An Improved and Versatile Method for the Rapid Synthesis of Aryldihydrobenzofuran Systems by a Boron Tribromide-Mediated Cyclization Reaction

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Boron tribromide is presented as a highly reactive reagent that *simultaneously* allows the demethylation and fully diastereoselective cyclization of different precursor molecules, obtained by an aldol-type reaction, to a series of hydroxylated aryldihydrobenzofuran systems in racemic form. The latter are often found as key structures in natural compounds of different classes. Syntheses of educts, which mainly took advantage of a versatile *Rieche* formylation, are also described.

1. Introduction. – Viewing a whole list of polyamine alkaloids [1], the spermine alkaloid aphelandrine[2]) and the related class of ephedradines (see **1**–**4**) attract attention in view of their structural complexity. Undoubtedly, this arises from the incorporation of two hydroxylated aromatic systems, which are linked together to form an aryldihydrobenzofuran system. Such a system is not only an integral part of the mentioned polyamine alkaloids but also of compounds that belong to other groups of natural products, for example the flavonoids [2], lignans [3][4], and depsides [5]. The latter group contains, in particular, the salvianolic acids, which will be discussed below. In contrast to the biological relevance of the aryldihydrobenzofuran moiety, only quite a few synthetic procedures for such compounds can be found in the literature. Most of the published work dealing with the preparation of aryldihydrobenzofuran systems involved a synthetic procedure is referred to as phenolic oxidation [6]. The importance of such a reaction for the biosynthesis of aphelandrine has been shown impressively by *Nezbedová et al.* [7]. In sharp contrast to its unquestioned relevance for *in vivo* synthesis, in the laboratory, this reaction proved to suffer from serious disadvantages, *e.g.*, the yields are usually low and the range of obtainable substitution patterns at the two aromatic rings is rather limited. So it became obvious to us that, in the course of our synthetic projects, we should look for an alternative procedure, which should not only allow the preparation of different hydroxylated aryldihydrobenzofurans but which also must be operationally simple and, in addition, require only inexpensive starting materials. A corresponding literature search revealed a strategy to construct the aryldihydrobenzofuran framework first published by *Nakatsubo* and *Higuchi* [8]; the same method was again mentioned almost one decade later by *Baker et al.* [9]. Therein,

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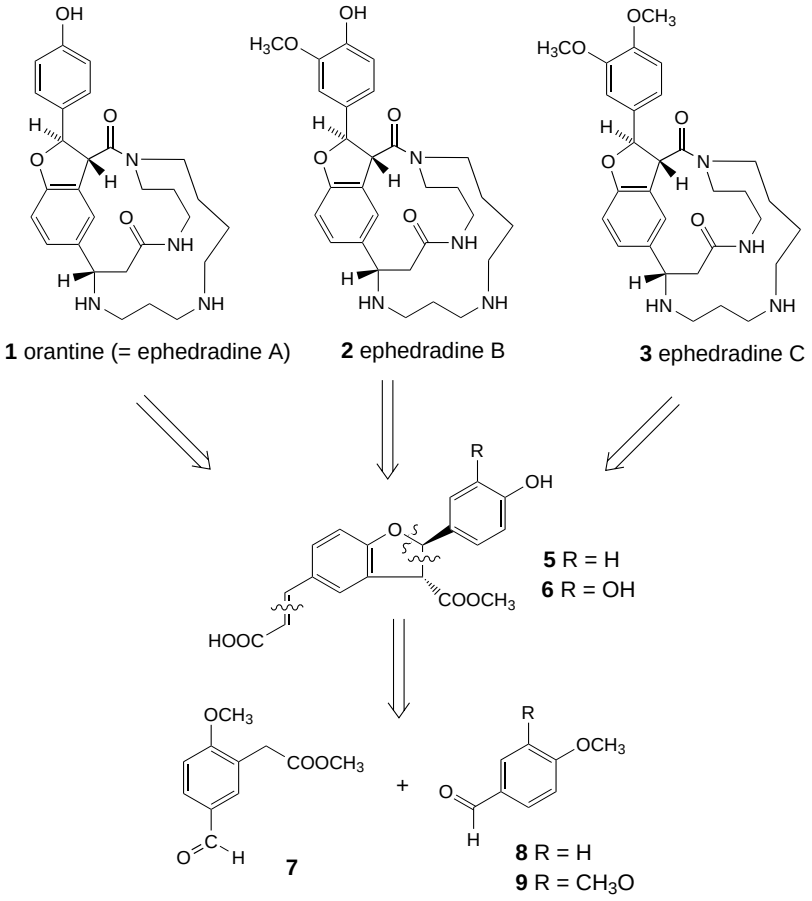
[1]) Part of the Ph.D. thesis of *R. D.*, University of Zürich, 2002.

[2]) Aphelandrine and orantine (=ephedradine A; **1**) are epimers with respect to the two stereogenic centers at the dihydrobenzofuran ring.

the key steps are an aldol-type reaction between an aromatic aldehyde and a phenylacetic ester derivative, followed by a ring closure mediated by the *Lewis* acid $BF_3 \cdot Et_2O$. Verifying these synthetic steps, we found them to satisfy our claims *in principal*. On the other hand, the procedures provided by these authors for preparing the necessary phenylacetic ester derivatives are rather tedious and, therefore, not at all satisfying. To make a long story short: literature offered us a valuable synthetic strategy, but we had to work out the scope and limitations of this process for ourselves and also to find a convenient access to the starting materials.

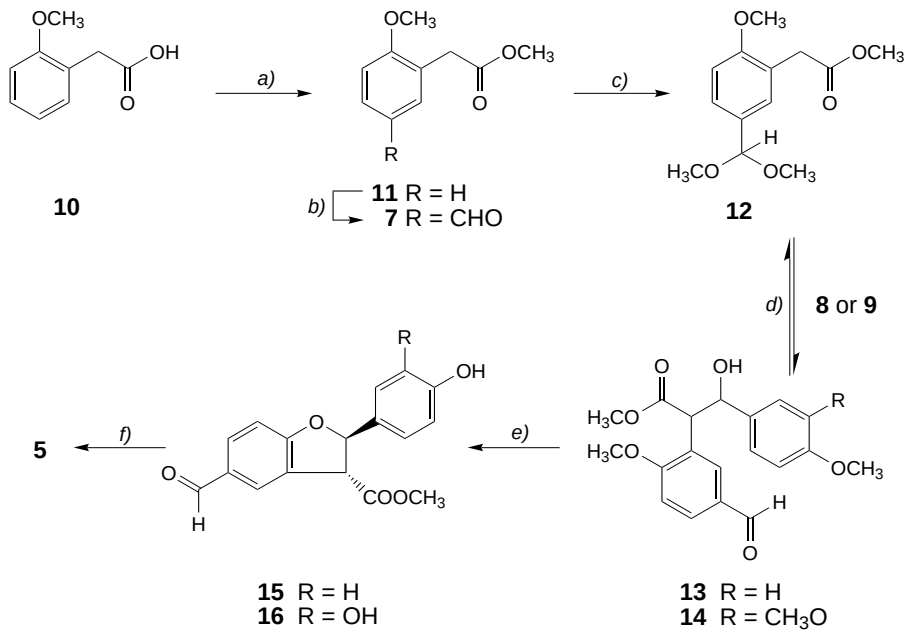
2. Results and Discussion. – The first synthetic targets we chose were the closely related aryldihydrobenzofuran systems **5** and **6** deduced from the macrocyclic spermine alkaloids orantine (=ephedradine A; **1**) and ephedradine B (**2**) and C (**3**). *retro*-Synthetic analysis according to the strategy of [8] – as shown in *Scheme 1* – revealed the building blocks **7** and **8** or **9** for a synthesis of **5** and **6**.

Scheme 1



Obviously, the availability of **8** and **9** represent no problem because **8** is anisaldehyde, and **9** is veratrumaldehyde, which are both inexpensive commercial compounds. So we focused on the synthesis of phenylacetic ester derivative **7**. Very surprisingly, for the formation of such a simple compound, the literature offers only the elaborate procedure of *Baker et al.* mentioned above. Recognizing the availability of (2-methoxyphenyl)acetic acid (**10**), we were able to prepare **7** easily in multigram amounts by a very smooth two-step reaction sequence (*Scheme 2*): an esterification with MeOH to **11** was accomplished by a comparatively unknown formylation method, the so-called *Rieche* formylation [10] involving as a formylating agent dichloromethyl methyl ether in combination with stoichiometric amounts of $SnCl_4$. Fortunately, this procedure not only allowed the isolation of almost quantitative yields of the desired **7** after a rapid reaction but also provided the product with complete regioselectivity, *i.e.*, apart from the normal extraction procedure, purification was unnecessary. The projected aldol-type reaction with the aldehydes **8** or **9** first required suitable protection of the formyl group of **7**, which was perfectly achieved by its transformation to the standard dimethyl acetal derivative **12** with trimethyl orthoformate. Acetal derivative **12** was stable enough to facilitate the following aldol-type reaction. On the other hand, the acetal moiety was easily hydrolyzed during the subsequent workup procedure, therefore uncovering the formyl moiety for the final *Knoevenagel* condensation. For the aldol-type reaction (an equilibrium reaction) of **12** with **8** or **9**,

Scheme 2



a) $SOCl_2$, MeOH, 0°, 1 h; 98%. *b*) Cl_2CHOMe, $SnCl_4$, CH_2Cl_2, 0° → r.t., 2 h; 98%. *c*) $HC(OMe)_3$, MeOH, NH_4Cl, reflux, 2 h; 88%. *d*) 1. LDA, Et_2O, −78°, 30 min; 77%; 2. aq. HCl soln., 1 min, r.t.; quant. *e*) BBr_3, CH_2Cl_2, 0°, 2 h; 68%. *f*) $CH_2(COOH)_2$, piperidine, pyridine, reflux, 2 h; 97%.

it proved to be of greatest importance to carry out the whole reaction, *including* the quenching process, at low temperature (−78°) because only then does the equilibrium favor the products. Deprotonation of **12** was best done by lithium diisopropylamide (LDA) in Et_2O, followed by addition of the appropriate aldehyde. As equilibrium was always attained rapidly, prolonged reaction times did not increase the yield. Workup under mildly acidic conditions liberated the aldol products **13** and **14**, respectively, each as an inseparable mixture of two diastereoisomers. Fortunately, this outcome was of no importance because the subsequent cyclization of **13** and **14** transformed both diastereoisomers of each aldol product into the desired aryldihydrobenzofuran systems **15** and **16**, respectively. We were very pleased to see that an excess of boron tribromide not only liberated from the MeO groups of **13** or **14** the phenolic OH groups needed for the cyclization step but also promoted the latter *in situ* to give the aryldihydrobenzofuran systems **15** or **16**, respectively, in good to excellent yields. It may be justified to emphasize the role of boron tribromide as a deprotecting *and* cyclization reagent, making, thus, the whole transformation highly user-friendly, especially when taking into account the simple reaction conditions, which do not even require any specially dried solvent or protecting atmosphere. The NMR spectra of the racemic products **15** and **16** clearly established the presence of just one diastereoisomer in each case, *i.e.*, the (hydroxylated) aryl moiety and the COOMe group both connected to the dihydrofuran moiety were in either *cis*- or *trans*-relationship, but definitely, no mixture was present. Since it is known that coupling constants – although easily observeable – are of no significance in such five-membered rings, we could not determine the *cis*- or *trans*-configuration from the NMR data. This difficulty, indeed, once led to a wrong presumption by *Stoessl* [11] about the relative configuration of hordatine A (an antifungal factor of barley) in which the aryldihydrobenzofuran system **5** is incorporated. Confronted with an analogous question, *Yoshihara et al.* [4] decided to solve the configuration problem by comparison and correlation of the chemical shifts of configurationally known derivatives. Therefore, they were able to establish the *trans*-configuration in their case. Even so, one may expect increased thermodynamic stability for the *trans*-configuration, we actually had no final proof in hand that the arguments of *Yoshihara* were also true in our case. Luckily, it was possible to crystallize **16**, so the assumed *trans*-configuration could be secured unequivocally by an X-ray single-crystal analysis (see *Fig. 1*).

