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New Highly Diastereoselective Perkin/Michael Addition Domino Reaction between Homophthalic Anhydride and Aromatic Aldehydes: A Facile Approach to Blue-Fluorescent Dibenzo[*c*,*h*]chromenones

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Dedicated to Professor Mariana Palamareva on the occasion of her 70th birthday

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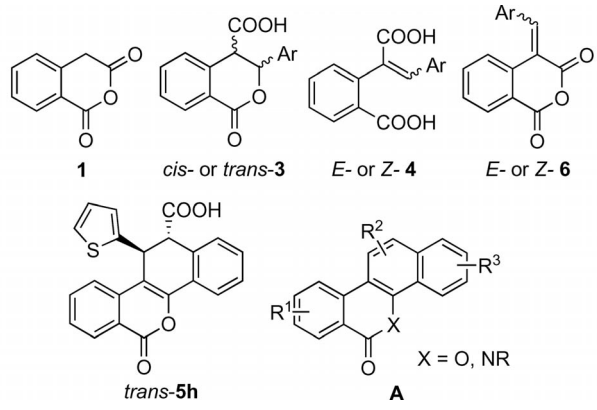
A series of new *trans*-11-aryl-6-oxo-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic acids has been synthesised through a new Perkin/Michael addition domino reaction between homophthalic anhydride and aromatic aldehydes. The synthesis is straightforward and gives good overall yields by taking into account the concomitant formation of four C–C, C–O and C=C bonds. The structures of the newly synthesised compounds were established by spectroscopic methods (^{1}H NMR, ^{13}C NMR and IR) and X-ray diffraction analysis, and the fluorescent properties were investigated. A probable reaction mechanism including three proven intermediates is proposed.

Introduction

For a long time, homophthalic anhydride (**1**) has been known as a useful reagent for the synthesis of various heterocyclic compounds. In particular, homophthalic anhydrides have been treated successfully with compounds containing polar double bonds, including aldehydes and ketones,[1] imines,[2] acyl chlorides and anhydrides,[3] alkenes, and alkynes[4] etc., giving rise to products of different heterocyclic families. These reactions can be considered as tandem (domino) reactions, because several transformations take place in a single synthetic step, affording products of varying complexity. The domino reactions typically consist of an initial reaction that produces an intermediate that undergoes further transformations with strategically positioned reactive centres either in the same molecule or with other compounds in the reaction mixture, after the initial transformation takes place.[5] Having both an activated methylene group and a cyclic anhydride fragment in its structure, **1** can thus be considered to be a very attractive starting material for a range of domino transformations[6] because it is able to act both as a C-nucleophile and as an acylating agent. A comprehensive review on the role of cyclic anhydrides (including **1**) in the formation of polycyclic compounds was recently published by Gonzales–López and Shaw.[7]



Amongst the above mentioned reactions of **1**, however, the reaction between homophthalic anhydrides and carbonyl compounds **2** has been less explored. Aromatic aldehydes and ketones have been demonstrated to react with **1** under Lewis acid or Lewis base mediated conditions,[1] affording predominantly the corresponding diastereomeric mixture of *cis*- and *trans*-3-substituted 3,4-dihydroisocoumarin-4-carboxylic acids **3**. Nevertheless, in some cases, by-products of concurrent reactions are observed in quantities that seem to depend on reaction conditions such as solvent, temperature, catalyst, etc. For example, small amounts of 2-(carboxyphenyl)cinnamic acids **4a** (depending on the aldehyde type) have been detected in the presence of 4-(di-

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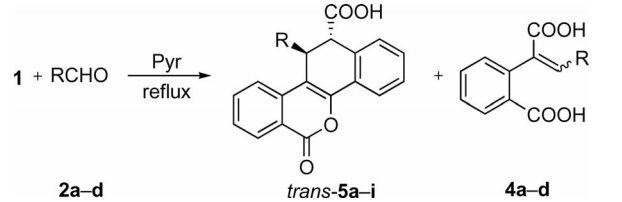
methylamino)pyridine (DMAP) as catalyst[1a] and not in the presence of $BF_3{\cdot}Et_2O$ complex.[1b] Furthermore, when the reaction between **1** and benzaldehyde was carried out in the presence of a strong base (NaH) for 33 h, formation of product **4a** predominated (85%).[1d]

Additionally, we have previously reported[1a] that the reaction between **1** and thiophene-2-carbaldehyde (**2h**) in pyridine, acting both as a solvent and a basic catalyst, proceeds at room temperature in four parallel directions: mainly cycloaddition to 3,4-dihydroisocoumarin acid *trans*-**3h**, but also Perkin reaction to acyclic diacid **4h**, an unknown reaction to form dibenzo[*c*,*h*]chromene **5h**, and a Knoevenagel condensation to give 4-substituted homophthalic anhydride **6h**, in a percent ratio amongst the products of 34:25:15:27, respectively. Whereas the formation of **3h**, **4h** and **6h** is expected, the presence of a by-product containing the dibenzo[*c*,*h*]chromene skeleton *trans*-**5h** (isolated and characterised as methyl ester) is unexpected, because, to the best of our knowledge, there are no protocols in the literature for the preparation of this type of compounds in a reaction between homophthalic anhydride and carbonyl compounds. It is noteworthy that the formation of a compound of type **5** was observed only in the reaction between **1** and thiophene-2-carbaldehyde at room temperature in pyridine. Under the same conditions, other aldehydes **2** react smoothly with **1** to give products of type **3** and **4** only. This fact prompted us to examine the above-mentioned reaction further to direct it to a one-step, selective preparation of compounds containing the dibenzo[*c*,*h*]chromene backbone. Compounds of this type are interesting from a synthetic point of view because of their conversion into benzo[*c*]-phenantridine alkaloids or into different antibiotics[8] with general structure **A** (see above). Thus, as part of our ongoing program on the synthesis of new heterocyclic compounds from cyclic anhydrides,[1a,2d–2i,9] in this paper we present a one-pot procedure for the preparation of (±)-*trans*-11-aryl-11,12-dihydro-6-oxo-6*H*-dibenzo[*c*,*h*]-chromene-12-carboxylic acids by a new Perkin/Michael addition domino reaction between homophthalic anhydride and aromatic aldehydes, both being commercial products.

