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Stereospecificity of Diels–Alder Reactions Validated Using Ab Initio Calculations: Synthesis of Novel Coumarin and Phenanthridine Derivatives

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Abstract: A new series of coumarin derivatives (**2–5**) was synthesized by reaction of phenylsulfonylacetonitrile (**1**) with 2-hydroxy-1-naphthaldehyde and/or salicyaldehyde. Compounds **3** and **5** were converted to the corresponding phenanthridine analogs **6** and **7**, respectively. Compound **9a** was treated with different dienophiles to furnish the *endo* adducts of compounds (**11a–d**) rather than the *exo* adducts. Ab initio calculations at the Hartree-Fock (HF) level using the basis set 6-31 G (d,p) was used to study and validate the stereospecificity of compounds **11a–d** and showed clearly that the *endo* adducts were thermodynamically favorable. PM3 parameters also showed that the *endo* adducts are thermodynamically and kinetically favorable. Tetrahydrobenzochromenone (**11**) was synthesized and allowed to react with different aromatic diazonium salts to give the corresponding 4-arylazo derivatives (**13**), which were converted to the corresponding diazaindenophenanthrene derivatives (**14**) by reaction with *o*-diamines.

Keywords: Aromatic diazonium salt, chromen, dienophiles, 2-hydroxy-1-naphthaldehyde, phenanthridines, phenylsulfonylacetonitrile, salicyaldehyde

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INTRODUCTION

This work is the continuation of a program to develop new, simple methods for the synthesis of functionally substituted heterocycles with anticipated biological activity. We have recently extended it to include the investigation of the pharmacological aspects of the newly synthesized heterocycles based on the finding that some heterocycles can achieve activity in both the pharmacological and pesticidal areas: coumarins, chromones, and flavones are pharmacologically important classes of plant products. The biological importance of coumarin has resulted in much interest in their synthesis and chemistry.[1] Some compounds of this class, notably 3-phenylcoumarins, are reported to possess anticoagulant[2] properties and are used as additives to food and cosmetics.[3] 3-Phenylcoumarins containing an azole ring have found applications as fluorescent-brightening agents.[4]

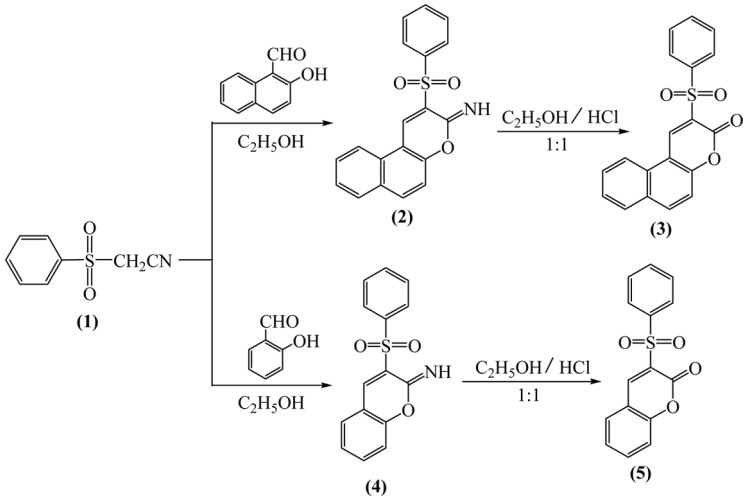
In contrast to most other types of tumor-inhibitory compounds, many of which exhibit toxicity, mutagenicity, and other undesirable properties, the coumarin and chromone compounds tend to show minimal side effects. In addition, some coumarins have been recently discovered in some natural products, many of which have been used as bactericides,[5] fungicides,[6] anti-inflammatory agents,[7] and antitumor agents.[8]

RESULTS AND DISCUSSION

In the past few years, Fadda et al. have been exploring the synthetic potential, scope, and limitations of activated nitriles in coumarins and different heterocycle synthesis.[9–11] Several new approaches for the synthesis of five- and six-membered rings and their fused heterocyclic derivatives have been developed during this work.[12,13] In view of these considerable efforts, our research group has been devoted to the development of a new synthetic methodology for this class of compounds.

In the present work, we explore the synthetic potential of phenylsulfonylacetonitrile (**1**) to form chromene derivatives via the reaction of **1** with 2-hydroxynaphthaldehyde and salicylaldehyde, respectively. Thus, compound **1** reacts with 2-hydroxy-1-naphthaldehyde and/or salicylaldehyde in the presence of a catalytic amount of triethylamine (TEA) in refluxing ethanol to give 2-imino-3-phenylsulfonylbenzo[f]chromene (**2**) and 2-imino-3-phenylsulfonylcoumarin (**4**) derivatives, respectively in good yields.

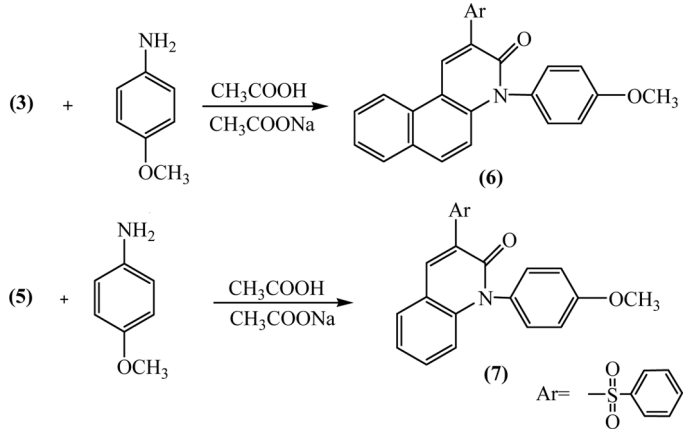
Mass spectral (MS) measurements and analytical data are in complete agreement with structure **2**, m/z 335 (M^+, 10%) (cf. Schemes 1 and 2, Table 3). The infrared (IR) spectra of both **2** and **4** showed bands at 3150 cm^{-1} attributable to the stretching frequency of the NH group.



Scheme 1. Conversion of phenylsulfonylacetonitrile to coumarin derivatives.

The ^{1}H NMR spectra of these compounds revealed two singlet signals at δ 8.8 and 9.2 ppm due to NH (exchangeable with D_2O) and C4-protons, respectively, in addition to the aromatic protons at δ (7.3–8.5) ppm.

