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Tandem [2+2] cycloaddition and Cope rearrangement in reactions of cross-conjugated azatrienes with conjugated ketenes: a facile single step synthesis of novel azocinone derivatives

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Abstract—A facile single step synthesis of novel azocinone derivatives involving tandem [2+2] cycloaddition and Cope rearrangement in the reactions of cross-conjugated azatrienes with vinyl/isopropenyl ketenes supported by theoretical calculations is reported.

1. Introduction

Nitrogen heterocycles are among the most useful and their utility has been widely demonstrated in the chemistry of natural products, in material sciences, and in pharmaceutical chemistry.[1] Their synthesis has attracted considerable attention due to their large importance as building blocks for many therapeutically useful materials, as well as for the wide range of potential biological activity of both synthetic and naturally occurring derivatives. The hetero Diels–Alder reactions of azadienes are one of the most versatile routes for the synthesis of such nitrogen heterocycles. Extensive efforts have been carried out toward the Diels–Alder cycloadditions involving azadienes containing one or more nitrogen atoms and the rapid developments in this area have been reviewed.[1] A large variety of nitrogen heterocycles have been synthesized in our laboratory by the cycloaddition reactions of azadienes with a number of dienophiles.[2]

Recently, Saito and co-workers[3] have reported the diene transmissive hetero Diels–Alder (DTHDA) reactions of some in situ generated cross-conjugated azatrienes, providing a synthetic access to ring fused heterocyclic frameworks.

However, despite being excellent synthons, their initial [4+2] cycloaddition reaction has been restricted to a few reactive heterocummulenes. The lack of extensive efforts in this area may be due to their reported sensitivity to varying reaction conditions and the non-availability of pure starting materials. Our continued interest in the utilization of azadienes in cycloaddition reactions,[2] coupled with the synthetic potential of cross-conjugated azatrienes prompted us to explore the isolation of azatrienes as stable synthons prior to their utilization in hetero DA reactions.

The procedure for the synthesis of stable cross-conjugated azatrienes involves the treatment of the corresponding ketone **1** (10 mmol) with aromatic amine **2** (15 mmol) in the presence of titanium tetrachloride (10 mmol) and triethylamine (22 mmol) in dry toluene at 0 °C (Scheme 1).

After completion, the reaction mixture was passed through a silica column and distillation of the solvent under reduced pressure yielded solid compounds in very good yields (71–88%).

Saito et al. examined the reactions of azatriene **3c** with disubstituted ketenes and obtained [2+2] cycloadducts, which upon heating in toluene underwent [1,3] sigmatropic rearrangement to yield pyridone derivatives.[3b] Recently, Alcaide and co-workers have reported that the reactions of 1-azabuta-1,3-dienes with vinyl/isopropenyl ketenes leading to the initial formation of *cis*-3,4-divinyl-β-lactams as [2+2] adducts, which upon thermolysis in refluxing toluene underwent [3,3] sigmatropic shift to yield azocinone derivatives.[5] However, the methodology used suffers several disadvantages, for example, 3,4-divinyl-β-lactams, used for these transformations, were prepared following a multiplet strategy with natural loss of yields. Also, despite being a novel synthetic route for few azocinones, the scope of this reaction

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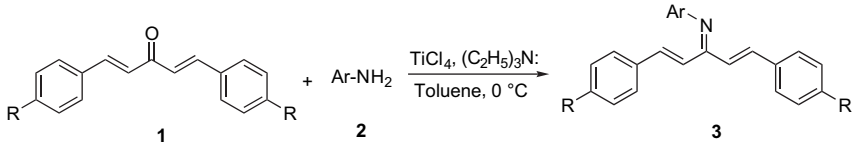


R = OCH_3, H, Cl
Ar = *p*-methoxyphenyl, *p*-tolyl, phenyl

3a. R = OCH_3, Ar = *p*-methoxyphenyl (79%)
3b. R = OCH_3, Ar = *p*-tolyl (82%)
3c. R = OCH_3, Ar = phenyl (88%)
3d. R = H, Ar = *p*-methoxyphenyl (84%)
3e. R = H, Ar = *p*-tolyl (87%)
3f. R = H, Ar = phenyl (83%)
3g. R = Cl, Ar = *p*-methoxyphenyl (76%)
3h. R = Cl, Ar = phenyl (81%)
3i. R = Cl, Ar = *p*-tolyl (71%)

Scheme 1.

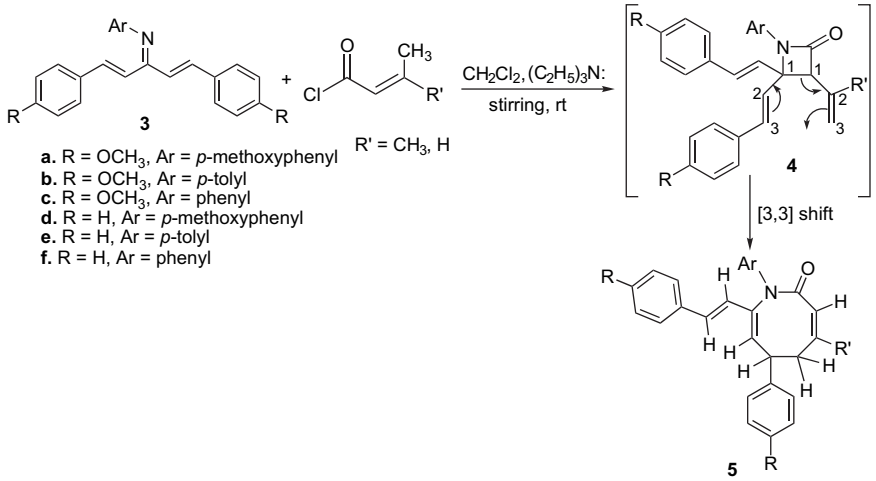
was limited to only few possible structural variants at N of 1-azabuta-1,3-diene.

