Solvent-Free and Efficient Synthesis of Highly Functionalized Cyclohexa-1,3-diene Derivatives via a Novel One-Pot Three-Component Reaction

Abdolali Alizadeh,* Atieh Rezvanian, Javad Mokhtari

Department of Chemistry, Tarbiat Modares University, P.O. Box 14115-175, Tehran, Iran
Fax +98(21)88006544; E-mail: abdol_alizad@yahoo.com; E-mail: aalizadeh@modares.ac.ir

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Abstract: A catalyst-free and convenient approach for the preparation of cyclohexa-1,3-dienecarboxylate derivatives is described. This three-component reaction between primary amines, alkyl acetoacetate, and dibenzylideneacetone proceeds under solvent-free condition in good to excellent yields.

Key words: primary amines, alkyl acetoacetate, dibenzylideneacetone, cyclohexa-1,3-dienecarboxylate, solvent-free

Cyclohexadienes are very important subunits in a number of biologically active compounds[1–3] such as antibacterially active agent **A**,[1a,b] antimicrobially active agent **B**,[1c] and calcium channel modulator **C**,[2] as well as versatile intermediates[4,5] in organic synthesis (Figure 1). Cyclohexa-1,3-diene has also been used successfully to produce a high-molecular-weight all-*cis* polymer.[6] Although several methods have been reported for the synthesis of cyclohexadienes,[7,8] they all rely on multistep reactions or their yields are low and the reaction times are long. New methodologies for rapid access to chemical diversity space include multicomponent reactions (MCRs), which are noteworthy tools for the quick and efficient synthesis of an extensive variety of organic compounds.

During the last two decades multicomponent reactions have been exploited by combinatorial chemists as a source of appendage diversity. One-pot multicomponent reactions are often resource-effective and environmentally acceptable and, thus, greener as compared to multistep reactions. They can offer significant advantages over conventional single-step syntheses by reducing time and saving money, energy, and raw materials, thus resulting in both economical and environmental benefits. At the same time, diversity can be achieved by building up libraries by varying each component.[9]

As part of our continuing effort in the design of new routes for the preparation of biologically active heterocycles and new organic compounds using the synthesis and reactions of enamines,[10] herein, we describe an efficient synthesis of fully substituted cyclohexadienes via a new one-pot three-component reaction. Our new synthetic route is shown in Table 1. Reaction between primary amines **1**, alkyl acetoacetates **2**, and dibenzylideneacetone under solvent-free conditions at room temperature (the amine and alkyl acetoacetate are mixed first and then dibenzylideneacetone is added) produces the alkyl 2-(alkylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate derivatives **3** in excellent yields.

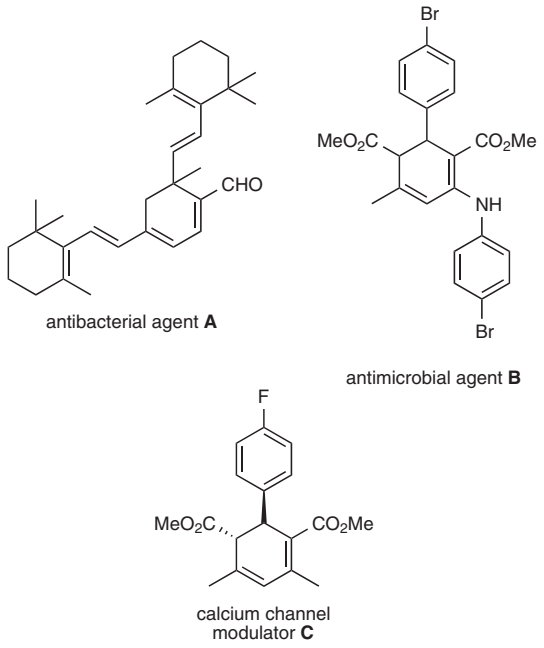

Figure 1

In order to establish the generality and scope of this new synthesis, we used different derivatives of primary amines **1a**–**e** and alkyl acetoacetate **2a**,**b** (Table 1). As anticipated from our initial results, these reactions proceed very cleanly under solvent-free conditions at room temperature and undesirable side-reactions are not observed.

