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First TDAE approach in quinonic series: synthesis of new 2-substituted 1,4-dimethoxy-9,10-anthraquinones

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ABSTRACT

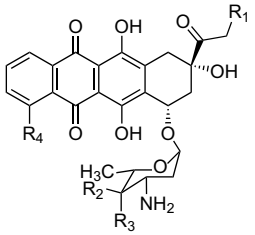
We report herein an original preparation of 2-substituted 1,4-dimethoxy-9,10-anthraquinones using the first example of TDAE strategy in quinonic series. This TDAE approach is an original and mild method to generate a quinonic anion, which cannot be formed via organometallic strategy.

1. Introduction

1,4-Dihydroxyanthraquinones are common structural sub-units of many biologically active quinonoids named, anthracyclines,[1] dynemicins,[2] mitoxantrones,[3] anthraquinone-steroid hybrids,[4] and naphthacenedione organic dyes.[5] They are particularly important for the synthesis of antitumor anthracyclines (daunorubicin, doxorubicin) that have proved to be the most effective drugs in the treatment of various tumors for the past 35 years (Fig. 1).[1] An analog development program has led to the discovery of second generation anthracyclines, including idarubicin (Zavedos) and epirubicin (Farmorubicin), presently available to oncologists. Currently, a few more synthetic analogs (WP744, WP769) with improved properties are undergoing clinical studies.[6]

Tetrakis(dimethylamino)ethylene (TDAE) is a reducing agent, which reacts with halogenated derivatives to generate an anion, under mild conditions, via a single electron transfer (SET).[7] According to this strategy, we have recently developed many reactions between nitrobenzylic substrates and a series of electrophiles such as aldehydes, ketones, α-keto-esters, α-keto-lactams, and ketomalonates leading to corresponding alcohol adducts.[8,9] Recently, this reactivity has been generalized in heterocyclic series.[10] Moreover, we have reported the reactions of dihalo- and trihalomethyl heterocyclic derivatives with aromatic aldehydes in the presence of TDAE, which have furnished, respectively, a mixture of cis/trans isomers of oxiranes and α-haloketone derivatives.[11,12]

As bioreductible alkylating agents, quinones constitute potential substrates for the radical nucleophilic substitution ($S_{RN}1$ reaction).[13] In connection with our program centered on the synthesis of new quinonic compounds using the electron transfer methodology, we developed various mechanistic studies and described different mechanisms as Bis-$S_{RN}1$, LD-$S_{RN}1$ (Long-Distance-$S_{RN}1$), $E_{RC}1$ (Unimolecular Radical Chain Elimination) or intramolecular $S_{RN}1$.[14] Since 2003, we have introduced a new program directed toward the development of original synthetic methods using TDAE methodology in medicinal chemistry and the preparation of new potentially bioactive compounds as anticancer agents. After the study of TDAE initiated reactions of benzenic and heterocyclic derivatives, we envisaged to prepare new quinonic compounds via such strategy. We report herein the preparation of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2**



R_1=R_2=H, R_3=OH, R_4=OCH_3: Daunorubicin
R_1=OH, R_2=H, R_3=OH, R_4=OCH_3: Doxorubicin
R_1=R_2=R_4=H, R_3=OH: Idarubicin
R_1=R_3=H, R_2=OH, R_4=OCH_3: Epirubicin
R_1=OH, R_2=H, R_3=$OCH_2C_6H_5$, R_4=OCH_3: WP744
R_1=OH, R_2=H, R_3=$OCH_2C_6H_5$, R_4=H: WP769

Figure 1. Structures of anthracyclines.

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and present the study of their reactivity with aromatic aldehydes, as electrophile, in the presence of TDAE.

2. Results and discussion

The choice of these substrates was dictated by the biological interest of 1,4-dimethoxy-9,10-anthraquinones but also by the preliminary studies of TDAE reactivity already conducted in quinonic series.

2.1. Preliminary studies

Firstly, we have envisaged the reaction of 2-chloromethyl-3-methyl-1,4-naphthoquinone with 4-nitrobenzaldehyde in the presence of TDAE. However, only untractable tarry matters were obtained, this result could be explained by the high reductivity of chloride (E_{pc1}=−0.404 V vs Ag/AgCl).[15] On the other hand, we have recently shown that some dimethoxybenzene derivatives, due to their particularly weak reductivity,[16] do not react with aromatic aldehydes under classical TDAE conditions.[8] In agreement with the biological interest of 1,4-dihydroxyanthraquinones, we have investigated the preparation of alternative quinonic substrates, which possess a dimethoxy substitution such as 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2**.

2.2. Synthesis of mono and dibromide substrates

The preparation of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2** was inspired by the previously described method.[17] The modifications brought to these previous protocols allowed us to increase certain yields. Condensation of phthalic anhydride with methyl-hydroquinone in an $AlCl_3$–NaCl melt at 200 °C afforded 2-methyl-1,4-dihydroxyanthraquinone in 88% yield. After methylation using dimethylsulfate, the obtained 2-methyl-1,4-dimethoxyanthraquinone was brominated with 1.5 equiv of *N*-bromosuccinimide in refluxing CCl_4 for 5 h to give 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** in 58% yield accompanied by 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2** in 27% yield. However, the preparation of this latter compound has been optimized (87%) using 3 equiv of *N*-bromosuccinimide in refluxing CCl_4 for 7 h (Scheme 1).

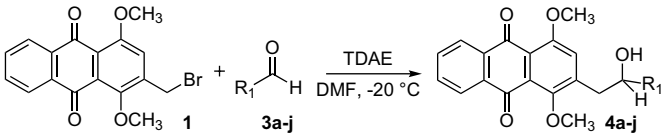
2.3. TDAE reactivity of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone 1

The reaction of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** with 3 equiv of various aromatic aldehydes **3a–j** in the presence of TDAE at −20 °C for 1 h followed by 2 h at rt led to the corresponding alcohol derivatives **4a–j** in moderate to good yields (43–92%) as shown in Table 1 (Scheme 2).