In order to explore their scope and synthetic potential, we have examined the reactions of the isolated azatrienes **3** with conjugated ketenes viz. vinyl/isopropenyl ketenes, which themselves are known to participate either as 2π or 4π component in [2+2] and [4+2] cycloaddition reactions,[4] generated in situ from the corresponding acid chlorides in the presence of triethylamine in dry dichloromethane at room temperature. Interestingly, these reactions resulted in a facile single step synthesis of novel azocinone derivatives in excellent yields (72–89%), instead of the expected trialkyl 3,4,4-azitidinin-2-ones.

The formation of azocinones **5** in these reactions is probably the result of initial [2+2] cycloadditions and highly efficient [3,3] sigmatropic rearrangements of the so formed [2+2] cycloadducts, 3,4,4-trisubstituted-2-azetidinones **4**, as transient intermediates. The comparison of tlc of the crude reaction mixture with that of the pure product clearly ruled out any possibility of the observed Cope rearrangement taking place during processes such as recrystallization, work up, etc.

The mechanism proposed above was further corroborated by the energy minimization calculations performed at AM1 level using MOPAC program.[6] The calculations reveal that the product **5** is more stable than the initial [2+2] cycloadduct **4** by 28.9 kcal mol^{-1} (Scheme 2).

The energy minimization calculations for 3,4,4-trisubstituted-2-azetidinones **4** indicate an energy of 130.8 kcal mol^{-1} with apical distance (C_{12}–C_{17}) of 3.54 Å and dihedral angles −89° (C_{14}–C_2–C_6–C_{12}) and −15° (C_2–C_{14}–C_{15}–C_{17}) (Fig. 1). On the other hand, the energy minimization



a. R = OCH_3, Ar = *p*-methoxyphenyl
b. R = OCH_3, Ar = *p*-tolyl
c. R = OCH_3, Ar = phenyl
d. R = H, Ar = *p*-methoxyphenyl
e. R = H, Ar = *p*-tolyl
f. R = H, Ar = phenyl

R' = CH_3, H

No.	R	Ar	R'	Yield(%)
5a.	OCH_3	*p*-methoxyphenyl	CH_3	85
5b.	OCH_3	*p*-methoxyphenyl	H	82
5c.	OCH_3	*p*-tolyl	CH_3	81
5d.	OCH_3	*p*-tolyl	H	88
5e.	OCH_3	phenyl	CH_3	89
5f.	OCH_3	phenyl	H	83
5g.	H	*p*-methoxyphenyl	CH_3	72
5h.	H	*p*-methoxyphenyl	H	78
5i.	H	*p*-tolyl	CH_3	86
5j.	H	*p*-tolyl	H	80
5k.	H	phenyl	CH_3	77
5l.	H	phenyl	H	76

Scheme 2.

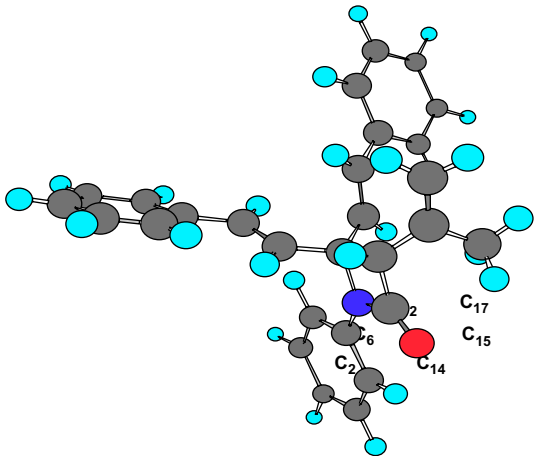


Figure 1. Energy minimized structure of intermediate **4**.

calculations on 3,4-divinyl azetidinone earlier utilized in thermolytic Cope rearrangement,[5] have shown its ground state energy as 80.6 kcal mol^{-1} with apical distance of 3.87 Å (Figs. 2 and 3).[6]

In line with the arguments advanced above, the reduction in dihedral angle increases the energy of the system to 102.2 kcal mol^{-1}, a difference of 21.6 kcal. The resultant energy barrier of 21.6 kcal mol^{-1} is naturally more difficult to attain than 4.1 kcal mol^{-1} required for conversion of **4** to **5**. This is also in agreement with the harsh conditions required for the earlier reported Cope rearrangement.[5]

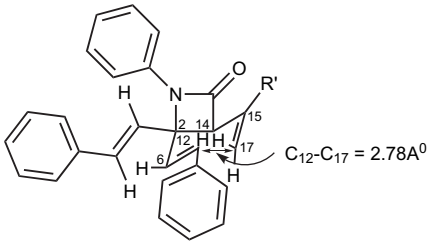


Figure 2. Most probable conformation of **4** for Cope rearrangement.

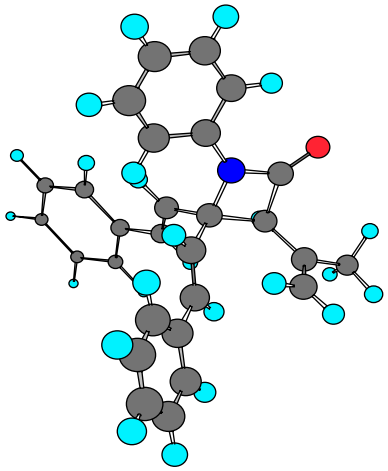


Figure 3. Energy minimized most probable conformer of [2+2] adduct **4** required for Cope rearrangement.