3-Phenylsulfonyl-*2H*-benzo[f]-2-chromenone (**3**) and 3-phenylsulfonyl-2-coumarinones (**5**) were synthesized via hydrolysis of **2** and **4** in a mixture of conc. hydrochloric acid and ethanol. The mass spectrum of **3** showed the expected molecular formula $C_{19}H_{12}O_4S$ *m/z* 336 (M^+, 15%). The IR



Scheme 2. Synthesis of phenanthridine derivatives.

spectra of compounds **3** and **5** showed a band at 1700 cm^{-1} assigned to the γ-lactone. The ^1H NMR spectrum of compound **3** revealed two doublet signals at δ 8.4 ($J = 8.1$ Hz) and 8.45 ppm ($J = 8.1$ Hz) attributable to C_9 and C_{10} protons, a singlet signal at δ 9.2 ppm due to the C_4 proton, in addition to the aromatic protons that appeared at δ 7.55–8.25 ppm.

Moreover, the resulting coumarin derivatives have latent functional substituents, which have the potential for further chemical transformations and give new routes for the preparation of substituted coumarin derivatives with possible biological activity.

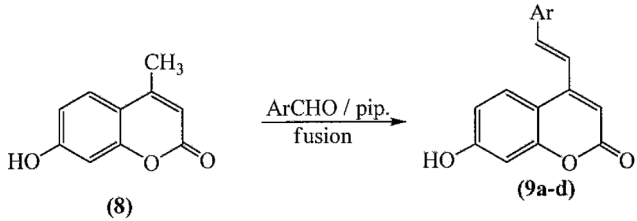
In addition to this evidence, the structures of compounds **3** and **5** were further confirmed by their transformation to the corresponding phenanthridine derivatives **6** and **7** by refluxing with *p*-anisidine in glacial acetic acid and freshly fused sodium acetate. Structures of compounds **6** and **7** were confirmed by both analytical and spectral data (cf. the Experimental section).

The importance of coumarin and its annulated substrates is well recognized by synthetic,[14] and biological chemists.[15] With the development of clinically useful anticonvulsant and analgesic drugs,[16] there has recently been remarkable interest in the synthetic manipulations of coumarins. The synthetic utilization of the nucleophilic double bond of coumarin is an important new field that offers great potential for the synthesis of a wide spectrum of novel products for different applications.

The heteroannulations of coumarin usually require either forcing conditions or relatively longer synthetic pathways. In addition, the readily available dienophiles are a class of important organic synthons that have exciting chemistry.

In view of the considerable chemical reactivity of activated dienophiles, we felt it would be valuable to investigate their reaction with strongly nucleophilic coumarin derivatives. In addition, phenanthridine alkaloids (e.g., *Amaryllidaceae* alkaloid) are known to inhibit protein synthesis in eukaryotic cells; they exhibit antineoplastic activity in ovarian sarcoma and lymphatic leukemia and therefore are considered antimitotics. In this article, we report our study on the synthesis of some new arylazobenzimidazolo and pyridoimidazolo phenanthridine derivatives of potential biological activity. Thus, we have found that fusion of a coumarin derivative (**8**) with different aryl aldehydes in the presence of a catalytic amount of piperidine gave the corresponding 4-arylidene coumarin derivatives **(9a–d)** (Scheme 3).

The structures of compounds **9a–d** were proposed on the basis of elemental analyses and spectral data. In general, the IR spectra of these compounds showed absorption bands at 3350, 1730, 1600, and 1175 cm^{-1}, attributable to the stretching frequencies of OH, γ-lactonic carbonyl, C=C, and C–O–C functional groups, respectively. The ^1H NMR spectra



9 a, Ar = C_6H_5
b, Ar = C_6H_4-NO_2-*p*
c, Ar = C_6H_4-Cl-*p*
d, Ar = C_6H_4-NO_2-*o*

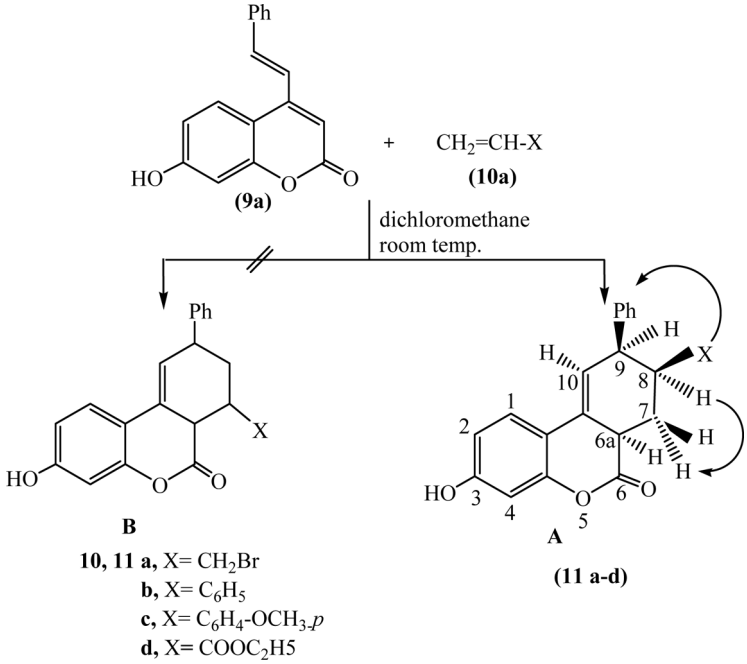
Scheme 3. Synthesis of 4-arylidene coumarin derivatives.

displayed a multiplet at 6.93–7.69 ppm, representing the aromatic protons, and a singlet peak at δ 6.89 ppm for the C_3 proton. In addition, two doublets appeared at 5.6 and 5.8 ppm, due to two olefinic protons. In ^{13}C NMR, the carbonyl carbon appeared at 169.01 ppm.

The coumarin derivative **(9a)** thus formed reacts with different dienophiles **(10a–d)** in dichloromethane (DCM) at room temperature to give the corresponding *endo*-cyclo adducts 3-hydroxy-8-substituted-9-phenyl-6a,7,8,9-tetrahydro-*6H*-benzo[c]chromen-6-one derivatives (**11a–d**) (Scheme 4).

The structures **(11a–d**) were established by both elemental and spectral results. For example, their ^1H NMR spectra, in general, showed a complex pattern that confirmed structure **A** rather than **B**. The ^1H NMR spectrum of **11b** showed a multiplet at 2.17 ppm due to C_7 protons, a multiplet at δ 3.31 for the C_8 proton, two doublets at δ 3.62 and δ 5.78 for a C_9 and C_{10} protons, a doublet doublet at δ 2.78 ppm for C_{6a} proton, and a multiplet of the aromatic protons at δ 6.5–7.3 ppm. The IR spectrum showed frequencies at 3350, 1730, 1600, and 1170 cm^{-1} due to OH, CO, C=C, and C–O–C functional groups respectively, whereas the ^{13}C NMR spectrum showed C-1 (128), C-2 (112.4), C-3 (156.9), C-4 (108.5), C-6 (169.0), C-7 (33.3), C-8 (38.8), C-9 (141.4), C-10 (120.7), C-11 (144.2), C-12 (45.8), C-13 (120.4), C-14 (152.2), C-8 phenyl (125.8–128.6), and C-9 phenyl (125.7–128.3).

