

### 53. Acid-Catalyzed Cyclization Reactions of Substituted Acetylenic Ketones: A New Approach for the Synthesis of 3-Halofurans, Flavones, and Styrylchromones<sup>1)</sup>

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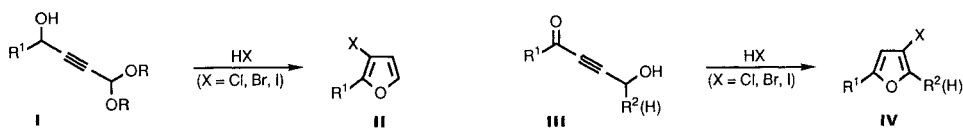
(23. I. 89)

Acetylenic acetals of type **I** (Scheme 1) and acetylenic ketones of type **III** (Scheme 1), **37** and **38** (Scheme 7) are versatile synthetic precursors for the synthesis of various heterocycles by acid-catalyzed cyclization reactions. By this way, substituted 3-halofurans of type **II** and **IV** (Scheme 1) and flavones and styrylchromones (Scheme 7) can be synthesized in good-to-excellent yields. The high degree of regioselectivity in the synthesis of the 3-halofurans (Scheme 4) is the result of the regioselective  $\beta$ -addition of HX (X = Cl, Br, I) to the acetylenic aldehyde and acetylenic ketone moieties. A possible mechanism is depicted in Scheme 5. Since 3-halofurans can easily be metalated and substituted, this approach constitutes a new synthesis of highly substituted furans.

**1. Introduction.** – In the past, acetylenic ketones have been widely used as synthons in a variety of reaction types [1][2]. They have been shown to be excellent substrates for the  $\beta$ -addition of amines, thiols, sulfinic acids, phenols, and HBr [3][4]. Their ability to trap nucleophiles has also been used for the synthesis of heterocycles such as for example 4*H*-thiopyran-4-ones [5] and 1,5-benzodiazepines [6]. Acetylenic ketones are furthermore excellent dienophiles for *Diels-Alder* reactions, and they have also been used by *Karpf* and *Dreiding* to synthesize a number of cyclopentenone-containing natural products (' $\alpha$ -Alkynone Cyclization') [7]. Recently, we have shown that substituted acetylenic ketones are good precursors for the synthesis of (*E*)-3-acylprop-2-enoic acids [8]. We present in this paper the use of acetylenic ketones for the synthesis of a number of interesting heterocycles by acid-catalyzed cyclisations.

**2. Synthesis of Substituted 3-Halofurans.** – 2.1. *General.* Among the large family of furans [9], the 3-halofurans [10a-e] have considerable potential as synthetic tools [11][12]. Their use, however, is somewhat limited due to the lack of generally applicable synthetic methods for their preparation. Recently, *Reich* and *Olson* have published an interesting synthesis of 3-iodo-4-methylfuran [10e]. We now describe a novel general synthesis of substituted 3-halofurans of type **II** and **IV** by acid-catalyzed cyclization of the corresponding acetylenic acetals of type **I** and the acetylenic ketones of type **III** (Scheme 1).

Scheme 1



<sup>1)</sup> Presented in part at the autumn meeting of the Swiss Chemical Society in Bern on October 21, 1988.

2.2. *Synthesis of the Acetylenic Acetals of Type I and the Acetylenic Ketones of Type III.* The synthesis of acetylenic acetals of type **I** was conveniently achieved in high yields by addition of the lithium acetylide of 3,3-diethoxyprop-1-yne (**1**; prepared by reaction of **1** with BuLi in THF at  $-78^\circ$ ) to the corresponding aldehyde **V** (see **2–4**; *Scheme 2* and *Table 1 (Method A)*) [13].

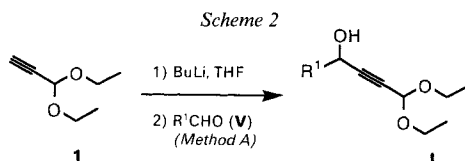


Table 1. *Synthesis of the Acetylenic Acetals I by Method A*

| Aldehyde <b>V</b> | <b>R</b> <sup>1</sup>                           | Acetylenic acetal <b>I</b> | Yield [%] <sup>a)</sup> |
|-------------------|-------------------------------------------------|----------------------------|-------------------------|
| <b>2</b>          | Ph                                              | <b>5</b>                   | 92                      |
| <b>3</b>          | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> | <b>6</b>                   | 92                      |
| <b>4</b>          | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub> | <b>7</b>                   | 82                      |

<sup>a)</sup> Yield of isolated, analytically pure material.

The acetylenic ketones of type **III** were prepared in two ways. Treatment of the tetrahydro-2*H*-pyranyl(THP)-protected propargyl alcohols of type **VI** (see **8** and **9**) with BuLi at  $-78^\circ$ , followed by addition of the aldehyde **V**, oxidation of the intermediate alcohols with MnO<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> and deprotection of the THP group using pyridinium *p*-toluenesulfonate (PPTS) in EtOH at  $50^\circ$  gave **III** (see **13–15** and **17**) in good overall yield without purification of the intermediates (*Scheme 3* and *Table 2 (Method B)*). As an alternative method, we used the reaction of the unprotected propargyl alcohols of type **VII** (see **12**) with 2.2 equiv. of BuLi in THF/hexamethylphosphoramide (HMPA) at  $0^\circ$

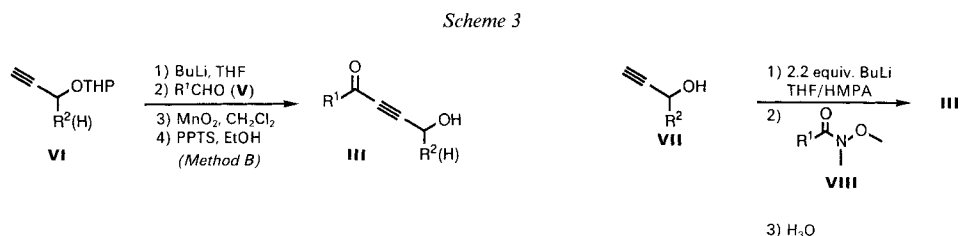


Table 2. *Synthesis of the Acetylenic Ketones III*

| <b>V</b> or <b>VIII</b> | <b>R</b> <sup>1</sup>                                  | Propargyl alcohol<br><b>VI</b> or <b>VII</b> | <b>R</b> <sup>2</sup> | Acetylenic ketones<br><b>III</b> | Yield [%] <sup>a)</sup> |
|-------------------------|--------------------------------------------------------|----------------------------------------------|-----------------------|----------------------------------|-------------------------|
| <b>2</b>                | Ph                                                     | <b>8</b>                                     | H                     | <b>13</b>                        | 68                      |
| <b>2</b>                | Ph                                                     | <b>9</b>                                     | CH <sub>3</sub>       | <b>14</b>                        | 78                      |
| <b>10</b>               | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | <b>8</b>                                     | H                     | <b>15</b>                        | 73                      |
| <b>11</b>               | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | <b>12</b>                                    | CH <sub>3</sub>       | <b>16</b>                        | 80                      |
| <b>3</b>                | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>        | <b>9</b>                                     | CH <sub>3</sub>       | <b>17</b>                        | 72                      |

<sup>a)</sup> Isolated yield, after purification by chromatography [13].

followed by addition of the *N*-methoxy-*N*-methylamides of type **VIII** (see **11**), to conveniently synthesize the acetylenic ketones of type **III** (see **16**; *Scheme 3* and *Table 2*). In cases where the aldehyde **V** was easily available, we preferred *Method B* because of easier handling and generally slightly better overall yields.