Table 1
Reaction of bromide **1** and aromatic aldehydes using TDAE[a]

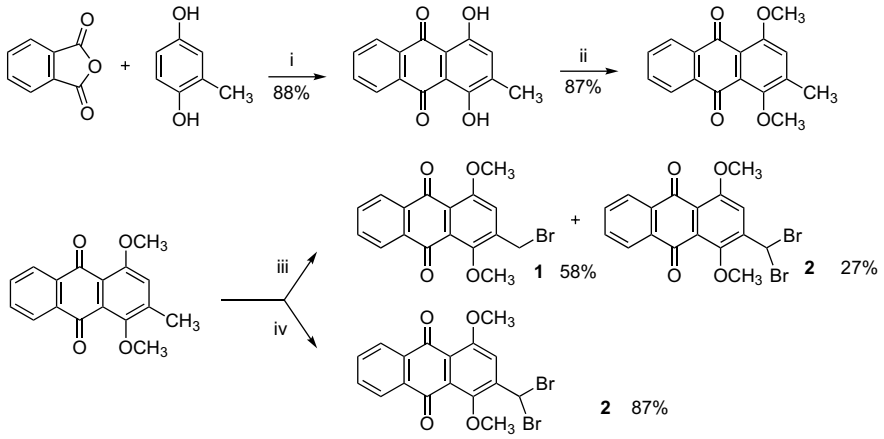
Entry[a]	Aromatic aldehyde	R_1	Product number	Yield[b] (%)
1	4-Nitrobenzaldehyde	4-NO_2–C_6H_4	**4a**	80
2	4-Bromobenzaldehyde	4-Br–C_6H_4	**4b**	46
3	4-Cyanobenzaldehyde	4-CN–C_6H_4	**4c**	57
4	Benzaldehyde	C_6H_5	**4d**	50
5	4-Tolualdehyde	4-CH_3–C_6H_4	**4e**	43
6	4-Chlorobenzaldehyde	4-Cl–C_6H_4	**4f**	52
7	4-Trifluoromethylaldehyde	4-CF_3–C_6H_4	**4g**	56
8	2-Nitrobenzaldehyde	2-NO_2–C_6H_4	**4h**	88
9	2-Bromobenzaldehyde	2-Br–C_6H_4	**4i**	92
10	3-Nitrobenzaldehyde	3-NO_2–C_6H_4	**4j**	84

[a] All the reactions are performed using 3 equiv of aromatic aldehyde **3a–j**, 1 equiv of bromide **1**, and 1 equiv of TDAE in anhydrous DMF stirred at −20 °C for 1 h and then warmed up to rt for 2 h.
[b] % Yield relative to bromide **1**.



Scheme 2. TDAE reactivity of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and aromatic aldehyde **3a–j**.

As observed in *p*-nitrobenzyl series,[8] aromatic aldehydes (**3a**, **3h**, and **3j**) with electron-withdrawing group as nitro group are more reactive (respectively, in 80, 88 and 84% yields) than aromatic aldehydes substituted by an electron-donor group such as methyl **3e** (43%) or than benzaldehyde **3d** (50%). In order to increase the moderate yield of reaction with 4-tolualdehyde (43%), we have investigated the influence of the reaction time (24 h at rt vs 2 h at rt) but no significant increase of yield has been observed. The



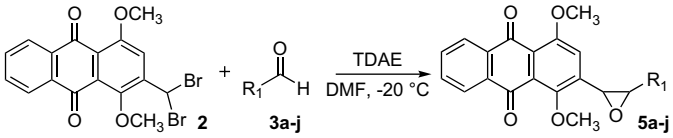
i) $AlCl_3$-NaCl, 200 °C, 3 min.; HCl/H_2O 100 °C, 2 h. ii) $SO_4(CH_3)_2$, acetone, 50 °C, 24h.
iii) NBS (1.5 eq.), hv, benzoyl peroxide, CCl_4, 80 °C, 5h. iv) NBS (3 eq.), hv, benzoyl peroxide, CCl_4, 80 °C, 7h

Scheme 1. Synthesis of 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2**.

formation of these alcohol derivatives may be explained by nucleophilic addition of quinonic carbanion, formed by action of TDAE with 2-bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1**, on carbonyl group of corresponding aldehyde. Moreover, this reaction is a regioselective method, only the carbonyl group reacts with quinonic anion. This TDAE strategy is an original and mild method to generate a quinonic anion, which cannot be formed via organometallic strategy.

2.4. TDAE reactivity of 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone 2

The reaction of 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2** with 2 equiv of aromatic aldehydes in the presence of TDAE at −20 °C for 1 h, followed by 2 h at rt led to a mixture of cis/trans isomers of corresponding oxiranes **5a–j** in good yields (63–86%) as shown in Scheme 3 and reported in Table 2. However, as with bromide **1**, the reaction of the substrate **2** and aromatic aldehyde with an electron-donor group such as methyl **3e** furnishes only 22% of corresponding oxirane **5e**. The formation of the oxiranes **4a–j** may be explained by nucleophilic addition of α-bromo carbanion, formed by action of TDAE with 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2**, on carbonyl group of aldehydes **3a–j** followed by an intramolecular nucleophilic substitution. ^{1}H NMR spectral studies reveal that oxiranes were identified as trans or cis isomers by their coupling constant. Two distinct doublets appeared in 3.76–4.73 ppm region with J=1.7–1.9 Hz or J=4.3–4.5 Hz each of the signal corresponding to one proton. The small value (1.7–1.9 Hz) of this coupling constant is consistent with a trans-isomer as reported in literature data[18,19] and large value (4.3–4.5 Hz) indicates the cis-isomer of oxirane.



Scheme 3. TDAE reactivity of 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2** and aromatic aldehyde **3a–j**.

