 136.0 (Ph–C), 140.1 (3-C), 141.2 (–*C*H=CH–Es), 165.2, 165.3, 166.2, 167.4 (CO_2). $C_{23}H_{27}NO_8$ (445.5): calcd C, 62.01; H, 6.58; N, 3.14%; found C, 62.44; H, 6.29; N, 3.25%. $C_{23}H_{27}NO_8$: calcd 445.1737; observed *m/z* (EI) 445.1730.

Carbonyl-ene reaction of 3-(alk-2-enyl)amino-2-(methoxycarbonyl)acrolein derivatives 3

Thermal Reaction of Acrolein Derivative 3a. Typical procedures. A solution of **3a** (0.232 g, 0.896 mmol) in toluene (10 ml) was heated under reflux for 6 h. After evaporating the toluene, the residue was subjected to column chromatography on silica-gel to afford **6** (0.019 g, 8%) and **7** (0.019 g, 8%) with hexane/ethyl acetate (10/1), **5a** (0.035 g, 15%) with hexane/ethyl acetate (5/1), and **4a** (0.128 g, 55%) with hexane/ethyl acetate (3/1), respectively.

1-Benzyl-4-hydroxy-3-(methoxycarbonyl)-4,5-dihydro-1*H*-azepine (4a). Pale yellow oil; IR (NaCl) $\tilde{\nu}$ = 3480, 1710, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.36 (1H, dddd, *J*=1.7, 4.3, 8.3, and 14.1 Hz, 5-H), 2.47–2.58 (2H, ov, 5-H and OH), 3.72 (3H, s, OMe), 4.57 (2H, s, C*H*$_2$Ph), 5.10 (1H, ddd, *J*=5.3, 8.3, and 8.6 Hz, 6-H), 5.20 (1H, br dd, *J*=4.3 and 5.3 Hz, 4-H), 5.94 (1H, ddd, *J*=1.2, 1.7, and 8.6 Hz, 7-H), 7.21–7.40 (5H, ov, Ph), 7.59 (1H, d, *J*=1.2 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=33.4 (5-C), 51.4 (OMe), 62.6 (*C*H$_2$Ph), 66.7 (4-C), 107.5 (3-C), 109.9 (6-C), 126.7, 127.9, 128.9, 136.8 (Ph–C), 132.4 (7-C), 145.7 (2-C), 169.0 (CO_2). $C_{15}H_{17}NO_3$: calcd 259.1200; observed *m/z* (EI) 259.1208.

3-Benzyl-5-(methoxycarbonyl)-3,6-dihydro-2,6-ethano-2*H*-[1,3]oxazine (5a). Pale yellow oil; IR (NaCl) $\tilde{\nu}$ = 1700, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.99–2.17 (4H, ov, 7-H$_2$ and 8-H$_2$), 3.67 (3H, s, OMe), 4.33 (2H, s, C*H*$_2$Ph), 4.99 (1H, dd, *J*=1.0 and 2.3 Hz, 2-H), 5.03 (1H, d, *J*=2.0 Hz, 6-H), 7.21(1H, d, *J*=1.0 Hz, 4-H), 7.25–7.39 (5H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ=35.7, 37.3 (7- and 8-C), 50.5 (OMe), 56.6 (*C*H$_2$Ph), 74.3 (6-C), 87.1 (2-C), 103.9 (5-C), 127.6, 127.9, 128.8, 136.5 (Ph–C), 142.7 (4-C), 166.3 (CO_2). $C_{15}H_{17}NO_3$ (259.3): calcd C, 69.48; H, 6.61; N, 5.40%; found C, 70.24; H, 6.72; N, 5.52%. $C_{15}H_{17}NO_3$: calcd 259.1199; observed *m/z* (EI) 259.1208.

