53. Acid-Catalyzed Cyclization Reactions of Substituted Acetylenic Ketones: A New Approach for the Synthesis of 3-Halofurans, Flavones, and Styrylchromones[1])

by **Daniel Obrecht**

Zentrale Forschungseinheiten, *F. Hoffmann-La Roche & Co. AG*, CH–4002 Basel

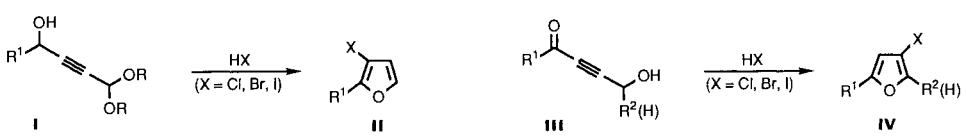
(23.I.89)

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 β-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 β-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 *4H*-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 ('α-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)*.

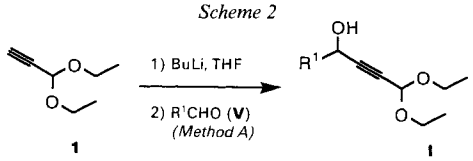
Scheme 1



[1]) 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°) to the corresponding aldehyde **V** (see **2**–**4**; *Scheme 2* and *Table 1* (*Method A*)) [13].

Scheme 2



1 **I**

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

Aldehyde **V**	R^1	Acetylenic acetal **I**	Yield [%][a])
2	Ph	**5**	92
3	$CH_3(CH_2)_4$	**6**	92
4	$CH_3(CH_2)_7$	**7**	82

[a]) 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°, followed by addition of the aldehyde **V**, oxidation of the intermediate alcohols with MnO_2 in CH_2Cl_2 and deprotection of the THP group using pyridinium *p*-toluenesulfonate (PPTS) in EtOH at 50° 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°

Scheme 3

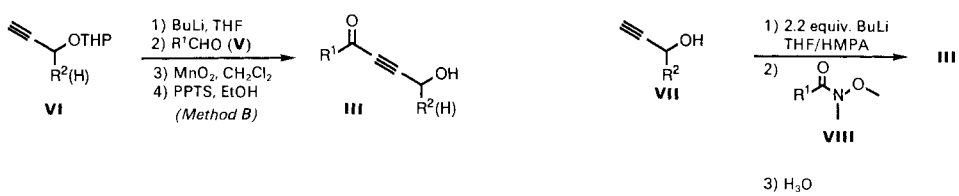


Table 2. *Synthesis of the Acetylenic Ketones* **III**

V or **VIII**	R^1	Propargyl alcohol **VI** or **VII**	R^2	Acetylenic ketones **III**	Yield [%][a])
2	Ph	**8**	H	**13**	68
2	Ph	**9**	CH_3	**14**	78
10	$3,4,5\text{-}(MeO)_3C_6H_2$	**8**	H	**15**	73
11	$3,4,5\text{-}(MeO)_3C_6H_2$	**12**	CH_3	**16**	80
3	$CH_3(CH_2)_4$	**9**	CH_3	**17**	72

[a]) 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 2–4N aq. HX (X = Cl, Br, I) in dioxane *(Method C)*, 2–4N aq. HX in toluene *(Method D)*, or 33% HBr/AcOH in CH_2Cl_2 *(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 2N aq. HI was purified by treatment with H_3PO_2 [14] to remove traces of I_2 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^1 and R^2 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^1 = Ph.