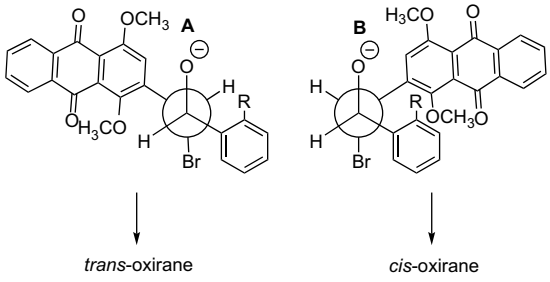
The relative cis/trans percentage of oxirane isomers reported in Table 2 showed that the stereoselectivity of these reactions was sensitive to steric hindrance. This stereoselectivity is better than previous results in quinoxaline series, probably due to the presence of OCH_3 substituents on anthraquinone. Moreover, the reactions with *ortho*-substituted aldehydes were most selective.

Table 2
Reaction of dibromide **2** and aromatic aldehyde **3a–j** using TDAE[a]

Entry[a]	Aromatic aldehyde	R_1	Oxirane	cis/trans isomers[b] (%)	Yield[c] (%)
1	4-Nitrobenzaldehyde	4-NO_2–C_6H_4	**5a**	26/74	72
2	4-Bromobenzaldehyde	4-Br–C_6H_4	**5b**	37/63	86
3	4-Cyanobenzaldehyde	4-CN–C_6H_4	**5c**	25/75	86
4	Benzaldehyde	C_6H_5	**5d**	46/54	63
5	4-Tolualdehyde	4-CH_3–C_6H_4	**5e**	39/61	22
6	4-Chlorobenzaldehyde	4-Cl–C_6H_4	**5f**	37/63	73
7	4-Trifluoromethylaldehyde	4-CF_3–C_6H_4	**5g**	25/75	73
8	2-Nitrobenzaldehyde	2-NO_2–C_6H_4	**5h**	0/100	82
9	2-Bromobenzaldehyde	2-Br–C_6H_4	**5i**	0/100	81
10	3-Nitrobenzaldehyde	3-NO_2–C_6H_4	**5j**	23/77	76

[a] All the reactions are performed using 2 equiv of aromatic aldehyde **3a–j**, 1 equiv of bromide **2**, and 1.5 equiv of TDAE in anhydrous DMF stirred at −20 °C for 1 h and then warmed up to rt for 2 h.
[b] % Isomers determined on ^{1}H NMR measurements from the crude product.
[c] % Yield relative to dibromide **2**.

Intramolecular substitution proceeds by an S_N2 mechanism and two conformations are possible for the transition state as shown in Scheme 4. However, the one that predominates is often determined by an eclipsing effect. In conformation **A**, the *ortho*-substituted benzene ring is placed between a hydrogen and a bromine atom, while in conformation **B**, it is between anthraquinone moiety and a bromine atom. This means that **A** is more stable, and most of the intramolecular substitution should occur from this conformation. These effects become greater while increasing the substituent size.



Scheme 4. Stereoselectivity of the oxirane formation.

3. Conclusion

In conclusion, this study presents the first approach of TDAE strategy in quinonic series. This methodology is an original and mild method to generate a quinonic carbanion or an α-bromo quinonic carbanion, which cannot be formed via organometallic strategy. The reactions of substrates **1** and **2** furnish, respectively, alcohols **4a–j** and oxiranes **5a–j** in good yields. Due to the basic properties of TDAE, the generalization of this strategy to enolizable carbonyl derivatives such as aliphatic aldehydes or ketones needs further studies to adapt this protocol. The extension of this strategy to other carbonyl derivatives as well as the pharmacological evaluation of all synthesized products is under active investigation.

4. Experimental section

Melting points were determined on a Buchi capillary melting point apparatus and are uncorrected. Elemental analyses were performed by the Centre de Microanalyses of the University of Aix-Marseille 3. Both ^{1}H and ^{13}C NMR spectra were determined on a Bruker AC 200 spectrometer. The ^{1}H chemical shifts are reported as parts per million downfield from tetramethylsilane (Me_4Si), and the ^{13}C chemical shifts were referenced to the solvents peaks: $CDCl_3$ (76.9 ppm) or Me_2SO-d_6 (39.6 ppm). Absorptions are reported with the following notations: s, singlet; d, doublet; t, triplet; q, quartet; m, a more complex multiplet or overlapping multiplets. The following adsorbents were used for column chromatography: silica gel 60 (Merck, particle size 0.063–0.200 mm, 70–230 mesh ASTM). TLC was performed on 5 cm×10 cm aluminum plates coated with silica gel 60 F-254 (Merck) in an appropriate solvent.

2-Bromomethyl-1,4-dimethoxy-9,10-anthraquinone **1** and 2-(dibromomethyl)-1,4-dimethoxy-9,10-anthraquinone **2** were prepared according to previously described method.[17]

4.1. General procedure for TDAE reaction of 1 with aromatic aldehydes

Into a two-necked flask equipped with a silica gel drying tube and a nitrogen inlet were added, under nitrogen at −20 °C, 10 mL of anhydrous DMF solution of **1** (0.2 g, 0.55 mmol) and aldehyde **3a–j** (1.65 mmol, 3 equiv). The solution was stirred and maintained at this temperature for 30 min and then was added dropwise (via

a syringe) TDAE (0.127 mL, 0.55 mmol, 1 equiv). A red color immediately developed with the formation of a white fine precipitate. The solution was vigorously stirred at −20 °C for 1 h and then warmed up to rt for 2 h. After this time TLC analysis (dichloromethane) clearly showed that **1** was totally consumed. The orange-red turbid solution was filtered (to remove the octamethyloxamidinium dichloride) and hydrolyzed with 80 mL of H_2O. The aqueous solution was extracted with toluene (3×40 mL), the combined organic layers washed with H_2O (3×40 mL), and dried over $MgSO_4$. Evaporation of the solvent left an orange viscous liquid as crude product. Purification by silica gel chromatography (dichloromethane) gave the corresponding alcohol **4a–j**.

