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Tributyltin(IV) Hydride Mediated Free-Radical Syntheses of Dehydrodibenzochromanones, Dehydrodibenzocoumaranones and Aristolactams.

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Abstract. We describe free radical cyclization of methyl bromophenylacetylphenylacetates to novel dehydrodibenzo[de,g]chromanones; oxidation of the latter compounds allowed the first total synthesis of dehydrodibenzo[cd,f]coumaranones, which are easily transformed into aristolactams.

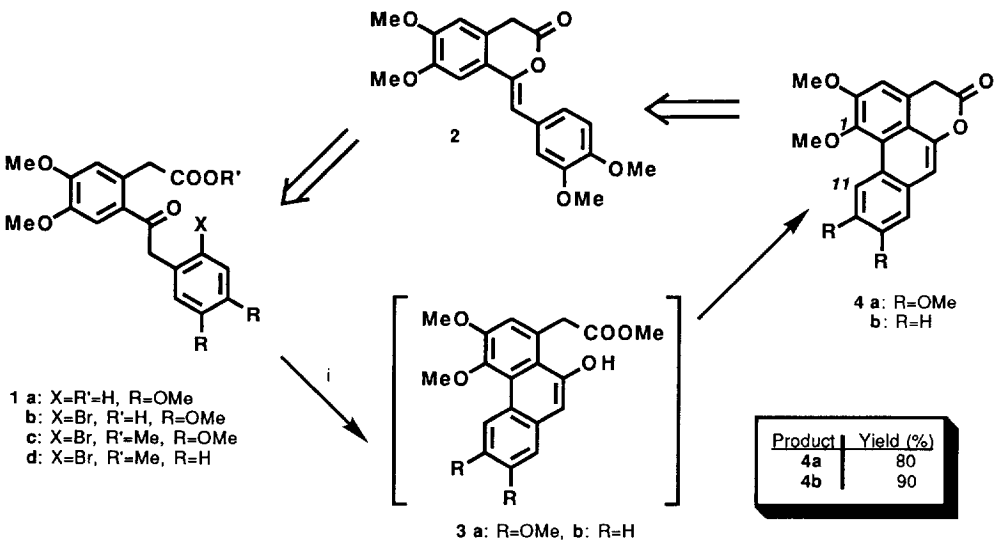
Preparation of many pharmacologically interesting classes of biologically-active natural compounds involves formation of biaryl bonds; a synthetic problem which has often been poorly solved[1]. For example, several approaches to the phenanthrene ring system of aporphinoids (alkaloids biogenetically derived from benzylisoquinolines) have used biaryl coupling reactions; in each case, only poor to moderate yields have resulted.[2]

We have recently reported[3] that the usually low-yielding biomimetic route to aporphines via photocyclization of 1-(2'-bromobenzyl)-1,2,3,4-tetrhydroisoquinolines[4] gives high yields when carried out in the presence of tributyltin(IV) hydride and AIBN;[5] and that, under the same conditions, bromobenzylisochromanones are transformed into novel dibenzo[de,g]chromanones, which can be easily converted into phenanthrene alkaloids.[6] However, we were forced to abandon this approach to dehydrodibenzo[de,g]chromanones **4**, because the Z isomer of the benzylideneisochromanone precursor, **2** (prepared[7] from ketoacids **1**), would not cyclize.[7]

Herein we describe how phenylacetylphenylacetic acids **1** can be cyclized to afford novel dehydrodibenzo[de,g]chromanones **4**; these latter compounds are easily transformed into aristolactams **10c** or **10f,** via dibenzo[cd,f]coumaranones **10b** or **10e**[8] (oxygen analogues of aristolactams) respectively, a new phenanthrene lactone class, whose only known natural member is aristololide (**10a**)[9].

In this approach, the phenanthrene ring system of **4** is formed by free radical cyclization of haloketoesters obtained from acids **1**. The starting bromoketoester, **1c**, was prepared in high yield by bromination of ketoacid **1a**,[10] and esterification of the bromoketoacid product, **1b**. The bromoketoester, **1c**, Bu_3SnH and AIBN were refluxed under argon for 18 h, and dehydrodibenzo[de,g]chromanone **4a**, the first reported compound of its class, was isolated in high yield from the reaction mixture. The initial reaction product was probably the phenanthrolic methyl ester, **3a**, which then cyclized to lactone **4a**. The spectroscopic properties of **4a** are similar to those of its nitrogen analogue **4c**:[3b] for example, the ^1H NMR spectra of both

show a singlet for H(11) which is deshielded (it appears at ∂ 9.12 ppm in the spectrum 4a) due to a steric interaction with C(1)OMe.



