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Thermal [4 + 2] Cycloadditions of 3-Acetyl-, 3-Carbamoyl-, and 3-Ethoxycarbonyl-Coumarins with 2,3-Dimethyl-1,3-butadiene under Solventless Conditions: A Structural Study

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Abstract: The thermal [4+2] cycloadditions of 3-acetyl-, 3-carbamoyl, and 3-ethoxycarbonylcoumarins with 2,3-dimethyl-1,3-butadiene under solvent free conditions are reported, as well as the epoxidation reactions of some adducts. Discussion is focused on the structural features of the Diels-Alder adducts and their epoxides, based upon NMR, X-ray, and mass spectral data, and supported by *ab initio* theoretical calculations.

Keywords: coumarins; Diels-Alder adducts; solventless reactions; 6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-6-oxo-6H-5,8-dioxacyclopropa[b]phenantrenes

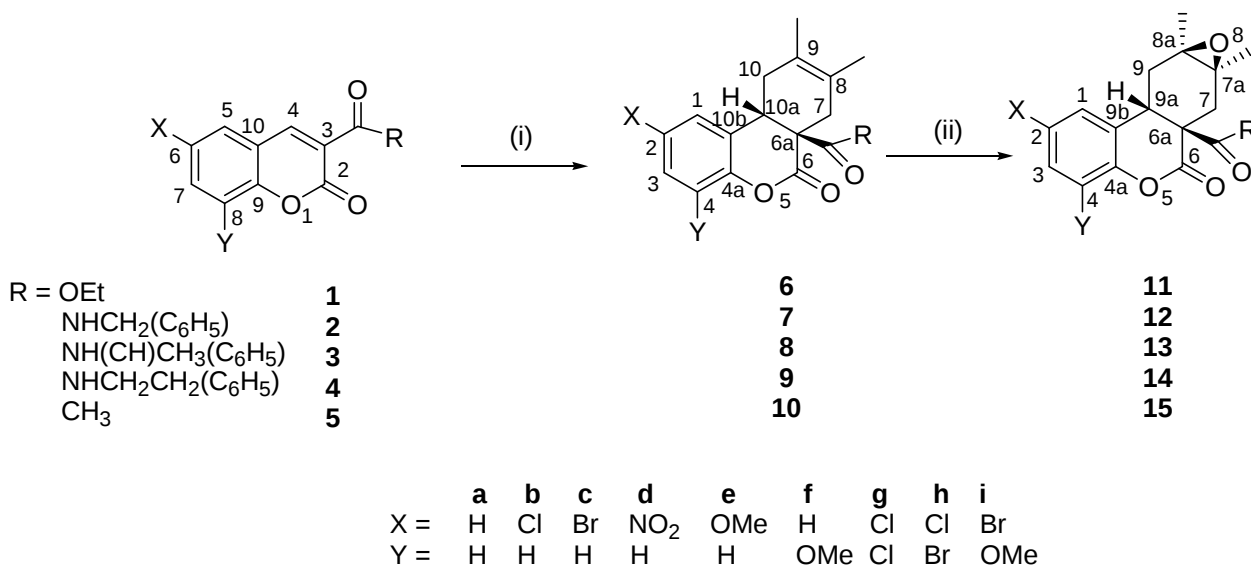
1. Introduction

Coumarins are widely known to undergo pericyclic reactions like photodimerization [1]. On this topic and in the context of crystal engineering, our group has reported the solid state photodimerization of ethyl coumarin-3-carboxylate (**1a**) and its 6-Cl and 6-Br derivatives **1b** and **1c** [2]. In contrast, the use of coumarins as 2π components in Diels-Alder (DA) cycloadditions has been less studied due to

their low reactivity in these reactions. Only 3-substituted coumarins with electron-withdrawing groups like COOEt [3], NO₂ [4], SO₂Ph, or heterocyclic rings [5], and very recently with CN [6], have been reported to undergo DA reactions under high pressure conditions.

The DA reaction of **1a** with 2,3-dimethyl-1,3-butadiene was realized in water alone and in CH₂Cl₂ under 9 kbar pressure [5]. The use of HfCl₄·2THF as catalyst, and solvent free conditions (SFC) significantly improve selectivity and yields [7]. However, independent results, obtained from our group, indicate that this reaction can be performed without catalyst under SFC [8]. Thus, in this work the synthesis of the (6*aR*,10*aR*)-rel-6*a*,7,10,10*a*-tetrahydro-8,9-dimethyl-6-oxodibenzo[*b,d*]pyran derivatives **6–10** from the DA reaction of 3-acetyl-, 3-carbamoyl-, and 3-ethoxycarbonyl-coumarins **1–5** with 2,3-dimethyl-1,3-butadiene under SFC as well as the synthesis of some of their epoxides **11–15** is reported (Scheme 1). The molecular structure of the compounds obtained is discussed on the basis of their NMR and X-ray data.

Scheme 1. Synthesis scheme and numbering.



(i) 2,3-Dimethyl-1,3-butadiene under SFC; (ii) *m*-Chloroperbenzoic acid in CHCl₃

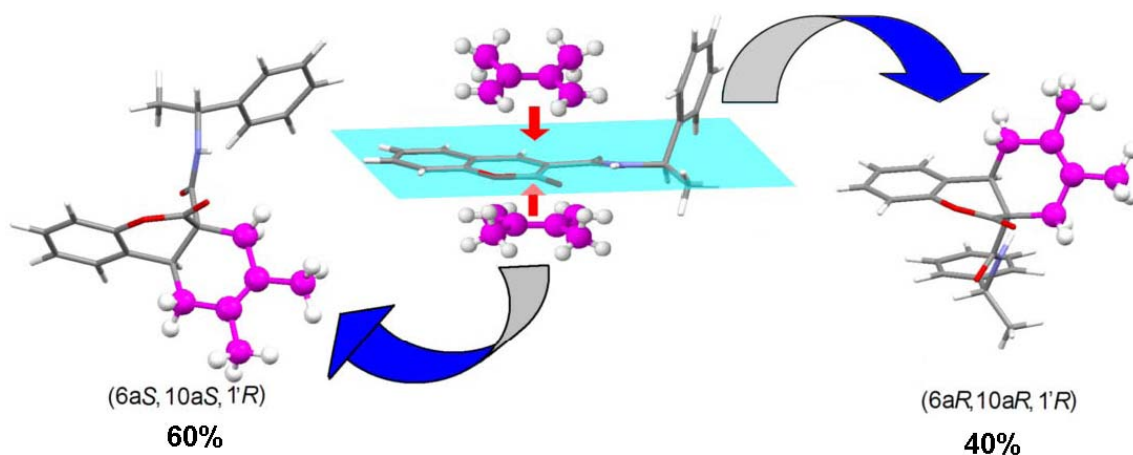
2. Results and Discussion

The synthesis of the cycloadducts was performed, starting from coumarins **1–5**, in a sealed glass ampoule with an excess of the diene (6 equivalents) at 160 °C, to give the corresponding DA cycloadducts **6–10**, in moderate to good yields (60–85%). The isolated yield of the adduct **6a** (80%), after purification by column chromatography, is lower than that reported in CH₂Cl₂ at high pressure [5] or under SFC in the presence of catalysts [7], but higher than that reported in water at 150 °C (58%) [5]. The cycloadduct **7a** was obtained in 85% yield, which is higher than the reported value (76%) using toluene as solvent [7].

In all cases racemic mixtures of the *cis* fused rings were formed, except in the case of **8a** which was synthesized using enantiopure (*R*)-1-phenylethylamine to generate coumarin **3a**. Thus, it is assumed that **8a** was obtained as a 60:40 mixture of (6*aS*,10*aS*,1'*R*) and (6*aR*,10*aR*,1'*R*) diastereomers, respectively. For this mixture, two sets of signals in the ¹H-NMR spectrum are clearly observed at δ

5.89, 1.21 (major) and 5.82, 1.37 (minor). They are doublets assigned to the NH and CH₃ protons of the amide moiety, respectively. In the former set, the signal for the CH₃ protons appears shielded because of the effect exerted by the coumarin aromatic ring diamagnetic currents. The *ab initio* calculated molecular geometry of (6a*S*,10a*S*,1'*R*) and (6a*R*,10a*R*,1'*R*) diastereomers predicts that the CH₃ protons, in the former, are in the appropriate position to be shielded by diamagnetic currents of the aromatic ring, with 1.24 kcal mol⁻¹ in favour of the (6a*S*,10a*S*,1'*R*) diastereomer. These results are in agreement with the preference of the diene approach to the less hindered face of the starting coumarin **3a** (Figure 1). However, the asymmetric induction of the chiral amine pendant group is poor in comparison with the results obtained for bulkier 3-alkoxides [10], because of its relatively long distance from the reactive double bond.

Figure 1. Calculated molecular structures of the (6a*S*,10a*S*,1'*R*) and (6a*R*,10a*R*,1'*R*) diastereomers of the cycloadduct **8a**. In the former (left) the methyl protons of the chiral amine residue lie in the shielding cone of the coumarin benzenoid ring.



In order to test the stereofacial selectivity of the addition reaction on the cyclohexene ring, the epoxidation of compounds **6a–10a** and **10d,f,i** with *m*-chloroperbenzoic acid (*m*-CPBA) was performed. The reaction proceeded in moderate 70–80% (**11a–15a**) to very good yields 90–96% (**15d,f,i**). The X-ray data (*vide infra*) show that the oxygen atom is stereoselectively added to the less hindered face of the cyclohexene ring, opposite to the benzopyrone ring. Therefore, the racemic mixture (6a*R*,7a*R*,8a*S*,9a*R*) and (6a*S*,7a*S*, 8a*R*,9a*S*) is formed except in the case of compound **13a**, which was obtained as a 60:40 mixture of diastereomers because of the presence of the amine moiety stereocentre. Thus, the original diastereomeric ratio of the starting adduct **8a** is preserved (*vide supra*).

