HETEROCYCLES, Vol. 73, 2007, pp. 689 - 698. © The Japan Institute of Heterocyclic Chemistry
Received, 1st July, 2007, Accepted, 5th September, 2007, Published online, 7th September, 2007. COM-07-S(U)48

A FACILE SODIUM ALKOXIDE MEDIATED RING OPENING OF UNACTIVATED α-DIENYL-β-LACTAMS: SYNTHESIS OF UNNATURAL MULTICOMPONENT β–AMINODIENOIC ESTERS

Amit Anand,[a] Gaurav Bhargava,[a] Maninder Singh Hundal,[b] and Mohinder P. Mahajan[a]*

[a] Department of Applied Chemistry, Guru Nanak Dev University, Amritsar – 143005, Punjab, India
[b] Department of Chemistry, Guru Nanak Dev University, Amritsar – 143005, Punjab, India
Phone +91 (0183)2258802-09*3320, Fax +91(183)2258819-20

E-mail: mahajanmohinderp@yahoo.co.in

Abstract – A convenient synthesis of variedly substituted, multi component unnatural β-aminodienoic esters by sodium alkoxide amidiolysis of unactivated α-dienyl-β-lactams is reported.

INTRODUCTION

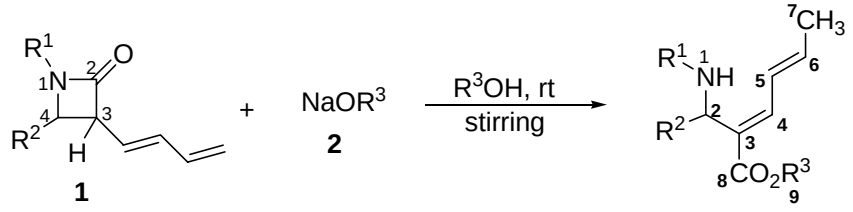
β-Amino esters have attracted considerable attention of scientific community worldwide, owing to their biological assets and as synthons to various medicinally active compounds.[1] Antibiotics like cynanovinfin RR, nodularin and microcystin LR,[2] to name a few, are some important drugs derived from β-amino carbonyls. Some β-amino esters are also known for their antifungal, hypoglycemic and antitumor (e.g. Taxol) activity.[3] Apart from their lesser abundance as compared to their α-analogues, they play a major role as segments in peptidic natural products with various biological activities. For example, (*R*)-β-dopa (5,3,4-dihydroxy- β-phenylalanine) is responsible for blue-violet color in mushroom,[5] β-tyrosine, a β-aryl-β-amino acid, is present in jasplakinolide which is a sponge metabolite with potent insecticidal, antifungal, and antihelminthic properties.[6] Other representative examples include cryptophycin, a potent tumor-selective depsipeptide,[7] and aminopeptidase inhibitors like bestatin and amastatin.[8] The various approaches available till date for synthesis of β-amino esters/acids include their homologation, enzymatic resolution, addition of enolates to imines, Curtius rearrangement, conjugate addition of a nitrogen nucleophiles to α, β-unsaturated esters or imides and

amino hydroxylation.[9] Recently Muraoka *et al.* and Ollevier *et al.* have engaged Mannich type reactions to construct such systems.[10] The β-lactam skeleton has attracted significant interest amongst synthetic and medicinal chemists over the years mainly because of its core structure of natural and synthetic β-lactam antibiotics. The strain on the β-lactam nucleus makes it susceptible to molecules which cleave one or more of its bonds and forms the basis of design in β-lactam antibiotics. Recently Ojima *et al.* have utilized β-lactam synthon methodology for the synthesis of various organic and medicinal systems including anti-tumor taxol derivatives. [11]

As part of our enduring interest in building heterocyclic systems of biological enormity, we have reported the synthesis[12] and π-facially selective DA cycloaddition reactions of variedly substituted α-dienyl β-lactams with various dienophiles.[13] In view of the importance of β-aminoesters and lack of reports on the amidiolysis of *N*-aryl/alkyl-β-lactams, we report herein, facile sodium alkoxide mediated amidiolysis of unactivated α-dienyl-β-lactams resulting in excellent yields of multicomponent β-aminodienoic esters.