The structures of compounds **3a**–**i** (Table 1) were deduced from their elemental analysis, IR, and high-field ^{1}H and ^{13}C NMR spectra. The mass spectrum of **3a** displayed the molecular ion peak at *m*/*z* 373, which is in agreement with the proposed structure. In the IR spectrum of **3a**, three absorption bands at 3264, 1643, 1607, and two absorption bands at 1561 and 1446 cm^{-1}, which are related to NH, CO_2Me, NC=C groups and aromatic stretching frequencies, clearly indicated the most significant functional groups of the product. The ^{1}H NMR spectrum of **3a** exhibited one triplet signal at δ = 1.04 (J = 7.4 Hz), readily recognized as methyl of propyl group. One sextet signal at

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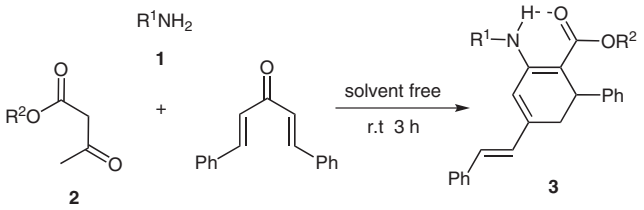
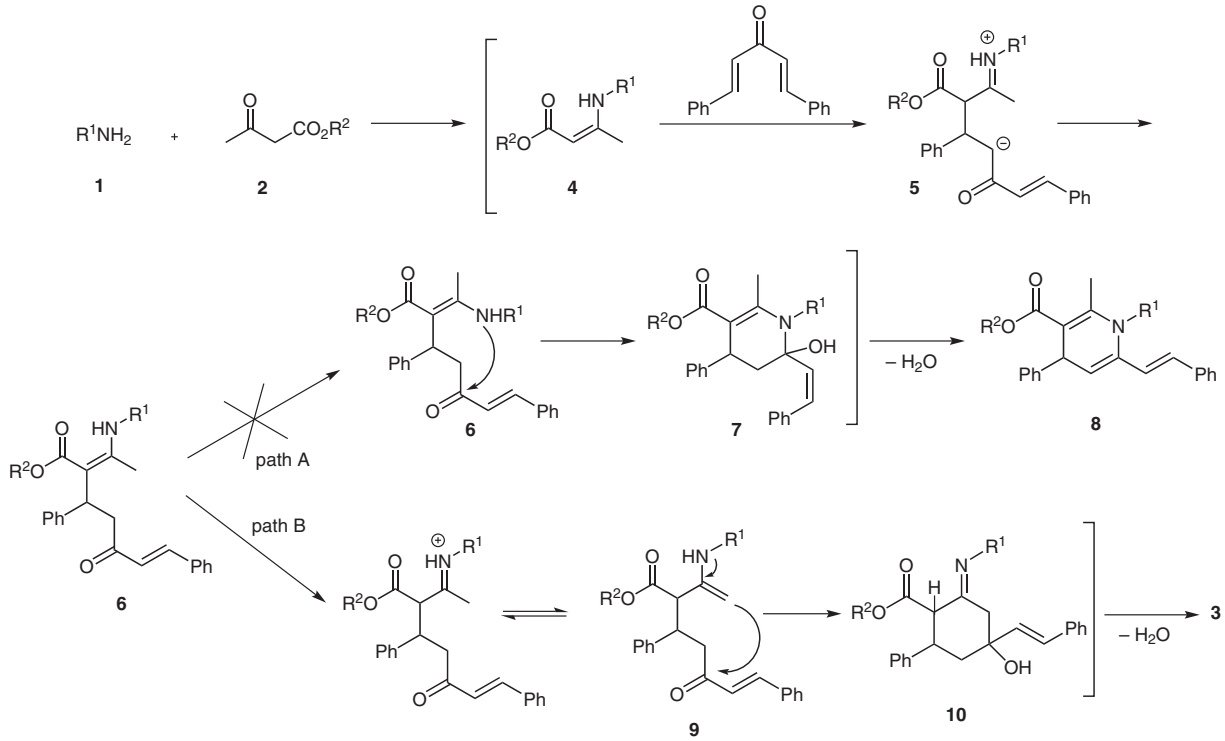
Table 1 Methyl or Ethyl 2-(Alkylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate Derivatives Prepared



Entry	R^1 **1**	R^2 **2**	Product **3**	Yield (%)
1	Pr (**1a**)	Me (**2a**)	**3a**	90
2	Pr (**1a**)	Et (**2b**)	**3b**	81
3	*i*-Bu (**1b**)	Me (**2a**)	**3c**	74
4	*i*-Bu (**1b**)	Et (**2b**)	**3d**	77
5	Bn (**1c**)	Me (**2a**)	**3e**	70
6	Bn (**1c**)	Et (**2b**)	**3f**	65
7	Bu (**1d**)	Me (**2a**)	**3g**	82
8	Bu (**1d**)	Et (**2b**)	**3h**	80
9	$CH_2CH=CH_2$ (**1e**)	Me (**2a**)	**3i**	64