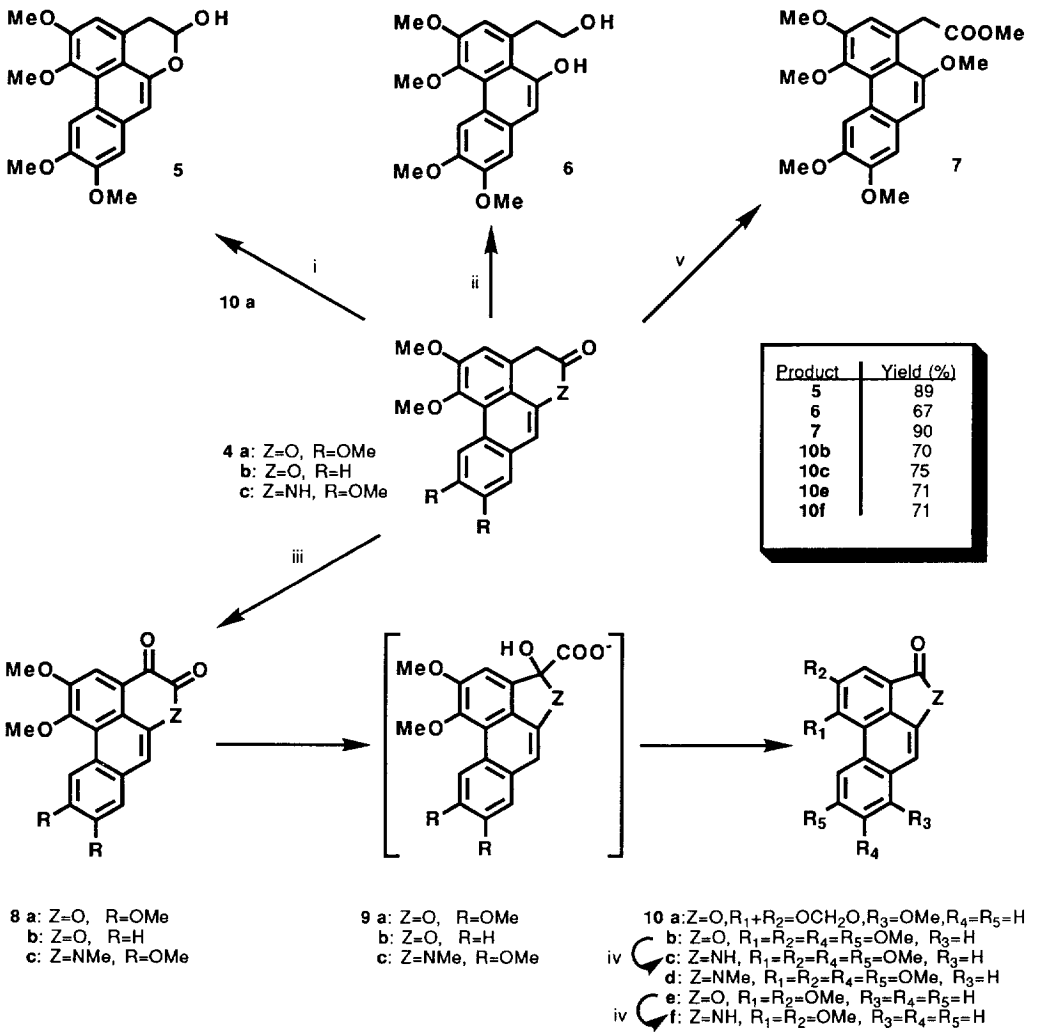
Scheme 1. *Reagents*: i) Bu_3SnH, AIBN, benzene, reflux, 18 h.

