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

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

INTRODUCTION

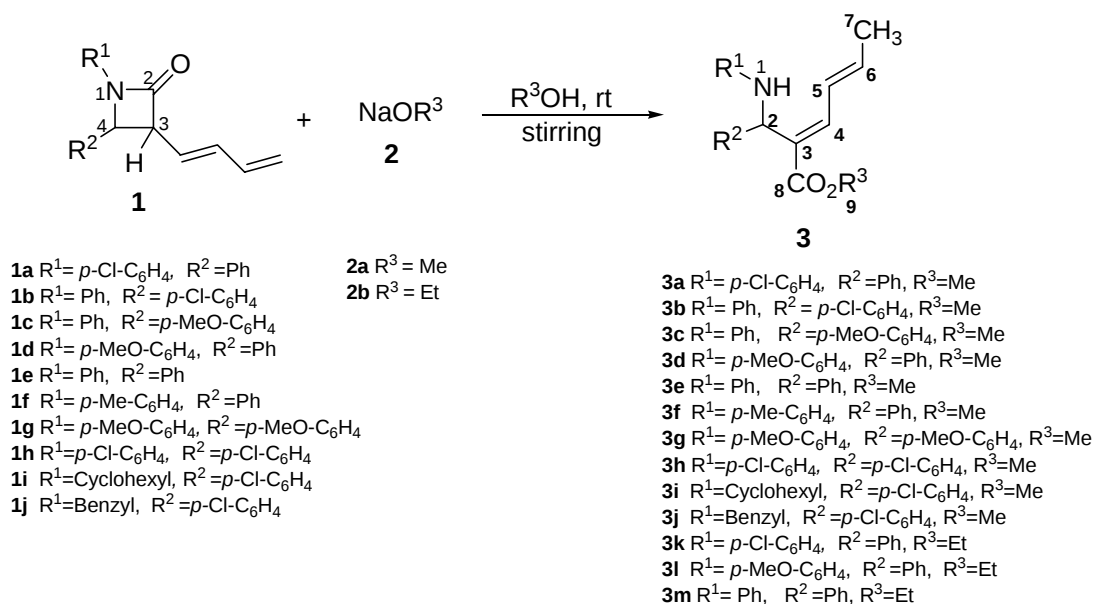
β -Amino esters have attracted considerable attention of scientific community worldwide, owing to their biological assets and as synthons to various medicinally active compounds.¹ Antibiotics like cyanovirin RR, nodularin and microcystin LR,² to name a few, are some important drugs derived from β -amino 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 synthesis¹² 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 amidolysis of *N*-aryl/alkyl- β -lactams, we report herein, facile sodium alkoxide mediated amidolysis of unactivated α -dienyl- β -lactams resulting in excellent yields of multicomponent β -aminodienoic esters.

RESULTS AND DISCUSSION

The treatment of α -dienyl- β -lactams¹⁵ **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**).



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 ($J=7.4\text{Hz}$, 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**).