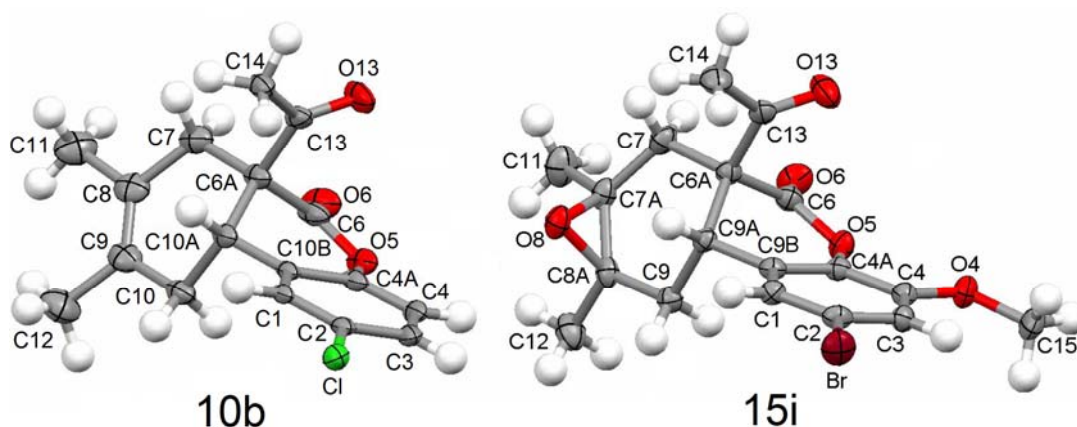
The molecular structure in solution was analyzed by ¹H- and ¹³C-NMR, the numbering scheme is given in Figure 1. Several differences in the ¹H-NMR spectra appear as a consequence of the cycloaddition. The H-4 signal in coumarins **1–5** usually appears as a singlet between 8.0 and 8.4 ppm [11], whereas in the cycloadducts **6–10** it becomes H-10a and appears as a doublet of doublets, by coupling with H₂-10, in the range 3.36–3.65 ppm. Irradiation of H-10a signal gave NOEs with H-1, H_{eq}-10, and alkyl protons of the R group, confirming the *cis* fusion between dihydropyrone and cyclohexene rings. Besides NOE experiments, the assignments of all ¹H signals were achieved through COSY experiments. The mean values of the coupling constants of H-10a with H_{ax}-10 (11.0–12.6 Hz)

and H_{eq} -10 (5.0–6.5 Hz), suggest a pseudo axial-axial and pseudo axial-equatorial relationship, respectively, and thus an anchored conformation for the cyclohexene ring. The nature of the carbonyl group at the 6a position exerts influence on the chemical shift of H-10a: for COOEt and COMe, H-10a appears in the range of 3.36–3.47 ppm whereas for CONHR it appears more deshielded, in the range 3.58–3.65 ppm, due to the effect of the amide mesomerism. The chemical shift of H_{ax} -7 in the acetylated adducts **10** appears at higher field (2.04–2.38 ppm) than in the carbamoyl and ethoxycarbonyl adducts **6a–8a** (2.47–2.50 ppm). This trend could be explained by a *syn* or *anti* conformational preference of the 3-CO with respect to the lactone carbonyl moiety. In compounds **6a–8a** the most populated conformer on the 1H -NMR time scale is the *anti* one with the 3-CO group appropriately positioned to exert a deshielding effect on H_{ax} -7, whereas the *syn* conformer is the predominant form in adducts **10a–i**. The chemical shift of H_{ax} -7, in the adduct **9a**, is out of range (δ 2.30) because of the protective effect exerted by the phenyl ring of the 2-phenylethyl amine residue. Finally, the chemical shift of H_{eq} -7 is in the range of 2.78 to 2.91 ppm, due to the deshielding effect of the dihydropyrone carbonyl moiety.

The change in the hybridization of C-3 and C-4 from sp^2 in coumarins **1–5** to sp^3 character in adducts **6–10** shifts the corresponding carbon atoms C-6a and C-10a, to lower frequencies, from 118–125 to 54–61 and from 147–149 to 36–37 ppm, respectively. The nature of the 3-substituent influences the chemical shift of the carbon atom carrying the substituent: thus C-6a appears in the range of 54–55 ppm for amide and ester adducts **6a–9a** and at 60–61 ppm for the acetylated adducts **10a–i**. The difference in chemical shifts is preserved from the starting coumarins: C-3 resonates at 118–120 ppm in compounds **1a–4a**⁹ and at 124–125 ppm in **5a–i**.

Epoxidation changes the hybridization of C-8 and C-9 atoms from sp^2 in the cycloadducts **6–10** to sp^3 character in epoxides **11a–15a** and **15d,f,i**, shifting the corresponding C-7a and C-8a carbon atoms approximately by 62 ppm to lower frequencies. Subtle changes are also observed in the 1H -NMR spectra: the oxirane methyl protons, H_{ax} -7, and H_{ax} -9 (these last H_{ax} -10 before the epoxidation) are shifted to low frequencies by approximately 0.3 ppm, owing to the effect of the steric compression exerted by the new formed three-membered ring.

Figure 2. Molecular structure of cycloadduct **10b** and **15i**. Thermal ellipsoids drawn at the 50% probability level.



The molecular structures of cycloadduct **10b** and epoxide **15i**, obtained by X-ray diffraction, are shown in Figure 2. Selected bond lengths and angles are listed in Table 1. In consequence of the transformation of C3—C4 double bond in coumarins to the single bond C6a—C10a in the adducts, this bond length enlarges by 0.18(2) Å, from 1.359(2) in **5a** [12] to 1.538(3) in **10b**. Epoxidation of adducts also changes the hybridization of C8 and C9 atoms enlarging C8—C9 bond length by 0.13(1) Å, in agreement with their new sp^3 character, from 1.331(3) in **10b** to 1.462(7) in **15i** (C7A—C8A), respectively.

Table 1. Selected bond lengths and angles from X-ray data of compounds **10b** and **15i**.

Atoms	10b (X = Cl)	15i (X = Br)
Bond lengths/Å		
O(5)C(6)	1.373(3)	1.364(6)
O(6)C(6)	1.190(3)	1.195(6)
C(6)C(6A)	1.526(3)	1.522(7)
C(6A)C(7)	1.536(3)	1.541(6)
C(6A)C(10A)	1.538(3)	1.551(6)
C(6A)C(13)	1.537(3)	1.527(6)
C(7)C(8)	1.509(3)	
C(7)C(7A)		1.501(7)
C(8)C(9)	1.331(3)	
C(7A)C(8A)		1.462(7)
C(9)C(10)	1.500(3)	
C(8A)C(9)		1.505(6)
C(10)C(10A)	1.530(3)	
C(9)C(9A)		1.523(6)
XC(2) ^a	1.742(2)	1.900(5)
Bond angles/°		
C(4A)O(5)C(6)	120.94(16)	120.2(4)
C(6A)C(7)C(8)	115.64(18)	117.2(4)
C(9)C(10)C(10A)	112.61(18)	
C(8A)C(9)C(9A)		113.7(4)
O(13)C(13)C(6A)	120.30(19)	121.1(5)
XC(2)C(1) ^a	119.68(15)	119.1(4)
Torsion angles/°		
C(6)O(5)C(4A)C(10B)	20.4(3)	23.2(6)
C(7)C(6A)C(6)O(5)	166.50(17)	163.0(4)
O(5)C(6)C(6A)C(13)	74.9(2)	77.6(5)
C(6)C(6A)C(13)O(13)	15.2(3)	2.6(6)
O(13)C(13)C(6A)C(7)	104.8(2)	116.7(5)
O(8)C(9)C(10)C(10A)	23.4(3)	
O(8)C(8A)C(9)C(9A)		-42.6(5)
C(10A)C(10B)C(4A)O(5)	-3.2(3)	
C(9A)C(9B)C(4A)O(5)		-1.6(7)
C(7)C(8)C(9)C(10)	0.4(3)	
C(7)C(7A)C(8A)C(9)		0.9(7)
C(9B)C(1)C(2)X	179.04(13)	177.9(3)

The X-ray structures of compounds **10b** and **15i** show that the CO of the acetyl group is pointing towards the lactone ring [C(7)C(6A)C(13)O(13) torsion angles of $-104.8(2)$, and $-116.7(5)^\circ$ for **10b** and **15i**, respectively. Thus, the *syn* conformation between both carbonyls is the preferred in the solid state, the same conformational preference being observed in solution by NMR (*vide supra*). The torsion angles C(10A)C(10B)C(4A)O(5) (**10b**) and C(9A)C(9B)C(4A)O(5) (**15i**) in dihydropyrene ring, and C(7)C(8)C(9)C(10) (**10b**) and C(7)C(7A)C(8A)C(9) (**15i**) in cyclohexene ring, take values near to zero, in agreement with a distorted twisted boat conformation for both rings. Epoxydation has a negligible influence on the conformation of the cyclohexane ring as observed in compound **15i**.

The supramolecular structure of DA adduct **10b** and epoxide **15i** is organized by weak $\text{CH}\cdots\text{A}$ ($\text{A} = \text{O}, \pi$) interactions. Nevertheless, they are scarce in comparison with those encountered in the crystal packing of the starting coumarins [12]. Thus, compound **15i** is worthy to mention, since its crystal network is organized by several $\text{CH}\cdots\text{O}$ and $\text{Br}\cdots\text{Br}$ polarization-induced interactions, in the *bc* plane [Figure 3(a)], and $\text{CH}\cdots\pi$ bifacial contacts developing the third dimension along the (7 0 3) direction [(Figure 3(b)]. The $\text{Br}\cdots\text{Br}'$ distance of $3.496(6)$ Å (symmetry code: (*i*) 1-*x*, 1-*y*, 2-*z*) is shorter than the reported value of $3.618(4)$ Å for 6-bromo-*N*-(2-hydroxyethyl)-2-oxo-2*H*-1-benzopyran-3-carboxamide [13]. The geometric parameters associated with non covalent interactions are listed in Table 2, $\text{C}\cdots\text{H}\cdots\text{O}$ [14] and $\text{C}\cdots\text{H}\cdots\pi$ [15] interactions are in agreement with accepted criteria and particularly with values reported for other coumarins [12,16].