4.1.1. 2-[2-Hydroxy-2-(4-nitrophenyl)ethyl]-1,4-dimethoxyanthracene-9,10-dione (*4a*)

Yellow solid; mp 199 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.01 (dd, J_{AB}=13.4 Hz, J=8.3 Hz, 1H, H_A), 3.25 (dd, J_{AB}=13.4 Hz, J=8.3 Hz, 1H, H_B), 3.90 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.20 (dd, J=8.3 Hz, J=3.9 Hz, 1H, CH), 7.06 (s, 1H, Ar-H), 7.55 (d, J=8.7 Hz, 2H, Ar-H), 7.73–7.75 (m, 2H, Ar-H), 8.14–8.18 (m, 2H, Ar-H), 8.20 (d, J=8.7 Hz, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.4, 56.8, 62.2, 73.1, 121.8, 121.9, 123.7, 126.5, 126.6, 127.2, 133.3, 133.7, 133.8, 134.2, 140.9, 147.4, 151.2, 152.4, 156.3, 182.6, 183.2. Anal. Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.36; H, 4.36; N, 3.15.

4.1.2. 2-[2-(4-Bromophenyl)-2-hydroxyethyl]-1,4-dimethoxyanthracene-9,10-dione (*4b*)

Yellow solid; mp 202 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.65 (d, J=3.3 Hz, 1H, OH), 3.06 (dd, J_{AB}=13.4 Hz, J=7.7, 1H, H_A), 3.19 (dd, J_{AB}=13.4 Hz, J=7.7 Hz, 1H, H_B), 3.87 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 5.05 (m, 1H, CH), 6.96 (s, 1H, Ar-H), 7.22 (d, J=8.7 Hz, 2H, Ar-H), 7.46 (d, J=8.7 Hz, 2H, Ar-H), 7.70–7.75 (m, 2H, Ar-H), 8.14–8.19 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.1, 56.7, 62.2, 73.4, 121.5, 121.8, 121.9, 126.4, 126.6, 127.0, 127.5, 131.6, 133.3, 133.7, 133.8, 134.3, 141.4, 142.8, 152.5, 156.1, 182.8, 183.4. Anal. Calcd for $C_{24}H_{19}BrO_5$: C, 61.68; H, 4.10. Found: C, 61.49; H, 4.28.

4.1.3. 4-[2-(1,4-Dimethoxy-9,10-dioxo-9,10-dihydro-anthracen-2-yl)-1-hydroxyethyl]-benzonitrile (*4c*)

Yellow solid; mp 153 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.00 (dd, J_{AB}=13.5 Hz, J=8.2 Hz, 1H, H_A), 3.23 (dd, J_{AB}=13.5 Hz, J=8.2 Hz, 1H, H_B), 3.88 (s, 3H, OCH_3), 3.92 (s, 3H, CH_3), 5.15 (dd, J=8.2 Hz, J=4.1 Hz, 1H, CH), 7.02 (s, 1H, Ar-H), 7.48 (d, J=8.1 Hz, 2H, Ar-H), 7.62 (d, J=8.1 Hz, 2H, Ar-H), 7.70–7.50 (m, 2H, Ar-H), 8.12–8.17 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.3, 56.7, 62.1, 73.2, 111.4, 118.6, 121.8, 126.4, 126.5, 126.6, 127.1, 132.3, 133.3, 133.7, 133.8, 134.2, 141.0, 149.2, 150.9, 152.4, 156.2, 182.6, 183.2. Anal. Calcd for $C_{25}H_{19}NO_5$: C, 72.63; H, 4.63; N, 3.39. Found: C, 72.40; H, 4.85; N, 3.34.

4.1.4. 2-(2-Hydroxy-2-phenylethyl)-1,4-dimethoxyanthracene-9,10-dione (*4d*)

Yellow solid; mp 140 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.45 (d, J=3.2 Hz, 1H, OH), 3.16 (dd, J_{AB}=7.2 Hz, J=4.8 Hz, 1H, H_A), 3.19 (dd, J_{AB}=7.2 Hz, J=4.8 Hz, 1H, H_B), 3.83 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.07 (m, 1H, CH), 6.97 (s, 1H, Ar-H), 7.31–7.37 (m, 5H, Ar-H), 7.70–7.74 (m, 2H, Ar-H), 8.15–8.19 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.0, 56.6, 62.2, 74.1, 121.6, 121.9, 125.8, 126.4, 126.5, 127.1, 127.8, 128.5, 133.2, 133.6, 133.9, 134.4, 141.8, 143.7, 152.6, 156.1, 182.9, 183.4. Anal. Calcd for $C_{24}H_{20}O_5$: C, 74.21; H, 5.19. Found: C, 73.55; H, 5.22.

4.1.5. 2-(2-Hydroxy-2-p-tolylethyl)-1,4-dimethoxyanthracene-9,10-dione (*4e*)

Yellow solid; mp 159 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.34 (s, 3H, CH_3), 3.15 (dd, J_{AB}=7.1 Hz, J=1.6 Hz, 1H, H_A), 3.19 (dd, J_{AB}=7.1 Hz, J=1.6 Hz, 1H, H_B), 3.86 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.04 (dd, J=1.6 Hz, J=0.9 Hz, 1H, CH), 7.00 (s, 1H, Ar-H), 7.16–7.29 (m, 4H, Ar-H), 7.70–7.75 (m, 2H, Ar-H), 8.16–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 21.1, 40.9, 56.6, 62.1, 73.9, 121.5, 121.9, 125.7, 126.4, 126.5, 127.0, 129.2, 133.2, 133.6, 133.9, 134.4, 137.5, 140.8, 142.0, 152.6, 156.1, 182.9, 183.4. Anal. Calcd for $C_{25}H_{22}O_5$: C, 74.61; H, 5.51. Found: C, 74.56; H, 5.61.