Exemplarily for **15**, we continued with the construction of such an α,β-unsaturated carboxylic acid side-chain – *via Knoevenagel* condensation – as one is present, *e.g.*, in the above-mentioned polyamine alkaloid hordatine A. By a standard procedure, **5** was obtained without any problems (*Scheme 2*), suggesting that **6** might be formed analogously. Following the general synthetic pathway, but varying the aldehyde used in the aldol-type reaction, there are surely a great range of different substitution patterns feasible.

Encouraged by these results, we went on to the *retro*-synthetic analysis of ephedradine D (**4**) with the focus on the aryldihydrobenzofuran system **17** integrated there. As shown in *Scheme 3*, the above-exemplified synthetic strategy required as starting materials phenylacetic acid derivative **18** and anisaldehyde (**8**).

This time, a literature search was completely unsuccessful. For obvious reasons of chemical similarity and inexpensiveness, we chose vanillin (**19**) as our starting material

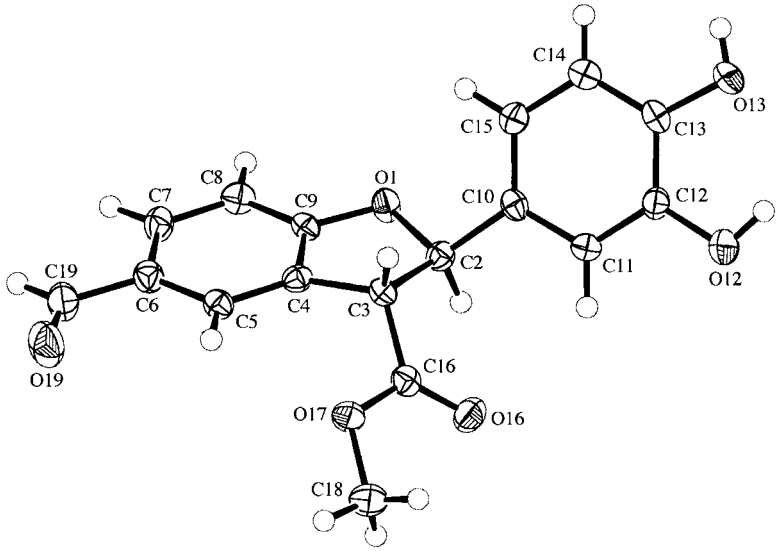
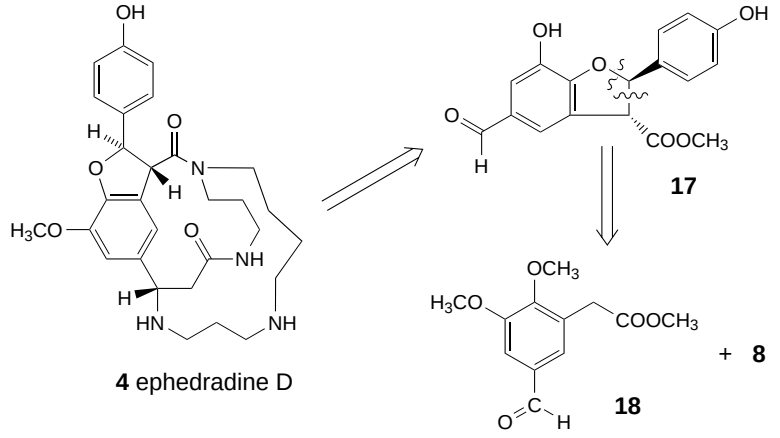


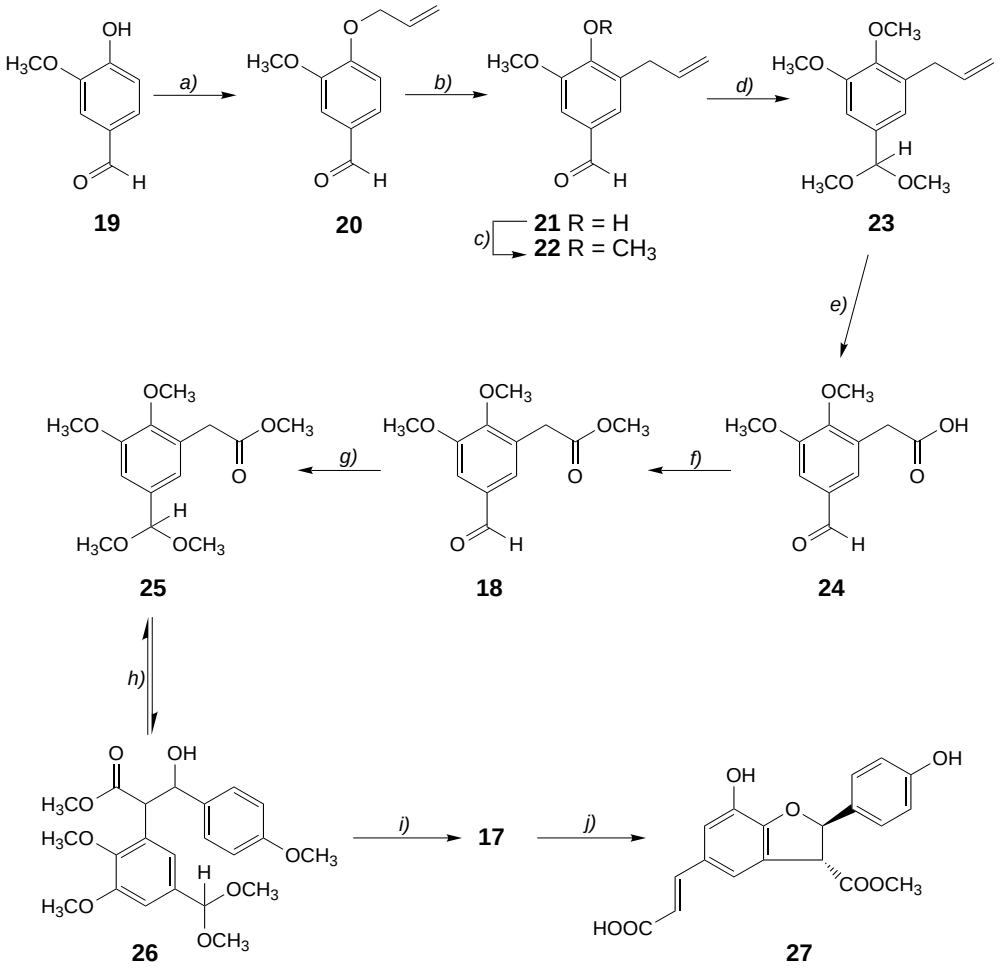
Fig. 1. *ORTEP Plot* [12] *of the aryldihydrobenzofuran skeleton* **16**

Scheme 3



for the synthesis of **18** (*Scheme 4*). First, **19** was allylated at the free OH group ($\rightarrow$**20**) by allyl bromide, and then an allyl migration yielding **21** was achieved according to a *Claisen* mechanism by means of heating **20** in mesitylene as an inert and high-boiling solvent. After methylation of the now free OH group by MeI ($\rightarrow$**22**) and subsequent acetalization, compound **23** was obtained in high overall yield. Unfortunately, the projected split-off of the C=C bond proved to be more problematic, so neither ozonolysis nor the attempted oxidation by means of $RuO_4/NaIO_4$ was successful. Finally, a *Lemieux–van Rudloff* oxidation (substoichiometric amounts of $KMnO_4$ together with an excess of $NaIO_4$) allowed the isolation of acid **24** in moderate yield. As

Scheme 4

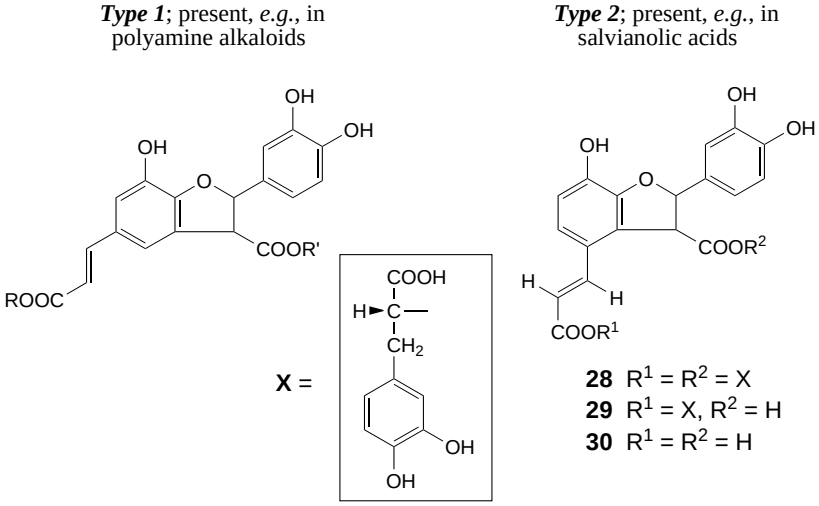


a) CH_2=$CHCH_2Br$, K_2CO_3, acetone, reflux, 8 h; 90%. *b*) Mesitylene, reflux, 24 h; 88%. *c*) MeI, K_2CO_3, DMF, r.t., 8 h; 92%. *d*) $HC(OMe)_3$, MeOH, NH_4Cl, reflux, 2 h; 95%. *e*) $KMnO_4$, $NaIO_4$, K_2CO_3, ^{t}BuOH/H_2O, r.t., 4 h; 51%. *f*) $SOCl_2$, MeOH, 0°, 1.5 h; 75%. *g*) $HC(OMe)_3$, MeOH, NH_4Cl, reflux, 2 h; 75%. *h*) LDA, **8**, Et_2O, −78°, 1 h; 73%. *i*) BBr_3, CH_2Cl_2, 0°, 1.5 h; 82%. *j*) $CH_2(COOH)_2$, piperidine, pyridine, reflux, 2 h; 92%.

the workup procedure required acidic conditions, the dimethyl acetal inevitably was also hydrolyzed. After two steps of routine synthesis, esterification (→**18**) and acetalization, the precursor **25** for the aldol-type reaction was obtained. The latter could be performed with anisaldehyde (**8**) as described above. Again, the aldol product **26** was formed as a mixture of diastereoisomers. All mentioned reactions before the aldol-type reaction could be optimized in such a manner that only the usual extractive workup but no chromatographic separation was necessary; despite the somewhat prolonged reaction sequence, rapid success was ensured. Also successful was the

application of boron tribromide as deprotecting/coupling reagent to furnish the desired aryldihydrobenzofuran **17** in one additional step, and, finally, the α,β-unsaturated acid side-chain was constructed by a *Knoevenagel* condensation yielding **27**. Attention may be drawn to the difference in reactivity of the two carboxylic acid functionalities of **27**, one being present as an ester and the other as the free acid, so regioselectivity for further synthetic operations is ensured effortlessly.

Concomitant to our work on the aryldihydrobenzofuran systems present in polyamine alkaloids, we were in search of a further substance class to test the usefulness of our new method. For this purpose, some natural products of the plant *Salvia miltiorrhiza* BUNGE (Labiatae) – the so-called salvianolic acids [5][13][14] – proved to be of high interest. Such compounds are well known in Chinese medicine for the treatment of coronary diseases [15]. At least in salvianolic acid B (**28**) [5] and the related compounds lithospermic acid (**29**) – isolated from *Lithospermum ruderale* DOUGL. ex LEHM. (Boraginaceae) [16] – as well as in przewalskinic acid (**30**) – isolated from *Salvia przewalskii* MAXIM. (Labiatae) [17] – there is also a aryldihydrobenzofuran skeleton present, which differs in substitution pattern from the already mentioned ones. A comparison of both aryldihydrobenzofuran skeletons is shown in *Fig. 2*.

