A short and efficient construction of the dibenzo[c,h]chromen-6-one skeleton

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Abstract
We hereby report a major revision of the synthetic methodology for construction of the dibenzochromenone skeleton. Homophthalic acid derivatives were reacted with thionylchloride/DMF in the presence of NaN₃. As the main product, dibenzochromenone derivatives were obtained. When the reaction was performed in the absence of NaN₃, only isochromenones were formed. The mechanism of the formation of these products is discussed.

Keywords: Homophthalic acid, acyl azide, isocoumarin, dibenzochromenone, arnottin I.

Introduction

Dibenzo[c,h]chromen-6-one 1 motifs are of considerable interest due to their biological activity and structural intricacies. They exhibit a wide range of biological activities.
Arnottin I 2, a dibenzo[c,h]chromen-6-one derivative was first isolated by Ishikawa and co-workers in 1977, as a minor constituent from the bark of Xanthoxylum arnottianum. However, the structure of this compound was not determined until 1993 since the producing plant yielded only small quantities of the material. Gilvocarcins 3, 4, a relatively small family of natural antibiotics having the dibenzo[c,h]chromenone skeleton, also exhibit diverse biological activity. The key step in syntheses of these compounds has been mainly metal-catalyzed aryl-aryl coupling reactions of the suitable substituted starting materials which were synthesized by multi-step procedures. James and Snieckus used mainly Negishi/Suzuki cross coupling followed by a remote metallation (DreM)-carbamoyl migration strategy. Ishikawa et al. used palladium-catalyzed coupling of o-bromobenzoates and 1-tetralones to construct the dibenzo[c,h]chromenone structure. Suzuki et al. used a three component system for the synthesis of defucogilvocarcin M 3. Nickel-catalyzed synthesis of benzocoumarin derivatives and its application to the total synthesis of arnottin I 2 was achieved by Madan and Cheng. In this paper, we describe a concise procedure leading directly to the core skeleton of dibenzo[c,h]chromenone structure with some substituents resembling the arnottin I structure. Furthermore, the position of the substituents in the products should provide information about the mechanism of formation of the products.

**Results and Discussion**

Recently, we have treated homophthalic acid 5 with thionyl chloride, DMF, and sodium azide in the presence of tetrabutylammonium bromide as a catalyst. Unfortunately, the expected diazide 7 was not formed. The dibenzo[c,h]chromenone 1 was formed in 41% yield. In order to test the
general applicability of this reaction for the formation of substituted dibenzo[c,h]chromenones, substituted homophthalic acids were used. First, the original reaction was reinvestigated.

\[ \text{N,N-Dimethyl(chlorosulfinyloxy)methaniminium chloride} \]

\[ \text{formed from thionyl chloride and dimethyl formamide is an efficient reagent for the synthesis of acyl azides from carboxylic acids.} \]

Therefore, homophthalic acid 5 was reacted with thionyl chloride, DMF, and sodium azide, in the presence of tetrabutylammonium bromide as a catalyst in methylene chloride, anticipating formation of the diazide 7. However, the desired diazide 7 was not formed. Besides the major product, 6H-dibenzo[c,h]chromen-6-one 1, an thioisocoumarin derivative 6 was isolated in 4% yield (Scheme 1).\(^{11,12}\)

\[ \text{Scheme 1} \]