δ = 1.68 (J = 7.2 Hz) was attributed to the methylenes (CH_2) of the propyl group. One of the hydrogens of the cyclohexadiene ring (CH_2) appears as doublet of doublet of doublet (ddd) at δ = 2.84 (^2J = 16.5 Hz, ^3J = 7.9 Hz, ^4J = 2.0 Hz), and the other hydrogen appears as doublet of doublet (dd) resonance at δ = 2.91 (^2J = 16.5 Hz, ^4J = 1.65 Hz). The appearance of these hydrogen signals could be explained as follows: due to the existence of a stereogenic center in the molecule, these hydrogens are diastereotopic to each other and one of them would be coupled with the geminal (^2J) and vicinal (^3J) hydrogens. The other hydrogen is probably positioned in a space so that it cannot couple with the vicinal hydrogen and it can only be split with the geminal hydrogen (^2J). However, both of them show a weak coupling with the hydrogen which is linked to C^3 of cyclohexadiene ring (^4J). The spectrum also contains one multiplet and one sharp singlet at δ = 3.27–3.36 and 3.68 which are attributed to the hydrogens of the CH_2N and OCH_3 groups, respectively. There are two doublet signals at δ = 4.24 (^3J = 6.9 Hz) and 6.38 (^4J = 1.6 Hz), which correspond to two CH groups of the cyclohexadiene ring. For both of the *trans* hydrogens of the CH=CH group, the signals appear as two doublets at δ = 6.72 (^3J = 16.1 Hz, C*H*=CHPh) and 6.86 (^3J = 16.1 Hz, CH=C*H*Ph). Ten aromatic hydrogens gave rise to characteristic signals in the aromatic region of the spectrum. Finally, the signal of NH group appears as singlet at δ = 9.01. The ^{1}H-decoupled ^{13}C NMR spectrum of **3a** showed 21 distinct resonances in agreement with the suggested structure.

Although no detailed mechanistic studies have been carried out at this point, a tentative mechanism for this transformation is proposed in Scheme 1. Initially the reaction of primary amine **1** and alkyl acetoacetate **2** leads to the enaminone intermediate **4**. Enaminone **4** attacks the double bond of dibenzylideneacetone to produce intermediate **5**, which in turn is converted into intermediate **6**. At this stage, considering the chemistry of enaminones,[11–15] we would normally expect nonbonding electron pairs of the nitrogen atom to attack to the carbonyl group and cause the creation of product **8** by elimination of a molecule of water (path A). But considering IR and ^{1}H and ^{13}C NMR



Scheme 1 Mechanism for the formation of alkyl 2-(alkylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylates **3**

spectra, this product was not created and another considerable event occurs. In fact, in this stage intermediate **6** undergoes an enamine–iminium ion–enamine isomerization process to form enamine **9**. Cyclization of the intermediate **9** to generate compound **10** and finally, by elimination of a molecule of water gives cyclohexa-1,3-dienecarboxylate derivatives **3** (path B). The reaction proceeds under path B, because of compounds **3** are more stable than compounds **8**. Compounds of type **3** are produced under equilibrium conditions and the vinylogous amide in all of the products (Table 1) is stabilized by an internal hydrogen bond.

In summary, we have developed a simple, one-pot, three-component synthesis of methyl or ethyl 2-(alkylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate derivatives, which are of potential synthetic interest. High yields of the products, relatively short reaction times, using simple and inexpensive starting materials as well as the solvent-free reaction condition are the main advantages of this method. Also, product could have high diversity via various functional groups instead of amine and ester groups. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.

All reactions were carried out in oven-dried glassware. Progress of reactions was monitored by TLC while purification was effected by column chromatography, using silica gel (Merck 230–240 mesh). Primary amines, and alkyl acetoacetate and dibenzylideneacetone were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ soln) with a Bruker DRX-500 Avance spectrometer at 500.13 and 125.8 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrophotometer.

Methyl 6-Phenyl-2-(propylamino)-4-styrylcyclohexa-1,3-dienecarboxylate (3a); Typical Procedure

To a magnetically stirred 5-mL flat-bottomed flask containing $PrNH_2$ (**1a**, 0.059 g, 1 mmol) was added methyl acetoacetate (**2a**, 0.116 g, 1 mmol). After 30 min, dibenzylideneacetone (0.234 g, 1 mmol) was added to the reaction mixture which was allowed to stir for 2.5 h. Purification of the crude product by column chromatography (silica gel, Merck 230–240 mesh, *n*-hexane–EtOAc, 12:1)] gave **3a** as an orange oil; yield: 0.31 g (90%).