Some chemical properties of lactone **4a** were evaluated (Scheme 2): **4a** slowly decomposes on standing in dichloromethane solution; it cannot be converted to the corresponding 5-oxoaporphine **4c** by treatment with ammonium hydroxide,[3b] but instead gives a complex mixture of products; it is reduced to lactol **5** when treated with $NaBH_4$ in methanol, but to diol **6** by $NaBH_4$ in THF containing traces of acetic acid.

Oxidation of lactone **4a** proved more interesting. An oxygenated solution of **4a** and sodium hydroxide in 1,4-dioxane was stirred at r.t. for 72 h. Work-up yielded a product which was shown by ^1H NMR to have lost the methylenic carbon of the starting lactone, but whose IR spectrum contained a vibration at 1780 cm^{-1} corresponding to the lactone carbonyl. This product was thus identified as the previously unknown homologous lactone **10b** (70% yield) and was probably formed via benzylic oxidation of **4a** to ketolactone **8a**, and, in the basic medium, benzil-benzilic acid rearrangement of the latter to **9a**, which was then oxidatively decarbonylated.

The ring-contraction reaction of the above sequence has been seen previously in the transformation of the 4,5-dioxoaporphine pontevedrine (**8c**) into the corresponding *N*-methylaristolactam **10d**;[11] treatment of **10b** with aqueous ammonia gave **10c** (75% yield), which could be methylated by NaH/MeI in THF to give a compound that was identical to **10d**, obtained by ring-contraction of pontevedrine.[11]

Lactone **4a** could be directly converted to the 10-methoxyphenanthrylacetic ester **7** in high yield by refluxing it in 1% methanolic hydrogen chloride; this was surprising, since all our previous attempts to prepare 10-alkoxyphenanthrylacetic acid derivatives (**7**) had been unsuccessful. For example, refluxing the isochromanone **2** (prepared[7] from **1a**) in 1% methanolic hydrogen chloride led to the expected methoxystilbene

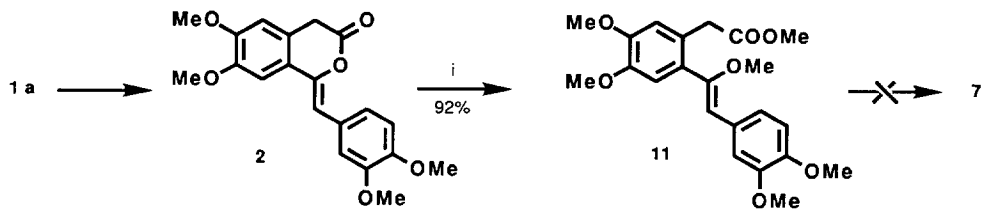


Scheme 2. *Reagents*: i) $NaBH_4$, methanol, rt, 2h. ii) $NaBH_4$, AcOH, THF, reflux, 30 min. iii) NaOH, O_2, dioxane, rt, 72 h. iv) NH_3, methanol, rt, 48 h. v) Methanol/ HCl (1%), reflux, 2h.

derivative **11**, but all attempts at photochemical electrocyclic ring closure[12] of the latter compound failed. The failure of **11** to cyclize was probably due to the methoxy group attached to its ethene bridge; this may have induced the stilbene chromophore to shift, thus disfavouring the electrocyclic reaction.[13]

By means of the free-radical cyclization approach described above, dibenzochromanone **4b** was prepared from bromoketoester **1d**[14] in even better yield than **4a**. Oxidation of **4b** under the conditions

described for **4a** afforded the expected dibenzocoumaranone **10e**, which could be converted to a compound identical to the natural aristolactam cepharanone B (**10f**)[15] by treatment with ammonia.



Scheme 3. *Reagents*: i) Methanol/ HCl (1%), reflux, 15 min.

In summary, by means of a synthetic approach involving free-radical cyclization of methyl bromophenylacetylphenylacetates, we prepared novel dehydrodibenzo[de,g]-chromanones **4** and dehydrodibenzo[cd,f]coumaranones **10** in high yield; the latter form a novel phenanthrene lactone class, whose only known natural member is aristololide (**10a**). This approach may be extended to the preparation of the pharmacologically interesting class of compounds, the aristolactams **10c**, **10d** or **10f**; current synthetic routes to the latter compounds often involve a cyclization step of precursors having a five-membered lactame ring,[15,16] and, perhaps because of that, are usually laborious and low-yielding.