The ^1H NMR spectra of **11a, c**, and **d** showed a pattern similar to that of structure **11b** in addition to a singlet at δ 3.73 attributed to $O\underline{CH_3}$ protons in structure **10c**, while in structure **10d** the ^1H NMR spectrum revealed a triplet at δ 1.02 ppm attributed to $CH_2\underline{CH_3}$ and a quartet at 3.55 ppm for $\underline{CH_2}CH_3$ protons. In structure **10a**, it showed a doublet at δ 1.9 ppm due to the CH_2Br proton and a multiplet at δ 3.4 ppm attributable to the C_8 proton.



Scheme 4. Synthesis of 3-hydroxy-9-phenyl tetrahydrobenzochromenone derivatives.

MOLECULAR MODELING

The Diels–Alder reaction between the diene (compound **9a**) and dienophiles (compounds **10a–d**) can lead to two stereoisomeric products through two different transition states: *endo* and *exo*. With this in mind, equilibrium molecular geometry for the *exo* and *endo* adducts of compounds **11a–d** were predicted using ab initio calculations at the Hartree–Fock (HF) level using the basis set 6-31 G (d, p). Table 1 shows the calculated heat of formation, the energy value of HOMO-LUMO gap, and dipole moment for the possible stereoisomers of compounds **11a–d** calculated following geometry optimization using the same level of theory and basis set. The heat of formation data presented in Table 1 clearly show that the *endo* adducts are more stable than the *exo* adduct for compounds **11a–d** by about 0.756–6.813 kcal/mol. Moreover, the HOMO-LUMO energy gap for the *endo* adducts is larger than that of the *exo* adducts, which indicates that the *endo* adducts are more stable. It was also observed that the dipole moments of the *endo* adducts are greater than those of the *exo* adducts. Based on the calculated heat of formation and HOMO-LUMO energy gap of the *endo* and *exo* adducts, it

Table 1. Total heat of formation, energy value of HOMO-LUMO gap, and dipole moment for compounds **11a–d**

	Total heat of formation (Hartree)		HOMO-LUMO gap (eV)		Dipole moment (Debye)	
Compound 11	*Endo*	*Exo*	*Endo*	*Exo*	*Endo*	*Exo*
a	−3486.935[a]	−3486.925	11.123	10.910	5.657	5.656
b	−1108.138[b]	−1108.127	11.109	10.837	4.280	4.156
c	−1222.019[c]	−1222.008	11.102	10.754	3.606	3.063
d	−1144.276[d]	−1144.274	11.113	11.06	6.153	4.467

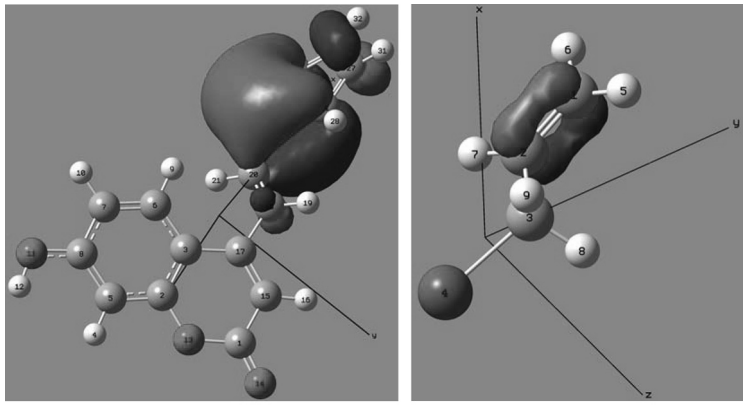
Note. 1 Hartree = 627.5 kcal/mol.
[a]*Endo* = *Exo*−6.139 (kcal/mol).
[b]*Endo* = *Exo*−6.813 (kcal/mol).
[c]*Endo* = *Exo*−6.717 (kcal/mol).
[d]*Endo* = *Exo*−0.756 (kcal/mol).

became clear that the *endo* adducts are thermodynamically more favorable than the *exo* adducts.

To further investigate the reaction stereospecificity between compounds **9a** and **10a**, the HOMO and LUMO energy values of each compound were computed at the HF level of theory using the basis set 6-31 G (d,p), and the molecular orbital (MO) isosurface was examined. It was found that the energy gap between the HOMO of compound **9a** and the LUMO of compound **10a** is smaller than that of the LUMO of compound **9a** and HOMO of compound **10a**. Hence, it was concluded that the reaction proceeds through the interaction of the HOMO of compound **9a** with the LUMO of compound **10a**.

To gain more understanding about the stereospecificity, the HOMO coefficients of compounds **9a** and the LUMO coefficients of **10a** were examined, and it was shown that carbon 20 of the former carries a bigger coefficient than carbon 15 (Fig. 1a), and carbon 2 of the latter carries a slightly bigger coefficient than that of carbon 1 (Fig. 1b), which favors *endo* adduct formation. Figures 1a and 1b show the HOMO and LUMO isosurface of compounds **9a** and **10a**, respectively, superimposed on their optimized molecular geometry computed using ab initio at the HF level of theory.

To gain more insights and deeper understanding of the kinetics of formation of compounds **11a–d**, the optimized geometry of the transition state of each product was predicted for both the *exo* and *endo* adducts, and their final energies were computed and compared with each other using PM3 parameters. Table 2 shows the heat of formation and the energy of the optimized geometry of the transition state of the *exo* and



(a) (b)

Figure 1. (a) HOMO isosurface of compound **9a**, and (b) the LUMO isosurface of compound **10a**.

endo adducts of compounds **11a–d**. The data in Table 1 clearly indicates that the *endo* adducts are thermodynamically and kinetically more favorable than the *exo* adducts.

Figure 2a shows the potential energy surface for the reaction of compound **9a** with compound **10a**. The potential energy (Fig. 2b) for the saddle point of compound **11a** with the ball cursor in the middle of the yellow band corresponds to the equilibrium molecular geometry of the transition state (Fig. 2c) of compound **11a**, which shows the bond formation between the diene and dienophile starting at the bond distance 2.2 Å.