IR (KBr): 3264 (NH), 1643 (CO_2Me), 1608 (NC=C), 1561 (Ph), 1446 (Ph), 1261 (ester C–O), 1207 cm^{-1} (ester C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 1.04 (t, ^3J = 7.4 Hz, 3 H, CH_3), 1.68 (sextet, ^3J = 7.2 Hz, 2 H, CH_2), 2.84 (ddd, ^2J = 16.5 Hz, ^3J = 7.9 Hz, ^4J = 2.0 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.5 Hz, ^4J = 1.65 Hz, 1 H, CH_2), 3.27–3.36 (m, 2 H, CH_2NH), 3.68 (s, 3 H, OCH_3), 4.24 (d, ^3J = 6.9 Hz, 1 H, CH^6), 6.38 (d, ^4J = 1.6 Hz, 1 H, CH^3), 6.72 (d, ^3J = 16.1 Hz, 1 H, C*H*=CHPh), 6.86 (d, ^3J = 16.1 Hz, 1 H, CH=C*H*Ph), 7.12 (t, ^3J = 6.7 Hz, 1 H, CH_{Ph}), 7.19–7.26 (m, 5 H, 5 CH_{Ph}), 7.31 (d, ^3J = 7.4 Hz, 2 H, 2 CH_{Ph}), 7.41 (d, ^3J = 7.6 Hz, 2 H, 2 CH_{Ph}), 9.01 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 11.4 (CH_3), 23.9 (*C*H_2CH_3), 31.5 (CH_2), 36.2 (CH_2NH), 44.6 (CH^6), 50.3 (OCH_3), 90.0 (CH^1), 119.6 (*C*=CPh), 125.8 (CH_{para}), 126.8 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 127.9 (2 CH_{Ph}), 128.2 (CH_{para}), 128.6 (2 CH_{Ph}), 129.7 (CH^3), 131.8 (C=*C*Ph), 136.6 (C_{ipso}), 144.1 (C^4), 145.8 (C_{ipso}), 155.2 (C^2), 170.5 (*C*O_2Me).

MS: *m*/*z* (%) = 373 (85) [M$^+$], 330 (15), 314 (100), 296 (88), 208 (19), 165 (14), 82 (27), 41 (14).

Anal. Calcd for $C_{25}H_{27}NO_2$ (373.49): C, 80.40; H, 7.29; N, 3.75. Found: C, 80.36; H, 7.24; N, 3.79.

Ethyl 6-Phenyl-2-(propylamino)-4-styrylcyclohexa-1,3-dienecarboxylate (3b)

Orange oil; yield: 0.31 g (81%).

IR (KBr): 3279 (NH), 1632 (CO_2Et), 1601 (NC=C), 1557 (Ph), 1445 (Ph), 1260 (ester C–O), 1226 cm^{-1} (ester C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 1.03 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.15 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.68 (sextet, ^3J = 7.1 Hz, 2 H, CH_2), 2.85 (ddd, ^2J = 16.2 Hz, ^3J = 7.9 Hz, ^4J = 1.9 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.2 Hz, ^4J = 1.8 Hz, 1 H, CH_2), 3.26–3.35 (m, 2 H, CH_2NH), 4.01–4.11 (m, 2 H, OCH_2CH_3), 4.24 (d, ^3J = 7.9 Hz, 1 H, CH^5), 6.39 (d, ^4J = 1.8 Hz, 1 H, CH^3), 6.73 (d, ^3J = 16.0 Hz, 1 H, C*H*=CHPh), 6.88 (d, ^3J = 16.0 Hz, 1 H, CH=C*H*Ph), 7.12 (t, ^3J = 7.0 Hz, 1 H, CH_{Ph}), 7.18–7.27 (s, 5 H, 5 CH_{Ph}), 7.31 (d, ^3J = 7.3 Hz, 2 H, 2 CH_{Ph}), 7.41 (d, ^3J = 7.3 Hz, 2 H, 2 CH_{Ph}), 8.98 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 11.5 (CH_3), 14.4 (OCH_2CH_3), 23.9 (*C*H_2CH_3), 31.3 (CH_2), 36.4 (CH_2NH), 44.6 (OCH_2CH_3), 58.6 (CH^6), 90.6 (CH^1), 119.7 (*C*=CPh), 125.7 (CH_{para}), 126.7 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 127.8 (2 CH_{Ph}), 128.2 (CH_{para}), 128.6 (2 CH_{Ph}), 129.8 (CH^3), 131.7 (C=*C*Ph), 136.6 (C_{ipso}), 144.0 (C^4), 146.2 (C_{ipso}), 154.9 (C^2), 170.1 (*C*O_2Me).