COSY, HMQC, and HMBC experiments were conducted to confirm the the assignment of the structure of 6. Two carbonyl carbons appeared at 191.3 and 183.1 ppm, the high field resonance being that for the five-membered ring carbonyl carbon. With the help a of COSY-spectrum we were able to distinguish between the aromatic protons of two benzene rings. The HMBC spectr um showed that the carbonyl carbon resonance at 183.1 (C-5) correlates with the doublet (H-4) resonating at 8.17 ppm. On the other hand, the carbonyl carbon resonance at 191.3 (C-11) correlated with the doublet at 7.5 ppm (H-10). These observations clearly show that the carbonyl groups are directly connected to different benzene rings. The quaternary carbon atom C-6a correlated with the doublet resonating at 7.17 (H-7) whereas the carbon atom C-11a correlated with the doublet at 8.95 ppm (H-1). Those findings support the proposed structure. The incorporation of a sulfur atom into the molecule was determined by elemental analysis as well as by its mass spectrum. With the isolation of this new isothiocoumarin derivative 6, the focus of the research was directed to the increase of its yield.
The same reaction was carried out but in the absence of DMF. This procedure increased the yield of the isothiocoumarin derivative 6 from 4% to 17%. On the other hand, elemental sulfur and new condensation products such as 8, 9 and 10 were isolated in 8, 14, and 7% yields, respectively (Scheme 2). Interestingly, the major product 1, which was formed when the reaction was carried out in the presence of DMF, was not detected. This observation shows that DMF is involved in the formation of 6H-dibenzo[c,h]chromen-6-one 1. The spectral data of 8 was in agreement with those reported in the literature. The presence of three benzene rings in 9 was easily established by analysis of the $^1$H-NMR spectrum. The $^{13}$C-NMR spectrum had 22 lines for aromatic carbons. The carbonyl resonances observed at 191.8, 158.0 ppm are in agreement with the proposed structures. COSY, HMQC, and HMBC spectra also support the structure. Again with the help of the COSY spectrum, the connection of the aromatic protons was easily determined. The HMBC spectrum showed correlation of the carbonyl resonance at 191.8 (C-11) ppm with the doublet resonating at 7.59 (H-12) ppm. The other carbonyl carbon at 160.4 (C-5) correlated with the doublet at 8.30 (H-4) ppm. Furthermore, the carbon atom at 151.2 (C-6a) correlated with the doublet at 8.25 (H-7) ppm. Additionally, the coupling constants between the protons H-7 and H-8 ($J_{7,8} = 8.4$ Hz) and H-8 and H-9 ($J_{8,9} = 6.9$ Hz) clearly showed the presence of a naphthalene unit in the proposed structure. The high resolution mass spectrum and the $^1$H-NMR spectrum of 10 clearly indicated the presence of a nitrogen atom in the molecule. Nine proton resonances between 7.2-8.3 ppm, where one of them resonates as singlet, support the structure. Furthermore, an IR absorption band at 2225 cm$^{-1}$ demonstrated the presence of a nitrile group. Two dimensional NMR spectra were also in agreement with the proposed structure 10.
The sulfur containing product, indeno[1,2-c]isothiochromenone-5,11-dione 6 was synthesized independently, in quantitative yield, by reacting 8 with Na$_2$S in THF and water (1:1). Therefore, we assume that sulfide anion formed under the reaction conditions by reduction of SOCl$_2$ by NaN$_3$, substitutes oxygen atom in 8 to give 6. Sulfide anions formed under reaction conditions can undergo further reaction with excess SOCl$_2$ present in the reaction media and produce elemental sulfur. In a separate reaction we successfully demonstrated that reaction of Na$_2$S with SOCl$_2$ in dichloromethane produces sulfur in a very fast process.

Scheme 3

In order to test the scope of the procedure shown in Scheme 1, the reaction was carried out with two substituted homophthalic acids. Bromohomophthalic acid 11 was synthesized by direct bromination of homophthalic acid. It is well known that the bromination of aromatic compounds containing electron-withdrawing groups has been an area of concern. Homophthalic acid 5 was reacted with potassium bromate in sulfuric acid to give the desired brominated diacid 11 in 44% yield. Bromohomophthalic acid 11 was reacted with thionyl chloride, DMF and sodium azide, under the same reaction conditions as described in Scheme 1, to give dibromodibenzochromenone derivative 12 in 37% yield. The $^1$H-NMR spectrum was consistent with the proposed structure. In contrast to 1, this dibromo derivative 11 was found to be poorly soluble in organic solvents so that a $^{13}$C-NMR spectrum could not be recorded. Additionally, a minor compound 13 (2%) was isolated. The structure was easily determined by comparison of the spectral data of 13 with those of 6.
Scheme 4

For the synthesis of 4-methoxyhomophthalic acid 16, a modified literature procedure was applied.\textsuperscript{17} Methoxybenzoic acid 14 was condensed with chloral hydrate to obtain the lactone 15, which was then reduced by zinc in acetic acid followed by hydrolysis to produce the methoxydiacid 16 (Scheme 4). With the synthesis of diacid 16, we were now able to assess its use for rapid and efficient generation of a dibenzochromenone skeleton, but with methoxyl substituents. Treatment of diacid 16 with thionyl chloride, DMF and sodium azide under the same reaction condition as reported for the synthesis of 12, resulted in the formation of the corresponding dimethoxydibenzochromenone derivative 17 in 45\% (Scheme 4). The structure and especially the exact positions of the methoxyl groups were determined with the help of COSY, HSQC and HMBC experiments.