4.1.6. 2-[2-(4-Chlorophenyl)-2-hydroxyethyl]-1,4-dimethoxyanthracene-9,10-dione (*4f*)

Yellow solid; mp 161 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.60 (d, J=3.4 Hz, 1H, OH), 3.01 (dd, J_{AB}=13.3 Hz, J=7.8 Hz, 1H, H_A), 3.20 (dd, J_{AB}=13.3 Hz, J=7.8 Hz, 1H, H_B), 3.87 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.06 (m, 1H, CH), 6.97 (s, 1H, Ar-H), 7.28–7.32 (m, 4H, Ar-H), 7.71–7.75 (m, 2H, Ar-H), 8.15–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.2, 56.6, 62.1, 73.2, 121.5, 121.9, 126.3, 126.4, 127.1, 128.5, 133.2, 133.3, 133.6, 133.7, 134.2, 141.6, 142.4, 144.7, 152.5, 156.1, 182.7, 183.3. Anal. Calcd for $C_{24}H_{19}ClO_5$: C, 68.10; H, 4.53. Found: C, 68.08; H, 4.65.

4.1.7. 2-{2-[4-(Trifluoromethyl)phenyl]-2-hydroxyethyl}-1,4-dimethoxyanthracene-9,10-dione (*4g*)

Yellow solid; mp 146 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.73 (d, J=3.3 Hz, 1H, OH), 3.07 (dd, J_{AB}=13.4 Hz, J=7.9 Hz, 1H, H_A), 3.25 (dd, J_{AB}=13.4 Hz, J=7.9 Hz, 1H, H_B), 3.85 (s, 3H, OCH_3), 3.95 (s, 3H, CH_3), 5.16 (m, 1H, CH), 6.95 (s, 1H, Ar-H), 7.45 (d, J=8.3 Hz, 2H, Ar-H), 7.45 (d, J=8.3 Hz, 2H, Ar-H), 7.70–7.76 (m, 2H, Ar-H), 8.16–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 41.3, 56.6, 62.1, 73.3, 121.8, 124.4, 125.4, 126.1, 126.4, 126.6, 129.6, 129.8, 130.2, 133.3, 133.7, 134.2, 141.2, 147.8, 152.4, 156.1, 182.7, 183.3. Anal. Calcd for $C_{25}H_{19}F_3O_5$: C, 65.79; H, 4.20. Found: C, 65.32; H, 4.46.

4.1.8. 2-[2-Hydroxy-2-(2-nitrophenyl)ethyl]-1,4-dimethoxyanthracene-9,10-dione (*4h*)

Yellow solid; mp 185 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.22 (dd, J_{AB}=14.0 Hz, J=7.7 Hz, 1H, H_A), 3.33 (dd, J_{AB}=14.0 Hz, J=7.7 Hz, 1H, H_B), 3.97 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 5.60 (dd, J=7.7 Hz, J=3.4 Hz, 1H, CH), 7.41–7.49 (m, 1H, Ar-H), 7.61–7.69 (m, 1H, Ar-H), 7.71–7.76 (m, 2H, Ar-H), 7.84–7.88 (m, 1H, Ar-H), 7.98–8.01 (m, 1H, Ar-H), 8.16–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 39.9, 56.8, 62.3, 70.5, 121.5, 121.8, 124.5, 126.5, 126.6, 127.3, 128.4, 133.3, 133.7, 133.8, 134.3, 139.5, 141.5, 147.6, 152.2, 156.6, 182.8, 183.3. Anal. Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.24; H, 5.53; N, 3.19.

4.1.9. 2-[2-(2-Bromophenyl)-2-hydroxyethyl]-1,4-dimethoxyanthracene-9,10-dione (*4i*)

Yellow solid; mp 203 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.01 (d, J=3.2 Hz, 1H, OH), 3.10 (dd, J_{AB}=13.8 Hz, J=7.9 Hz, 1H, H_A), 3.33 (dd, J_{AB}=13.8 Hz, J=7.9 Hz, 1H, H_B), 3.87 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 5.42 (m, 1H, CH), 7.04 (s, 1H, Ar-H), 7.15–7.18 (m, 1H, Ar-H), 7.25–7.35 (m, 1H, Ar-H), 7.51–7.56 (m, 2H, Ar-H), 7.71–7.75 (m, 2H, Ar-H), 8.16–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 38.9, 56.7, 62.3, 73.1, 121.7, 121.8, 126.5, 126.6, 127.2, 127.7, 127.8, 129.1, 132.7, 133.3, 133.6, 133.7, 133.9, 134.3, 141.5, 142.5, 152.6, 156.2, 182.8, 183.4. Anal. Calcd for $C_{24}H_{19}BrO_5$: C, 61.68; H, 4.10. Found: C, 61.51; H, 3.96.

4.1.10. 2-[2-Hydroxy-2-(3-nitrophenyl)ethyl]-1,4-dimethoxyanthracene-9,10-dione (*4j*)

Yellow solid; mp 218 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.92 (d, J=3.2 Hz, 1H, OH), 3.09 (dd, J_{AB}=13.4 Hz, J=8.2 Hz, 1H, H_A), 3.24 (dd, J_{AB}=13.4 Hz, J=8.2 Hz, 1H, H_B), 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 5.18 (m, 1H, CH), 7.08 (s, 1H, Ar-H), 7.52 (m, 1H, Ar-H), 7.67–7.76 (m, 3H, Ar-H), 8.12–8.20 (m, 3H, Ar-H), 8.32 (m, 1H, Ar-H). ^{13}C NMR (50 MHz, DMSO-d_6) δ_C 40.2, 56.5, 62.1, 71.8, 120.4, 120.5, 121.9, 122.4, 125.8, 125.9, 126.3, 129.6, 132.7, 133.4, 133.7, 133.9, 142.4,

147.7, 147.8, 152.2, 155.4, 181.5, 182.5. Anal. Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.18; H, 4.54; N, 3.19.