RESULTS AND DISCUSSION

The treatment of α-dienyl-β-lactams[15] **1a-j** with sodium alkoxide in their corresponding alcohol solvent for 1-2h resulted in the isolation of products **3a-m** in excellent yields (75-92 %; **Scheme 1).**



1a R^1= *p*-Cl-C_6H_4, R^2 =Ph
1b R^1= Ph, R^2 = *p*-Cl-C_6H_4
1c R^1= Ph, R^2 =*p*-MeO-C_6H_4
1d R^1= *p*-MeO-C_6H_4, R^2 =Ph
1e R^1= Ph, R^2 =Ph
1f R^1= *p*-Me-C_6H_4, R^2 =Ph
1g R^1= *p*-MeO-C_6H_4, R^2 =*p*-MeO-C_6H_4
1h R^1=*p*-Cl-C_6H_4, R^2 =*p*-Cl-C_6H_4
1i R^1=Cyclohexyl, R^2 =*p*-Cl-C_6H_4
1j R^1=Benzyl, R^2 =*p*-Cl-C_6H_4

2a R^3 = Me
2b R^3 = Et

3a R^1= *p*-Cl-C_6H_4, R^2 =Ph, R^3=Me
3b R^1= Ph, R^2 = *p*-Cl-C_6H_4, R^3=Me
3c R^1= Ph, R^2 =*p*-MeO-C_6H_4, R^3=Me
3d R^1= *p*-MeO-C_6H_4, R^2 =Ph, R^3=Me
3e R^1= Ph, R^2 =Ph, R^3=Me
3f R^1= *p*-Me-C_6H_4, R^2 =Ph, R^3=Me
3g R^1= *p*-MeO-C_6H_4, R^2 =*p*-MeO-C_6H_4, R^3=Me
3h R^1=*p*-Cl-C_6H_4, R^2 =*p*-Cl-C_6H_4, R^3=Me
3i R^1=Cyclohexyl, R^2 =*p*-Cl-C_6H_4, R^3=Me
3j R^1=Benzyl, R^2 =*p*-Cl-C_6H_4, R^3=Me
3k R^1= *p*-Cl-C_6H_4, R^2 =Ph, R^3=Et
3l R^1= *p*-MeO-C_6H_4, R^2 =Ph, R^3=Et
3m R^1= Ph, R^2 =Ph, R^3=Et

Scheme 1

The isolated and purified products were characterized as β-aminodienoic esters with the help of analytical data and spectral evidences. The mass spectrum of **3a,** for example, showed the molecular ion peak at 341

and its IR spectrum exhibited a sharp absorption at 1682 cm^{-1} due to the unsaturated ester carbonyl. The ^1H spectrum of **3a** showed a doublet of a doublet at δ 1.93 corresponding to the terminal methyl protons (J=7.4Hz, 1.5Hz), a singlet at δ 3.66 corresponding to the methoxy protons of ester group, a doublet at δ 5.07 corresponding to NH and an another doublet at δ 5.78 assigned to H^2, a multiplet at δ 6.26 corresponding to H^6 proton and two multiplets at δ 6.56 and δ 6.62 due to H^5 and H^4. Its ^{13}C spectra showed characteristic carbonyl at δ 167.4. The assigned structure was unambiguously supported by X-ray crystallographic studies. **(Figure 1)**.

