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PAPER

Regiospecific Inverse Electron Demand Diels-Alder reactions of 7-methylcoumarin-4-azadienes

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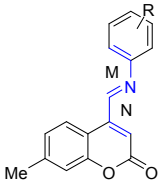
Condensation of 7-methylcoumarin-4-carbaldehyde with different anilines affords 7-methylcoumarin-4-azadienes. The 7-methylcoumarin-4-azadienes do not undergo normal electron demand Diels-Alder reaction with *N*-phenylmaleimide, but react with dihydropyran, dihydrofuran, and styrene *via* inverse electron demand Diels-Alder reaction in the presence of anhydrous $ZnCl_2$. The diene involves azomethine group and the aniline ring. The product is a mixture of two diastereomers in which the major diastereomer has all the hydrogens at the ring junction in *cis* configuration.

Introduction

The Coumarins are versatile molecules because many of them, natural as well as synthetic, exhibit a broad spectrum of biological properties such as antitumour [1], antimicrobial [2] and antiviral [3] activities. Polycyclic benzopyrones embedding a coumarin ring also show diverse activities. One of the strategies of building of such molecules is annulation over a coumarin ring. This strategy works very well with the 3,4-double bond in coumarin. The 3,4-double bond function as a dienophile [4] due to activation by adjacent carbonyl group and it also undergoes addition reaction [5]. 3-Vinyl and 4-styryl substituted coumarins perform as dienes and the corresponding Diels-Alder reaction gives 3,4-annulated coumarins [6]. Inverse electron demand Diels-Alder reaction of coumarins containing electron deficient diene with electron rich dienophiles is known to give 3,4-annulated coumarins [7].

The aza Diels-Alder reaction of coumarin-3-azadienes derived from 3-aminocoumarin and its intramolecular version are known [8]. Conjugated polyenes containing more than one diene component are interesting substrates for Diels-Alder reaction, as the reaction involves a challenge of regioselection. Diels-Alder reaction of dendralene and biscoumarinylethene types of polyene systems are reported in literature to give regioselective product [9]. Diels–Alder reaction of heteropolyene (cross conjugated) system like [3]-3-heterodendralenes (thia-[10], oxa-[11], and aza-[12] with an suitable dienophiles gives diversified heterocycles. More recently Saito et al reported the Diels-Alder reaction of [3]-1-azadendralenes in which cross-conjugated 1-azatriene underwent an initial hetero Diels–Alder reaction on the 1-*aza*-1,3-butadiene system with tosyl isocyanate to afford the mono-cycloadduct pyrimidinone which on further subsequent Diels–Alder reaction with dienophiles provides hexahydroquinazolin-2(1*H*)-ones with high stereoselectivity [13].

As a part of our interest in the Diels-Alder reaction of coumarins containing diene component, we thought that coumarin-4-azadienes (**1**) which contain a 3,4-double bond of coumarin ring conjugated to phenylimino group, would be an interesting diene system to study the Diels-Alder reaction; targeting coumarin containing polycyclic compounds.



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Azadiene **1** is an interesting substrate for Diels-Alder reaction as it contains two potentially reactive azadiene: a 2-azadiene (involving the aniline ring i.e. **M**) and a 1-azadiene (involving the C3-C4 coumarin double bond i.e. **N**) with different orbital characteristics and electron demands; possibly providing regioselectivity in the reaction. In general, simple 1- and 2-azadienes, due to their electron-deficient nature favor participation in `inverse electron demand' (LUMO diene-controlled) Diels-Alder reaction [14]. A major difference between the two systems is the efficacy of Lewis acid catalysis in the 2-azadiene cycloadditions. However reactivity of both the azadienes can be tuned by introducing either electron-withdrawing or electron-donating substituents at proper positions of the diene [15]. The introduction of electron-withdrawing substituents at the 2, 3, or 4 positions of the 1-azadiene may further accelerate reaction rates through LUMO diene-controlled pathway. Sufficiently electron-donating substituents placed at the C-1 and/or C-3 position in the 2-azadiene can enhance the Diels-Alder reactivity through the HOMO diene-controlled pathway [15]. Herein, we report a comprehensive study on the inverse electron demand Diels-Alder reaction of 7-methylcoumarin-4-azadienes (**1**).

7-Methylcoumarin-4-acetic acid (**5**) was prepared by the condensation of *m*-cresol (**4**) with acetone dicarboxylic acid (**3**),

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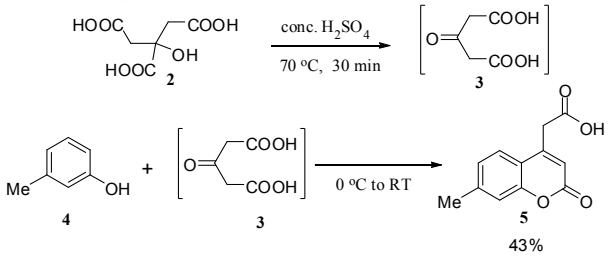
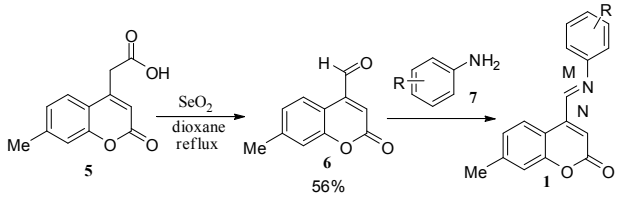
which in turn was prepared *in situ* by reacting citric acid (**2**) with conc. H_2SO_4 (**Scheme 1**) [16].



Scheme 1 Synthesis of 7-methylcoumarin-4-acetic acid (**5**)

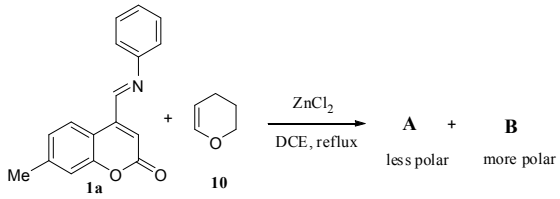
The compound **5** was subjected to oxidation using SeO_2 to obtain 7-methylcoumarin-4-carbaldehyde (**6**), which on condensation with anilines (**7**) gave 7-methylcoumarin-4-azadienes (**1**) (**Scheme 2**) [17].



Scheme 2 Synthesis of 7-methylcoumarin-4-azadienes (**1**)

Diels-Alder reaction of 4-styrylcoumarins with *N*-phenylmaleimide (NPMA) (**8**) is known to give 2,11-diphenyl-3a,10,11,11a-tetrahydro[1]benzopyrano[3,4-*e*]isoindole-1,3,4(2*H*)-triones [18]. Taking inspiration from this, we carried out the Diels-Alder reaction of **1a** (R = H) with NPMA (**8**) at different temperatures in dioxane, nitrobenzene, and *o*-dichlorobenzene (*o*-DCB). In dioxane **1a** remained unconsumed, while in nitrobenzene and *o*-DCB it decomposed to form other side products (TLC). The same reaction under microwave irradiation at different temperatures also failed to give the desired product. The use of Lewis acid ($ZnCl_2$, $AlCl_3$, $BF_3.OEt_2$) catalysts (thermal and MW conditions) did not show any further beneficial effect on the reaction. Thus, **1a** did not undergo normal electron demand Diels-Alder reaction.

Azadienes are known to undergo Diels-Alder reaction by inverse electron demand pathway. Hence, the reaction of **1a** with electron rich dienophiles was carried out. Accordingly, when 3,4-dihydro-2*H*-pyran (DHP) (1 equiv) (**10**) was reacted with **1a**, in the presence of $ZnCl_2$ (1 equiv), a mixture of compounds **A** (less polar) and **B** (more polar) was obtained (**Scheme 3**).