Figure 3. Supramolecular structure of compound **15i**. (a) View in the *bc* plane showing $\text{CH}\cdots\text{O}$ and $\text{Br}\cdots\text{Br}$ contacts. (b) View of bifacial $\text{CH}\cdots\pi$ contacts developing the third dimension along the (7 0 3) direction. Dashed lines represents intermolecular $\text{CH}\cdots\text{A}$ ($\text{A} = \text{O}, \pi$) contacts.

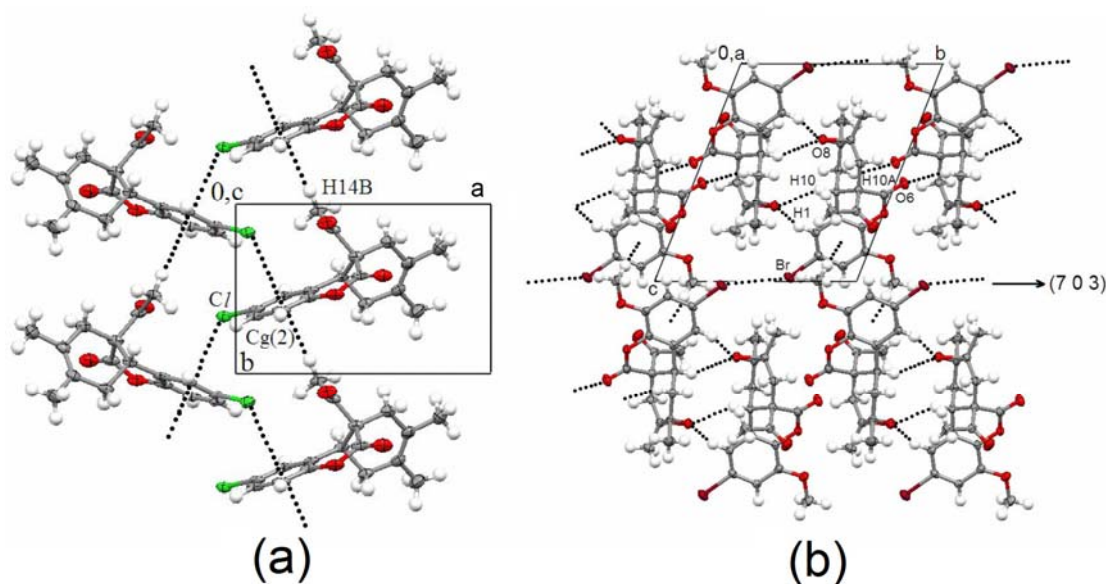
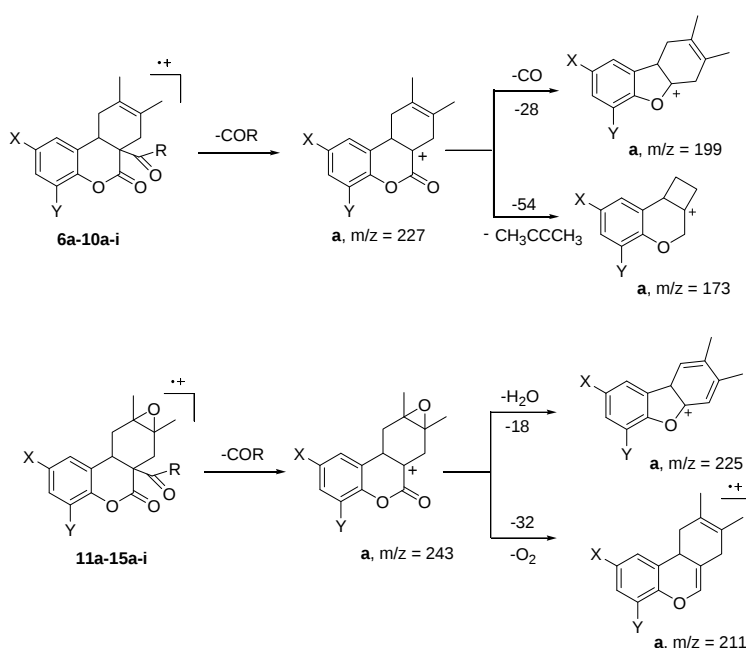


Table 2. Geometric parameters associated with intermolecular hydrogen interactions in compounds **10b** and **15i**.

Compound	D—H···A (symmetry code)	D—H/Å	H···A/Å	D···A/Å	D—H···A/°
10b	C(14)—H(14B)···Cg(2) (x, y+1, z)		2.66	3.626(2)	169
	C(10)—H(10)···O(13) (x, ½-y, z+½)		2.37	3.199(2)	140
15i	C(1)—H(1)···O(8) (-x, 1-y, 1-z)	0.93	2.56	3.317(6)	139
	C(9)—H(10A)···O(8) (-x, 1-y, 1-z)	0.98	2.59	3.491(6)	153
	C(14)—H(14A)···O(8) (-x, 1-y, 1-z)	0.96	2.51	3.421(7)	160
	C(9)—H(9A)···O(6) (1-x, 2-y, 1-z)	0.97	2.51	3.428(6)	157
	C(14)—H(14C)···Cg(3) ^a (x-1, y, z)		2.76	3.603(6)	147
	C(15)—H(15A)···Cg(3) ^a (1-x, 2-y, 2-z)		2.92	3.764(6)	148

^a Cg(3) is the centroid of the benzenoid ring (C1-C4/C4a/C9B).

The molecular peaks of 3-acetylcoumarin adducts **10** and their epoxides **15a,d,f,i** are barely observed (1%) by mass spectrometry. Nevertheless all compounds are cleaved and rearranged following the typical fragmentation path depicted in Scheme 2. Cycloadducts and epoxides give the corresponding fragments, m/z 227 for **6a-10a** and 243 for **11a-15a**, by the loss of 3-ethoxycarbonyl, 3-carbamoyl, or 3-acetyl angular groups. The species derived from **6-10** are further broken by the loss of CO and rearranged to the 2,3-dimethyl-1,4,4a,9b-tetrahydro-dibenzofuran ion (m/z 199) or by the loss of dimethylacetylene (m/z 54) to form the oxacyclobutanaphthalene species (m/z 173). The species derived from epoxides **11-15** mainly rearrange to the corresponding dibenzofuran (m/z 225) or chromene species (m/z 211) after the loss of water or O₂, respectively. Both fragmentation paths are in agreement with those found for other coumarins [17]. It is worthy to mention that retro-DA conversion was observed only in compound **10e**.

Scheme 2. Typical fragmentation path of DA adducts **6a-10ai** and epoxides **11a-15a-i** by mass spectrometry.

3. Experimental

3.1. General methods

All chemicals and solvents were of reagent grade and used as received. Melting points were measured on an Electrothermal IA 9100 apparatus and were uncorrected. IR spectra were recorded in KBr disks using a Perkin-Elmer 16F PC IR spectrophotometer. Mass spectra were obtained in a GC/MS system (Varian) with an electron ionization mode. Elemental analyses (EA) were performed on a Perkin-Elmer 2400 elemental analyzer. ^1H - and ^{13}C -NMR spectra were recorded on a Varian Mercury 300 (^1H , 300.08; ^{13}C , 75.46 MHz) instrument in CDCl_3 solutions, unless otherwise specified, measured with SiMe_4 as the internal reference, δ are in ppm and coupling constants nJ in Hz. ^1H - and ^{13}C -NMR assignments were achieved on the basis of NOE, COSY and HETCOR experiments. Single-crystal X-ray diffraction data for molecules **10b** and **15i** were collected on a Bruker Apex II area detector diffractometer at 100 and 293 K, respectively, with Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$. A semiempirical absorption correction was applied using SADABS [18], and the program SAINT [18] was used for integration of the diffraction profiles. The structures were solved by direct methods using SHELXS97 [19] program of WinGX package [20]. The final refinement was performed by full-matrix least-squares methods on F^2 with SHELXL97 [19] program. H atoms on C, N and O were positioned geometrically and treated as riding atoms, with $\text{C—H} = 0.93\text{--}0.98 \text{ \AA}$, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. Mercury was used for visualization, molecular graphics and analysis of crystal structures [21], software used to prepare material for publication was PLATON [22]. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC numbers 735605 (**10b**) and 721872 (**15i**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (Fax: +44-01223-336033 or E-Mail: deposit@ccdc.cam.ac.uk). Crystals suitable for X-ray analysis were obtained from saturated CHCl_3 solutions. The program GAUSSIAN98 [23] was used to perform the *ab initio* molecular orbital calculations at RHF-631G** level of theory.

3.2. General synthetic procedure for coumarins 1-5

The starting coumarins 1a-4a were synthesized according with the methodology reported elsewhere [11,16,24]. 6-Substituted acetyl coumarins **5a-i** were synthesized by Knoevenagel condensation of ethyl acetoacetate and the corresponding 5-substituted 2-hydroxybenzaldehyde, the spectroscopic data of **5a-d** are in agreement with literature [25].