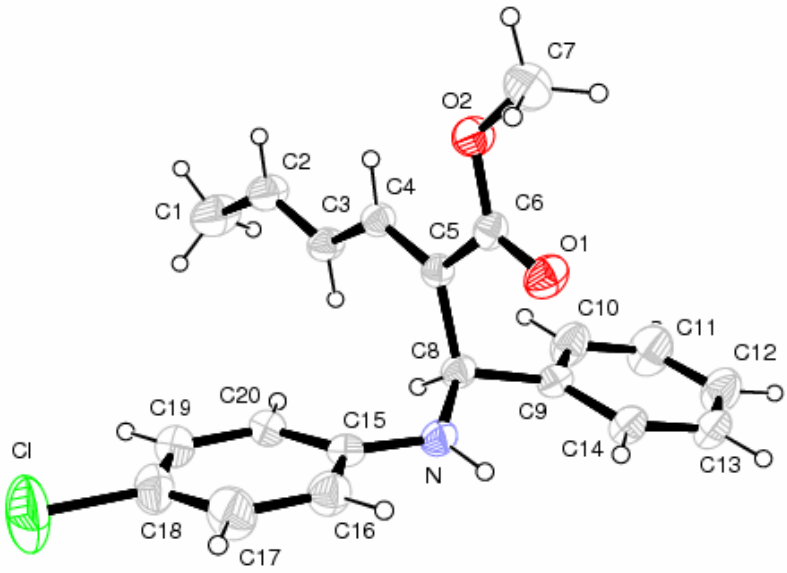
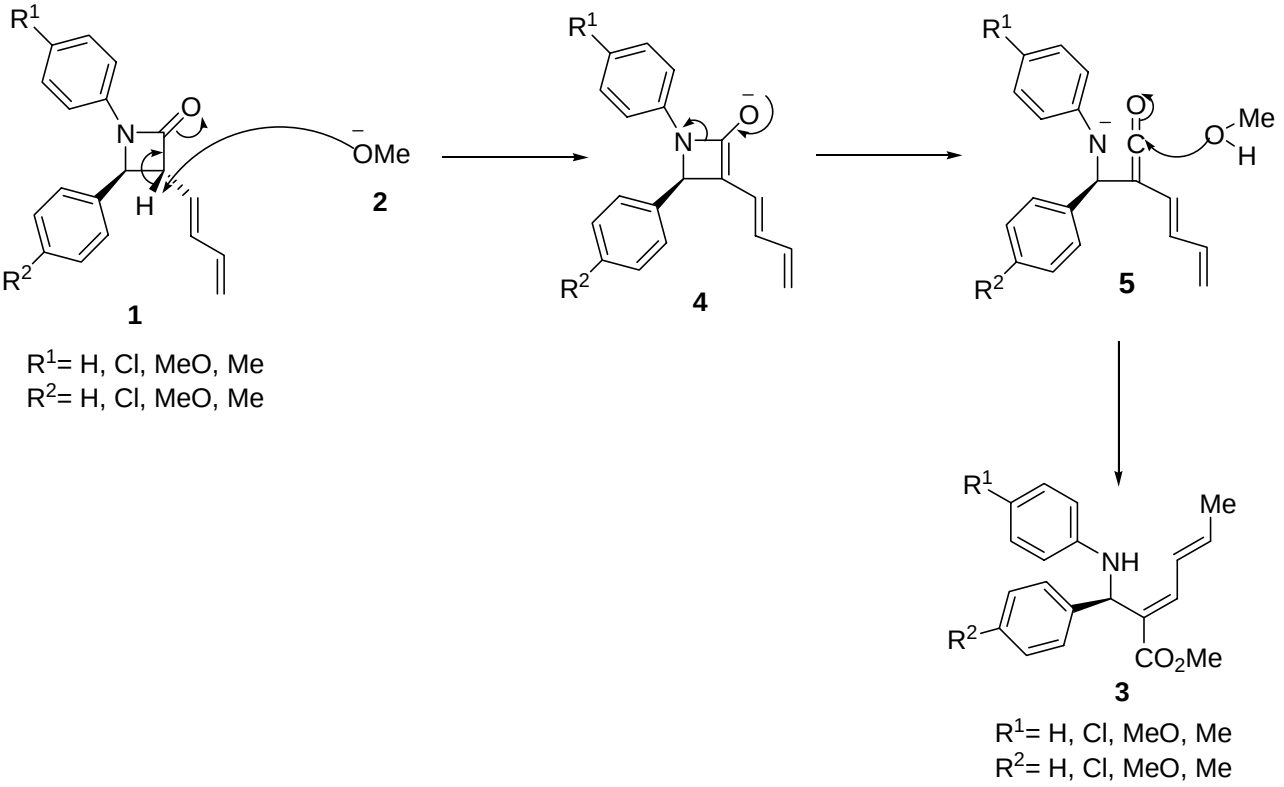


Figure: 1 An ORTEP diagram of **3a**

A plausible mechanism for the formation of β-aminodienoic esters utilizing *trans*-α-dienyl β-lactams probably involves the alkoxide abstraction of H^3 proton generating intermediate **4** which is followed by N1-C2 ring cleavage resulting in the formation of another intermediate **5.** Nucleophilic attack by a molecule of alcohol on ketene carbonyl then leads to resultant β-aminodienoic esters **3. (Scheme 2)**