Scheme 3 The aza Diels-Alder reaction of 7-methylcoumarin-4-azadiene (**1a**) with DHP (**10**)

A and **B** were separated and purified by flash column chromatography on silica gel using chloroform. Gratifyingly, a mixture of **A** and **B** was isolated in 67% yield with **A** (169 mg, 49%) and **B** (62 mg, 18%). Six different products are possible for this reaction as shown in **figure 1.**

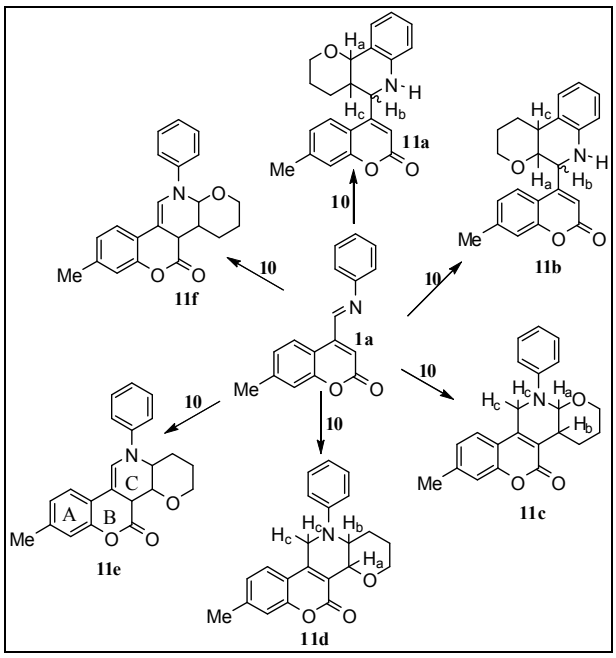


Fig.1 Possible products in the aza Diels-Alder reaction of 7-methylcoumarin-4-azadiene (**1a**) with dihydropyran (**10**)

The IR spectra of compounds **A** and **B** showed secondary NH group, as sharp medium intensity peaks at 3348 and 3322 cm^{-1} respectively, and the carbonyl groups showed peaks at 1720 and 1708 cm^{-1} respectively. ^1H NMR spectra of **A** and **B** had ratio of aliphatic protons to aromatic protons 10:8 (without considering 3 protons of methyl group). Based on these observations, structures **11e** and **11f** were ruled out, as they contain the ratio 9:9. Moreover, in **11e** and **11f** the newly formed double bond remain in ring C, exocyclic to ring B, which we have shown earlier to be improbable [12]. In **11c** and **11d**, NH is absent and Hc is expected to give two closely spaced doublets around 3.0 - 3.5 δ. This feature was not seen in the ^1H NMR spectra of **A** and **B**. Hence, **11c** and **11d** were ruled out. Among **11a** and **11b**, the distinguishing proton appears to be Ha, which in the case of **11b** would come downfield compared to that in **11a**. In the D_2O exchanged ^1H NMR spectra of **A** and **B**, the NH peak disappeared

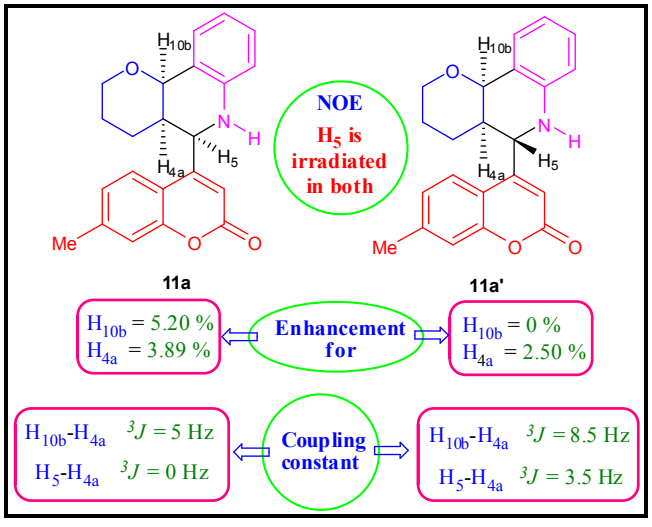


Fig. 2 Stereochemical relationship between products **11a** and **11a'**

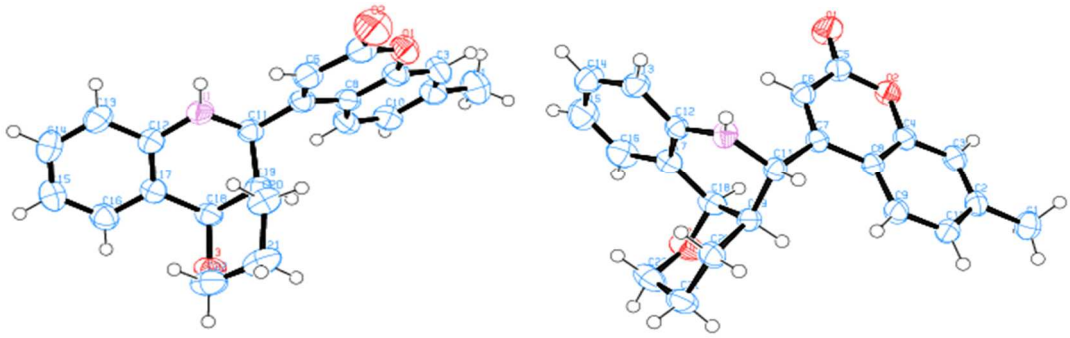


Fig.3 ORTEP diagram of products **11a** (**A**) and **11a'** (**B**)

and DHO peak appeared at 4.7 δ. Hence, the structures **11c** and and **11d** were ruled out, as they do not contain NH proton. Based on ^{13}C NMR spectra structure **11c** was ruled out, as it contains a carbon atom which is flanked by two electronegative atoms, oxygen and nitrogen, and is expected to give a peak around 80-85 δ. Such a peak was not observed in both the spectra. To throw more light on the structure, DQF-COSY spectra of **A** and **B** were recorded and the spectra supported structure **11a**. Based on the stereochemical restriction in the Diels-Alder reaction, compound **11a** can exists in two diastereomeric forms **11a** and **11a'**. The most diagnostic parameter for the structural assignment is the scalar coupling constant between protons H_{4a} and H_5. As depicted in Figure 2, the *cis* isomer has small coupling constants $J_{H\text{-}5,\ H\text{-}4a}$ = 0 Hz, $J_{H\text{-}10b,\ H\text{-}4a}$ = 5 Hz, consistent with an all *cis* configuration of the hydrogen atoms of 4a, 5, and 10b positions. In the *trans* isomer, the value of $J_{H\text{-}5,\ H\text{-}4a}$ = 8.5 Hz is large and indicates the *anti* orientation of the hydrogen atoms of 4a and 5 positions. To get more clarification about the stereochemical relationship NOE spectra were recorded. In both the spectra the signal corresponding to H_5 (5.10 δ in compound A, 4.56 δ in compound B) was irradiated. In the case of **A** the irradiation resulted in intensification of H_{4a} by 3.89% and H_{10b} by 5.20%; which confirmed the *cis* arrangement between H_5, H_{4a} and H_{10b}. In the case of **B** there was enhancement of H_{4a} by 2.50% and there was no NOE observed for H_{10b}, because of *trans* relationship between H_5-H_{4a} and H_5-H_{10b} (**figure 2**). By observing the NOE effect it was clear that in the less polar compound (**A** = **11a**) the stereochemical relation between H_5 and H_{4a} was *cis*, while in the more polar compound (**B** = **11a'**) the relation was *trans*.

To establish the structures unequivocally, single crystal XRD was recorded on a Bruker axs kappa apex 2 CCD Diffractometer using graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The ORTEP diagram of **A** and **B** are shown in figure 3. Thus the two compounds, **A** and **B**, are diastereomers of each other.

Compound **A** (**11a**) is 4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline.

Compound **B** (**11a'**) is 4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline.

In structure **1**, diene N appears to be more electron deficient than diene M. However, in the case of an unsymmetrical polyene system, particularly the one like in the present case, where there is a combination of heteroatoms, electron donating groups and electron withdrawing groups, the regioselection is difficult to predict. To through more light on the selectivity, **6** was condensed with benzylamine to obtain corresponding anil (**1i**). **1i** is devoid of diene component M and has only diene component N. **1i** failed to react with NPMA as well as DHP.