Results and Discussion

In our attempts to find appropriate conditions for the preparation of compounds of type **5**, first, the reaction between a two- or three-fold molar excess of **1** (the stoichiometry of the reaction requires **1** to be in excess) and aromatic aldehydes **2a**–**d** was carried out in boiling pyridine (Table 1). Thus, by favouring thermodynamic control of the reaction through the application of increased temperature, we tried to eliminate the formation of **3**, because the corresponding acids of type **3** seem to be kinetically controlled products.[1d] To examine the influence of the substituents on the reactivity, aromatic aldehydes containing electron-donating or -withdrawing groups (benzaldehyde, *p*-methoxybenzaldehyde, piperonal and *p*-nitrobenzaldehyde, **2a**–**d**, respectively) were used as model compounds (Table 1, Entries 1–4). The process was monitored by means of thin layer chromatography (TLC). At the end of the reaction the products formed were identified as the dibenzo[*c*,*h*]-chromenes **5a**–**d** and Perkin-type compounds **4a**–**d**, which were formed in a ratio that depended on the molar excess of **1**. Table 1 shows the yields of compounds **5** after isolation and recrystallisation when two- and three-fold molar excess of **1** were used. It is noteworthy that the product ratio of **4**/**5** was changed from 1:1 with 2 equiv. of **1** to 1:4 (in favour of **5**) with threefold molar excess of **1**, regardless of the aldehyde type. On the one hand, this increase in yield in the latter case identified suitable conditions for the preparation of the target compounds **5a**–**h** (Table 1, entries 1–8) and, on the other hand, suggests that compounds of type **4** could be assumed as probable intermediates in the reaction, reacting with a second molecule of **1** to give **5** (the probable mechanism is discussed below).

Table 1. Effect of the molar ratio of homophthalic anhydride (**1**) upon the yield of **5**.



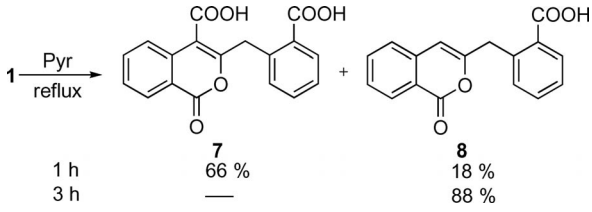
2a–d *trans*-**5a–i** **4a–d**

Entry	**2**	RCHO	Yield of **5** [%][a]	
			3 mol of **1**	2 mol of **1**
1	**a**	benzaldehyde	86 (70)	48 (31)
2	**b**	*p*-methoxybenzaldehyde	80 (75)	55 (45)
3	**c**	piperonal[b]	65 (56)	50 (34)
4	**d**	*p*-nitrobenzaldehyde	72 (65)	52 (38)
5	**e**	2,4-dimethoxybenzaldehyde	50 (33)	n.a.
6	**f**	3,4-dimethoxybenzaldehyde	75 (47)	n.a.
7	**g**	2,4-dichlorobenzaldehyde	62 (47)	n.a.
8	**h**	thiophene-2-carbaldehyde	75 (59)	n.a.
9	**i**	paraformaldehyde	44 (25)	n.a.
10	**j**	octanal[c]	–	–
11	**k**	undecanal[c]	–	–

[a] Yield after recrystallisation are given in parentheses. [b] Benzo[1,3]dioxole-5-carbaldehyde. [c] No formation of **4** or **5** was observed.

Furthermore, two alternative ways of mixing the starting materials were examined: portionwise addition of an aldehyde to a solution of homophthalic anhydride in pyridine, and vice versa. Improved reaction outcomes were observed in the case of portionwise addition of **1**, resulting in the formation of **4** and **5** as the only products. In contrast, when a solution of the aldehyde was added dropwise to a boiling solution of **1** in pyridine, a concurrent dimerisation reaction took place (as shown in Scheme 1), and the isocoumarin **8** was isolated as a major product. Its structure (as a methyl ester) was unequivocally established recently by means of X-ray diffraction.[9e] It was previously reported[3b,6f] that **8** was isolated as a by-product in the reaction of homophthalic anhydrides in basic media, and a dimerisation reaction of the anhydride was proposed for its formation,

which suggests that the dimerisation of **1** is probably faster than the formation of the intermediate that has to react to **5**. To verify this independently, **1** was heated to reflux in pyridine, which first gave a mixture of isocoumarins **7** and **8** after 1 h, and then **8**, quantitatively, after 3 h of heating (Scheme 1). Consequently, the order of mixing the reagents is of great importance for successful reaction.

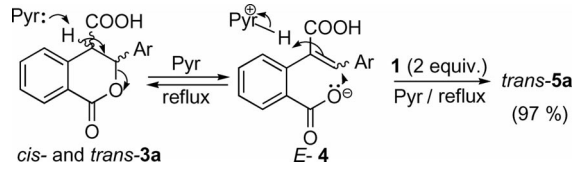


Scheme 1. Dimerisation of **1** in pyridine leading to isocoumarins **7** and **8**.

To study the effects of the aldehyde on the reaction, **1** was further treated with a range of aliphatic aldehydes (Table 1, Entries 9–11). Only paraformaldehyde (the precursor for formation of formaldehyde in situ) reacted with **1** under the reaction conditions, to give a mixture of the corresponding dibenzo[*c*,*h*]chromene **5i** and the dimerisation product **8**. Octanal and undecanal did not produce **5**, with the predominant products formed in these cases being the isocoumarins **7** and **8**. These results suggest that only aldehydes with no α-hydrogen atoms can be used in the reaction.