Scheme 5

During these reactions a nitrogen atom, arising from azide anion used in the reaction, was not incorporated in the products 12, 13 as well as 17. To determine the function of azide anion, the
reaction with 16 was run in the absence of NaN$_3$. Instead of the formation of a dibenzochromenone 17, an aminomethylene compound 18 was formed, which was converted to the isocoumarin derivative 19$^{18}$ by reaction with methanol saturated with hydrogen chloride (Scheme 5).

**Conclusions**

The reactions performed in our work show that the dibenzochromenone structure 1 can be easily generated, even with the substituted homophthalic acid derivatives, in 37–45% yields in a one-pot reaction. Furthermore, the attempted azidination reactions of homophthalic acid derivatives 5, 11, and 16 show that NaN$_3$ plays an important role in determination the mode of the reaction. In the absence of NaN$_3$, isocoumarin derivative 19 was formed from the reaction of 16 instead of the dibenzocoumarin derivative 17. The mechanism we propose is shown in Scheme 6.

![Scheme 6](image)

We suggest that the first step is the formation of the anhydride 20, which could then be regiospecifically opened up by the azide anion to the corresponding monoazide 21. Formation of an acyl azide activates the methylenic protons for further reaction. Intermolecular acylation of 21 with acyl chloride 22 followed by ring-closure would result in the formation of 24. This anhydride might undergo again ring-opening by azide anion attack to form β-keto-acid carboxylate 25. Decarboxylation of 25 would lead to cyclization to form the key intermediate 26, which could easily be converted in the dibenzochromenone derivatives 1, 12, and 17 as well as into the nitrile 10. Recently, Threadgill et al.$^{19}$ obtained relevant information about the
mechanism of the acylation of isocoumarin derivatives which strongly support our suggestion. Furthermore, the exact determination of the positions of the substituents in 12 and 17 supports our proposed mechanism.

The formation of the compounds having cyclopentadienone structures such 6, 8, 13 as well as 9, however, cannot be explained via this mechanism. As one can easily recognize from the position of the substituents in 13, for the construction of this skeleton requires a C–C connection of methylene groups of two homophthalic acid units.

Before such a C–C connection between the two methylene groups can take place, one of these groups should contain a good leaving group. We therefore assume, that firstly a chlorination on one of the methylene goup20 takes place under the reaction conditions, followed by attack of the enol form of the second methylene group. Decarboxylation and cyclization can then lead to the compounds 8 and 13.

**Experimental Section**

**General.** Melting points were determined on a Thomas-Hoover capillary melting point apparatus. IR spectra were recorded on a Perkin Elmer 980 spectrometer. NMR spectra were recorded on a Bruker-Avance instrument at 400 MHz for $^1$H and 100 MHz for $^{13}$C NMR. Apparent splitting is given in all cases. Mass spectra were recorded on an Agilent 5975C spectrometer operating at an ionization potential of 70 eV. Column chromatography was performed on silica gel (60-mesh, Merck). TLC was carried out on Merck 0.2 mm silica gel 60 F$_{254}$ analytical aluminum plates.

**Synthesis of 6H-dibenzo[c,h]chromen-6-one (1).** In a 25 mL dropping funnel, benzene (7 mL), dimethyl formamide (2.8 mL) and thionyl chloride (2.3 mL) were consecutively added. The formed solution was allowed to form two separate layers. The lower layer was added to a suspension of the homophthalic acid 5 (2.5 g, 13.9 mmol), sodium azide (2.6 g, 44 mmol), tetrabutylammonium bromide (0.6 g, 2.3 mmol), and pyridine (3.2 mL) in dichloromethane (100 mL). The mixture was then stirred at room temperature overnight and washed with saturated aqueous sodium bicarbonate solution (3 x 50 mL), with 1.0 M HCl solution (3 x 50) three times and finally with water (2 x 25 mL). The organic phase was dried over magnesium sulfate and
concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 40 g, CH₂Cl₂) to give colorless crystals 1 (0.7 g, mp, 182-183 °C⁰, Lit. mp. 179-180 °C¹¹) in 41% yield. The product was recrystallized from ethyl acetate. The NMR spectra were in agreement with those reported in the literature.⁹,¹¹ As the second fraction indeno[1,2-c]isothiochromene-5,11-dione 6 was isolated.