MS: *m*/*z* (%) = 387 (74) [M$^+$], 344 (11), 314 (100), 234 (10), 208 (23), 194 (15), 91 (23), 77 (12), 43 (7).

Anal. Calcd for $C_{26}H_{29}NO_2$ (387.52): C, 80.59; H, 7.54; N, 3.61. Found: C, 80.53; H, 7.59; N, 3.66.

Methyl 2-(Isobutylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate (3c)

Orange oil; yield: 0.28 g (74%).

IR (KBr): 3270 (NH), 1641 (CO_2Me), 1605 (NC=C), 1559 (Ph), 1445 (Ph), 1285 (ester C–O), 1223 cm^{-1} (ester C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 0.98 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.03 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.87–1.92 (m, 1 H, Me_2CH), 2.86 (ddd, ^2J = 16.3 Hz, ^3J = 7.6 Hz, ^4J = 2.3 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.3 Hz, ^4J = 2.1 Hz, 1 H, CH_2), 3.17 (q, ^3J = 6.7 Hz, 2 H, CH_2NH), 3.61 (s, 3 H, OCH_3), 4.25 (d, ^3J = 6.8 Hz, 1 H, CH^6), 6.37 (d, ^4J = 2.1 Hz, 1 H, CH^3), 6.72 (d, ^3J = 16.0 Hz, 1 H, C*H*=CHPh), 6.86 (d, ^3J = 16.0 Hz, 1 H, CH=C*H*Ph), 7.12 (t, ^3J = 6.6 Hz, 1 H, CH_{Ph}), 7.18–7.26 (5 CH_{Ph}), 7.31 (d, ^3J = 7.3 Hz, 2 H, 2 CH_{Ph}), 7.40 (d, ^3J = 7.3 Hz, 2 H, 2 CH_{Ph}), 9.12 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 20.3 (2 CH_3), 29.5 (CH), 31.5 (CH_2), 36.2 (CH_2NH), 50.3 (OCH_3), 50.6 (CH^6), 89.9 (CH^1), 119.6 (*C*=CPh), 125.8 (CH_{para}), 126.8 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 127.9 (2 CH_{Ph}), 128.2 (CH_{para}), 128.6 (2 CH_{Ph}), 129.8 (CH^3), 131.8 (C=*C*Ph), 136.6 (C_{ipso}), 144.1 (C^4), 145.8 (C_{ipso}), 155.3 (C^2), 170.5 (*C*O_2Me).

MS: *m*/*z* (%) = 387 (93) [M$^+$], 328 (100), 310 (92), 272 (24), 208 (21), 194 (18), 91 (26), 77 (10), 41 (13).

Anal. Calcd for $C_{26}H_{29}NO_2$ (387.52): C, 80.59; H, 7.54; N, 3.61. Found: C, 80.63; H, 7.49; N, 3.55.

Ethyl 2-(Isobutylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate (3d)

Orange oil; yield: 0.30 g (77%).

IR (KBr): 3277 (NH), 1633 (CO_2Et), 1600 (NC=C), 1559 (Ph), 1438 (Ph), 1260 (ester C–O), 1228 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 0.96 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.03 (d, ^3J = 6.7 Hz, 3 H, CH_3), 1.15 (t, ^3J = 7.1 Hz, 3 H, CH_2CH_3), 1.85–1.91 (m, 1 H, $CHMe_2$), 2.85 (ddd, ^2J = 16.5 Hz, ^3J = 7.8 Hz, ^4J = 1.9 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.5 Hz, ^4J = 1.6 Hz, 1 H, CH_2), 3.16 (t, ^3J = 6.1 Hz, 2 H, CH_2NH), 4.01–4.12 (m, 2 H, OCH_2CH_3), 4.24 (d, ^3J = 7.8 Hz, 1 H, CH^6), 6.38 (s, 1 H, CH^3), 6.73 (^3J = 16.1 Hz, 1 H, CH=CHPh), 6.88 (d, ^3J = 16.1 Hz, 1 H, CH=CHPh), 7.13 (t, ^3J = 5.5 Hz, 1 H, 1 CH_{Ph}), 7.18–7.27 (m, 5 H, 5 CH_{Ph}), 7.30 (t, ^3J = 7.7 Hz, 2 H, 2 CH_{Ph}), 7.41 (d, ^3J = 7.7 Hz, 2 H, 2 CH_{Ph}), 9.08 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 15.3 (OCH_2CH_3), 21.0 (2 CH_3), 30.4 (CH), 32.2 (CH_2), 37.3 (CH_2NH), 51.5 (OCH_2CH_3), 59.5 (CH^6), 91.5 (CH^1), 120.7 (CH=CHPh), 126.6 (CH_{Ph}), 127.6 (2 CH_{Ph}), 128.0 (2 CH_{Ph}), 128.7 (2 CH_{Ph}), 129.0 (CH_{Ph}), 129.5 (2 CH_{Ph}), 130.7 (CH^3), 132.6 (C=CPh), 137.5 (C_{ipso}), 144.8 (C^4), 147.1 (C_{ipso}), 155.9 (C^2), 171.0 (CO_2Me).