13,14-Dibenzyl-3,9-bis(methoxycarbonyl)-13,14-diaza-tricyclo[6.4.1.1^{2,7}]tetradecan-3,5,9,11-tetraene (6). Colorless prisms from hexane–propan-2-ol; mp 183–184°C; IR (KBr) $\tilde{\nu}$ = 1700, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.41 (2H, dd, *J*=4.3 and 4.9 Hz, 1- and 7-H), 3.47 (4H, s, 2×C*H*$_2$Ph), 3.66 (6H, s, 2×OMe), 4.02 (2H, t, *J*=1.3 Hz, 2- and 8-H), 6.15–6.28 (4H, ov, 5-, 6-, 11-, and 12-H), 7.13–7.23 (10H, ov, Ph), 7.39 (2H, dd, *J*=1.6 and 6.9 Hz, 4- and 10-H); ^{13}C NMR ($CDCl_3$) δ=51.8 (MeO), 56.8 (*C*H$_2$Ph), 59.6 (1- and 7-C), 60.9 (2- and 8-C), 124.1 (5- and 11-C), 126.8, 128.0, 128.1, 135.0 (Ph–C), 134.8 (6- and 12-C), 138.7 (3- and 9-C), 143.4 (4- and 10-C), 168.1 (CO_2). $C_{30}H_{30}N_2O_4$ (482.6): calcd C, 74.67; H, 6.27; N, 5.81%; found C, 74.56; H, 6.32; N, 5.82%. The structure of this compound was confirmed by X-ray crystal structure analysis.[11]

13,14-Dibenzyl-3,12-bis(methoxycarbonyl)-13,14-diaza-tricyclo[6.4.1.1^{2,7}]tetradecan-3,5,9,11-tetraene (7). Yellow oil. We did not succeed in isolating this compound as a pure form and, however, its structure was deduced by the spectroscopic data as follows. ^{1}H NMR ($CDCl_3$) δ=3.28 (1H, d, *J*=5.9 Hz, 7- and 8-H), 3.41, 3.51 (each 2H, each d, *J*=13.5 Hz, 2×C*H*$_2$Ph), 3.74 (6H, s, 2×OMe), 4.20 (2H, br s, 1- and 2-H), 5.93 (2H, dd, *J*=5.9 and 11.2 Hz, 6- and 12-H), 6.25 (1H, dd, *J*=7.9 and 11.2 Hz, 5- and 11-H), 7.17–7.25 (10H, ov, Ph), 7.32 (2H, d, *J*=7.9 Hz, 4- and 10-H); ^{13}C NMR ($CDCl_3$) δ=51.9 (MeO), 56.8 (*C*H$_2$Ph), 58.1 (1- and 2-C), 61.2 (7- and 8-C), 124.7 (5 and 11-C), 126.8, 127.9,

128.3, 135.8 (Ph–C), 133.9 (6- and 12-C), 138.6 (3- and 9-C), 141.7 (4- and 10-C), 168.3 (CO_2); MS (EI) *m*/*z*: 482 (M^+), 364, 241.

Similarly, thermal reaction of acrolein derivatives **3b**–**e** gave azepine **4b**–**e** and/or [1,3]oxazines **5b**–**d** and the results are demonstrated in Table 1.

4*S,5*S**)-(±)-1-Benzyl-4-hydroxy-3-(methoxycarbonyl)-5-methyl-4,5-dihydro-1*H*-azepine (4b).** Pale yellow oil; IR (NaCl) $\tilde{\nu}$ = 3480, 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.22 (3H, d, *J*=6.9 Hz, 5-Me), 1.77 (1H, br s, OH), 2.58 (1H, m, 5-H), 3.72 (3H, s, OMe), 4.56 (2H, s, C*H*$_2$Ph), 4.75 (1H, ddd, *J*=1.0, 4.3, and 8.9 Hz, 6-H), 4.98 (1H, s, 4-H), 5.86 (1H, td, *J*=1.7 and 8.9 Hz, 7-H), 7.21–7.40 (5H, ov, Ph), 7.60 (1H, d, *J*=1.0 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=19.5 (5-Me), 37.7 (5-C), 51.4 (OMe), 62.6 (*C*H$_2$Ph), 71.7 (4-C), 107.7 (3-C), 115.5 (6-C), 126.8, 128.0, 128.9, 136.9 (Ph–C), 130.0 (7-C), 145.7 (2-C), 168.8 (CO_2). $C_{16}H_{19}NO_3$ (273.3): calcd C, 70.31; H, 7.01; N, 5.12%; found C, 70.38; H, 7.06; N, 5.13%.