3-Acetyl-6-methoxy-2H-1-benzopyran-2-one (5e). Prepared from 0.41 mL (3.3 mmol) of 2-hydroxy-5-methoxybenzaldehyde and 0.42 mL (3.3 mmol) of ethyl acetoacetate. Yellow solid 89% yield, mp 180–183 °C. IR $\nu(\text{cm}^{-1})$: 1723 (OC=O), 1677 (C=O), 1226, 1197 (C-O). ^1H -NMR: 8.44 (s, 1H, H4), 7.28 (d, 1H, $^3J = 9.1$, H8), 7.20 (dd, 1H, $^3J = 9.1$, $^4J = 2.9$, H7), 7.02 (d, 1H, $^4J = 2.6$, H5), 3.85 (s, 3H, OCH_3), 2.70 (s, 3H, CH_3); ^{13}C -NMR: 195.9 (CO), 159.7 (OCO), 156.6 (C6), 150.1 (C10), 147.6 (C4), 124.8 (C3), 123.2 (C7), 117.9 (C5), 118.7 (C9), 111.3 (C8), 56.1 (OCH_3), 30.9 (CH_3); EA (%) calculated for $\text{C}_{12}\text{H}_{10}\text{O}_4$: 66.05 C, 4.62 H; found: 66.04 C, 4.61 H.

3-Acetyl-8-methoxy-2H-1-benzopyran-2-one (5f). Prepared from 0.5 g (3.3 mmol) of 2-hydroxy-3-methoxybenzaldehyde and 0.42 mL (3.3 mmol) of ethyl acetoacetate. Yellow solid, 88% yield, mp 171–174 °C. IR $\nu(\text{cm}^{-1})$: 1727 (OC=O), 1682 (C=O), 1278, 1197 (C-O). $^1\text{H-NMR}$: 8.42 (s, 1H, H4), 7.25 (d, 1H, $^4J = 1.1$, $^3J = 5.7$, H7), 7.14 (d, 1H, $^4J = 2.0$, $^3J = 5.7$, H5), 7.18 (t, 1H, $^3J = 5.5$, $^4J = 2.0$, H6), 3.94 (s, 3H, OCH₃), 2.68 (s, 3H, CH₃); $^{13}\text{C-NMR}$: 195.8 (CO), 158.9 (OCO), 145.1 (C10), 147.9 (C4), 147.2 (C8), 125.0 (C5), 124.8 (C3), 121.5 (C6), 116.0 (C7), 118.9 (C9), 56.5 (OCH₃), 30.8 (CH₃); EA (%) calculated for C₁₂H₁₀O₄: 66.05 C, 4.62 H; found: 66.15 C, 4.60 H.

3-Acetyl-6,8-dichloro-2H-1-benzopyran-2-one (5g). Prepared from 0.5 g (2.6 mmol) of 3,5-dichlorosalicylaldehyde and 0.33 mL (2.6 mmol) of ethyl acetoacetate. White solid in 48% yield, mp 172–175 °C. IR $\nu(\text{cm}^{-1})$: 1749 (OC=O), 1676 (C=O), 1217 (C-O), 769 (C-Cl). $^1\text{H-NMR}$: 8.37 (s, 1H, H4), 7.54 (d, 1H, $^4J = 2.4$, H7), 7.66 (d, 1H, $^4J = 2.4$, H5), 2.71 (s, 3H, CH₃); $^{13}\text{C-NMR}$: 194.8 (CO), 157.7 (OCO), 149.7 (C10), 145.4 (C4), 122.9 (C8), 127.8 (C5), 126.2 (C3), 130.5 (C6), 134.2 (C7), 120.1 (C9), 30.7 (CH₃); EA (%) calculated for C₁₁H₆O₃Cl₂: 51.39 C, 2.35 H; found: 51.53 C, 2.42 H.

3-Acetyl-8-bromo-6-chloro-2H-1-benzopyran-2-one (5h). Prepared from 0.5 g (2.1 mmol) of 3-bromo-5-chloro-salicylaldehyde and 0.27 mL of ethyl acetoacetate (2.1 mmol). Yellow solid in 60% yield, mp 192–196 °C. IR $\nu(\text{cm}^{-1})$: 1740 (OC=O), 1675 (C=O), 1202 (C-O), 760 (C-Cl), 556 (C-Br). $^1\text{H-NMR}$ (DMSO-*d*₆): 8.55 (s, 1H, H4), 8.05 (d, 1H, $^4J = 2.2$, H7), 8.12 (d, 1H, $^4J = 2.2$, H5), 2.56 (s, 3H, CH₃); $^{13}\text{C-NMR}$: 195.4 (CO), 158.0 (OCO), 150.7 (C10), 146.1 (C4), 110.5 (C8), 129.8 (C5), 126.6 (C3), 129.5 (C6), 136.5 (C7), 121.1 (C9), 30.7 (CH₃); EA (%) calculated for C₁₁H₆O₃ClBr: 43.82 C, 2.01 H; found: 43.70 C, 2.12 H.

3-Acetyl-6-bromo-8-methoxy-2H-1-benzopyran-2-one (5i). Prepared from 0.5 g (2.2 mmol) of 5-bromo-2-hydroxy-3-methoxybenzaldehyde and 0.28 mL of ethyl acetoacetate (2.2 mmol). Yellow solid in 89% yield, mp 215–218 °C. IR $\nu(\text{cm}^{-1})$: 1735 (OC=O), 1674 (C=O), 1235, 1128 (C-O), 662 (C-Br). $^1\text{H-NMR}$: 8.36 (s, 1H, H4), 7.24 (d, 1H, $^4J = 2.1$, H7), 7.34 (d, 1H, $^4J = 2.1$, H5), 3.96 (s, 3H, OCH₃), 2.71 (s, 3H, CH₃); $^{13}\text{C-NMR}$: 195.1 (CO), 158.0 (OCO), 144.0 (C10), 146.3 (C4), 147.6 (C8), 123.1 (C5), 125.5 (C3), 117.1 (C6), 118.8 (C7), 119.7 (C9), 56.5 (OCH₃), 30.5 (CH₃); EA (%) calculated for C₁₂H₉O₄Br: 48.5 C, 3.1 H; found: 48.45 C, 2.95.

3.3. General synthetic procedure for DA adducts 6-10

1 mmol (typically 100–300 mg) of the corresponding coumarin **1-5** and the appropriate volume equivalent to 6 mmol of 2,3-dimethyl-1,3-butadiene (typically 0.3–1.0 mL) were placed in a glass ampoule; the sealed ampoule was placed inside a metallic capsule and heated in a sand bath at 160 °C for a period of 24 hours. The ampoule content was dissolved in CHCl₃ and evaporated to dryness. The resultant solid was washed with hot hexane and the insoluble solid was purified by CC in SiO₂-gel, using CHCl₃ as eluent. Cycloadducts **6a** [5], **7a** [9] are reported elsewhere.

(6aR,10aR)- and (6aS,10aS)-N-[(R)-1-Phenylethyl]-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxo-dibenzo[b,d]pyran-6a-carboxamide (**8a**). White crystalline solid in 77% yield, mp 168.9–171.4 °C.

IR/ ν (cm^{-1}): 3312 (NH), 1784 (OC=O), 1629 (NC=O), 1532 (C=C), 1222 (N-C), 1146 (C-O). ^1H -NMR: 7.30 (m, 1H, H3), 7.26 (t, 2H, $^3J = 7.3$ and 7.7, Hm), 7.13 (t, 1H, $^3J = 7.3$, Hp), 7.14 (d, 2H, $^3J = 7.3$, Ho), 7.07 (t, 1H, $^3J = 8.1$ and 8.4, H2), 7.00 (d, 1H, $^3J = 8.1$, H1), 6.83 (dd, 1H, $^3J = 5.3$, $^4J = 2.2$, H4), 5.89, 5.82 (d, 1H each, $^3J = 7.5$, N-H), 4.88 (dq, 1H, $^3J = 7.3$, CH₃), 3.58 (m, 1H, H10a), 2.90 (t, 1H, $^3J = 18.3$, H_{eq}-7), 2.49 (d, 1H, $^3J = 17.4$, H_{ax}-7), 2.32 (t, 1H, $^3J = 18.7$ and 12.3, H_{eq}-10), 2.02 (m, 1H, H_{ax}-10), 1.67, 1.60 (s, 3H each, 2CH₃), 1.37, 1.21 (d, 3H, $^3J = 7.0$, CH₃); ^{13}C -NMR: 170.6, 170.5 (NCO), 167.6, 167.4 (OCO), 150.2 (C4a), 142.5, 142.2 (Ci), 129.0 (C3), 128.7, 128.6 (Cm), 128.5, 128.4 (C1), 128.1 (C10b), 128.0, 127.7 (C2), 127.4, 126.1 (Cp), 125.5, 125.7 (Co), 123.5, 123.6 (C9), 123.2, 123.3 (C8), 116.8, 116.7 (C4), 55.0, 54.8 (C6a), 49.5, 49.2 (NCH), 37.0, 36.9 (C7), 36.8, 36.8 (C10), 36.3 (C10a), 21.6, 21.4 (CH₃CH), 18.8, 18.8 (CH₃); GC/MS m/z (%): 375 (M^+ , 24), 281 (38), 227 (100), 211 (5), 199 (3), 105 (29), 79 (12), 44 (5).