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

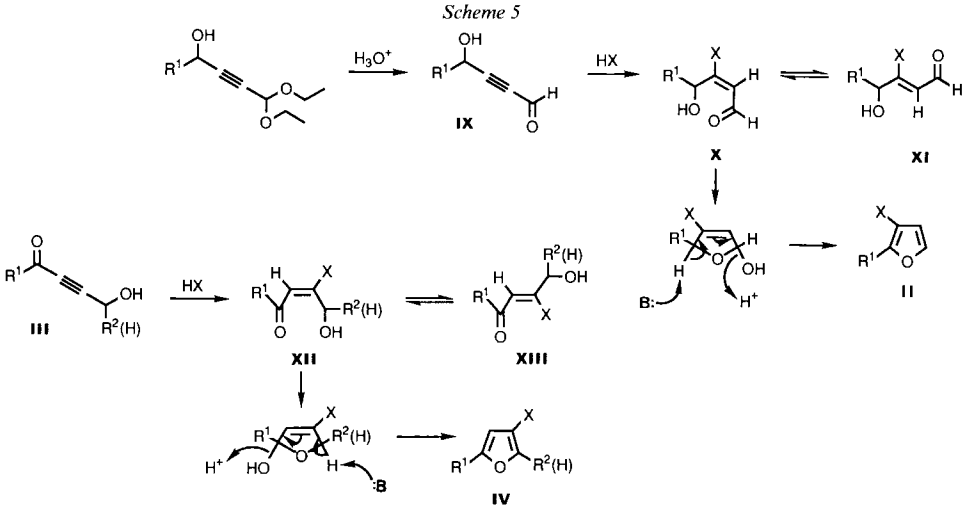
Starting material I or III	*Method*	Temp. [°C]	Time [h]	3-halofurans of type II or IV	X	R^1	R^2	Yield [%][a]
5	*C*	50	24	**18**	Br	Ph		60
5	*D*	50	2	**18**	Br	Ph		93
6	*C*	40	3.5	**19**	Br	$CH_3(CH_2)_4$		82(97)
7	*C*	50	6	**20**	Br	$CH_3(CH_2)_7$		76(99)
7	*E*	0–r.t.	0.5	**20**	Br	$CH_3(CH_2)_7$		86
7	*C*	50	4	**21**	Cl	$CH_3(CH_2)_7$		72(96)
13	*D*	50	3	**22**	Br	Ph	H	95
13	*D*	r.t.	4	**23**	I	Ph	H	77
14	*C*	50	4.5	**24**	Cl	Ph	CH_3	91
14	*C*	50	8	**25**	Br	Ph	CH_3	92
14	*C*	50	0.5	**26**	I	Ph	CH_3	91
15	*C*	50	4	**27**	Cl	3,4,5-$(MeO)_3C_6H_2$	H	86
15	*C*	50	2.5	**28**	Br	3,4,5-$(MeO_3)C_6H_2$	H	93
16	*C*	50	15	**29**	Cl	3,4,5-$(MeO)_3C_6H_2$	CH_3	81
16	*C*	50	20	**30**	Br	3,4,5-$(MeO)_3C_6H_2$	CH_3	82
16	*C*	50	0.5	**31**	I	3,4,5-$(MeO)_3C_6H_2$	CH_3	88
17	*D*	50	4	**32**	Br	$CH_3(CH_2)_4$	CH_3	81
17	*C*	r.t.	1	**33**	I	$CH_3(CH_2)_4$	CH_3	76

[a]) 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

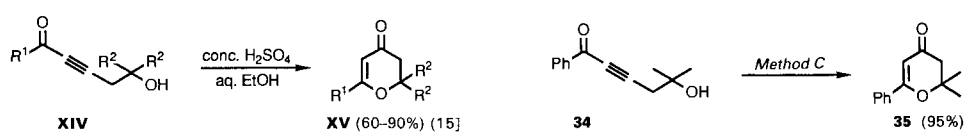
2.4. *Mechanistic Aspects.* To explain the outcome of these reactions, we postulate that the acetylenic acetal **I** is first hydrolyzed to the acetylenic aldehyde **IX**. The latter or the acetylenic ketone **III** is then regioselectively attacked by HX giving rise to a mixture of (*E*)- and (*Z*)-products 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 β-diketones. It is noteworthy that the observed position of X in **II** and **IV** is completely controlled by the acetylenic aldehyde and acetylenic ketone moieties.

Scheme 5



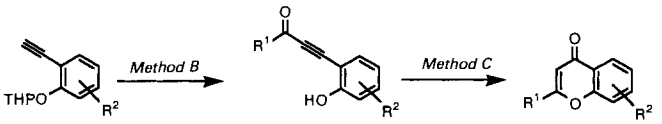
3. Synthesis of Flavones and Styrylchromones. – 3.1. *General.* During the course of our investigations to find further interesting applications of acid-catalyzed cyclizations of substituted acetylenic ketones, we turned our attention to an interesting publication of *Vereshchagin* and coworkers, who cyclized the acetylenic ketones of type **XIV** to 4*H*-pyran-4-ones of type **XV** using conc. H_2SO_4 in aq. EtOH *(Scheme 6)* [15]. We have shown now that the reaction of 5-hydroxy-5-methylhex-2-ynophenone (**34**) with 4N aq. HBr in dioxane (1:3) for 2.5 h at 90° gave a 95% yield of the 4*H*-pyran-4-one **35** *(Scheme 6)*. This comparison shows that the use of HBr is clearly superior to H_2SO_4 for these cyclizations.

Scheme 6



XIV **XV** (60–90%) [15] **34** **35** (95%)

Scheme 7



36 $R^2 = H$

37 $R^1 = PH$, $R^2 = H$
38 $R^1 = (E)$-PhCH=CH, $R^2 = H$

39 $R^1 = Ph$, $R^2 = H$
40 $R^1 = (E)$-PhCH=CH, $R^2 = H$

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-2*H*-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-4*H*-[1]benzopyran-4-one (**40**, 82%), respectively.

