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One-Pot Three-Component Synthesis of 3-Halofurans and 3-Chloro-4-iodofurans

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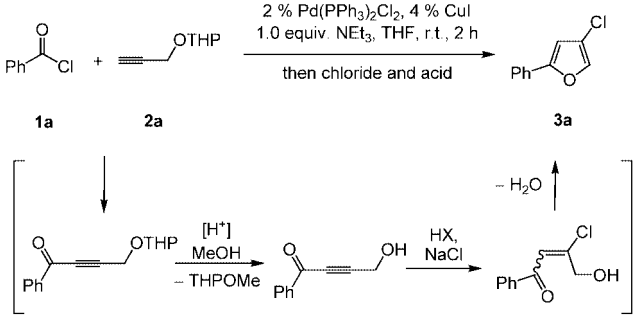
A novel sequence of Sonogashira coupling and acid-mediated nucleophilic addition to the ynone intermediate with concomitant deprotection and cyclocondensation opens a new one-pot synthetic access to 3-chloro-, 3-iodo-, and 3-chloro-4-iodo-furans in moderate to good yields.

Introduction

The furan core is a ubiquitous structural unit in numerous natural products,[1] in pharmaceuticals,[2] and even in photonic chromophores.[3] As a consequence of the highly versatile transformation potential of furans (e.g. as dienes in Diels–Alder reactions, by regioselective metallation, electrophilic substitution and addition in 2 position) they have become important synthetic building blocks. Among many furan syntheses the two major approaches to furans[4] are either based upon the construction of the furan ring starting from acyclic precursors[5] or substitution reactions on the furan core. In particular, by regiospecific substitutions halofurans are ideal starting materials for highly sophisticated derivatives since they can be applied as electrophiles in cross-coupling reactions,[6] or they can be easily transformed by halogen–metal exchange into nucleophiles for subsequent electrophilic trapping.[7] However, efficient and concise syntheses of 3-mono- and 3,4-disubstituted halofurans are still a methodological challenge.[8,9] Recently, we have communicated a novel consecutive one-pot three-component synthesis of 3-halofurans[10] as part of our program directed to develop new one-pot multi-component heterocycle syntheses based upon transition-metal-catalyzed in situ activation of alkynes by cross-coupling,[11] here, we report novel consecutive one-pot three-component syntheses of 3-halofurans and 3-chloro-4-iodofurans.

Results and Discussion

Recently, we have developed a modification[11f] of the mild, straightforward, and catalytic Sonogashira coupling of acyl chlorides and terminal alkynes to alkynones,[12] where *only one stoichiometrically necessary equivalent* of triethylamine as the hydrochloric acid scavenging base is applied in the cross-coupling step. Therefore, the reaction medium can be considered to be essentially base-free, now setting the stage for catalytic acid-catalyzed consecutive steps. Because ynones are important 1,3-dicarbonyl synthetic equivalents with an enormous potential as key intermediates in heterocycle synthesis,[13] we first scouted the possibility to convert benzoyl chloride (**1a**) and the tetrahydropyranyl propargyl ether (**2a**) under modified Sonogashira conditions, followed by the subsequent addition of various acids and chloride sources through the intermediacy of an γ-hydroxy alkynone[14] into 4-chloro-2-phenylfuran (**3a**) (Scheme 1, Table 1). Mechanistically, it is very likely that the acid not only catalyzes the deprotection of the THP ether by transacetalization, but also mediates the Michael addition of the chloride to the alkynone intermediate. Hence, the *E*-configured β-chloro hydroxy enone subsequently undergoes a cyclocondensation to furnish the chlorofuran **3a**. The *Z*-configured β-chloro hydroxy enone, which does not undergo cyclocondensation at comparable rate, is only detected in trace amounts according to TLC (as a highly polar byproduct) and GC-MS (the mass corresponds to a chloro hydroxy enone isomer).



Scheme 1. Coupling-addition-cyclocondensation sequence to the 4-chlorofuran **3a**.