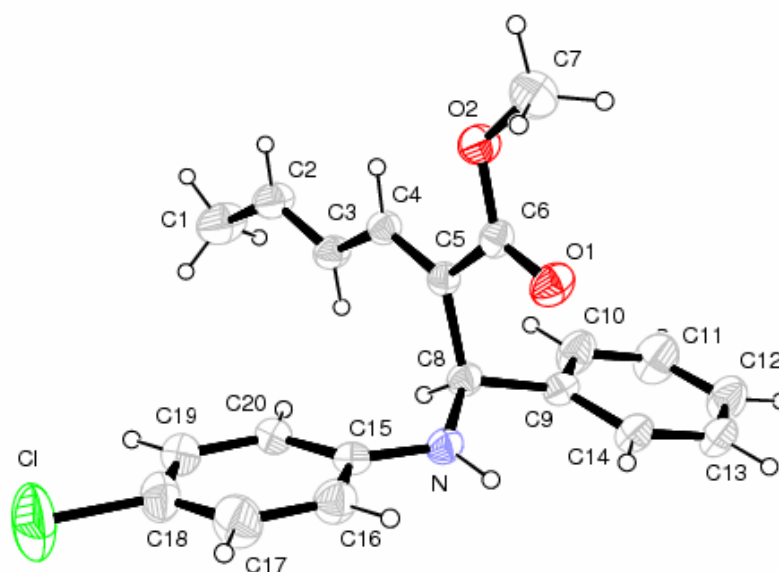
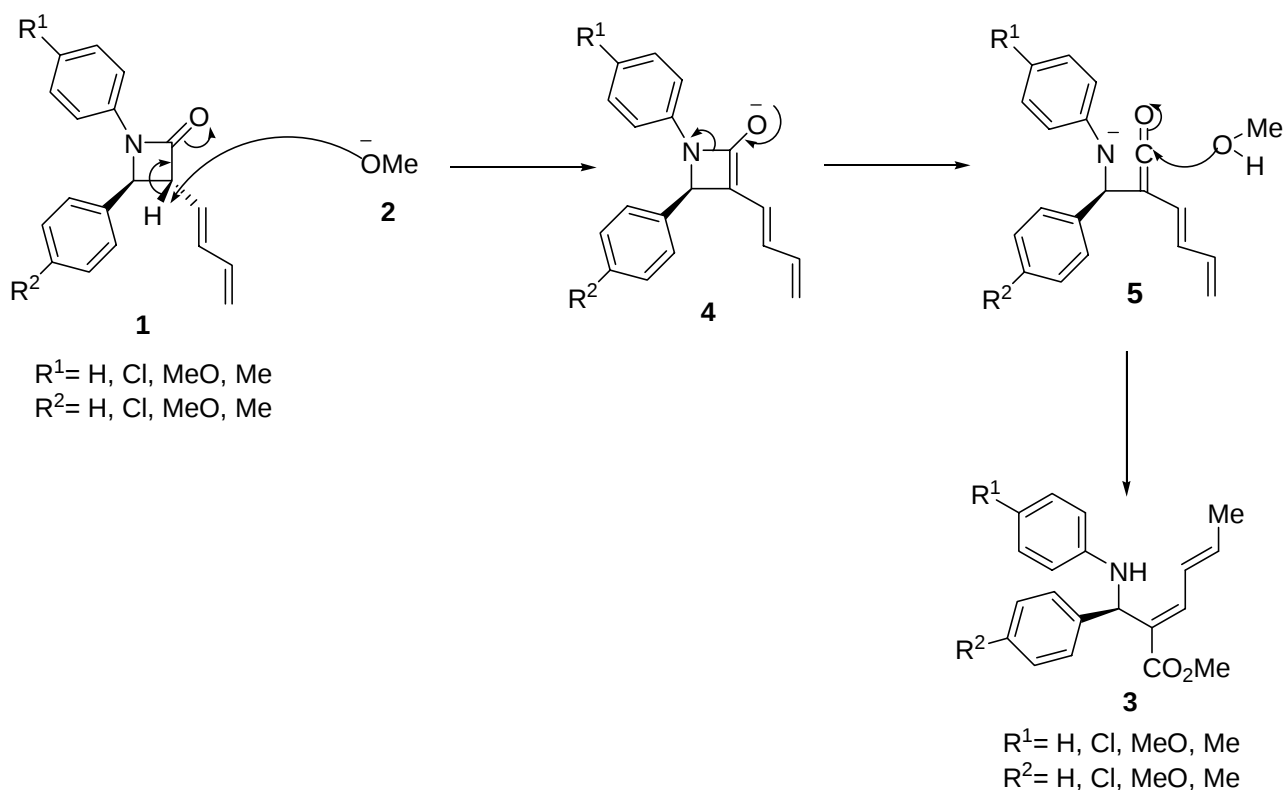


Figure: 1 An ORTEP diagram of **3a**

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**)