**2.3. Synthesis of the Substituted 3-Halofurans by Acid-Catalyzed Cyclization of I and III.** The 3-halofurans of type **II** and **IV** (*Scheme 1*) were obtained by treatment of the acetylenic acetal **I** (see **5–7**) and the acetylenic ketone **III** (see **13–16**), respectively, with 2–4*N* aq. HX (X = Cl, Br, I) in dioxane (*Method C*), 2–4*N* aq. HX in toluene (*Method D*), or 33% HBr/AcOH in CH<sub>2</sub>Cl<sub>2</sub> (*Method E*) at temperatures ranging from 0 to 50° (*Table 3*). Usually, toluene gave very clean reactions and is, therefore, the solvent of choice for these cyclizations. Furthermore, the 2*N* aq. HI was purified by treatment with H<sub>3</sub>PO<sub>2</sub> [14] to remove traces of I<sub>2</sub> in order to avoid the formation of diiodinated products. As it can be seen from *Table 3*, the yields were generally good-to-excellent. It is interesting to note that the yields were not very much dependent on the substituents R<sup>1</sup> and R<sup>2</sup> as long as they were compatible with the dilute aq. acid conditions. The presented strategy allows to synthesize regioselectively the isomeric 2- and 5-substituted 3-halofurans as shown in *Scheme 4* for R<sup>1</sup> = Ph.

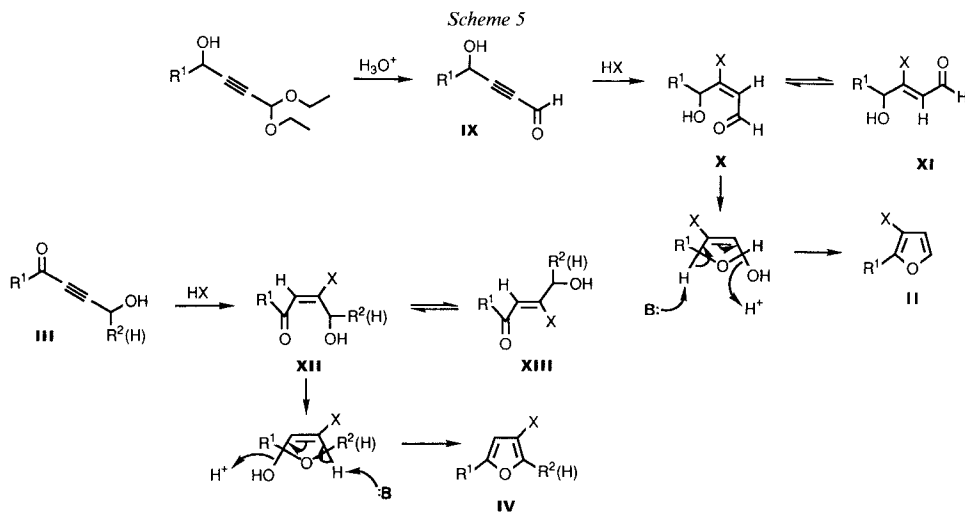
Table 3. Synthesis of the 3-Halofurans **II** and **IV**

| Starting material<br><b>I</b> or <b>III</b> | Method   | Temp.<br>[°C] | Time<br>[h] | 3-halofurans of type<br><b>II</b> or <b>IV</b> | X  | R <sup>1</sup>                                         | R <sup>2</sup>  | Yield<br>[%] <sup>a)</sup> |
|---------------------------------------------|----------|---------------|-------------|------------------------------------------------|----|--------------------------------------------------------|-----------------|----------------------------|
| <b>5</b>                                    | <i>C</i> | 50            | 24          | <b>18</b>                                      | Br | Ph                                                     |                 | 60                         |
| <b>5</b>                                    | <i>D</i> | 50            | 2           | <b>18</b>                                      | Br | Ph                                                     |                 | 93                         |
| <b>6</b>                                    | <i>C</i> | 40            | 3.5         | <b>19</b>                                      | Br | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>        |                 | 82(97)                     |
| <b>7</b>                                    | <i>C</i> | 50            | 6           | <b>20</b>                                      | Br | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub>        |                 | 76(99)                     |
| <b>7</b>                                    | <i>E</i> | 0–r.t.        | 0.5         | <b>20</b>                                      | Br | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub>        |                 | 86                         |
| <b>7</b>                                    | <i>C</i> | 50            | 4           | <b>21</b>                                      | Cl | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub>        |                 | 72(96)                     |
| <b>13</b>                                   | <i>D</i> | 50            | 3           | <b>22</b>                                      | Br | Ph                                                     | H               | 95                         |
| <b>13</b>                                   | <i>D</i> | r.t.          | 4           | <b>23</b>                                      | I  | Ph                                                     | H               | 77                         |
| <b>14</b>                                   | <i>C</i> | 50            | 4.5         | <b>24</b>                                      | Cl | Ph                                                     | CH <sub>3</sub> | 91                         |
| <b>14</b>                                   | <i>C</i> | 50            | 8           | <b>25</b>                                      | Br | Ph                                                     | CH <sub>3</sub> | 92                         |
| <b>14</b>                                   | <i>C</i> | 50            | 0.5         | <b>26</b>                                      | I  | Ph                                                     | CH <sub>3</sub> | 91                         |
| <b>15</b>                                   | <i>C</i> | 50            | 4           | <b>27</b>                                      | Cl | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | H               | 86                         |
| <b>15</b>                                   | <i>C</i> | 50            | 2.5         | <b>28</b>                                      | Br | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | H               | 93                         |
| <b>16</b>                                   | <i>C</i> | 50            | 15          | <b>29</b>                                      | Cl | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | CH <sub>3</sub> | 81                         |
| <b>16</b>                                   | <i>C</i> | 50            | 20          | <b>30</b>                                      | Br | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | CH <sub>3</sub> | 82                         |
| <b>16</b>                                   | <i>C</i> | 50            | 0.5         | <b>31</b>                                      | I  | 3,4,5-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> | CH <sub>3</sub> | 88                         |
| <b>17</b>                                   | <i>D</i> | 50            | 4           | <b>32</b>                                      | Br | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>        | CH <sub>3</sub> | 81                         |
| <b>17</b>                                   | <i>C</i> | r.t.          | 1           | <b>33</b>                                      | I  | CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>        | CH <sub>3</sub> | 76                         |

<sup>a)</sup> Isolated yield, after chromatography [13] and bulb-to-bulb distillation or crystallization as indicated in the *Exper. Part* (yields in parentheses are based on chromatographed material).

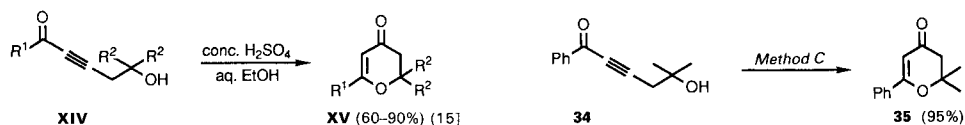
*Scheme 4*

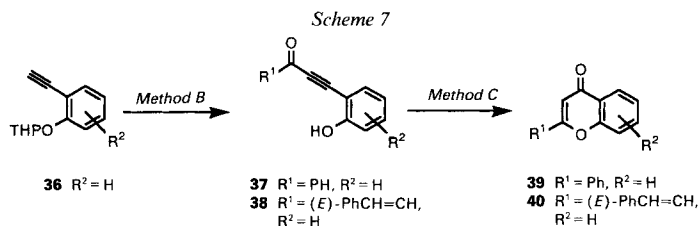
**2.4. Mechanistic Aspects.** To explain the outcome of these reactions, we postulate that the acetylenic acetal **I** is first hydrolyzed to the acetylenic aldehyde **IX**. The latter or the acetylenic ketone **III** is then regioselectively attacked by  $\text{HX}$  giving rise to a mixture of (*E*)- and (*Z*)-products of type **X–XIII** (Scheme 5). The (*E*)-isomers **X** and **XII** afford, after cyclization and dehydration, the products **II** and **IV**, respectively. Interconversion of (*E*)- and (*Z*)-isomers appears to be rapid under the reaction conditions, since the (*Z*)-addition products **XI** and **XIII** were the only by-products isolated, when the reactions were stopped before completion. This fact is also a strong indication that the intermediate addition products **X–XIII** are not further hydrolyzed to  $\beta$ -diketones. It is noteworthy that the observed position of  $\text{X}$  in **II** and **IV** is completely controlled by the acetylenic aldehyde and acetylenic ketone moieties.