The separation of **4** and **5** at the end of the reaction was achieved by extraction with ethyl acetate at pH = 8. At this pH value the acyclic acids **4** are soluble in water, whereas the dibenzo[*c*,*h*]chromene compounds **5** remain in the organic layer. This fact can be attributed to the larger organic moiety of **5** in comparison to **4** and to the presence of two carboxylate groups in **4**, which contribute to their higher solubility in water than that of **5**. The structure of compounds **5a**–**i** was established by spectroscopic analysis (^{1}H NMR, ^{13}C NMR and IR) and by microanalysis. The signals for the methyne protons 11-H and 12-H were observed as singlets in the region δ = 3.92–4.07 and 4.90–5.11 ppm, respectively, which is in agreement with a torsion angle of approximately 80–90°.[10] This allowed a *trans* configuration to be attributed to compounds **5a**–**h**, with an antiperiplanar (diaxial) conformation being adopted by the bulky substituents (aryl and carboxylate groups) at C-11 and C-12. The proposed *trans* configuration was further confirmed independently by X-ray diffraction analysis of **5a** (Figure 1, left; for details see the Supporting Information). The data is in agreement with a previously reported X-ray study of the methyl ester of **5h**,[9f] which showed that it is a conformationally rigid compound. Furthermore, the observed $^3J_{11,12}$ coupling constant of 1.2 Hz did not depend on the polarity of the solvent used for recording the NMR spectra, in contrast to the conformationally more flexible 3,4-disubstituted 3,4-dihydroisocoumarin.[9g] The data obtained shows that the reaction between **1** and **2**, under the conditions used, is highly diastereoselective towards the target compounds **5** with *trans* configuration. This stereocontrol suggests that if chiral catalysts are used, the corresponding enantiopure derivatives could be obtained; this proposal is currently under investigation.

The assumption mentioned above that **4** can be an intermediate in the reaction scheme leading to **5** prompted us to investigate the thermal stability of acids **3**. Such acids are the main products when the reaction between **1** and aromatic aldehydes is performed under mild conditions, e.g., low temperature and short reaction time, regardless of the catalyst. Thus, when **3a** was heated in pyridine, rapid lactone ring opening occurred, resulting in the formation of an equilibrium mixture of **3** and **4** (in favour of **4**), with no other observable products (Scheme 2).



Scheme 2. One-pot transformation of **3** to **5**, showing the equilibrium between **3** and **4**.

Subsequent addition of **1** (two-fold molar excess) to the reaction mixture led to the quantitative formation of *trans*-**5a**. Thus, acids of type **3** could be considered to be intermediates in the formation of **4**, and could participate further

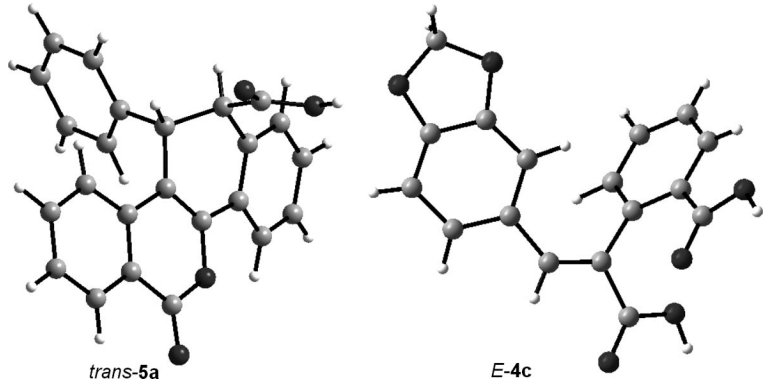


Figure 1. X-ray crystal structures: *trans*-**5a**, showing synclinal 11-H and 12-H atoms; *E*-**4c**, showing the *cis* orientation of the phenyl substituents.

in a reaction leading to **5**. It is noteworthy that **4** was obtained as a single diastereomer with (*E*) configuration, regardless of the relative configuration of the starting 3,4-dihydroisocoumarin acid **3a**. The existence of **4a** as the (*E*) diastereomer was established by means of a comprehensive NMR study, and was further proven for **4c**, which is another compound of this type, by X-ray diffraction analysis. The latter was obtained from **3c** in boiling pyridine (Figure 1, right; for details see the Supporting Information).

Subsequent participation of compounds of type **4** in the reaction scheme as intermediates was further studied by carrying out a reaction between **4a** and homophthalic anhydride in boiling pyridine. At the end of the reaction (which was monitored by TLC), the only observable product was the corresponding acid *trans*-**5a**. It should be mentioned that a twofold molar excess of **1** was still needed for full conversion of **4**, which suggests that an additional interaction between **4** and **1** takes place. To further clarify the reaction scheme, dimethyl ester **9a**, monomethyl ester **10a** and cinnamic acid (Table 2) were submitted to the same conditions, but no reaction took place. Consequently, for the reaction to proceed successfully, two free carboxylate groups are needed. Thus, compounds **6** (Scheme 3), which were previously considered to be by-products, can be assumed to be a third intermediate, which needs 1 equiv. of **1** for the formation from **4**. To verify this hypothesis, **4a** was heated to reflux in acetic anhydride. Under these conditions, **6a** was obtained as a single product, which was subsequently transformed into *trans*-**5a** (consuming 1 equiv. of **1**; Scheme 3). This result supports the participation of compounds of type **6** as intermediates in the reaction.

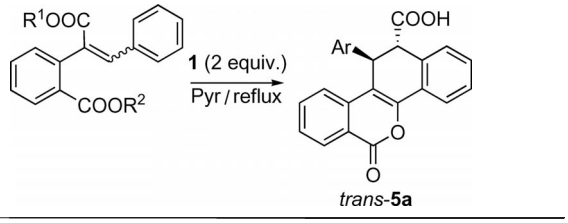
By considering the above reasoning, a probable reaction mechanism can be put forward that involves pyridine acting as a base to give the protonated form that is capable of proton liberation (Scheme 4); it should be mentioned that not all the acid–base reactions are depicted in the this scheme.