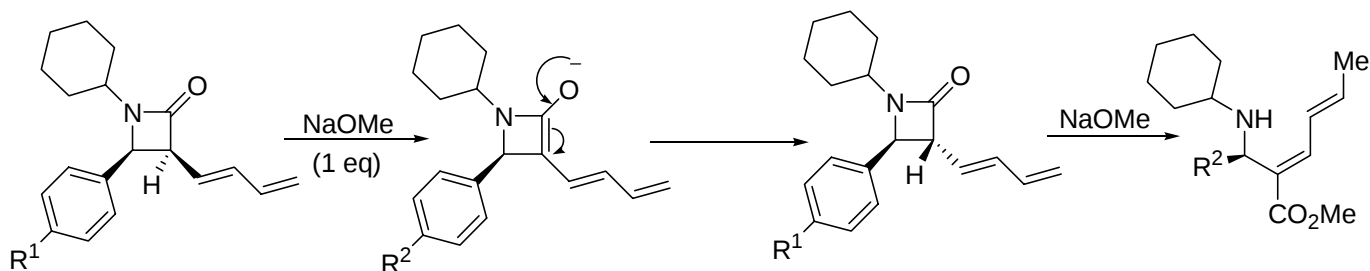
Recently, Troisi *et al.* have also reported the sodium methoxide amidolysis of α -vinyl- β -lactam to afford *E:Z* (1:1) mixture of α -ethylidene- β -aminobenzenepropanoic acid methyl esters.¹⁶ The stereoselectivity observed in the present case of sodium alkoxide amidolysis of 3-butadienyl-2-azetidinones 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. ^1H NMR spectra were recorded in deuteriochloroform 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 deuteriochloroform using TMS as internal standard. Mass spectra were recorded on Shimadzu GCMS-QP-2000 mass spectrometer. Elemental analyses were performed on Heraeus 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-azetidinones¹⁰ (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} . ^1H 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_i), 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 $\text{C}_{20}\text{H}_{20}\text{ClNO}_2$ (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): $\nu_{\max}$ = 1689.6, 3393.4 cm^{-1} . ^1H 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 $\text{C}_{20}\text{H}_{20}\text{ClNO}_2$ (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): $\nu_{\max}$ = 1682.5, 3389.5 cm^{-1} . ^1H 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, $-\text{OCH}_3\text{C}_6\text{H}_4$), 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 $\text{C}_{21}\text{H}_{23}\text{NO}_3$ (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): $\nu_{\max}$ = 1689.5, 3388.5 cm^{-1} . ^1H 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, $-\text{OCH}_3\text{C}_6\text{H}_4$), 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 $\text{C}_{21}\text{H}_{23}\text{NO}_3$ (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): $\nu_{\max}$ = 1681.1, 3396.4 cm^{-1} . ^1H 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 $\text{C}_{20}\text{H}_{20}\text{NO}_2$ (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): $\nu_{\max}$ = 1678.1, 3390.4 cm^{-1} . ^1H NMR (CDCl_3 , 300

MHz): $\delta_{\text{H}} = 1.92(\text{dd}, J = 6.6, 1.5 \text{ Hz}, 3 \text{ H}, \text{H}_7)$, $2.42(\text{s}, 3 \text{ H}, -\text{CH}_3\text{C}_6\text{H}_4)$, $3.67(\text{s}, 3 \text{ H}, \text{H}_9)$, $5.09(\text{d}, J=9.3 \text{ Hz}, 1 \text{ H}, \text{H}_1)$, $5.79(\text{d}, J = 9.0 \text{ Hz}, 1 \text{ H}, \text{H}_2)$, $6.28(\text{m}, 1 \text{ H}, \text{H}_6)$, $6.63(\text{m}, 1 \text{ H}, \text{H}_5)$, $6.66(\text{m}, 1 \text{ H}, \text{H}_4)$, $6.63\text{--}7.40(\text{m}, 9 \text{ H}, \text{aromatic})$ ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta_{\text{C}} = 19.1, 21.2, 51.8, 54.0, 113.6, 117.6, 126.1, 126.3, 126.8, 128.3, 129.3, 141.0, 141.2, 141.5, 147.1, 168.0$ ppm. MS m/z 321 $[M]^+$. Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_2$ (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-methoxyphenylamino)methyl]hexa-2,4-dienoic acid methyl ester (3g):