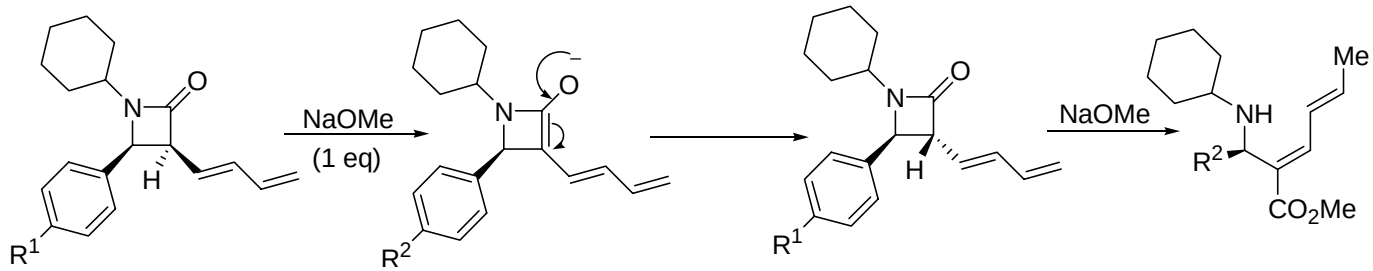
Recently, Troisi *et al.* have also reported the sodium methoxide amidiolysis of α-vinyl-β-lactam to afford *E:Z* (1:1) mixture of α-ethylidine-β-aminobenzenepropanoic acid methyl esters.[16] The stereoselectivity observed in the present case of sodium alkoxide amidiolysis of 3-butadienyl-2-azetidinones leading to a single *E*-isomer **3** may be ascribed to the greater stability of butadienyl ketene intermediate **5.** The reaction proceeds through the preferred formation of this intermediate which is stable enough to exist in an all *E*-form / *S*-transoid conformation (Scheme-2) leading to the formation of thermodynamic product **3**. This is in contrast to the mixture of *E* and *Z* isomers (kinetically controlled products) when 3-vinyl-2-azetidinones were used as substrates. [16]



Scheme 2

In order to generalize the mechanistic pathway and to rationalize the results, we have examined alkoxide mediated amidolysis of *cis*-*N*-cyclohexyl-α-dienyl-β-lactam derivatives. These reaction also resulted in the formation of *N*-cyclohexyl-β-aminodienoic esters, albeit, in lower yields (60%) by using excess of sodium methoxide. However, the reactions resulted in the conversion of *cis*-*N*-cyclohexyl-α-dienyl-β-lactams to the corresponding *trans*-*N*-cyclohexyl-α-dienyl-β-lactams when equimolar quantities of sodium methoxide were employed.

This is probably due to the abstraction of the H^3 by one equivalent of base followed by reprotonation to form more stable *trans* isomer, further confirmed from the coupling constant of J=2.1 Hz between H^3-H^4 protons of the 2-azetidinone ring (**Scheme 3**)



Scheme 3 Mechanism showing the ring opening of *N*-cyclohexyl-α-dienyl-β-lactams

In conclusion, a facile single step base catalyzed route for the synthesis of multicomponent *β*-aminodienoic esters through the ring opening reactions of unactivated *N*-alkyl/aryl-*α*-dienyl-*β*-lactam derivatives has been devised. Further work for the utilization of the diene moiety in construction of novel heterocyclic compounds containing *β*-amino ester group is in progress.

EXPERIMENTAL

GENERAL REMARKS

Melting points were determined by open capillary using Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. IR spectra were recorded on a Shimadzu D-8001 spectrophotometer. ^{1}H NMR spectra were recorded in deuterochloroform with Bruker AC-E 200 (200 MHz) spectrometers using TMS as internal standard. Chemical shift values are expressed as ppm downfield from TMS and *J* values are in Hz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet, q: quartet, br: broad peak and brs: broad singlet. ^{13}C NMR spectra were also recorded on Bruker AC-200E (50.4 MHz) spectrometers in deuterochloroform using TMS as internal standard. Mass spectra were recorded on Shimadzu GCMS-QP-2000 mass spectrometer. Elemental analyses were performed on Heraus CHN-O-Rapid Elemental Analyzer. Column chromatography was performed on a silica gel (60–120) mesh or Harrison Research Chromatotron using 2 mm plates (Silica gel 60 PF254).