In the first step, homophthalic anhydride reacts in a Perkin-type reaction with an aldehyde to give a mixture of *cis*- and *trans*-3-substituted 3,4-dihydroisocoumarin-4-carboxylic acids **3**, which (as shown in Scheme 2) undergo rapid lactone ring opening leading to an equilibrium mixture with **4**. The latter reacts further with a second molecule of homophthalic anhydride (according to Scheme 3) to give the 4-arylidenehomophthalic anhydride **6**. This step can be considered as an activation of **4**, which facilitates participation in the Michael addition reaction that takes place in the next step. The resulting intermediate **10** yields the further intermediate **11** after intramolecular acylation. Subsequent pyridine-supported anhydride ring opening of **11** leads to intermediate **12**, which undergoes an easy decarboxylation as a β-oxo carboxylic acid and, after intramolecular lactionisation, forms compound **5**. Thus, according to the proposed mechanism, the target dibenzo[*c*,*h*]chromene compounds *trans*-**5a**–**i** are formed through a seven-step reaction scheme with concomitant formation of four C–C, C–O and C=C bonds in overall yields of 50–86%.

These studies demonstrate that domino reactions can be used as a powerful bond-forming tool that allows the preparation of polycyclic compounds by connecting several components in a one-pot, sequential and efficient manner.[5]

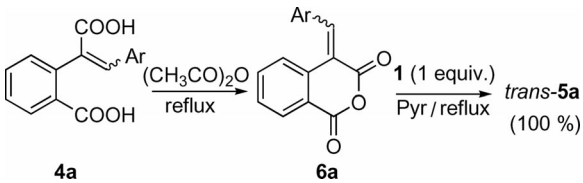
The planar structure of compounds **5a**–**i** suggests that they should be photochemically active.[11a] Moreover, it has been reported[11b] that compounds containing a 6*H*-benzo[*c*]chromen-6-one moiety exhibit fluorescence in the visible region. This prompted us to carry out a preliminary study on their fluorescence properties. The results obtained for **5a**–**d** (labelled as **I**, **II**, **III** and **IV**, respectively) are depicted in Figure 2 (for further details see the Supporting Information). It should be noted that compounds **5a**–**c** show blue fluorescence, which deserves additional investigation because blue fluorescence is rarer than fluorescence at longer wavelengths.[11b] As seen in Figure 2, an aryl substituent at position 11 has little influence on the absorption and fluorescence maxima, except in the case of **5d** (**III**) in which the presence of a nitro group causes a hypsochromic shift of the fluorescence into the UV, rather than in the visible region. The Stokes shifts are in the range 76–117 nm, which suggests structural differences between the species in both the ground and excited states, which deserve additional comprehensive examination. However, the combination of fluorescence properties and a carboxylic function in **5** allowed us to speculate that these compounds can be useful as fluorescent markers for different molecules bearing functional groups capable of bonding with the carboxylic group in **5**.

Table 2. Effect of carboxylate groups of **4** on the yield of **5**.

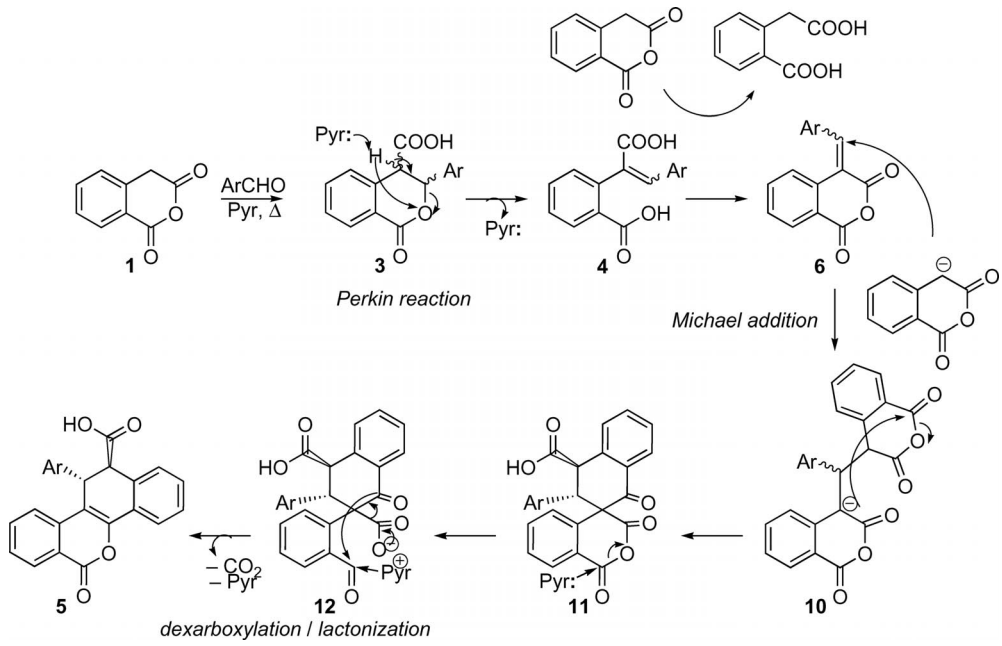


Entry	Reagent	R^1	R^2	Product
1	**4a**[a]	H	H	**5a** (100%)
2	**9a**[b]	CH_3	CH_3	–
3	**10a**[c]	CH_3	H	–
4	cinnamic acid	H		–

[a] (*E*)-2-(1-Carboxy-2-phenylvinyl)benzoic acid. [b] Methyl (*E*)-2-(3-methoxy-3-oxo-1-phenylprop-1-en-2-yl)benzoate. [c] (*E*)-2-(3-Methoxy-3-oxo-1-phenylprop-1-en-2-yl)benzoic acid.



Scheme 3. Synthesis of *trans*-**5a** from **6a**, suggesting the participation of compounds of type **6** as intermediates in the reaction.