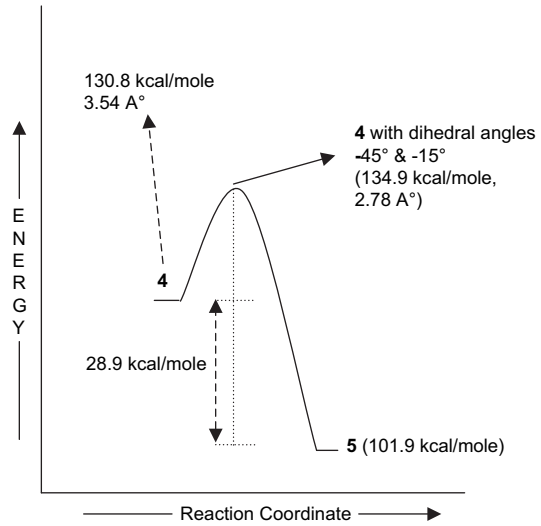


Figure 4. A probable graphical representation of reaction pathway.

The methodology has been generalized for the synthesis of other azocinone derivatives **5** (**c–l**) in the reactions of cross-conjugated azatrienes (**3b–3f**) with conjugated ketenes without even traces of corresponding [2+2] cycloadducts. Since, the synthesis of eight- and nine-membered rings is comparatively difficult due to their unfavorable enthalpic and entropic factors,[7,8] an easy and convenient route for the synthesis of such eight membered lactams has been developed (Fig. 4).

In conclusion, an unprecedented single pot synthesis of stable cross-conjugated azatrienes **3** (**a–f**) along with the tandem [2+2] cycloaddition and highly facile [3,3] sigmatropic rearrangement in their reactions with conjugated ketenes, leading to facile synthesis of various functionalised azocinone derivatives, has been reported. Alcaide and co-workers in their communication exploited just the azadienic system having limited variants thus imposing structural limitations on the reaction site and restraining the diversity of the formed azocinone derivatives. Whereas the systems considered in our manuscript widens the scope of this methodology, as many structural variants present in the cross-conjugated system acting as 1-azadiene opens up a channel to obtain novel functionalized azocinones. The facile nature of the observed [3,3] sigmatropic shift has been supported by the theoretical studies.

2. Experimental

2.1. General

Melting points were determined by open capillary method using Veego Precision Digital Melting Point apparatus (MP-D) and are uncorrected. IR spectra were recorded on a Shimadzu D-8001 FT-spectrophotometer. ^{1}H NMR spectra were recorded in deuterochloroform with Bruker AC-E 200 (200 MHz) spectrometer using TMS as an internal standard. Chemical shift values are expressed as parts per million downfield from TMS and *J* values are in hertz. Splitting patterns are indicated as s: singlet, d: doublet and br s: broad singlet. ^{13}C NMR spectra were also recorded on a Bruker

AC-E 200 (50.4 MHz) spectrometer in a deuterochloroform using TMS as an 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 PF_{254}).

2.2. Starting materials

Cross-conjugated ketones **1** were prepared according to the reported procedure.[9] Crotyl and 3,3-dimethylacryl chlorides were prepared from their corresponding acids and thionyl chloride. Thionyl chloride was distilled before use. Aromatic amines used were commercially available. Dichloromethane was dried over di-phosphorous pentoxide and stored over molecular sieves (4 Å).

2.3. General procedure for the preparation of cross-conjugated azatrienes (3)

To the solution of **1** (10 mmol) and aryl amine **2** (15 mmol) in toluene (30 mL) was added triethylamine (22 mmol) and reaction mixture was stirred. After stirring for 5 min $TiCl_4$ (10 mmol) was added to the reaction mixture dropwise by keeping the reaction temperature at 0 °C. After completion (tlc), the reaction mixture was passed through a silica column and distillation of the solvent under reduced pressure yielded solid compounds, which were recrystallized using ethyl acetate–hexane mixture (1:5, v/v).

2.4. General procedure for the reaction of azatrienes with isopropenyl/vinyl ketenes

To a well-stirred solution of azatrienes **3** (10 mmol) and triethylamine (15 mmol) in dry methylene chloride (30 mL) was added dropwise a solution of 3,3-dimethylacryl chloride/crotyl chloride in dry methylene chloride (30 mL) over a period of 0.5 h at room temperature. After completion of the reaction (tlc), the reaction mixture was first washed with saturated sodium bicarbonate solution (2×25 mL) and water (2×50 mL) and the organic layer was dried over anhydrous sodium sulfate. Removal of solvent under reduced pressure yielded the crude product, which was purified by silica gel column chromatography using a mixture of ethyl acetate and hexane (1:10, v/v).

2.4.1. (4-Methoxy-phenyl)-{3-(4-methoxy-phenyl)-1-[2(4-methoxy-phenyl)-vinyl]-allylidene}-amine (3a). Reddish yellow prismatic crystalline solid, Yield: 79%; mp 161–163 °C; Anal. Calcd for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.34; H, 6.42; N, 3.42%. IR (KBr): ν_{max}=1602, 1510, 1463, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=3.82 (s, 6H, 2×–OCH_3), 3.84 (s, 3H, –OCH_3), 6.68 (d, J=16.5 Hz, 1H, olefinic), 6.84–6.93 (m, 7H, 6ArH and 1H, olefinic), 7.10 (d, J=16.5 Hz, 1H, olefinic), 7.13 (d, J=16.5 Hz, 1H, olefinic), 7.25–7.55 (m, 6H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=55.2 (–OCH_3), 55.3 (–OCH_3), 114.0, 114.1, 114.2, 120.7, 122.7, 124.2, 128.3, 128.6, 128.9, 129.1, 136.9, 137.3, 144.2, 156.3, 160.2, 160.4, and 163.0. *m/z*: 399 (M^+).