GENERAL PROCEDURE:

The synthesis of *β*-aminodienoic esters was realized by addition of sodium methoxide **2** (15mmol) to MeOH (20 mL) solution of *trans*-3-butadienyl-*2*-azetidinones[10] (10mmol) **1a-j**. After completion of the reaction, (monitored through tlc) reaction mixture was washed with water and extracted with CH_2Cl_2. The removal of solvent under reduced pressure resulted in crude product, which was purified through silica gel column chromatography resulted in isolation of compound **3a-m** in excellent yields.

2-[(4-Chlorophenylamino)phenylmethyl]hexa-2,4-dienoic acid methyl ester (3a):

Pale yellow solid (92 %), mp 120–121 °C. IR (KBr): ν_{max} = 1689.5, 3392.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.93(dd, *J* = 6.9, 1.5 Hz, 3 H, H_7), 3.66 (s, 3H, H_9), 5.07 (d, *J*=9.3 Hz, 1 H, H_1), 5.78 (d, *J* = 9.0 Hz, 1 H, H_2), 6.26 (m, 1 H, H_6), 6.68 (m, 1 H, H_5), 6.72 (m, 1 H, H_4), 6.68-7.22 (m, 9 H, aromatic), ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.1, 51.6, 54.1, 113.5, 117.6, 126.2, 126.3, 126.6, 128.3, 129.2, 141.0, 141.2. 141.5, 147.2, 167.4 ppm. MS *m*/*z* 341 $[M]^+$. Anal. Calcd for $C_{20}H_{20}ClNO_2$ (341.1): C 70.27, H 5.90, N 4.10. Found: C 70.41, H 6.00, N 3.97.

2-[(4-Chlorophenyl)phenylaminomethyl]hexa-2,4-dienoic acid methyl ester (3b):

Pale yellow solid (90 %), mp 118–119 °C. IR (KBr): ν_{max} = 1689.6, 3393.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.92(dd, J = 6.8, 1.5 Hz, 3 H, H_7), 3.68 (s, 3 H, H_9), 5.05(d, J=9.3 Hz, 1 H, H_1), 5.72 (d, J = 9.0 Hz, 1 H, H_2), 6.25(m, 1 H, H_6), 6.68 (m, 1 H, H_5), 6.73 (m, 1 H, H_4), 6.99 (m, 9 H, aromatic), ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.2, 51.8, 54.1, 114.7, 117.9, 126.3, 127.0, 128.4, 129.1, 129.4, 141.2, 141.8, 142.0, 147.0, 167.3, MS m/z 341 $[M]^+$. Anal. Calcd for $C_{20}H_{20}ClNO_2$ (341.1): C 70.27, H 5.90, N 4.10. Found: C 70.42, H 6.04, N 4.19.

2-[(4-Methoxyphenyl)phenylaminomethyl]hexa-2,4-dienoic acid methyl ester (3c):

White solid (80 %), mp 132–135 °C. IR (KBr): ν_{max} = 1682.5, 3389.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.90(dd, J = 6.8, 1.4 Hz, 3 H, H_7), 3.63 (s, 3 H, -$OCH_3C_6H_4$), 3.68 (s, 3 H, H_9) 5.10(d, J=9.3 Hz, 1 H, H_1), 5.85 (d, J = 9.0 Hz, 1 H, H_2), 6.28(m, 1 H, H_6), 6.70 (m, 1 H, H_5), 6.73 (m, 1 H, H_4), 6.70-7.48 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.2, 51.7, 54.5, 56.2, 113.8, 117.9, 126.8, 126.9, 127.2, 129.6, 130.4, 142.2, 142.6. 142.7, 148.2, 167.4, 169.2 ppm. MS m/z 337 $[M]^+$. Anal. Calcd for $C_{21}H_{23}NO_3$ (337.4): C 74.75, H 6.87, N 4.15. Found: C 74.92, H 7.02, N 3.97.