As we demonstrated for the synthesis of 3-halofurans, these cyclizations tolerate a wide range of substituents R^1 and 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.

We wish to thank our colleagues from the Central Research Units, *F. Hoffmann-La Roche & Co. AG* for IR (Mr. *A. Bubendorf*), NMR (Dr. *W. Arnold*), mass spectra (Dr. *W. Vetter* and Mr. *W. Meister*), and elemental analyses (Dr. *W. Dirscherl*). We thank also Dr. *Max Schmid*, Prof. *H.-J. Hansen*, Dr. *A. Knierzinger*, and especially Dr. *Rudolf Schmid* for fruitful discussions.

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. CH_2Cl_2 was distilled from powdered CaH_2. All other reactants were 'reagent-grade' unless described otherwise. Anal. TLC: 2.5 × 10 cm precoated TLC plates, SiO_2 *60F-254*, layer thickness 0.25 mm (*E. Merck & Co.*, Darmstadt, FRG). Flash chromatography (FC): *E. Merck* 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 cm^{-1}. ^{1}H-NMR: at 250 MHz, *Bruker-AC-250* apparatus, TMS as internal standard; chemical shifts of signal centres and ranges in ppm (δ), 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°. The mixture was stirred for 30 min at −78°, followed by addition of 11.0 mmol of freshly distilled aldehyde **V** at −78°. The mixture was stirred for 2 h at −78°, allowed to warm to −40°, and quenched with sat. $NaHCO_3$ soln. (50 ml), ice (50 g), and Et_2O 100 ml). The aq. layer was extracted with Et_2O (2 × 50 ml), the combined org. fractions were washed with sat. brine (50 ml), dried ($MgSO_4$), and the solvents were removed. The residue was chromatographed on SiO_2 (80 g) with Et_2O/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°. The mixture was stirred for 30 min at −30°, followed by addition of 11.0 mmol of the aldehyde **V** at −78°. The mixture was stirred for 30 min at −78°, allowed to slowly warm up to 0°, and stirred for 30 min at 0°, and poured into Et_2O (50 ml)/sat. NH_4Cl soln. (30 ml) and ice (50 g). The aq. layer was extracted with AcOEt (2 × 50 ml), the combined org. fractions were washed with sat. brine (2 × 50 ml), dried ($MgSO_4$), and the solvents removed. The residue was dissolved in CH_2Cl_2 (10 ml) and added to a mechanically stirred suspension of MnO_2 (80 g) in CH_2Cl_2 (50 ml) at 0°. The mixture was stirred for 45 min at 0°, filtered through $MgSO_4$ (20 g) and the solvents were removed. To the residue in EtOH (50 ml), 0.5 g of PPTS were added at r.t., and the mixture was stirred at 50°, until no more **V** was detectable by TLC (1–2.5 h). The cold mixture was diluted with H_2O (50 ml) and AcOEt (80 ml). The aq. phase was extracted with AcOEt (2 × 50 ml), the combined org. fractions were washed with sat. brine (2 × 50 ml), dried, and the solvents were removed. The residue was chromatographed on SiO_2 (80 g) and crystallized from 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° as indicated in *Table 3*, cooled to r.t., diluted with Et_2O or AcOEt (100 ml), and poured onto ice (50 g). The aq. phase was extracted with Et_2O or AcOEt (100 ml), the combined org. fractions were washed with sat. brine (50 ml) and the solvents removed. The residue was chromatographed on SiO_2 (80 g), distilled under reduced pressure (bulb-to-bulb) or crystallized as indicated.

1.4. *Method D.* Same procedure as *Method C*, exept 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 CH_2Cl_2 (50 ml), a soln. of 33% HBr/AcOH (4 ml) in CH_2Cl_2 (5 ml) was added at 0°. The mixture was stirred for 1 h at 0°, allowed to warm up to r.t., and quenched with sat. $NaHCO_3$ soln. (30 ml), ice (50 g), and Et_2O (100 ml). The org. phase was washed with sat. brine (75 ml), dried ($MgSO_4$) and the solvents were removed. The residue was purified as described in *Method C*.

2. Acetylenic Acetals I. – 2.1. *(±)-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): 3417*w*, 2977*m*, 2868*w*, 1495*w*, 1453*w*, 1328*w*, 1136*s*, 1050*s*, 1014*s*, 699*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.6–7.5, 7.45–7.3 (2*m*, 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*, $(CH_3CH_2O)_2CH$); 2.32 (*d*, *J* = 6.2, OH); 1.3–1.15 (*m*, $(CH_3CH_2O)_2CH$). MS: 233 (2, $M^+ - H$), 189 (76), 133 (79), 115 (100), 105 (36), 103 (32), 77 (48), 55 (48). Anal. calc. for $C_{14}H_{18}O_3$ (234.30): C 71.77, H 7.74; found: C 71.64, H 7.73.