4.2. General procedure for TDAE reaction of 2 with aromatic aldehydes

Into a two-necked flask equipped with a silica gel drying tube and a nitrogen inlet were added, under nitrogen at −20 °C, 10 mL of anhydrous DMF solution of **2** (0.2 g, 0.45 mmol) and aldehyde **3a–j** (0.90 mmol, 2 equiv). The solution was stirred and maintained at this temperature for 30 min and then was added dropwise (via a syringe) TDAE (0.157 mL, 0.675 mmol, 1.5 equiv). A red color immediately developed with the formation of a white fine precipitate. The solution was vigorously stirred at −20 °C for 1 h and then warmed up to rt for 2 h. After this time TLC analysis (dichloromethane) clearly showed that **2** was totally consumed. The orange-red turbid solution was filtered (to remove the octamethyloxamidinium dibromide) and hydrolyzed with 80 mL of H_2O. The aqueous solution was extracted with toluene (3×40 mL), the combined organic layers washed with H_2O (3×40 mL), and dried over $MgSO_4$. Evaporation of the solvent left an orange viscous liquid as crude product. Purification by silica gel chromatography (dichloromethane/Et_2O, 98/2) gave the corresponding mixture of cis/trans-isomer oxiranes **5a–j** as solids.

*4.2.1. 1,4-Dimethoxy-2-[3-(4-nitrophenyl)oxiran-2-yl]-anthracene-9,10-dione (**5a**)*

trans-isomer: yellow solid; mp 202 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.86 (s, 3H, OCH_3), 3.92 (d, J=1.7 Hz, 1H, CH), 4.06 (s, 3H, OCH_3), 4.31 (d, J=1.7 Hz, 1H, CH), 7.31 (s, 1H, Ar-H), 7.55 (d, J=8.8 Hz, 2H, Ar-H), 7.72–7.77 (m, 2H, Ar-H), 8.14–8.20 (m, 2H, Ar-H), 8.28 (d, J=8.8 Hz, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.9, 58.8, 61.5, 62.6, 114.6, 122.5, 124.2, 126.4, 126.5, 126.7, 127.5, 133.5, 133.7, 133.9, 134.3, 139.4, 143.2, 148.2, 152.4, 157.2, 182.6, 183.1. *cis-isomer*: yellow solid; mp 248 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.89 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 4.62 (d, J=4.4 Hz, 1H, CH), 4.70 (d, J=4.4 Hz, 1H, CH), 7.21 (s, 1H, Ar-H), 7.44 (d, J=8.8 Hz, 2H, Ar-H), 7.67–7.71 (m, 2H, Ar-H), 8.06 (d, J=8.8 Hz, 2H, Ar-H), 8.09–8.14 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 57.3, 59.2, 62.1, 117.8, 122.3, 123.4, 124.2, 126.3, 126.6, 126.9, 127.4, 133.3, 133.4, 133.8, 134.2, 136.7, 140.9, 147.7, 152.4, 156.0, 182.5, 182.9. Anal. Calcd for $C_{24}H_{17}NO_7$: C, 66.82; H, 3.97; N, 3.25. Found: C, 66.76; H, 4.16; N, 3.25.

*4.2.2. 2-[3-(4-Bromophenyl)oxiran-2-yl]-1,4-dimethoxyanthracene-9,10-dione (**5b**)*

trans-isomer: yellow solid; mp 227 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.77 (d, J=1.7 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.28 (d, J=1.7 Hz, 1H, CH), 7.25 (d, J=8.4 Hz, 2H, Ar-H), 7.29 (s, 1H, Ar-H), 7.55 (d, J=8.4 Hz, 2H, Ar-H), 7.70–7.76 (m, 2H, Ar-H), 8.13–8.21 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.3, 62.1, 62.5, 114.6, 122.1, 122.8, 126.4, 126.7, 127.2, 127.4, 132.0, 133.3, 133.7, 133.8, 134.3, 135.1, 140.1, 152.3, 157.2, 182.6, 183.2. *cis-isomer*: yellow solid; mp 175 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.87 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.51 (d, J=4.4 Hz, 1H, CH), 4.65 (d, J=4.4 Hz, 1H, CH), 7.13 (d, J=8.5 Hz, 2H, Ar-H), 7.16 (s, 1H, Ar-H), 7.34 (d, J=8.5 Hz, 2H, Ar-H), 7.67–7.72 (m, 2H, Ar-H), 8.10–8.16 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 56.9, 59.7, 62.1, 118.0, 122.0, 122.2, 126.4, 126.6, 126.8, 128.3, 131.3, 132.6, 133.3, 133.6, 133.7, 134.3, 137.5, 152.6, 156.0, 182.6, 183.1. Anal. Calcd for $C_{24}H_{17}BrO_5$: C, 61.95; H, 3.68. Found: C, 61.60; H, 3.76.

*4.2.3. 4-[3-(9,10-Dihydro-1,4-dimethoxy-9,10-dioxo-anthracen-2-yl)oxiran-2-yl]benzonitrile (**5c**)*