A series of 7-methylcoumarin-4-azadienes was prepared as per literature method by reacting 7-methylcoumarin-4-carbaldehyde (**6**) and anilines (**7**) in benzene at reflux condition (Table 1) [17]. All anilines (**7**) react with 7-methylcoumarin-4-carbaldehyde (**6**) to give high yield of **1**. Primary aliphatic benzyl amine reacts very rapidly as compared to other aromatic amines (entry 9). Due to electron deficient nature of 3-nitroaniline (**1f**) and 4-nitroaniline (**1e**) it took maximum time for condensation (entry 5 & 6). As expected steric effect is pronounced in the reaction of **1h** with **6,** reaction required more time for completion.

The effect of Lewis acid catalyst and solvent on the reaction was then investigated (Table 2). The reaction of **1a** and DHP (**10**) could not be effected without a catalyst. Different catalysts were used for the reaction in 1,2-dichloroethane. Anhydrous Lewis acids were very effective in catalyzing the reaction, while hydrated Lewis acids were much less active. Bronsted acids also were not very effective in catalyzing the reaction. In the case of $AlCl_3$ and $FeCl_3$, the reaction at 0 °C gave about 50-55% combined yield of **11a** and **11a'**. When the same reaction was carried out at room temperature, the combined yield of **11a** and **11a'** decreased and substantial amount of a sticky material was formed, which was insoluble in organic solvents. $SnCl_4$ was also effective. $ZnCl_2$ was found to be not only effective, but was very convenient to use. At room temperature the reaction was slow and the combined yield was 77% (entry 8). At reflux condition the reaction was fast and gave 83% of yield (entry 9). Hence, all the reactions were carried out at the reflux temperature. CAN was

Table 1 Preparation of 7-methylcoumarin-4-azadienes (**1**) by the reaction of anilines (**7**) and 7-methylcoumarin-4-carbaldehyde (**6**)[a]

Entry	R	Product (**1**)	Time[b] (min)	Yield[c] of **1** (%)
1	H	**1a**	60	83
2	2-OMe	**1b**	30	84
3	4-Me	**1c**	30	86
4	4-Br	**1d**	40	85
5	4-NO_2	**1e**	120	72
6	3-NO_2	**1f**	110	76
7	4-OMe	**1g**	30	89
8	2,6-$(Me)_2$	**1h**	110	80
9	-	**1i**	20	84

[a]Reaction conditions: 7-methylcoumarin-4-carbaldehyde (1 mmol), aniline (1 mmol), Benzene (5 mL), Reflux temp, [b]Time required for total consumption of **6**, [c]Isolated yield

Table 2 The effect of Lewis acids on the aza Diels-Alder reaction of **1a** and **10** in 1,2-dichloroethane[a]

Entry	Catalyst[b]	Condition (Time)[c]	Yield[d] (%)	
			11a	**11a'**
1	Without catalyst	Reflux (24 h)	NR	
2	$BF_3.OEt_2$	rt (15 min)	57	10
3	$BF_3.OEt_2$	reflux (5 min)	44	8
4	$AlCl_3$	0 °C (2 h)	40	10
5	$FeCl_3$	0 °C (2 h)	32	22
6	$AlCl_3$	rt (5 min)	31	06
7	$FeCl_3$	rt (5 min)	24	16
8	$ZnCl_2$	rt (9 h)	59	18
9	$ZnCl_2$	reflux (3 h)	60	23
10	$AlCl_3$. $6H_2O$	rt (25 min)	27	08
11	$FeCl_3$. $6H_2O$	rt (15 min)	29	05
12	$ZnCl_2$. $2H_2O$	reflux (10 h)	33	14
13	methanolic HCl	rt (14 h)	12	18
14	conc. H_2SO_4	0 °C (5 min)	20	-
15	$SnCl_4$	rt (15 min)	46	14
16	CAN	rt (3 h)	20	34

[a]**Reaction conditions:** 7-methylcoumarin-4-azadiene (1 mmol), dihydropyran (3 mmol), 1,2-dichloroethane (5 mL), [b]Catalyst (1 mmol), [c]Time for which reaction was continued, [d]Isolated yield.

also effective and in 3 h, 54% of combined yield was obtained. Except CAN, with all the catalysts **11a** was obtained as the major product, while with CAN, **11a'** was the major product.

Based on this study, $ZnCl_2$ was selected as the catalyst for the reaction and using this catalyst different solvents such as methanol, ethanol, acetonitrile, dioxane, tetrahydrofuran, 1,2-dichloroethane and toluene were tried. Except, 1,2-dichloroethane and acetonitrile the reaction did not take place in other solvents. 1,2-Dichloroethane was the best solvent found for reaction and gave 83% of combined yield of **11a** and **11a'**.

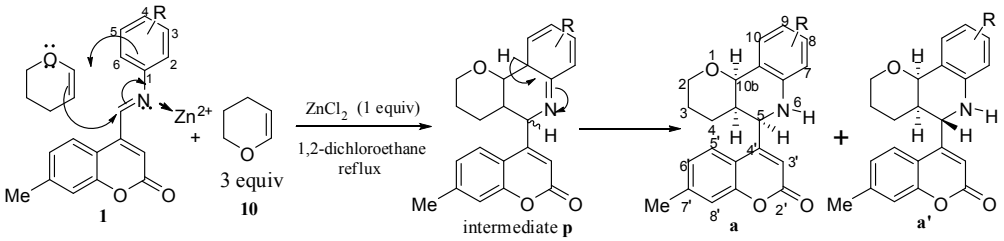
At this stage, other parameters, i.e. catalyst loading and molar ratio of the reactants were studied (Table **3**). The yield of the product considerably improved (83%) using 3 equiv. of DHP. Further increase in the amount of DHP did not increase the yield (Entries 8 and 9). Also the yield was not significantly increased by increasing the amount of 7-methylcoumarin-4-azadiene (**1a**) with respect to dienophile. The yield was considerably improved (67%) when one equivalent of $ZnCl_2$ was used (Entry 2). Further increase in the catalyst loading did not improve the yield (Entries 3 and 4).

Table 3 Effect of catalyst loading, concentration of **1a**, and molar ratio of **1a:10** on the reaction of **1a** and **10**[a]

Entry	$ZnCl_2$ (equiv)	Molar ratio (**1a:10**)	Time[b] (h)	% Yield[c] (**11a**+**11a'**)	Combined Yield (**11a**+**11a'**) (%)
1	0.5	1:1	6	39+14	53
2	1	1:1	6	49+18	67
3	2	1:1	6	51+18	69
4	3	1:1	6	42+18	60
5	1	1:1	6	46+20	66
6	1	1:2	5	52+23	75
7	1	1:3	3	60+23	83
8	1	1:4	3	61+20	81
9	1	1:5	3	61+21	82

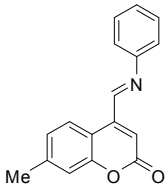
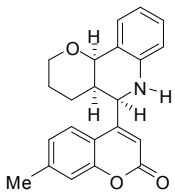
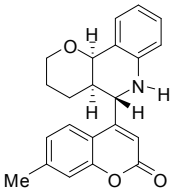
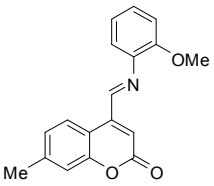
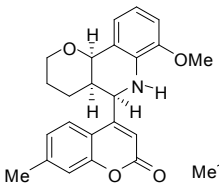
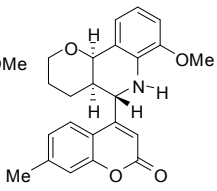
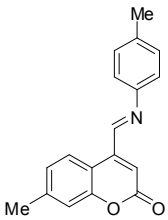
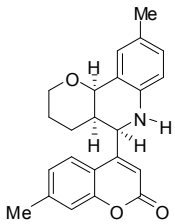
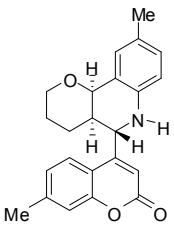
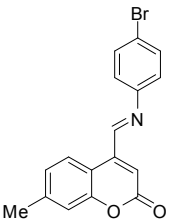
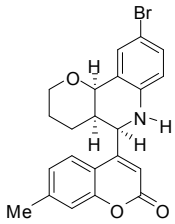
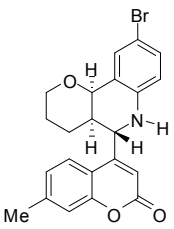
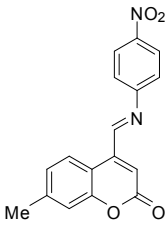
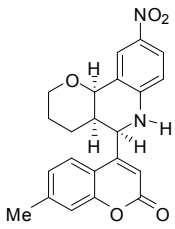
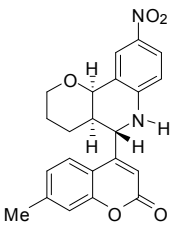
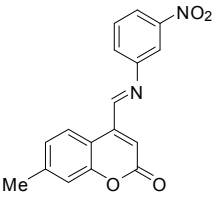
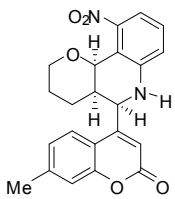
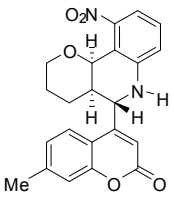
[a]**Reaction conditions:** 7-methylcoumarin-4-azadiene (1 mmol), 1,2-dichloroethane (5 mL), reflux temp, [b]Time for which reaction was continued, [c]Isolated yield.