2.2. *(±)-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°/12 Torr). IR (film): 3421*w*, 2932*s*, 2871*m*, 2235*w*, 1460*w*, 1357*w*, 1328*m*, 1148*s*, 1118*m*, 1052*s*, 1011*m*. ^{1}H-NMR ($CDCl_3$, 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*, $(CH_3CH_2O)_2CH$); 1.99 (*d*, *J* = 6.6, OH); 1.8–1.65, 1.55–1.25 (2*m*, 6 aliph. H); 1.24 (*t*, *J* = 7.2, $(CH_3CH_2O)_2CH$); 0.95–0.85 (*m*, 3 aliph. H). MS: 227 (2, $M^+ - H$), 183 (33), 109 (25), 85 (47), 67 (29), 57 (100), 55 (47), 43 (51).

2.3. *(±)-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°/0.1 mbar). IR (film): 3431*w*, 2927*w*, 2856*m*, 2220*w*, 1720*w*, 1450*w*, 1327*w*, 1145*m*, 1119*m*, 1053*s*, 1011*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.31 (*d*, *J* = 1.3, H–C(1)); 4.5–4.4 (*m*, H–C(4)); 3.85–3.55 (*m*, $(CH_3CH_2O)_2CH$); 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, $M^+ - H$), 225 (95), 95 (43), 85 (99), 57 (100). Anal. calc. for $C_{16}H_{30}O_3$ (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 SiO_2 with AcOEt/hexane 1:3, 10.75 g (68%) of **13** as a pale yellow oil. IR (film): 3416*m* (br.), 2895*w*, 2231*m*, 1643*s*, 1597*s*, 1450*s*, 1315*s*, 1267*s*, 1177*m*, 1102*s*, 1023*s*, 901*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.2–8.05, 7.7–7.4 (2*m*, 5 arom. H); 4.58 (*d*, *J* = 6.4, 2 H–C(4)); 2.39 (*t*, *J* = 6.4, OH).