trans-isomer: yellow solid; mp 234 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.83 (s, 3H, OCH_3), 3.86 (d, J=1.8 Hz, 1H, CH), 4.02 (s, 3H, OCH_3), 4.27 (d, J=1.8 Hz, 1H, CH), 7.27 (s, 1H, Ar-H), 7.48 (d, J=8.1 Hz, 2H, Ar-H), 7.68 (d, J=8.1 Hz, 2H, Ar-H), 7.70–7.78 (m, 2H, Ar-H), 8.10–8.18 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.6, 61.6, 62.4, 112.5, 114.5, 118.3, 122.3, 126.2, 126.3, 126.6, 127.3, 132.6, 133.3, 133.6, 133.8, 134.2, 139.4, 141.3, 152.3, 157.1, 182.5, 183.0. *cis-isomer*: yellow solid; mp 175 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.87 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.58 (d, J=4.4 Hz, 1H, CH), 4.68 (d, J=4.4 Hz, 1H, CH), 7.18 (s, 1H, Ar-H), 7.37 (d, J=8.3, 2H, Ar-H), 7.50 (d, J=8.3, 2H, Ar-H), 7.67–7.78 (m, 2H, Ar-H), 8.10–8.21 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 57.2, 59.4, 62.1, 112.1, 117.8, 126.3, 126.6, 127.2, 127.3, 127.8, 131.9, 132.5, 133.3, 133.5, 133.8, 134.2, 136.8, 138.9, 152.4, 156.0, 182.5, 182.9. Anal. Calcd for $C_{25}H_{17}NO_5$: C, 72.99; H, 4.16; N, 3.40. Found: C, 72.68; H, 4.20; N, 3.45.

*4.2.4. 1,4-Dimethoxy-2-(3-phenyloxiran-2-yl)anthracene-9,10-dione (**5d**)*

trans-isomer: yellow solid; mp 183 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.81 (d, J=1.8 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.34 (d, J=1.8 Hz, 1H, CH), 7.31 (s, 1H, Ar-H), 7.36–7.45 (m, 5H, Ar-H), 7.70–7.74 (m, 2H, Ar-H), 8.13–8.21 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.2, 60.4, 62.8, 114.7, 122.0, 125.6, 126.3, 126.7, 127.4, 128.7, 128.8, 133.3, 133.7, 133.8, 134.4, 136.0, 140.6, 152.4, 157.2, 182.6, 183.2. *cis-isomer*: yellow solid; mp 218 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.88 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.57 (d, J=4.5 Hz, 1H, CH), 4.66 (d, J=4.5 Hz, 1H, CH), 7.16 (s, 1H, Ar-H), 7.18–7.25 (m, 5H, Ar-H), 7.67–7.76 (m, 2H, Ar-H), 8.10–8.18 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.6, 56.7, 60.3, 62.0, 118.2, 121.7, 126.5, 126.7, 128.1, 128.7, 128.8, 133.2, 133.6, 133.7, 133.9, 134.0, 134.3, 137.9, 142.4, 152.6, 155.9, 156.3, 182.8, 183.6. Anal. Calcd for $C_{24}H_{18}O_5$: C, 74.60; H, 4.70. Found: C, 74.30; H, 5.18.

*4.2.5. 1,4-Dimethoxy-2-(3-p-tolyloxiran-2-yl)anthracene-9,10-dione (**5e**)*

trans-isomer: yellow solid; mp 188 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.38 (s, 3H, CH), 3.76 (d, J=1.7 Hz, 1H, CH), 3.84 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.32 (d, J=1.7 Hz, 1H, CH), 7.23 (m, 2H, Ar-H), 7.25 (s, 1H, Ar-H), 7.30 (m, 2H, Ar-H), 7.69–7.74 (m, 2H, Ar-H), 8.12–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 21.2, 56.8, 58.1, 62.4, 62.9, 114.6, 121.9, 125.6, 126.3, 126.6, 127.3, 129.4, 133.0, 133.2, 133.7, 133.8, 134.4, 138.7, 140.8, 152.3, 157.2, 182.6, 183.2. *cis-isomer*: yellow solid; mp 179 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 2.23 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.54 (d, J=3.7 Hz, 1H, CH), 4.64 (d, J=3.7 Hz, 1H, CH), 7.00 (d, J=8.1 Hz, 2H, Ar-H), 7.14 (d, J=8.1 Hz, 2H, Ar-H), 7.17 (s, 1H, Ar-H), 7.66–7.71 (m, 2H, Ar-H), 8.10–8.14 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 21.1, 56.7, 56.8, 60.4, 62.1, 118.2, 121.6, 126.3, 126.5, 126.6, 126.7, 128.8, 130.4, 133.2, 133.6, 133.7, 134.3, 137.9, 138.2, 152.7, 155.9, 182.8, 183.1. Anal. Calcd for $C_{25}H_{20}O_5$: C, 74.99; H, 5.03. Found: C, 74.09; H, 5.50.

*4.2.6. 2-[3-(4-Chlorophenyl)oxiran-2-yl]-1,4-dimethoxyanthracene-9,10-dione (**5f**)*

trans-isomer: yellow solid; mp 218 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.78 (d, J=1.8 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.28 (d, J=1.8 Hz, 1H, CH), 7.28 (s, 1H, Ar-H), 7.31 (d, J=8.5 Hz, 2H, Ar-H), 7.39 (d, J=8.5 Hz, 2H, Ar-H), 7.70–7.77 (m, 2H, Ar-H), 8.12–8.20 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.3, 62.1, 62.4, 114.6, 122.1, 126.4, 126.7, 127.0, 127.4, 129.0, 133.3, 133.7, 133.8, 134.4, 134.6, 134.7, 140.2, 152.3, 157.2, 182.6, 183.2. *cis-isomer*: yellow solid; mp 184 °C; ^{1}H NMR (50 MHz, $CDCl_3$) δ_H 3.87 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.52 (d, J=4.4 Hz, 1H, CH), 4.63 (d, J=4.4 Hz, 1H, CH), 7.15 (s, 1H, Ar-H), 7.18 (m, 4H, Ar-H), 7.66–7.71 (m, 2H, Ar-H), 8.08–8.14 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.7, 56.8, 59.6, 62.0, 118.0, 121.9, 126.3, 126.6, 126.8, 127.9, 128.4, 132.0, 133.2, 133.6, 133.7, 134.0, 134.3, 137.5, 152.5, 155.9, 182.6, 183.0. Anal. Calcd for $C_{24}H_{17}ClO_5$: C, 68.50; H, 4.07. Found: C, 68.31; H, 4.09.