2-[(4-Methoxyphenylamino)phenylmethyl]hexa-2,4-dienoic acid methyl ester (3d):

White solid (68 %), mp 138–140 °C. IR (KBr): ν_{max} = 1689.5, 3388.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.92(dd, J = 6.8, 1.4 Hz, 3 H, H_7), 3.62 (s, 3 H, -$OCH_3C_6H_4$), 3.69 (s, 3 H, H_9) 5.08(d, J=9.3 Hz, 1 H, H_1), 5.78 (d, J = 9.0 Hz, 1 H, H_2), 6.25(m, 1 H, H_6), 6.72 (m, 1 H, H_5), 6.76 (m, 1 H, H_4), 6.72-7.52 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.5, 51.8, 54.8, 57.2, 114.2, 118.2, 128.1, 128.2, 128.9, 129.2, 130.6, 142.2, 142.6. 142.8, 148.2, 167.6, 169.6 ppm. MS m/z 337 $[M]^+$. Anal. Calcd for $C_{21}H_{23}NO_3$ (337.4): C 74.75, H 6.87, N 4.15. Found: C 74.92 H 6.98, N 4.28.

2-(Phenylphenylaminomethyl)hexa-2,4-dienoic acid methyl ester (3e):

White solid (72 %), mp 90-91 °C. IR (KBr): ν_{max} = 1681.1, 3396.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.92(dd, J = 6.6, 1.5 Hz, 3 H, H_7), 3.66 (s, 3 H, H_9) 5.08(d, J=9.3 Hz, 1 H, H_1), 5.79 (d, J = 9.0 Hz, 1 H, H_2), 6.27(m, 1 H, H_6), 6.64 (m, 1 H, H_5), 6.68 (m, 1 H, H_4), 6.64-7.39 (m, 10 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.1, 51.7, 54.1, 113.5, 117.6, 126.2, 126.4, 126.9, 128.4, 129.3, 141.1, 141.2. 141.6, 147.2, 168.0 ppm. MS m/z 307 $[M]^+$. Anal. Calcd for $C_{20}H_{20}NO_2$ (307.4): C 78.15, H 6.89, N 4.56. Found: C 78.29, H 7.05, N 4.39.

2-(Phenyl-*p*-tolylaminomethyl)hexa-2,4-dienoic acid methyl ester (3f):

Pale cream solid (70 %), mp 98-100 °C. IR (KBr): ν_{max} = 1678.1, 3390.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300

MHz): δ_H = 1.92(dd, *J* = 6.6, 1.5 Hz, 3 H, H_7), 2.42(s, 3 H, -$CH_3C_6H_4$), 3.67 (s, 3 H, H_9) 5.09(d, *J*=9.3 Hz, 1 H, H_1), 5.79 (d, *J* = 9.0 Hz, 1 H, H_2), 6.28(m, 1 H, H_6), 6.63 (m, 1 H, H_5), 6.66 (m, 1 H, H_4), 6.63-7.40 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.1, 21.2, 51.8, 54.0, 113.6, 117.6, 126.1, 126.3, 126.8, 128.3, 129.3, 141.0, 141.2. 141.5, 147.1, 168.0 ppm. MS *m*/*z* 321 $[M]^+$. Anal. Calcd for $C_{21}H_{23}NO_2$ (321.4): C 78.47, H 7.21, N 4.36. Found: C 78.60, H 7.35, N 4.21.

2-[(4-Methoxyphenyl)-(4-methoxyphenyamino)methyl]hexa-2,4-dienoic acid methyl ester (3g):

White solid (65 %), mp 135-138 °C. IR (KBr): ν_{max} = 1679.1, 3388.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.91(dd, *J* = 6.6, 1.5 Hz, 3 H, H_7), 3.64(s, 3 H, -$OCH_3C_6H_4$N-), 3.65(s, 3 H, -$OCH_3C_6H_4$), 3.72 (s, 3 H, H_9) 5.08(d, *J*=9.3 Hz, 1 H, H_1), 5.78 (d, *J* = 9.0 Hz, 1 H, H_2), 6.29(m, 1 H, H_6), 6.66 (m, 1 H, H_5), 6.70 (m, 1 H, H_4), 6.66-7.38 (m, 8 H, H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.1, 21.2, 51.8, 54.0, 56.2, 56.8, 113.6, 117.6, 126.1, 126.3, 126.8, 128.3, 129.3, 141.0, 141.2. 141.5, 147.1, 168.0 ppm. MS *m*/*z* 367 $[M]^+$. Anal. Calcd for $C_{22}H_{25}NO_4$ (367.4): C 71.91, H 6.86, N 3.81. Found: C 72.12, H 6.97, N 3.70.