Scheme 4. Proposed reaction mechanism for the developed Perkin/Michael addition domino reaction between homophthalic anhydride and aromatic aldehydes.

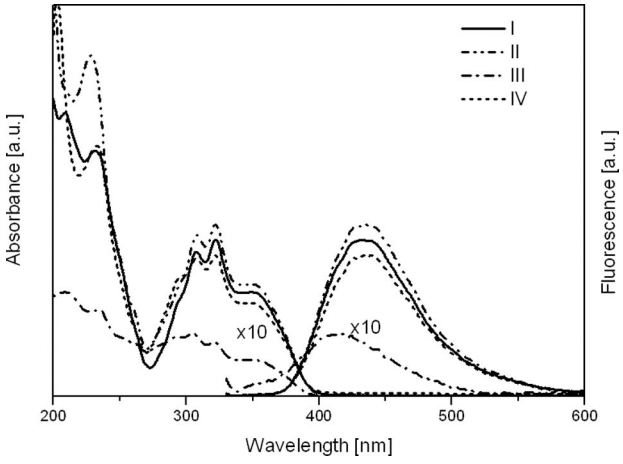


Figure 2. Absorbance and fluorescence spectra of compounds **5a**–**d**.

Conclusions

We present a new, one-pot protocol for the synthesis of blue-fluorescent *trans*-11-aryl-11,12-dihydro-6-oxo-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic acid derivatives by a Perkin/Michael addition domino reaction between homophthalic anhydride and aromatic aldehydes in pyridine, being both a basic catalyst and a solvent. The reaction is highly diastereoselective towards the *trans* cycloadducts **5a**–**h**. A probable reaction mechanism is proposed that includes Perkin-type compounds and their intra- and intermolecular anhydrides as intermediates. A systematic study of the scope, limitations and stereochemical course of this promising method, as well as possible chemical transformation of the resulting dibenzo[*c*,*h*]chromene compounds is in progress.

Experimental Section

General: Melting points were determined with a Kofler microscope Boetius PHMK 0.5. IR spectra were acquired in chloroform, if not stated otherwise, with a Specord 75 and are reported in cm^{-1}. NMR spectra were obtained with a Bruker DRX 250 NMR spectrometer at 250.13/62.5 MHz and Bruker Avance 600 spectrometer at 600/150 MHz for ^{1}H and ^{13}C, respectively, in the given solvent. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard. Elemental analyses were obtained at the Faculty of Chemistry, University of Sofia. TLC was performed on precoated 0.2 mm Merck silica gel 60F254 plates.

X-ray Data for *trans*-5a and *E*-4c: CCDC-773190 (*trans*-**5a**) and -773191 (*E*-**4c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Preparation of 11-Substituted 6-Oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acids 5a–i: To a refluxing solution of the corresponding aldehyde **2a**–**i** in anhydrous pyridine, homophthalic anhydride (3 equiv.) was added portionwise within 3 h (1 equiv. per 1 h). At the end of the reaction (monitored by TLC), the mixture was diluted with ethyl acetate and washed with 10% hydrochloric acid to remove the pyridine. The organic layer was combined with water and the pH was adjusted to 8 with 10% $NaHCO_3$. At this pH value the acyclic acids **4** were soluble in water, whereas the dibenzo[*c*,*h*]chromene compounds **5a**–**i** remained in the organic layer. After the separation of the two layers, the organic layer was washed with water, dried with sodium sulfate and the solvent was then evaporated under reduced pressure. The products **5a**–**i** were isolated after recrystallisation of the residue from methanol/dichloromethane.

(±)-*trans*-6-Oxo-11-phenyl-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5a): From the reaction of homophthalic anhydride (2.641 g, 16.287 mmol) and benzaldehyde (0.575 g, 0.55 mL, 5.423 mmol) in pyridine (10 mL), an oil (1.728 g, 86%) was iso-

lated, which gave, after recrystallisation, colourless crystals containing 1 equiv. CH_3OH. Yield: 1.402 g (70%); m.p. 239–241 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 0.9 Hz, 1 H, ArH), 8.01 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 7.63 (ddd, $^3J_{H,H}$ = 8.3, $^3J_{H,H}$ = 7.3, $^4J_{H,H}$ = 1.4 Hz, 1 H, ArH), 7.52 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, ArH), 7.45 (dt, $^3J_{H,H}$ = 7.2, $^4J_{H,H}$ = 1.1 Hz, 1 H, ArH), 7.42 (ddd, $^3J_{H,H}$ = 7.7, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.2 Hz, 1 H, ArH), 7.31 (dt, $^3J_{H,H}$ = 7.5, $^4J_{H,H}$ = 1.3 Hz, 1 H, ArH), 7.22 (d, $^3J_{H,H}$ = 7.1 Hz, 1 H, ArH), 7.20–7.13 (m, 5 H, $CH_{11\text{-}Ph}$), 5.07 (s, 1 H, 11-H), 3.95 (s, 1 H, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 173.6 (CO_{COOH}), 161.9 ($CO_{lactone}$), 148.3, 140.1, 136.7, 134.9 (CH_{Ar}), 131.4, 130.5 (CH_{Ar}), 129.9 (CH_{Ar}), 129.6 (CH_{Ar}), 128.8 (CH_{Ar}), 128.2 (CH_{Ar}), 128.0, 127.7 (CH_{Ar}), 127.2 (CH_{Ar}), 122.8 (CH_{Ar}), 122.7 (CH_{Ar}), 121.1, 110.3, 52.1 (C-12), 40.4 (C-11) ppm. IR (Nujol): $\tilde{\nu}$ = 1710 (C=O), 1700 (C=O), 1630 (C=C) cm^{-1}. $C_{24}H_{16}O_4 \cdot CH_3OH$ (400.42): calcd. C 74.99, H 5.03, O 19.98; found C 75.39, H 5.14, O 19.47.