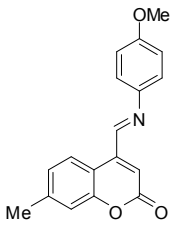
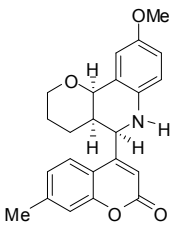
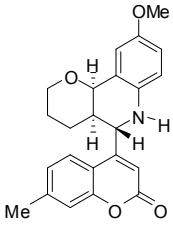
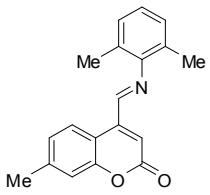
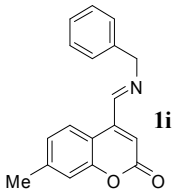
Under the optimized conditions, different 7-methylcoumarin-4-azadienes (**1a-1g**) were reacted with DHP (**10**) in the presence of $ZnCl_2$ to obtain the corresponding aza Diels-Alder adducts (Scheme 4, Table 4). All the dienes were reactive and gave the adducts in good yield; however, the time required for complete consumption of the diene varied substantially from diene to diene. The reaction with highly electron deficient diene (**1e**) was very fast, however we were unable to isolate the more polar product **15a'** and only less polar product **15a** was isolated in low yield. Reaction of electron rich dienes **1b** and **1g**, gave high percentage of **1a**. The reaction of **1h** and **1i** did not take place even up to 18 h. It also supported that adduct was derived from the M diene system. In all the cases "**a**" was obtained as the major isomer; the highest being found in the case of dienes **1a** and **1b**. **1** with 2,6-dimethylphenyl ring (**1h**) on the N atom failed to react with DHP.



Scheme 4 The aza Diels-Alder reaction of 7-methylcoumarin-4-azadienes (**1**) with DHP (**10**)

Table 4 The aza Diels-Alder reaction of 7-methylcoumarin-4-azadienes (**1**) with DHP (**10**)[a]

Entry	Azadiene (**1**)	(**a**)	Products	(**a'**)	Time[b] (h)	Ratio[c] (**a:a'**) (%)	Yield[d] **a (%)**	Yield[d] **a' (%)**
1	 **1a**	 **11a**	 **11a'**		3	72:28	60	23
2	 **1b**	 **12a**	 **12a'**		4.5	87:13	68	10
3	 **1c**	 **13a**	 **13a'**		4	56:44	45	35
4	 **1d**	 **14a**	 **14a'**		4	56:44	43	34
5[e]	 **1e**	 **15a**	 **15a'**		10	-	36	unable to isolate
6	 **1f**	 **16a**	 **16a'**		1	69:31	45	20

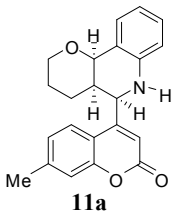
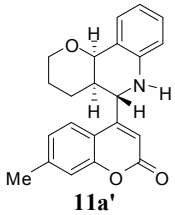
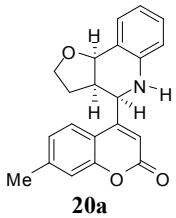
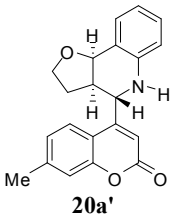
7	 **1g**	 **17a**  **17a'**	4	59:41	47	33
8	 **1h**	No Reaction	18			
9	 **1i**	No Reaction	18			

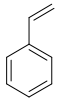
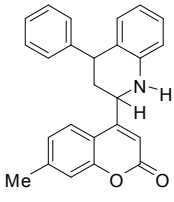
[a]**Reaction conditions**: 7-methylcoumarin-4-azadiene (1 mmol), dihydropyran (3 mmol), 1,2-dichloroethane (5 mL), Reflux temp, $ZnCl_2$ (1 mmol), [b]Time for which reaction was continued, [c]Ratio **a/a'** obtained by isolating both the products, [d]Isolated yield, [e]Reaction was carried out at room temperature

Other dienophiles like dihydrofuran (DHF) (**18**) and styrene (**19**) were reacted with **1a** under the similar conditions (Table 5). As expected, the reaction proceeded rapidly with electron rich dienophile; the order being: styrene < DHP < DHF. The reaction with DHF was very fast as compared to that with DHP. The diastereomeric ratio was almost the same in the case of DHP and DHF, but changed when the styrene was the dienophile. In the case of DHF, we were unable to isolate the more polar product **20a'** and only less polar **20a** was isolated in low yield.

To ascertain whether the adducts equilibrated, diastereomer **11a** was subjected to the same reaction conditions, i.e. 1 equivalent of $ZnCl_2$ in dichloroethane. No sign of conversion to the diastereomer **11a'** was observed at room temperature (3 h) or even after 24 h at reflux. Also, a 50:50 mixture of the diastereomers (**11a+11a'**) did not show any change in the ratio when heated to reflux in 1,2-dichloroethane in the presence of 1 equiv of $ZnCl_2$. These results suggested that the 1,3 prototropic shift is not reversible under the reaction conditions.

Table 5 The aza Diels-Alder Reaction of **1a** and dihydropyran/ dihydrofuran/ styrene[a]

Entry	Dienophile	**(a)** Products **(a')**	Time[b] (h)	Ratio[c] (**a:a'**) (%)	Yield[d] **a** (%)	Yield[d] **a'** (%)
1	 **10**	 **11a**  **11a'**	3	72:28	60	23
2[e]	 **18**	 **20a**  **20a'**	1.5	66:34	30	unable to isolate

3	 **19**	 **21a** **21a'**	4	60:40	48	32

[a]**Reaction conditions**: 7-methylcoumarin-4-azadiene (1 mmol), dienophile (3 mmol), 1,2-dichloroethane (5 mL), Reflux temp, $ZnCl_2$ (1 mmol), [b]Time for which reaction was continued, [c]Ratio **a**/**a'** obtained by isolating both the product, [d]Isolated yield, [e]Ratio **a/a'** obtained from mixture of ^{1}H NMR.

In the Diels-Alder reaction of 2-azadiene; both the concerted and stepwise mechanism have been postulated [19]. It has also been postulated that the reaction mechanism depends on relative face of approach of reactants, nature of the solvent and dienophile used [19b, 20]. In a stepwise mechanism it is postulated that dipolar intermediate can be trapped by nucleophiles like methanol, acetic acid [21]. To ascertain the mechanism of the reaction, an azadiene **1a** was reacted with **10** using optimized reaction conditions. Addition of nucleophilic solvent like methanol, acetic acid in the reaction of **1a** and **10** does not have any effect on trapping of polar reaction intermediate which support concerted mechanism for the reaction

Experimental

7-Methylcoumarin-4-acetic acid, 7-methylcoumarin-4-carbaldehyde, 7-methylcoumarin-4-azadienes were prepared by following the reported methods [16,17]. 1,2-Dichloroethane was freshly distilled from calcium hydride. The products were separated and purified by column chromatography using 100-200 mesh silica gel. Melting points were determined on an Analab melting point apparatus (Model- µThermocal 10) in open capillary tubes and are uncorrected. The IR spectra were recorded on a Jasco-4100 spectrophotometer. ^{1}H NMR spectra were recorded on 300 MHz or 500 MHz spectrometers. ^{13}C NMR spectra were recorded on 75 MHz or 100 MHz. Chemical shifts are reported in parts per million relative to the central line of the multiplet at 77.0 ppm for $CDCl_3$, 39.5 ppm for DMSO. The mass spectra were recorded on a Finnigan LCQ Advantage Max spectrometer. Elemental analysis was carried out with a Thermo finnigan, Flash EA 1112 instrument.