Coupling of **11b** with some selected diazotized aromatic amines **(12a–e)** afforded the corresponding 3-hydroxyl-8,9-diphenyl-4-arlyazo-6a,7,8,9-tetrahydrobenzo[c]chromen-6-one derivatives (**13a–e**). Structures

Table 2. Total heat of formation (HF) and final energy of the transition-state compound (**11a–d**) calculated using PM3 parameters

	HF (kcal/mol), PM3		Energy of transition state (kcal/mol)	
Compound 11	*Endo*	*Exo*	*Endo*	*Exo*
a	−17.329	−15.311	45.415	47.055
b	10.842	12.8750	72.276	73.621
c	−28.229	−25.209	34.126	35.497
d	−102.105	−99.464	−38.145	−37.5077

Table 3. Fragments and their relative abundance of compound **2**

Mass	RA (%)	RIC (%)
51	23.42	6.44
63	4.15	1.14
77	25.97	7.14
89	4.85	1.33
113	5.77	1.59
135	8.30	2.28
137	6.41	1.76
138	13.08	3.60
139	59.92	1.65
140	11.60	3.19
164	20.89	5.74
165	14.21	3.91
166	5.35	1.47
193	17.23	4.74
194	5.56	1.15
270*	100.00	27.49
271	28.42	7.81
272	4.80	1.32
335**	5.86	1.61
	$\varepsilon = 363.79$	

*Base peak. **M^+ (molecular ion peak).

13a–e were established on the basis of both elemental and spectral data. The ^{1}H NMR spectrum of compound **13a** revealed a multiplet at δ 2.17 due to CH_2 protons, a doublet at δ 2.79 (C_{6a} proton), two doublets at δ 3.31 (C_8 proton), two doublets at δ 3.62 (C_9 proton), and two doublets at δ 5.78 (C_{10} proton), in addition to a multiplet of aromatic protons at δ 6.7–7.93. On the other hand, the IR spectrum of compounds **13a–e** showed absorption frequencies at 3310, 1730, 1610, 1580, and 1170 cm^{-1} due to OH, γ-lactonic carbonyl, C=C, N=N, and C–O–C functional groups, respectively.

Condensation of **13a** with *o*-phenylenediamine and/or 2,3-diamino pyridine in boiling glacial acetic acid in the presence of a catalytic amount of freshly fused sodium acetate gave the corresponding 2,3-diphenyl-8-phenylazo-1,2,3,13b-tetrahydro-8b,13-diaza-indeno[1,2-I]phenanthren-7-ol(**14a**) and its **8b**, 12,13-triaza derivative (**14b**), respectively.

Structures **14a** and **b** were suggested for the reaction product on the basis of elemental analyses and spectral evidence. In addition, structures **14a** and **b** were confirmed by independent synthesis via the condensation

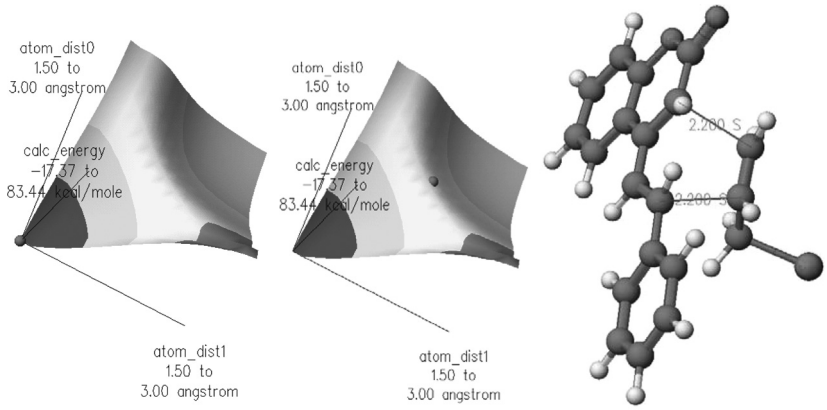


Figure 2. (a) Potential energy surface for the reaction of compound **9a** with compound **10a**, (b) potential energy surface showing the transition state of compound **11a**, and (c) the optimized geometry of the transition state of compound **11a.**

of coumarin derivative **11b** with *o*-phenylenediomine and/or 2,3-diaminopyridine in the presence of freshly fused sodium acetate in glacial acetic acid to give the corresponding benzimidazolo or pyridoimidazolo phenarthridine derivatives (**15a** and **b**) followed by coupling with the appropriate diazotied aromatic amine (**12a**) to give the corresponding 8-phenylazo derivatives (**14a** and **b**). Elemental analysis and spectral data are in good agreement with structures of the hitherto prepared azo dyes (cf. Scheme 5). The IR spectrum of **14a** showed the disappearance of the bands at 1730 and 1170 cm^{-1} of δ-carbonyl lactone and C–O–C functional groups, and a new band appeared at 1625 cm^{-1} due to the absorption stretching frequency of the C=N function group. The ^{13}C NMR spectrum revealed a signal of C=N at 141.5 ppm, and in the ^{1}H NMR spectrum, the C_{13a} proton appeared as a doublet at a lower field (δ 3.24 ppm) than that of compound **13a** because of the electronegativity of nitrogen atoms in compound **14a** (cf. Experimental section). The mass spectrum of compound **2** exhibits abundant parent ions for the structure $Ar_1SO_2C_6H_5$, where Ar_1 represents the iminobenzocoumarin moiety. It was found that the prominent peaks in the mass spectra were due to Ar_1SO^+, Ar_1O^+, $C_6\ H_5\ SO^{+\bullet}$, and $C_6H_5O^{+\bullet}$ as shown in Fig. 3. Also, the ions $Ar_1SO_2^{+\bullet}$ are of low abundance. On the other hand, fragmentation does occur in which neutral Ar_1SO_2 fragments seem to be eliminated. Both $Ar_1^{+\bullet}$ and $C_6H_5^{+\bullet}$ ions are observed at high abundance.

An ion of mass corresponding to M–$SO_2C_6H_5$ units ($Ar_1^{+\bullet}$) with a loss mass unit of 27 gives a neutral fragment (Ar_1–HCN) of mass 167 (Fig. 4).

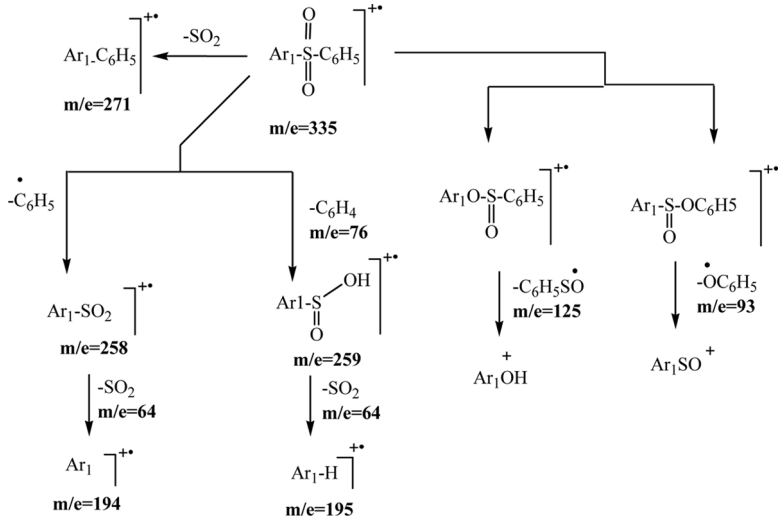


Figure 3. Fragmentation pattern of arylsulfonyl compounds.