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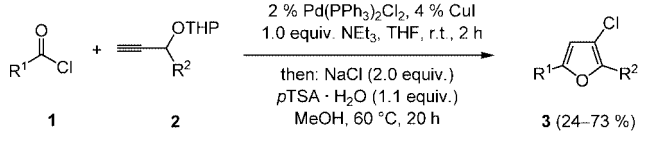
Table 1. Optimization of conditions for the coupling–addition–cyclocondensation sequence to the 4-chlorofuran **3a**.

Entry	Acid and chloride source	Solvent	Temperature, time	Yield of **3a**
1	2 equiv. of 2 M HCl	THF	60 °C, 10 h	53%
2	2 equiv. of 2 M HCl	THF	60 °C, 40 h	64%
3	2 equiv. of 2 M HCl	CH_3CN	60 °C, 40 h	0%
4	2 equiv. of 2 M HCl	toluene	60 °C, 40 h	28%
5	1.1 equiv. of *p*TSA·H_2O, 2 equiv. of NaCl	THF, CH_3OH	60 °C, 20 h	63%
6	1.1 equiv. *p*TSA·H_2O	THF, CH_3OH	60 °C, 40 h	47%

The most favorable solvent system for the addition–cyclocondensation step turns out to be THF or THF/methanol (Entries 1, 2, 5 and 6), however, heating to 60 °C for 40 h was necessary for complete conversion if aqueous HCl is used as a proton and chloride source (Entry 2). Interestingly, the reaction time can be considerably reduced if a mixture of NaCl (as chloride source) and *p*-tolylsulfonic acid (*p*TSA) is applied (Entry 5). Most elegantly and most atom-economically is the use of the acyl chloride as the only chloride donor (Entry 6), but, obviously, the concentration of chloride is relatively low, and as a consequence of the weaker nucleophilicity the yield of the 4-chlorofuran **3a** is significantly lower. Therefore, this novel sequence can be rationalized as follows. After the cross-coupling of the acyl chloride **1a** and the THP-protected propargyl alcohol **2a** the resulting THP-protected 3-hydroxy alkynone is solvolyzed under acid catalysis to furnish the γ-hydroxy alkynone that instantaneously reacts in the sense of an acid-assisted Michael addition of HCl and the subsequent cyclocondensation to conclude the three-component sequence to give the 4-chlorofuran **3a**.

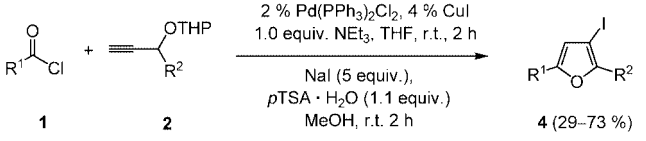
According to these optimal conditions (Entry 5) and the extension to sodium iodide as a halide source, various acyl chlorides **1** and tetrahydropyranyl propargyl ethers **2** can be successfully and efficiently transformed into 3-chlorofurans **3** (Scheme 2, Table 2) or 3-iodofurans **4** (Scheme 3, Table 3) in the sense of a one-pot coupling–addition–cyclocondensation sequence. The obtained products are oils or crystalline compounds, which have to be rapidly isolated by chromatography on neutral aluminium oxide (the column chromatography on silica gel causes red coloring), and can be stored at low temperatures (0 °C) and under nitrogen without traces of decomposition.



Scheme 2. One-pot three-component synthesis of chlorofurans **3**.

Table 2. One-pot three-component synthesis of chlorofurans **3**.