(2*R,6*S**,7*S**)-(±)-3-Benzyl-5-(methoxycarbonyl)-7-methyl-3,6-dihydro-2,6-ethano-2*H*-[1,3]oxazine (5b).** Colorless prisms from hexane; mp 82–83°C; IR (KBr) $\tilde{\nu}$ = 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.01 (3H, d, *J*=7.3 Hz, 7-Me), 1.59 (1H, ddd, *J*=2.6, 6.3, and 13.2 Hz, 8-H), 2.22 (1H, dd, *J*=8.3 and 13.2 Hz, 8-H), 2.57 (1H, m, 7-H), 3.67 (3H, s, OMe), 4.31 (2H, s, C*H*$_2$Ph), 4.60 (1H, s, 6-H), 5.01 (1H, d, *J*=5.9 Hz, 2-H), 7.19 (1H, s, 4-H), 7.24–7.39 (5H, ov, Ph); ^{13}C NMR ($CDCl_3$) δ=21.2 (7-Me), 44.1, 45.6 (7- and 8-C), 50.5 (OMe), 56.6 (*C*H$_2$Ph), 79.9 (6-C), 87.6 (2-C), 103.3 (5-C), 127.5 (5-C), 127.5, 127.9, 128.8, 136.6 (Ph–C), 142.1 (4-C), 166.2 (CO_2). $C_{16}H_{19}NO_3$ (273.3): calcd C, 70.31; H, 7.01; N, 5.12%; found C, 70.38; H, 7.06; N, 5.13%.

(4*S,5*S**)-(±)-1-Benzyl-4-hydroxy-3-(methoxycarbonyl)-5-phenyl-4,5-dihydro-1*H*-azepine (4c).** Colorless prisms from hexane; mp 128–129°C; IR (KBr) $\tilde{\nu}$ = 3490, 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.92 (1H, br d, *J*=5.6 Hz, OH), 3.70 (4H, ov, OMe and 5-H), 4.63 (2H, s, C*H*$_2$Ph), 5.16 (1H, ddd, *J*=1.3, 4.9, and 8.9 Hz, 6-H), 5.28 (1H, br d, *J*=5.6 Hz, 4-H), 6.02 (1H, ddd, *J*=1.3, 2.3, and 8.9 Hz, 7-H), 7.25–7.43 (10H, ov, Ph), 7.70 (1H, s, 2-H); ^{13}C NMR ($CDCl_3$) δ=49.5 (5-C), 51.6 (OMe), 62.8 (*C*H$_2$Ph), 71.6 (4-C), 108.2 (3-C), 113.2 (6-C), 126.7, 126.9, 128.1, 128.3, 128.5, 129.0, 136.8, 143.6 (Ph–C), 130.1 (7-C), 145.2 (2-C), 168.4 (CO_2). $C_{21}H_{21}NO_3$ (335.4): calcd C, 75.20; H, 6.31; N, 4.18%; found C, 75.22; H, 6.48; N, 4.29%.

(2*R,6*S**,7*R**)-(±)-3-Benzyl-5-(methoxycarbonyl)-7-phenyl-3,6-dihydro-2,6-ethano-2*H*-[1,3]oxazine (5c).** Colorless prisms from hexane; mp 121–123°C; IR (KBr) $\tilde{\nu}$ = 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.17 (1H, ddd, *J*=3.3, 6.3, and 13.5 Hz, 8-H), 2.58 (1H, dd, *J*=8.9 and 13.5 Hz, 8-H), 3.65–3.68 (4H, ov, OMe and 7-H), 4.39 (2H, s, C*H*$_2$Ph), 4.96 (1H, s, 6-H), 5.19 (1H, d, *J*=5.9 Hz, 2-H), 7.18–7.38 (11H, ov, Ph and 4-H); ^{13}C NMR ($CDCl_3$) δ=45.3 (8-C), 50.6 (OMe), 56.6 (*C*H$_2$Ph), 56.8 (7-C), 80.5 (6-C), 87.6 (2-C), 103.5 (5-C), 126.3, 126.7, 127.8, 128.0, 128.4, 128.9, 136.5, 142.3 (Ph–C), 144.9 (4-C), 166.1 (CO_2). $C_{21}H_{21}NO_3$ (335.4): calcd C, 75.20; H, 6.31; N, 4.18%; found C, 75.37; H, 6.28; N, 4.22%.