**3. Synthesis of Flavones and Styrylchromones.** – 3.1. *General.* During the course of our investigations to find further interesting applications of acid-catalyzed cyclizations of substituted acetylenic ketones, we turned our attention to an interesting publication of *Vereshchagin* and coworkers, who cyclized the acetylenic ketones of type **XIV** to 4*H*-pyran-4-ones of type **XV** using conc.  $\text{H}_2\text{SO}_4$  in aq. EtOH (Scheme 6) [15]. We have shown now that the reaction of 5-hydroxy-5-methylhex-2-ynophenone (**34**) with 4*N* aq.  $\text{HBr}$  in dioxane (1:3) for 2.5 h at  $90^\circ$  gave a 95% yield of the 4*H*-pyran-4-one **35** (Scheme 6). This comparison shows that the use of  $\text{HBr}$  is clearly superior to  $\text{H}_2\text{SO}_4$  for these cyclizations.

Scheme 6





As an extension of these cyclizations, we describe a new approach to flavones and styrylchromones (Scheme 7). Cyclization of the substituted acetylenic ketones **37** and **38** using aq. HBr should lead to flavone **39** and styrylchromone **40** (Scheme 7).

3.2. *Synthesis of the Acetylenic Ketones 37 and 38.* Acetylenic ketones **37** and **38** were synthesized by treatment of 2-(2-ethynylphenoxy)-3,4,5,6-tetrahydro-2H-pyran (**36**) [16] according to Method B with aldehydes of type V (Scheme 7).

3.3. *Cyclizations.* The acetylenic ketones **37** and **38** were treated with 4N aq. HBr in dioxane (1:3) at 80° for 2 h to yield 3',4',5'-trimethoxyflavone (**39**, 80%) and 2-styryl-4H-[1]benzopyran-4-one (**40**, 82%), respectively.

As we demonstrated for the synthesis of 3-halofurans, these cyclizations tolerate a wide range of substituents  $\text{R}^1$  and  $\text{R}^2$  (Scheme 7). Applications toward pharmacologically interesting styrylchromones [17] will be published later.

**4. Conclusions.** – This work shows that substituted acetylenic acetals of type I and acetylenic ketones of type III (Scheme 1) are excellent cyclization precursors for the synthesis of various substituted 3-halofurans of type II and IV in high yields. It is worth to point out that, by this method, the previously hardly known class of 2-substituted 3-halofurans of type II now has become readily accessible. Since 3-bromo- and 3-iodofurans can be metalated and substituted [11], the present work constitutes a novel general synthesis of highly substituted furans. Moreover, cyclizations of substituted acetylenic ketones **37** and **38** allow a new entry into flavones and styrylchromones in good yields (Scheme 7). Further applications of this type of cyclizations for the synthesis of other interesting heterocycles will be reported in due course.

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#### Experimental Part

(The author likes to thank Mr. O. Heitzelmann for his excellent work and enthusiasm.)

*General.* All reactions with air – or moisture – sensitive reactants and solvents were carried out in oven – or flame-dried glassware under a positive pressure of dry Ar. Reaction solvents and liquid reagents were purified by distillation shortly before use. THF was distilled under Ar from Na with benzophenone ketyl as indicator.  $\text{CH}_2\text{Cl}_2$  was distilled from powdered  $\text{CaH}_2$ . All other reactants were 'reagent-grade' unless described otherwise. Anal. TLC: 2.5 × 10 cm precoated TLC plates,  $\text{SiO}_2$  60F-254, layer thickness 0.25 mm (E. Merck & Co., Darmstadt, FRG). Flash chromatography (FC): E. Merck  $\text{SiO}_2$  60 (230–400 mesh ASTM) according to [13]. M.p.: Büchi-SMP-20 apparatus, uncorrected. IR: Nicolet 7199 FT-IR spectrometer; solids in KBr pellets, liquids as thin films; characteristic bands in  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$ : at 250 MHz, Bruker-AC-250 apparatus, TMS as internal standard; chemical shifts of signal centres and ranges in ppm ( $\delta$ ), J in Hz.

**1. General Procedures.** – 1.1. *Method A.* To a stirred soln. of 1.43 ml (10.0 mmol) of 3,3-diethoxyprop-1-yne (**1**; *Fluka*) in THF (30 ml), 6.88 ml (11.0 mmol) of BuLi soln. (1.6M in hexane) were added at  $-78^{\circ}$ . The mixture was stirred for 30 min at  $-78^{\circ}$ , followed by addition of 11.0 mmol of freshly distilled aldehyde **V** at  $-78^{\circ}$ . The mixture was stirred for 2 h at  $-78^{\circ}$ , allowed to warm to  $-40^{\circ}$ , and quenched with sat.  $\text{NaHCO}_3$  soln. (50 ml), ice (50 g), and  $\text{Et}_2\text{O}$  (100 ml). The aq. layer was extracted with  $\text{Et}_2\text{O}$  ( $2 \times 50$  ml), the combined org. fractions were washed with sat. brine (50 ml), dried ( $\text{MgSO}_4$ ), and the solvents were removed. The residue was chromatographed on  $\text{SiO}_2$  (80 g) with  $\text{Et}_2\text{O}$ /hexane 1:2 and further purified by bulb-to-bulb distillation under reduced pressure.

1.2. *Method B.* To a stirred soln. of 10.0 mmol of the THP-protected propargylic alcohol **VI** in THF (30 ml), 6.88 ml (1.1 equiv.) of BuLi soln. (1.6M in hexane) were added at  $-78^{\circ}$ . The mixture was stirred for 30 min at  $-30^{\circ}$ , followed by addition of 11.0 mmol of the aldehyde **V** at  $-78^{\circ}$ . The mixture was stirred for 30 min at  $-78^{\circ}$ , allowed to slowly warm up to  $0^{\circ}$ , and stirred for 30 min at  $0^{\circ}$ , and poured into  $\text{Et}_2\text{O}$  (50 ml)/sat.  $\text{NH}_4\text{Cl}$  soln. (30 ml) and ice (50 g). The aq. layer was extracted with  $\text{AcOEt}$  ( $2 \times 50$  ml), the combined org. fractions were washed with sat. brine ( $2 \times 50$  ml), dried ( $\text{MgSO}_4$ ), and the solvents removed. The residue was dissolved in  $\text{CH}_2\text{Cl}_2$  (10 ml) and added to a mechanically stirred suspension of  $\text{MnO}_2$  (80 g) in  $\text{CH}_2\text{Cl}_2$  (50 ml) at  $0^{\circ}$ . The mixture was stirred for 45 min at  $0^{\circ}$ , filtered through  $\text{MgSO}_4$  (20 g) and the solvents were removed. To the residue in  $\text{EtOH}$  (50 ml), 0.5 g of PPTS were added at r.t., and the mixture was stirred at  $50^{\circ}$ , until no more **V** was detectable by TLC (1–2.5 h). The cold mixture was diluted with  $\text{H}_2\text{O}$  (50 ml) and  $\text{AcOEt}$  (80 ml). The aq. phase was extracted with  $\text{AcOEt}$  ( $2 \times 50$  ml), the combined org. fractions were washed with sat. brine ( $2 \times 50$  ml), dried, and the solvents were removed. The residue was chromatographed on  $\text{SiO}_2$  (80 g) and crystallized from  $\text{AcOEt}$ /hexane as indicated.