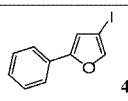
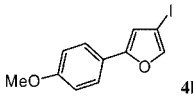
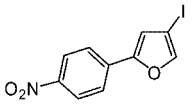
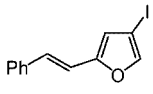
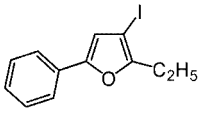
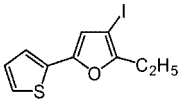
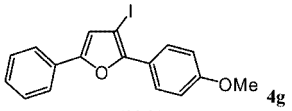
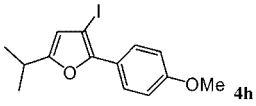
Entry	Acyl chloride **1**	Alkyne **2**	Chlorofuran **3** (yield)
1	R^1 = Ph (**1a**)	R^2 = H (**2a**)	**3a** (63 %)
2	R^1 = *p*-$MeOC_6H_4$ (**1b**)	**2a**	**3b** (71 %)
3	R^1 = *p*-$O_2NC_6H_4$ (**1c**)	**2a**	**3c** (24 %)
4	R^1 = *o*-FC_6H_4 (**1d**)	**2a**	**3d** (47 %)
5	R^1 = 1-cyclohexenyl (**1e**)	**2a**	**3e** (64 %)
6	**1a**	R^2 = Et (**2b**)	**3f** (70 %)
7	R^1 = 2-thienyl (**1f**)	R^2 = Et (**2b**)	**3g** (59 %)
8	R^1 = Ph-CH=CH (**1g**)	R^2 = Et (**2b**)	**3h** (73 %)



Scheme 3. One-pot three-component synthesis of iodofurans **4**.

The structures of the 3-halofurans **4** were unambiguously supported by spectroscopic (^1H, ^{13}C and DEPT, COSY, NOESY, HETCOR and HMBC NMR experiments, IR, UV/Vis, mass spectrometry) and combustion analyses, and they are in agreement with structural assignments of previously reported derivatives.[15] The formation of the halofuran core is unambiguously supported by the spectroscopic and analytical data. For the 2-substituted 4-halofurans **3a**–**e** and **4a**–**d** in the ^1H NMR spectra two doublets in the region of δ = 6.34–7.35 and 7.49–7.90 ppm with ^4J coupling constants of 0–1.1 Hz were assigned as 3-H and 5-H furan protons, respectively. Accordingly, for the 2,5-disubstituted 3-halofurans **3f**–**h** and **4e**–**h** the singlets at δ = 6.27–7.11 ppm can be assigned to the 4-H methine protons. Most characteristically, in the ^{13}C NMR quaternary C3-halo carbon nuclei appear between δ = 117.8 and 118.6 ppm for chlorofurans and, as a consequence of the heavy atom ef-

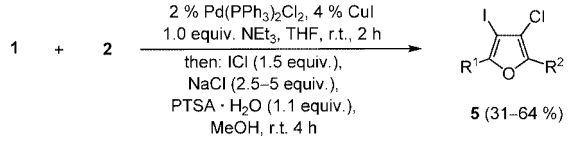
Table 3. One-pot three-component synthesis of iodofurans **4**.

Entry	Acyl chloride **1**	Alkyne **2**	3-Iodofuran **4** (yield)
1	**1a**	**2a**	 **4a** (63 %)
2	**1b**	**2a**	 **4b** (63 %)
3	**1c**	**2b**	 **4c** (40 %)
4	**1g**	**2b**	 **4d** (61 %)
5	**1a**	**2b**	 **4e** (72 %)
6	**1f**	**2b**	 **4f** (49 %)
7	**1a**	$R^2 = p$-$MeOC_6H_4$ (**2c**)	 **4g** (39 %)
8	$R^1 = i$Pr (**1h**)	**2c**	 **4h** (29 %)

fect,[16] between δ = 60.2 and 67.1 ppm for iodofurans, respectively. The resonances of β-methine signals are found at δ = 105.2–116.8 ppm, whereas the resonances of α-methine signals are detected at δ 137.8–148.4 ppm.