(4*S,5*R**)-(±)-1-Benzyl-5-(2-furyl)-4-hydroxy-3-(methoxycarbonyl)-4,5-dihydro-1*H*-azepine (4d).** Colorless prisms from hexane–propan-2-ol; mp 116–117°C; IR (KBr) $\tilde{\nu}$ = 3480, 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.05 (1H, br, OH), 3.78 (3H, s, OMe), 3.80 (1H, br, 5-H), 4.62 (2H, s, C*H*$_2$Ph), 5.21 (1H, ddd, *J*=1.0, 4.3, and 8.9 Hz, 6-H), 5.49 (1H, s, 4-H), 6.02 (1H, td, *J*=1.7 and 8.9 Hz, 7-H), 6.25 (1H, d, *J*=3.3 Hz, furyl 3-H), 6.34 (1H, dd, *J*=2.0 and 3.3, furyl 4-H), 7.23–7.41 (6H, ov, Ph and furyl 5-H), 7.60 (1H, s, 2-H); ^1H NMR ($CDCl_3$) δ=43.6 (3-C), 51.6 (OMe), 62.7 (*C*H$_2$Ph), 69.9 (4-C), 105.5, 110.3, 141.4, 155.8 (furyl-C), 106.9 (3-C), 110.0 (6-C), 126.8, 128.1, 129.0, 136.6 (Ph–C), 130.6 (7-C), 146.0 (2-C), 168.3 (CO_2). $C_{19}H_{19}NO_4$ (325.4): calcd 70.14; H, 5.89; N, 4.31%; found C, 70.15; H, 5.93; N, 4.36%.

(2*R,6*S**,7*R**)-(±)-3-Benzyl-7-(2-furyl)-5-(methoxycarbonyl)-3,6-dihydro-2,6-ethano-2*H*-[1,3]oxazine (5d).** Colorless prisms from hexane, mp 93–94°C; IR (KBr) $\tilde{\nu}$ = 1710, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.28 (1H, ddd, *J*=3.3, 5.9, and 13.5 Hz, 8-H), 2.43 (1H, dd, *J*=8.9 and 13.2 Hz, 8-H), 3.70 (3H, s, OMe), 3.74 (1H, dd, *J*=3.3 and 8.6 Hz, 7-H), 4.37 (2H, s, C*H*$_2$Ph), 5.08 (1H, s, 6-H), 5.15 (1H, br d, *J*=5.9 Hz, 2-H), 6.03 (1H, d, *J*=3.3 Hz, furyl 3-H), 6.25 (1H, dd, *J*=2.0 and 3.3 Hz, furyl 4-H), 7.26–7.37 (7H, ov, furyl 5-H and Ph and 4-H); ^{13}C NMR ($CDCl_3$) δ=41.7 (8-C), 49.7 (7-C), 50.7 (OMe), 56.8 (*C*H$_2$Ph), 78.3 (6-C), 87.3 (2-C), 102.8 (5-C), 104.3, 110.0, 141.1, 156.0 (furyl-C), 127.6, 128.0, 128.9, 136.4 (Ph–C), 142.5 (4-C), 156.7 (CO_2). $C_{19}H_{19}NO_4$ (325.4): calcd C, 70.14; H, 5.89; N, 4.31%; found C, 70.14; H, 5.90; N, 4.31%.

(4*S,5*S**)-(±)-1-Benzyl-5-ethoxycarbonyl-4-hydroxy-3-(methoxycarbonyl)-4,5-dihydro-1*H*-azepine (4e).** Colorless prisms from hexane–ethyl acetate; mp 126–127°C; IR (KBr) $\tilde{\nu}$ = 3480, 1725, 1700, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.30 (3H, t, *J*=7.3 Hz, CH_2CH_3), 2.22 (1H, br s, OH), 3.29 (1H, br d, *J*=5.6 Hz, 5-H), 3.74 (3H, s, OMe), 4.23 (2H, q, *J*=7.3 Hz, CH_2CH_3), 4.59 (2H, s, C*H*$_2$Ph), 5.42 (1H, dd, *J*=5.6 and 8.9 Hz, 6-H), 5.69 (1H, s, 4-H), 6.03 (1H, br d, *J*=8.9 Hz, 7-H), 7.21–7.39 (5H, ov, Ph), 7.66 (1H, s, 2-H); ^{13}C NMR ($CDCl_3$) δ=14.5 (CH_2CH_3), 49.0 (5-C), 51.6 (OMe), 61.3 (CH_2CH_3), 62.7 (*C*H$_2$Ph), 68.5 (4-C), 106.4 (3-C), 107.3 (6-C), 126.8, 128.1, 129.0, 136.5 (Ph–C), 130.9 (7-C), 146.0 (2-C), 168.2, 171.9 (CO_2). $C_{18}H_{21}NO_5$ (331.36): calcd C, 65.24; H, 6.39; N, 4.23%; found C, 64.99; H, 6.40; N, 4.30%. The structure of this compound was confirmed by X-ray crystal structure analysis.[11]