EXPERIMENTAL SECTION

Melting points were determined in a Kofler Thermogerate apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1420 spectrophotometer; the nuclear magnetic resonance spectra were recorded in a Bruker WM-250 apparatus in deuterochloroform solutions containing tetramethylsilane as internal standard; mass spectra were obtained in a Kratos MS 50 TC mass spectrometer. Thin layer chromatography (tlc) was performed using Merck GF-254 type 60H silica gel, eluting with methylene chloride-methanol mixtures; samples spots were visualized under ultraviolet light or by developing plates with iodine vapour; column chromatography was carried out using Merck type 9385 silica gel. Solvents were purified as per ref. 17. Where indicated, solutions of compounds in organic solvents were dried over anhydrous sodium sulphate.

Methyl 2 -(2'-bromo-4',5'-dimethoxyphenylacetyl)-4,5-dimethoxyphenylacetate (1c).
Bromoketoacid **1b**[10] (5g, 11 mmol) was dissolved in 150 ml of methanol and 3 drops of concentrated sulfuric acid were added. After refluxing the mixture for 2 h, the methanol was evaporated and the residue was redissolved in 100 ml of dichloromethane, and washed with two 50 ml portions of water. The combined

organic layers were dried and the solvent was removed *in vacuo*, leaving a solid residue which was recrystallized from methanol to afford methyl 2-(2'-bromo-4',5'-dimethoxyphenylacetyl)-4,5-dimethoxyphenylacetate (**1c**) as a white solid (96% yield). M.p. 121-122 °C. IR (KBr, ν/cm^{-1}): 2960, 1740 (C=O), 1670 (C=O), 1600, 1510. ^{1}H NMR, δ/ppm: 3.67 (s, 3H, -OCH$_3$), 3.81 (s, 3H, -OCH$_3$), 3.84 (s, 3H, -OCH$_3$), 3.91 (s, 8H, 2x-OCH$_3$ and -CH$_2$-), 4.30 (s, 2H, -CH$_2$-), 6.71 (s, 1H, Ar-H), 6.74 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 7.40 (s, 1H, Ar-H). Anal.: $C_{21}H_{23}O_7Br$ requires C 53.96, H 4.92, Br 17.13; found, C 54.10, H 5.15, Br 16.81.

1,2,9,10-Tetramethoxy-6a,7-dehydrodibenzo[de,g]chromanone (4a).

AIBN (125 mg) and tributyltin hydride (0.64 ml, 2.3 mmol) were added to a solution of bromoketoester **1c** (500 mg, 1.1 mmol) in 250 ml of dry benzene, and refluxed under an argon atmosphere for 18 hours . The benzene was removed *in vacuo* and the residue was dissolved in 250 ml of acetonitrile, which was washed with three 50 ml portions of hexane, dried and then concentrated *in vacuo*. After flash chromatography of the solid residue (eluant: dichloromethane), 1,2,9,10-tetramethoxy-6a,7-dehydro-dibenzo[de,g]chromanone (**4a**) was isolated as a white solid (80% yield). M.p. 180-181 °C (methanol). IR (KBr, ν/cm^{-1}): 2940, 1760 (C=O), 1640 (C=C-O), 160
0, 1450, 1240, 1120. ^{1}H NMR, δ/ppm: 3.95 (s, 3H, -OCH$_3$), 4.05 (s, 6H, 2x-OCH$_3$), 4.07 (s, 3H, -OCH$_3$), 4.26 (s, 2H, -CH$_2$-), 7.05 (s, 1H, Ar-H), 7.17 (s, 1H, Ar-H), 7.18 (s, 1H, Ar-H), 9.12 (s, 1H, Ar-H). FAB-MS, m/e(%): 355 [(M+1)$^+$, 24], 354 (M$^+$, 100), 339 (30), 311 (17), 252 (8), 165 (16). Anal.: $C_{20}H_{18}O_6$ requires C 67.80, H 5.08; found, C 67.65, H 5.15.

1,2,9,10-Tetramethoxy-6a,7-dehydrodibenzo[de,g]chroman-5-ol (5).