General procedure for the synthesis coumarin-4-azadienes (8)

7-Methylcoumarin-4-carbaldehyde (**6**) (1 mmol), and aniline (**7**) (1 mmol) were refluxed in benzene (5 mL) for an appropriate time shown in Table 1. After complete consumption of **6**, the solution was cooled to room temperature. The solid was separated by filtration, followed by washing with cold benzene and hexane. The mother liquor and washings were combined and concentrated under reduced pressure. The product **8** was purified by recrystallization from ethyl acetate.

General procedure for the aza Diels-Alder reaction between 1 and 10

7-Methylcoumarin-4-azadiene (**1**) (1 mmol) and anhydrous $ZnCl_2$ (0.136 g, 1 mmol) were stirred in 1,2-dichloroethane (5 mL) for 15 min and dihydropyran (**10**) (0.252 g, 3 mmol) was added slowly at room temperature. The solution was heated to reflux till complete consumption of **1**. The solution was cooled to room temperature, quenched with water (10 mL) and extracted with chloroform (10 mL). The extract was dried over anhydrous Na_2SO_4. The decanted organic layer was evaporated to obtain a sticky mass which was purified by column chromatography on silica gel using chloroform.

7-Methylcoumarin-4-azadiene (1a)

Brown solid; 83%; mp 148-150 ^{o}C; FT-IR (KBr): 3054 (aromatic C-H), 2896 (aliphatic C-H), 1729 (C=O); 1622, 1600 and 1547 (aromatic C=C, C=N); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.78 (s, 1H, C_3H), 7.18 (d, 1H, C_6H, J = 8.4 Hz), 8.66 (s, 1H, H-C=N-), 7.28-7.38 (m, 3H, C4'-H, C5'-H and C6'-H), 7.45-7.50 (t, 2H, C3'-H and C7'-H, J = 7.5 Hz), 8.67 (d, 1H, C5-H, J = 8.4 Hz).

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (11a)

White Solid; 209 mg, 60%; mp 275-276 ^{o}C; FT-IR (KBr): 3348 (NH), 3049 (aromatic C-H), 2947 (aliphatic C-H), 1720 (C=O); 1615, 1588 and 1553 (aromatic C=C); 1478, 1321, 1252, 1139, 1073, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41-1.61 (m, 4H, C3-H and C4-H), 2.47 (m, 1H, C4a-H), 2.53 (s, 3H, CH_3) 3.48 (td, 1H, C2a-H, J = 2.5 and 10.5 Hz), 3.66 (dd, 1H, C2b-H, J = 2.5 and 10.5 Hz), 3.82 (bs, 1H, NH), 5.10 (s, 1H, C5-H), 5.47 (d, 1H, C10b-H, J = 5 Hz), 6.74 (d, 1H, C7-H, J = 8 Hz), 6.77 (s, 1H, C3'-H), 6.93 (t, 1H, C9-H, J = 7.5 Hz), 7.18-7.21 (m, 2H, C8-H and C6'-H), 7.26 (s, 1H, C8'-H), 7.51 (d, 2H, C10-H and C5'-H, J = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): 18.5 (C3), 21.5 (CH_3), 25.2 (C4), 35.6 (C4a), 54.3 (C5), 60.4 (C2), 72.1 (C10b), 112.1 (C3'), 114.9 (C4a'), 115.3 (C8'), 117.8 (C7), 119.2 (C9), 119.9 (C10a), 122.9, 125.6, 127.5, 128.3, 143.2 (C7'), 144.3 (C6a), 154.0 (C4' and C8a'), 160.8 (C2'); MS = 348.5 (M+H); Anal. Calcd. for $C_{22}H_{21}NO_3$ (347.41): C, 76.06; H, 6.09; N, 4.03% Found: C, 76.19; H, 6.04; N, 4.11%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (11a')

Brown Solid; 80 mg, 23%; mp 174-176 ^{o}C; FT-IR (KBr): 3322 (NH), 2941 (aliphatic C-H), 1708 (C=O); 1619, 1533 and 1494 (aromatic C=C); 1315, 1268, 1144, 1067, 756 cm^{-1}; ^{1}H NMR ((500 MHz, $CDCl_3$): δ 1.53-1.56 (m, 1H, C3a-H), 1.68-1.91 (m, 3H, C3b-H and C4-H), 2.47 (bs, 1H, C4a-H), 2.52 (s, 3H, CH_3) 3.75 (td, 1H, C2a-H, J = 3.5 and 10.5 Hz), 4.01 (bd, 1H, C2b-H), 4.25 (bs, 1H, NH), 4.56 (d, 1H, C5-H, J = 3.5 Hz), 4.97 (d, 1H, C10b-H, J = 8.5 Hz), 6.54 (s, 1H, C3'-H), 6.66 (d, 1H, C7-H, J = 8 Hz), 6.85 (t, 1H, C9-H, J = 7 Hz), 7.16 (d, 1H, C6'-H, J = 8.0 Hz), 7.20 (dt, 1H, C8-H, J = 1.5 and 7 Hz), 7.26 (s, 1H, C8'-H),

7.35 (dd, 1H, C10-H, *J* = 1.5 and 7.0 Hz), 7.88 (bs, 1H, C5'-H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.6 (CH_3), 23.0 (C3), 24.3 (C4), 36.5 (C4a), 53.0 (C5), 66.1 (C2), 72.3 (C10b), 113.8 (C3'), 114.2 (C4a'), 115.4 (C8'), 117.7 (C7), 118.3 (C9), 119.5 (C8), 124.6 (C10a), 125.4, 129.3, 130.0, 143.2 (C6a), 143.3 (C7'), 154.2 (C4'), 156.2 (C8a'), 161.0 (C2'); MS = 348.5 (M+H); Anal. Calcd. for $C_{22}H_{21}NO_3$ (347.41): C, 76.06; H, 6.09; N, 4.03% Found: C, 76.14; H, 6.13; N, 3.96%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-7-methoxy-2H-pyrano[3,2-c]quinoline (12a)

Pale yellow solid; 257 mg, 68%; mp 291-293 ^{o}C; FT-IR (neat): 3324 (NH), 2865 (aliphatic C-H), 1702 (C=O); 1611, 1553 and 1504 (aromatic C=C); 1330, 1254, 1172, 1138, 1087, 866, 815 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.44 (bd, 1H, C3a-H), 1.55-1.67 (m, 3H, C3b-H and C4-H), 2.49-2.51 (m, 1H, C4a-H), 2.55 (s, 3H, CH_3), 3.52 (td, 1H, C2a-H, *J* = 2.5 and 10.5 Hz), 3.68 (dd, 1H, C2b-H, *J* = 2.5 and 10.5 Hz), 3.95 (s, 3H, OCH_3), 4.26 (bs, 1H, NH), 5.08 (s, 1H, C5-H), 5.51 (d, 1H, C10b-H, *J* = 5 Hz), 6.83 (d, 1H, C10-H, *J* = 7.5 Hz), 6.88-6.91 (m, 2H, C3'-H and C9-H), 7.17 (d, 1H, C8-H, *J* = 7.5 Hz), 7.21 (d, 1H, C6'-H, *J* = 8 Hz), 7.29 (s, 1H, C8'-H), 7.53 (d, 1H, C5'-H, *J* = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.7 (C3), 21.6 (CH_3), 25.2 (C4), 35.6 (C4a), 54.2 (OCH_3) 55.5 (C5), 60.7 (C2), 72.3 (C10b), 108.6 (C8), 112.4 (C3'), 115.0 (C4a'), 117.9 (C8'), 118.1 (C7), 118.1 (C9), 119.3 (C10), 120.0 (C10a), 122.9 (C6'), 125.6 (C5'), 134.0 (C6a), 143.3 (C7'), 146.7 (C7), 154.0 (C4'), 154.1 (C8a'), 161.0 (C2'); MS = 378.5 (M+H); Anal. Calcd. for $C_{23}H_{23}NO_4$ (377.43): C, 73.19; H, 6.14; N, 3.71%. Found: C, 73.03; H, 6.19; N, 3.57%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-7-methoxy-2H-pyrano[3,2-c]quinoline (12a')