Red crystals (73 mg, 4%) from methylene chloride, mp 235-236 °C (Found: C, 71.32; H, 3.09; S, 12.34% C₁₆H₃₅O₂S requires : C, 72.71; H, 3.05; S, 12.13% IR νmax (KBr)/cm⁻¹ 2989, 1699, 1654, 1275, 1262, 764, 750; ¹H-NMR (400 MHz, CDCl₃) δ 8.95 (d, J = 8.1 Hz, H-1), 8.17 (d, J = 8.0 Hz, H-4), 7.72 (t, J = 7.5 Hz, H-2), 7.50 (d, J = 7.1 Hz, H-10), 7.47 (t, J = 7.7 Hz, H-3), 7.40 (t, J = 7.4, H-8), 7.31 (t, J = 7.4 Hz, H-9), 7.17 (d, J = 7.3 Hz, H-7). ¹³C-NMR (100 MHz, CDCl₃) δ 191.3 (C-11), 183.1 (C-5), 156.2 (C-6a), 140.6 (C-6b), 135.0 (C-2), 134.1 (C-8), 133.8 (C-11b), 133.3 (C-9), 131.1 (C-10a), 128.6 (C-3), 127.0 (C-4), 126.5 (C-11a), 126.3 (C-1), 123.1 (C-10), 119.9 (C-4a), 119.7 (C-7). MS, m/z: 264 (M⁺+, 100%), 236 (M⁺-CO, 81%), 208 (M⁺-2CO, 27%), 176 (M⁺-2CO, -S, 10%), 163 (35%), 104 (22%).

**Reaction of homophthalic acid with thionyl chloride and sodium azide in the absence of dimethyl formamide**

To a suspension of homophthalic acid (5.0 g, 27.8 mmol), NaN₃ (7.2 g, 111 mmol), tetrabutylammonium bromide (0.75 g, 2.3 mmol), and pyridine (9 mL) in dichloromethane (100mL), thionyl chloride (4.6 mL, 63.4 mL) was added dropwise under a nitrogen atmosphere and the mixture was stirred at room temperature for 10 h. The inorganic salts were separated by filtration. The filtrate was washed with 1.0 M HCl solution three times, followed by water extraction. The organic phase was dried (MgSO₄) and solvent removed under reduced pressure. The residue was purified by chromatography over silica gel (60 g) eluting with methylene chloride.

Sulfur (340 mg, 10.6 mmol) was isolated as the first fraction. The compound 6 (623 mg, 17%) was isolated as the second fraction. The third fraction was characterized as 8. **Indeno[1,2-c]isochromene-5,11-dione (8).** Yellow solid (275 mg, 8%), m.p. 257-258 °C (Lit. 258-259 °C¹³b) 403 mg, 8%, yellow solid; ¹H-NMR (CDCl₃, TMS) δ 8.31 (d, J = 7.9 Hz, H-1), 8.23 (d, J = 8.0 Hz, H-4), 7.74 (t, J = 7.6 Hz, H-2), 7.52 (d, J = 7.1, H-10), 7.48 (d, J = 7.4 Hz, H-3), 7.45-7.39 (m, 2H, H-7 and H-8), 7.34 (dt, J = 6.8 and 1.8 Hz, H-9). ¹³C-NMR (400 MHz, CDCl₃) δ 189.9 (C-11), 170.6 (C-5), 160.8 (C-6a), 136.4 (C-6b), 136.0 (C-2), 133.6 (C-8), 132.8 (C-10 or C-11b), 132.8 (C-10 or C-11b), 131.6 (C-8), 130.9 (C-4), 128.4 (C-3), 123.3 (C-1), 123.1 (C-10), 119.9 (C-7), 119.0 (C-4a), 107.7 (C-11a). MS m/z (C₁₆H₁₅O₃) 248 (M⁺+, 100%), 220 (M⁺-CO, 19), 163 (30).