2.4.2. {3-(4-Methoxy-phenyl)-1-[2-(4-methoxy-phenyl)-vinyl]-allylidene}-*p*-tolyl-amine (3b). Reddish yellow solid, Yield: 82%; mp 148–149 °C; Anal. Calcd for $C_{26}H_{25}NO_2$: C, 81.43; H, 6.57; N, 3.65. Found: C, 81.37; H, 6.51; N, 3.59%. IR (KBr) ν_{max}=1602, 1510, 1463, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.35 (s, 3H, –CH_3), 3.81 (s, 3H, –OCH_3), 3.84 (s, 3H, –OCH_3), 6.66 (d, J=16.5 Hz, 1H, olefinic), 6.80–6.94 (m, 6H, ArH), 7.12 (d, J=15.9 Hz, 1H, olefinic), 7.15 (d, J=15.9 Hz, 1H, olefinic), 7.25–7.36 (m, 4H, ArH), 7.47 (d, J=16.5 Hz, 1H, olefinic), 7.53 (d, J=8.9 Hz, 2H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.9, 55.3, 55.4, 114.2, 114.4, 120.7, 121.2, 123.4, 124.0, 128.3, 129.1, 129.3, 129.7, 130.3, 133.1, 137.5, 148.3, 160.3, 160.5, and 163.2. *m/z*: 383 (M^+).

2.4.3. {3-(4-Methoxy-phenyl)-1-[2-(4-methoxy-phenyl)-vinyl]-allylidene}-phenyl-amine (3c). Yellow solid, Yield: 88%; mp 155–156 °C; Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.35; H, 6.34; N, 3.73%. IR (KBr): ν_{max}=1603, 1510, 1462, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=3.83 (s, 6H, 2×–OCH_3), 6.66 (d, J=16.5 Hz, 1H, olefinic), 6.78–7.05 (m, 7H, ArH), 7.11 (d, J=15.9 Hz, 1H, olefinic), 7.13 (d, J=15.9 Hz, 1H, olefinic), 7.21–7.33 (m, 4H, ArH), 7.49 (d, J=16.5 Hz, 1H, olefinic), 7.55 (d, J=8.9 Hz, 2H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=55.4, 114.1, 114.5, 120.2, 121.7, 122.6, 123.7, 125.6, 127.8, 128.5, 129.6, 130.2, 132.9, 136.8, 149.5, 159.9, 160.2, and 163.1. *m/z*: 369 (M^+).

2.4.4. (4-Methoxy-phenyl)-(3-phenyl-1-styryl-allylidene)-amine (3d). Yellow solid, Yield: 84%; mp 119–120 °C; Anal. Calcd for $C_{24}H_{21}NO$: C, 84.92; H, 6.24; N, 4.13. Found: C, 85.02; H, 6.29; N, 4.18%. IR (KBr): ν_{max}=1602, 1510, 1460, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=3.83 (s, 3H, –OCH_3), 6.70 (d, J=16.5 Hz, 1H, olefinic), 6.86–6.97 (m, 7H, ArH), 7.13 (d, J=15.8 Hz, 1H, olefinic), 7.15 (d, J=16.5 Hz, 1H, olefinic), 7.29–7.38 (m, 5H, ArH), 7.41 (d, J=15.8 Hz, 1H, olefinic), 7.56 (d, J=8.7 Hz, 2H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=55.3, 113.9, 114.6, 121.6, 122.6, 124.7, 127.3, 128.4, 128.6, 128.9, 129.4, 137.2, 138.5, 145.9, 156.8, 160.1, 160.7, and 162.9. *m/z*: 339 (M^+).

2.4.5. (3-Phenyl-1-styryl-allylidene)-*p*-tolyl-amine (3e). Yellow solid, Yield: 87%; mp 107–108 °C; Anal. Calcd for $C_{24}H_{21}N$: C, 89.12; H, 6.54; N, 4.33. Found: C, 89.22; H, 6.47; N, 4.38%. IR (KBr): ν_{max}=1603, 1512, 1465, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.37 (s, 3H, –CH_3), 6.81 (d, J=16.5 Hz, 1H, olefinic), 6.85 (d, J=8.4 Hz, 2H, ArH), 7.17 (d, J=15.9 Hz, 1H, olefinic), 7.19–7.64 (m, 14H, 12ArH and 2 olefinic) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.9, 121.1, 122.5, 126.3, 127.3, 127.5, 128.7, 128.8, 128.9, 129.2, 129.4, 133.5, 135.8, 136.2, 137.8, 138.1, 148.0, and 162.8. *m/z*: 323 (M^+).

2.4.6. Phenyl-(3-phenyl-1-styryl-allylidene)-amine (3f). Reddish yellow solid, Yield: 83%; mp 79–80 °C; Anal. Calcd for $C_{23}H_{19}N$: C, 89.28; H, 6.19; N, 4.53. Found: C, 89.21; H, 6.25; N, 4.48%. IR (KBr): ν_{max}=1602, 1510, 1463, 1033 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=6.76 (d, J=16.5 Hz, 1H, olefinic), 6.90–7.13 (m, 3H,

2ArH and 1 olefinic), 7.18 (d, J=16.5 Hz, 1H, olefinic), 7.22–7.63 (m, 13H, ArH), 7.75 (d, J=16.5 Hz, 1H, olefinic) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=120.9, 122.3, 123.8, 125.9, 127.5, 128.3, 128.7, 128.9, 129.0, 130.4, 134.7, 135.7, 136.1, 138.0, 143.3, 150.7, and 162.9. m/z: 309 (M^+).