1.3. *Method C.* To a stirred soln. of 10.0 mmol of the acetylenic acetal **I** or acetylenic ketone **III** in dioxane (30 ml), 2–4N aq. HX (10 ml) was added at r.t. The mixture was stirred at r.t. to  $50^{\circ}$  as indicated in Table 3, cooled to r.t., diluted with  $\text{Et}_2\text{O}$  or  $\text{AcOEt}$  (100 ml), and poured onto ice (50 g). The aq. phase was extracted with  $\text{Et}_2\text{O}$  or  $\text{AcOEt}$  (100 ml), the combined org. fractions were washed with sat. brine (50 ml) and the solvents removed. The residue was chromatographed on  $\text{SiO}_2$  (80 g), distilled under reduced pressure (bulb-to-bulb) or crystallized as indicated.

1.4. *Method D.* Same procedure as *Method C*, except that toluene was used as solvent instead of dioxane.

1.5. *Method E.* To a stirred soln. of 10.0 mmol of the acetylenic acetal **I** or the acetylenic ketone **III** in  $\text{CH}_2\text{Cl}_2$  (50 ml), a soln. of 33%  $\text{HBr}/\text{AcOH}$  (4 ml) in  $\text{CH}_2\text{Cl}_2$  (5 ml) was added at  $0^{\circ}$ . The mixture was stirred for 1 h at  $0^{\circ}$ , allowed to warm up to r.t., and quenched with sat.  $\text{NaHCO}_3$  soln. (30 ml), ice (50 g), and  $\text{Et}_2\text{O}$  (100 ml). The org. phase was washed with sat. brine (75 ml), dried ( $\text{MgSO}_4$ ) and the solvents were removed. The residue was purified as described in *Method C*.

**2. Acetylenic Acetals I.** – 2.1. ( $\pm$ )-4-Hydroxy-4-phenylbut-2-ynal Diethyl Acetal (**5**) [18a]. A soln. of 6.54 g (51.0 mmol) of **1** in THF was treated according to *Method A* with 5.95 g (1.1 equiv.) of benzaldehyde (**2**): 11.0 g (92%) of **5** as a colorless oil after FC. IR (film): 3417w, 2977m, 2868w, 1495w, 1453w, 1328w, 1136s, 1050s, 1014s, 699m.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 250 MHz): 7.6–7.5, 7.45–7.3 (2m, 5 arom. H); 5.53 (br. d,  $J = 6.2$ , H–C(4)); 5.36 (d,  $J = 1.4$ , H–C(1)); 3.85–3.55 (m,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{CH}$ ); 2.32 (d,  $J = 6.2$ , OH); 1.3–1.15 (m,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{CH}$ ). MS: 233 (2,  $M^+ - \text{H}$ ), 189 (76), 133 (79), 115 (100), 105 (36), 103 (32), 77 (48), 55 (48). Anal. calc. for  $\text{C}_{14}\text{H}_{18}\text{O}_3$  (234.30): C 71.77, H 7.74; found: C 71.64, H 7.73.

2.2. ( $\pm$ )-4-Hydroxynon-2-ynal Diethyl Acetal (**6**) [18b]. A soln. of 15.0 ml (0.105 mol) of **1** in THF was treated according to *Method A*: 22.0 g (92%) **6** after bulb-to-bulb distillation ( $160^{\circ}/12$  Torr). IR (film): 3421w, 2932s, 2871m, 2235w, 1460w, 1357w, 1328m, 1148s, 1118m, 1052s, 1011m.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 250 MHz): 5.31 (d,  $J = 1.2$ , H–C(1)); 4.5–4.3 (m,  $J = 6.6$ , H–C(4)); 3.85–3.5 (m,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{CH}$ ); 1.99 (d,  $J = 6.6$ , OH); 1.8–1.65, 1.55–1.25 (2m, 6 aliph. H); 1.24 (t,  $J = 7.2$ ,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{CH}$ ); 0.95–0.85 (m, 3 aliph. H). MS: 227 (2,  $M^+ - \text{H}$ ), 183 (33), 109 (25), 85 (47), 67 (29), 57 (100), 55 (47), 43 (51).

2.3. ( $\pm$ )-4-Hydroxydodec-2-ynal Diethyl Acetal (**7**) [18c]. A soln. of 20.0 ml (0.14 mol) of **1** in THF was treated according to *Method A* with **4** (*Fluka*): 31.8 g (82.2%) of **7** as a colorless liquid after bulb-to-bulb distillation ( $138^{\circ}/0.1$  mbar). IR (film): 3431w, 2927w, 2856m, 2220w, 1720w, 1450w, 1327w, 1145m, 1119m, 1053s, 1011w.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 250 MHz): 5.31 (d,  $J = 1.3$ , H–C(1)); 4.5–4.4 (m, H–C(4)); 3.85–3.55 (m,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{CH}$ ); 1.88 (br. d,  $J = 6.0$ , OH); 1.8–1.7 (m, 2 H–C(5)); 1.55–1.15 (m, 14 aliph. H); 0.95–0.85 (m, 3 H–C(12)). MS: 269 (3,  $M^+ - \text{H}$ ), 225 (95), 95 (43), 85 (99), 57 (100). Anal. calc. for  $\text{C}_{16}\text{H}_{30}\text{O}_3$  (270.41): C 71.07, H 11.18; found: C 71.23, H 11.36.

**3. Acetylenic Ketones III.** – 3.1. 4-Hydroxybut-2-ynophenone (**13**). A soln. of 19.8 g (0.141 mol) of **8** in THF was treated according to *Method B* to yield, after FC on  $\text{SiO}_2$  with  $\text{AcOEt}$ /hexane 1:3, 10.75 g (68%) of **13** as a pale yellow oil. IR (film): 3416m (br.), 2895w, 2231m, 1643s, 1597s, 1450s, 1315s, 1267s, 1177m, 1102s, 1023s, 901m.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 250 MHz): 8.2–8.05, 7.7–7.4 (2m, 5 arom. H); 4.58 (d,  $J = 6.4$ , 2 H–C(4)); 2.39 (t,  $J = 6.4$ , OH).

MS: 160 (100,  $M^+$ ), 131 (84), 105 (55), 77 (82), 51 (44). Anal. calc. for  $C_{10}H_8O_2$  (160.17): C 74.99, H 5.03; found: C 74.44, H 5.02.

3.2. ( $\pm$ )-4-Hydroxyphenyl-2-ynophenone (**14**). A soln. of 21.8 g (0.143 mol) of **9** in THF was treated according to *Method B* with **2** to yield, after FC on  $SiO_2$  with AcOEt/hexane 1:3, 19.43 g (78%) of **14** as a pale yellow oil. IR (film): 3410m (br.), 2985w, 2222w, 1644s, 1597m, 1450m, 1314m, 1266s, 1130m, 1082w, 1012m.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 8.2–8.1, 7.7–7.45 (2m, 5 arom. H); 4.9–4.8 (m, H–C(4)); 2.33 (d,  $J = 5.6$ , OH); 1.62 (d,  $J = 5.6$ ,  $CH_3$ –C(4)). MS: 174 (22,  $M^+$ ), 159 (15), 131 (100), 105 (51), 77 (54), 53 (44). Anal. calc. for  $C_{11}H_{10}O_2$  (174.20): C 75.84, H 5.79; found: C 75.60, H 5.91.