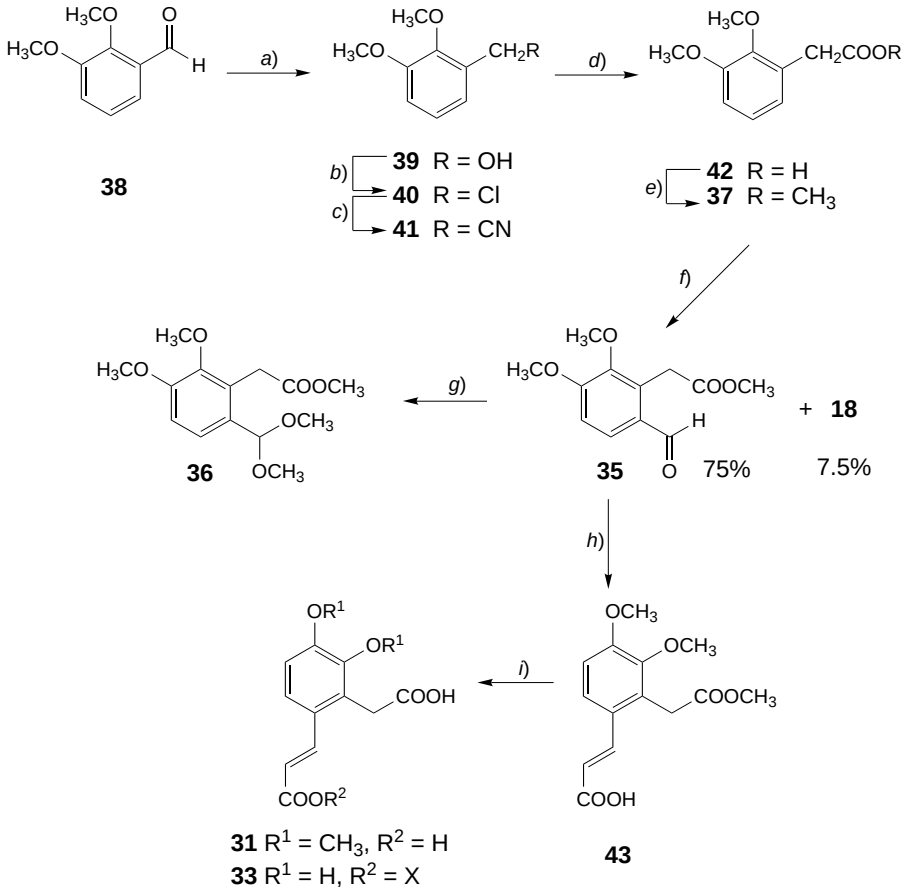


derived from (2*R*)-3-(3,4-dihydroxyphenyl)lactic acid

Fig. 2. *Comparison of the substitution patterns of different aryldihydrobenzofuran skeletons present in natural products*

Moreover, below we would like to exemplify that our synthetic strategy, initially focussed on the preparation of przewalscinic acid (**30**), allowed *en passant* the synthesis of the principal skeletons **31** and **32** of two more natural products – salvianolic acid D (**33**) and salvianolic acid E (**34**) (see below, *Schemes 5* and *6*). Following the *retro*-synthetic analysis, it was obvious that we needed access to the aromatic aldehyde **35** and its dimethyl acetal **36**. For the synthesis of **35** (*Scheme 5*) on a multigram scale, we once

Scheme 5



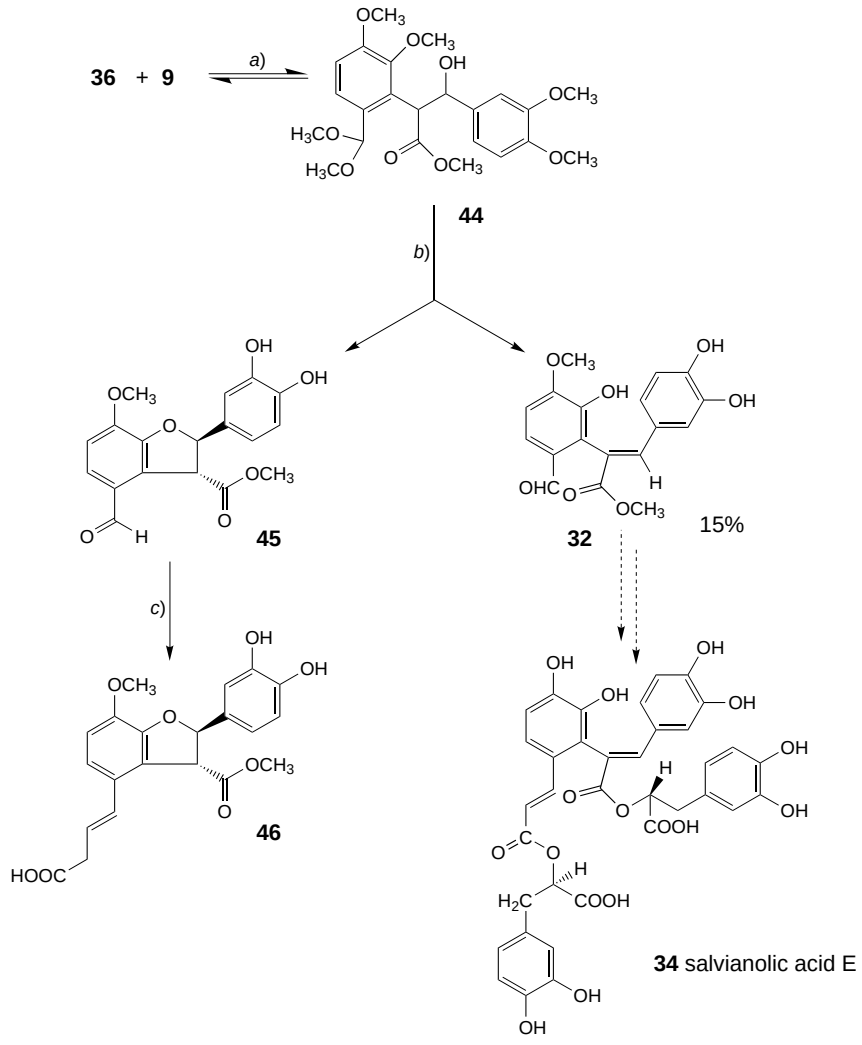
a) $NaBH_4$, MeOH, r.t., 2 h; 99%. *b*) $SOCl_2$, pyridine, $CHCl_3$, r.t., 45 min; 95%. *c*) KCN, EtOH/H_2O, reflux, 1 h; 99%. *d*) 2N NaOH, EtOH, reflux, 10 h; 90%. *e*) $SOCl_2$, MeOH, 0°, 1.5 h; 97%. *f*) Cl_2CHOMe, $SnCl_4$, CH_2Cl_2, 0° → r.t., 2 h. *g*) $HC(OMe)_3$, MeOH, NH_4Cl, reflux, 2 h; 90%. *h*) $CH_2(COOH)_2$, pyridine, piperidine, reflux, 2 h; 81%. *i*) 2N KOH, MeOH, r.t., 2 h; 73%.

more trusted the highly reliable *Rieche* formylation of precursor **37**. The latter was accessible in a straightforward reaction cascade starting from easily available 2,3-dimethoxybenzaldehyde (**38**). Reduction of **38** by means of $NaBH_4$ (→**39**), transformation of the OH functionality into Cl (→**40**) resulted, after substitution with potassium cyanide, in nitrile **41**. Hydrolysis under basic conditions gave acid **42**, which finally could be esterified to **37**. *Rieche* formylation of **37** under standard conditions resulted in the desired aldehyde **35** in good yield. Regioselectivity of this formylation proved to be high again, but a small amount (7.5%) of regioisomer **18** was also observed. On the one hand, aldehyde **35** was transformed into acetal **36**, the important intermediate for the subsequent aldol-type reaction. On the other hand, a *Knoevenagel*

condensation of **35** with malonic acid gave **43**, which, after simple ester hydrolysis, furnished **31**, the above-mentioned skeleton of salvianolic acid D (**33**). This natural compound – isolated from *Salvia miltiorhizza* – also contains the (2*R*)-3-(3,4-dihydroxyphenyl)lactic acid residue.

For the ongoing synthesis of **30**, acetal **36** was subjected to an aldol-type reaction with veratrumaldehyde (**9**) (*Scheme 6*). Again, an equilibrium was reached quickly, enabling the isolation of product **44** in a somewhat lower yield in comparison to the above-mentioned aldol-type reactions. More conspicuously, **44** was obtained as a *single*

Scheme 6



a) LDA, Et_2O, – 78°, 1 h; 60%. *b*) BBr_3, CH_2Cl_2, 0°, 2 h; 42% (**45**). *c*) $CH_2(COOH)_2$, pyridine, piperidine, 100°, 2 h; 35%.

diastereoisomer. Treatment of **44** with boron tribromide resulted in the formation of the expected aryldihydrobenzofuran system **45**. Due to the occurrence of a by-product (see below), the yields were always lower than in former cases. Although an excess of boron tribromide was used, one phenolic methyl ether was not cleaved under the reaction conditions. The product **46** of a subsequent *Knoevenagel* condensation, therefore, represented the monomethyl ether of przewalskinic acid (**30**). Structure **46** – in particular the position of the remaining ether MeO group – was secured by two-dimensional NMR analysis. Clearly, with **46** in hand, a projected synthesis of lithospermic acid (**29**) and salvianolic acid B (**28**) necessitates a one- or two-fold esterification with (2*R*)-3-(3,4-dihydroxyphenyl)lactic acid. Once more, the intrinsic diversification of the two carboxy groups in **46** greatly supports such a purpose.

In addition to that, the described cyclization also resulted in *ca*. 15% of the interesting by-product **32**. The latter was obviously produced by dehydration of **44** and is surely utilizable as a key compound in the synthesis of salvianolic acid E (**34**). The phenolic MeO group also present in **32** means that boron tribromide, at least under the chosen reaction conditions, is not suitable for full deprotection. Larger amounts of **32** should be amenable from **44** in a well-directed synthesis.

Conclusions. – In summary, it could be shown that boron tribromide is a highly useful reagent for the *simultaneous* demethylation and cyclization within the context of the synthesis of different hydroxylated aryldihydrobenzofuran systems that occur, *e.g.*, in the structures of polyamine alkaloids or depsides. The presented methodology is flexible enough to enable the construction of the different substitution patterns essential for the total synthesis of such a natural product. Besides the simple reaction conditions for the cyclization step, all starting materials are available by straightforward procedures from common inexpensive chemicals without needing any special methods or reagents. Finally, the possibility to exchange both components of the aldol-type reaction against other substituted ones, offers the chance for a substance library, which may be of pharmaceutical interest regarding the physiological properties of the original natural compounds.

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Experimental Part

General. All commercially available reagents were used without further purification. Solvents were either *puriss. p.a.* grade (*Fluka*) or were distilled prior to use. Reactions were normally *not* carried out under N_2, unless otherwise stated; they were monitored by TLC (*Merck* precoated silica gel plates *60* F_{254}). All extracts were dried ($MgSO_4$) before evaporation, unless otherwise stated. Column chromatography (CC): silica gel *60* (230–400 mesh ASTM) from *Merck*. Melting points (M.p.): *Mettler FP5*. IR [cm^{-1}]: in $CHCl_3$ (*Fluka* for IR spectroscopy); *Perkin-Elmer 781*. NMR Spectra: in $CDCl_3$, except where noted, *Bruker ARX-300* (^1H at 300 and ^{13}C at 75 MHz) or *Bruker DRX-600* (^1H at 600 and ^{13}C at 150 MHz); chemical shifts δ in ppm rel. to Me_4Si as internal standard; coupling constants *J* in Hz. MS: *Finnigan SSQ-700* for chemical ionization (CI) with NH_3, *Finnigan MAT-90* for electron impact (EI, 70 eV), and *Finnigan TSQ-700* for electrospray ionization (ESI); *m*/*z* (rel. intensity in %).