Methodologically, this one-pot three-component coupling–addition–cyclocondensation synthesis of 3-halofurans proceeds in moderate to good yields for acyl chlorides bearing electron-rich (Table 1 and Table 2, Entries 2), electron-withdrawing (Table 1 and Table 2, Entries 3) and electron-neutral substituents (Table 1, Entries 1, 6, 2, Table 2 and Table 1, Table 5, Table 6, Table 7). For the nitro-substituted acyl chloride **1c**, however, the obtained yield is somewhat lower (Table 1 and Table 2, Entries 3). Alkenyl (**1e** and **1g**) and heterocyclic acyl chlorides (**1f**) react smoothly to furnish the desired halofurans. Both unsubstituted (**2a**) and substituted (**2b**, **2c**) THP-protected propargylic alcohols can be involved in this sequence. Applying sodium iodide as a halide source leads to even milder reaction conditions and shorter reaction times, now furnishing extremely valuable 3-iodofurans. Therefore, due to the acid sensitivity of iodofurans, this methodology has significant advantages over existing protocols using HI as an acid.[14] It is worth to mention that the deprotection step of the THP-protected propargylic alcohols and immediate cyclization to the desired products has to be performed in 2 h, as a prolongation of the reaction time leads to a significant decrease in yields, which can be explained by the high acid sensitivity of β-iodofurans. Additionally, the number of isolation steps in this sequence is reduced to a single one and offers a high degree of molecular diversity. In attempts to extend this strategy to bromofurans always a mixture of bromo- and chlorofurans was obtained. However, because iodofurans are more reactive in cross-coupling reactions than the corresponding bromo derivatives, the possibility to apply acid bromides for the synthesis of β-bromofurans was not further considered.

Furthermore, the concept of a sequential nucleophilic addition in acidic medium was probed by the conversion of the ynone intermediates with iodine monochloride[17] and subsequent cyclization[18] into chloro(iodo)furans in a one-pot fashion. Therefore, upon reacting the acyl chlorides **1** and the tetrahydropyranyl propargyl ethers **2** in THF at room temperature – in the presence of one equiv. of triethylamine and catalytic amounts of $Pd(Ph_3P)_2Cl_2$ and CuI – for 2 h, and after subsequent addition of 2.5–5 equiv. of NaCl, 1.5 equiv. of iodine monochloride, and 1.1 equiv. of *p*TSA, after 4 h of stirring at room temperature, the substituted 3-chloro-4-iodofurans **5** were obtained in moderate to decent yields (Scheme 4, Table 4).



Scheme 4. One-pot three-component synthesis of chloro-iodofurans **5**..

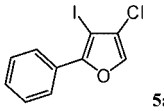
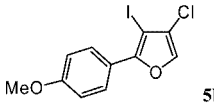
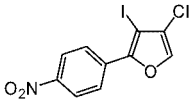
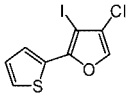
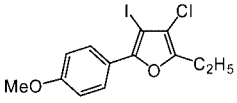
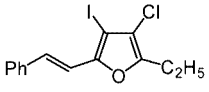
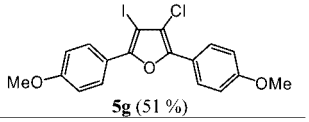
The obtained products **5** are oils or crystalline compounds, which have to be rapidly isolated on neutral aluminium oxide (the column chromatography on silica gel causes red coloring), and can be stored at low temperatures (0 °C) under nitrogen.

The structures of the 3-chloro-4-iodofurans **5** were unambiguously assigned by ^{1}H NMR and ^{13}C NMR spectra and the regiochemistry was unequivocally corroborated by an X-ray structure analysis of the chloro(iodo)furan **5c** (Figure 1).[19]

In the ^{1}H NMR spectra of the monosubstituted 4-chloro-3-iodofurans **5a**–**d** the α-methine protons give rise to distinct singlets at δ = 7.56–8.12 ppm. In the ^{13}C NMR spectra the indicative quaternary C3–Cl and C4–I carbon nuclei appear between δ = 116.9–123.5 ppm and δ = 66.2–72.2 ppm, respectively.

Amazingly, dihalofurans with different halides in 3 and 4 positions are hitherto unknown to the best of our knowledge. Interestingly, no electrophilic addition to the double bond as a competing side reaction can be detected (Entry 6), and only the desired product **5f** was isolated. Although only few acyl chlorides were tested in this study, the usual range of (hetero)aromatic and alkenyl acyl chlorides should be applicable without any problem. Compound **5g** was synthesized in 51% with 11% of 3,4-diiodo-2,5-bis(4-methoxyphenyl)furan, if the reaction mixture was stirred after

Table 4. One-pot synthesis of chloro-iodofurans **5**.