3.3. 4-Hydroxy-3',4',5'-trimethoxybut-2-ynophenone (**15**). A soln. of 10.0 g (71.3 mmol) of **8** in THF was treated according to *Method B* with 3,4,5-trimethoxybenzaldehyde (**10**, Fluka): 13.0 g (73%) of **15** after recrystallization from AcOEt/hexane. M.p. 104–105°. IR (KBr): 3380m (br.), 2940w, 2840w, 2240w, 1630s, 1580m, 1505m, 1420m, 1340s, 1230s, 1130s, 1005m, 750m.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 7.38 (s, 2 arom. H); 4.57 (br. s, 2 H–C(4)); 3.94, 3.93 (2s, 3  $CH_3O$ ); 2.37 (br. s, OH). MS: 250 (100,  $M^+$ ), 235 (40). Anal. calc. for  $C_{13}H_{14}O_5$  (250.25): C 62.39, H 5.64; found: C 62.43, H 5.80.

3.4. ( $\pm$ )-4-Hydroxy-3',4',5'-trimethoxyphenyl-2-ynophenone (**16**). To a soln. of 0.66 g (9.42 mmol) of *but-3-yn-2-ol* (**12**) in THF (20 ml) and HMPA (6 ml), 12.55 ml BuLi soln. (1.6M in hexane) were added at  $-78^\circ$ . The mixture was allowed to warm up to  $0^\circ$  and stirred at  $0^\circ$  for 1 h. To the mixture, a soln. of 2.0 g (7.83 mmol) of **N**, 3,4,5-tetramethoxy-*N*-methylbenzamide (**11**) [8] in THF (20 ml) was added at  $-40^\circ$ . The mixture was stirred at  $-40^\circ$  for 30 min, slowly warmed up to r.t., stirred at r.t. for 1 h, and quenched with a mixture of ice (20 g) 0.5N aq. HCl (10 ml)  $Et_2O$  (100 ml). The org. phase was washed with  $H_2O$  ( $2 \times 40$  ml), the combined aq. phase extracted with  $Et_2O$  (50 ml), the combined org. fractions were washed with sat. brine ( $2 \times 50$  ml), dried ( $MgSO_4$ ) and the solvents removed. The residue was chromatographed on  $SiO_2$  (100 g) with AcOEt/hexane 1:1 and crystallized from AcOEt/hexane affording 1.65 g (80%) of **16** as a pale yellow solid. M.p. 77–79°. IR (KBr): 3460m (br.), 2975w, 2940w, 2215m, 1688m, 1580s, 1500m, 1420m, 1335s, 1220s, 1180m, 1130s, 995m, 750m.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 7.39 (s, 2 arom. H); 4.9–4.75 (m,  $J = 5.6$ , H–C(4)); 3.95, 3.93 (2s, 3  $CH_3O$ ); 2.31 (d,  $J = 5.6$ , OH); 1.61 (d,  $J = 5.6$ ,  $CH_3$ –C(4)). MS: 264 (100,  $M^+$ ), 249 (34), 53 (16), 43 (21). Anal. calc. for  $C_{14}H_{16}O_5$  (264.28): C 63.63, H 6.10; found: C 63.54, H 6.18.

3.5. ( $\pm$ )-2-Hydroxydec-3-yn-5-one (**17**). A soln. of 23.1 g (0.15 mol) of **9** in THF was treated according to *Method B* with **3** affording, after FC on  $SiO_2$  with AcOEt/hexane 1:2, 18.17 g (72%) of **17** as a pale yellow oil. IR (film): 3406m (br.), 2933m, 2870m, 2215m, 1676s, 1458w, 1404w, 1371w, 1235w, 1163m, 1086w, 1038w.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 4.69 (q,  $J = 5.6$ , H–C(2)); 2.56 (t,  $J = 7.3$ , 2 H–C(6)); 2.18 (d,  $J = 5.6$ , OH); 1.8–1.55 (m, 2 H–C(7)); 1.52 (d,  $J = 5.6$ ,  $CH_3$ –C(2)); 1.45–1.2 (m, 4 aliph. H); 1.0–0.85 (m, 3 aliph. H). MS: 153 (1,  $M^+ - CH_3$ ), 112 (31), 97 (100), 69 (22), 53 (62), 43 (60). Anal. calc. for  $C_{10}H_{16}O_2$  (168.24): C 71.39, H 9.59; found: C 70.96, H 9.70.

4. 3-Halofurans **II** and **IV**. – 4.1. 3-Bromo-2-phenylfuran (**18**). *Method C*: a soln. of 1.0 g (4.27 mmol) of **5** in dioxane was treated with 2N aq. HBr at  $50^\circ$  for 24 h. FC on  $SiO_2$  with AcOEt/hexane 1:3 and bulb-to-bulb distillation ( $150^\circ/0.08$  mbar) afforded 540 mg (60.2%) of **18** as a colorless liquid. IR (film): 3150w, 3120w, 3057w, 1580w, 1510m, 1480m, 1449w, 1379w, 1186w, 1157w, 1056m, 949m, 883m, 764s, 669s, 663s.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 8.0–7.9, 7.5–7.3 (2m, 5 arom. H); 7.42, 6.53 (2d,  $J = 1.9$ , H–C(5), H–C(4)). MS: 224, 222 (100,  $M^+$ ), 195, 193 (31), 115 (84). Anal. calc. for  $C_{10}H_7BrO$  (223.07): C 53.84, H 3.16, Br 35.82; found: C 53.82, H 3.20, Br 35.99. *Method D*: a soln. of 1.0 g (4.27 mmol) of **5** in toluene was treated with 4N aq. HBr at  $50^\circ$  for 2 h to yield, after chromatography and distillation (see above), 830 mg (92.7%) of **18** as a colorless liquid.

4.2. 3-Bromo-2-pentylfuran (**19**). A soln. of 2.0 g (8.76 mmol) of **6** in dioxane was treated according to *Method C* with 4N aq. HBr at  $40^\circ$  for 3.5 h to afford 1.90 g (96.7%) of **19** after FC on  $SiO_2$  with AcOEt/hexane 1:4. Bulb-to-bulb distillation ( $155^\circ/16$  mbar) gave 1.55 g (81.5%) of **19** as a colorless liquid. IR (film): 3127w, 2923s, 2861s, 1597w, 1507m, 1461w, 1180w, 1140m, 1041w, 775s.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 7.25, 6.34 (2d,  $J = 2.0$ , H–C(5), H–C(4)); 2.63 (t,  $J = 7.3$ , 2 aliph. H); 1.75–1.55, 1.4–1.2, 0.95–0.85 (3m, 9 aliph. H). MS: 218, 216 (49,  $M^+$ ), 161, 159 (100), 137 (53), 81 (85), 51 (78). Anal. calc. for  $C_9H_{13}BrO$  (217.11): C 49.79, H 6.04, Br 36.80; found: C 50.17, H 6.15, Br 37.20.