MS: *m*/*z* (%) = 401 (83) [M^+], 344 (18), 328 (100), 312 (19), 272 (25), 208 (31), 142 (29), 96 (57), 57 (25), 41 (26).

Anal. Calcd for $C_{27}H_{31}NO_2$ (401.55): C, 80.76; H, 7.78; N, 3.49. Found: C, 80.82; H, 7.71; N, 3.44.

Methyl 2-(Benzylamino)-6-phenyl-4-styrylcyclohexa-1,3-diene-carboxylate (3e)
Orange oil; yield: 0.29 g (70%).

IR (KBr): 3262 (NH), 1642 (CO_2Me), 1608 (NC=C), 1561 (Ph), 1445 (Ph), 1284 (ester C–O), 1228 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 2.85 (ddd, ^2J = 16.4 Hz, ^3J = 7.6 Hz, ^4J = 2.0 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.5 Hz, ^4J = 2.1 Hz, 1 H, CH_2), 3.61 (s, 3 H, OCH_3), 4.26 (dd, ^3J = 7.6 Hz, 1 H, CH^5), 4.58 (t, ^3J = 5.5 Hz, 2 H, CH_2), 6.33 (d, ^4J = 2.1 Hz, 1 H, CH^3), 6.68 (d, ^3J = 16.1 Hz, 1 H, CH=CHPh), 6.76 (d, ^3J = 16.1 Hz, 1 H, CH=CHPh), 7.11–7.40 (m, 15 H, 15 CH_{Ph}), 9.36 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 31.6 (CH_2), 36.3 (CH_2NH), 46.7 (OCH_3), 50.5 (CH^6), 91.3 (CH^1), 119.5 (C=CPh), 125.9 (CH_{para}), 126.7 (CH_{para}), 126.8 (2 CH_{Ph}), 126.8 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 128.0 (2 CH_{Ph}), 128.2 (CH_{para}), 128.6 (2 CH_{Ph}), 128.8 (2 CH_{Ph}), 129.7 (CH^3), 131.9 (C=CPh), 136.5 (C_{ipso}-CH_2), 139.3 (C_{ipso}), 144.3 (C^4), 145.6 (C_{ipso}), 155.1 (C^2), 170.5 (CO_2Me).

MS: *m*/*z* (%) = 421 (34) [M^+], 387 (10), 362 (23), 332 (27), 300 (17), 141 (14), 91 (100), 69 (18), 43 (17).

Anal. Calcd for $C_{29}H_{27}NO_2$ (421.53): C, 82.63; H, 6.46; N, 3.32. Found: C, 82.69; H, 6.43; N, 3.27.

Ethyl 2-(Benzylamino)-6-phenyl-4-styrylcyclohexa-1,3-diene-carboxylate (3f)
Orange oil; yield: 0.28 g (65%).