Methyl (2-Methoxyphenyl)acetate (**11**). To an ice-cooled soln. of (2-methoxyphenyl)acetic acid (**10**; 10.0 g, 60.0 mmol) in MeOH (100 ml), thionyl chloride (11.9 g, 7.25 ml, 0.1 mol) was added dropwise and slowly. After

1 h stirring, evaporation yielded **11** (10.6 g, 98%). Colorless liquid, pure enough for the next step. IR: 3000*w*, 2950*m*, 2840*w*, 1730*s*, 1600*m*, 1590*m*, 1490*s*, 1460*s*, 1435*s*, 1340*s*, 1290*s*, 1250*s*, 1160*s*, 1110*s*, 1050*w*, 1030*m*. ^{1}H-NMR ($CDCl_3$): 7.24 (*dt*, *J* = 9.7, 1.7, 1 H); 7.17 (*dd*, *J* = 7.4, 1.7, 1 H); 6.92 (*dd*, *J* = 7.4, 1.1, 1 H); 6.86 (*dd*, *J* = 10.3, 2.0, 1 H); 3.81 (*s*, 3 H); 3.68 (*s*, 3 H); 3.63 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 172.2 (*s*); 157.4 (*s*); 130.7 (*d*); 128.4 (*d*); 122.9 (*s*); 120.4 (*d*); 110.4 (*d*); 5.4 (*q*); 51.7 (*q*); 35.6 (*t*). CI-MS: 198 (100, $[M+NH_4]^+$), 181 (10, $[M+H]^+$).

Methyl (5-Formyl-2-methoxyphenyl)acetate (**7**). $SnCl_4$ (22.8 g, 10.3 ml, 87.0 mmol) was added to an ice-cooled soln. of **11** (10.5 g, 58.0 mmol) in CH_2Cl_2 (150 ml). Then, dichloromethyl methyl ether (13.4 g, 10.3 ml, 116.0 mmol) was added dropwise within 30 min. Stirring was continued at r.t. for 90 min before the mixture was hydrolyzed by careful pouring into ice-water. Extraction with CH_2Cl_2 and evaporation of the org. phase yielded 11.8 g (98%) of **7**. Oil, which was considered sufficiently pure for use in the next step. IR: 3000*w*, 2950*w*, 2840*w*, 2740*w*, 1735*s*, 1685*s*, 1605*s*, 1585*m*, 1500*m*, 1460*w*, 1440*m*, 1340*m*, 1325*m*, 1260*s*, 1170*m*, 1120*m*, 1025*m*, 910*w*. ^{1}H-NMR ($CDCl_3$): 9.87 (*s*, 1 H); 7.81 (*dd*, *J* = 8.5, 2.1, 1 H); 7.73 (*d*, *J* = 2.1, 1 H); 6.99 (*d*, *J* = 8.5, 1 H); 3.91 (*s*, 3 H); 3.70 (*s*, 3 H); 3.68 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 190.7 (*d*); 171.4 (*s*); 162.5 (*s*); 132.1 (*d*); 131.8 (*d*); 129.6 (*s*); 124.0 (*s*); 110.3 (*d*); 55.8 (*q*); 51.9 (*q*); 35.4 (*t*). CI-MS: 226 (100, $[M+NH_4]^+$), 209 (8, $[M+H]^+$).

Methyl [5-(Dimethoxymethyl)-2-methoxyphenyl]acetate (**12**). A mixture of **7** (11.0 g, 53.0 mmol), trimethyl orthoformate (11.3 g, 11.6 ml, 106.0 mmol) and a cat. amount (*ca.* 0.1 g) of NH_4Cl in MeOH (100 ml) was refluxed for 2 h. After cooling to r.t., the mixture was poured into ice-cooled aq. 2N NaOH and extracted quickly with Et_2O. Evaporation gave 11.9 g (88%) of **12**. Yellowish oil of sufficient purity. IR: 2995*m*, 2950*s*, 2900*m*, 2840*m*, 1735*s*, 1615*m*, 1500*s*, 1460*m*, 1435*s*, 1405*w*, 1340*s*, 1310*w*, 1255*s*, 1160*s*, 1125*m*, 1100*s*, 1050*m*, 990*w*. ^{1}H-NMR ($CDCl_3$): 7.32 (*dd*, *J* = 8.4, 2.2, 1 H); 7.26 (*d*, *J* = 2.2, 1 H); 6.85 (*d*, *J* = 8.4, 1 H); 5.34 (*s*, 1 H); 3.80 (*s*, 3 H); 3.67 (*s*, 3 H); 3.63 (*s*, 2 H); 3.30 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 172.0 (*s*); 157.5 (*s*); 130.1 (*s*); 129.3 (*d*); 126.8 (*d*); 122.7 (*s*); 110.0 (*d*); 102.8 (*d*); 55.4 (*q*); 52.4 (*q*); 51.7 (2*q*); 35.6 (*t*). CI-MS: 223 ($[M-MeOH+H]^+$)[3]).

Methyl 2-(5-Formyl-2-methoxyphenyl)-3-hydroxy-3-(4-methoxyphenyl)propanoate (**13**). A freshly prepared LDA soln. (^{i}Pr$_2$NH (0.4 ml) and 1.6M BuLi (1.8 ml) in abs. Et_2O (10 ml)) was cooled to −78°, and then **12** (0.48 g, 1.90 mmol) was added. After 10 min, anisaldehyde (**8**; 0.26 g, 1.90 mmol) was introduced and the mixture stirred at −78° for 30 min. The *cold* soln. was quenched by addition of dil. aq. HCl soln. and extracted with Et_2O. Evaporation and separation of **13** from starting material was achieved by CC (SiO_2, hexane/AcOEt 2:1 → 1:1): **13** (0.57 g, 77%). Colorless oil. IR: 3520 (br.), 3020*w*, 3000*w*, 2950*m*, 2900*w*, 2840*m*, 2740*w*, 1730*s*, 1590*s*, 1600*s*, 1580*m*, 1500*s*, 1460*m*, 1440*m*, 1370*w*, 1300*w*, 1260*s*, 1105*m*, 1025*m*, 830*m*. ^{1}H-NMR ($CDCl_3$)[4]): *isomer A:* 9.88 (*s*, 1 H); 7.93 (*d*, *J* = 2.1, 1 H); 7.82 (*dd*, *J* = 8.6, 2.1, 1 H); 7.11 (*d*, *J* = 8.7, 2 H); 6.89 (*d*, *J* = 8.6, 1 H); 6.77 (*d*, *J* = 8.7, 2 H); 5.40 (*d*, *J* = 6.0, 1 H); 4.51 (*d*, *J* = 6.0, 1 H); 3.76 (*s*, 3 H); 3.68 (*s*, 3 H); 3.61 (*s*, 3 H); *isomer B:* 9.79 (*s*, 1 H); 7.70 (*dd*, *J* = 8.5, 2.1, 1 H); 7.65 (*d*, *J* = 2.1, 1 H); 7.02 (*d*, *J* = 6.7, 2 H); 6.81 (*d*, *J* = 8.5, 1 H); 6.68 (*d*, *J* = 6.7, 2 H); 5.15 (*d*, *J* = 8.8, 1 H); 4.35 (*d*, *J* = 8.8, 1 H); 3.71 (*s*, 9 H). ^{13}C-NMR ($CDCl_3$)[5]): 190.7 (*d*); 190.5 (*d*); 173.9 (*s*); 173.0 (*s*); 162.2 (*s*); 161.4 (*s*); 159.0 (*s*); 158.9 (*s*); 133.1 (*s*); 132.7 (*s*); 132.0 (*d*); 131.2 (*d*); 131.1 (*d*); 130.9 (*d*); 129.6 (*s*); 127.6 (*d*); 127.5 (*d*); 125.5 (*s*); 124.2 (*s*); 113.3 (*d*); 113.1 (*d*); 110.7 (*d*); 74.8 (*d*); 73.7 (*d*); 55.7 (*q*); 55.1 (*q*); 52.2 (*d*); 52.0 (*q*); 50.5 (*d*). CI-MS: 362 (19, $[M+NH_4]^+$), 344 (46, $[M-H_2O+NH_4]^+$), 327 (30, $[M-H_2O+H]^+$).

Methyl 3-(3,4-Dimethoxyphenyl)-2-(5-formyl-2-methoxyphenyl)-3-hydroxypropanoate (**14**). As described for **13**, with **7** (0.56 g, 19.0 mmol) and veratrumaldehyde (**9**; 0.36 g, 2.19 mmol). CC (SiO_2, hexane/AcOEt 1:1) yielded **14** (0.63 g, 77%). Colorless solid (mixture of two diastereoisomers). IR: 3500 (br.), 3020*w*, 3000*w*, 2950*m*, 2840*m*, 2740*w*, 1740*s*, 1690*s*, 1600*s*, 1580*m*, 1500*m*, 1460*m*, 1435*m*, 1320*w*, 1260*s*, 1150*w*, 1140*m*, 1100*w*, 1025*m*, 910*s*, 855*w*. ^{1}H-NMR ($CDCl_3$): 9.87 (*s*); 9.79 (*s*); 7.97 (*d*); 7.80 (*dd*); 7.71–7.68 (*m*); 6.88 (*d*); 6.83–6.59 (*m*); 5.39 (*d*); 5.15 (*d*); 4.50 (*d*); 4.38 (*d*); 3.83–3.44 (8*s*). ^{13}C-NMR ($CDCl_3$): 90.8 (*d*); 190.5 (*d*); 173.8 (*s*); 173.0 (*s*); 162.3 (*s*); 161.5 (*s*); 148.4 (*s*); 148.3 (*s*); 133.6 (*s*); 133.1 (*s*); 132.0 (*d*); 131.2 (*d*); 131.0 (*d*); 130.9 (*d*); 129.5 (*s*); 129.4 (*s*); 125.4 (*s*); 124.2 (*s*); 119.0 (*d*); 118.6 (*d*); 110.65 (*d*); 110.56 (*d*); 110.51 (*d*); 110.27 (*d*); 109.57 (*d*); 109.48 (*d*); 75.1 (*d*); 73.7 (*d*); 55.7 (*q*); 55.60 (*q*); 52.2 (*q*); 52.1 (*q*); 52.0 (*d*); 50.4 (*d*). ESI-MS: 397 ($[M+Na]^+$).

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[3]) The loss of MeOH from the $[M+H]^+$ or $[M+NH_4]^+$ ion under the CI-measurement conditions proved to be very characteristic for such dimethoxy acetals. Without exception, all measured compounds of this type showed such a behavior, whereas for none of them, a $[M+NH_4]^+$ or $[M+H]^+$ signal could be observed (*cf.* also [18]).

[4]) Product **13** was obtained as a mixture of two diastereoisomers *A* and *B* in a ratio of *ca.* 1:2 (see *General Part*). Separation of the ^{1}H-NMR signals of these isomers was possible with the help of signal integration.

[5]) No separation of the ^{13}C-NMR signals of the diastereoisomers *A* and *B* was possible.