2.4.7. {3-(4-Chloro-phenyl)-1-[2-(4-chloro-phenyl)-vinyl]-allylidene}-(4-methoxy-phenyl)-amine (3g). Yellow crystalline solid, Yield: 76%; mp 110–111 °C; Anal. Calcd for $C_{24}H_{19}Cl_2NO$: C, 70.60; H, 4.69; N, 3.43. Found: C, 70.66; H, 4.62; N, 3.52%. IR (KBr): ν_{max}=1603, 1510, 1462, 1033 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=3.81 (s, 3H, –OCH_3), 6.76 (d, J=16.5 Hz, 1H, olefinic), 7.01 (d, J=15.9 Hz, 1H, olefinic), 7.08 (d, J=16.5 Hz, 1H, olefinic), 7.19–7.31 (m, 4H, ArH), 7.36 (d, J=8.9 Hz, 2H, ArH), 7.37 (d, J=8.9 Hz, 2H, ArH), 7.49 (d, J=8.4 Hz, 2H, ArH), 7.52 (d, J=8.4 Hz, 2H, ArH), 7.66 (d, J=15.9 Hz, 1H, olefinic) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=55.4, 114.1, 120.8, 122.9, 124.7, 126.5, 127.6, 128.2, 128.7, 129.5, 130.1, 134.8, 135.6, 137.6, 137.8, 141.5, 152.6, and 161.1. m/z: 408 (M^+).

2.4.8. {3-(4-Chloro-phenyl)-1-[2-(4-chloro-phenyl)-vinyl]-allylidene}-*p*-tolyl-amine (3h). Yellow solid, Yield: 81%; mp 124–125 °C; Anal. Calcd for $C_{24}H_{19}Cl_2N$: C, 73.47; H, 4.88; N, 3.57. Found: C, 73.51; H, 4.83; N, 3.62%. IR (KBr): ν_{max}=1602, 1512, 1462, 1033 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.39 (s, 3H, –CH_3), 6.78 (d, J=16.5 Hz, 1H, olefinic), 6.99 (d, J=8.6 Hz, 2H, ArH), 7.05 (d, J=15.9 Hz, 1H, olefinic), 7.18 (d, J=16.5 Hz, 1H, olefinic), 7.21 (d, J=8.7 Hz, 2H, ArH), 7.19–7.31 (m, 4H, ArH), 7.35–7.52 (m, 4H, ArH), 7.66 (d, J=15.9 Hz, 1H, olefinic) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.8, 114.2, 121.6, 122.5, 124.9, 126.5, 127.8, 128.4, 128.9, 129.1, 129.5, 134.8, 135.6, 137.6, 137.8, 141.5, 152.6, and 161.1. m/z: 391 (M^+).

2.4.9. {3-(4-Chloro-phenyl)-1-[2-(4-chloro-phenyl)-vinyl]-allylidene}-phenyl-amine (3i). Yellow solid, Yield: 71%; mp 131–132 °C; Anal. Calcd for $C_{23}H_{17}Cl_2N$: C, 73.02; H, 4.53; N, 3.70. Found: C, 72.94; H, 4.59; N, 3.61%. IR (KBr): ν_{max}=1603, 1510, 1464, 1033 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=6.74 (d, J=16.5 Hz, 1H, olefinic), 7.01 (d, J=8.7 Hz, 2H, ArH), 7.03 (d, J=15.9 Hz, 1H, olefinic), 7.16 (d, J=16.5 Hz, 1H, olefinic), 7.23 (d, J=8.7 Hz, 2H, ArH), 7.14–7.35 (m, 4H, ArH), 7.36–7.51 (m, 5H, ArH), 7.67 (d, J=15.9 Hz, 1H, olefinic) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=114.1, 121.8, 122.6, 125.1, 126.3, 127.9, 128.2, 129.2, 129.9, 131.5, 134.5, 135.9, 137.2, 137.8, 141.8, 152.7, and 161.5. m/z: 377 (M^+).

2.4.10. 1,6-Bis-(4-methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-4-methyl-5,6-dihydro-1*H*-azocinone (5a). Colorless crystalline solid, Yield: 85%; mp 202–203 °C; Anal. Calcd for $C_{31}H_{31}NO_4$: C, 77.31; H, 6.49; N, 2.91. Found: C, 77.39; H, 6.53; N, 2.99. IR (KBr): ν_{max}=1662, 1508, 1338, 1299, 1031 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.84 (s, 3H, –CH_3), 2.28 (unresolved dd, J=13.1 Hz, 1H, –CH_2), 2.72 (unresolved dd, J=13.1 Hz, 1H, –CH_2), 3.77 (s, 6H, 2×–OCH_3), 3.83 (s, 3H, –OCH_3), 4.08–4.12 (m, 1H, –CH), 5.93 (d, J=10.0 Hz, 1H, olefinic), 5.99 (br s, 1H, olefinic), 6.34 (d, J=16.2 Hz, 1H, olefinic), 6.42 (d, J=16.2 Hz, 1H, olefinic), 6.74–6.94 (m, 6H, ArH), 7.15–7.35 (m, 6H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=26.1 (–CH_3), 39.9 (–CH_2), 42.6 (–CH), 55.2 (–OCH_3), 55.3(–OCH_3), 96.1, 113.9, 114.3, 120.1, 122.3, 126.4, 127.7, 127.9, 129.1, 130.7, 132.1, 132.3, 134.5, 138.7, 140.2, 157.6, 158.6, 159.4, and 168.5. m/z: 481 (M^+).

2.4.11. 1,6-Bis-(4-methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-5,6-dihydro-1*H*-azocin-2-one (5b). Colorless solid, Yield: 82%; mp 191–192 °C; Anal. Calcd for $C_{30}H_{29}NO_4$: C, 77.06; H, 6.21; N, 3.00. Found: C, 77.13; H, 6.13; N, 2.93%. IR (KBr): ν_{max}=1660, 1512, 1338, 1299, 1030 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.41–2.47 (m, 1H, –CH_2), 2.76–2.82 (m, 1H, –CH_2), 3.81 (s, 6H, 2×–OCH_3), 3.83 (s, 3H, –OCH_3), 4.13–4.18 (m, 1H, –CH), 5.93 (br s, 1H, olefinic), 5.99 (d, J=10.1 Hz, 1H, olefinic), 6.02 (br s, 1H, olefinic), 6.43 (br s, 2H, olefinic), 6.71–6.89 (m, 6H, ArH), 7.13–7.38 (m, 6H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=37.5, 40.8, 55.2, 55.5, 96.2, 114.1, 114.5, 120.5, 122.3, 123.7, 126.4, 127.7, 129.8, 131.4, 132.2, 133.8, 135.4, 137.6, 138.9, 141.2, 142.5, 157.4, and 168.5. m/z: 467 (M^+).