Over a period of 10 min, sodium borohydride (200 mg) was added in small portions to a solution of chromanone **4a** (300 mg, 0.85 mmol) in 15 ml of methanol, and then stirred for 2 h at r.t. The solvent was removed *in vacuo*, and the residue was mixed with 60 ml of water and then extracted with three 25 ml portions of dichloromethane. The combined organic layers were washed with a further 60 ml of water, dried, and then concentrated *in vacuo*. After flash chromatography of the residue (eluant: 99:1 dichloromethane/methanol) 1,2,9,10-tetramethoxy-6a,7-dehydrodibenzo[de,g]-chroman-5-ol (**5**) was isolated as a white solid (89% yield). M.p. 194-195 °C (methanol). IR (KBr, ν/cm^{-1}): 3020 (-OH), 2990, 1640 (C=C-O), 1600, 1420, 1270, 1130. ^{1}H NMR, δ/ppm: 3.21-3.52 (m, 2H, -CH$_2$-), 3.93 (s, 3H, -OCH$_3$), 4.00 (s, 3H, -OCH$_3$), 4.02 (s, 3H, -OCH$_3$), 4.04 (s, 3H, -OCH$_3$), 5.81 (m, 1H, -CH-), 7.00 (s, 1H, Ar-H), 7.05 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 9.10 (s, 1H, Ar-H). EI/MS, m/e (%): 357 [(M+1)$^+$, 21], 356 (M$^+$, 100), 341 (43), 245 (36), 243 (36). Anal.: $C_{20}H_{20}O_6$ requires C 67.41, H 5.70; found, C 67.59, H 5.83.

2-(10'-Hydroxy-3',4',6',7'-tetramethoxy-1'-phenanthryl)ethanol (6).

In a flask fitted with a drying tube ($CaCl_2$), chromanone **4a** (400 mg, 1.13 mmol), sodium borohydride (300 mg, 0.84 mmol) and 6 ml of dry THF were stirred under a dry atmosphere at 0°C. Glacial acetic acid (470 mg) was added dropwise over 10 min to the mixture, which was then refluxed for 30 min. The solvent was removed *in vacuo* and the residue was suspended in 100 ml of water and extracted into three 25 ml portions of dichloromethane; the combined organic extracts were then dried and concentrated *in vacuo*. After flash chromatography of the residue (eluant: 95:5 dichloromethane/methanol), 2-(10'-hydroxy-3',4',6',7'-

tetramethoxy-1'-phenanthryl)ethanol (**6**) was isolated as an oil (67% yield). IR (film, ν/cm^{-1}): 3300 (-OH), 2990, 1630 (C=C-O), 1600, 1500, 1470, 1420, 1260. ^{1}H NMR, δ/ppm: 3.26 (t, J=5.6 Hz, 2H, -CH_2-), 3.94 (s, 3H, -OCH_3), 4.03 (s, 3H, -OCH_3), 4.04 (s, 3H, -OCH_3), 4.05 (s, 3H, -OCH_3), 4.39 (t, J=5.6 Hz, 2H, -CH_2-), 6.96 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 7.36 (s, 1H, Ar-OH), 9.13 (s, 1H, Ar-H). EI/MS, m/e (%): 359 [(M+1)$^+$, 20), 358 (M$^+$, 100). Anal.: $C_{20}H_{22}O_6$ requires C 67.03, H 6.19; found, C 67.08, H 6.10.

3,4,6,7-Tetramethoxy-9,10-dehydrodibenzo[cd,f]coumaranone (10b).

Oxygen was bubbled through a solution of chromanone **4a** (250 mg, 0.7 mmol) in 20 ml of 1,4-dioxane for 15 min; excess of sodium hydroxide (250 mg) was added and the mixture was stirred at r.t. for 72 hours. The solvent was removed *in vacuo* and the residue dissolved in 30 ml of dichloromethane and washed with two 15 ml portions of water. The organic layer was then dried and concentrated *in vacuo* and. After flash chromatography of the residue (eluant: 99:1 dichloromethane/methanol), 3,4,6,7-tetramethoxy-9,10-dehydrodibenzo[cd,f]coumaranone (**10b**) was isolated as a yellow solid (70% yield). M.p. 196-197 °C (methanol). IR (KBr, ν/cm^{-1}): 2940, 1780 (C=O), 1620 (C=C-O), 1540, 1270, 1100. ^{1}H NMR, δ/ppm: 4.05 (s, 3H, -OCH_3), 4.08 (s, 6H, 2x-OCH_3), 4.17 (s, 3H, -OCH_3), 7.17 (s, 1H, Ar-H), 7.26 (s, 1H, Ar-H), 7.78 (s, 1H, Ar-H), 8.74 (s, 1H, Ar-H). EI/MS, m/e (%): 340 (M$^+$, 100), 324 (23), 282 (12), 170 (11). Anal.: $C_{19}H_{16}O_6$ requires C 67.06, H 4.71; found, C 67.35, H 4.60.