(±)-*trans*-11-(4-Methoxyphenyl)-6-oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5b): From the reaction of homophthalic anhydride (2.027 g, 12.501 mmol) and 4-methoxybenzaldehyde (0.568 g, 0.51 mL, 4.171 mmol) in pyridine (10 mL), an oil (1.323 g, 80%) was isolated, which gave, after recrystallisation, colourless crystals containing 0.5 equiv. CH_3OH. Yield: 1.253 g (75%); m.p. 158–160 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 8.00 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, ArH), 7.65–7.62 (m, 1 H, ArH), 7.52 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH), 7.46–7.43 (m, $^4J_{H,H}$ = 1.1 Hz, 1 H, ArH), 7.41 (dt, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 1.1 Hz, 1 H, ArH), 7.32–7.30 (m, 1 H, ArH), 7.22 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 7.05 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, $CH_{11\text{-}Ph}$), 6.71 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, $CH_{11\text{-}Ph}$), 5.01 (s, 1 H, 11-H), 3.92 (s, 1 H, 12-H), 3.69 (s, 3 H, OCH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 173.7 (CO_{COOH}), 161.9 ($CO_{lactone}$), 158.6, 148.1, 136.7, 134.9 (CH_{Ar}), 132.0, 131.5, 130.6 (CH_{Ar}), 130.0 (CH_{Ar}), 129.6 (CH_{Ar}), 128.3 ($CH_{11\text{-}Ph}$), 128.2, 128.0, 127.7 (CH_{Ar}), 122.9 (CH_{Ar}), 122.7 (CH_{Ar}), 121.2, 114.1 ($CH_{11\text{-}Ph}$), 110.7, 55.0 (OCH_3), 52.3 (C-12), 39.7 (C-11) ppm. IR (Nujol): $\tilde{\nu}$ = 1690 (C=O), 1640 (C=C) cm^{-1}. $C_{25}H_{18}O_5 \cdot 0.5CH_3OH$ (414.43): calcd. C 73.90, H 4.86, O 21.23; found C 74.16, H 4.76, O 21.08.

(±)-*trans*-11-(Benzo[*d*][1,3]dioxol-5-yl)-6-oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5c): From the reaction of homophthalic anhydride (0.534 g, 3.293 mmol) and benzo[*d*][1,3]-dioxol-5-carbaldehyde (0.165 g, 1.099 mmol) in pyridine (3 mL), an oil (0.296 g, 65%) was isolated, which gave, after recrystallisation, colourless crystals. Yield: 0.252 g (56%); m.p. 246–248 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 7.99 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, ArH), 7.67–7.64 (m, 1 H, ArH), 7.52 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, ArH), 7.45 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, ArH), 7.41 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, ArH), 7.31 (ddd, $^3J_{H,H}$ = 7.4, $^3J_{H,H}$ = 7.3, $^4J_{H,H}$ = 0.8 Hz, 1 H, ArH), 7.24 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 6.66 (dd, $^3J_{H,H}$ = 8.1, $^4J_{H,H}$ = 1.5 Hz, 1 H, $CH_{11\text{-}Ph}$), 6.62 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, $CH_{11\text{-}Ph}$), 6.56 (d, $^4J_{H,H}$ = 1.5 Hz, 1 H, $CH_{11\text{-}Ph}$), 5.85 (d, $^3J_{H,H}$ = 3.1 Hz, 2 H, $CH_{11\text{-}Ph}$), 4.98 (s, 1 H, 11-H), 3.92 (s, 1 H, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 173.5 (CO_{COOH}), 161.7 ($CO_{lactone}$), 148.1, 147.7, 146.5, 136.6, 134.8 (CH_{Ar}), 133.9, 131.3, 130.5 (CH_{Ar}), 129.9 (CH_{Ar}), 129.6 (CH_{Ar}), 128.2 (CH_{Ar}), 127.8, 127.7 (CH_{Ar}), 122.8 (CH_{Ar}), 122.7 (CH_{Ar}), 121.1, 120.3 (CH_{Ar}), 110.4, 108.4 (CH_{Ar}), 107.4 (CH_{Ar}), 100.8 (CH_2), 52.2 (C-12), 40.0 (C-11) ppm. IR (Nujol): $\tilde{\nu}$ = 1730 (C=O), 1680 (C=O), 1650 (C=C) cm^{-1}. $C_{25}H_{16}O_6$ (412.39): calcd. C 72.81, H 3.91, O 23.28; found C 72.92, H 4.19, O 22.89.

(±)-*trans*-11-(4-Nitrophenyl)-6-oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]-chromene-12-carboxylic Acid (5d): From the reaction of homophthalic anhydride (1.973 g, 12.168 mmol) and 4-nitrobenzaldehyde (0.611 g, 4.043 mmol) in pyridine (10 mL), an oil (1.216 g, 72%) was isolated, which gave, after recrystallisation, colourless crystals. Yield: 1.101 g (65%); m.p. 237–239 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.35 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 0.7 Hz, 1 H, ArH), 8.05 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, $CH_{11\text{-}Ph}$), 8.01 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, ArH), 7.68–7.65 (m, 1 H, ArH), 7.48 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, ArH), 7.45–7.43 (m, 2 H, ArH), 7.36–7.32 (m, 3 H, ArH), 7.23 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 5.20 (s, 1 H, 11-H), 3.93 (s, 1 H, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 172.7 (CO_{COOH}), 161.4 ($CO_{lactone}$), 148.6, 147.6, 146.9, 136.0, 135.0 (CH_{Ar}), 130.6, 130.5 (CH_{Ar}), 130.1 (CH_{Ar}), 129.9 (CH_{Ar}), 128.5 (CH_{Ar}), 128.2 (CH_{Ar}), 128.0 (CH_{Ar}), 127.5, 124.0 (CH_{Ar}), 122.8 (CH_{Ar}), 122.2 (CH_{Ar}), 121.0, 109.2, 51.6 (C-12), 40.0 (C-11) ppm. IR (Nujol): $\tilde{\nu}$ = 1720 (C=O), 1680 (C=O) cm^{-1}. $C_{24}H_{15}NO_6$ (413.38): calcd. C 69.73, H 3.66, N 3.39, O 23.22; found C 69.71, H 3.91, N 3.45, O 22.93.