MS: 160 (100, $M^{+\cdot}$), 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. *(±)-4-Hydroxypent-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): 3410*m* (br.), 2985*w*, 2222*w*, 1644*s*, 1597*m*, 1450*m*, 1314*m*, 1266*s*, 1130*m*, 1082*w*, 1012*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.2–8.1, 7.7–7.45 (2*m*, 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, $M^{+\cdot}$), 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): 3380*m* (br.), 2940*w*, 2840*w*, 2240*w*, 1630*s*, 1580*m*, 1505*m*, 1420*m*, 1340*s*, 1230*s*, 1130*s*, 1005*m*, 750*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.38 (*s*, 2 arom. H); 4.57 (br. *s*, 2 H–C(4)); 3.94, 3.93 (2*s*, 3 CH_3O); 2.37 (br. *s*, OH). MS: 250 (100, $M^{+\cdot}$), 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. *(±)-4-Hydroxy-3′,4′,5′-trimethoxypent-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°. The mixture was allowed to warm up to 0° and stirred at 0° 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°. The mixture was stirred at −40° 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 × 40 ml), the combined aq. phase extracted with Et_2O (50 ml), the combined org. fractions were washed with sat. brine (2 × 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): 3460*m* (br.), 2975*w*, 2940*w*, 2215*m*, 1688*m*, 1580*s*, 1500*m*, 1420*m*, 1335*s*, 1220*s*, 1180*m*, 1130*s*, 995*m*, 750*m*. ^{1}H-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 (2*s*, 3 CH_3O); 2.31 (*d*, J = 5.6, OH); 1.61 (*d*, J = 5.6, CH_3–C(4)). MS: 264 (100, $M^{+\cdot}$), 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. *(±)-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): 3406*m* (br.), 2933*m*, 2870*m*, 2215*m*, 1676*s*, 1458*w*, 1404*w*, 1371*w*, 1235*w*, 1163*m*, 1086*w*, 1038*w*. ^{1}H-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*, 2H–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, $M^{+\cdot} - CH_3$), 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 wit 2N aq. HBr at 50° for 24 h. FC on SiO_2 with AcOEt/hexane 1:3 and bulb-to-bulb distillation (150°/0.08 mbar) afforded 540 mg (60.2%) of **18** as a colorless liquid. IR (film): 3150*w*, 3120*w*, 3057*w*, 1580*w*, 1510*m*, 1480*m*, 1449*w*, 1379*w*, 1186*w*, 1157*w*, 1056*m*, 949*m*, 883*m*, 764*s*, 669*s*, 663*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.0–7.9, 7.5–7.3 (2*m*, 5 arom. H); 7.42, 6.53 (2*d*, J = 1,9, H–C(5), H–C(4)). MS: 224, 222 (100, $M^{+\cdot}$), 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° 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° 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°/16 mbar) gave 1.55 g (81.5%) of **19** as a colorless liquid. IR (film): 3127*w*, 2923*s*, 2861*s*, 1597*w*, 1507*m*, 1461*w*, 1180*w*, 1140*m*, 1041*w*, 775*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.25, 6.34 (2*d*, 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 (3*m*, 9 aliph. H). MS: 218, 216 (49, $M^{+\cdot}$), 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° 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°/0.1 mbar) gave 2.90 g (75.7%) of **20** as a colorless liquid. IR (film): 3127*w*, 2917*s*, 2854*s*, 1597*w*, 1556*w*, 1508*w*, 1462*w*, 1347*m*, 1188*w*, 1138*m*, 1059*w*, 975*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.25, 6.34 (2*d*, 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 (3*m*, 15 aliph. H). MS: 260,258 (15, $M^{+\cdot}$), 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_2 with Et_2O/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): 2960*m*, 2927*s*, 2885*m*, 1605*m*, 1515*m*, 1470*w*, 1205*w*, 1145*w*, 995*w*, 724*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.23, 6.30 (2*d*, 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 (3*m*, 15 aliph. H). MS: 214 (14, M^+), 179 (25), 115 (100). Anal. calc. for $C_{12}H_{19}ClO$ (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_2 with Et_2O/hexane 1:5, 530 mg (95%) of **22** as a white solid. M.p. 41–42°. IR (KBr): 3112*w*, 3033*w*, 1603*w*, 1566*w*, 1513*w*, 1474*w*, 1276*w*, 1069*w*, 1019*w*, 930*m*, 909*m*, 803*w*, 764*s*, 680*s*, 585*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.7–7.6 (*m*, 2 arom. H); 7.46, 6.68 (2*d*, J = 0.8, H–C(3), H–C(5)); 7.45–7.25 (*m*, 3 arom. H). MS: 224, 222 (50, M^+), 143 (17), 115 (100). Anal. calc. for $C_{10}H_7BrO$ (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_2 with Et_2O/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): 3110*w*, 3031*w*, 2923*w*, 1604*w*, 1563*w*, 1502*w*, 1423*m*, 1441*m*, 1272*m*, 1136*w*, 1067*m*, 1013*m*, 905*s*, 793*m*, 760*s*, 687*s*, 582*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.7–7.55 (*m*, 2 arom. H); 7.46, 6.72 (2*d*, J = 0.7, H–C(3), H–C(5)); 7.45–7.25 (*m*, 3 arom. H). MS: 270 (100, M^+), 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_2 with Et_2O/hexane 1:5, 2.0 g (90.5%) of **24** as a slightly yellow oil. IR (film): 3070*w*, 3040*w*, 2930*w*, 1601*m*, 1487*m*, 1088*s*, 1026*m*, 757*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.65–7.55, 7.45–7.2 (2 *m*, 5 arom. H); 6.56 (*s*, H–C(4)); 2.34 (*s*, CH_3–C(2)). Anal. calc. for $C_{11}H_9C10$ (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_2 with Et_2O/hexane 1:3, 2.51 g (92.3%) of **25** as a pale yellow oil. IR (film): 3130*w*, 3060*w*, 2920*w*, 1597*s*, 1554*m*, 1487*s*, 1147*m*, 1075*s*, 1021*s*, 758*s*, 690*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.65–7.55, 7.4–7.2 (2 *m*, 5 arom. H); 6.59 (*s*, H–C(4)); 2.35 (*s*, CH_3–C(2)). MS: 238, 236 (100, M^+), 195, 193 (17), 157 (26), 129 (24), 105 (43), 77 (96), 51 (35), 43 (43). Anal. calc. for $C_{10}H_{15}BrO$ (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_2 with Et_2O/hexane 1:5, 2.95 g (90.5%) of **26** as a pale yellow oil. IR (film): 3120*w*, 3060*w*, 2910*w*, 1587*m*, 1551*m*, 1446*m*, 1143*m*, 1071*m*, 1014*s*, 799*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.65–7.55, 7.45–7.2 (2*m*, 5 arom. H); 6.62 (*s*, H–C(4)); 2.40 (*s*, CH_3–C(2)). MS: 284 (100, M^+), 157 (16), 128 (19), 115 (27), 105 (62), 77 (39), 51 (28), 43 (17). Anal. calc. for $C_{11}H_9IO$ (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_2 with Et_2O/hexane 1:2, 462 mg (86%) as white solid. M.p. 81–82°. IR (KBr): 3140*w*, 2930*w*, 2835*w*, 1590*m*, 1575*s*, 1500*s*, 1418*m*, 1250*s*, 1242*s*, 1132*s*, 995*m*, 945*m*, 800*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.44, 6.59 (2*s*, H–C(3), H–C(5)); 6.84 (*s*, 2 arom. H); 3.91, 3.87 (2*s*, 3 CH_3O). MS: 268 (100, M^+), 253 (83), 225 (22), 195 (20), 139 (15). Anal. calc. for $C_{13}H_{13}ClO_4$ (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_2 with Et_2O/hexane 1:1, 580 mg (93%) of **28** as white solid. M.p. 73–74°. IR (KBr): 3120*w*, 3100*w*, 2935*w*, 2830*w*, 1595*m*, 1570*m*, 1495*s*, 1420*m*, 1300*s*, 1130*s*, 1005*m*, 835*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.45, 6.63 (2*d*, J = 0.8, H–C(3), H–C(5)); 6.84 (*s*, 2 arom. H); 3.91, 3.87 (2*s*, 3 CH_3O). MS: 314, 312 (100, M^+), 299, 297 (97), 269 (19), 239 (22). Anal. calc. for $C_{13}H_{13}BrO_4$ (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_2 with Et_2O/hexane 1:1, 260 mg (80.6%) of **29** as a white solid. M.p. 101–102°. IR (KBr): 3130*w*, 2940*w*, 1595*m*, 1500*s*, 1450*m*, 1420*m*, 1340*m*, 1245*s*, 1135*s*, 1100*m*, 1010*m*, 840*m*, 790*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 6.80 (*s*, 2 arom. H); 6.51 (*s*, H–C(4)); 3.91, 3.86 (2*s*, 3 CH_3O); 2.35 (*s*, CH_3–C(2)). MS: 282 (100, M^+), 267 (88), 239 (15), 209 (15), 43 (27). Anal. calc. for $C_{14}H_{15}C10_4$ (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_2 with Et_2O/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): 3131*w*,