**Dibenzo[c,h]indeno[2,1-f]chromene-5,11-dione (9)** was isolated as the fourth fraction. Yellow solid, m.p. 212-213 °C (451 mg, 14%); HRMS caled for C₂₅H₁₂O₃ (M⁺ + H) 349.0865; found 349.0871; IR νmax/cm⁻¹ 2955, 2922 2852, 1727, 1706, 1286, 1259, 1103, 742; ¹H-NMR (400 MHz, benzene-d₆) δ 9.33 (d, J = 8.4 Hz, 1H, H-10), 8.30 (dd, J = 7.8 and 1.3 Hz, 1H, H-4), 8.25 (d, J = 8.4 Hz, 1H, H-7), 7.89 (d, J = 7.6 Hz, 1H, H-1), 7.59 (dd, J = 7.0 and 1.0 Hz, 1H, H-12),
7.40 (d, J = 7.5 Hz, 1H, H-15), 7.26 (ddd, J = 8.4, 6.9 and 1.2 Hz, 1H, H-9), 7.09 (ddd, J = 8.4, 6.9 and 1.2 Hz, 1H, H-8), 7.05 (ddd, J = 7.8, 7.4 and 1.5 Hz, 1H, H-2), 6.98 (d, J = 7.8 and 1.5 Hz, 1H, H-3), 6.87 (dd, J = 7.5 and 1.3 Hz, 1H, H-14), 6.80 (d, J = 7.5 and 0.9 Hz, 1H, H-13).

\(^{13}\text{C-}
\text{NMR}\) (100 MHz, CDCl\(_3\)) \(\delta\) 191.8 158.0, 151.2, 142.3, 141.7, 133.8, 132.3, 131.6, 131.4, 129.4, 129.1, 128.7, 128.0, 127.4, 126.2, 125.5, 124.3, 123.0, 122.7, 122.4, 121.2, 121.4, 121.0, 109.5. MS \(m/z\) 348 (M\(^+\), 1%), 296 (100), 268 (17), 240 (45), 195 (18), 120 (36).

2-(1-Oxo-1\(H\)-isochromen-3-yl)benzonitrile (10) was isolated as the fifth fraction. M.p. 201-202 \(^{\circ}\)C, (225 mg, 7%); HRMS calcd for C\(_{13}\)H\(_{15}\)N\(_4\)O (M + K\(^+\)) 286.0270; found 286.0260; IR \(v_{\text{max}}\) (KBr)/cm\(^{-1}\) 2962, 2921, 2851, 2225, 1732, 1645, 1606, 1458, 1259, 1232, 1033, 1008, 794; \(^1\text{H-NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 8.33 (d, \(J = 8.4\) Hz, 1H, H-8), 7.99 (dd, \(J = 8.0\) Hz, 1H, H-6), 7.80 (dd, \(J = 7.8\) and 1.1 Hz, 1H, H-3), 7.76 (ddd, \(J = 7.8\) and 1.3 Hz, 1H, H-6), 7.71 (dd, \(J = 7.95\) and 1.37 Hz, 1H, H-5), 7.58 (dd, \(J = 7.3\) and 1.5 Hz, 1H, H-5), 7.57 (dd, \(J = 8.4\) and 7.8 Hz, 1H, H-7), 7.52 (dd, \(J = 7.6\) and 1.2 Hz, 1H, H-4), 7.32 (s, 1H, H-4); \(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)) \(\delta\) 160.0, 148.2, 134.9, 133.6, 133.5, 132.8, 131.4, 128.9, 128.06, 127.7, 127.1, 125.1, 119.3, 116.4, 107.8, 105.5; MS (70 eV) 247 (M\(^+\) 100%), 219 (39), 190 (51), 164 (11), 130 (13), 89 (32).

5-Bromo-2-(carboxymethyl)benzoic acid (11). Homophtalic acid 5 (5.0 g, 27 mmol) and potassium bromate (6.58 g, 43 mmol) were mixed in water (30 mL) and the mixture was heated at 90 °C. A mixture of sulfuric acid (24 ml, 95%) and water (40 mL) was added dropwise to the resulting mixture at 90 °C over a period of 30 min. After completion of addition the mixture was stirred 2 h at the same temperature. Then the mixture was cooled to the room temperature and the product was filtered off and washed with water (3 x 50 mL) to give 11 (3.2 g, 44%). The product was recrystallized from EtOAc/hexane (4/1), m.p. 216-217, m.p. 215\(^{16}\). \(^1\text{H-NMR}\) (400 MHz, DMSO-\(d_6\)) \(\delta\) 7.99 (d, \(J_{6,2} = 2.4\) Hz, 1H, H-6), 7.71 (dd, \(J_{2,26} = 8.0\) Hz, \(J_{2,6} = 2.4\) Hz, 1H, H-2), 7.31 (d, \(J_{3,32} = 8.0\) Hz, 1H, H-3), 3.92 (s, 2H, -CH\(_2\)); \(^{13}\text{C-NMR}\) (100 MHz, DMSO-\(d_6\)) \(\delta\) 172.0, 166.9, 135.9, 134.5, 134.4, 132.7, 132.6, 119.7, 39.2.