(6a*R*,10a*R*)-*rel*-N-(2-Phenylethyl)-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[b,d]pyran-6a-carboxamide (**9a**). White crystalline powder in 84% yield, mp 138.6–140.0 °C. IR/ ν (cm^{-1}): 3333 (NH), 1771 (OC=O), 1634 (NC=O), 1546 (C=C), 1222 (C–O), 1144 (C–N). ^1H -NMR: 7.25 (t, 2H, $^3J = 7.3$, Hm), 7.27 (d, 1H, $^3J = 7.3$, H1), 7.21 (dt, 1H, 7.0 Hz, H3), 7.11 (ddt, 1H, $^3J = 7.2$ and 7.7, $^4J = 1.3$, H2), 7.05 (dd, 2H, $^3J = 7.1$, Ho), 7.00 (dd, 1H, $^3J = 7.5$, H4), 5.79 (t, 1H, $^3J = 5.4$, NH), 3.58 (dd, 1H, $^3J = 11.7$ and 11.7, H10a), 3.34 (dt, 2H, $^3J = 7.2$ and 7.2, $^4J = 2.0$, NCH₂), 2.79 (d, 1H, $^3J = 17.1$, H_{eq}-7), 2.61 (m, 2H, CH₂), 2.30 (d, 1H, $^3J = 16.7$, H_{ax}-7), 2.26 (d, 1H, H_{eq}-10), 2.00 (dd, 1H, $^3J = 15.5$ and 12.0, H_{ax}-10), 1.58, 1.65 (s, 3H, 2CH₃); ^{13}C -NMR: 170.4 (NC=O), 168.4 (OC=O), 150.0 (C4a), 138.4 (Ci), 129.0 (C10b), 128.9 (Co,m), 128.6 (Cp), 128.4 (C3), 127.9 (C1), 126.8 (C3), 125.4 (C2), 123.7 (C9), 123.1 (C8), 116.8 (C4), 41.3 (NCH₂), 37.3 (C7), 36.5 (C10a), 36.3 (C13), 35.5 (CH₂), 18.8, 18.7 (CH₃); GC/MS m/z (%): 375 (M^+ , 20), 227 (100), 199 (3), 173 (7); EA (%) calculated for C₂₄H₂₅O₃N: 76.77 C, 6.71 H, 3.73 N; found: 76.70C, 6.72 H, 3.82 N.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[b,d]pyran (**10a**). White crystalline powder in 83% yield, mp 86–88 °C. IR/ ν (cm^{-1}): 1763 (OC=O), 1702 (C=O), 1159, 1140 (C–O). ^1H -NMR: 7.25 (m, 1H, H3), 7.22 (dd, 1H, $^3J = 12.1$, $^4J = 1.8$, H1), 7.10 (td, 1H, $^3J = 7.3$, $^4J = 1.2$, H2), 7.03 (dd, 1H, $^3J = 7.9$, $^4J = 1.1$, H4), 3.47 (dd, 1H, $^3J = 11.2$ and 11.4, H10a), 2.87 (d, 1H, $^3J = 17.3$, H_{eq}-7), 2.31 (dd, 1H, $^3J = 18.0$, H_{ax}-7), 2.24 (d, 1H, $^3J = 12.0$, H_{eq}-10), 2.12 (s, 3H, CH₃), 2.06 (dd, 1H, H_{ax}-10), 1.70, 1.62 (s, 3H, CH₃); ^{13}C -NMR 204.1 (CO), 168.6 (OCO), 150.4 (C4a), 128.9 (C3), 127.6 (C1), 127.5 (C10b), 125.1 (C2), 123.5 (C9), 122.8 (C8), 117.2 (C4), 60.6 (C6a), 36.8 (C10a), 35.9 (C10), 34.8 (C7), 26.2 (C14), 18.8, 18.9 (CH₃); GC/MS m/z (%): 270 (M^+ , 4), 227 (100), 199 (8), 185 (7), 173 (10), 43 (22); EA (%) calculated for C₁₇H₁₈O₃: 75.53 C, 6.73 H; found: 75.50, 6.70 H.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-2-chloro-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[b,d]pyran (**10b**). Pale yellow solid in 50% yield, mp 102–106 °C. IR/ ν (cm^{-1}): 1781 (OC=O), 1699 (C=O), 1212, 1139 (C–O), 814 (C–Cl). ^1H -NMR: 7.27 (dd, 1H, $^3J = 8.0$, $^4J = 1.98$, H3), 7.19 (d, 1H, $^4J = 2.0$, H1), 6.94 (d, 1H, $^3J = 8.0$ Hz, H4), 3.43 (dd, 1H, $^3J = 6.2$, 11.3, H10a), 2.86 (d, 1H, $^2J = 16.0$, H_{eq}-7), 2.28 (dd, 1H, $^2J = 18.3$, $^3J = 6.2$, H_{eq}-10), 2.13 (d, 1H, $^2J = 16.0$, H_{ax}-7), 2.11 (s, 3H, H14), 2.02 (dd, 1H, $^2J = 18.3$, $^3J = 11.3$, H_{ax}-10), 1.67 (s, 3H, CH₃), 1.59 (s, 3H, CH₃); ^{13}C -NMR: 203.5 (CO), 167.9

(OCO), 148.9 (C4a), 130.1 (C10b), 129.3 (C2), 128.8 (C3), 127.6 (C1), 123.8 (C9), 122.9 (C8), 118.5 (C4), 60.2 (C6a), 36.6 (C10a), 35.7 (C10), 34.8 (C7), 26.3 (C14), 18.8, 18.9 (CH₃); GC/MS *m/z* (%): 306 (M⁺, 1), 261 (100), 233 (11), 219 (11), 207 (10), 165 (5), 70 (7), 43 (26); EA (%) calculated for C₁₇H₁₇O₃Cl·0.4H₂O: 65.45 C, 5.75 H; found 65.58 C, 5.79 H.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-2-bromo-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[*b,d*]pyran (**10c**). Pale yellow solid in 55% yield, mp 50–54 °C. IR/ ν (cm⁻¹): 1773 (OC=O), 1711 (C=O), 1205, 1138 (C-O), 821 (C-Br). ¹H-NMR: 7.30 (dd, 1H, ³*J* = 7.2, ⁴*J* = 1.7, H3), 7.27 (d, 1H, ⁴*J* = 1.7 Hz, H1), 6.86 (d, 1H, ³*J* = 7.2, H4), 3.41 (dd, 1H, ³*J* = 6.4, 11.4 Hz, H10a), 2.83 (d, 1H, ²*J* = 16.8, H_{eq}-7), 2.14 (dd, 1H, ²*J* = 16.9, ³*J* = 11.4, H_{eq}-10), 2.09 (s, 3H, H14), 2.04 (d, 1H, ²*J* = 16.9, H_{ax}-7), 1.92 (dd, 1H, ²*J* = 16.8, ³*J* = 6.4, H_{ax}-10), 1.57 (s, 3H, CH₃), 1.66 (s, 3H, CH₃); ¹³C-NMR: 203.6 (CO), 167.9 (OCO), 149.4 (C4a), 130.4 (C1), 131.8 (C3), 129.6 (C2), 123.4 (C9), 122.8 (C8), 118.9 (C4), 117.7 (C10b), 60.3 (C6a), 36.5 (C10a), 35.7 (C10), 34.7 (C7), 26.2 (C14), 18.8, 18.9 (CH₃); GC/MS *m/z* (%): 348 (M⁺, 1), 305 (100), 277 (5), 251 (6), 198 (10), 165 (10), 43 (58); EA (%) calculated for C₁₇H₁₇O₃Br: C 58.47 C, 4.91 H; found: C 58.43 C, 4.82 H.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-6a,7,10,10a-tetrahydro-8,9-dimethyl-2-nitro-6-oxodibenzo[*b,d*]pyran (**10d**). Pale yellow powder in 81% yield, mp 142–147 °C. IR/ ν (cm⁻¹): 1782 (OC=O), 1726 (C=O), 1525 (NO₂), 1339, 1230 (C-O). ¹H-NMR: 8.16 (d, 1H, ⁴*J* = 2.5, H1), 8.14 (dd, 1H, ³*J* = 9.3, ⁴*J* = 2.5, H3), 7.15 (d, 1H, ³*J* = 9.3, H4), 3.60 (dd, 1H, ³*J* = 6.4, 11.1, H10a), 2.90 (d, 1H, ²*J* = 17.3, H_{eq}-7), 2.38 (d, 1H, ²*J* = 17.3, H_{ax}-7), 2.27 (dd, 1H, ²*J* = 16.7, ³*J* = 6.2, H_{eq}-10), 2.15 (s, 3H, H14), 2.05 (dd, 1H, ²*J* = 16.7, ³*J* = 11.1, H_{ax}-10), 1.62 (s, 3H, CH₃), 1.71 (s, 3H, CH₃); ¹³C-NMR: 202.7 (CO), 166.9 (OCO), 154.7 (C4a), 144.6 (C2), 128.9 (C10b), 124.8 (C3), 123.6 (C1), 123.3 (C9), 122.9 (C8), 118.1 (C4), 60.1 (C6a), 36.5 (C10a), 35.6 (C10), 34.6 (C7), 26.1 (C14), 18.8, 18.9 (CH₃); GC/MS *m/z* (%): 315 (M⁺, 1), 272 (100), 244 (8), 230 (8), 218 (8), 204 (6), 67 (7), 43 (25); EA (%) calculated for C₁₇H₁₇O₅N: 64.75 C, 5.43 H, 4.44 N; found 65.10 C, 5.65 H, 4.20 N.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-6a,7,10,10a-tetrahydro-2-methoxy-8,9-dimethyl-6-oxodibenzo[*b,d*]pyran (**10e**). Pale yellow solid in 55% yield, m.p 44–46 °C. IR/ ν (cm⁻¹): 1761 (OC=O) 1710 (C=O) 1190, 1147 (C-O). NMR: ¹H-NMR: 6.89 (d, 1H, ⁴*J* = 3.5, H1), 6.87 (d, 1H, ³*J* = 6.5, H4), 6.68 (dd, 1H, ³*J* = 6.5, ⁴*J* = 3.2, H3), 3.71 (s, 3H, OCH₃), 3.36 (dd, 1H, ³*J* = 6.5, 11.0, H10a), 2.78 (d, 1H, ²*J* = 16.7, H_{eq}-7), 2.19 (dd, 1H, ²*J* = 18.2, ³*J* = 6.5, H_{eq}-10), 2.06 (s, 3H, H14), 2.09 (d, 1H, ²*J* = 16.7, H_{ax}-7), 2.00 (dd, 1H, ²*J* = 18.2, ³*J* = 11.0, H_{ax}-10), 1.59 (s, 3H, CH₃), 1.63 (s, 3H, CH₃); ¹³C-NMR: 203.7 (CO), 168.3 (OCO), 156.2 (C2), 143.8 (C4a), 128.0 (C3), 123.0 (C9), 122.4 (C8), 117.5 (C1), 113.2 (C10b), 112.3 (C4), 60.0 (C6a), 55.4 (OCH₃), 36.7 (C10a), 35.4 (C10), 34.4 (C7), 25.9 (C14), 18.4, 18.5 (CH₃); GC/MS *m/z* (%): 300 (M⁺, 1), 218 (80), 190 (5), 175 (15); EA (%) calculated for C₁₈H₂₀O₄: 71.98 C, 6.71 H; found: 71.91 C, 6.65 H.