An ion m/z 139 may find its origin in the loss of carbon monoxide from mass of 167. The great intensity of the ions 271 and 270 demonstrates the overall stability of these ions, while the formation of an m/z

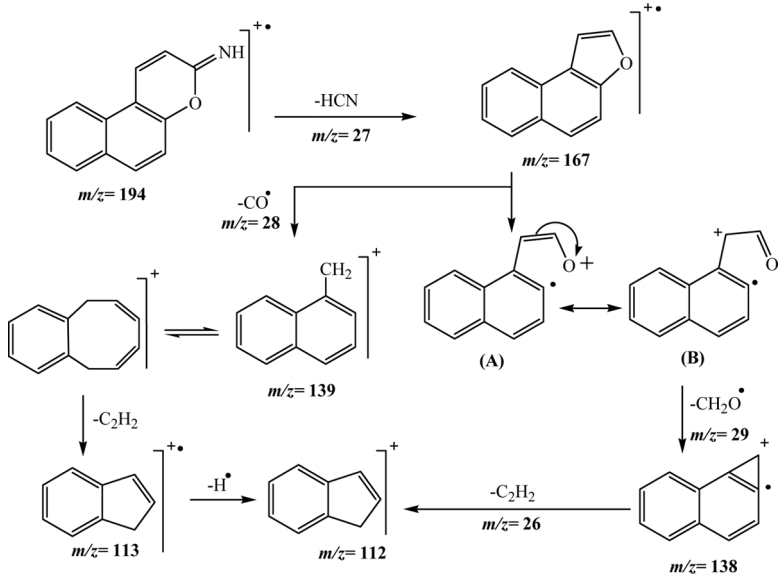
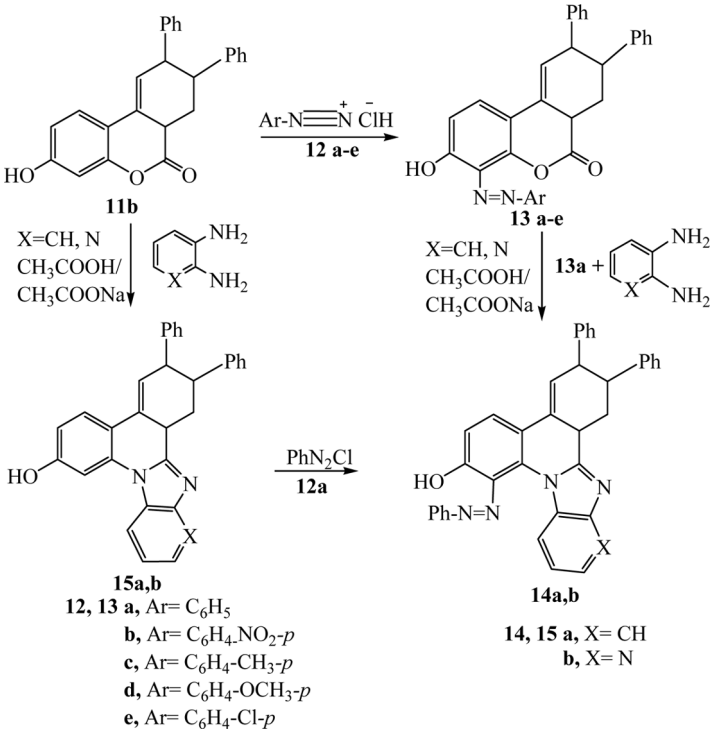


Figure 4. General route of fragmentation of coumarin derivatives.



Scheme 5. Synthesis of tetrahydrodiaza- and triaza-indenophenanthrene derivatives.

138 fragment is reminiscent of the behavior of furan and may conceivably proceed from ion **B** with the production of ion 138 or a related troplium species. It is postulated that the latter ion has the nephthcyclo propenyl structure and is formed in a manner similar to the $C_3H_3^{+\bullet}$ ion in furan.

Compound **3** showed a similar fragmentation behavior route as that discussed for compound **2** (cf. Fig. 4).

EXPERIMENTAL

General

All melting points are recorded on Gallenkamp electric melting-point apparatus and are uncorrected. The IR spectra $\upsilon\,cm^{-1}$ (KBr) were obtained on a Perkin-Elmer IR spectrophotometer model 157. The ^1H NMR spectra were recorded on a Varian spectrometer at 200 MHz using

tetramethylsilane (TMS) as an internal reference and dimethylsulfoxide (DMSO)-d_6 as solvent. The mass spectra (EI) were run at 70 eV with Kratos MS equipment and/or a Varian MAT 311 A spectrometer.

Molecular Modeling

All molecular geometries were fully optimized using either Gaussian 03 W[17] or CAChe 12.12.33.[18] In the case of transition-state calculations, harmonic vibration frequencies were calculated using PM3 implemented in CAChe for all stationary points to verify that for energy minima all frequencies are real but for the transition state there is only one imaginary frequency. In the case of ab initio calculations, geometry optimization was performed using HF/6–31 G (d,p).[19]

Synthesis of 2-Imino-3-phenylsulfonyl-benzo[f]chromene (2) and 2-Imino-3-phenylsulfonyl Coumarin (4)

2-Hydroxy-1-naphthaldehyde and/or salicylaldehyde (0.01 mol) were added to a solution of phenylsulfonyl acetonitrile (**1**, 0.01 mol) in absolute ethanol (30 ml) in the presence of a catalytic amount of triethylamine (4 drops). The reaction mixture was refluxed for 4 h and allowed to cool to room temperature. The resulting precipitate was filtered, dried, and recrystallized from ethanol to yield compounds **2** and **4**, respectively (cf. Table 1). Compound **2:** 185°C; 76%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3150 (NH), 1561 (phenyl); ^1H NMR ($CDCl_3$) δ 7.3–8.5 (m, 9H, Ar-H), 8.4 (d, 1H, C_9-H), 8.45 (d, 1H, C_{10}-H), 8.8 (s, 1H, NH exchangeable with D_2O), 9.2 (s, 1H, C_4-H); m/z 335 (M^+, 10%); calcd. for $C_{19}H_{13}NO_3S$: 335.38; C, 68.1; H, 3.9; found: C, 68.1; H, 4.1. Compound **4:** 223°C; 66%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3120 (NH), 1550 (phenyl); ^1H NMR ($CDCl_3$) δ 7.3–8.5 (m, 9H, Ar-H), 8.7 (s, 1H, C_4-H), 9.7 (s, 1H, C_4-H); m/z 285 (M^+, 20%); calcd. for $C_{15}H_{11}NO_3S$: 285.32; C, 63.2; H, 3.9; found: C, 63.2; H, 3.9.