White solid (65 %), mp $135\text{--}138^\circ\text{C}$. IR (KBr): $\nu_{\text{max}} = 1679.1, 3388.4 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.91(\text{dd}, J = 6.6, 1.5 \text{ Hz}, 3 \text{ H}, \text{H}_7)$, $3.64(\text{s}, 3 \text{ H}, -\text{OCH}_3\text{C}_6\text{H}_4\text{N}-)$, $3.65(\text{s}, 3 \text{ H}, -\text{OCH}_3\text{C}_6\text{H}_4)$, $3.72(\text{s}, 3 \text{ H}, \text{H}_9)$, $5.08(\text{d}, J=9.3 \text{ Hz}, 1 \text{ H}, \text{H}_1)$, $5.78(\text{d}, J = 9.0 \text{ Hz}, 1 \text{ H}, \text{H}_2)$, $6.29(\text{m}, 1 \text{ H}, \text{H}_6)$, $6.66(\text{m}, 1 \text{ H}, \text{H}_5)$, $6.70(\text{m}, 1 \text{ H}, \text{H}_4)$, $6.66\text{--}7.38(\text{m}, 8 \text{ H}, \text{aromatic})$ ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta_{\text{C}} = 19.1, 21.2, 51.8, 54.0, 56.2, 56.8, 113.6, 117.6, 126.1, 126.3, 126.8, 128.3, 129.3, 141.0, 141.2, 141.5, 147.1, 168.0$ ppm. MS m/z 367 $[M]^+$. Anal. Calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_4$ (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 $122\text{--}124^\circ\text{C}$. IR (KBr): $\nu_{\text{max}} = 1690.6, 3392.4 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.91(\text{dd}, J = 6.6, 1.5 \text{ Hz}, 3 \text{ H}, \text{H}_7)$, $3.68(\text{s}, 3 \text{ H}, \text{H}_9)$, $5.06(\text{d}, J=9.3 \text{ Hz}, 1 \text{ H}, \text{H}_1)$, $5.72(\text{d}, J = 9.0 \text{ Hz}, 1 \text{ H}, \text{H}_2)$, $6.26(\text{m}, 1 \text{ H}, \text{H}_6)$, $6.64(\text{m}, 1 \text{ H}, \text{H}_5)$, $6.71(\text{m}, 1 \text{ H}, \text{H}_4)$, $6.64\text{--}7.38(\text{m}, 8 \text{ H}, \text{aromatic})$ ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta_{\text{C}} = 19.2, 51.8, 54.1, 114.7, 117.9, 126.3, 127.1, 128.4, 129.2, 129.4, 141.3, 141.8, 142.2, 147.0, 167.3$ ppm. MS m/z 375 $[M]^+$. Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{Cl}_2\text{NO}_2$ (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 $102\text{--}104^\circ\text{C}$. IR (KBr): $\nu_{\text{max}} = 1682.6, 3388 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.1\text{--}1.97(\text{m}, 10 \text{ H}, \text{cyclohexyl})$, $1.18(\text{dd}, J = 6.4, 1.4 \text{ Hz}, 3 \text{ H}, \text{H}_7)$, $3.42(\text{m}, 1 \text{ H}, -\text{H}(\text{cyclohexyl}))$, $3.64(\text{s}, 3 \text{ H}, \text{H}_9)$, $5.08(\text{d}, J=9.3 \text{ Hz}, 1 \text{ H}, \text{H}_1)$, $5.68(\text{d}, J = 9.0 \text{ Hz}, 1 \text{ H}, \text{H}_2)$, $6.28(\text{m}, 1 \text{ H}, \text{H}_6)$, $6.69(\text{m}, 1 \text{ H}, \text{H}_5)$, $6.71(\text{m}, 1 \text{ H}, \text{H}_4)$, $6.70\text{--}7.25(\text{m}, 5 \text{ H}, \text{aromatic})$ ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta_{\text{C}} = 16.4, 17.5, 33.8, 44.5, 51.3, 54.5, 56.9, 114.8, 117.9, 126.6, 127.5, 127.8, 128.1, 130.4, 132.5, 132.9, 141.4, 144.2, 147.5, 166.3$ ppm. MS m/z 347 $[M]^+$. Anal. Calcd for $\text{C}_{20}\text{H}_{26}\text{ClNO}_2$ (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 $108\text{--}110^\circ\text{C}$. IR (KBr): $\nu_{\text{max}} = 1692.6, 3390.4 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.82(\text{dd}, J = 6.4, 1.4 \text{ Hz}, 3 \text{ H}, \text{H}_7)$, $3.64(\text{s}, 3 \text{ H}, \text{H}_9)$, $3.92(\text{s}, 2 \text{ H}, -\text{CH}_2(\text{benzyl}))$, $5.09(\text{d},$