(6a*R*,10a*R*)-*rel*-6a-Acetyl-6a,7,10,10a-tetrahydro-4-methoxy-8,9-dimethyl-6-oxodibenzo[*b,d*]pyran (**10f**). Pale yellow powder 85% yield, mp 115–119 °C. IR ν (cm⁻¹): 1769 (OC=O), 1706 (C=O), 1196, 1095 (C-O). ¹H-NMR: 7.03 (dd, 1H, ³*J* = 8.4, 7.7 Hz, H2), 6.82 (d, 1H, ³*J* = 8.4, Hz, H1), 6.78 (d, 1H,

$^3J = 7.7$, H3), 3.85 (s, 3H, OCH₃), 3.44 (dd, 1H, $^3J = 6.4$, 11.4, H10a), 2.88 (d, 1H, $^2J = 16.7$, H_{eq}-7), 2.21 (dd, 1H, $^2J = 18.2$, $^3J = 6.4$, H_{eq}-10), 2.12 (s, 3H, H14), 2.11 (d, 1H, $^2J = 16.7$, H_{ax}-7), 2.03 (dd, 1H, $^2J = 18.5$, $^3J = 11.4$, H_{ax}-10), 1.68 (s, 3H, CH₃), 1.59 (s, 3H, CH₃); ^{13}C -NMR: 203.9 (CO), 167.9 (OCO), 147.8 (C10), 139.9 (C8), 128.7 (C9), 125.2 (C6), 123.5 (C9), 122.8 (C8), 119.1 (C7), 111.6 (C5), 60.4 (C6a), 56.2 (OCH₃), 36.9 (C10a), 35.8 (C10), 34.9 (C7), 26.4 (C14), 18.8, 18.9 (CH₃); GC/MS m/z (%): 300 (M^+ , 1), 257 (100), 229 (7), 203 (8), 105 (2), 105 (2), 91 (4), 77 (4), 43 (17); EA (%) calculated for C₁₈H₂₀O₄: 71.98 C, 6.71 H; found: 72.25 C, 6.80 H.

(6aR,10aR)-rel-6a-Acetyl-2,4-dichloro-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[b,d]pyran (**10g**). Pale yellow powder in 71% yield, mp 148–151 °C. IR/ ν (cm⁻¹): 1787 (OC=O), 1703 (C=O), 1233, 1192 (C-O), 810 (C-Cl). ^1H -NMR: 7.28 (d, 1H, $^4J = 2.4$, H3), 7.11 (d, 1H, $^4J = 2.4$, H1), 3.47 (dd, 1H, $^3J = 6.2$, 11.5, H10a), 2.89 (d, 1H, $^2J = 17.0$, H_{eq}-7), 2.28 (dd, 1H, $^2J = 17.9$, $^3J = 6.2$, H_{eq}-10), 2.17 (d, 1H, $^2J = 18.7$, H_{ax}-7), 2.14 (s, 3H, H14), 1.97 (dd, 1H, $^2J = 18.9$, $^3J = 9.3$, H_{ax}-10), 1.69 (s, 3H, CH₃), 1.59 (s, 3H, CH₃); ^{13}C -NMR: 202.8 (CO), 166.8 (OCO), 144.9 (C4a), 130.7 (C4), 130.1 (C2), 129.2 (C3), 126.1 (C1), 123.3 (C9), 122.9 (C8), 60.1 (C6a), 36.9 (C10a), 35.5 (C10), 34.9 (C7), 26.5 (C14), 18.8, 18.9 (CH₃); GC/MS m/z (%): 339 (M^+ , 1), 296 (100), 268 (9), 253 (12), 241 (12), 232 (9), 91 (5), 67 (8), 43 (37); EA (%) calculated for C₁₇H₁₆O₃Cl₂: 60.19 C, 4.75 H; found 60.15 C, 4.85 H.

(6aR,10aR)-rel-6a-Acetyl-4-bromo-2-chloro-6a,7,10,10a-tetrahydro-8,9-dimethyl-6-oxodibenzo[b,d]pyran (**10h**). Pale yellow powder in 62% yield, mp 152–155 °C. IR ν (cm⁻¹): 1785 (OC=O), 1703 (C=O), 1232, 1131 (C-O), 787 (C-Cl), 524 (C-Br). ^1H -NMR: 7.45 (d, 1H, $^4J = 2.4$, H1), 7.15 (d, 1H, $^4J = 2.4$, H3), 3.46 (dd, 1H, $^3J = 6.4$, 11.4, H10a), 2.89 (d, 1H, $^2J = 17.1$, H_{eq}-7), 2.31 (dd, 1H, $^2J = 17.6$, $^3J = 6.4$, H_{eq}-10), 2.19 (d, 1H, $^2J = 16.9$, H_{ax}-7), 2.14 (s, 3H, H14), 1.99 (dd, 1H, $^2J = 17.6$, $^3J = 11.4$, H_{ax}-10), 1.69 (s, 3H, CH₃), 1.60 (s, 3H, CH₃); ^{13}C -NMR: 202.8 (CO), 166.9 (OCO), 146.1 (C4a), 132.0 (C3), 130.6 (C2), 130.4 (C4), 126.8 (C1), 123.3 (C9), 122.9 (C8), 111.4 (C10b), 60.1 (C6a), 37.0 (C10a), 35.5 (C10), 34.9 (C7), 26.6 (C14), 18.8, 18.9 (CH₃); GC/MS m/z (%): 384 (M^+ , 1), 341 (100), 325 (5), 313 (6), 287 (10), 232 (15), 67 (16), 43 (27); EA (%) calculated for C₁₇H₁₆O₃ClBr: 53.22 C, 4.2 H; found 53.60 C, 4.25 H.

(6aR,10aR)-rel-6a-Acetyl-2-bromo-6a,7,10,10a-tetrahydro-4-methoxy-8,9-dimethyl-6-oxodibenzo[b,d]pyran (**10i**). Pale yellow powder in 83% yield, mp 160–164 °C. IR/ ν (cm⁻¹): 1769 (OC=O), 1706 (C=O), 1275, 1196 (C-O), 506 (C-Br). ^1H -NMR: 6.94 (s, 1H, H1), 6.94 (s, 1H, H3), 3.84 (s, 3H, OCH₃), 3.41 (dd, 1H, $^3J = 6.2$, 11.3, H10a), 2.88 (d, 1H, $^2J = 16.9$, H_{eq}-7), 2.36 (dd, 1H, $^2J = 17.0$, $^3J = 6.2$, H_{eq}-10), 2.18 (d, 1H, $^2J = 16.9$, H_{ax}-7), 2.13 (s, 3H, H14), 1.97 (dd, 1H, $^2J = 17.0$, $^3J = 11.3$, H_{ax}-10), 1.68 (s, 3H, CH₃), 1.59 (s, 3H, CH₃); ^{13}C -NMR: 203.4 (C=O), 167.4 (OCO), 148.4 (C4a), 138.5 (C4), 130.3 (C2), 123.4 (C9), 122.8 (C8), 121.9 (C3), 117.6 (C10b), 114.9 (C1), 60.2 (C6a), 56.5 (s, 3H, OCH₃), 36.7 (C10a), 35.6 (C10), 34.9 (C7), 26.4 (C14), 18.8, 18.8 (CH₃); GC/MS m/z (%): 380 (M^+ , 1), 337 (100), 309 (4), 283 (8), 256 (8), 228 (14), 115 (5), 91 (5), 43 (31); EA (%) calculated for C₁₈H₁₉O₄Br: 57.01 C, 5.05 H; found 57.20 C, 5.06 H.

3.4. General synthetic procedure for epoxides 11-15

Prepared from 200 mg of compounds **6-10** and two equivalents of *m*-CPBA dissolved in CHCl₃ (25 mL) and refluxed for 24 h. The CHCl₃ solution was extracted with an aqueous saturated NaHCO₃ solution. The organic layer was dried with Na₂SO₄, then filtered and concentrated.

Ethyl (6aR,7aR,8aS,9aR)-rel-6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-6-oxo-5,8-dioxacyclopropa[b]phenantrene-6a(6H)-carboxylate (11a). White crystalline solid in 73% yield, mp 79.8–82.5 °C. IR/v (cm⁻¹): 1772 (OC=O), 1735 (EtOC=O), 1248, 1230, 1150 (C-O). ¹H-NMR: 7.19 (ddd, 1H, ³J = 7.7, 7.7, ⁴J = 1.8 Hz, H3), 7.09 (dd, 1H, ³J = 7.5, ⁴J = 1.8, H1), 7.03 (dd, 1H, ³J = 7.5, ⁴J = 1.1, H2), 6.98 (d, 1H, ³J = 8.6, H4), 3.87 (m, 2H, OCH₂), 3.36 (dd, 1H, ³J = 12.4 and 5.5, H9a), 2.83 (d, 1H, ³J = 15.2, H_{eq}-7), 2.24 (d, 1H, ³J = 15.4, H_{ax}-7), 2.21 (dd, 1H, ³J = 10.3 and 5.5, H_{eq}-9), 1.60 (dd, 1H, ³J = 15.6 and 12.5, H_{ax}-9), 1.40, 1.24 (s, 3H c/u, 2CH₃), 0.83 (t, 3H, CH₃-CH₂). ¹³C-NMR: 169.9 (OCO), 167.4 (OCO lactone), 150.9 (C4a), 129.1 (C1), 127.8 (C3), 126.4 (C9b), 125.1 (C2), 117.0 (C4), 62.3 (CH₂-O), 61.7 (C8a), 60.3 (C7a), 53.3 (C6a), 35.6 (C9a), 34.5 (C9), 34.4 (C7), 21.0 (CH₃-C8a), 19.2 (CH₃-C7a), 13.9 (CH₃-CH₂); GC/MS *m/z* (%): 316 (M⁺, 2), 259 (38), 243 (100), 225 (50), 214 (34), 199 (24), 145 (11), 115 (17), 91 (6), 43 (52); EA (%) calculated for C₁₈H₂₀O₅: 68.34 C, 6.37 H; found: 68.35 C, 6.32 H.