Synthesis of 3-Phenylsulfonyl-*2H*-benzo[f]-2-chromenone (3) and 3-Phenylsulfonyl-2-coumarinone (5)

A solution of compounds **2–4** (0.01 mol) in a mixture of conc. HCl and ethanol (1:1, 20 ml) was heated for 15 min. The reaction mixture was left to stand at room temperature overnight, and the solid product was filtered off and recrystallized from ethanol to give compounds **3** and **5**,

respectively (cf. Table 1). Compound **3**: 218°C; 55%; IR (KBR) ν_{max} cm^{-1}: 1700 (δ-lactonic CO), 1555 (phenyl); ^1H NMR ($CDCl_3$) δ 7.55–8.25 (m, 9H, Ar-H), 8.4 (d, C_9-H), 8.50 (d, 1H, C_{10}-H), 9.2 (s, 1H, C_4-H); m/z 336 (M^+, 15%); calcd. for $C_{19}H_{12}O_4S$: 336.36; C, 67.9; H, 3.6; found: C, 67.3; H, 3.5. Compound **5**: 244°C; 50%; IR (KBR) ν_{max} cm^{-1}: 1710 (δ-lactonic CO), 1550 (phenyl); ^1H NMR ($CDCl_3$) δ 7.5–8.5 (m, 9H, Ar-H), 9.2 (s, 1H, C_4-H); m/z 286 (M^+, 35%), calcd. for $C_{15}H_{10}O_4S$: 286.30; C, 62.9; H, 3.5; found: C, 62.8; H, 3.3.

Synthesis of *N*-(*p*-Methoxyphenyl)-3-phenylsulfonylquinolin-2-one (7)

A mixture of compound **3** (0.01 mol) and/or compound **5** (0.01 mol) and *p*-anisidine (0.01 mol) in glacial acetic acid (30 ml) containing freshly fused sodium acetate (0.3 g) was refluxed for 4 h. The reaction mixture was left to cool at room temperature. The precipitated solid materials were filtered off, dried well and recrystallized from acetic acid to yield compounds **6** and **7**, respectively (cf. Table 1). Compound **6**: 265°C; 43%; IR (KBR) ν_{max} cm^{-1}: 1680 (amidic CO), 1540 (phenyl); ^1H NMR ($CDCl_3$) δ 3.74 (s, 3H, OCH_3), 8.45 (d, 1H, C_9-H), 8.6 (d, 1H, C_{10}-H), 7.4–8.35 (m, 9H, Ar-H), 9.3 (s, 1H, C_4-H); calcd. for $C_{26}H_{19}NO_4S$: 441.5; C, 70.7; H, 4.3; found: C, 70.6; H, 4.1. Compound **7**: 282°C; 40%; IR (KBR) ν_{max} cm^{-1}: 1680 (amidic CO), 1550 (phenyl); ^1H NMR ($CDCl_3$) δ 3.75 (s, 3H, OCH_3), 7.30–8.40 (m, Ar-H), 9.1 (s, 1H, C_4-H); calcd. for $C_{22}H_{17}NO_4S$: 391.44; C, 67.5; H, 4.3; found: C, 67.5; H, 4.3.

Synthesis of 7-Hydroxy-4-arylidene Coumarino Derivatives (9a–d)

A mixture of coumarin derivative (**8**, 0.01 mol) and different aryl aldehydes (0.01 mol) was heated in an oil bath at 150°C for 3 h in the presence of a catalytic amount of piperdine. The reaction mixture was recrystallized from acetic acid to yield the corresponding 4-arylidene-coumarino derivatives **9a–d** (cf. Table 1). Compound **9a**: 146°C; 85%; IR (KBR) ν_{max} cm^{-1}: 3350 (OH), 1720 (δ-lactonic CO), 1600 (C=C), 1175 (C–O–C); ^1H NMR ($CDCl_3$) δ 5.6–5.8 (two-d, 2H, CH=CH), 6.89 (s, 1H, C_3-H), 6.93–7.69 (m, 8H, Ar-H); calcd. for $C_{18}H_{14}O_2$: 262.30; C, 77.3; H, 4.6; found: C, 77.1; H, 4.5. Compound **9b**: 160°C; 73%; IR (KBR) ν_{max} cm^{-1}: 3315 (OH), 1720 (δ-lactonic CO), 1600 (C=C), 1175 (C–O–C), 1350, 1530 (NO_2); ^1H NMR ($CDCl_3$) δ 5.6, 5.8 (2d, 2H, CH=CH), 6.89 (s, 1H, C_3-H), 6.93–7 (m, 7H, Ar-H); calcd. for $C_{18}H_{13}NO_4$: 307.30; C, 66.0; H, 3.6; found: C, 66.0; H, 3.5.

Compound **9c**: 173°C; 65%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3380 (OH), 1700 (γ-lactonic CO), 1600 (C=C), 1180 (C–O–C); ^1H NMR ($CDCl_3$) δ 5.6, 5.8 (2d, 2H, CH=CH), 6.9 (s, 1H, C_3-H), 6.95–7.80 (m, 7H, Ar-H); calcd. for $C_{18}H_{13}ClO_2$: 296.75; C, 68.3; H, 3.7; found: C, 68.2; H, 3.5. Compound **9d**: 182°C; 70%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3315 (OH), 1720 (γ-lactonic CO), 1600 (C=C), 1175 (C–O–C), 1350, 1530 (NO_2); ^1H NMR ($CDCl_3$) δ 5.6, 5.8 (2-d, 2H, CH=CH), 6.9 (s, 1H, C_3-H), 6.95–7.80 (m, 7H, Ar-H); calcd. for $C_{18}H_{13}ClO_2$: 296.75; C, 66.0; H, 3.6; found: C, 66.0; H, 3.5.