2.4.12. 6-(4-Methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-4-methyl-1-*p*-tolyl-5,6-dihydro-1*H*-azocin-2-one (5c). Pale white solid, Yield: 81%; mp 212–213 °C; Anal. Calcd for $C_{31}H_{31}NO_3$: C, 79.97; H, 6.71; N, 3.01. Found: C, 80.05; H, 6.78; N, 2.96%. IR (KBr): ν_{max}=1663, 1510, 1330, 1290, 1030 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.83 (s, 3H, –CH_3), 2.34 (s, 3H, –CH_3), 2.39–2.43 (m, 1H, –CH_2), 2.64–2.74 (m, 1H, –CH_2), 3.83 (s, 6H, 2×–OCH_3), 4.09–4.13 (m, 1H, –CH), 5.88 (br s, 1H, olefinic), 6.01 (br s, 1H, olefinic), 6.45 (br s, 2H, olefinic), 6.77 (d, J=8.7 Hz, 2H, ArH), 6.88 (d, J=8.8 Hz, 2H, ArH), 6.99–7.41 (m, 8H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.8 (CH_3), 25.9 (–CH_3), 40.3 (–CH_2), 42.9 (–CH), 55.3 (–OCH_3), 96.2, 113.8, 114.4, 120.5, 121.8, 123.5, 125.6, 126.7, 129.4, 130.7, 131.8, 134.2, 135.2, 136.1, 138.4, 142.4, 156.5, 157.2, and 168.2. m/z: 465 (M^+).

2.4.13. 6-(4-Methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-1-*p*-tolyl-5,6-dihydro-1*H*-azocin-2-one (5d). Colorless solid, Yield: 88%; mp 183–184 °C; Anal. Calcd for $C_{30}H_{29}NO_3$: C, 79.80; H, 6.47; N, 3.10. Found: C, 79.85; H, 6.51; N, 3.01%. IR (KBr): ν_{max}=1661, 1514, 1330, 1293, 1030 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.34 (s, 3H, –CH_3), 2.43–2.48 (m, 1H, –CH_2), 2.74–2.80 (m, 1H, –CH_2), 3.82 (s, 6H, 2×–OCH_3), 4.17–4.20 (m, 1H, –CH), 5.87–5.91 (m, 1H, olefinic), 5.97 (d, J=10.2 Hz, 1H, olefinic), 6.02 (br s, 1H, olefinic), 6.45 (br s, 2H, olefinic), 6.77 (d, J=8.7 Hz, 2H, ArH), 6.89 (d, J=8.7 Hz, 2H, ArH), 6.99–7.42 (m, 8H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=21.0, 37.7, 40.6, 55.4, 96.1, 113.9, 114.4, 120.3, 121.6, 122.8, 125.9, 127.3, 129.4, 132.5, 133.4, 135.6, 136.7, 137.4, 138.8, 140.9, 141.8, 156.9, and 168.3. m/z: 451 (M^+).

2.4.14. 6-(4-Methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-4-methyl-1-phenyl-5,6-dihydro-1*H*-azocin-2-one (5e). Colorless prismatic crystalline solid, Yield: 89%; mp 196–197 °C; Anal. Calcd for $C_{30}H_{29}NO_3$: C, 79.80; H,

6.47; N, 3.10. Found: C, 79.89; H, 6.51; N, 3.14%. IR (KBr): ν_{max}=1660, 1510, 1335, 1295, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.82 (s, 3H, $-CH_3$), 2.29 (unresolved dd, J=13.1 Hz, 1H, $-CH_2$), 2.74 (unresolved dd, J=13.1 Hz, 1H, $-CH_2$), 3.79 (s, 6H, 2×$-OCH_3$), 4.09–4.14 (m, 1H, –CH), 5.94 (d, J=10.1 Hz, 1H), 6.02 (br s, 1H, olefinic), 6.33 (d, J=16.2 Hz, 1H), 6.44 (d, J=16.2 Hz, 1H), 6.79–7.39 (m, 13H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=26.2 ($-CH_3$), 39.8 ($-CH_2$), 42.9 (–CH), 55.2 ($-OCH_3$), 96.2, 114.1, 114.5, 120.7, 121.8, 124.4, 125.8, 126.2, 128.5, 129.6, 132.3, 133.7, 135.5, 138.9, 141.8, 156.5, 158.4, 159.2, and 168.2. m/z: 451 (M^+).

2.4.15. 6-(4-Methoxy-phenyl)-8-[2-(4-methoxy-phenyl)-vinyl]-1-phenyl-5,6-dihydro-1*H*-azocin-2-one (5f). White solid, Yield: 83%; mp 178–179 °C; Anal. Calcd for $C_{29}H_{27}NO_3$: C, 79.61; H, 6.22; N, 3.20. Found: C, 79.68; H, 6.29; N, 3.13%. IR (KBr): ν_{max}=1663, 1510, 1330, 1295, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.37–2.42 (m, 1H, $-CH_2$), 2.73–2.79 (m, 1H, $-CH_2$), 3.82 (s, 6H, 2×$-OCH_3$), 4.16–4.21 (m, 1H, –CH), 5.93 (br s, 1H, olefinic), 6.05 (br s, 1H, olefinic), 6.43 (br s, 2H, olefinic), 6.79 (d, J=8.8 Hz, 2H, ArH), 6.87–7.39 (m, 11H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=39.1, 41.1, 55.2, 96.1, 113.8, 114.2, 120.4, 121.8, 122.6, 124.9, 126.7, 128.3, 130.7, 133.2, 133.7, 135.1, 136.3, 137.2, 141.5, 143.5, 156.8, and 168.2. m/z: 437 (M^+).