$J=9.3$ 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): $\delta_{\text{C}} = 19.2, 51.8, 52.6, 54.1, 114.7, 117.9, 126.4, 128.1, 129.0, 129.2, 129.5, 141.4, 141.9, 142.8, 147.2, 167.6$ ppm. MS m/z 356 $[M]^+$. Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{ClNO}_2$ (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): $\nu_{\text{max}} = 1689.5, 3392.5 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.06(\text{t}, 3 \text{ H}, -\text{CH}_3-\text{CH}_2)$, 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): $\delta_{\text{C}} = 14.2, 20.2, 51.6, 54.1, 113.5, 117.6, 126.2, 126.3, 126.6, 128.3, 129.2, 141.0, 141.2, 141.5, 147.2, 167.4$ ppm. MS m/z 355 $[M]^+$. Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{ClNO}_2$ (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): $\nu_{\text{max}} = 1689.5, 3388.5 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.08(\text{t}, 3 \text{ H}, -\text{CH}_3-\text{CH}_2)$, 1.97(m, 2 H, H_7), 3.63 (s, 3H, $-\text{OCH}_3\text{C}_6\text{H}_4$), 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): $\delta_{\text{C}} = 14.4, 20.2, 51.8, 54.8, 57.2, 114.2, 118.2, 128.1, 128.2, 128.9, 129.2, 130.6, 142.2, 142.6, 142.8, 148.2, 167.6, 169.6$ ppm. MS m/z 351 $[M]^+$. Anal. Calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_3$ (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): $\nu_{\text{max}} = 1681.1, 3396.4 \text{ cm}^{-1}$. ^1H NMR (CDCl_3 , 300 MHz): $\delta_{\text{H}} = 1.10(\text{t}, 3 \text{ H}, -\text{CH}_3-\text{CH}_2)$, 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): $\delta_{\text{C}} = 14.6, 20.2, 51.7, 54.1, 113.5, 117.6, 126.2, 126.4, 126.9, 128.4, 129.3, 141.1, 141.2, 141.6, 147.2, 168.0$ ppm. MS m/z 321 $[M]^+$. Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_2$ (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. $\text{C}_{20}\text{H}_{20}\text{ClNO}_2$, $M = 341.82$, triclinic, space group $P-1$, $a = 8.380(5)$, $b = 10.941(5)$, $c = 11.215(5)$ Å, $\alpha = 111.360(5)^\circ$, $\beta = 103.700(5)^\circ$, $\gamma = 90.840(5)^\circ$, $V = 924.6(8)$ Å³, $Z = 2$, D calcd. = 1.228 Mg/m³, $\mu(\text{Abs. Coeff.}) = 0.217 \text{ mm}^{-1}$, $T = 298(2)$ K, $\lambda = 0.71073$ Å, Final R indices [$I \geq 2.0\sigma(I)$] $R_1 = 0.0602$,

$wR2 = 0.1548$, R indices (all data) [$I \geq 2.0\sigma(I)$] $R1 = 0.1037$, $wR2 = 0.1904$ (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.