2-[(4-Chlorophenyl)-(4-chlorophenylamino)methyl]hexa-2,4-dienoic acid methyl ester (3h):

Pale yellow solid (82 %), mp 122-124 °C. IR (KBr): ν_{max} = 1690.6, 3392.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.91(dd, *J* = 6.6, 1.5 Hz, 3 H, H_7), 3.68 (s, 3 H, H_9) 5.06(d, *J*=9.3 Hz, 1 H, H_1), 5.72 (d, *J* = 9.0 Hz, 1 H, H_2), 6.26(m, 1 H, H_6), 6.64 (m, 1 H, H_5), 6.71 (m, 1 H, H_4), 6.64-7.38 (m, 8 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.2, 51.8, 54.1, 114.7, 117.9, 126.3, 127.1, 128.4, 129.2, 129.4, 141.3, 141.8, 142.2, 147.0, 167.3 ppm. MS *m*/*z* 375 $[M]^+$. Anal. Calcd for $C_{20}H_{20}Cl_2NO_2$ (376.3): C 63.84, H 5.09, N 3.72. Found: C 64.02, H 5.24, N 3.66.

2-[(4-Chlorophenyl)-cyclohexylaminomethyl]hexa-2,4-dienoic acid methyl ester (3i):

Pale yellow solid (70 %), mp 102-104 °C. IR (KBr): ν_{max} = 1682.6, 3388 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.1-1.97(m, 10 H, cyclohexyl) 1.18(dd, *J* = 6.4, 1.4 Hz, 3 H, H_7), 3.42(m, 1 H. –H(cyclohexyl)) , 3.64 (s, 3 H, H_9) 5.08(d, *J*=9.3 Hz, 1 H, H_1), 5.68 (d, *J* = 9.0 Hz, 1 H, H_2), 6.28(m, 1 H, H_6), 6.69 (m, 1 H, H_5), 6.71 (m, 1 H, H_4), 6.70-7.25 (m, 5 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 16.4, 17.5, 33.8, 44.5, 51.3, 54.5, 56.9, 114.8, 117.9, 126.6, 127.5, 127.8, 128.1, 130.4, 132.5, 132.9, 141.4, 144.2, 147.5, 166.3 ppm. MS *m*/*z* 347 $[M]^+$. Anal. Calcd for $C_{20}H_{26}ClNO_2$ (347.9): C 69.05, H 7.53, N 4.03. Found: C 69.21, H 7.70, N 4.15.

2-[Benzylamino-(4-Chlorophenyl)methyl]hexa-2,4-dienoic acid methyl ester (3j):

Pale yellow solid (66 %), mp 108-110 °C. IR (KBr): ν_{max} = 1692.6, 3390.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.82(dd, *J* = 6.4, 1.4 Hz, 3 H, H_7), 3.64 (s, 3 H, H_9), 3.92(s, 2 H. –CH_2(benzyl)), 5.09(d,

J=9.3 Hz, 1H, H_1), 5.66 (d, *J* = 9.0 Hz, 1 H, H_2), 6.26(m, 1 H, H_6), 6.68 (m, 1H, H_5), 6.72 (m, 1H, H_4), 6.68-7.25 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 19.2, 51.8, 52.6, 54.1, 114.7, 117.9, 126.4, 128.1, 129.0, 129.2, 129.5, 141.4, 141.9, 142.8, 147.2, 167.6 ppm. MS *m*/*z* 356 $[M]^+$. Anal. Calcd for $C_{21}H_{22}ClNO_2$ (355.9): C 70.88, H 6.23, N 3.94. Found: C 71.04, H 6.42, N 3.82.