2988*w*, 2939*w*, 1591*m*, 1554*w*, 1499*m*, 1416*m*, 1244*m*, 1129*s*, 1065*w*, 825*w*, 707*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 6.80 (*s*, 2 arom. H); 6.54 (*s*, H–C(4)); 3.91, 3.86 (2*s*, 3 CH_3O); 2.36 (*s*, CH_3–C(2)). MS: 328, 326 (100, M^+), 311 (86), 285, 283 (18), 253 (25), 43 (50). Anal. calc. for $C_{14}H_{15}BrO_4$ (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_2 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): 3112*w*, 2948*w*, 2835*w*, 1595*m*, 1553*m*, 1498*s*, 1461*m*, 1422*m*, 1240*m*, 1131*s*, 1000*m*, 848*w*, 821*w*, 765*w*, 674*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 6.80 (*s*, 2 arom. H); 6.57 (*s*, H–C(4)); 3.91, 3.86 (2*s*, 3 CH_3O); 2.41 (*s*, CH_3–C(2)). MS: 374 (100, M^+), 359 (67), 331 (11), 219 (14), 43 (17). Anal. calc. for $C_{14}H_{15}IO_4$ (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_2 with Et_2O/hexane 1:7 and bulb-to-bulb distillation (180°/19 mbar). IR (film): 2958*m*, 2928*s*, 1614*w*, 1575*w*, 1461*w*, 1380*w*, 1225*m*, 1041*m*, 987*w*, 935*w*, 786*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.93 (*s*, H–C(4)); 2.53 (*t*, J = 7.5, 2 aliph. H); 2.23 (*s*, CH_3–C(2)); 1.7–1.5, 1.4–1.25, 0.95–0.85 (3*m*, 9 aliph. H). MS: 232, 230 (17, M^+), 175, 173 (100), 43 (29). Anal. calc. for $C_{10}H_{15}BrO$ (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_2 with Et_2O/hexane 1:4 and bulb-to-bulb distillation (185°/0.04 mbar). IR (film): 2955*s*, 2929*s*, 2858*m*, 1602*w*, 1571*m*, 1462*w*, 1380*w*, 1218*w*, 1177*w*, 1128*w*, 1087*w*, 1029*m*, 983*m*, 935*w*, 789*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 5.95 (*s*, H–C(4)); 2.54 (*t*, J = 7.5, 2 aliph. H); 2.28 (*s*, CH_3–C(2)); 1.7–1.5, 1.4–1.25, 0.95–0.85 (3*m*, 9 aliph. H). MS: 278 (30, M^+), 221 (100), 43 (21). Anal. calc. for $C_{10}H_{15}IO$ (278.13): C 43.18, H 5.44, I 45.63; found: C 43.01, H 5.51, I 45.91.