2.4.16. 1-(4-Methoxy-phenyl)-4-methyl-6-phenyl-8-styryl-5,6-dihydro-1*H*-azocin-2-one (5g). Pale white solid, Yield: 72%; mp 217–218 °C; Anal. Calcd for $C_{29}H_{27}NO_2$: C, 82.63; H, 6.46; N, 3.32. Found: C, 82.52; H, 6.41; N, 3.24%. IR (KBr): ν_{max}=1661, 1517, 1333, 1295, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.92 (s, 3H, $-CH_3$), 2.32–2.38 (m, 1H, $-CH_2$), 2.76–2.79 (m, 1H, $-CH_2$), 3.78 (s, 3H, $-OCH_3$), 4.14–4.20 (m, 1H, –CH), 6.02 (br s, 1H, olefinic), 6.03 (br s, 1H, olefinic), 6.50 (br s, 2H, olefinic), 6.87 (d, J=8.8 Hz, 2H, ArH), 7.16–7.43 (m, 12H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=26.1 ($-CH_3$), 37.9 ($-CH_2$), 41.1(–CH), 55.3 ($-OCH_3$), 96.2, 114.0, 120.2, 124.8, 126.5, 127.2, 127.9, 128.2, 130.3, 132.4, 132.9, 133.1, 136.5, 138.8, 140.2, 142.4, 145.8, 157.3, and 168.6. m/z: 421 (M^+).

2.4.17. 1-(4-Methoxy-phenyl)-6-phenyl-8-styryl-5,6-dihydro-1*H*-azocin-2-one (5h). Colorless solid, Yield: 78%; mp 189–190 °C; Anal. Calcd for $C_{28}H_{25}NO_2$: C, 82.53; H, 6.18; N, 3.44. Found: C, 82.57; H, 6.12; N, 3.36%. IR (KBr): ν_{max}=1660, 1515, 1330, 1295, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.42–2.48 (m, 1H, $-CH_2$), 2.80–2.83 (m, 1H, $-CH_2$), 3.79 (s, 3H, $-OCH_3$), 4.16–4.19 (m, 1H, –CH), 5.90 (br s, 1H, olefinic), 6.03 (d, J=10.0 Hz, 1H, olefinic), 6.17 (d, J=10.0 Hz, 1H, olefinic), 6.52 (br s, 2H, olefinic), 6.89 (d, J=8.8 Hz, 2H, ArH), 7.17–7.46 (m, 12H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=37.4 ($-CH_2$), 40.7 (–CH), 55.2 ($-OCH_3$), 96.1, 114.1, 124.5, 126.4, 126.5, 127.0, 127.2, 127.9, 128.5, 129.1, 131.3, 131.5, 131.9, 133.1, 136.2, 139.1, 142.2, 157.8, and 168.1. m/z: 407 (M^+).

2.4.18. 4-Methyl-6-phenyl-8-styryl-1-*p*-tolyl-5,6-dihydro-1*H*-azocin-2-one (5i). Colorless solid, Yield: 86%; mp 167–168 °C; Anal. Calcd for $C_{29}H_{27}NO$: C, 85.89; H, 6.71; N, 3.45. Found: C, 85.83; H, 6.62; N, 3.39%. IR (KBr): ν_{max}=1664, 1513, 1331, 1292, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.83 (s, 3H, $-CH_3$), 2.35 (s, 3H, $-CH_3$), 2.25–2.33 (m, 1H, $-CH_2$), 2.73–2.82 (m, 1H, $-CH_2$), 4.15–4.19 (m, 1H, –CH), 5.99 (br s, 1H, olefinic), 6.05 (br s, 1H, olefinic), 6.53 (br s, 2H, olefinic), 6.78 (d, J=8.8 Hz, 2H, ArH), 6.89 (d, J=8.8 Hz, 2H, ArH), 7.10–7.45 (m, 10H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.9, 25.8 ($-CH_3$), 37.6 ($-CH_2$), 40.7 (–CH), 96.1, 114.2, 121.5, 122.6, 123.3, 124.9, 126.7, 127.9, 129.8, 130.8, 131.9, 132.2, 132.8, 133.4, 134.5, 135.4, 142.9, 157.8, and 168.2. m/z: 405 (M^+).

2.4.19. 6-Phenyl-8-styryl-1-*p*-tolyl-5,6-dihydro-1*H*-azocin-2-one (5j). Colorless solid, Yield: 80%; mp 159–160 °C; Anal. Calcd for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 86.01; H, 6.52; N, 3.49%. IR (KBr): ν_{max}= 1662, 1511, 1330, 1299, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.37 (s, 3H, $-CH_3$), 2.35–2.43 (m, 1H, $-CH_2$), 2.72–2.80 (m, 1H, $-CH_2$), 4.13–4.18 (m, 1H, –CH), 5.92 (br s, 1H, olefinic), 6.07 (d, J=8.9 Hz, 1H, olefinic), 6.17 (br s, 1H, olefinic), 6.53 (br s, 2H, olefinic), 6.79 (d, J=8.8 Hz, 2H, ArH), 6.93 (d, J=8.8 Hz, 2H, ArH), 7.05–7.41 (m, 10H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=20.9, 37.5 ($-CH_2$), 40.4 (–CH), 96.2, 114.2, 120.8, 122.5, 123.1, 123.7, 125.5, 126.8, 127.3, 127.9, 129.1, 130.3, 132.7, 134.5, 136.3, 136.8, 142.5, 158.1, and 168.3. m/z: 391 (M^+).