(±)-*trans*-11-(2,4-Dimethoxyphenyl)-6-oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5e): From the reaction of homophthalic anhydride (0.568 g, 3.501 mmol) and 2,4-dimethoxybenzaldehyde (0.194 g, 1.167 mmol), an oil (0.248 g, 50%) was isolated. This compound was obtained as colourless crystals containing 0.5 equiv. CH_3OH. Yield: 0.166 g (33%); m.p. 144–146 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.32 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 0.9 Hz, 1 H, ArH), 7.97 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, ArH), 7.61–7.58 (m, 1 H, ArH), 7.42 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, ArH), 7.39 (dt, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 7.36 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH), 7.27–7.25 (m, 1 H, ArH), 7.16 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 6.49 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H, $CH_{11\text{-}Ph}$), 6.48 (d, $^4J_{H,H}$ = 2.8 Hz, 1 H, $CH_{11\text{-}Ph}$), 6.07 (dd, $^3J_{H,H}$ = 8.6, $^4J_{H,H}$ = 2.4 Hz, 1 H, $CH_{11\text{-}Ph}$), 5.33 (s, 1 H, 11-H), 3.95 (s, 3 H, OCH_3), 3.93 (s, 1 H, 12-H), 3.65 (s, 3 H, OCH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 177.7 (CO_{COOH}), 162.0 ($CO_{lactone}$), 160.1, 157.1, 148.4, 136.7, 135.1 (CH_{Ar}), 130.8, 130.7 (CH_{Ar}), 130.1 (CH_{Ar}), 129.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.2 (CH_{Ar}), 127.9, 123.0 (CH_{Ar}), 122.8 (CH_{Ar}), 121.3, 118.9, 110.5, 103.8 (CH_{Ar}), 98.8 (CH_{Ar}), 55.6 (OCH_3), 55.2 (OCH_3), 49.5 (C-12), 32.2 (C-11) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1690 (C=O) cm^{-1}. $C_{26}H_{20}O_6 \cdot 0.5CH_3OH$ (444.45): calcd. C 71.61, H 4.99, O 23.40; found C 71.78, H 4.65, O 23.57.

(±)-*trans*-11-(3,4-Dimethoxyphenyl)-6-oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5f): From the reaction of homophthalic anhydride (0.568 g, 3.501 mmol) and 3,4-dimethoxybenzaldehyde (0.194 g, 1.167 mmol), an oil (0.373 g, 75%) was isolated. The compound was obtained as colourless crystals containing 1.5 equiv. H_2O. Yield: 0.236 g (47%); m.p. 157–159 °C. ^1H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 7.99 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 7.65–7.63 (m, 1 H, ArH), 7.49 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH), 7.47–7.44 (m, 1 H, ArH), 7.42 (dt, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 1.2 Hz, 1 H, ArH), 7.30 (dt, $^3J_{H,H}$ = 7.5, $^4J_{H,H}$ = 1.2 Hz 1 H, ArH), 7.18 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 6.63–6.59 (m, 3 H, $CH_{11\text{-}Ph}$), 4.89 (s, 1 H, 11-H), 3.94 (s, 1 H, 12-H), 3.74 (s, 1 H, OCH_3), 3.65 (s, 3 H, OCH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 176.9 (CO_{COOH}), 161.9 ($CO_{lactone}$), 149.1, 148.3, 148.0, 136.5, 135.1 (CH_{Ar}), 131.8, 130.6 (CH_{Ar}), 130.3, 130.3 (CH_{Ar}), 129.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.2, 128.1 (CH_{Ar}), 123.0 (CH_{Ar}), 122.7 (CH_{Ar}), 121.3, 119.3 (CH_{Ar}), 111.2 (CH_{Ar}), 110.6, 110.1 (CH_{Ar}), 55.7 (OCH_3), 55.7 (OCH_3), 52.0 (C-12), 40.0 (C-11) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1690 (C=O) cm^{-1}. $C_{26}H_{20}O_6 \cdot 1.5H_2O$ (455.46): calcd. C 68.56, H 5.09, O 26.35; found C 68.22, H 4.76, O 27.02.

(±)-*trans*-11-(2,4-Dichlorophenyl)-6-oxo-11,12-dihydro-6*H*-dibenzo-[*c*,*h*]chromene-12-carboxylic Acid (5g): From the reaction of homophthalic anhydride (0.556 g, 3.430 mmol) and 2,4-dichlorobenzaldehyde (0.200 g, 1.143 mmol), an oil (0.308 g, 62%) was isolated. This compound was obtained as pale-yellow crystals, containing 0.5 equiv. CH_3OH. Yield: 0.236 g (47%); m.p. 176–178 °C. ^{1}H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.34 (dd, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, ArH), 8.00 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 1.1 Hz, 1 H, ArH), 7.64 (ddd, $^3J_{H,H}$ = 8.1, $^3J_{H,H}$ = 7.4, $^4J_{H,H}$ = 1.4 Hz, 1 H, ArH), 7.48–7.46 (m, 2 H), 7.43 (ddd, $^3J_{H,H}$ = 7.7, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.2 Hz, 1 H, ArH), 7.31 (ddd, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 7.5, $^4J_{H,H}$ = 1.3 Hz, 1 H, ArH), 7.28 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, ArH), 7.19 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, ArH), 6.87 (dd, $^3J_{H,H}$ = 8.5, $^4J_{H,H}$ = 2.1 Hz, 1 H, $CH_{11\text{-}Ph}$), 6.63 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H, $CH_{11\text{-}Ph}$), 5.44 (s, 1 H, 11-H), 3.92 (s, 1 H, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 176.3 (CO_{COOH}), 161.6 ($CO_{lactone}$), 148.9, 135.9, 135.3 (CH_{Ar}), 134.6, 134.1, 133.7, 130.8 (CH_{Ar}), 130.4 (CH_{Ar}), 130.1 (CH_{Ar}), 130.0 (CH_{Ar}), 129.7, 129.5 (CH_{Ar}), 129.0 (CH_{Ar}), 128.4 (CH_{Ar}), 127.8, 127.6 (CH_{Ar}), 123.3 (CH_{Ar}), 122.3 (CH_{Ar}), 121.3, 109.3, 49.1 (C-12), 35.9 (C-11) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1710 (C=O), 1690 (C=O) cm^{-1}. $C_{24}H_{14}Cl_2O_4 \cdot 0.5CH_3OH$ (453.29): calcd. C 64.92, H 3.56; found C 64.95, H 3.61.