3,8-Dibromo-6\(H\)-dibenzo[e,h]chromen-6-one (12). 5-Bromo-2-(carboxymethyl)-benzoic acid (11) (1.45 g, 5.6 mmol), NaN\(_3\) (1.45 g, 43 mmol), tetrabutylammonium bromide (0.3 g, 1.15 mmol) and pyridine (1.8 mL) were added to 100 mL of CH\(_2\)Cl\(_2\). In a dropping funnel, 2.0 mL of dry benzene, 1.2 mL of \(N,N\)-dimethylformamide and 0.92 mL SOCl\(_2\) were mixed and the solution was left to form two separate layers. After 10 min, the bottom phase was added dropwise to the mixture prepared above. The resulting mixture was stirred for 18 h. Inorganic non-reacted starting materials were removed by filtration. The filtrate was washed with 0.1 M HCl (3 x 50 mL) followed by water (3 x 100 mL) and dried over MgSO\(_4\). Removal of the solvent under reduced pressure gave the crude product, which was purified by chromatography on silica gel (40 g) eluting with CH\(_2\)Cl\(_2\). As the first fraction the thioisocoumarin derivative 13, which could not be purified, was isolated, 24 mg (orange solid), 2%, purity about 85% according to the \(^1\text{H-NMR}\).

3,8-Dibromoindeno[1,2-c]thioisochromene-5,11-dione (13). Orange solid. \(^{1}\text{H-NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 8.80 (d, \(J = 8.7\) Hz, H-1), 8.30 (d, \(J = 2.0\) Hz, H-4), 7.8 (dd, \(J = 8.7\) and 2.0 Hz, 2.8).
The second fraction was identified as dibromobenzochromenone 12. 433 mg (37%) as a white solid, m.p. 312-323 °C. (Found: C, 50.11; H, 2.00% C₁₇H₈Br₂O₂ requires C, 50.53; H, 2.00%); IR νmax(KBr)/cm⁻¹ 3079, 2919, 1711, 1482, 1262, 1185, 827; ¹H-NMR (400 MHz, CDCl₃) δ 8.73 (d, J = 1.9 Hz, H-4), 8.60 (d, J = 2.1 Hz, H-7), 8.05 (d, J = 8.6 Hz, H-10), 8.02 (d, J = 8.9 Hz, H-11), 7.96 (dd, J = 8.6 and 2.1 Hz, H-9), 7.74 (2d, J = 8.4 Hz, H-1 and H-12) 7.68 (dd, J = 8.7 and 1.9 Hz, H-2). ¹³C-NMR spectrum could not be taken due to the poor solubility of the compound. MS Spectrum: 70 eV, m/z; 402/404/406 (M⁺, 52, 100, 49%), 295/297 (M⁺-Br, 17%), 267/269 (M⁺-Br, and -CO, 11%), 216 (9%), 187 (41%).