2-[(4-Chlorophenylamino)phenylmethyl]hepta-2,4-dienoic acid ethyl ester (3k):

Pale Yellow solid (78 %), mp 110-112 °C. IR (KBr): ν_{max} = 1689.5, 3392.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.06(t, 3 H, -CH_3-CH_2), 1.98(m, 2 H, H_7), 3.65 (s, 3 H, H_9), 5.08 (d, *J*=9.3 Hz, 1 H, H_1), 5.76 (d, *J* = 9.0 Hz, 1 H, H_2), 6.24(m, 1 H, H_6), 6.64 (m, 1 H, H_5), 6.69 (m, 1 H, H_4),6.64-7.40 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.2, 20.2, 51.6, 54.1, 113.5, 117.6, 126.2, 126.3, 126.6, 128.3, 129.2, 141.0, 141.2. 141.5, 147.2, 167.4 ppm. MS *m*/*z* 355 $[M]^+$. Anal. Calcd for $C_{21}H_{22}ClNO_2$ (355.1): C 70.88, H 6.23, N 3.94. Found: C 70.97, H 6.38, N 3.85.

2-[(4-Methoxyphenylamino)phenylmethyl]hepta-2,4-dienoic acid ethyl ester (3l):

White solid (62 %), mp 142-145 °C. IR (KBr): ν_{max} = 1689.5, 3388.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.08(t, 3 H, -CH_3-CH_2), 1.97(m, 2 H, H_7), 3.63 (s, 3H, -$OCH_3C_6H_4$), 3.69 (s, 3 H, H_9), 5.09(d, *J*=9.3 Hz, 1 H, H_1), 5.76 (d, *J* = 9.0 Hz, 1 H, H_2), 6.26(m, 1 H, H_6), 6.72 (m, 1 H, H_5), 6.78 (m, 1 H, H_4), 6.72-7.52 (m, 9 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.4, 20.2, 51.8, 54.8, 57.2, 114.2, 118.2, 128.1, 128.2, 128.9, 129.2, 130.6, 142.2, 142.6. 142.8, 148.2, 167.6, 169.6 ppm. MS *m*/*z* 351 $[M]^+$. Anal. Calcd for $C_{22}H_{25}NO_3$ (351.4): C 75.19, H 7.17, N 3.99. Found: C 75.32, H 7.29, N 3.81.

2-(Phenyl-phenylaminomethyl)hepta-2,4-dienoic acid ethyl ester (3m):

White solid (66 %), mp 96-97 °C. IR (KBr): ν_{max} = 1681.1, 3396.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H = 1.10(t, 3 H, -CH_3-CH_2), 1.99(m, 2 H, H_7), 3.64 (s, 3 H, H_9), 5.08(d, *J*=9.3 Hz, 1 H, H_1), 5.80 (d, *J* = 9.0 Hz, 1 H, H_2), 6.26(m, 1 H, H_6), 6.69 (m, 1 H, H_5), 6.69 (m, 1 H, H_4), 6.63-7.39 (m, 10 H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.6, 20.2, 51.7, 54.1, 113.5, 117.6, 126.2, 126.4, 126.9, 128.4, 129.3, 141.1, 141.2. 141.6, 147.2, 168.0 ppm. MS *m*/*z* 321 $[M]^+$. Anal. Calcd for $C_{21}H_{23}NO_2$ (321.4): C 78.47, H 7.21, N 4.36. Found: C 78.62, H 7.35, N 4.18.

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15. The starting materials α-dienyl-β-lactams are *trans* with *N*-aryl substituents and *cis* with *N*-alkyl substituents.
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17. X-Ray crystal data and structure refinement for **3a**.

CCDC-634260 (for **3a)** contains the supplementary crystallographic data for this paper. $C_{20}H_{20}ClNO_2$, M = 341.82, triclinic, space group P-1, a = 8.380(5), b = 10.941(5), c = 11.215(5) Å, α = 111.360(5)°, β = 103.700(5)°, γ = 90.840(5)°, V = 924.6(8) Å^3, Z = 2, D calcd. = 1.228 Mg/m^3, μ(Abs. Coeff.)= 0.217 mm^{-1}, T = 298(2) K, λ= 0.71073 Å, Final R indices [I _ 2.0σ(I)] R1=.0602,

*wR*2 = 0.1548, R indices (all data) [I _ 2.0σ(I)] R1 = 0.1037, wR2 = 0.1904 (3412 collections), GOF = 1.068 (311 parameters). Diffraction data were measured on a Bruker APEX CCD-Detector X-ray diffractometer. Structure solution, refinements were carried out with Shelx-97.