Entry	Acyl chloride **1**	Alkyne **2**	Chloro-iodofuran **5** (yield)
1	**1a**	**2a**	 **5a** (52 %)
2	**1b**	**2a**	 **5b** (42 %)
3	**1c**	**2a**	 **5c** (31 %)
4	**1f**	**2a**	 **5d** (31 %)
5	**1b**	**2b**	 **5e** (64 %)
6	**1g**	**2b**	 **5f** (57 %)
7	**1b**	**2c**	 **5g** (51 %)

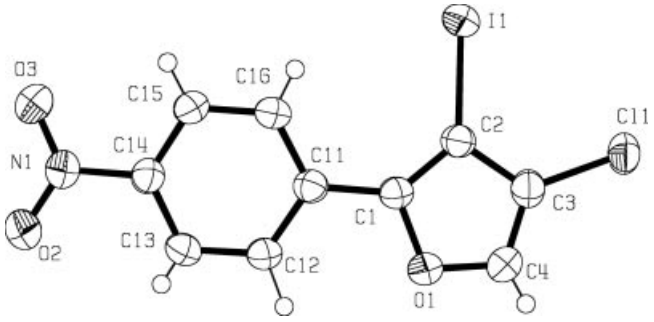
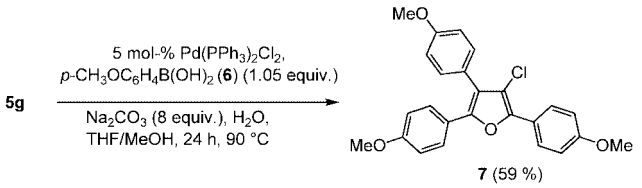


Figure 1. Molecular structure of 4-chloro-3-iodo-2-(4-nitrophenyl) furan (**5c**). Selected bond lengths [Å]: C(1)–C(11): 1.454(5), C(1)–C(2): 1.369(4), C(2)–C(3): 1.429(5), C(3)–C(4): 1.340(5), O(1)–C(4): 1.346(4), C(1)–O(1): 1.376(4), C(2)–I(1): 2.055(3), C(3)–Cl(1): 1.735(4).

addition of ICl and NaCl for 2 h before the *p*TSA·H_2O and methanol were added. This result emphasizes the importance of order and sequence of addition of all reagents.

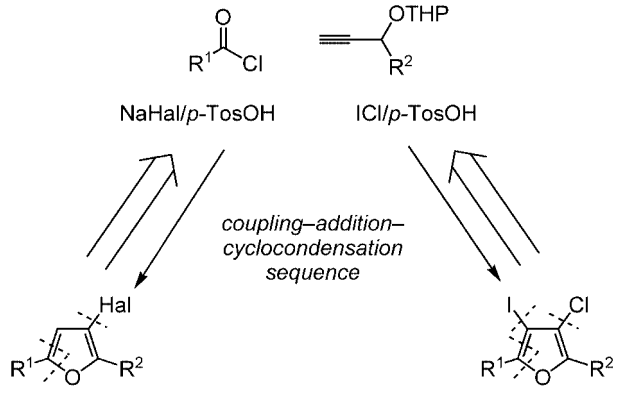
Dihalofurans **5** can be valuable building blocks for the synthesis of highly substituted furans, as illustrated by the Suzuki coupling of the chloro(iodo)furan **5g** with the boronic acid **6** furnishing the trisubstituted chlorofuran **7** in 59% yield (Scheme 5). As expected, the coupling selectively occurs at the carbon–iodine bond.



Scheme 5. Synthesis of a trisubstituted chlorofuran **7**.

Conclusions

In conclusion, we have developed a novel consecutive three-component coupling–addition–cyclocondensation synthesis of 3-halofurans and 3-chloro-4-iodofurans. Based upon a modification of the Sonogashira coupling of acyl chlorides and alkynes, the reaction medium is essentially base free after the cross-coupling event and sets the stage for Michael additions in acidic media. The subsequent acid-catalyzed cyclocondensation gives rise to a one-pot multi-component access to synthetically valuable 3-halofurans and 3-chloro-4-iodofurans (Scheme 6).