*4.2.7. 2-{3-[4-(Trifluoromethyl)phenyl]oxiran-2-yl}-1,4-dimethoxyanthracene-9,10-dione (**5g**)*

trans-isomer: yellow solid; mp 217 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.84 (s, 3H, OCH_3), 3.86 (d, J=1.6 Hz, 1H, CH), 4.03 (s, 3H, CH_3), 4.28 (d, J=1.6 Hz, 1H, CH), 7.28 (s, 1H, Ar-H), 7.49 (d, J=8.0 Hz, 2H, Ar-H), 7.67 (d, J=8.0 Hz, 2H, Ar-H), 7.70–7.77 (m, 2H, Ar-H), 8.12–8.19 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.4, 61.8, 62.4, 114.6, 121.2, 124.7, 125.7, 125.8, 126.3, 126.6, 130.9, 133.3, 133.6, 133.7, 134.3, 139.8, 140.0, 152.3, 157.1, 182.5, 183.0. *cis-isomer*: yellow solid; mp 194 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.88 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.59 (d, J=4.1 Hz, 1H, CH), 4.68 (d, J=4.1 Hz, 1H, CH), 7.18 (s, 1H, Ar-H), 7.47 (d, J=7.9 Hz, 2H, Ar-H), 7.51 (d, J=7.9 Hz, 2H, Ar-H), 7.65–7.77 (m, 2H, Ar-H), 8.10–8.18 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 57.0, 59.6, 62.1, 118.0, 122.1, 125.2, 126.4, 126.6, 126.8, 126.9, 127.0, 130.4, 133.3, 133.6, 133.7, 134.3, 137.1, 137.6, 152.6, 156.0, 182.6, 183.0. Anal. Calcd for $C_{25}H_{17}F_3O_5$: C, 66.08; H, 3.77. Found: C, 65.90; H, 3.97.

*4.2.8. 1,4-Dimethoxy-2-[3-(2-nitrophenyl)oxiran-2-yl]-anthracene-9,10-dione (**5h**)*

trans-isomer: yellow solid; mp 224 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.90 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 4.32 (d, J=1.8 Hz, 1H, CH), 4.52 (d, J=1.8 Hz, 1H, CH), 7.34 (s, 1H, Ar-H), 7.57 (m, 2H, Ar-H), 7.73–7.76 (m, 4H, Ar-H), 8.15–8.23 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.9, 57.6, 60.3, 62.7, 114.9, 122.5, 125.0, 126.5, 126.7, 127.0, 127.5, 129.2, 132.9, 133.4, 133.7, 133.8, 134.4, 134.6, 139.5, 147.8, 153.1, 157.1, 182.7, 183.2. Anal. Calcd for $C_{24}H_{17}NO_7$: C, 66.82; H, 3.97; N, 3.25. Found: C, 66.30; H, 4.01; N, 3.21.

*4.2.9. 2-[3-(2-Bromophenyl)oxiran-2-yl]-1,4-dimethoxyanthracene-9,10-dione (**5i**)*

trans-isomer: yellow solid; mp 176 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.94 (s, 3H, OCH_3), 4.06 (s, 3H, CH_3), 4.17 (d, J=1.9 Hz, 1H, CH), 4.25 (d, J=1.9 Hz, 1H, CH), 7.24–7.31 (m, 2H, Ar-H), 7.33 (s, 1H, Ar-H), 7.40–7.61 (m, 2H, Ar-H), 7.71–7.76 (m, 2H, Ar-H), 8.15–8.22 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.9, 57.8, 62.4, 62.8, 114.7, 122.3, 122.6, 126.1, 126.4, 126.7, 127.5, 127.9, 129.9, 132.6, 133.3, 133.7, 133.8, 134.4, 135.7, 140.1, 152.7, 157.2, 182.7, 183.2. Anal. Calcd for $C_{24}H_{17}BrO_5$: C, 61.95; H, 3.68. Found: C, 62.04; H, 3.86.

*4.2.10. 1,4-Dimethoxy-2-[3-(3-nitrophenyl)oxiran-2-yl]-anthracene-9,10-dione (**5j**)*

trans-isomer: yellow solid; mp 170 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.85 (s, 3H, OCH_3), 3.92 (d, J=1.7 Hz, 1H, CH), 4.03 (s, 3H, OCH_3), 4.31 (d, J=1.7 Hz, 1H, CH), 7.28 (s, 1H, Ar-H), 7.59–7.65 (m, 1H, Ar-H), 7.69–7.74 (m, 4H, Ar-H), 8.11–8.22 (m, 2H, Ar-H), 8.24 (s, 1H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 58.5, 61.3, 62.5, 114.6, 120.6, 122.3, 123.6, 126.4, 126.6, 127.3, 129.9, 131.5, 133.3, 133.7, 133.8, 134.3, 138.4, 139.4, 148.7, 152.4, 157.1, 182.5, 183.0. *cis-isomer*: yellow solid; mp 243 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ_H 3.88 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.64 (d, J=4.3 Hz, 1H, CH), 4.72 (d, J=4.3 Hz, 1H, CH), 7.29 (s, 1H, Ar-H), 7.36–7.44 (m, 1H, Ar-H), 7.59–7.64 (m, 1H, Ar-H), 7.66–7.71 (m, 2H, Ar-H), 8.06–8.10 (m, 2H, Ar-H), 8.11–8.18 (m, 2H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C 56.8, 57.5, 59.1, 62.1, 117.7, 121.5, 122.1, 123.2, 126.4, 126.6, 126.9, 129.3, 132.6, 133.3, 133.5, 133.8, 134.3, 135.9, 136.6, 148.0, 152.4, 156.1, 182.6, 183.0. Anal. Calcd for $C_{24}H_{17}NO_7$: C, 66.82; H, 3.97; N, 3.25. Found: C, 66.33; H, 4.46; N, 3.18.

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