4.3. 3-Bromo-2-octylfuran (**20**). A soln. of 4.0 g (14.79 mmol) of **7** in dioxane was treated according to *Method C* with 4N aq. HBr at  $50^\circ$  for 6 h to yield 3.80 g (99%) of **20**, after FC on  $SiO_2$  with AcOEt/hexane 1:7. Bulb-to-bulb distillation ( $150^\circ/0.1$  mbar) gave 2.90 g (75.7%) of **20** as a colorless liquid. IR (film): 3127w, 2917s, 2854s, 1597w, 1556w, 1508w, 1462w, 1347m, 1188w, 1138m, 1059w, 975w.  $^1H$ -NMR ( $CDCl_3$ , 250 MHz): 7.25, 6.34 (2d,  $J = 2.0$ , H–C(4), H–C(5)); 2.62 (t,  $J = 8.0$ , 2 aliph. H); 1.8–1.5, 1.4–1.15, 0.95–0.8 (3m, 15 aliph. H). MS: 260, 258 (15,  $M^+$ ), 179 (38), 161, 159 (100), 81 (66). Anal. calc. for  $C_{12}H_{19}BrO$  (259.19): C 55.61, H 7.39, Br 30.83; found: C 55.66, H 7.43, Br 30.81.

4.4. *3-Chloro-2-octylfuran* (**21**). A soln. of 2.0 g (7.40 mmol) of **7** in dioxane was treated according to *Method C* with 4N aq. HCl at 50° for 4 h to yield 1.52 g (95.7%) of **21**, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:7. Bulb-to-bulb distillation (130°/0.1 mbar) gave 1.14 g (72.2%) of **21** as a colorless liquid. IR (film): 2960m, 2927s, 2885m, 1605m, 1515m, 1470w, 1205w, 1145w, 995s, 724w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.23, 6.30 (2d, *J* = 2.0, H–C(5), H–C(4)); 2.62 (t, *J* = 7.3, 2 aliph. H); 1.7–1.5, 1.4–1.15, 0.95–0.8 (3m, 15 aliph. H). MS: 214 (14, *M*<sup>+</sup>), 179 (25), 115 (100). Anal. calc. for C<sub>17</sub>H<sub>19</sub>ClO (214.73): C 67.12, H 8.92, Cl 16.51; found: C 67.47, H 9.08, Cl 16.32.

4.5. *4-Bromo-2-phenylfuran* (**22**). A soln. of 400 mg (2.5 mmol) of **13** in toluene was treated according to *Method D* with 4N aq. HBr at 50° for 3 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:5, 530 mg (95%) of **22** as a white solid. M.p. 41–42°. IR (KBr): 3112w, 3033w, 1603w, 1566w, 1513w, 1474w, 1276w, 1069w, 1019w, 930m, 909m, 803w, 764s, 680s, 585m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.7–7.6 (m, 2 arom. H); 7.46, 6.68 (2d, *J* = 0.8, H–C(3), H–C(5)); 7.45–7.25 (m, 3 arom. H). MS: 224, 222 (50, *M*<sup>+</sup>), 143 (17), 115 (100). Anal. calc. for C<sub>10</sub>H<sub>7</sub>BrO (223.07): C 53.84, H 3.16, Br 35.82; found: C 53.92, H 3.12, Br 35.45.

4.6. *4-Iodo-2-phenylfuran* (**23**). A soln. of 170 mg (1.06 mmol) of **13** in toluene was treated according to *Method D* with 2N aq. HI [14] to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:5, 220 mg (77%) of **23** as a white solid (which turns red after a while, even in the freezer). M.p. 64–65°. IR (KBr): 3110w, 3031w, 2923w, 1604w, 1563w, 1502w, 1423m, 1441m, 1272m, 1136w, 1067m, 1013m, 905s, 793m, 760s, 687s, 582s. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.7–7.55 (m, 2 arom. H); 7.46, 6.72 (2d, *J* = 0.7, H–C(3), H–C(5)); 7.45–7.25 (m, 3 arom. H). MS: 270 (100, *M*<sup>+</sup>), 143 (61), 115 (99), 77 (40), 63 (28), 51 (20).

4.7. *3-Chloro-2-methyl-5-phenylfuran* (**24**). A soln. of 2.0 g (11.48 mmol) of **14** in dioxane was treated according to *Method C* with 4N aq. HCl at 50° for 4.5 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:5, 2.0 g (90.5%) of **24** as a slightly yellow oil. IR (film): 3070w, 3040w, 2930w, 1601m, 1487m, 1088s, 1026m, 757s. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.65–7.55, 7.45–7.2 (2m, 5 arom. H); 6.56 (s, H–C(4)); 2.34 (s, CH<sub>3</sub>–C(2)). Anal. calc. for C<sub>11</sub>H<sub>9</sub>ClO (192.64): C 68.58, H 4.71, Cl 18.40; found: C 68.55, H 4.92, Cl 18.08.

4.8. *3-Bromo-2-methyl-5-phenylfuran* (**25**). A soln. of 2.0 g (11.48 mmol) of **14** in dioxane was treated according to *Method C* with 4N aq. HBr to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:3, 2.51 g (92.3%) of **25** as a pale yellow oil. IR (film): 3130w, 3060w, 2920w, 1597s, 1554m, 1487s, 1147m, 1075s, 1021s, 758s, 690s. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.65–7.55, 7.4–7.2 (2m, 5 arom. H); 6.59 (s, H–C(4)); 2.35 (s, CH<sub>3</sub>–C(2)). MS: 238, 236 (100, *M*<sup>+</sup>), 195, 193 (17), 157 (26), 129 (24), 105 (43), 77 (96), 51 (35), 43 (43). Anal. calc. for C<sub>10</sub>H<sub>13</sub>BrO (231.13): C 51.97, H 6.54, Br 34.57; found: C 52.31, H 6.69, Br 34.56.

4.9. *3-Iodo-2-methyl-5-phenylfuran* (**26**). A soln. of 2.0 g (11.48 mmol) of **14** in dioxane was treated according to *Method C* with 2N aq. HI [14] at 50° for 35 min to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:5, 2.95 g (90.5%) of **26** as a pale yellow oil. IR (film): 3120w, 3060w, 2910w, 1587m, 1551m, 1446m, 1143m, 1071m, 1014s, 799m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.65–7.55, 7.45–7.2 (2m, 5 arom. H); 6.62 (s, H–C(4)); 2.40 (s, CH<sub>3</sub>–C(2)). MS: 284 (100, *M*<sup>+</sup>), 157 (16), 128 (19), 115 (27), 105 (62), 77 (39), 51 (28), 43 (17). Anal. calc. for C<sub>11</sub>H<sub>9</sub>IO (284.10): C 46.51, H 3.19, I 44.67; found: C 46.04, H 3.17, I 45.15.

4.10. *4-Chloro-2-(3,4,5-trimethoxyphenyl)furan* (**27**). A soln. of 500 mg (2.0 mmol) of **15** in dioxane was treated according to *Method C* with 4N aq. HCl at 50° for 4 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:2, 462 mg (86%) as white solid. M.p. 81–82°. IR (KBr): 3140w, 2930w, 2835w, 1590m, 1575s, 1500s, 1418m, 1250s, 1242s, 1132s, 995m, 945m, 800m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.44, 6.59 (2s, H–C(3), H–C(5)); 6.84 (s, 2 arom. H); 3.91, 3.87 (2s, 3 CH<sub>3</sub>O). MS: 268 (100, *M*<sup>+</sup>), 253 (83), 225 (22), 195 (20), 139 (15). Anal. calc. for C<sub>13</sub>H<sub>13</sub>ClO<sub>4</sub> (268.69): C 58.11, H 4.88, Cl 13.19; found: C 58.07, H 4.94, Cl 13.00.