2.4.20. 4-Methyl-1,6-diphenyl-8-styryl-5,6-dihydro-1*H*-azocin-2-one (5k). Colorless solid, Yield: 77%; mp 172–173 °C; Anal. Calcd for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 85.97; H, 6.49; N, 3.63%. IR (KBr): ν_{max}= 1661, 1510, 1326, 1290, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=1.86 (s, 3H, $-CH_3$), 2.30–2.36 (m, 1H, $-CH_2$), 2.74–2.81 (m, 1H, $-CH_2$), 4.21–4.26 (m, 1H, –CH), 5.91 (br s, 1H, olefinic), 6.02 (br s, 1H, olefinic), 6.56 (br s, 2H, olefinic), 6.79–7.15 (m, 6H, ArH), 7.20–7.41 (m, 9H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=26.1 ($-CH_3$), 37.6 ($-CH_2$), 40.5 (–CH), 96.2, 114.3, 121.3, 122.6, 123.7, 125.5, 126.4, 127.2, 129.5, 130.6, 132.2, 132.8, 133.4, 134.5, 135.4, 136.1, 142.7, 156.7, and 168.4. m/z: 391 (M^+).

2.4.21. 1,6-Diphenyl-8-styryl-5,6-dihydro-1*H*-azocin-2-one (5l). Colorless solid, Yield: 76%; mp 208–209 °C; Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.82; H, 6.19; N, 3.65%. IR (KBr): ν_{max}=1660, 1515, 1327, 1290, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, Me_4Si): δ=2.35–2.41 (m, 1H, $-CH_2$), 2.70–2.78 (m, 1H, $-CH_2$), 4.15–4.22 (m, 1H, –CH), 5.98 (br s, 1H, olefinic), 6.06 (d, J=10.1 Hz, 1H, olefinic), 6.13 (br s, 1H, olefinic), 6.57 (br s, 2H, olefinic), 6.73–7.39 (m, 15H, ArH) ppm; ^{13}C NMR (50.4 MHz, $CDCl_3$, Me_4Si): δ=37.9 ($-CH_2$), 40.6 (–CH), 96.1, 113.9, 120.5, 121.9, 122.6, 123.2, 125.1, 125.4, 127.6, 129.4, 130.3, 131.6, 131.8, 133.6, 135.9, 136.8, 141.9, 157.8, and 168.5. m/z: 377(M^+).

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References and notes

1. For recent reviews on azadienes see: (a) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869; (b) Boger, D. L. *Chem. Tract-Org. Chem.* **1996**, *9*, 149; (c) Barluenga, J.; Tomas, M. *Adv. Heterocycl. Chem.* **1993**, *57*, 1; (d) Boger, D. L. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 4.3; (e) Ghosez, L. *Stereocontrolled Organic Synthesis*; Blackwell: London, 1994; p 193; (f) Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic: San Diego, 1987; (g) Behforonz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259; (h) Jayakumar, S.; Ishar, M. P. S.; Mahajan, M. P. *Tetrahedron Report* **2002**, *58*, 379; (i) Attanasi, O. A.; Filippone, P. *Synlett* **1997**, 1128; (j) Boger, D. L. *Chem. Rev.* **1986**, *86*, 781; (k) Radl, S. *Aldrichim. Acta* **1997**, *30*, 97; (l) Sandhu, J. S.; Sain, B. *Heterocycles* **1987**, *26*, 777; (m) Ghosez, L.; Serckx-Ponchin, B.; Rivera, M.; Bayard, P.; Sainte, F.; Demoulin, A.; Frisque-Hesbain, A. M.; Mockel, A.; Munoz, L.; Bernard-Henriet, C. *J. Heterocycl. Chem.* **1985**, *22*, 69; (n) Boger, D. L. *Bull. Soc. Chim. Belg.* **1990**, *99*, 599.
2. (a) Jayakumar, S.; Singh, P.; Mahajan, M. P. *Tetrahedron* **2004**, *60*, 4315; (b) Mazumdar, S. N.; Mukherjee, S.; Sharma, A. K.; Sengupta, D.; Mahajan, M. P. *Tetrahedron* **1994**, *50*, 7579; (c) Dey, P. D.; Sharma, A. K.; Bharatam, P. V.; Mahajan, M. P. *Tetrahedron* **1997**, *53*, 13829; (d) Jayakumar, S.; Kumar, V.; Mahajan, M. P. *Tetrahedron Lett.* **2001**, *42*, 2235; (e) Mohan, C.; Singh, P.; Mahajan, M. P. *Tetrahedron* **2005**, *61*, 10774; (f) Singh, P.; Marwaha, A.; Singh, H.; Mahajan, M. P. *Tetrahedron* **2005**, *61*, 11999; (g) Bhargava, G.; Mahajan, M. P.; Saito, T.; Otani, T.; Kurashima, M.; Sakai, K. *Eur. J. Org. Chem.* **2005**, 2397.
3. (a) Saito, T.; Kimura, H.; Sakamaki, K.; Karakasa, T.; Moriyama, S. *Chem. Commun.* **1996**, 811; (b) Saito, T.; Kobayashi, S.; Ohgaki, M.; Wada, M.; Nagahiro, C. *Tetrahedron Lett.* **2002**, *43*, 2627.
4. (a) Berge, J. M.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1982**, *65*, 2230; (b) Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1987**, *52*, 3289.
5. Alcaide, B.; Rodriguez-Ranera, C.; Rodriguez-Vicente, A. *Tetrahedron Lett.* **2001**, *42*, 3081.
6. The structures are made in Chem. Pro 7.0 and subjected to semi-empirical energy minimization calculations at AM1 level using MOPAC in gas phase (neglecting solvent effect).
7. Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774.
8. (a) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95; (b) Galli, L.; Mandolini, L. *Eur. J. Org. Chem.* **2000**, 3117.
9. Elnagdi, M. H.; Mousawi, S. M.; Abdel-Khalik, M. M.; El-Sheriny, S.; John, E. *J. Heterocycl. Chem.* **2001**, *38*, 949.