Yellow Solid; 38 mg, 10%; mp 163-165 ^{o}C; FT-IR (neat): 3416 (NH), 2923 and 2855 (aliphatic C-H), 1713 (C=O); 1620, 1556 and 1503 (aromatic C=C); 1299, 1266, 1187, 1134, 1085, 865, 822 cm^{-1}; ^{1}H NMR ((500 MHz, CDCl3): δ 1.57-1.60 (m, 1H, C3a-H), 1.72-1.82 (m, 3H, C3b-H and C4-H), 2.49 (bs, 1H, C4a-H), 2.54 (s, 3H, CH_3), 3.76 (td, 1H, C2a-H, *J* = 2.5 and 10.5 Hz), 3.90 (s, 3H, OCH_3), 4.00 (bd, 1H, C2b-H), 4.25 (bs, 1H, NH), 4.62 (d, 1H, C5-H, *J* = 3.5 Hz), 4.97 (d, 1H, C10b-H, *J* = 8 Hz), 6.54 (s, 1H, C3'-H), 6.80-6.84 (m, 2H, C8-H and C10-H), 7.02 (t, 1H, C9-H, *J* = 8 Hz), 7.18 (d, 1H, C6'-H, *J* = 8 Hz), 7.28 (s, 1H, C8'-H), 7.88 (bs, 1H, C5'-H); MS = 378.6 (M+H); Anal. Calcd. for $C_{23}H_{23}NO_4$ (377.43): C, 73.19; H, 6.14; N, 3.71%. Found: C, 73.09; H, 6.22; N, 3.63%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-methyl-2H-pyrano[3,2-c]quinoline (13a)

Yellow solid; 163 mg, 45%; mp 184-186 ^{o}C; FT-IR (neat): 3370 (NH), 2926 (aliphatic C-H), 1728 (C=O); 1617, 1585 and 1554 (aromatic C=C); 1487, 1326, 1244, 1179, 1135, 1089, 861, 744 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.43 (bd, 1H, C4-H), 1.55-1.66 (m, 3H, C3-H and C4b-H), 2.37 (s, 3H, CH_3), 2.46-2.49 (m, 1H, C4a-H), 2.55 (s, 3H, CH_3), 3.52 (td, 1H, C2a-H, *J* = 2.5 and 10.5 Hz), 3.68 (m, 2H, C2b-H and NH), 5.07 (s, 1H, C5-H), 5.46 (d, 1H, C10b-H, *J* = 5.5 Hz), 6.69 (d 1H, C7-H, *J* = 8 Hz), 6.80 (s, 1H, C3'-H), 7.03 (d, 1H, C8-H, *J* = 8 Hz), 7.21 (d, 1H, C6'-H, *J* = 8 Hz), 7.28 (s, 1H, C10-H), 7.35 (s, 1H, C8'-H), 7.53 (d, 1H, C5'-H, *J* = 8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 18.5 (C3), 20.7 (CH_3), 21.6 (CH_3), 25.27 (C4), 35.9 (C4a), 54.5 (C5), 60.6 (C2), 72.3 (C10b), 112.3 (C3'), 115.0 (C4a'), 115.4 (C8'), 117.9 (C7), 119.9 (C10a), 122.9 (C8), 125.7 (C10), 127.8 (C6'), 128.7 (C6a'), 129.1 (C5'), 141.8 (C9), 143.3 (C7'), 154.0 (C4'), 154.1 (C8a'), 161.0 (C2'); MS = 362.5 (M+H). Anal. Calcd. for $C_{23}H_{23}NO_3$ (361.43): C, 76.43; H, 6.41; N, 3.88%. Found: C, 76.58; H, 6.62; N, 3.92%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-methyl-2H-pyrano[3,2-c]quinoline (13a')

White Solid; 127 mg, 35%; mp 234 - 235 ^{o}C; FT-IR (neat): 3408 (NH), 3062 (aromatic C-H), 1710 (C=O); 1620, 1586, 1557 and 1499 (aromatic C=C); 1447, 1313, 1244, 1141, 1082, 822, 749 cm^{-1}; ^{1}H NMR ((500 MHz, $CDCl_3$): δ 1.53-1.58 (m, 1H, C3a-H), 1.70-1.88 (m, 3H, C3b-H and C4-H), 2.35 (s, 3H, CH_3), 2.47 (bs, 1H, C4a-H), 2.54 (s, 3H, CH_3) 3.77 (td, 1H, C2a-H, *J* = 2.5 and 10.5 Hz), 4.05 (bd, 1H, C2b-H), 4.52 (bs, 1H, NH), 4.54 (d, 1H, C5-H, *J* = 3 Hz), 4.97 (d, 1H, C10b-H, *J* = 8.5 Hz), 6.55 (s, 1H, C3'-H), 6.61 (d, 1H, C7-H, *J* = 8.0), 7.04 (d, 1H, C8-H, *J* = 8.0 Hz), 7.16-7.18 (m, 2H, C10-H and C6'-H), 7.27 (s, 1H, C8'-H), 7.93 (bs, 1H, C5'-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7 (2xCH_3), 23.1 (C3), 24.5 (C4), 36.6 (C4a), 55.6 (C5), 60.1 (C2), 72.1 (C10b), 109.3 (C3'), 113.8 (C8'), 115.5 (C4a'), 117.3 (C7), 117.8 (C8), 119.4 (C10a), 121.6 (C10), 124.7 (C6'), 125.5 (C5'), 133.3 (C6a), 143.3 (C7'), 146.0 (C9), 154.3 (C4'), 156.2 (C8a'), 161.2 (C2'); MS = 362.5 (M+H); Anal. Calcd. for $C_{23}H_{23}NO_3$ (361.43): C, 76.43; H, 6.41; N, 3.88%. Found: C, 76.63; H, 6.33; N, 3.75%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-bromo-2H-pyrano[3,2-c]quinoline (14a)

White solid; 186 mg, 43%; mp 215-217 ^{o}C; FT-IR (KBr): 3345 (NH), 2923 and 2854 (aliphatic C-H), 1699 (C=O); 1615, 1599 and 1500 (aromatic C=C); 1322, 1265, 1087, 1039, 871, 810 cm^{-1}; ^{1}H NMR ((300 MHz, $CDCl_3$): δ 1.25-1.65 (m, 4H, C3-H and C4-H), 2.39-2.41 (bd, 1H, C4a-H), 2.46 (s, 3H, CH_3), 3.41 (td, 1H, C2a-H, *J* = 2.5 and 10.0 Hz), 3.60 (dd, 1H, C2b-H, *J* = 2.5 and 10.0 Hz), 3.89 (s, 1H, NH), 5.00 (s, 1H, C5-H), 5.34 (d, 1H, C10b-H, *J* = 5.7 Hz), 6.59 (d, 1H, C7-H, *J* = 8.4 Hz), 6.66 (s, 1H, C3'-H), 7.13 (d, 1H, C6'-H, *J* = 8 Hz), 7.17 (s, 1H, C8'-H) 7.20 (dd, 1H, C8-H, *J* = 2.4 and 8 Hz), 7.43 (d, 1H, C5'-H, *J* = 8 Hz), 7.54 (d, 1H, C10-H, *J* = 2.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.6 (C3), 21.6 (CH_3), 25.1 (C4), 35.3 (C4a), 54.3 (C5), 60.8 (C2), 71.5 (C10b), 111.4 (C4a'), 112.2 (C3'), 114.8 (C9), 117.0 (C8'), 118.0 (C7'), 122.2 (C10a), 122.9 (C6'), 125.8 (C5'), 130.2 (C8), 131.3 (C10), 143.3 (C6a), 143.6 (C7'), 153.7 (C4'), 154.0 (C8a'), 160.8 (C2'); MS = 427.4 (M+H). Anal. Calcd. for $C_{22}H_{20}BrNO_3$ (426.30): C, 61.98; H, 4.73; N, 3.29%. Found: C, 61.89; H, 4.80; N, 3.43%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-bromo-2H-pyrano[3,2-c]quinoline (14a')