IR (KBr): 3440 (NH), 1632 (CO_2Et), 1608 (NC=C), 1567 (Ph), 1445 (Ph), 1264 (ester C–O), 1224 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 1.17 (t, ^3J = 6.8 Hz, 3 H, CH_3), 2.85 (ddd, ^2J = 16.4 Hz, ^3J = 7.6 Hz, ^4J = 2.0 Hz, 1 H, CH_2), 2.87 (dd, ^2J = 16.4 Hz, ^4J = 2.1 Hz, 1 H, CH_2), 4.06–4.12 (s, 2 H, OCH_2CH_3), 4.26 (dd, ^3J = 7.6 Hz, 1 H, CH^5), 4.58 (t, ^3J = 5.8 Hz, 2 H, CH_2), 6.33 (d, ^4J = 2.1 Hz, 1 H, CH^3), 6.70 (d, ^3J = 16.0 Hz, 1 H, CH=CHPh), 6.82 (d, ^3J = 16.0 Hz, 1 H, CH=CHPh), 7.12–7.46 (m, 15 H, 15 CH_{Ph}), 9.08 (s, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 14.4 (OCH_2CH_3), 31.3 (CH_2), 36.4 (CH_2NH), 45.0 (CH^6), 58.7 (OCH_2CH_3). 91.8 (CH^1), 119.6 (C=CPh), 125.7 (CH_{para}), 126.7 (CH_{para}), 127.0 (2 CH_{Ph}), 127.5 (2 CH_{Ph}), 127.9 (2 CH_{Ph}), 128.1 (2 CH_{Ph}), 128.3 (CH_{para}), 128.6 (2 CH_{Ph}), 128.8 (2 CH_{Ph}), 129.7 (CH^3), 131.8 (C=CPh), 135.3 (C_{ipso}-CH_2), 139.1 (C_{ipso}), 143.9 (C^4), 146.0 (C_{ipso}), 154.1 (C^2), 170.1 (CO_2Et).

MS: *m*/*z* (%) = 435 (1) [M^+], 385 (19), 312 (62), 234 (49), 181 (17), 149 (27), 131 (54), 103 (61), 91 (75), 77 (69), 43 (100).

Anal. Calcd for $C_{30}H_{29}NO_2$ (435.56): C, 82.73; H, 6.71; N, 3.22. Found: C, 82.77; H, 6.68; N, 3.20.

Methyl 2-(Butylamino)-6-phenyl-4-styrylcyclohexa-1,3-diene-carboxylate (3g)
Orange oil; yield: 0.31 g (82%).

IR (KBr): 3276 (NH), 1634 (CO_2Me), 1610 (NC=C), 1571 (Ph), 1445 (Ph), 1275 (ester C–O), 1234 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.44–1.51 (m, 2 H, CH_2), 1.62–1.69 (m, 2 H, CH_2), 2.85 (ddd, ^2J = 16.5 Hz, ^3J = 7.9 Hz, ^4J = 1.9 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.5 Hz, ^4J = 1.7 Hz, 1 H, CH_2), 3.29–3.42 (m, 2 H, CH_2NH), 3.60 (s, 3 H, OCH_3), 4.24 (d, ^3J = 7.9 Hz, 1 H, CH^6), 6.39 (d, ^4J = 1.7 Hz, 1 H, CH^3), 6.72 (d, ^3J = 16.0 Hz, 1 H, CH=CHPh), 6.87 (d, ^3J = 16.0 Hz, 1 H, CH=CHPh), 7.12 (t, ^3J = 7.1 Hz, 1 H, CH_{Ph}), 7.18–7.28 (m, 5 H, 5 CH_{Ph}), 7.31 (t, ^3J = 7.7 Hz, 2 H, 2 CH_{Ph}), 7.41 (d, ^3J = 7.7 Hz, 2 H, 2 CH_{Ph}), 8.99 (br, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.1 (CH_2), 31.5 (CH_2), 32.7 ($EtCH_2$), 36.2 (CH_2NH), 42.5 (CH^6), 50.3 (CH_3), 89.9 (CH^1), 119.6 (C=CPh), 125.8 (CH_{para}), 126.7 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 127.9 (2 CH_{Ph}), 128.2 (CH_{para}), 128.6 (2 CH_{Ph}), 129.7 (CH^3), 131.8 (C=CPh), 136.6 (C_{ipso}), 144.2 (C^4), 145.8 (C_{ipso}), 155.2 (C^2), 170.5 (CO_2Me).

MS: *m*/*z* (%) = 387 (58) [M^+], 91 (72), 81 (64), 280 (27), 234 (40), 199 (62), 91 (49), 71 (68), 57 (79), 43 (100).

Anal. Calcd for $C_{26}H_{29}NO_2$ (387.52): C, 80.59; H, 7.54; N, 3.61. Found: C, 80.55; H, 7.49; N, 3.64.

Ethyl 2-(Butylamino)-6-phenyl-4-styrylcyclohexa-1,3-dienecarboxylate (3h)
Orange oil; yield: 0.32 g (80%).