4.11. *4-Bromo-2-(3,4,5-trimethoxyphenyl)furan* (**28**). A soln. of 500 mg (2.0 mmol) of **15** in dioxane was treated according to *Method C* with 4N aq. HBr at 50° for 2.5 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:1, 580 mg (93%) of **28** as white solid. M.p. 73–74°. IR (KBr): 3120w, 3100w, 2935w, 2830w, 1595m, 1570m, 1495s, 1420m, 1300s, 1130s, 1005m, 835m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.45, 6.63 (2d, *J* = 0.8, H–C(3), H–C(5)); 6.84 (s, 2 arom. H); 3.91, 3.87 (2s, 3 CH<sub>3</sub>O). MS: 314, 312 (100, *M*<sup>+</sup>), 299, 297 (97), 269 (19), 239 (22). Anal. calc. for C<sub>13</sub>H<sub>13</sub>BrO<sub>4</sub> (313.15): C 49.86, H 4.18, Br 25.52; found: C 49.87, H 4.18, Br 25.63.

4.12. *3-Chloro-2-methyl-5-(3,4,5-trimethoxyphenyl)furan* (**29**). A soln. of 300 mg (1.14 mmol) of **16** in dioxane was treated according to *Method C* at 50° for 20 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:1, 260 mg (80.6%) of **29** as a white solid. M.p. 101–102°. IR (KBr): 3130w, 2940w, 1595m, 1500s, 1450m, 1420m, 1340m, 1245s, 1135s, 1100m, 1010m, 840m, 790m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 6.80 (s, 2 arom. H); 6.51 (s, H–C(4)); 3.91, 3.86 (2s, 3 CH<sub>3</sub>O); 2.35 (s, CH<sub>3</sub>–C(2)). MS: 282 (100, *M*<sup>+</sup>), 267 (88), 209 (15), 43 (27). Anal. calc. for C<sub>14</sub>H<sub>15</sub>ClO<sub>4</sub> (282.72): C 59.48, H 5.35, Cl 12.54; found: C 59.20, H 5.35, Cl 12.21.

4.13. *3-Bromo-2-methyl-5-(3,4,5-trimethoxyphenyl)furan* (**30**). A soln. of 1.0 g (3.78 mmol) of **16** in dioxane was treated according to *Method C* with 4N aq. HBr at 50° for 20 h to yield, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:1 and crystallization from AcOEt/hexane, 1.02 g (82.4%) of **30** as a pale yellow solid. M.p. 94–95°. IR (KBr): 3131w,



2988w, 2939w, 1591m, 1554w, 1499m, 1416m, 1244m, 1129s, 1065w, 825w, 707w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 6.80 (s, 2 arom. H); 6.54 (s, H–C(4)); 3.91, 3.86 (2s, 3 CH<sub>3</sub>O); 2.36 (s, CH<sub>3</sub>–C(2)). MS: 328, 326 (100, M<sup>+</sup>), 311 (86), 285, 283 (18), 253 (25), 43 (50). Anal. calc. for C<sub>14</sub>H<sub>15</sub>BrO<sub>4</sub> (327.17): C 51.40, H 4.62, Br 24.42; found: C 51.39, H 4.64, Br 24.75.

4.14. *3-Iodo-2-methyl-3-(3,4,5-trimethoxyphenyl)furan (31)*. A soln. of 6.0 g (22.7 mmol) of **16** in dioxane was treated according to *Method C* with 2N aq. HI [14] at 50° for 30 min to yield, after FC on SiO<sub>2</sub> with AcOEt/hexane 1:8 and crystallization from AcOEt/hexane, 7.50 g (88.4%) of **31** as a brownish solid. M.p. 131–132°. IR (KBr): 3112w, 2948w, 2835w, 1595m, 1553m, 1498s, 1461m, 1422m, 1240m, 1131s, 1000m, 848w, 821w, 765w, 674w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 6.80 (s, 2 arom. H); 6.57 (s, H–C(4)); 3.91, 3.86 (2s, 3 CH<sub>3</sub>O); 2.41 (s, CH<sub>3</sub>–C(2)). MS: 374 (100, M<sup>+</sup>), 359 (67), 331 (11), 219 (14), 43 (17). Anal. calc. for C<sub>14</sub>H<sub>15</sub>IO<sub>4</sub> (374.18): C 44.94, H 4.04, I 33.92; found: C 44.79, H 4.04, I 33.67.

4.15. *3-Bromo-2-methyl-5-pentylfuran (32)*. A soln. of 400 mg (2.38 mmol) of **17** in toluene was treated according to *Method D* with 4N aq. HBr at 50° for 4 h: 450 mg (81.1%) of **32** as a colorless oil, after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:7 and bulb-to-bulb distillation (180°/19 mbar). IR (film): 2958m, 2928s, 1614w, 1575w, 1461w, 1380w, 1225m, 1041m, 987w, 935w, 786w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 5.93 (s, H–C(4)); 2.53 (t, *J* = 7.5, 2 aliph. H); 2.23 (s, CH<sub>3</sub>–C(2)); 1.7–1.5, 1.4–1.25, 0.95–0.85 (3m, 9 aliph. H). MS: 232, 230 (17, M<sup>+</sup>), 175, 173 (100), 43 (29). Anal. calc. for C<sub>10</sub>H<sub>15</sub>BrO (231.13): C 51.97, H 6.54, Br 34.57; found: C 52.31, H 6.69, Br 34.56.

4.16. *3-Iodo-2-methyl-5-pentylfuran (33)*. A soln. of 2.0 g (11.89 mmol) of **17** in dioxane was treated with 2N aq. HI [14] at r.t. for 1 h: 2.51 g (75.9%) of **33** as a pale yellow oil after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:4 and bulb-to-bulb distillation (185°/0.04 mbar). IR (film): 2955s, 2929s, 2858m, 1602w, 1571m, 1462w, 1380w, 1218w, 1177w, 1128w, 1087w, 1029m, 983m, 935w, 789w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 5.95 (s, H–C(4)); 2.54 (t, *J* = 7.5, 2 aliph. H); 2.28 (s, CH<sub>3</sub>–C(2)); 1.7–1.5, 1.4–1.25, 0.95–0.85 (3m, 9 aliph. H). MS: 278 (30, M<sup>+</sup>), 221 (100), 43 (21). Anal. calc. for C<sub>10</sub>H<sub>15</sub>IO (278.13): C 43.18, H 5.44, I 45.63; found: C 43.01, H 5.51, I 45.91.

**5. 4H-Pyran-2-one Derivative 35.** – 5.1. *5-Hydroxy-5-methylhex-2-ynophenone (34)* [15]. To a soln. of 5.0 g (50.94 mmol) of 2-methylpent-4-yn-2-ol (prepared according to [19]) in THF (150 ml), 66.9 ml of BuLi soln. (1.6M in hexane) were added at –60°. The mixture was stirred at 0° for 1 h, and 7.03 g (66.24 mmol) of benzaldehyde (**2**) were added at –78°. The mixture was allowed to slowly warm up to 0°, stirred at 0° for 2 h, and quenched with sat. NH<sub>4</sub>Cl soln. (100 ml), ice (100 g), and Et<sub>2</sub>O (150 ml). The aq. layer was extracted with Et<sub>2</sub>O (2 × 100 ml), the combined org. fractions were washed with sat. brine (200 ml), dried (MgSO<sub>4</sub>) and the solvents removed. The residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) and added at 0° to a mechanically stirred suspension of 133 g of MnO<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> (200 ml). The mixture was stirred at 0° for 30 min, filtered through MgSO<sub>4</sub>, and evaporated. The residue was chromatographed on SiO<sub>2</sub> (250 g) with Et<sub>2</sub>O/hexane 1:1: 7.3 g (70.9%) of **34** as a pale yellow oil. IR (film): 3421w (br.), 2933w, 2240w, 2202m, 1640s, 1598w, 1451w, 1313m, 1268s, 1169w, 900w, 702s. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 8.2–8.15, 7.65–7.55, 7.55–7.45 (3m, 5 arom. H); 2.71 (s, 2 H–C(4)); 2.17 (s, OH); 1.43 (s, CH<sub>3</sub>–C(5)). MS: 144 (100), 115 (23), 105 (23), 77 (25), 66 (28), 59 (83).