Methyl trans-*5-Formyl-2,3-dihydro-2-(4-hydroxyphenyl)benzofuran-3-carboxylate* (**15**). To an ice-cooled soln. of **13** (0.13 g, 0.38 mmol) in CH_2Cl_2 (10 ml), a freshly prepared soln. of BBr_3 (0.95 g, 0.36 ml, 3.8 mmol) in CH_2Cl_2 (5 ml; *Merck puriss.*) was added dropwise (→ rapid precipitation of a brown solid). The temp. was raised to r.t. within 2 h before the mixture was carefully quenched with MeOH (vigorous generation of HBr!). Dilution with aq. NaCl soln. and extraction with CH_2Cl_2 yielded, after evaporation and CC (SiO_2, hexane/AcOEt 1:1), **15** (77 mg, 68%). Small yellow crystals. IR: 3600*m*, 3500–3100 (br.), 3020*w*, 2960*w*, 2840*w*, 2740*w*, 1740*s*, 1690*s*, 1600*s*, 1515*m*, 1485*m*, 1440*m*, 1325*w*, 1280*w*, 1245*s*, 1170*s*, 1105*m*, 1035*w*, 970*w*, 940*w*, 920*w*, 830*m*, 630*w*. ^{1}H-NMR ($CDCl_3$): 9.86 (*s*, 1 H); 7.94 (*d*, *J* = 1.5, 1 H); 7.80 (*dd*, *J* = 8.3, 1.6, 1 H); 7.25 (*d*, *J* = 8.5, 2 H); 6.99 (*d*, *J* = 8.3, 1 H); 6.85 (*d*, *J* = 8.6, 2 H); 6.15 (*d*, *J* = 7.5, 1 H); 5.81 (br. *s*, 1 H); 4.32 (*d*, *J* = 7.5, 1 H); 3.84 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 190.6 (*d*); 170.5 (*s*); 164.4 (*s*); 156.3 (*s*); 134.0 (*d*); 131.4 (*s*); 130.6 (*s*); 127.4 (*d*); 126.8 (*d*); 125.5 (*s*); 115.7 (*d*); 110.3 (*d*); 87.1 (*d*); 54.5 (*d*); 52.9 (*q*). CI-MS: 316 (100, $[M+NH_4]^+$), 299 (36, $[M+H]^+$).

Methyl trans-*2-(3,4-Dihydroxyphenyl)-5-formyl-2,3-dihydrobenzofuran-3-carboxylate* (**16**). As described for **15**, with **14** (0.36 g, 0.96 mmol) and BBr_3 (2.41 g, 0.91 ml, 9.60 mmol). CC (SiO_2, hexane/AcOEt 2:1) gave **16** (0.27 g, 90%). Yellow oil, which was crystallized for X-ray-analysis from $CDCl_3$[6]). M.p. 116–117° ($CDCl_3$). IR: 3540*m*, 3200(br.), 2980*w*, 2950*w*, 2840*w*, 1730*s*, 1685*s*, 1600*s*, 1520*w*, 1480*w*, 1440*m*, 1370*m*, 1220*s*, 1105*m*, 1040*w*, 975*w*, 940*w*, 915*w*. ^{1}H-NMR ((D_6)DMSO): 9.87 (*s*, 1 H); 9.0 (br., 2 H); 7.89–7.84 (*m*, 2 H); 7.08 (*d*, *J* = 8.2, 1 H); 6.75–6.66 (*m*, 3 H); 5.96 (*d*, *J* = 6.8, 1 H); 4.50 (*d*, *J* = 6.8, 1 H); 3.75 (*s*, 3 H). ^{13}C-NMR ((D_6)DMSO): 191.0 (*d*); 170.6 (*s*); 163.8 (*s*); 145.9 (*s*); 145.4 (*s*); 133.5 (*d*); 130.4 (*s*); 130.1 (*s*); 126.7 (*d*); 126.0 (*s*); 117.4 (*d*); 115.5 (*d*); 113.3 (*d*); 109.9 (*d*); 87.2 (*d*); 53.4 (*d*); 52.7 (*q*). CI-MS: 332 (100, $[M+NH_4]^+$), 315 (55, $[M+H]^+$).

Methyl trans-*5-[(1E)-2-Carboxyethenyl]-2,3-dihydro-2-(4-hydroxyphenyl)benzofuran-3-carboxylate* (**5**). To a soln. of **15** (52 mg, 0.17 mmol) in pyridine (5 ml) were added malonic acid (36 mg, 0.35 mmol) and two drops of piperidine. The mixture was refluxed for 2 h and then poured into an excess of dil. aq. HCl soln. Extraction with AcOEt and evaporation gave **5** (57 mg, 97%). Yellow solid. IR: 3590*m*, 3500–2400(br.), 1735*s*, 1685*s*, 1630*m*, 1600*s*, 1510*m*, 1485*s*, 1435*s*, 1370*w*, 1330*w*, 1200*s*, 1170*s*, 1110*m*, 1035*w*, 980*m*, 910*m*, 865*w*, 835*m*, 820*m*. ^{1}H-NMR ($CDCl_3$): 9.30 (br., 2 H); 7.76 (*d*, *J* = 15.9, 1 H); 7.59 (*d*, *J* = 1.7, 1 H); 7.45 (*dd*, *J* = 8.3, 1.7, 1 H); 7.26 (*d*, *J* = 8.5, 2 H); 6.90 (*d*, *J* = 8.3, 1 H); 6.84 (*d*, *J* = 8.6, 2 H); 6.33 (*d*, *J* = 15.9, 1 H); 6.10 (*d*, *J* = 7.5, 1 H); 4.28 (*d*, *J* = 7.5, 1 H); 3.85 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 172.0 (*s*); 170.8 (*s*); 161.4 (*s*); 156.1 (*s*); 146.6 (*d*); 131.8 (*s*); 131.1 (*d*); 127.4 (*s*+*d*); 125.1 (*s*+*d*); 115.6 (*d*); 114.5 (*d*); 110.3 (*d*); 86.4 (*d*); 54.9 (*d*); 52.8 (*q*). CI-MS: 358 (100, $[M+NH_4]^+$), 341 (64, $[M+H]^+$), 340 (18, $[M-H_2O+NH_4]^+$), 323 (86, $[M-H_2O+H]^+$), 297 (35, $[M-CO_2+H]^+$).

3-Methoxy-4-[(prop-2-enyl)oxy]benzaldehyde (= O-*Allylvanillin*; **20**). To vanillin (**19**, 20.0 g, 0.13 mol) in acetone (150 ml), allyl bromide (19.90 g, 13.9 ml, 0.16 mol) and K_2CO_3 (27.25 g, 0.20 mol) were added. Then the mixture was refluxed for 8 h. After pouring into H_2O and extraction with Et_2O, the org. phase was washed with dil. aq. NaOH soln. and evaporated: **20** (22.5 g, 90%). Slightly yellow oil. IR: 3080*w*, 3030*w*, 3000*w*, 2960*w*, 2940*m*, 2840*m*, 2740*w*, 1675*s*, 1595*s*, 1585*s*, 1500*s*, 1460*s*, 1420*s*, 1390*m*, 1360*w*, 1335*w*, 1270*s*, 1160*s*, 1130*s*, 1030*m*, 995*s*, 935*m*, 870*m*. ^{1}H-NMR ($CDCl_3$): 9.85 (*s*, 1 H); 7.44–7.41 (*m*, 2 H); 6.98 (*d*, *J* = 8.7, 1 H); 6.15–6.02 (*m*, 1 H); 5.48–5.41 (*m*, 2 H); 4.70 (*dt*, *J* = 5.4, 1.5, 2 H); 3.94 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 190.7 (*d*); 153.4 (*s*); 149.8 (*s*); 132.1 (*d*); 130.1 (*s*); 126.4 (*d*); 118.6 (*t*); 111.9 (*d*); 109.3 (*d*); 69.7 (*t*); 55.9 (*q*). CI-MS: 210 (11, $[M+NH_4]^+$), 193 (100, $[M+H]^+$).

4-Hydroxy-3-methoxy-5-(prop-2-enyl)benzaldehyde (**21**). A soln. of **20** (19.7 g, 0.10 mol) in mesitylene (75 ml) was refluxed for 20 h. The cooled soln. was poured into aq. 2N NaOH and washed with Et_2O twice. The org. phase was discarded and the ice-cooled aq. phase acidified with aq. conc. HCl soln. and extracted with AcOEt. Evaporation yielded **21** (17.4 g, 88%). Orange oil, which was considered to be sufficiently pure for the next step. IR: 3520*s*, 3080*w*, 3000*w*, 2970*w*, 2940*w*, 2840*w*, 2730*w*, 1680*s*, 1640*w*, 1595*s*, 1490*m*, 1460*m*, 1435*m*, 1400*m*, 1370*w*, 1300*s*, 1140*s*, 1105*w*, 1070*m*, 995*w*, 950*w*, 920*w*, 860*w*. ^{1}H-NMR ($CDCl_3$): 9.80 (*s*, 1 H); 7.31 (*s*, 2 H); 6.39 (*s*, 1 H); 6.07–5.94 (*m*, 1 H); 5.15–5.18 (*m*, 2 H); 3.95 (*s*, 3 H); 3.46 (*dt*, *J* = 6.6, 1.4, 2 H). ^{13}C-NMR ($CDCl_3$): 191.0 (*d*); 149.3 (*s*); 146.8 (*s*); 135.4 (*d*); 129.0 (*s*); 127.8 (*d*); 126.0 (*s*); 116.2 (*t*); 107.0 (*d*); 56.1 (*q*); 33.3 (*t*).

3,4-Dimethoxy-5-(prop-2-enyl)benzaldehyde (**22**). K_2CO_3 (10.1 g, 72.8 mmol) and MeI (7.75 g, 3.4 ml, 54.6 mmol) were added to a soln. of **21** (7.0 g, 36.4 mmol) in DMF (40 ml). The mixture was stirred at r.t. for 8 h, then taken up in H_2O, and extracted with Et_2O. Washing the org. phase with dil. aq. NaOH soln. and evaporation gave **22** (6.91 g, 92%). Colorless liquid. IR: 3070*w*, 2940*m*, 2830*m*, 2740*w*, 1690*s*, 1635*w*, 1580*s*, 1480*m*, 1460*m*, 1420*m*, 1380*s*, 1330*w*, 1300*s*, 1220*w*, 1140*s*, 1110*w*, 1070*m*, 1000*s*, 915*m*, 860*m*. ^{1}H-NMR ($CDCl_3$): 9.87 (*s*, 1 H);

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[6]) See *Fig. 1* and *Table*.

7.33 (*d*, *J* = 1.9, 1 H); 7.31 (*d*, *J* = 1.9, 1 H); 6.04–5.91 (*m*, 1 H); 5.12–5.05 (*m*, 2 H); 3.92 (*s*, 3 H); 3.90 (*s*, 3 H); 3.46 (*dt*, *J* = 6.5, 1.4, 2 H). ^{13}C-NMR ($CDCl_3$): 191.2 (*d*); 153.2 (*s*); 152.5 (*s*); 136.2 (*d*); 134.2 (*s*); 132.2 (*s*); 126.4 (*d*); 116.2 (*t*); 109.0 (*d*); 60.6 (*q*); 55.8 (*q*); 33.9 (*t*). CI-MS: 224 (34, $[M+NH_4]^+$), 207 (100, $[M+H]^+$).

5-(Dimethoxymethyl)-1,2-dimethoxy-3-(prop-2-enyl)benzene (**23**). As described for **12**, with **22** (2.66 g, 12.9 mmol): **23** (3.1 g, 95%). Colorless liquid. IR: 3070*w*, 2940*s*, 2900*w*, 2820*m*, 1635*w*, 1590*s*, 1490*s*, 1460*s*, 1420*m*, 1355*s*, 1300*s*, 1230*w*, 1210*w*, 1190*m*, 1150*s*, 1100*s*, 1070*m*, 1050*s*, 1010*m*, 990*m*, 910*m*, 855*m*. ^{1}H-NMR ((D_6)benzene): 7.12 (*d*, *J* = 1.9, 1 H); 7.05 (*d*, *J* = 1.9, 1 H); 6.06–5.97 (*m*, 1 H); 5.35 (*s*, 1 H); 5.10–4.99 (*m*, 2 H); 3.73 (*s*, 3 H); 3.47 (*dt*, *J* = 6.5, 1.4, 2 H); 3.39 (*s*, 3 H); 3.19 (*s*, 6 H). ^{13}C-NMR ((D_6)benzene): 153.3 (*s*); 147.9 (*s*); 137.9 (*d*); 134.4 (*s*); 133.7 (*s*); 121.1 (*d*); 115.6 (*t*); 109.9 (*d*); 103.1 (*d*); 60.3 (*q*); 55.4 (*q*); 52.1 (2*q*); 34.7 (*t*).