5. 4*H*-Pyran-4-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_4Cl soln. (100 ml), ice (100 g), and Et_2O (150 ml). The aq. layer was extracted with Et_2O (2 × 100 ml), the combined org. fractions were washed with sat. brine (200 ml), dried ($MgSO_4$) and the solvents removed. The residue was dissolved in CH_2Cl_2 (10 ml) and added at 0° to a mechanically stirred suspension of 133 g of MnO_2 in CH_2Cl_2 (200 ml). The mixture was stirred at 0° for 30 min, filtered through $MgSO_4$, and evaporated. The residue was chromatographed on SiO_2 (250 g) with Et_2O/hexane 1:1: 7.3 g (70.9%) of **34** as a pale yellow oil. IR (film): 3421*w* (br.), 2933*w*, 2240*w*, 2202*m*, 1640*s*, 1598*w*, 1451*w*, 1313*m*, 1268*s*, 1169*w*, 900*w*, 702*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.2–8.15, 7.65–7.55, 7.55–7.45 (3*m*, 5 arom. H); 2.71 (*s*, 2 H–C(4)); 2.17 (*s*, OH); 1.43 (*s*, CH_3–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_2 with Et_2O/hexane 1:1. M.p. 36–37°. IR (KBr): 3064*w*, 2978*w*, 1661*s*, 1599*s*, 1571*s*, 1492*w*, 1448*m*, 1367*s*, 1278*m*, 1251*m*, 1055*m*, 770*m*, 693*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.8–7.7, 7.5–7.4 (2*m*, 5 arom. H); 5.99 (*s*, H–C(3)); 2.59 (*s*, 2 H–C(5)); 1.55 (*s*, 2 CH_3–C(6)). MS: 202 (42, M^+), 187 (37), 105 (100), 77 (37), 69 (49), 56 (23). Anal. calc. for $C_{13}H_{14}O_2$ (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-2*H*-pyran were added. The mixture was heated at 50° for 48 h, cooled to r.t., and quenched with sat. $NaHCO_3$ soln. (50 ml) and Et_2O (100 ml). The aq. phase was extracted with Et_2O (2 × 50 ml), the combined org. fractions were washed with sat. brine (2 × 50 ml), dried ($MgSO_4$) and the solvents removed. The residue was chromatographed on SiO_2 (400 g) with Et_2O/hexane 1:5: 23.4 g (91%) of **36** as a colorless liquid. IR (film): 3283*m*, 2945*m*, 2874*w*, 2105*w*, 1576*w*, 1485*s*, 1447*m*, 1356*w*, 1282*m*, 1181*m*, 1119*s*, 1032*m*, 960*s*, 873*w*, 755*s*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.5–7.4, 7.35–7.2, 7.15–7.1, 7.0–6.9 (4*m*, 4 arom. H); 5.6–5.5 (*m*, OCHO); 4.05–3.8, 3.65–3.55 (2*m*, CH_2O); 3.25 (*s*, $CH{\equiv}C$); 2.2–1.5 (*m*, 6 aliph. H). MS: 202 (6, M^+), 118 (21), 85 (100), 67 (22), 57 (25), 43 (24). Anal. calc. for $C_{13}H_{14}O_2$ (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): 3344*m*, 3269*w*, 2998*w*, 2941*w*, 2185*s*, 1619*m*, 1577*s*, 1501*m*, 1453*m*, 1415*m*, 1335*s*, 1235*m*, 1161*m*, 1003*w*, 739*m*. ^{1}H-NMR ($CDCl_3$, 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_3O). MS: 312 (100, $M^{+\cdot}$), 297 (12), 281 (12), 281 (12), 269 (14), 168 (28), 143 (23), 89 (13). Anal. calc. for $C_{18}H_{16}O_5$ (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_2 (200 g) with Et_2O/hexane 1:1 and crystallization from AcOEt/hexane. M.p. > 105° (dec.). IR (KBr): 3208*m* (br.), 3055*w*, 2223*w*, 2183*s*, 1625*s*, 1590*s*, 1499*w*, 1450*m*, 1343*m*, 1325*m*, 1182*m*, 1100*w*, 981*w*, 751*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 7.95, 6.89 (2*d*, 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, $M^{+\cdot}$), 247 (47), 231 (100), 219 (31), 191 (24), 103 (27), 89 (32), 77 (32). Anal. calc. for $C_{17}H_{12}O_2$ (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)-4*H*-[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_2O. M.p. 174–175°. IR (KBr): 3070*w*, 2941*w*, 2839*w*, 1639*s*, 1603*m*, 1568*m*, 1506*m*, 1470*m*, 1419*s*, 1372*m*, 1338*m*, 1245*m*, 1127*s*, 1006*w*, 771*w*, 750*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.3–8.2, 7.75–7.65, 7.6–7.55, 7.5–7.4 (4*m*, 4 arom. H); 7.15 (*s*, 2 arom. H); 6.79 (*s*, H–C(3)); 3.97, 3.94 (2*s*, 3 CH_3O). MS: 312 (100, $M^{+\cdot}$), 297 (42), 269 (18), 121 (21). Anal. calc. for $C_{18}H_{16}O_5$ (312.32): C 69.22, H 5.16; found: C 68.99, H 5.20.