Olefin-ene reaction of conjugated diene compounds 10 from 3-(alk-2-enyl)amino-2-(methoxycarbonyl)acrolein derivatives 3

Thermal Reaction of Diene 10a. Typical procedures. A solution of diene **10a** (0.102 g, 0.27 mmol) in toluene (5 ml) was heated under reflux for 12 h and the solvent was evaporated. The residue was subjected to column chromatography

on silica-gel to afford azepine **11a** (0.092 g, 90%) with hexane/ethyl acetate (1/1).

1-Benzyl-3-methoxycarbonyl-4-{[bis(methoxycarbonyl)]-methyl}-4,5-dihydro-1*H*-azepine (11a). Pale yellow oil; IR (NaCl) $\tilde{\nu}=1700$, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.39 (1H, br d, J=15.5 Hz, 5-H), 2.53 (1H, ddd, J=4.6, 8.9, and 15.5 Hz, 5-H), 3.43 (1H, d, J=10.6 Hz, 4-C*H*Es_2), 3.63, 3.67, 3.71 (each 3H, each s, OMe), 4.20 (1H, ddd, J=4.0, 4.6, and 10.6 Hz, 4-H), 4.54 (2H, s, CH_2Ph), 4.84 (1H, td, J=8.9 and 9.2 Hz, 6-H), 5.85 (1H, br td, J=4.3 and 9.2 Hz, 7-H), 7.24–7.40 (5H, ov, Ph), 7.53 (1H, dd, J=1.0 and 1.6 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=30.9 (5-C), 38.5 (4-C), 51.5, 52.2, 52.3 (OMe), 57.6 (4-*C*HEs_2), 62.8 (*C*H_2Ph), 105.8 (3-C), 108.5 (6-C), 126.8, 127.9, 128.9, 137.2 (Ph–C), 131.6 (7-C), 145.2 (2-C), 168.7, 168.8 (CO_2). $C_{20}H_{23}NO_6$ (373.4): calcd C, 64.33; H, 6.21; N, 3.75%; found C, 64.69; H, 6.29; N, 3.69%. $C_{20}H_{23}NO_6$: calcd 373.1526; observed *m/z* (EI) 373.1518.

Similarly, thermal reaction of conjugated dienes **10b**,**c**,**e** gave azepine **11b**,**c**,**e** and the results are demonstrated in Table 2.

(4*R,5*S**)-(±)-1-Benzyl-3-methoxycarbonyl-4-{[bis-(methoxycarbonyl)]methyl}-5-methyl-4,5-dihydro-1*H*-azepine (11b).** Yellow oil; IR (NaCl) $\tilde{\nu}=1700$, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.03 (3H, d, J=7.6 Hz, 5-Me), 2.75 (1H, m, 5-H), 3.32 (1H, d, J=8.3 Hz, 4-C*H*Es_2), 3.54, 3.69. 3.74 (each 3H, each s, OMe), 4.29 (1H, br d, J=8.3 Hz, 4-H), 4.53 (2H, s, CH_2Ph), 4.63 (1H, ddd, J=1.0, 4.0, and 9.2 Hz, 6-H), 5.81 (1H, ddd, J=1.6, 2.3, and 9.2 Hz, 7-H), 7.20–7.41 (5H, ov, Ph), 7.51 (1H, dd, J=1.0 and 1.6 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=21.0 (5-Me), 37.4 (5-C), 44.4 (4-C), 51.5, 52.0, 52.4 (OMe), 57.6 (4-*C*HEs_2), 62.4 (*C*H_2Ph), 106.2 (3-C), 114.5 (6-C), 126.8, 127.9, 128.8, 137.0 (Ph–C), 129.4 (7-C), 144.9 (2-C), 168.7, 168.9, 169.3 (CO_2). $C_{21}H_{25}NO_6$ (387.4): calcd C, 65.10; H, 6.50; N, 3.62%; found C, 64.71; H, 6.54; N, 3.35%. $C_{21}H_{25}NO_6$: calcd 387.1682; observed *m/z* (EI) 387.1672.