Synthesis of 3-Hydroxy-9-phenyl-6a,7,8,9-tetrahydrobenzo[c] chromen-6-one Derivatives (11a–d)

A solution of coumarin derivative **9a** (0.01 mol) and vinyl derivatives **10a–d** (0.01 mol) in DCM (20 ml) was left to stand at room temperature overnight. The precipitated solid product was filtered off, dried well, and recrystallized from dioxane to give compounds **11a–d** (cf. Table 1). Compound **11a**: 201°C; 77%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3350 (OH), 1720 (γ-lactonic CO), 1610 (C=C), 1770 (C–O–C); ^1H NMR ($CDCl_3$) δ 1.9 (d, 2H, CH_2Br), 2.17 (m, 2H, C_7-H), 2.78 (d-d, 1H, C_{6a}-H), 3.4 (m, 1H, C_8-H), 3.62 (d, 1H, C_9-H), 5.78 (d, 1H, C_{10}-H), 6.5–7.3 (m, 8H, Ar-H); calcd. for $C_{20}H_{17}BrO_3$: 385.25; C, 62.3; H, 4.4; found: C, 62.1; H, 3.9. Compound **11b**: 223°C; 60%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3350 (OH), 1730 (γ-lactonic CO), 1600 (C=C), 1170 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.17 (m, 2H, C_7-H), 2.78 (d-d, 1H, C_{6a}-H), 3.31 (m, 1H, C_8-H), 3.62 (d, 1H, C_9-H), 5.78 (d, 1H, C_{10}-H), 6.5–7.3 (m, 13H, Ar-H); ^{13}C NMR δ C_{-1} (128), C_{-2} (112.4), C_{-3} (156.9), C_{-4} (108.5), C_{-6} (169.0), C_{-7} (33.3), C_{-8} (138.8), C_{-9} (141.4), C_{-10} (120.7), C_{-11} (144.2), C_{-12} (45.5), C_{-13} (120.4), C_{-14} (152.2), $C_{-8\text{-phenyl}}$ (125.8–128.6); calcd. for $C_{25}H_{20}O_3$: 368.42; C, 81.5; H, 5.4; found: C, 81.3; H, 4.9. Compound **11c**: 210°C; 72%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3320 (OH), 1710 (γ-lactonic CO), 1180 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.17 (m, 2H, C_7-H), 2.78 (d-d, 1H, C_{6a}-H), 3.31 (m, 1H, C_8-H), 3.62 (d, 1H, C_9-H), 3.72 (s, 3H, OCH_3), 5.78 (d, 1H, C_{10}-H), 6.5–7.3 (m, 12H, Ar-H); calcd. for $C_{26}H_{22}O_4$: 398.45; C, 78.4; H, 5.5; found: C, 78.5; H, 5.2. Compound **11d**: 272°C; 68%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3300 (OH), 1740 (carbonyl ester), 1710 (δ-lactonic CO), 1640 (C=N), 1170 (C–O–C); ^1H NMR ($CDCl_3$) δ 1.02 (t, 3H, $CH_2\underline{CH_3}$), 2.17 (m, 2H, C_7-H), 2.75 (d-d, 1H, C_{6a}-H), 3.31 (m, 1H, C_8-H), 3.55 (q, 2H, $\underline{CH_2}CH_3$), 3.62 (d, 1H, C_9-H), 5.78 (d, 1H, C_{10}-H), 6.5–7.3 (m, 8H, Ar-H); calcd. for $C_{22}H_{20}O_5$: 364.39; C, 72.5; H, 5.5; found: C, 72.2; H, 5.1.

Synthesis of 3-Hydroxy-8,9-diphenyl-4-arylazo-6a,7,8,9-tetrahydrobenzo[c]chromen-6-one Derivatives (13a–e)

A well-stirred solution of appropriate aryl amines (**12a–e**, 0.2 mol) in 2 N HCl (125 ml) was cooled in an ice bath and diazotized with 0.1 N sodium nitrite solution (100 ml). The reaction mixture was stirred at 0–5 °C for 1 h. The cold diazonium solution was added dropwise to a well stirred cold solution of compound **11b** (0.2 mol) in sodium hydroxide solution (5%, 30 ml). The reaction mixture was stirred for 2 h until coupling was complete. The precipitated solid material was filtered off, washed with water, dried well, and recrystallized from aqueous ethanol to give **13a–e** derivatives (cf. Table 1). Compound **13a**: 260°C; 62%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3310 (OH), 1730 (δ-lactonic CO), 1610 (C=), 1580 (N=N), 1170 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.17 (m, 2H, C_7-H), 2.79 (d-d, 1H, C_{6a}-H), 3.31 (m, 1H, C_8-H), 3.61 (d, 1H, C_9-H), 5.78 (d,d-1H, C_{10}-H), 6.7–7.93 (m, 17H, Ar-H); ^{13}C NMR C_{-1} (130.2), C_{-2} (112.7), C_{-3} (151.1), C_{-4} (132.5), C_{-6} (169.0), C_{-6a} (45.8), C_{-7} (33.3), C_{-8} (138.8), C_{-9} (141.5), C_{-10} (120.2), C_{-10a} (144.2), C_{-11a} (120.7), C_{-12a} (146.4), N=N-phenyl (122.7–152.5) $C_{-8\text{-phenyl}}$ (125.8–128.6), $C_{-9\text{-phenyl}}$ (125.7–128.3); calcd. for $C_{31}H_{24}N_2O_3$: 472.53; C, 78.8; H, 4.1; found: C, 78.3; H, 4.5. Compound **13b**: 281°C; 55%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3310 (OH), 1725 (δ-lactonic CO), 1610 (C=C), 1580 (N=N), 1530 (NO_2 sym), 1350 (NO_2 sym), 1170 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.20 (m, 2H, C_7-H), 2.79 (d, 1H, C_{6a}-H), 3.32 (d, d, 1H, C_8-H), 3.60 (d, d, 1H,C_9-H), 5.8 (d,d-1H, C_{10}-H), 6.7–7.93 (m, 16H, Ar-H); calcd. for $C_{31}H_{23}N_3O_5$: 517.53; C, 72.0; H, 4.5; found: C, 71.6; H, 4.2. Compound **13c**: 279°C; 58%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3310 (OH), 1720 (δ-lactonic CO), 1600 (C=C), 1580 (N=N), 1180 (C–O–C); ^1H NMR ($CDCl_3$) δ 1.90 (s, 3H, CH_3), 2.18 (m, 2H, C_7-H), 2.79 (d, 1H, C_{6a}-H), 3.40 (d, d, 1H, C_8-H), 3.60 (d, d, 1H, C_9-H), 5.78 (d, d-1H, C_{10}-H), 6.65–7.8 (m, 16H, Ar-H); calcd. for $C_{32}H_{26}N_2O_3$: 486.56; C, 79.0; H, 5.4; found: C, 79.2; H, 5.1. Compound **13d**: 285°C; 49%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3380 (OH), 1710 (δ-lactonic CO), 1620 (C=C), 1580 (N=N), 1175 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.18 (m, 2H, C_7-H), 2.79 (d, 1H, C_{6a}-H), 3.45 (d, d, 1H, C_8-H), 3.60 (d, d, 1H, C_9-H), 3.90 (s, 3H, OCH_3), 5.75 (d, d-1H, C_{10}-H), 6.70–7.90 (m, 16H, Ar-H); calcd. for $C_{32}H_{26}N_2O_4$: 502.56; C, 76.5; H, 5.2; found: C, 76.5; H, 5.1. Compound **13e**: 252°C; 55%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3300 (OH), 1710 (δ-lactonic CO), 1600 (C=C), 1575 (N=N), 1185 (C–O–C); ^1H NMR ($CDCl_3$) δ 2.17 (m, 2H, C_7-H), 2.77 (d, 1H, C_{6a}-H), 3.33 (d, d, 1H, C_8-H), 3.61 (d, d, 1H, C_9-H), 5.75 (d, d-1H, C_{10}-H), 6.7–7.91 (m, 16H, Ar-H); calcd. for $C_{31}H_{23}ClN_2O_3$: 506.98; C, 73.5; H, 4.5; found: C, 73.2; H, 4.2.