(5-Formyl-2,3-dimethoxyphenyl)acetic Acid (**24**). To **23** (3.90 g, 15.5 mmol) in ^{t}BuOH (25 ml) was added a soln. of K_2CO_3 (6.40 g, 46.0 mmol) in H_2O (50 ml). To the resulting suspension were added $NaIO_4$ (13.6 g, 46.0 mmol) and $KMnO_4$ (2.0 g, 12.4 mmol). The mixture started to warm and was stirred for 4 h at r.t. The mixture was washed with AcOEt and this org. phase discarded. The aq. phase was acidified with dil. aq. HCl soln. and again extracted with AcOEt exhaustively. Evaporation yielded **24** (1.80 g, 52%). Slightly yellowish oil. IR: 3600–2400 (br.), 2940*w*, 2840*w*, 1710*s*, 1690*s*, 1590*s*, 1485*m*, 1460*m*, 1430*w*, 1385*m*, 1300*s*, 1140*s*, 1090*s*, 1000*s*, 860*w*. ^{1}H-NMR ($CHCl_3$): 9.86 (*s*, 1 H); 8.4 (br., 1 H); 7.41 (*d*, *J* = 1.9, 1 H); 7.36 (*d*, *J* = 1.9, 1 H); 3.94 (*s*, 3 H); 3.92 (*s*, 3 H); 3.74 (*s*, 2 H). ^{13}C-NMR ($CHCl_3$): 191.1 (*d*); 176.6 (*s*); 152.9 (*s*); 152.8 (*s*); 131.9 (*s*); 128.0 (*s*); 126.9 (*d*); 110.6 (*d*); 60.6 (*q*); 55.8 (*q*); 35.4 (*t*). CI-MS: 242 (100, $[M+NH_4]^+$), 225 (6, $[M+H]^+$).

Methyl (5-Formyl-2,3-dimethoxyphenyl)acetate (**18**). As described for **11**, with **24** (2.13 g, 9.50 mmol): 1.69 g (75%) of **18**. Colorless oil. IR: 3000*w*, 2940*w*, 2840*w*, 1735*s*, 1690*s*, 1590*s*, 1485*w*, 1460*m*, 1430*m*, 1390*m*, 1350*w*, 1300*s*, 1220*w*, 1140*s*, 1090*m*, 1010*m*, 1000*m*. ^{1}H-NMR ($CHCl_3$): 9.87 (*s*, 1 H); 7.40 (*d*, *J* = 1.9, 1 H); 7.36 (*d*, *J* = 1.9, 1 H); 3.92 (2*s*, 6 H); 3.72 (2*s*, 5 H). ^{13}C-NMR ($CHCl_3$): 190.8 (*d*); 171.4 (*s*); 153.0 (*s*); 152.7 (*s*); 132.0 (*s*); 128.6 (*s*); 126.9 (*d*); 110.3 (*d*); 60.6 (*q*); 55.8 (*q*); 52.0 (*q*); 35.4 (*t*). CI-MS: 256 (100, $[M+NH_4]^+$), 239 (15, $[M+H]^+$).

Methyl [5-(Dimethoxymethyl)-2,3-dimethoxyphenyl]acetate (**25**). As described for **12**, with **18** (1.69 g, 7.10 mmol): 1.51 g (75%) of **25**. Yellow oil. IR: 2995*m*, 2940*s*, 2830*s*, 1735*s*, 1595*s*, 1490*s*, 1460*s*, 1430*m*, 1360*s*, 1310*w*, 1270*w*, 1150*s*, 1090*s*, 1050*s*, 1000*s*, 950*w*, 855*m*. ^{1}H-NMR ((D_6)benzene): 7.11 (*d*, *J* = 1.9, 1 H); 7.05 (*d*, *J* = 1.9, 1 H); 5.32 (*s*, 1 H); 3.78 (*s*, 3 H); 3.62 (*s*, 2 H); 3.35 (*s*, 3 H); 3.34 (*s*, 3 H); 3.18 (*s*, 6 H). ^{13}C-NMR ((D_6)benzene): 171.6 (*s*); 153.1 (*s*); 148.2 (*s*); 134.3 (*d*); 128.6 (*s*); 121.9 (*d*); 110.8 (*t*); 102.9 (*d*); 60.2 (*q*); 55.4 (*q*); 52.1 (2*q*); 51.4 (*q*); 36.0 (*t*). CI-MS: 253 ($[M-MeOH+H]^+$).

Methyl 2-[5-(Dimethoxymethyl)-2,3-dimethoxyphenyl]-3-hydroxy-3-(4-methoxyphenyl)propanoate (**26**). As described for **13**, with **25** (1.51 g, 5.31 mmol) and anisaldehyde (**8**; 0.82 g, 0.73 ml, 6.0 mmol). CC (SiO_2, hexane/AcOEt 2:1 → 1:1) yielded 1.65 g (73%) of **26**. Mixture of two diastereoisomers. IR: 3500 (br.), 3020*w*, 2980*m*, 2940*s*, 2900*m*, 2830*s*, 1725*s*, 1610*s*, 1590*s*, 1510*m*, 1485*m*, 1460*s*, 1430*m*, 1350*s*, 1300*s*, 1240*s*, 1170*w*, 1140*m*, 1100*s*, 1050*s*, 1000*s*, 940*w*, 910*w*, 860*m*, 830*s*. ^{1}H-NMR ((D_6)benzene)[7]): isomer *A:* 7.62 (*d*, *J* = 1.8, 1 H); 7.33 (*d*, *J* = 8.6, 2 H); 7.06 (*d*, *J* = 1.8, 1 H); 6.72 (*d*, *J* = 8.7, 2 H); 5.48 (*d*, overlap with isomer *B*, 1 H); 5.34 (*s*, 1 H); 4.74 (*d*, *J* = 7.2, 1 H); 3.74 (*s*, 3 H); 3.35–3.10 (4*s*, overlap with isomer *B*, 15 H); 2.81 (br. *s*, 1 H); isomer *B:* 7.25 (*d*, *J* = 1.8, 1 H); 7.21 (*d*, *J* = 8.6, 2 H); 6.92 (*d*, *J* = 1.8, 1 H); 6.59 (*d*, *J* = 8.7, 2 H); 5.48 (*d*, overlap with isomer *A*, 1 H); 5.25 (*s*, 1 H); 4.59 (*d*, *J* = 9.4, 1 H); 3.62 (br. *s*, 1 H); 3.59 (*s*, 3 H); 3.35–3.10 (4*s*, overlap with isomer *A*, 15 H). ^{13}C-NMR ((D_6)benzene): 174.6 (*s*); 173.3 (*s*); 1597 (*s*); 159.5 (*s*); 153.2 (*s*); 153.0 (*s*); 147.7 (*s*); 134.9 (*s*); 134.4 (*s*); 134.1 (*s*); 130.0 (*s*); 129.6 (*s*); 128.3 (*d*); 128.2 (*d*); 120.4 (*d*); 120.3 (*d*); 113.7 (*d*); 113.5 (*d*); 110.7 (*d*); 110.6 (*d*); 103.2 (*d*); 102.9 (*d*); 75.6 (*d*); 74.8 (*d*); 60.3 (*q*); 60.1 (*q*); 55.2 (*q*); 54.6 (*q*); 53.9 (*d*); 52.6 (*d*); 52.1 (*q*); 51.6 (*q*). CI-MS: 389 (100, $[M-MeOH+H]^+$), 371 (7, $[M-MeOH-H_2O+H]^+$), 340 (23, $[M-MeOH-MeO-H_2O+H]^+$).

Methyl trans-*5-Formyl-2,3-dihydro-7-hydroxy-2-(4-hydroxyphenyl)benzofuran-3-carboxylate* (**17**). As described for **15**, with **26** (0.14 g, 0.33 mmol) and BBr_3 (0.84 g, 0.32 ml, 3.30 mmol). CC (SiO_2, hexane/AcOEt 1:1) yielded 85 mg (82%) of **17**. Yellow foam. IR: 3580*m*, 3300 (br.), 2950*w*, 2840*w*, 1740*s*, 1690*s*, 1600*s*, 1490*m*, 1450*w*, 1435*w*, 1350*s*, 1270*s*, 1170*s*, 1120*s*, 1035*w*, 995*w*, 940*w*, 910*w*, 870*w*, 830*w*. ^{1}H-NMR ((D_6)acetone): 9.83 (*s*, 1 H); 8.69 (*s*, 1 H); 8.52 (*s*, 1 H); 7.49 (*m*, 1 H); 7.38 (*m*, 1 H); 7.31 (*d*, *J* = 8.6, 2 H); 6.88 (*d*, *J* = 8.6, 2 H); 6.11

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[7]) Product **26** was obtained as a mixture of two diastereoisomers *A* and *B* in a ratio of *ca.* 1:2 (see *General Part*). Separation of the ^{1}H-NMR signals of these isomers was at least partly possible with the help of signal integration. No separation was obtained for the ^{13}C-NMR signals.

(d, J = 7.5, 1 H); 4.48 (d, J = 7.4, 1 H); 3.81 (s, 3 H). ^{13}C-NMR ((D$_6$)acetone): 191.0 (d); 171.5 (s); 158.9 (s); 153.2 (s); 143.0 (s); 132.8 (s); 131.5 (s); 128.7 (d); 127.6 (s); 120.1 (d); 118.3 (d); 116.4 (d); 88.5 (d); 55.7 (d); 53.1 (q). CI-MS: 332 (100, $[M+NH_4]^+$), 315 (65, $[M+H]^+$).

Methyl trans-*5-(2-Carboxyethenyl)-2,3-dihydro-7-hydroxy-2-(4-hydroxyphenyl)benzofuran-3-carboxylate* (**27**). As described for **5**, with **17** (0.11 g, 0.36 mmol) and malonic acid (0.11 g, 1.07 mmol): 0.12 g (92%) of **27**. Yellow oil. IR (KBr): 3500–2300 (br.), 2954*w*, 1683*s*, 1603*s*, 1516*m*, 1495*m*, 1445*m*, 1340*s*, 1274*s*, 1210*s*, 1170*s*, 1137*s*, 1073*w*, 978*m*, 914*w*, 853*w*, 835*m*, 752*w*. ^{1}H-NMR ((D$_6$)acetone): 8.50 (br., 2 H); 7.58 (d, J = 15.9, 1 H); 7.31 (d, J = 8.5, 2 H); 7.21 (d, J = 1.7, 1 H); 7.14 (d, J = 1.7, 1 H); 6.88 (d, J = 8.6, 2 H); 6.33 (d, J = 15.9, 1 H); 6.03 (d, J = 7.6, 1 H); 4.40 (d, J = 7.6, 1 H); 3.81 (s, 3 H). ^{13}C-NMR ((D$_6$)acetone): 171.7 (s); 168.0 (s); 158.7 (s); 150.0 (s); 145.6 (d); 142.6 (s); 131.8 (s); 129.6 (s); 128.6 (d); 127.5 (s); 117.7 (d); 117.4 (d); 116.6 (d); 116.4 (d); 88.0 (d); 56.2 (d); 53.0 (q). ESI-MS: 357 (100, $[M+H]^+$), 339 (45, $[M-H_2O+H]^+$).