(4*R,5*S**)-(±)-1-Benzyl-3-methoxycarbonyl-4-{[bis-(methoxycarbonyl)]methyl}-5-phenyl-4,5-dihydro-1*H*-azepine (11c).** Yellow oil; IR (NaCl) $\tilde{\nu}=1700$, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.20, 3.51, 3.72 (each 3H, each s, OMe), 3.52 (1H, d, J=8.6 Hz, 4-C*H*Es_2), 3.97 (1H, m, 5-H), 4.59 (2H, s, CH_2Ph), 4.61 (1H, br d, J=8.6 Hz, 4-H), 5.23 (1H, ddd, J=1.3, 3.6, and 9.9 Hz, 6-H), 6.04 (1H, ddd, J=0.6, 2.6, and 9.9 Hz, 7-H), 7.17–7.42 (10H, ov, Ph), 7.59 (1H, d, J=0.6 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=45.7 (5-C), 47.1 (4-C), 51.4, 51.6, 52.0 (OMe), 57.3 (4-*C*HEs_2), 62.5 (*C*H_2Ph), 106.6 (3-C), 110.0 (6-C), 126.6, 127.0, 127.8, 127.9, 128.3, 128.8, 136.8, 142.3 (Ph-C), 130.5 (C-7), 145.0 (2-C), 167.8, 168.5, 168.6 (CO_2). $C_{26}H_{27}NO_6$ (449.5): calcd C, 69.47; H, 6.05; N, 3.12%; found C, 68.94; H, 6.25; N, 3.07%. $C_{26}H_{27}NO_6$: calcd 449.1839; observed *m/z* (EI) 449.1818.

(4*R,5*S**)-(±)-1-Benzyl-5-ethoxycarbonyl-3-methoxycarbonyl-4-{[bis(methoxycarbonyl)]methyl}-4,5-dihydro-1*H*-azepine (11e).** Colorless prisms from hexane–benzene; mp 112–123°C; IR (KBr) $\tilde{\nu}=1700$, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.32 (3H, t, J=7.3 Hz, CH_2CH_3), 3.34 (1H, m, 5-H), 3.37 (1H, d, J=9.6 Hz, 4-C*H*Es_2), 3.56, 3.66, 3.71 (each 3H, each s, OMe), 4.10–4.27 (2H, ov, CH_2CH_3), 4.58 (2H, s, CH_2Ph), 4.83 (1H, d, J=9.6 Hz, 4-H), 5.33 (1H, ddd, J=1.0, 4.3, and 9.2 Hz, 6-H), 5.99 (1H, td, J=2.0 and 9.2 Hz, 7-H), 7.23–7.42 (5H, ov, Ph), 7.56 (1H, br s, 2-H); ^{13}C NMR ($CDCl_3$) δ=14.1 (CH_2CH_3), 47.2 (5-C), 51.6 (4-C), 51.7, 52.2, 52.5 (OMe), 57.5 (4-*C*HEs_2), 61.4 (*C*H_2CH_3), 62.8 (*C*H_2Ph), 105.5 (3-C), 106.6 (6-C), 126.9, 128.1, 129.0, 136.8 (Ph–C), 130.5 (7-C), 144.8 (2-C), 167.8, 168.5, 168.6, 172.2 (CO_2). $C_{23}H_{27}NO_8$ (445.5): calcd C, 62.01; H, 5.75; N, 3.14%; found C, 61.97; H, 6.09; N, 3.20%. The structure of this compound was confirmed by X-ray crystal structure analysis.[11]

Single-crystal X-Ray structure analyses of diazatricyclotetradecantriene 6 and azepines 4e and 11e[11]