3,4,6,7-Tetramethoxyaristolactam (10c).

A mixture of coumaranone **10b** (100 mg, 0.29 mmol), and 20 ml each of methanol and concentrated aqueous ammonia solution was stirred at r.t. for 48 h. The bulk of the methanol was removed *in vacuo* and the aqueous suspension was diluted with 30 ml of water and then extracted with three 15 ml portions of dichloromethane. The combined organic layers were then dried and concentrated *in vacuo* . After flash chromatography of the residue (eluant: 95:5 dichloromethane/methanol), 3,4,6,7-tetramethoxyaristolactam (**10c**) was isolated as a yellow solid (75% yield). M.p. 208-209 °C (methanol). IR (KBr, ν/cm^{-1}): 3190 (N-H), 2920, 1680 (C=O), 1500, 1260, 1120. ^{1}H NMR, δ/ppm: 4.04 (s, 3H, -OCH_3), 4.08 (s, 6H, 2x-OCH_3), 4.12 (s, 3H, -OCH_3), 7.00 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 7.70 (b.s., 1H, N-H), 7.79 (s, 1H, Ar-H), 8.80 (s, 1H, Ar-H). EI/MS, m/e (%): 340 [(M+1)$^+$, 26], 339 (M$^+$, 100), 324 (21), 309 (48), 294 (18). Anal.: $C_{19}H_{17}O_5N$ requires C 67.25, H 5.05, N 4.13; found, C 67.06, H 4.99, N 4.09.

***N*-Methyl-3,4,6,7-tetramethoxyaristolactam (10d).**

To a suspension of aristolactam **10c** (100 mg, 0.29 mmol) and sodium hydride (10 mg) in 10 ml of DMF, an excess of methyl iodide was added dropwise while the mixture was stirred under an argon atmosphere for 30 minutes. The excess of sodium hydride was destroyed by addition of ethanol to the reaction mixture, which was then poured into 50 ml of water, neutralized with 5% hydrochloric acid, and extracted with two 15 ml portions of chloroform. The extract was washed with water, dried and concentrated to give N-Methyl-3,4,6,7-tetramethoxyaristolactam (**10d**) as yellow crystals (quantitative yield). Analytical data for this sample were identical to those for a sample of **10d** obtained from pontevedrine[11] (tlc, MS, ^{1}H NMR).

Methyl 3,4,6,7,10-pentamethoxy-1-phenanthrylacetate (7).

A solution of chromanone **4a** (100 mg, 0.28 mmol) in 10 ml of 1% methanolic hydrogen chloride was refluxed for 2 h. The solvent was removed *in vacuo* and the residue was dissolved in 30 ml of dichloromethane and then washed with two 15 ml portions of water; the organic layer was then dried and concentrated *in vacuo* . After flash chromatography of the residue (eluant: 99:1 dichloromethane/methanol), methyl 3,4,6,7,10-pentamethoxy-1-phenanthrylacetate (**7**) was isolated as a white solid (90% yield). M.p. 181-183 °C (methanol). IR (KBr, ν/cm^{-1}): 2935, 1733 (C=O), 1623 (CH=C-O), 1593, 1463, 1250, 1189. ^{1}H NMR, δ/ppm: 3.70 (s, 3H, -OCH_3), 3.87 (s, 3H, -OCH_3), 3.89 (s, 3H, -OCH_3), 3.95 (s, 6H, 2x-OCH_3), 4.02 (s, 3H, -OCH_3), 4.16 (s, 2H, -CH_2-), 6.78 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 7.06 (s, 1H, Ar-H), 9.19 (s, 1H, Ar-H). EI/MS, m/e (%): 400 (M^+, 100), 353 (14), 325 (17), 200 (12), 163 (14), 58 (24). Anal.: $C_{22}H_{24}O_7$ requires C 65.99, H 6.04; found, C 66.17, H 6.14.