White solid; 144 mg, 34%; mp 275-276 ^{o}C; FT-IR (KBr): 3369 (NH), 2952 and 2869 (aliphatic C-H), 1711 (C=O); 1617, 1600, 1513 and 1484 (aromatic C=C); 1303, 1271, 1133, 1087, 806 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49-1.86 (m, 4H, C3-H and C4-H), 2.35 (bs, 1H, C4a-H), 2.45 (s, 3H, CH_3), 3.63-3.70 (m,

1H, C2a-H), 3.85-3.89 (m, 1H, C2b-H), 4.27 (s, 1H, NH), 4.46 (d, 1H, C5-H, *J* = 3.6 Hz), 4.83 (d, 1H, C10b-H, *J* = 8 Hz), 6.38 (s, 1H, C3'-H), 6.54 (d, 1H, C7-H, *J* = 8.4), 7.10 (d, 1H, C6'-H), 7.16 (s, 1H, C8'-H), 7.23 (dd, 1H, C8-H, 2.1 and 8.7 Hz), 7.40 (d, 1H, C10-H, *J* = 2.1 Hz), 7.70 (d, 1H, C5'-H, *J* = 8.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 21.7 (CH_3), 23.8 (C3), 24.3 (C4), 36.1 (C4a), 55.6 (C5), 60.7 (C2), 71.5 (C10b), 109.9 (C4a'), 113.7 (C3'), 115.2 (C9), 115.8 (C8'), 117.9 (C7'), 121.3 (C10a), 124.2 (C6'), 125.6 (C5'), 132.1 (C8), 132.3 (C10), 142.2 (C6a), 143.5 (C7'), 154.2 (C4'), 155.6 (C8a'), 161.0 (C2'); MS = 427.4 (M+H); Anal. Calcd. for $C_{22}H_{20}BrNO_3$ (426.30): C, 61.98; H, 4.73; N, 3.29%. Found: C, 61.87; H, 4.76; N, 3.44%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-nitro-2H-pyrano[3,2-c]quinoline (15a)

Yellow solid; 142 mg, 36%; mp 303-305 °C; FT-IR (neat): 3302 (NH), 2933 and 2889 (aliphatic C-H), 1702 (C=O); 1612, 1587 and 1497 (aromatic C=C); 1552 and 1365 (NO_2), 1316, 1267, 1132, 1089, 822, 748 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO): δ 1.25-1.53 (m, 4H, C3-H and C4-H), 2.48 (s, 3H, CH_3), 2.59 (bt, 1H, C4a-H, merged in DMSO), 2.89 (bs, 1H, NH, merged in shifted DMSO water), 3.41 (td, 1H, C2a-H, *J* = 2.5 and 10.5 Hz), 3.65 (dd, 1H, C2b-H, *J* = 2.5 and 10.5 Hz), 5.18 (s, 1H, C5-H), 5.38 (d, 1H, C10b-H, *J* = 5.7 Hz), 6.61 (s, 1H, C3'-H), 6.86 (d, 1H, C7-H, *J* = 9.3 Hz), 7.18 (d, 1H, C6'-H, *J* = 8 Hz), 7.20 (s, 1H, C8'-H) 7.54 (d, 1H, C5'-H, *J* = 8 Hz), 7.96 (dd, 1H, C8-H, *J* = 2.7 and 9.3 Hz), 8.26 (d, 1H, C10-H, *J* = 2.4 Hz). MS = 393.3 (M+H); Anal. Calcd. for $C_{22}H_{20}N_2O_5$ (392.40): C, 67.34; H, 5.14; N, 7.14%. Found: C, 67.47; H, 5.08; N, 7.06%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-10-nitro-2H-pyrano[3,2-c]quinoline (16a)

Yellow solid; 177 mg, 45%; mp 270-272 °C; FT-IR (neat): 3419 (NH), 3066 (aromatic C-H), 2953 and 2865 (aliphatic C-H), 1715 (C=O); 1612, 1528 and 1484 (aromatic C=C); 1577 and 1377 (NO2), 1334, 1271, 1136, 1079, 798, 723 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25-1.58 (m, 4H, C3-H and C4-H), 2.42-2.47 (m, 4H, CH_3 and C4a-H), 3.09-3.14 (m, 1H, C2a-H), 3.57 (d, 1H, C2b-H, *J* = 10.5 Hz), 4.19 (s, 1H, NH), 5.02 (s, 1H, C5-H), 5.70 (d, 1H, C10b-H, *J* = 6.0 Hz), 6.63 (s, 1H, C3'-H), 6.88 (d, 1H, C7-H, *J* = 8.4 Hz), 6.98 (d, 1H, C9-H, *J* = 7.8 Hz) 7.15-7.44 (m, 4H, C8-H, C6'-H, C8'-H and C5'-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.7 (C3), 20.8 (CH3), 23.8 (C4), 33.7 (C4a), 53.0 (C5), 60.9 (C2), 68.6 (C10b), 111.4 (C4), 111.7 (C3'), 111.8 (C8'), 114.0 (C4a'), 116.9 (C7), 117.7 (C8), 122.5, 125.1, 128.0 (C9), 142.7 (C7'), 146.5 (C6a), 150.5 (C10), 152.4 (C8a'), 153.1 (C4'), 160.0 (C2'); MS = 393.3 (M+H); Anal. Calcd. for $C_{22}H_{20}N_2O_5$ (392.40): C, 67.34; H, 5.14; N, 7.14%. Found: C, 67.22; H, 5.02; N, 7.00%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-10-nitro-2H-pyrano[3,2-c]quinoline (16a')

Brown solid;79 mg, 20%; mp 178-180 °C; FT-IR (neat): 3351 (NH), 2955 and 2859 (aliphatic C-H), 1713 (C=O); 1617, 1589 and 1496 (aromatic C=C); 1528 and 1361 (NO_2), 1319, 1270, 1134, 1079, 824, 720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.4-1.9 (m, 4H, C3-H and C4-H), 2.46-2.47 (m, 4H, CH_3 and C4a-H), 3.64-3.99 (m, 2H, C2a-H and C2b-H), 4.46 (bs, 1H, NH), 4.58 (d, 1H, C5-H, *J* = 3.6 Hz), 5.13 (d, 1H, C10b-H, *J* = 8 Hz), 6.37 (s, 1H, C3'-H), 6.80 (t, 1H, C8-H, *J* = 8.0), 7.13 (d, 1H, C6'-H, *J* = 8.1 Hz), 7.22 (m, 2H, C7-H and C8'-H, *J* = 2.1 and 9 Hz), 7.60 (dd, 1H, C9-H, 2.1 and 8.0 Hz), 7.64 (d, 1H, C5'-H, *J* = 8.1 Hz); MS = 393.5 (M+H); Anal. Calcd. for $C_{22}H_{20}N_2O_5$ (392.40): C, 67.34; H, 5.14; N, 7.14%. Found: C, 67.17; H, 5.10; N, 7.23%.