(6aR,7aR,8aS,9aR)-rel-N-benzyl-6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-6-oxo-5,8-dioxacyclopropa[b]phenantrene-6a(6H)-carboxamide (12a). White crystalline solid in 78% yield, mp 205.4–207 °C. IR/v (cm⁻¹): 3342 (NH), 1773 (OC=O), 1637 (NC=O), 1538 (C=C), 1234 (C-O), 1152 (C-N). ¹H-NMR: 7.27 (m, 1H, H3), 7.21 (m, 5H, 5H-C₆H₅), 7.12 (t, 1H, ³J = 7.4, H6), 7.01 (d, 1H, ³J = 8.0, H5), 6.82 (m, 1H, H4), 5.82 (t, 1H, NH), 4.22 (m, 2H, AA'BB', NCH₂), 3.52 (dd, 1H, ²J = 12.5, ³J = 5.3, H9a), 2.94 (d, 1H, ²J = 15.5, H_{eq}-7), 2.32 (dd, 1H, ²J = 15.5, ³J = 5.2, H_{eq}-9), 2.27 (d, 1H, ²J = 15.5, H_{ax}-7), 1.69 (dd, 1H, ²J = 15.6, ³J = 12.7, H_{ax}-9), 1.43 (s, 3H, CH₃), 1.30 (s, 3H, CH₃); ¹³C-NMR: 169.4 (NCO), 168.0 (OCO lactone), 150.3 (C4a), 137.4 (Ci), 128.9 (C-*m* and C1), 128.0 (C3), 127.8 (Cp), 127.5 (Co), 127.0 (C9b), 125.6 (C2), 117.0 (C4), 61.8 (C8a), 60.5 (7a), 54.6 (C6a), 43.9 (NCH₂), 36.0 (C9a), 35.7 (C9), 34.7 (C8a), 21.0 (CH₃-C8a), 19.1 (CH₃-C7a); GC/MS *m/z* (%): 377 (M⁺, 2), 318 (10), 243 (40), 227 (15), 225 (30), 211 (32), 199 (8), 173 (8), 150 (100), 131 (10), 91 (95), 43 (30); EA (%) calculated for C₂₃H₂₃O₄N: 73.19 C, 6.14 H; found: 73.09 C, 6.14 H.

(6aR,7aR,8aS,9aR)- and (6aS,7aS,8aR,9aS)-6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-6-oxo-N-[(R)-1-phenylethyl]-5,8-dioxacyclopropa[b]phenantrene-6a(6H)-carboxamide (13a). White crystalline powder in 78% yield, mp 163.9–165.0 °C; IR v (cm⁻¹): 3256 (NH), 1759 (OC=O), 1638 (NC=O), 1230, 1161, 1151 (C-O); GC/MS *m/z* (%) 391 (M⁺, 4), 332 (15), 243 (58), 227 (28), 225 (35), 211 (42), 199 (8), 173 (15), 105 (100), 43 (20). *Minor (6aR,7aR,8aS,9aR) isomer 13a*: ¹H-NMR: 7.3–6.9 (m, 9H, ArH), 5.67 (d, 1H, ³J = 1.5, NH), 3.48 (dd, 1H, ³J = 5.1, ³J = 12.0, H9a), 2.92 (dd, 1H, ²J = 15.4, H_{eq}-7), 2.27 (d, 1H, ²J = 15.6, H_{ax}-7), 2.29 (m, 1H, H_{eq}-9), 1.68 (dd, 1H, ²J = 15.6, ³J = 5.6, H_{ax}-9), 4.84 (dq, 1H, ³J = 6.9, CHCH₃), 1.43 and 1.30 (two s, 2 × 3H, 7a- and 8a-CH₃), 1.26 (d, 3H, ³J = 7.0, CHCH₃); ¹³C-NMR: 169.6 (NCO), 167.1 (C-6), 150.3 (C-4a), 142.0 (C-1'), 128.8 (C-3',5'), 128.0 (C-1), no (C-3), 127.6 (C-9b), 127.0 (C-4'), 125.9 (C-2',6'), 125.5 (C-2), 117.0 (C-4), 61.8 (C-8a),

60.6 (C-7a), 54.6 (C-6a), 49.1 (NCH), 35.9 (C-9a), 34.9 (C-9), 34.8 (C-7), 21.1, 21.0, and 19.1 ($3 \times \text{CH}_3$). *Major (6aS,7aS,8aR,9aS) isomer 13a*: $^1\text{H-NMR}$: 7.3–6.9 (m, 9H, ArH), 5.71 (d, 1H, $^3J = 1.5$, NH), 3.44 (dd, 1H, $^3J = 5.1$, $^3J = 12.0$, H-9a), 2.90 (dd, 1H, $^2J = 15.4$, H_{eq}-7), 2.19 (d, 1H, $^2J = 15.6$, H_{ax}-7), 2.29 (m, 1H, H_{eq}-9), 1.68 (dd, 1H, $^2J = 15.6$, $^3J = 5.6$, H_{ax}-9), 4.83 (dq, 1H, $^3J = 6.9$, CHCH₃), 1.42 and 1.29 (two s, $2 \times 3\text{H}$, 7a- and 8a-CH₃), 1.22 (d, 3H, $^3J = 7.0$, CHCH₃); $^{13}\text{C-NMR}$: 169.3 (NCO), 167.1 (C-6), 150.4 (C-4a), 142.1 (C-1'), 129.0 (C-3',5'), no (C-1), 127.9 (C-3), 127.7 (C-9b), 126.8 (C-4'), 126.1 (C-2',6'), 125.5 (C-2), 117.0 (C-4), 61.8 (C-8a), 60.6 (C-7a), 54.5 (C-6a), 49.2 (NCH), 36.0 (C-9a), 35.5 (C-9), 34.8 (C-7), 21.1, 21.0, and 19.1 ($3 \times \text{CH}_3$).

(6aR,7aR,8aS,9aR)-rel-6a,7,7a,8a,9,9a-Hexahydro-7a,8a-dimethyl-6-oxo-N-(2-phenylethyl)-5,8-dioxacyclopropa[b]phenantrene-6a(6H)-carboxamide (14a). White crystalline powder in 78% yield, mp 189.4–191.6 °C. IR/v (cm^{-1}): 3322 (NH), 1789 (OC=O), 1640 (CONH), 1146 y 1129 (C-O). $^1\text{H-NMR}$: 7.25(m, 5H, Ph), 7.15 (dd, 1H, $^3J = 7.4$, $^4J = 1.9$, H3), 7.10 (dd, 1H, $^3J = 7.4$, $^4J = 1.2$, H2), 7.03 (d, 1H, $^3J = 6.7$, H1), 7.00 (d, 1H, $^3J = 8.1$, H4), 5.54 (a, 1H, NH), 3.48 (dd, 1H, $^3J = 5.2$, $^3J = 12.6$, H9a), 3.29 (q, 2H, $^3J = 7.2$, NCH₂), 2.81 (d, 1H, $^3J = 5.5$, H_{eq}-7), 2.56 (t, 2H, $^3J = 7.2$, CH₂), 2.28 (dd, 1H, $^3J = 5.2$, $^2J = 15.7$, H_{eq}-9), 2.11 (d, 1H, $^3J = 15.7$, H_{ax}-7), 1.65 (dd, 1H, $^3J = 5.5$ Hz, $^3J = 12.6$, H_{ax}-9), 1.40, 1.29 (s, 3H c/u, 2CH₃); $^{13}\text{C-NMR}$: 169.5 (NCO), 167.9 (OCO), 150.2 (C4a), 138.3 (Ci), 128.9 (Cm), 128.9 (Co), 128.8 (C1), 127.9 (C3), 126.9 (Cp), 125.7 (C2), 116.9 (C4), 127.1 (C9b), 61.8 (C8a), 60.5 (C7a), 54.4 (C6a), 41.2 (NCH₂), 36.0 (CH₂), 35.9 (C9a), 35.4 (C9), 34.5 (C7), 21.0 (CH₃C8a), 19.1 (CH₃C7a); GC/MS m/z (%): 391 (M^+ , 8), 332 (20), 243 (100), 227 (43), 225 (95), 211 (68), 173 (43); EA (%) calculated for C₂₄H₂₅O₄N: 73.64 C, 6.44 H, 3.58 N; found: 73.27 C, 6.24 H, 3.44 N.