Methyl (Z)-4,5-dimethoxy-2-(3',4'-dimethoxy-α'-methoxystyryl)phenylacetate (11).

A solution of isochroman-3-one **2**[7] (100 mg, 0.28 mmol) in 10 ml of 1% methanolic hydrogen chloride (1%) (10 ml) was refluxed for 15 min. The solvent was removed *in vacuo* and the residue was dissolved in 30 ml of dichloromethane and then washed with two 15 ml portions of water (2x15 ml). The organic layer was dried and concentrated *in vacuo*. After flash chromatography of the residue (eluant: 99:1 dichloromethane/methanol), methyl *(Z)*-4,5-dimethoxy-2-(3',4'-dimethoxy-α'-methoxystyryl)phenylacetate (**11**) was isolated as a white solid (92% yield). M.p. 127-128 °C (methanol). IR (KBr, ν/cm^{-1}): 2950, 1736 (C=O), 1679 (C=C-O), 1602, 1520, 1267, 1128. ^{1}H NMR, δ/ppm: 3.67 (s, 3H, -OCH_3), 3.84 (s, 6H, 2x-OCH_3), 3.87 (s, 3H, -OCH_3), 3.88 (s, 3H, -OCH_3), 3.91 (s, 3H, -OCH_3), 4.15 (s, 2H, -CH_2-), 6.70-6.80 (m, 5H, 5xAr-H), 7.39 (s, 1H, Ar-H). EI/MS, m/e (%): 402 (M^+, 3), 237 (29), 209 (100), 151 (12). Anal.: $C_{22}H_{26}O_7$ requires C 65.66, H 6.51; found, C 65.39, H 6.35.

1,2-Dimethoxy-6a,7-dehydrodibenzo[de,g]chromanone (4b).

Starting from bromoketoester **1d**[14] (500 mg, 1.2 mmol), and following the procedure above, 1,2-dimethoxy-6a,7-dehydrodibenzo[de,g]chromanone (**4b**) was isolated as a white solid (90% yield). M.p. 160-162 °C (methanol). IR (KBr, ν/cm^{-1}): 2935, 1760 (C=O), 1640 (C=C-O), 1603, 1456, 1245. ^{1}H NMR, δ/ppm: 3.95 (s, 3H, -OCH_3), 4.04 (s, 3H, -OCH_3), 4.27 (s, 2H, -CH_2-), 7.09 (s, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.56-7.61 (m, 2H, 2xAr-H), 7.77-7.81 (m, 1H, Ar-H), 9.51-9.54 (m, 1H, Ar-H). EI/MS, m/e (%): 294 (M^+, 14), 280 (100), 166 (28), 138 (31), 83 (61). Anal.: $C_{18}H_{14}O_4$ requires C 73.46, H 4.79; found, C 73.51, H 4.70.

3,4-Dimethoxy-9,10-dehydrodibenzo[cd,f]coumaranone (10e).

Starting from coumaranone **4b** (500 mg, 1.7 mmol), and following the procedure described above for the preparation of **10b**, 3,4-dimethoxy-9,10-dehydrodibenzo[cd,f]coumaranone (**10e**) was isolated as a yellow solid (71% yield). M.p. 176-178 °C (methanol). IR (KBr, ν/cm^{-1}): 2944, 1780 (C=O), 1620 (C=C-O), 1545, 1266. ^{1}H NMR, δ/ppm: 4.10 (s, 3H, -OCH_3), 4.18 (s, 3H, -OCH_3), 7.26 (s, 1H, Ar-H), 7.62-7.66 (m, 2H, 2xAr-H), 7.84 (s, 1H, Ar-H), 8.89-8.93 (m, 1H, Ar-H), 9.22-9.25 (m, 1H, Ar-H). MS EI/MS, m/e (%): 280 (M^+, 100), 264 (12), 77 (31). Anal.: $C_{17}H_{12}O_4$ requires C 72.85, H 4.32; found, C 72.60, H 4.50.