IR (KBr): 3275 (NH), 1635 (CO_2Et), 1603 (NC=C), 1558 (Ph), 1446 (Ph), 1260 (ester C–O), 1220 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.15 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.44–1.47 (m, 2 H, CH_2), 1.61–1.66 (m, 2 H, CH_2), 2.86 (ddd, ^2J = 16.0 Hz, ^3J = 6.4 Hz, ^4J = 1.9 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.0 Hz, ^4J = 1.7 Hz, 1 H, CH_2), 3.28–3.41 (m, 2 H, CH_2NH), 4.00–4.12 (s, 2 H, OCH_2CH_3), 4.24 (d, ^3J = 6.4 Hz, 1 H, CH^6), 6.39 (d, ^4J = 1.7 Hz, 1 H, CH^3), 6.72 (d, ^3J = 16.1 Hz, 1 H, CH=CHPh), 6.88 (d, ^3J = 16.1 Hz, 1 H, CH=CHPh), 7.10 (t, ^3J = 7.05 Hz, 1 H, CH_{Ph}), 7.18–7.26 (m, 5 H, 5 CH_{Ph}), 7.31 (t, ^3J = 7.6 Hz, 2 H, 2 CH_{Ph}), 7.41 (d, ^3J = 7.6 Hz, 2 H, 2 CH_{Ph}), 9.01 (br, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 14.4 (OCH_2CH_3), 20.1 (CH_2), 31.2 (CH_2), 32.7 (CH_2), 36.4 (CH_2NH), 42.6 (CH^6), 58.6 (OCH_2CH_3), 90.5 (CH^1), 119.7 (C=CPh), 125.7 (CH_{para}), 126.7 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 127.8 (2 CH_{Ph}), 128.1 (CH_{para}), 128.6 (2 CH_{Ph}), 129.8 (CH^3), 131.7 (C=CPh), 136.6 (C_{ipso}), 144.0 (C^4), 146.2 (C_{ipso}), 154.8 (C^2), 170.1 (CO_2Me).

MS: *m*/*z* (%) = 401 (76) [M^+], 328 (100), 234 (55), 208 (26), 103 (30), 91 (27), 77 (27), 41 (16), 91 (100).

Anal. Calcd for $C_{27}H_{51}NO_2$ (401.55): C, 80.76; H, 7.78; N, 3.49. Found: C, 80.71; H, 7.74; N, 3.55.

Methyl 2-(Allylamino)-6-phenyl-4-styrylcyclohexa-1,3-diene-carboxylate (3i)
Orange oil; yield: 0.23 g (64%).

IR (KBr): 3434 (NH), 1649 (CO_2Me), 1621 (NC=C), 1594 (Ph), 1446 (Ph), 1266 (ester C–O), 1226 cm^{-1} (ester C–O).

^1H NMR (500.13 MHz, $CDCl_3$): δ = 2.86 (ddd, ^2J = 16.4 Hz, ^3J = 7.5 Hz, ^4J = 2.0 Hz, 1 H, CH_2), 2.91 (dd, ^2J = 16.4 Hz, ^4J = 2.1 Hz, 1 H, CH_2), 3.61 (s, 3 H, OCH_3), 3.99 (br, 2 H, CH_2), 4.27 (d, ^3J = 7.5 Hz, 1 H, CH^5), 5.23 (d, ^3J = 10.5 Hz, 1 H, CH=CH_2), 5.35 (d, ^3J = 14.5 Hz, 1 H, CH=CH_2), 5.94–6.02 (m, 1 H, CH=CH_2), 6.32 (d, ^4J = 2.1 Hz, 1 H, CH^3), 6.72 (d, ^3J = 16.4 Hz, 1 H, CH=CHPh), 6.82 (d, ^3J = 16.4 Hz, 1 H, CH=CHPh), 7.08–7.77 (m, 10 H, 10 CH_{Ph}), 9.12 (br, 1 H, NH).

^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 31.5 (CH_2), 36.3 (CH_2NH), 45.0 (OCH_3), 50.4 (CH^1), 90.9 (CH^3), 116.0 (CH=CH$_2$), 119.5 (CH^5), 125.4 (CH_{para}), 125.9 (2 CH_{Ph}), 127.1 (2 CH_{Ph}), 128.3 (2 CH_{Ph}), 128.6 (CH_{para}), 128.9 (2 CH_{Ph}), 130.4 (C=CPh), 131.9 (C=CPh), 134.8 (C_{ipso}), 143.3 (CH=CH_2), 144.1 (C^4), 145.6 (C_{ipso}), 155.2 (C^2), 170.5 (CO_2Me).

MS: *m*/*z* (%) = 371 (3) [M^+], 312 (6), 280 (4), 234 (100), 205 (29), 191 (17), 165 (16.5), 131 (58), 103 (90), 91 (35), 77 (79), 51 (35).

Anal. Calcd for $C_{25}H_{25}NO_2$ (371.48): C, 80.83; H, 6.78; N, 3.77. Found: C, 80.79; H, 6.73; N, 3.81.

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