7.2. *2-Styryl-4*H*-[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): 3372*w*, 3057*w*, 3020*w*, 1652*s*, 1624*s*, 1560*m*, 1404*s*, 1392*s*, 1327*w*, 1323*w*, 1124*w*, 969*m*, 755*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 8.25–8.15 (*m*, H–C(5)); 7.75–7.3 (*m*, 8 arom. H); 7.62, 6.79 (2*d*, J = 16.1, 2 olef. H); 6.34 (*s*, H–C(3)). MS: 248 (63, $M^{+\cdot}$), 247 (100), 231 (43), 128 (62), 92 (24). Anal. calc. for $C_{17}H_{12}O_2$ (248.28): C 82.24, H 4.87; found: C 82.18, H 5.07.

REFERENCES

[1] L.I. Vereshchagin, R.I. Katkevich, *Usp. Khim.* **1969**, *38*, 1964.
[2] L.I. Vereshchagin, R.L. Bol'shedvorska, *Usp. Khim.* **1973**, *42*, 511.
[3] J. Chauvelier, *Ann. Chim. Fr.* **1966**, 1721.
[4] K. Bowden, E.A. Braude, E.R.H. Jones, *J. Chem. Soc.* **1946**, 945.
[5] W.D. Rudorf, R. Schwarz, *Tetrahedron Lett.* **1987**, 4267.
[6] W. Ried, E. König, *Liebigs Ann. Chem.* **1972**, *755*, 24.
[7] M. Karpf, *Angew. Chem.* **1986**, 98, 413; J. Huguet, M. Karpf, A.S. Dreiding, *Tetrahedron Lett.* **1983**, 4177.
[8] D. Obrecht, B. Weiss, *Helv. Chim. Acta* **1989**, *72*, 117.
[9] P. Bosshard, C.H. Eugster, *Adv. Heterocycl. Chem.* **1966**, *7*, 378; F.M. Dean; *ibid.* **1982**, 30, 167; *ibid.* **1983**, 31, 238.
[10] a) Y. Fukuyama, Y. Kawashima, T. Miwa, T. Tokorayama, *Synthesis* **1974**, 443; b) R.E. Lutz, M.G. Reese, *J. Am. Chem. Soc.* **1959**, *81*, 127; c) R.E. Larock, C.-L. Liu, *J. Org. Chem.* **1983**, *48*, 2151; d) D. Caine, W.D. Samuels, *Tetrahedron Lett.* **1980**, 4057; e) H. Reich, R.E. Olson, *J. Org. Chem.* **1987**, *52*, 2315.
[11] N. Dinh Ly, M. Schlosser, *Helv. Chim. Acta* **1977**, *60*, 2085.
[12] T.L. Gilchrist, D.P.J. Pearson, *J. Chem. Soc., Perkin Trans. 1* **1976**, 989.
[13] W.C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923.
[14] 'Reagentienanhang in Organikum', Ed. K. Schwetlick, 13th edn., VEB-Verlag, Berlin, 1974, p. 713.
[15] L.I. Vereshchagin, L.D. Gavrilov, E.I. Titova, L.G. Tikhonova, S.R. Buzilova, *Khim. Geterotsikl. Soedin* **1976**, 1471.
[16] N. Nakagawa, *J. Chem. Soc. Jpn.* **1951**, *72*, 1471.
[17] W.H. Gerwick, A. Lopez, G.D. van Duyne, J. Clardy, W. Ortiz, A. Bay, *Tetrahedron Lett.* **1986**, 1979.
[18] a) A. Gorgues, A. LeCoq, *Tetrahedron Lett.* **1979**, 4825; b) H. Esterbauer, *Monatsh. Chem.* **1967**, *98*, 1994; c) H. Esterbauer, *ibid.* **1971**, *102*, 824.
[19] L. Miginiac, *Ann. Chim. Fr.* **1961**, 1071.
[20] H.L. Gaggad, K.N. Wadokar, B.J. Ghiya, *Ind. J. Chem.* **1985**, *24B*, 1244.