(±)-*trans*-6-Oxo-11-(thiophen-2-yl)-11,12-dihydro-6*H*-dibenzo[*c*,*h*]-chromene-12-carboxylic Acid (5h): From the reaction of homophthalic anhydride (0.316 g, 1.950 mmol) and 4-(thiophen-2-ylmethylene)isochroman-1,3-dione (0.500 g, 1.950 mmol), an oil (0.534 g, 75%) was isolated which gave, after recrystallisation, colourless crystals. Yield: 0.430 g (59%); m.p. 263–265 °C. ^{1}H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.35 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, ArH), 7.97 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, ArH), 7.74–7.71 (m, 1 H, ArH), 7.69 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, ArH), 7.50–7.47 (m, 1 H, ArH), 7.43 (dt, $^3J_{H,H}$ = 7.4, $^4J_{H,H}$ = 1.3 Hz, 1 H, ArH), 7.36 (dt, $^3J_{H,H}$ = 7.3, $^4J_{H,H}$ = 1.2 Hz, 1 H, ArH), 7.33–7.32 (m, 1 H, ArH), 7.02 (dd, $^3J_{H,H}$ = 4.7, $^3J_{H,H}$ = 1.6, Hz, 1 H, CH_{Th}), 6.78–6.76 (m, 2 H, CH_{Th}), 5.37 (s, 1 H, 11-H), 4.09 (s, 1 H, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 172.5 (CO_{COOH}), 161.3 ($CO_{lactone}$), 147.3, 143.3, 136.0, 134.7 (CH_{Ar}), 131.467, 130.4, 129.7 (CH_{Ar}), 129.5 (CH_{Ar}), 128.0 (CH_{Ar}), 127.6 (CH_{Ar}), 127.2, 126.4 (CH_{Ar}), 124.6 (CH_{Ar}), 123.9 (CH_{Ar}), 122.5 (CH_{Ar}), 122.3 (CH_{Ar}), 120.7, 111.0, 77.2, 77.0, 76.8, 51.8 (C-12), 35.3 (C-11) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1700 (C=O), 1690 (C=O) cm^{-1}. $C_{22}H_{14}O_4S$ (374.41): calcd. C 70.55, H 3.77, O 17.09, S 8.56; found C 70.46, H 3.92, O 17.31, S 8.31.

(±)-6-Oxo-11,12-dihydro-6*H*-dibenzo[*c*,*h*]chromene-12-carboxylic Acid (5i): From the reaction of homophthalic anhydride (0.838 g, 5.168 mmol) and paraformaledhyde (0.052 g, 1.722 mmol) in pyridine (10 mL), an oil (0.218 g, 44%) was isolated, which gave, after recrystallisation, white crystals containing 0.5 equiv. CH_3OH. Yield: 0.126 g (25%); m.p. 237–239 °C. ^{1}H NMR (600 MHz, $CDCl_3$, 20 °C, TMS): δ = 8.35 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, ArH), 7.90 (d, $^3J_{H,H}$ = 7.3 Hz, 1 H, ArH), 7.80 (t, $^3J_{H,H}$ = 7.6 Hz, 1 H, ArH), 7.70 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, ArH), 7.52 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, ArH), 7.42–7.35 (m, 3 H, ArH), 3.98 (d, $^3J_{H,H}$ = 6.9, $^3J_{H,H}$ = 4.9 Hz, 1 H, 12-H), 3.56 (dd, $^2J_{H,H}$ = 16.0, $^3J_{H,H}$ = 4.8 Hz, 1 H, 11-H), 3.07 (dd, $^2J_{H,H}$ = 16.0, $^3J_{H,H}$ = 7.2 Hz, 1 H, 11-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C, TMS): δ = 174.2 (CO_{COOH}), 161.8 ($CO_{lactone}$), 146.9, 136.9, 134.7 (CH_{Ar}), 133.3, 129.9 (CH_{Ar}), 129.2 (CH_{Ar}), 128.7 (CH_{Ar}), 127.9, 127.8 (CH_{Ar}), 127.6 (CH_{Ar}), 122.7 (CH_{Ar}), 122.2 (CH_{Ar}), 120.8, 108.0, 42.8 (C-12), 23.6 (CH_2) ppm. IR (Nujol): $\tilde{\nu}$ = 1710 (C=O), 1670 (C=O), 1620 (C=C) cm^{-1}. $C_{18}H_{12}O_4 \cdot 0.5CH_3OH$ (308.31): calcd. C 72.07, H 4.58, O 23.35; found C 72.26, H 4.36, O 23.38.

Supporting Information (see footnote on the first page of this article): Procedures for the preparation of compounds **5a**–**i**, for confirming compounds **3**, **4** and **6** as intermediates, and for the dimerization reaction of homophthalic anhydride; ^{1}H and ^{13}C NMR spectra for compounds **5a**–**i**, **4a**, *E*-**6a**, *Z*-**6a**, **7** and **8**; X-ray data for *trans*-**5a** and **4c**; determination of the (*E*)/(*Z*) configuration of compounds **4**; fluorescence data for compounds **5a**–**d**.

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