Scheme 6. Retrosynthetic analysis of substituted 3-halofurans and 3-chloro-4-iodofurans.

With this facile multi-component access to 3-halofurans and 3-chloro-4-iodofurans in hand, the stage now is set for sequential catalytic transformations[20] for the synthesis of substituted furan derivatives in a one-pot fashion.[10] Studies addressing the scope and limitation of coupling–addition–cyclocondensation–coupling sequences and related sequential transformations to enhance molecular diversity are currently under investigation.

Experimental Section

All reactions involving water-sensitive compounds were carried out in oven-dried Schlenk glassware under nitrogen unless stated otherwise. Reagents, catalysts and ligands were purchased reagent grade and used without further purification. Solvents were dried and distilled according to standard procedures.[21] THP-protected alcohols **2** were synthesized according to literature procedures.[22] Column chromatography: silica gel 60, mesh 70–230 or aluminium oxide 90 active neutral (mesh 70–230) Merck. TLC: silica gel plates. Melting points: uncorrected values. ^{1}H-, ^{13}C-, DEPT-, NOESY-, COSY-, HMQC-, and HMBC spectra were recorded with Bruker ARX 250, Bruker DRX 300, Varian VXR 400S or Bruker DRX 500 spec-

trometers by using [D$_6$]acetone, CD_2Cl_2, or [D$_6$]DMSO as solvents unless otherwise stated. The assignments of quaternary C, CH, CH_2 and CH_3 were made on the basis of DEPT spectra. IR spectra were obtained for thin films on KBr plates with a Bruker Vector 22 FT-IR spectrophotometer. UV/Vis spectra were recorded with Hewlett–Packard HP8452 A spectrometer. Mass spectra were recorded with JEOL JMS-700 und Finnigan TSQ 700 spectrometers. The melting points (uncorrected) were measured with Reichert–Jung Thermovar and Büchi Melting Point B-540 apparatus. Elemental analyses were carried out in the microanalytical laboratory of the Organisch-Chemisches Institut der Universität Heidelberg.

X-ray Structure Determination of Compound 5c: A suitable crystal was mounted on a Hampton Research Cryo Loop and transferred to a Bruker Smart CCD 1 K diffractometer. The structure was solved by direct methods and refined anisotropically on F^2 (programs SHELXTL V6.12 and SADABS V2.03 for absorption correction; G. M. Sheldrick, University of Göttingen, and Bruker Analytical X-ray-Division, Madison, Wisconsin 2001). Hydrogen atoms were found from differential Fourier synthesis and refined isotropically. The data of the X-ray structure analysis of **5c** are summarized in Table 5.

Table 5. Crystal data and structure refinements for **5c**.

Compound	**5c**
Empirical formula	$C_{10}H_5ClINO_3$
Formula weight	349.50
Temperature [K]	200(2) K
Wavelength [Å]	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/c$
Z	4
Unit cell dimensions	a = 7.0636(7) Å, α = 90.0° b = 10.335(1) Å, β = 92.961(2)° c = 14.921(1) Å, γ = 90.0°
Volume [Å]^3	1087.8(2)
Density (calculated) [g/cm^3]	2.134
Absorption coefficient [mm^{-1}]	3.178
Crystal size [mm]	0.28 × 0.18 × 0.09
Theta range for data collection [°]	2.7 to 28.3
Index ranges	$-9 \le h \le 9$ $-13 \le k \le 13$ $-19 \le l \le 19$
Reflections collected	10899
Independent reflections	2711 [R(int) = 0.0228]
Observed reflections	2588 [$I > 2\sigma(I)$]
Absorption correction	semi-empirical from equivalents
Max. and min. transmission	0.76 and 0.47
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	2711/0/165
Goodness-of-fit on F^2	1.20
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.035, wR_2 = 0.085
Largest diff. peak and hole [e•Å^{-3}]	1.22 and –0.30