(6aR,7aR,8aS,9aR)-rel-6a-Acetyl-6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-6-oxo-6H-5,8-dioxacyclopropa[b]phenantrene (15a). White crystalline powder in 70% yield, mp 125.6–126.9 °C. IR/v (cm^{-1}): 1772 (OC=O), 1699 (C=O), 1300, 1258, 1150 (C-O). $^1\text{H-NMR}$: 7.25 (dd, 1H, $^3J = 7.6$, 7.4, H2), 7.16 (d, $^3J = 7.6$, H1), 7.09 (dd, 1H, $^3J = 7.4$, 8.1, H3), 7.02 (d, 1H, $^3J = 8.1$, H4), 3.45 (dd, 1H, $^3J = 12.2$, 5.0, H9a), 2.83 (d, 1H, $^2J = 15.0$, H_{eq}-7), 2.31 (dd, 1H, $^2J = 15.4$, $^3J = 5.0$, H_{eq}-9), 2.08 (d, 1H, $^2J = 15.0$, H_{ax}-7), 2.02 (s, 3H, CH₃O), 1.68 (dd, 1H, $^2J = 15.4$, $^3J = 12.2$, H_{ax}-9), 1.45, 1.31 (s, 3H c/u, 2CH₃); $^{13}\text{C-NMR}$: 203.5 (COCH₃), 170.4 (OCO), 150.6 (C4a), 134.9 (C9b), 130.5 (C1), 128.5 (C2), 125.4 (C3), 117.4 (C4), 62.0 (C8a), 60.4 (C7a), 60.3 (C6a), 35.9 (C9a), 34.3 (C9), 33.2 (C7), 25.5 (CH₃CO), 21.0 (CH₃C8a), 19.2 (CH₃C7a); GC/MS m/z (%): 286 (M^+ , 1), 243 (16), 225 (28), 211 (100), 184 (14), 114 (17), 91 (9), 43 (60); EA (%) calculated for C₁₇H₁₈O₄: 71.31 C, 6.34 H; found: 71.28 C, 6.44 H.

(6aR,7aR,8aS,9aR)-rel-6a-Acetyl-6a,7,7a,8a,9,9a-hexahydro-7a,8a-dimethyl-2-nitro-6-oxo-6H-5,8-dioxacyclopropa[b]phenantrene (15d). White solid in 96% yield, mp 216–220 °C. IR/v(cm^{-1}): 1786 (OC=O), 1700 (C=O), 1526 (NO₂), 1338, 1237, 1142 (C-O). $^1\text{H-NMR}$: 8.18 (dd, 1H, $^4J = 2.6$, $^3J = 8.8$, H3), 8.15 (d, 1H, $^4J = 2.6$, H1), 7.18 (d, 1H, $^3J = 8.8$, H4), 3.63 (dd, 1H, $^3J = 5.2$, 12.1, H9a), 2.89 (d, 1H, $^2J = 15.5$, H_{eq}7), 2.38 (dd, 1H, $^2J = 15.5$, $^3J = 5.2$, H_{eq}-9), 2.15 (d, 1H, $^2J = 15.5$, H_{ax}-7), 2.09 (s, 3H, H14), 1.70 (dd, 1H, $^2J = 15.5$, $^3J = 12.1$, H_{ax}-9), 1.35 (s, 3H, CH₃), 1.48 (s, 3H, CH₃); $^{13}\text{C-NMR}$: 202.2 (CO), 166.8 (OCO), 154.8 (C4a), 144.7 (C2), 127.4 (C9b), 125.2 (C3), 123.6 (C1), 118.2 (C4),

61.6 (C6a), 60.0 (C8a), 59.9 (C7a), 35.6 (C9), 34.2 (C9a), 32.9 (C7), 25.4 (C14), 20.9, 19.0 (CH₃); GC/MS *m/z* (%): 331 (M⁺, 1), 288 (19), 256 (100), 230 (26), 115 (5), 91 (4), 43 (78); EA (%) calculated for C₁₇H₁₇O₆N: 61.63 C, 5.17 H, 4.23 N; found: 61.44 C, 5.25 H, 4.14 N.

(6aR,7aR,8aS,9aR)-rel-6a-Acetyl-6a,7,7a,8a,9,9a-hexahydro-4-methoxy-7a,8a-dimethyl-6-oxo-6H-5,8-dioxacyclopropa[b]phenantrene (**15f**). White solid in 92% yield, mp 188–192 °C. IR/v(cm⁻¹): 1764 (OC=O), 1702 (C=O), 1281, 1153, 1095 (C-O). ¹H-NMR: 7.05 (t, 1H, H2, ³J = 7.9), 6.85 (dd, 1H, ³J = 7.9, H1), 6.74 (dd, 1H, ³J = 7.9, H3), 3.85 (s, 3H, OCH₃), 3.44 (dd, 1H, ³J = 5.0, 12.3, H9a), 2.85 (d, 1H, ²J = 15.2, H_{eq}-7), 2.31 (dd, 1H, ²J = 15.5, ³J = 5.0, H_{eq}-9), 2.07 (d, 1H, ²J = 15.2, H_{ax}-7), 2.04 (s, 3H, H14), 1.70 (dd, 1H, ²J = 15.5, ³J = 12.3, H_{ax}-9), 1.45 (s, 3H, CH₃), 1.31 (s, 3H, CH₃); ¹³C-NMR: 203.4 (CO), 167.8 (OCO), 147.8 (C4a), 139.6 (C4), 127.2 (C9b), 125.5 (C2), 118.9 (C1), 111.9 (C3), 61.9 (C6a), 60.3 (C8a), 60.1 (C7a), 56.3 (OCH₃), 35.6 (C9), 34.4 (C9a), 33.2 (C7), 25.6 (C14), 19.2, 21.0 (CH₃); GC/MS *m/z* (%): 316 (M⁺, 1), 273 (53), 255 (100), 245(4), 241 (60), 211 (11), 115 (13), 91 (8), 43 (47); EA (%) calculated for C₁₈H₂₀O₅: 68.34 C, 6.37 H; found: 64.83 C, 6.28 H.

(6aR,7aR,8aS,9aR)-rel-6a-Acetyl-2-bromo-6a,7,7a,8a,9,9a-hexahydro-4-methoxy-7a,8a-dimethyl-6-oxo-6H-5,8-dioxacyclopropa[b]phenantrene (**15i**). White powder in 95% yield, mp 169–172 °C. IR/v(cm⁻¹): 1768 (OC=O), 1702 (C=O), 1198, 1154, 1123 (C-O), 512 (C-Br). ¹H-NMR: 6.97 (d, 1H, ⁴J = 2.1, H1), 6.91 (d, 1H, ⁴J = 2.1, H3), 3.86 (s, 3H, OCH₃), 3.42 (dd, 1H, ³J = 5.0, 12.3, H9a), 2.85 (d, 1H, ²J = 15.5, H_{eq}-7), 2.30 (dd, 1H, ²J = 15.5, ³J = 5.0, H_{eq}-9), 2.07 (s, 3H, H14), 2.06 (d, 1H, ²J = 15.5, H_{ax}-7), 1.68 (dd, 1H, ²J = 15.5, ³J = 12.3, H_{ax}-9), 1.45 (s, 3H, CH₃), 1.32 (s, 3H, CH₃); ¹³C-NMR: 202.8 (CO), 167.2 (OCO), 148.5 (C4a), 138.7 (C4), 128.8 (C2), 121.7 (C3), 117.8 (C9b), 115.4 (C1), 61.7 (C8a), 60.2 (C7a), 59.9 (C6a), 56.4 (OCH₃), 35.4 (C9), 34.3 (C9a), 33.2 (C7), 25.7 (C14), 20.9, 19.2 (CH₃); GC/MS *m/z* (%): 395 (M⁺, 1), 351 (27), 334 (10), 321 (100), 255 (8), 240 (28), 115 (12), 91 (5), 43 (80); EA (%) calculated for C₁₈H₁₉O₅Br: 54.70 C, 4.85 H; found: 54.26 C, 4.74 H.

3.5. Crystal structures

Compound 10b: C₁₇H₁₇O₃, colorless crystals, monoclinic, *P*2₁/*c*, *Z* = 4, *a* = 18.809(2) Å, *b* = 7.1461(9) Å, *c* = 11.4261(14) Å, α = 90°, β = 105.493(2)°, γ = 90°, *V* = 1480.0(3) Å³, *D*_{calcd} = 1.368 g/cm³, μ = 0.265 mm⁻¹, 10086 reflections collected, 2603 independent (*R*_{int} = 0.025), 2414 observed, *R*1 = 0.0411, *wR*2 = 0.1198 (*I* > 2σ(*I*)).

Compound 15i: C₁₈H₁₉BrO₅, colorless crystals, triclinic, *P*-1, *Z* = 2, *a* = 7.3676(18) Å, *b* = 10.851(3) Å, *c* = 12.154(3) Å, α = 108.055(4)°, β = 97.784(4)°, γ = 106.789(4)°, *V* = 857.0(4) Å³, *D*_{calcd} = 1.532 g/cm³, μ = 2.423 mm⁻¹, 8373 reflections collected, 3017 independent (*R*_{int} = 0.046), 2455 observed, *R*1 = 0.0575, *wR*2 = 0.1149 (*I* > 2σ(*I*)).

4. Conclusions

The thermal reactions of ethyl coumarin-3-carboxylate (**1a**), 3-carboxyamides **2a-4a** and 3-acetylcoumarins **5a-i** with 2,3-dimethyl-1,3-butadiene under SFC yielded the corresponding DA adducts in 60 to 85%, as a racemic mixture of the *cis* fused rings. Poor asymmetric induction is observed when the enantiopure compound **3a** was used. Epoxidation of DA cycloadducts **6a-10a** proceeded in 70–80% yield, whereas starting from **10d**, **10f**, and **10i**, the isolated yields were in the 90–96% range. NMR and X-ray data demonstrated that the oxygen atom is stereoselectively added to the less hindered face of the cyclohexene ring, opposite to the benzopyrone ring fusion. ¹H-NMR and X-ray data supported an anchored twisted boat conformation for both dihydropyrone and cyclohexene rings. Data on the supramolecular structure of DA adducts and epoxides is scarce, although it is directed by CH $\cdots$ A (A = O, π) and, in the case of **15i**, also by Br $\cdots$ Br interactions.

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Sample Availability: Samples of compounds **10a**, **11-12a** and **15a** are available from the authors.

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