Single crystals of compounds **6** ($C_{30}H_{30}N_2O_4$: 482.52) as prisms from hexane–propan-2-ol, **4e** ($C_{18}H_{21}NO_5$: 331.37) as prisms from hexane, and **11e** ($C_{23}H_{27}NO_8$: 445.47) as prisms from hexane were obtained. A crystal of approximate dimensions 0.24×0.32×0.38 mm^3 for **6**, 0.28×0.42×0.64 mm^3 for **4e**, and 0.16×0.48×0.68 mm^3 for **11e** were used for data collection, respectively. All measurements were made on a Rigaku AFC5S diffractometer by employing graphite-monochromated Mo–Kα radiation. The unit-cell dimensions were obtained by least-squares analysis of 25 reflections within the range of $39.09<2\theta<39.94°$ for **6**, 18 reflections within the range of $20.10<2\theta<22.48°$ for **4e**, and 13 reflections within the range of $12.39<2\theta<23.74°$ for **11e**, respectively. The crystal data for compound **6** are given: crystal system: triclinic; space group: P1 (#2); cell constants: *a*: 8.530(3) Å, *b*: 9.586(4) Å, *c*: 8.162(7) Å, V: 636.8(3) $Å^3$; α=98.56(5)°, β=100.78(6)°, γ=77.86(3)°; *Z* value: 2; Dc: 2.517 g cm^{-3}. Similarly, the crystal data for compound **4e** are given: crystal system: triclinic; space group: P1 (#2); cell constants: *a*: 10.37(3) Å, *b*: 10.42(1) Å, *c*: 9.40(2) Å, *V*: 865(3) $Å^3$; α=109.5(1)°, β=108.1(2)°, γ=67.5(1)°; *Z* value: 2; Dc: 1.272 g cm^{-3}. The crystal data for compound **11e** are given: crystal system: monoclinic; space group: $P2_1/n$ (#14); cell constants: *a*: 8.12(1) Å, *b*: 11.27(3) Å, *c*: 25.11(2) Å, *V*: 2275(4) $Å^3$; β=97.9(1)°; *Z* value: 4; Dc: 1.300 g cm^{-3}. The $\omega-2\theta$ scan technique to a maximum 2θ-value of 54.9° was used and scans of $(1.63+0.30\tan\theta)°$ were made at a speed 16° min^{-1} for **6**. The $\omega-2\theta$ scan technique to a maximum 2θ-value of 55.1° was used and scans of $(1.10+0.30\tan\theta)°$ were made at a speed 16° min^{-1} for **4e**. The ω-2θ scan technique to a maximum 2θ-value of 55.1° was used and scans of $(0.97+0.30\tan\theta)°$ were made at a speed 16° min^{-1} for **11e**. A total of 3111 observed reflections (unique: 2914; R_{int}=0.029) for **6**, 4190 observed reflections (unique: 3968; R_{int}=0.083) for **4e**, and 4873 observed reflection (unique: 4491; R_{int}=0.083) was collected for **11e**, respectively. All calculations were performed using texan program.[15] Atoms other than hydrogen were refined anisotropically. The structure of compound **6** was solved by direct methods (SIR)[16] and refined by least-squares to *R* 0.048 (R_w 0.051). The structure of compound **4e** was solved by direct methods (MITHRIL)[17] and refined by least-squares to *R* 0.106 (R_w 0.106). The structure of

compound **11e** was solved by direct methods (MITHRIL)[17] and refined by least-squares to R 0.073 (R_w 0.070).

Kinetics on thermal reaction of conjugated Diene 10c

The apparatus and procedures for the measurement of the conversion rates are same as those in the previous paper.[4e] To measure the rates of the disappearance of the diene **10c**, dichlorobenzene was utilized as internal standard. A Wakosil-II5C18HG (id 4.6×250 mm^2) column was used and the flow rate of the elution was 1 ml min^{-1} and the component of the elution was acetonitrile–H_2O (1:1). All rates of conversion of **10c** in several solvents were first-order with respect to the diene concentration. The obtained rate constants [k (s^{-1})×10^5] at 97°C were as bellows: 2.78 (relative rate: 1.00) in dioxane, 1.79 (0.39) in DMF, 1.42 (0.51) in propionitrile, and 1.13 (0.41) in butan-1-ol.

Acknowledgements

We thank Mr. Tetsuhiro Maeda for his experimental assistance. The author (M. N.) is also grateful for the financial support by the Grant-in-Aid for Scientific Research No. 09650940 from the Ministry of Education, Science, Sports and Culture of Japan.

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