General Procedure for the Three-Component Synthesis of Chlorofurans 3: In a screw-cap pressure vessel $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol) and CuI (7 mg, 0.04 mmol) were dissolved in 5 mL of degassed THF. Then acyl chloride **1** (1.00 mmol), THP-protected propargyl alcohol **2** (1.00 mmol), as well as triethylamine (0.14 mL, 1.00 mmol) were successively added to the solution (for experimental details see Table 6). The reaction mixture was stirred for 2 h at room temperature until the conversion was complete (monitored by TLC). Then sodium chloride (117 mg, 2.00 mmol), *p*-toluenesulfonic acid monohydrate (209 mg, 1.10 mmol) and 3 mL of methanol were added, and the reaction mixture was heated at 60 °C for 20 h. After complete conversion of the ynone to the furan (TLC), the reaction mixture was diluted with a saturated solution of $NaHCO_3$ (10 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic layers were dried with sodium sulfate and the solvents evaporated in vacuo. The residue was chromatographed on the neutral aluminium oxide (hexane/ethyl acetate) to give the analytically pure 3(4)-chlorofurans **3** as oils or solids (crystallization from hexane).

4-Chloro-2-phenylfuran (3a): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3a** was obtained as a colorless solid (sublimes under high vacuum), R_f = 0.75, m.p. 53–54 °C. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 6.68 (d, J = 0.7 Hz, 1 H), 7.24–7.34 (m, 1 H), 7.37–7.44 (m, 2 H), 7.49 (d, J = 0.7 Hz, 1 H), 7.61–7.65 (m, 2 H) ppm.^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 106.8 (CH), 117.8 (C_{quat}), 124.2 (CH), 128.6 (CH), 129.2 (CH), 130.3 (C_{quat}), 138.5 (CH), 154.7 (C_{quat}) ppm. MS (EI +Q1): m/z (%) = 180 (33) [^{37}Cl – M$^+$], 178 (100) [^{35}Cl – M$^+$], 149 (29) [^{35}Cl – M$^+$ – CHO], 115 (57) [M$^+$ – COCl]. IR (KBr): $\tilde{\nu}$ 3143 cm^{-1}, 1569, 1518 1445, 1355, 1282, 1205, 1121, 1071, 1014, 941, 908, 804, 764, 689, 588. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 282 nm (19700), 298 (1000). $C_{10}H_7ClO$ (178.6): calcd. C 67.24, H 3.95; found C 67.52, H 4.44.

4-Chloro-2-(4-methoxyphenyl)furan (3b): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3b** was obtained as a colorless solid (sublimes under high vacuum), R_f = 0.60, m.p. 82–83 °C. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 3.81 (s, 3 H), 6.52 (d, J = 1.1 Hz, 1 H), 6.92 (d, J = 8.8 Hz, 2 H), 7.43 (d, J = 1.1 Hz, 1 H), 7.55 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 55.7 (CH_3), 105.2 (CH), 114.6 (CH), 117.7 (C_{quat}), 123.2 (C_{quat}), 125.7 (CH), 137.8 (CH), 154.8 (C_{quat}), 160.2 (C_{quat}) ppm. MS (EI +Q1): m/z (%) = 210 (33) [^{37}Cl – M], 208 (100) [^{35}Cl – M$^+$], 195 (17) [^{37}Cl – M$^+$ – CH_3], 193 (61) [^{35}Cl – M$^+$ – CH_3], 179 (11) [^{35}Cl – M$^+$ – CHO], 145 (49) [M$^+$ – COCl]. IR (KBr): $\tilde{\nu}$ 1614 cm^{-1}, 1526, 1496, 1296, 1279, 1252, 1126, 1035, 909, 835, 794, 592. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 284 nm (23800), 306 (11500). $C_{11}H_9ClO_2$ (208.7): calcd. C 63.32, H 4.35, Cl 16.99; found C 63.34, H 4.38, Cl 17.01.

4-Chloro-2-(4-nitrophenyl)furan (3c): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate,

Table 6. Experimental details of the synthesis of chlorofurans **3**.