3,8-Dimethoxyindeno[1,2-c]isochromene-5,11-dione (17). 2-(Carboxymethyl)-5-methoxybenzoic acid (1.275 g, 6.07 mmol) NaN₃ (1.574 g, 46.7 mmol), tetrabutylammonium bromide (0.32 g, 1.23 mmol) and 2.0 mL pyridine, 1.2 mL of N,N-dimethylformamide and 0.92 mL SOCl₂ were reacted as described above. After the normal work-up procedure, the residue was purified by chromatography on silica gel (40 g) eluting with CH₂Cl₂. 3,8-Dimethoxy-6H-dibenzo[c,h]chromen-6-one (17) was isolated as white solid (0.08 g, 45%), m.p. 244-245 °C; (Found: C, 73.98; H, 4.71%; C₁₀H₁₄O₄ requires C, 74.50; H, 4.61%); IR νmax(KBr)/cm⁻¹ 3075, 2945, 2840, 1712, 1609, 1498, 1223, 1061, 1020, 8228; ¹H-NMR (400 MHz, CDCl₃) δ 7.99 (d, J = 8.9 Hz, H-10), 7.74 (d, J = 2.8 Hz, H-7), 7.75 (d, J = 8.7 Hz, H-12), 7.69 (d, J = 2.4 Hz, H-1), 7.65 (d, J = 8.9 Hz, H-4), 7.57 (d, J = 8.7 Hz, H-11), 7.34 (dd, J = 8.9 and 2.8 Hz, H-9), 7.12 (dd, J = 8.9 and 2.5 Hz, H-3), 3.95 (s, 3H), 3.92 (s, 3H). ¹³C-NMR (100 MHz, CDCl₃) δ 161.5 (C-6), 159.8 (C-8), 158.7 (C-2), 145.3 (C-4b), 129.3 (C-4), 129.1 (C-10a), 129.0 (C-4a), 125.0 (C-9), 124.5 (C-3), 124.2 (C-12a), 123.9 (C-10), 122.3 (C-6a), 120.3 (C-3), 116.5 (C-11), 113.7 (C-10b), 100.1 (C-1), 55.84 (OCH₃), 55.78 (OCH₃). MS m/z 306 (M⁺, 100%), 263 (21%), 220 (10), 192 (9), 163 (12), (Z)-4-[(Dimethylamino)methylene]-7-methoxysichroman-1,3-dione (18). 2-(Carboxymethyl)-5-methoxybenzoic acid (16) (130 mg, 0.62 mmol) tetrabutylammonium bromide (32 mg g, 0.12 mmol) and pyridine (0.3 mL) benzene (0.4 mL) N,N-dimethylformamide 0.15 mL and SOCl₂ (0.12 mL) in 40 mL of CH₂Cl₂ were reacted as described above. The resulting mixture was stirred overnight. Inorganic non-reacted starting materials were removed. The filtrate was washed with 0.3 M HCl solution three times. The organic phase was dried over MgSO₄. Removal of the solvent gave the crude product, which was purified by chromatography on silica gel (10 g) eluting with ethyl acetate to give a yellow solid 123 mg, 82%). ¹H-NMR (400 MHz, CDCl₃) δ 7.78 (bs, H-5), 7.49 (t, J = 1.6 Hz, H-8), 7.09 (dd, J = 7.2 and 2.4 Hz, H-6), 3.87 (s, 3H, -OCH₃), 3.24 (bs, 6H, -NCH₃). ¹³C-NMR (100 MHz, CDCl₃) δ 163.2 , 156.6, 156.2, 132.9, 124.2, 120.4, 117.5, 111.4 , 88.2, 55.6, 47.5, 45.0 MS m/z, (C₁₃H₁₃NO₄) 247 (M⁺, 100%), 204.0 (85), 188.1 (18), 160.1 (19), 132.1 (61).
Methyl 7-methoxy-1-oxo-1H-isochromene-4-carboxylate (19). (Z)-4-((dimethylamino)-methylene)-7-methoxyisochroman-1,3-dione (18) (65 mg, 0.26 mmol) was dissolved in methanol (20 mL). Dry HCl gas produced from sulfuric acid and sodium chloride was passed slowly through this solution. After the saturation was completed, it was refluxed for 2 h. The solvent was removed under reduced pressure, water was added to the residue which was then extracted with chloroform (3x10 mL). The combined extracts were dried (MgSO4) and the solvent was removed at reduced pressure. The residue was purified by chromatography on silica gel eluting with ethyl acetate/hexane (3:2) to yield 17.5 mg 29% (isolated yield) of methyl 7-methoxy-1-oxo-1H-isochromene-4-carboxylate (19), as a white solid (m.p. 121-123 °C, 124-125 °C); \( ^1H \)-NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.57 (d, \( J = 9.1 \) Hz , H-5), 8.10 (s, H-3), 7.71 (d, \( J =2.9 \) Hz, H-8), 7.37 (dd, \( J = 9.1 \) and 2.9 Hz, H-6), 3.90 (s, 3H, -OCH\(_3\)), 3.89 (s, 3H, -OCH\(_3\)). \( ^13C \)-NMR (100 MHz, CDCl\(_3\)) \( \delta \) 164.7, 161.0, 159.9, 150.5, 127.3, 127.0, 124.5, 121.91 (C-), 110.7, 109.9, 55.7, 52.1. MS m/z, (C\(_{12}\)H\(_{10}\)O\(_5\)) 234.1/235.1 (M\(^+\), 8/1), 203.0 (M\(^+\) -OCH\(_3\)), 202.0 (-H), 174.1 (-CO), 163.1.

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References and Notes

14. We have recently found that sodium azide can reduce 1,4-benzoquinones to the corresponding hydroquinones in high yields. Algi, F.; Balci, M. *Synth. Commun.* **2006**, *36*, 2293.