Synthesis of 2,3-Diphenyl-1,2,3,13b-tetrahydro-8b,13-diaza-indeno(1,2-I) phenthren-7-o1 (14a) and Its 8b,12,13-Triaza Derivative (14b)

Method A

A mixture of compound **13a** (0.005 mol) and *o*-phenylenediamine (0.005 mol) and/or 2,3-diaminopyridine (0.005 mol) was refluxed in glacial acetic acid (30 ml) in the presence of freshly fused sodium acetate (0.3 g) for 6 h. The reaction mixture was left to stand overnight for complete precipitation. The resulting precipitate was filtered, dried, and recrystallized from acetic acid to yield the corresponding **14a** and **b**, respectively (cf. Table 1).

Method B

A well-stirred solution of aniline (0.2 mol) in 2 N HCl (125 ml) was cooled in an ice bath (0–5°C), diazotized with 0.1 N sodium nitrite solution (100 ml), and stirred for 1 h at 0–5°C. The diazonium solution was added dropwise to a well-stirred cold solution of compounds **15a** and **b** (0.2 mol) in sodium hydroxide solution (5%, 30 ml). The reaction mixture was stirred for 2 h until coupling was complete. The resulting precipitate was filtered, washed with water, dried, and recrystallized from aqueous ethanol to yield compounds **14a** and **b**. Compound **14a**: >300°C; 40%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3340 (OH), 1625 (C=N), 1600 (C=C), 1580 (N=N); ^1H NMR ($CDCl_3$) δ 2.3 (m, 2H, CH_2), 3.23 (d, 1H, C_{13a}-H), 3.31 (m, 1H, C_2-H), 3.62 (d, 1H, C_3-H), 5 (s, 1H, OH), 5.78 (d, 1H, C_4-H), 6.9–7.93 (m, 21H, Ar-H); ^{13}C NMR: C_{-1} (90.3), C_{-2} (42.8), $C_{-2\text{-phenyl}}$ (125–138.8), C_{-3} (41.8), $C_{-3\text{-phenyl}}$ (135.7–139.4), C_{-4} (120.7), C_{-4a} (144.2), C_{-5} (130.7), C_{-6} (115.4), C_{-7} (151.6), C_{-8} (132.1), N=N-phenyl (122.7–152.5), C_{-8a} (130), C_{-8b} (120.3), C_{-9a} (137.9), C_{-9} (115.4), C_{-10} (122.9), C_{-11} (122.9), C_{-12} (115.4), C_{-12a} (137.9), C_{13a} (141.5), (36.3); calcd. for $C_{37}H_{28}N_4O$: 544.64; C, 81.6; H, 5.2; found: C, 81.4; H, 4.6. Compound **14b**: >300°C; 46%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3350 (OH), 1620 (C=N), 1600 (C=C), 1580 (N=N); ^1H NMR ($CDCl_3$) δ 2.20 (m, 2H, CH_2), 2.23 (d, 1H, C_{13a}-H), 3.34 (m, 1H, C_2-H), 3.62 (d, 1H, C_3-H), 5.0 (s-1H, OH), 5.57 (d, 1H, C_4-H), 6.85–7.42 (m, 20H, Ar-H); calcd. for $C_{36}H_{27}N_5O$: 545.63; C, 79.3; H, 5.0; found: C, 79.1; H, 4.7.

Synthesis of 2,3-Diphenyl-1,2,3,13b-tetrahydro-8b,13-diaza-indeno (1,2-I)phenanthren-7-ol (15a) and Its 8b,12,13-Triaza Derivatives (15b)

Equimolar amounts of compound **11a** (0.005 mol) and *o*-phenylendiamine (0.005 mol) and/or 2,3-diamino pyridine (0.005 mol) were refluxed

in glacial acetic acid (30 ml) in the presence of freshly fused sodium acetate (0.3 g m) for 4 h and allowed to cool to room temperature. The resulting precipitate was filtered, dried, and recrystallized from acetic acid to yield compounds **15a** and **b** (cf. Table 1). Compound **15a**: 277°C; 50%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3310 (OH), 1640 (C=N), 1600 (C=C); ^1H NMR ($CDCl_3$) δ 2.23 (m, 2H, CH_2), 3.21 (d, 1H, C_{13a}-H), 3.25 (m, 1H, C_2-H), 3.61 (d, 1H, C_3-H), 5.2 (s-1H, OH), 5.71 (d, 1H, C_4-H), 6.6–7.4 (m, 17H, Ar-H); calcd. for $C_{31}H_{24}N_2O$: 440.54; C, 84.6; H, 5.5; found: C, 84.1; H, 4.9. Compound **15b**: 283°C; 43%; IR (KBR) $\nu_{max}\,cm^{-1}$: 3320 (OH), 1640 (C=N), 1600 (C=C); ^1H NMR ($CDCl_3$) δ 2.23 (m, 2H, CH_2), 2.21 (d, 1H, C_{13a}-H), 3.35 (m, 1H, C_2-H), 3.6 (d, 1H, C_3-H), 5.3 (s-1H, OH), 5.51 (d, 1H, C_4-H), 6.5–7.4 (m, 16H, Ar-H); calcd. for $C_{30}H_{23}N_3O$: 441.52; C, 81.6; H, 5.2; found: C, 81.6; H, 5.1.

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