5.2. *2,2-Dimethyl-6-phenyl-2,3-dihydro-4H-pyran-4-one (35)* [15]. A soln. of 4.46 g (22.03 mmol) of **34** in dioxane was treated according to *Method C* at 90° for 2.5 h: 4.23 g (94.8%) of **35** as a white solid after FC on SiO<sub>2</sub> with Et<sub>2</sub>O/hexane 1:1. M.p. 36–37°. IR (KBr): 3064w, 2978w, 1661s, 1599s, 1571s, 1492w, 1448m, 1367s, 1278m, 1251m, 1055m, 770m, 693m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.8–7.7, 7.5–7.4 (2m, 5 arom. H); 5.99 (s, H–C(3)); 2.59 (s, 2 H–C(5)); 1.55 (s, 2 CH<sub>3</sub>–C(6)). MS: 202 (42, M<sup>+</sup>), 187 (37), 105 (100), 77 (37), 69 (49), 56 (23). Anal. calc. for C<sub>13</sub>H<sub>14</sub>O<sub>2</sub> (202.25): C 77.20, H 6.98; found: C 76.87, H 6.96.

**6. Acetylenic Ketones 37 and 38.** – 6.1. *2-(2-Ethynylphenoxy)-3,4,5,6-tetrahydro-2H-pyran (36)*. To a soln. of 15.0 g (0.127 mol) of 2-ethynylphenol [16] in AcOEt (25 ml) at 0°, 3 drops of conc. aq. HCl and 23 ml of 3,4-dihydro-2H-pyran were added. The mixture was heated at 50° for 48 h, cooled to r.t., and quenched with sat. NaHCO<sub>3</sub> soln. (50 ml) and Et<sub>2</sub>O (100 ml). The aq. phase was extracted with Et<sub>2</sub>O (2 × 50 ml), the combined org. fractions were washed with sat. brine (2 × 50 ml), dried (MgSO<sub>4</sub>) and the solvents removed. The residue was chromatographed on SiO<sub>2</sub> (400 g) with Et<sub>2</sub>O/hexane 1:5: 23.4 g (91%) of **36** as a colorless liquid. IR (film): 3283m, 2945m, 2874w, 2105w, 1576w, 1485s, 1447m, 1356w, 1282m, 1181m, 1119s, 1032m, 960s, 873w, 755s. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.5–7.4, 7.35–7.2, 7.15–7.1, 7.0–6.9 (4m, 4 arom. H); 5.6–5.5 (m, OCHO); 4.05–3.8, 3.65–3.55 (2m, CH<sub>2</sub>O); 3.25 (s, CH≡C); 2.2–1.5 (m, 6 aliph. H). MS: 202 (6, M<sup>+</sup>), 118 (21), 85 (100), 67 (22), 57 (25), 43 (24). Anal. calc. for C<sub>13</sub>H<sub>14</sub>O<sub>2</sub> (202.25): C 77.20, H 6.98; found: C 77.06, H 7.18.

6.2. *3-(2-Hydroxyphenyl)-3',4',5'-trimethoxyprop-2-ynophenone (37)*. A soln. of 2.0 g (9.89 mmol) of **36** in THF was treated according to *Method B* with **10**: 2.3 g (74.5%) of **37** as a white solid after recrystallization from AcOEt/hexane. M.p. > 135° (dec.). IR (KBr): 3344m, 3269w, 2998w, 2941w, 2185s, 1619m, 1577s, 1501m, 1453m, 1415m, 1335s, 1235m, 1161m, 1003w, 739m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.55–7.45 (m, 1 arom. H); 7.52 (s, 2

arom. H); 7.45–7.35, 7.05–6.9 (2m, 3 arom. H); 6.88 (br. s, OH); 3.95 (s, 3 CH<sub>3</sub>O). MS: 312 (100, M<sup>+</sup>), 297 (12), 281 (12), 281 (12), 269 (14), 168 (28), 143 (23), 89 (13). Anal. calc. for C<sub>18</sub>H<sub>16</sub>O<sub>5</sub> (312.32): C 69.22, H 5.16; found: C 68.82, H 5.36.

6.3. (E)-5-(2-Hydroxyphenyl)-1-phenylpent-1-en-4-yn-3-one (38). A soln. of 2.0 g (9.89 mmol) of **36** in THF was treated according to *Method B* with cinnamic aldehyde: 2.0 g (81%) of **36** as a pale yellow solid, after FC on SiO<sub>2</sub> (200 g) with Et<sub>2</sub>O/hexane 1:1 and crystallization from AcOEt/hexane. M.p. > 105° (dec.). IR (KBr): 3208m (br.), 3055w, 2223w, 2183s, 1625s, 1590s, 1499w, 1450m, 1343m, 1325m, 1182m, 1100w, 981w, 751m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 7.95, 6.89 (2d, J = 16.1, H–C(1), H–C(2)); 7.65–7.35 (m, 7 arom. H); 7.05–6.85 (m, 2 arom. H, OH). MS: 248 (48, M<sup>+</sup>), 247 (47), 231 (100), 219 (31), 191 (24), 103 (27), 89 (32), 77 (32). Anal. calc. for C<sub>17</sub>H<sub>12</sub>O<sub>2</sub> (248.28): C 82.24, H 4.87; found: C 82.28, H 4.98.

7. Flavone **39** and Styrylchromone **40**. – 7.1. 3',4',5'-Trimethoxyflavone (= 2-(3,4,5-Trimethoxyphenyl)-4H-[1]benzopyran-4-one; **39**). A soln. of 300 mg (0.96 mmol) of **37** in dioxane was treated according to *Method C* with 4N aq. HBr at 65° for 3.5 h to yield 240 mg (80%) of **39** as a pale yellow solid, after recrystallization from EtOH/H<sub>2</sub>O. M.p. 174–175°. IR (KBr): 3070w, 2941w, 2839w, 1639s, 1603m, 1568m, 1506m, 1470m, 1419s, 1372m, 1338m, 1245m, 1127s, 1006w, 771w, 750w. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 8.3–8.2, 7.75–7.65, 7.6–7.55, 7.5–7.4 (4m, 4 arom. H); 7.15 (s, 2 arom. H); 6.79 (s, H–C(3)); 3.97, 3.94 (2s, 3 CH<sub>3</sub>O). MS: 312 (100, M<sup>+</sup>), 297 (42), 269 (18), 121 (21). Anal. calc. for C<sub>18</sub>H<sub>16</sub>O<sub>5</sub> (312.32): C 69.22, H 5.16; found: C 68.99, H 5.20.

7.2. 2-Styryl-4H-[1]benzopyran-4-one (**40**) [20]. A soln. of 300 mg (1.21 mmol) of **38** in dioxane was treated according to *Method C* with 4N aq. HBr at 80° for 2 h to yield 235 mg (82%) of **40** as a pale yellow solid. M.p. 139–140°. IR (KBr): 3372w, 3057w, 3020w, 1652s, 1624s, 1560m, 1404s, 1392s, 1327w, 1323w, 1124w, 969m, 755m. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 250 MHz): 8.25–8.15 (m, H–C(5)); 7.75–7.3 (m, 8 arom. H); 7.62, 6.79 (2d, J = 16.1, 2 olef. H); 6.34 (s, H–C(3)). MS: 248 (63, M<sup>+</sup>), 247 (100), 231 (43), 128 (62), 92 (24). Anal. calc. for C<sub>17</sub>H<sub>12</sub>O<sub>2</sub> (248.28): C 82.24, H 4.87; found: C 82.18, H 5.07.

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