(2,3-Dimethoxyphenyl)methanol (**39**). To a soln. of 2,3-dimethoxybenzaldehyde (**38**; 34.0 g, 0.21 mmol) in MeOH (120 ml) was carefully added $NaBH_4$ (4.7 g, 0.124 mmol) in some portions. Then the mixture was stirred for 1 h at r.t. After evaporation, the residue was diluted with H_2O. Extraction with CH_2Cl_2, washing with H_2O, and evaporation yielded **35** (34.0 g, 99%). Slightly brownish liquid. IR: 3600*m*, 3450 (br.), 3020*w*, 2990*w*, 2960*w*, 2940*s*, 2840*m*, 1600*w*, 1585*s*, 1480*s*, 1430*m*, 1390*m*, 1305*m*, 1270*s*, 1170*m*, 1080*s*, 1010*s*, 960*m*, 900*w*. ^{1}H-NMR ($CHCl_3$): 7.06–7.01 (m, 1 H); 6.94–6.85 (m, 2 H); 4.68 (s, 2 H); 3.87 (s, 3 H); 3.86 (s, 3 H); 2.37 (s, 1 H). ^{13}C-NMR ($CHCl_3$): 152.4 (s); 146.9 (s); 134.5 (s); 124.1 (d); 120.5 (d); 112.1 (d); 61.2 (t); 60.7 (q); 55.7 (q).

1-(Chloromethyl)-2,3-dimethoxybenzene (**40**). To a soln. of **39** (32.2 g, 0.19 mol) in $CHCl_3$ (200 ml) were added pyridine (6 ml) and then dropwise thionyl chloride (42.6 g, 26.0 ml, 0.36 mol) (*caution:* strongly exothermic reaction!). After cooling to r.t., the mixture was diluted with H_2O and extracted with CH_2Cl_2. Subsequent washing of the org. phase with H_2O and aq. $NaHCO_3$ soln. yielded, after evaporation, **40** (33.9 g, 95%). Slightly brownish liquid. IR: 3020*w*, 2990*w*, 2960*w*, 2940*m*, 2900*w*, 2840*m*, 1590*s*, 1480*s*, 1460*w*, 1430*m*, 1310*m*, 1270*s*, 1170*w*, 1150*w*, 1080*s*, 1000*s*, 945*m*. ^{1}H-NMR ($CHCl_3$): 7.07–7.02 (m, 1 H); 6.99–6.95 (m, 1 H); 6.91–6.88 (m, 1 H); 4.65 (s, 2 H); 3.92 (s, 3 H); 3.86 (s, 3 H). ^{13}C-NMR ($CHCl_3$): 152.7 (s); 147.4 (s); 131.5 (s); 124.1 (d); 122.1 (d); 112.9 (d); 61.1 (q); 55.7 (q); 41.0 (t).

(2,3-Dimethoxyphenyl)acetonitrile (**41**). To a hot soln. of KCN (10.25 g, 0.16 mol) in H_2O (20 ml) was added **40** (24.9 g, 0.13 mol) in EtOH (50 ml). The mixture was refluxed for 1 h, poured in ice-water, and extracted with CH_2Cl_2. Evaporation gave **41** (23.4 g, 99%). Thin oil. IR: 2990*w*, 2960*w*, 2940*m*, 2900*w*, 2840*m*, 2250*w*, 1600*m*, 1590*m*, 1480*s*, 1460*w*, 1430*m*, 1410*w*, 1310*w*, 1270*s*, 1170*m*, 1075*s*, 1000*s*. ^{1}H-NMR ($CHCl_3$): 7.08–7.03 (m, 1 H); 6.96–6.89 (m, 2 H); 3.91 (s, 3 H); 3.87 (s, 3 H); 3.71 (s, 2 H). ^{13}C-NMR ($CHCl_3$): 152.6 (s); 146.7 (s); 124.2 (d); 124.1 (s); 120.9 (d); 118.1 (s); 112.7 (d); 60.5 (q); 55.7 (q); 18.4 (t).

(2,3-Dimethoxyphenyl)acetic Acid (**42**). A mixture of **41** (10.0 g, 56.4 mmol) in H_2O (40 ml) and aq. 2N NaOH (160 ml) was refluxed for 10 h. After concentration to half of the volume, the mixture was washed once with Et_2O and the org. phase was discarded. The aq. phase was acidified with conc. aq. HCl soln. and extracted with AcOEt. Washing with H_2O and evaporation yielded **42** (9.90 g, 90%). Oil. IR: 3500–2400 (br.), 2940*m*, 2840*m*, 1710*s*, 1600*w*, 1590*m*, 1470*s*, 1430*w*, 1400*w*, 1270*s*, 1170*m*, 1080*s*, 1040*w*, 1005*s*, 955*m*. ^{1}H-NMR ($CHCl_3$): 10.5 (br., 1 H); 7.03–7.00 (m, 1 H); 6.98–6.80 (m, 2 H); 3.85 (s, 3 H); 3.84 (s, 3 H); 3.68 (s, 2 H). ^{13}C-NMR ($CHCl_3$): 177.8 (s); 152.6 (s); 147.3 (s); 127.6 (s); 123.8 (d); 122.5 (d); 111.9 (d); 60.4 (q); 55.6 (q); 35.4 (t).

Methyl (2,3-Dimethoxyphenyl)acetate (**37**). As described for **11**, with **42** (9.1 g, 46.4 mmol) and thionyl chloride (8.27 g, 5.0 ml, 69.6 mmol): 9.5 g (97%) of **37**. Colorless liquid. IR: 3020*w*, 3000*m*, 2940*m*, 2900*w*, 2840*m*, 1735*s*, 1600*m*, 1590*m*, 1475*s*, 1430*s*, 1340*m*, 1275*s*, 1160*s*, 1080*s*, 1010*s*, 955*w*. ^{1}H-NMR ($CHCl_3$): 7.03–6.97 (m, 1 H); 6.86–6.80 (m, 2 H); 3.85 (s, 3 H); 3.82 (s, 3 H); 3.69 (s, 3 H); 3.66 (s, 2 H). ^{13}C-NMR ($CHCl_3$): 172.0 (s); 152.6 (s); 147.3 (s); 128.2 (s); 123.7 (d); 122.5 (d); 111.7 (d); 60.4 (q); 55.6 (q); 51.8 (q); 35.4 (t).

Methyl (6-Formyl-2,3-dimethoxyphenyl)acetate (**35**). As described for **7**, with **37** (1.0 g, 4.76 mmol), $SnCl_4$ (1.86 g, 0.84 ml, 7.13 mmol), and dichloromethyl methyl ether (1.09 g, 0.84 ml, 9.5 mmol). CC (SiO_2, hexane/AcOEt 3:1) yielded **35** (0.85 g, 75%). Oil. IR: 2940*w*, 2840*w*, 2740*w*, 1735*s*, 1690*s*, 1595*m*, 1570*m*, 1490*w*, 1460*m*, 1430*w*, 1340*w*, 1280*s*, 1170*w*, 1090*s*, 1005*m*, 980*m*. ^{1}H-NMR ($CHCl_3$): 9.92 (s, 1 H); 7.57 (d, J = 8.5, 1 H); 7.00 (d, J = 8.5, 1 H); 4.18 (s, 2 H); 3.96 (s, 3 H); 3.82 (s, 3 H); 3.71 (s, 3 H). ^{13}C-NMR ($CHCl_3$): 191.6 (d); 171.6 (s); 157.2 (s); 148.0 (s); 132.3 (d); 129.7 (s); 128.3 (s); 110.3 (d); 60.8 (q); 55.8 (q); 51.8 (q); 30.9 (t).

Methyl [6-(Dimethoxymethyl)-2,3-dimethoxyphenyl]acetate (**36**). As described for **12**, with **35** (0.76 g, 3.19 mmol) and trimethyl orthoformate (1.02 g, 1.05 ml, 9.6 mmol): 0.82 g (90%) of **36**. Yellow oil. IR: 2995*w*, 2940*m*, 2840*m*, 1730*s*, 1600*m*, 1490*m*, 1455*m*, 1435*w*, 1420*w*, 1375*w*, 1340*m*, 1310*m*, 1275*s*, 1160*m*, 1110*m*, 1080*s*, 1045*s*, 1010*w*, 990*w*, 960*w*. ^{1}H-NMR ((D$_6$)benzene): 7.42 (d, J = 8.5, 1 H); 6.54 (d, J = 8.5, 1 H); 5.39 (s, 1 H); 4.07

(*s*, 2 H); 3.82 (*s*, 3 H); 3.38 (*s*, 3 H); 3.28 (*s*, 3 H); 3.15 (*s*, 6 H). ^{13}C-NMR ((D$_6$)benzene): 171.9 (*s*); 153.2 (*s*); 148.8 (*s*); 130.0 (*s*); 123.2 (*d*); 110.8 (*d*); 102.3 (*d*); 60.2 (*q*); 55.2 (*q*); 52.4 (2*q*); 51.3 (*q*); 31.8 (*t*)[8]. CI-MS: 253 ([$M - CH_3OH + H$]$^+$).

3-{3,4-Dimethoxy-2-[(methoxycarbonyl)methyl]phenyl}prop-2-enoic Acid (**43**). As described for **5**, with **35** (0.20 g, 0.84 mmol) and malonic acid (0.20 g, 1.9 mmol): 0.19 g (81%) of **43**. Powder. IR: 3500–2400 (br.), 2940*w*, 2840*w*, 1735*s*, 1690*s*, 1630*m*, 1595*s*, 1490*m*, 1460*w*, 1435*w*, 1275*s*, 1165*w*, 1125*w*, 1080*m*, 1040*w*, 1005*w*, 980*w*. ^{1}H-NMR (CHCl$_3$): 7.93 (*d*, *J* = 15.6, 1 H); 7.41 (*d*, *J* = 8.7, 1 H); 6.90 (*d*, *J* = 8.7, 1 H); 6.28 (*d*, *J* = 15.6, 1 H); 4.90 (br., 1 H); 3.91 (*s*, 3 H); 3.88 (*s*, 2 H); 3.83 (*s*, 3 H); 3.71 (*s*, 3 H). ^{13}C-NMR (CHCl$_3$): 171.5 (2*s*); 154.2 (*s*); 147.5 (*s*); 143.5 (*d*); 128.6 (*s*); 126.8 (*s*); 123.0 (*d*); 117.4 (*d*); 111.5 (*d*); 60.6 (*q*); 55.7 (*q*); 52.1 (*q*); 31.6 (*t*). CI-MS: 298 (100, [$M + NH_4$]$^+$), 280 (32, [$M - H_2O + NH_4$]$^+$), 263 (60, [$M - H_2O + H$]$^+$).

3-[2-(Carboxymethyl)-3,4-dimethoxyphenyl]prop-2-enoic Acid (**31**). To a soln. of **43** (90 mg, 0.32 mmol) in MeOH (5 ml) was added aq. 2N KOH (2 ml). Stirring at r.t. for 2 h was followed by pouring into dil. aq. HCl soln. and extraction with AcOEt. Evaporation yielded **31** (62 mg, 73%). Brownish oil. IR (KBr): 3500–2400 (br.), 2947*m*, 1687*s*, 1621*m*, 1591*s*, 1494*s*, 1465*w*, 1418*m*, 1272*s*, 1209*w*, 1079*s*, 1043*m*, 973*m*, 947*m*, 807*m*, 782*w*. ^{1}H-NMR ((D$_6$)acetone): 7.88 (*d*, *J* = 15.7, 1 H); 7.51 (*d*, *J* = 8.7, 1 H); 7.04 (*d*, *J* = 8.7, 1 H); 6.98 (br., 2 H); 6.33 (*d*, *J* = 15.7, 1 H); 3.92 (*s*, 3 H); 3.88 (*s*, 2 H); 3.81 (*s*, 3 H). ^{13}C-NMR ((D$_6$)acetone): 172.4 (*s*); 167.9 (*s*); 155.1 (*s*); 148.6 (*s*); 142.7 (*d*); 129.9 (*s*); 128.2 (*s*); 123.6 (*d*); 119.0 (*d*); 112.6 (*d*); 60.7 (*q*); 56.1 (*q*); 31.9 (*t*). CI-MS: 284 (100, [$M + NH_4$]$^+$), 266 (11, [$M - H_2O + NH_4$]$^+$), 249 (19, [$M - H_2O + H$]$^+$), 240 (84, [$M - CO_2 + NH_4$]$^+$), 223 (48, [$M - CO_2 + H$]$^+$), 205 (13, [$M - H_2O - CO_2 + H$]$^+$).