3,4-Dimethoxyaristolactam (10f).

Starting from coumaranone **10e** (100 mg, 0.36 mmol), and following the procedure described above for preparation of **10c**, 3,4-dimethoxyaristolactam (**10f**) was isolated as a yellow solid (71 % yield), and identified by comparison (tlc, MS, ^{1}H NMR) with an authentical sample of **10f**[15].

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REFERENCES AND NOTES

1. Bringmann, G.; Walter, R.; Weirich, R. *Angew Chem. Int. Ed. Engl.*, **1990**, *29*, 977.
2. a) Shamma, M., *The Isoquinoline Alkaloids: Chemistry and Pharmacology*. Academic Press, 1972. b) Shamma, M.; Moniot, J.L. *Isoquinoline Alkaloids Research, 1972-77*, Plenum Press, 1978. c) Guinaudeau, H.; Leboeuf, M.; Cavé, A. *J. Nat. Prod.*, **1988**, *51*, 389. d) Cavé, A.; Leboeuf, M.; Cassels, B.K. in *The Alkaloids*, vol. 35, A. Brossi (ed.) , Academic Press, 1989. e) Guinaudeau, H.; Leboeuf, M.; Cavé, A. *J. Nat. Prod.*, **1990**, *53*, 235. e) Kametani, T. In *The Total Synthesis of Natural Products*, ApSimon J. (ed.), Wiley Interscience, 1977. f) Chang, Z-L.; Zhu, D-Y. In *The Alkaloids*, vol. 31, p. 29, A. Brossi (ed.), Academic Press, 1987. g) Castedo, L.; Tojo, G. In *The Alkaloids*, vol. 39, p. 99, A. Brossi (ed.), Academic Press, 1990.
3. a) Estévez, J.C.; Villaverde, M.C.; Estévez, R.J.; Castedo, L. *Tetrahedron Lett.*, **1991**, *32*, 529. b) Estévez, J.C.; Villaverde, M.C.; Estévez, R.J.; Castedo, L. *Tetrahedron*, **1994**, *50*, 2107.
4. Cava, M.P.; Mitchell, M.J.; Havlicek, S.C.; Lindert, A. *J. Org. Chem.*, **1970**, *35*, 175.
5. a) Narasimhan, N.S.; Aidhen, I.S. *Tetrahedron Lett.*, **1988**, *29*, 2987. b) Curran, D.P. *Synthesis*, **1988**, 417.
6. Estévez, J.C.; Villaverde, M.C.; Estévez, R.J.; Castedo, L. *Tetrahedron*, **1993**, *49*, 2783.
7. Elliot, I.W., Jr. *J. Heterocycl. Chem.*, **1972**, *9*, 853.
8. Estévez, J.C.; Villaverde, M.C.; Estévez, R.J.; Castedo, L. *Tetrahedron Lett.*, **1992**, *33*, 5145.
9. Achari, B.; Bandyopadhyay, S.; Saha, C.R.; Pakarshi, S.C. *Heterocycles*, **1983**, *20* , 771.
10. Castedo, L.; Estévez, R.J.; Saá, J.M.; Suau, R. *J. Heterocycl. Chem.*, **1982**, *19*, 1469.
11. Castedo, L.; Suau, R.; Mouriño, A. *Tetrahedron Lett.*, **1976**, 501.
12. Seijas, J.A.; De Lera, A.R.; Villaverde, M.C.; Castedo, L. *J. Chem. Soc. Chem. Commun.*, **1985**, 893.
13. Floyd, A.J.; Dyke, S.F.; Ward, S.E. *Chem. Rev.*, **1976**, *76*, 509.
14. Castedo, L.; Estévez, R.J.; Saá, J.M.; Suau, R. *An. Quím. (C)*, **1983**, *79*, 329.
15. Castedo, L.; Guitián, E.; Saá, J.M.; Suau, R. *Heterocycles*, **1982**, *19*, 279.
16. Castedo, L.; Guitián, E.; Saá, J.M.; Suau, R. *Tetrahedron Lett*, **1982**, *23*, 457.
17. Perrin, D.D.; Armarego, W.L.F. *Purification of Laboratory Chemicals*, Pergamon Press, **1988**.

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