4aR*, 5R*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-methoxy-2H-pyrano[3,2-c]quinoline (17a)

Yellow solid; 177 mg, 47%; mp 232-234 °C; FT-IR (KBr): 3344 (NH), 2945 (aliphatic C-H), 1711 (C=O); 1619, 1550 and 1501 (aromatic C=C); 1443, 1320, 1262, 1232, 1147, 1067, 862, 817 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48-1.83 (m, 4H, C3-H and C4-H), 2.38-2.39 (bd, 1H, C4a-H), 2.45 (s, 3H, CH_3), 3.64-3.72 (m, 1H, C2a-H), 3.77 (s, 3H, OCH_3), 3.92 (m, 2H, NH, C2b-H), 4.48 (d, 1H, C5-H, *J* = 3.6 Hz), 4.85 (d, 1H, C10b-H, *J* = 8 Hz), 6.46 (s, 1H, C3'-H), 6.56 (d, 1H, C7-H, *J* = 8.4), 6.77 (dd, 1H, C8-H, *J* = 2.7 and 8.4 Hz), 6.87 (d, 1H, C10-H, *J* = 2.7 Hz), 7.09 (d, 1H, C6'-H, *J* = 8 Hz), 7.19 (s, 1H, C8'-H), 7.81 (d, 1H, C5'-H, *J* = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.5 (C3), 21.6 (CH_3), 25.2 (C4), 35.8 (C4a), 54.6 (OCH_3), 55.9 (C5), 60.8 (C2), 72.4 (C10b), 111.8 (C3), 112.3 (C8), 115.0 (C4a'), 115.4 (C9), 116.6 (C7'), 117.9 (C8'), 121.2 (C10a), 122.9 (C6'), 125.6 (C5'), 138.1 (C6a), 143.3 (C7'), 153.5 (C9), 154.0 (C4'), 154.2 (C8a'), 161.0 (C2'); MS = 378.4 (M+H); Anal. Calcd. for $C_{23}H_{23}NO_4$ (377.43): C, 73.19; H, 6.14; N, 3.71%. Found: C, 73.34; H, 6.21; N, 3.66%.

4aR*, 5S*, 10bR*-5-(7-methylcoumarin-4-yl)-3,4,4a,5,6,10b-hexahydro-9-methoxy-2H-pyrano[3,2-c]quinoline (17a')

Greenish yellow solid; mp 180-181 °C; FT-IR (KBr): 3329 (NH), 2970 (aliphatic C-H), 125 mg, 33%; 1712 (C=O); 1611, and 1501 (aromatic C=C); 1442, 1366, 1230, 1218, 1158, 1077, 1038, 921, 821 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34-1.60 (m, 4H, C3-H and C4-H), 2.39 (bs, 1H, C4a-H) 2.46 (s, 3H, CH_3) 3.42 (td, 1H, C2a-H), 3.53 (s, 1H, NH) 3.61 (dd, 1H, C2b-H), 3.79 (s, 3H, OCH_3) 4.96 (s, 1H, C5-H), 5.38 (d, 1H, C10b-H, *J* = 5.5 Hz), 6.64 (d 1H, C7-H, *J* = 9.0 Hz), 6.73 (s, 1H, C3'-H), 6.76 (dd, 1H, C8-H, *J* = 2.7 and 8 Hz), 7.03 (d, 1H, C10-H), 7.13 (d, 1H, C6'-H, *J* = 8 Hz), 7.19 (s, 1H, C8'-H), 7.45 (d, 1H, C5'-H, *J* = 8 Hz); MS = 378.6 (M+H); Anal. Calcd. for $C_{23}H_{23}NO_4$ (377.43): C, 73.19; H, 6.14; N, 3.71%. Found: C, 73.29; H, 6.23; N, 3.79%.

3a, 4, 9b (all cis)-4-(7-methylcoumarin-4-yl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-c]quinoline (20a)

White Solid; 100 mg, 30%; mp 284-285 °C; FT-IR (KBr): 3365 (NH), 3062 (aromatic C-H), 2962 and 2871 (aliphatic C-H), 1714 (C=O); 1608, 1591 and 1485 (aromatic C=C); 1362, 1261, 1187, 1151, 872, 829, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76-1.83 (m, 1H, C3a-H) 2.1-2.25 (m, 1H, C3b-H), 2.46 (s, 3H, CH_3), 2.64-2.74 (bm, 1H, C3a-H), 3. 87 (m, 1H, C2a-H), 4.03 (m, 1H, C2b-H), 4.17 (bs, 1H, NH), 4.23 (d, 1H, C4-H, *J* = 10.2 Hz), 4.65 (d, 1H, C9a-H, *J* = 5.7 Hz), 6.55 (s, 1H, C3'-H), 6.67 (d, 1H, C6-H, *J* = 7.5 Hz), 6.87 (t, 1H, C8-H, *J* = 2 and 8 Hz), 7.10 (d, 1H, C6'-H, *J* = 8.1 Hz), 7.17 (dd, 1H, C7-H, *J* = 8), 7.21 (s, 1H, C8'-H), 7.42 (d, 1H, C9-H, *J* = 7.8 Hz), 7.85 (d, 1H, C5'-H, *J* = 7.8 Hz); MS = 334.5 (M+H); Anal. Calcd. for $C_{21}H_{19}NO_3$ (333.38): C, 75.66; H, 5.74; N, 4.20%. Found: C, 75.78; H, 5.85; N, 4.12%.

2,4(cis)-2-(7-methylcoumarin-4-yl)-1,2,3,4-tetrahydro-4-phenylquinoline (21a)

Pale yellow solid; 176 mg, 48%; mp 195-196 ^{o}C; FT-IR (neat): 3328 (NH), 2962 and 2863 (aliphatic C-H), 1703 (C=O); 1615, 1555 and 1486 (aromatic C=C); 1321, 1255, 1186, 1061, 867, 772, 701, 755 cm^{-1}; ^{1}H NMR (400 MHz, DMSO): δ 1.96-2.02 (m, 1H, C3a-H) 2.39 (d, 1H, C3b-H, *J* = 12 Hz), 2.41 (s, 3H, CH_3), 4.44 (dd, 1H, C4-H, *J* = 5 and 12 Hz), 5.08 (d, 1H, C2-H, *J* = 8.8 Hz), 6.17 (s, 1H, C3'-H), 6.39-6.47 (m, 2H, C6-H and C8-H, *J* = 8 Hz), 6.58 (s, 1H, C8'-H) 6.74 (d, 1H, C5-H, *J* = 7.8 Hz), 6.95 (t, 1H, PhH, *J* = 7 Hz), 7.19-7.33 (m, 6H, C6'-H, C7-H, 4PhH), 7.92 (d, 1H, C5'-H, *J* = 8.3 Hz); MS = 368.3 (M+H). Anal. Calcd. for $C_{25}H_{21}NO_2$ (367.44): C, 81.72; H, 5.76; N, 3.81%. Found: C, 81.64; H, 5.85; N, 3.74%.

2,4 (trans)-2-(7-methylcoumarin-4-yl)-1,2,3,4-tetrahydro-4-phenylquinoline (21a')

Greenish yellow solid; 119 mg, 32%; mp 226-228 ^{o}C; FT-IR (neat): 3366 (NH), 3025 (aromatic C-H), 2871 (aliphatic C-H), 1714 (C=O); 1615, 1554 and 1503 (aromatic C=C); 1321, 1259, 1186, 1146, 870, 755 cm^{-1}; ^{1}H NMR (400 MHz, DMSO): δ 1.83-1.90 (bs, 1H, C3a-H) 2.35 (bs, 1H, C3b-H), 2.40 (s, 3H, CH_3), 4.35-4.43 (m, 1H, C4-H), 5. 04 (bs, 1H, NH), 5.39-5-41 (m, 1H, C2-H), 6.54 (s, 1H, C3'-H), 6.67-6.69 (m, 2H, ArH), 6.95-7.22 (m, 9H, ArH), 7.90 (d, 1H, C5'-H, *J* = 8.0 Hz); MS = 368.4 (M+H); Anal. Anal. Calcd. for $C_{25}H_{21}NO_2$ (367.44): C, 81.59; H, 5.76; N, 3.81%. Found: C, 81.59; H, 5.82; N, 3.75%.

Conclusions

In conclusion, the reaction of 7-methylcoumarin-4-carbaldehyde with substituted anilines gives 7-methylcoumarin-4-azadienes (**1**). These azadienes provide two azadiene components, one involving coumarin 3,4-double bond (N) and the other involving the aniline ring (M). The two dienes differ markedly in reactivity. Compound **1** does not undergo normal electron demand Diels-Alder reaction similar to 4-styrylcoumarin. It undergoes regiospecific inverse electron demand Diels-Alder reaction involving diene M, with dienophiles dihydropyran, dihydrofuran, and styrene. The reaction requires a Lewis acid catalyst and the $ZnCl_2$ is the best catalyst. The solvent has profound effect on the reaction; 1,2- dichloroethane is the best solvent. In the reaction unequal amounts of two diastereomeric products are formed. The reaction provides an entry into coumarinyl substituted pyranoquinolines.

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Notes and references

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