Methyl 2-[6-(Dimethoxymethyl)-2,3-dimethoxyphenyl]-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoate (**44**). As described for **13**, with **36** (0.82 g, 2.88 mmol) and veratrumaldehyde (0.50 g, 3.0 mmol) (**9**). CC (SiO$_2$, hexane/AcOEt 1:1) yielded 0.78 g (60%) of **44**. IR: 3500 (br.), 3020*w*, 2980*m*, 2940*s*, 2900*m*, 2840*m*, 1720*s*, 1600*m*, 1510*m*, 1490*m*, 1450*s*, 1460*s*, 1420*w*, 1370*w*, 1260*s*, 1150*w*, 1135*m*, 1110*m*, 1085*s*, 1040*s*, 990*m*, 930*w*, 900*w*, 860*w*, 830*w*. ^{1}H-NMR (CHCl$_3$): 7.09 (*d*, *J* = 8.5, 1 H); 7.00–6.87 (*m*, 4 H); 5.74 (*s*, 1 H); 5.32 (*d*, *J* = 4.1, 1 H); 4.06 (*d*, *J* = 4.1, 1 H); 3.91 (*s*, 3 H); 3.90 (*s*, 3 H); 3.87 (*s*, 3 H); 3.76 (*s*, 3 H); 3.51 (*s*, 3 H); 3.47 (*s*, 3 H); 3.36 (*s*, 3 H); 1.40 (br. *s*, 1 H). ^{13}C-NMR (CHCl$_3$): 171.0 (*s*); 152.0 (*s*); 148.7 (*s*); 148.4 (*s*); 145.7 (*s*); 131.5 (*s*); 126.8 (*s*); 126.6 (*s*); 123.0 (*d*); 118.2 (*d*); 112.3 (*d*); 110.7 (*d*); 109.0 (*d*); 98.3 (*d*); 69.3 (*d*); 60.0 (*q*); 55.83 (*q*); 55.79 (2*q*); 55.76 (*q*); 55.5 (*q*); 51.5 (*q*); 45.6 (*d*). ESI-MS: 473 ([$M + Na$]$^+$).

Methyl trans-*2-(3,4-Dihydroxyphenyl)-4-formyl-2,3-dihydro-7-methoxybenzofuran-3-carboxylate* (**45**) *and Methyl (2*E*)-3-(3,4-Dihydroxyphenyl)-2-(6-formyl-2-hydroxy-3-methoxyphenyl)prop-2-enoate* (**32**). As described for **15**, with **44** (0.10 g, 0.22 mmol) and BBr_3 (0.556 g, 0.21 ml, 2.20 mmol). CC (SiO$_2$, CH$_2$Cl$_2$/MeOH 19:1) yielded 32 mg (42%) of **45** and 12 mg (15%) of **32**.

Data for **45**: IR: 3700–2900 (br.), 3020*w*, 2950*w*, 2840*w*, 1735*s*, 1685*s*, 1615*s*, 1580*s*, 1510*w*, 1450*s*, 1435*s*, 1400*w*, 1285*s*, 1165*m*, 1095*s*, 1015*w*. ^{1}H-NMR (CHCl$_3$): 9.81 (*s*, 1 H); 7.39 (*d*, *J* = 8.3, 1 H); 6.96 (*d*, *J* = 8.3, 1 H); 6.88 (*s*, 1 H); 6.80 (*s*, 1 H); 6.79 (*s*, 1 H); 5.95 (br. *s*, 2 H); 5.79 (*d*, *J* = 6.5, 1 H); 4.67 (*d*, *J* = 6.5, 1 H); 3.97 (*s*, 3 H); 3.76 (*s*, 3 H). ^{13}C-NMR (CHCl$_3$): 191.0 (*d*); 172.2 (*s*); 149.7 (2*s*); 144.2 (*s*); 144.0 (*s*); 132.5 (*s*); 128.7 (*d*); 126.5 (*s*); 124.4 (*s*); 118.3 (*d*); 115.4 (*d*); 112.6 (*d*); 111.8 (*d*); 88.4 (*d*); 56.7 (*d*); 56.2 (*q*); 52.8 (*q*). CI-MS: 345 ([$M + H$]$^+$).

Data for **32**: IR: 3540*m*, 3500–3000 (br.), 2940*w*, 2840*w*, 1685*s*, 1600*s*, 1505*w*, 1435*m*, 1375*m*, 1335*w*, 1280*s*, 1110*m*, 1090*m*, 1030*w*, 980*w*, 940*w*, 860*w*. ^{1}H-NMR ((D$_6$)acetone): 9.82 (*s*, 1 H); 8.38 (*s*, 1 H); 7.95 (*s*, 1 H); 7.92 (*s*, 1 H); 7.88 (*s*, 1 H); 7.52 (*d*, *J* = 8.5, 1 H); 7.18 (*d*, *J* = 8.5, 1 H); 6.66 (*d*, *J* = 8.2, 1 H); 6.59–6.57 (*m*, 2 H); 3.98 (*s*, 3 H); 3.67 (*s*, 3 H). ^{13}C-NMR ((D$_6$)acetone): 190.9 (*d*); 168.3 (*s*); 153.3 (*s*); 148.0 (*s*); 145.8 (*s*); 145.4 (*s*); 143.0 (*d*); 128.9 (*s*); 127.8 (*s*); 126.7 (*s*); 124.6 (*d*); 123.0 (*s*); 122.5 (*d*); 117.7 (*d*); 116.0 (*d*); 111.4 (*d*); 56.6 (*q*); 52.3 (*q*).

Methyl trans-*4-(2-Carboxyethenyl)-2-(3,4-dihydroxyphenyl)-2,3-dihydro-7-methoxybenzofuran-3-carboxylate* (**46**). As described for **5**, with **45** (30 mg, 0.087 mmol) and malonic acid (45 mg, 0.44 mmol). CC (SiO$_2$, CH$_2$Cl$_2$/MeOH 10:1) gave 12 mg (35%) of **46**. IR: 3600–2400 (br.), 2940*w*, 2840*w*, 1725*s*, 1610*s*, 1500*m*, 1435*m*, 1380*m*, 1280*s*, 1120*w*, 1080*m*, 1010*w*, 980*w*. ^{1}H-NMR ((D$_4$)MeOH): 7.68 (*d*, *J* = 15.9, 1 H); 7.27 (*d*, *J* = 8.6, 1 H); 6.99 (*d*, *J* = 8.6, 1 H); 6.76–6.70 (*m*, 2 H); 6.29 (*d*, *J* = 15.9, 1 H); 5.86 (*d*, *J* = 5.3, 1 H); 3.91 (*s*, 3 H); 3.77 (*s*, 3 H). ^{13}C-NMR ((D$_4$)MeOH): 173.7 (*s*); 170.6 (*s*); 150.0 (*s*); 147.7 (*s*); 147.0 (*s*); 146.8 (*s*); 142.7 (*d*); 133.3 (*s*);

[8]) One signal of a quaternary C-atom is overlapped by the solvent signal.

126.7 (*s*); 126.0 (*s*); 121.6 (*d*); 119.0 (*d*); 118.4 (*d*); 116.5 (*d*); 114.8 (*d*); 113.5 (*d*); 88.9 (*d*); 57.2 (*d*); 56.8 (*q*); 53.3 (*q*). ESI-MS: 385 (100, $[M-H]^-$), 353 (22, $[M-MeOH-H]^-$)[9]).

X-Ray Crystal-Structure Determination of Compound **16**[10]). – The data collection and refinement parameters are summarized in the *Table*, and a view of the molecule is shown in *Fig. 1*. All measurements were made on a *Nonius-KappaCCD* diffractometer [19], with graphite-monochromated Mo$K\alpha$ radiation (λ 0.71073 Å) and an *Oxford-Cryosystems Cryostream-700* cooler. Data reduction was performed with HKL Denzo and Scalepack [20]. The intensities were corrected for *Lorentz* and polarization effects but not for absorption. The structure was solved by direct methods with SIR92 [21], which revealed the positions of all non-H-atoms. The crystal lattice contains $CHCl_3$ molecules that lie close to and are, thus, necessarily disordered about centres of inversion. Formally, the site-occupation factors for the atoms of the $CHCl_3$ molecule should, therefore, be 0.5, but the best refinement results were obtained when the site-occupation factors were allowed to refine and then were held fixed at 0.444. This suggests that some of the $CHCl_3$ has diffused out of the crystal leaving some sites unoccupied. However, the parameters in the *Table* were calculated assuming a 1:2 ratio. The non-H-atoms were refined anisotropically. The hydroxy H-atoms were placed in the positions indicated by a difference electron density map and their positions were allowed to refine together with individual isotropic displacement parameters. All remaining H-atoms were fixed in geometrically calculated positions

Table. *Crystallographic Data for Compound* **16**

Crystallized from	$CDCl_3$
Empirical formula	$C_{17}H_{14}O_6 \cdot 0.5(CDCl_3)$
Formula weight [g mol^{-1}]	373.98
Crystal color, habit	colorless, plate
Crystal dimensions [mm]	$0.08 \times 0.25 \times 0.25$
Temperature [K]	160 (1)
Crystal system	orthorhombic
Space group	*Pbca*
Z	8
Reflections for cell determination	5263
2θ range for cell determination [°]	4 – 60
Unit cell parameters a [Å]	16.1842 (2)
b [Å]	7.5777 (1)
c [Å]	26.1527 (4)
V [Å^3]	3207.34 (8)
D_x [g cm^{-3}]	1.549
μ(Mo$K\alpha$) [mm^{-1}]	0.354
Scan type	ϕ and ω
$2\theta_{(max)}$ [°]	60
Total reflections measured	53748
Symmetry-independent reflections	4692
Reflections used ($I > 2\sigma(I)$)	2867
Parameters refined	253
Final R	0.0461
wR	0.0465
Weights	$[\sigma^2(F_o) + (0.015F_o)^2]^{-1}$
Goodness-of-fit	1.668
Secondary extinction coefficient	$2\,(1) \cdot 10^{-7}$
Final λ_{max}/σ	0.0004
$\delta\rho$ (max; min) [e Å^{-3}]	0.25; −0.21

[9]) Measurement in the negative mode. The pseudomolecular ion is expected as $[M-1]^-$.

[10]) Crystallographic data (excluding structure factors) for the structure of **16** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication No. CCDC-187704. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 (1223) 336033; e-mail: deposit@ccdc.cam.ac.uk).

(d(C–H) = 0.95 Å), and each was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent C-atom. Refinement of the structure was carried out on F by full-matrix least-squares procedures which minimized the function $\Sigma w(|F_o|-|F_c|)^2$. A correction for secondary extinction was applied. Two reflections, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Neutral-atom scattering factors for non-H-atoms were taken from *Maslen*, *Fox* and *O'Keefe* [22], and the scattering factors for H-atoms were taken from [23]. Anomalous dispersion effects were included in F_c [24]; the values for f' and f'' were those of [25]. The values of the mass attenuation coefficients are those of [26]. All calculations were performed with the teXsan crystallographic software package [27].

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