Entry	Acyl chloride **1**	Alkyne **2**	Chlorofuran **3** (yield)
1	141 mg (1.00 mmol) of **1a**	141 mg (1.00 mmol) of **2a**	113 mg (63%) of **3a**
2	171 mg (1.00 mmol) of **1b**	141 mg (1.00 mmol) of **2a**	138 mg (71%) of **3b**
3	186 mg (1.00 mmol) of **1c**	141 mg (1.00 mmol) of **2a**	56 mg (24%) of **3c**
4	159 mg (1.00 mmol) of **1d**	141 mg (1.00 mmol) of **2a**	92 mg (47%) of **3d**
5	145 mg (1.00 mmol) of **1e**	141 mg (1.00 mmol) of **2a**	117 mg (64%) of **3e**
6	141 mg (1.00 mmol) of **1a**	168 mg (1.00 mmol) of **2b**	145 mg (70%) of **3f**
7	147 mg (1.00 mmol) of **1f**	168 mg (1.00 mmol) of **2b**	125 mg (59%) of **3g**
8	167 mg (1.00 mmol) of **1g**	168 mg (1.00 mmol) of **2b**	170 mg (73%) of **3h**

4:1), **3c** was obtained as a yellow solid (sublimes under high vacuum), R_f = 0.78, m.p. 128–130 °C. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 6.89 (d, J = 0.7 Hz, 1 H), 7.59 (d, J = 0.7 Hz, 1 H), 7.77 (d, J = 8.8 Hz, 2 H), 8.24 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 110.3 (CH), 118.6 (C_{quat}), 124.6 (CH), 124.7 (CH), 135.8 (C_{quat}), 140.6 (CH), 147.5 (C_{quat}), 152.4 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 225 (33) [^{37}Cl – M$^+$], 223 (100) [^{35}Cl – M$^+$], 100), 195 (9) [^{37}Cl – M$^+$ – NO], 193 (20) [^{35}Cl – M$^+$ – NO]. IR (KBr): $\tilde{\nu}$ 1602 cm^{-1}, 1577, 1511, 1339, 1110, 943, 910, 853, 801, 586. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 242 nm (10500), 346 (18800). $C_{10}H_6ClNO_3$ (223.6): calcd. C 53.71, H 2.70, N 6.26, Cl 15.85; found C 53.75, H 2.86, N 6.27, Cl 15.91.

4-Chloro-2-(2-fluorophenyl)furan (3d): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3d** was obtained as colorless crystals, R_f = 0.66, m.p. 38–39 °C. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 6.83 (d, J = 3.8 Hz, 1 H), 7.10–7.35 (m, 3 H), 7.52 (s, 1 H), 7.78 (dt, J = 7.5 Hz, J = 1.9 Hz, 1 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 111.6 (d, J = 11.9 Hz, CH), 116.4 (d, J = 21.5 Hz, CH), 118.0 (C_{quat}), 118.5 (d, J = 11.9 Hz, C_{quat}), 124.9 (d, J = 3.4 Hz, CH), 126.3 (d, J = 2.8 Hz, CH), 129.8 (d, J = 8.5 Hz, CH), 138.5 (d, J = 1.1 Hz, CH), 148.7 (C_{quat}), 159.0 (d, J = 251.0 Hz, C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 199 (33) [^{37}Cl – M$^+$], 196 (100) [^{35}Cl – M$^+$], 169 (12) [^{37}Cl – M$^+$ – CHO], 167 (37) [^{35}Cl – M$^+$ – CHO], 133 (90) [M$^+$ – COCl]. IR (KBr): $\tilde{\nu}$ 3150 cm^{-1}, 3071, 2920, 1590, 1519, 1487, 1354, 1264, 1206, 1128, 1104, 1036, 1014, 943, 910, 819, 760, 590. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 268 nm (22700), 278 (23900), 290 (19900), 298 (16500), 330 (4600). HRMS calcd. for $C_{10}H_6{}^{37}ClFO$: 198.0062; found 198.0024. HRMS calcd. for $C_{10}H_6{}^{35}ClFO$: 196.0091; found 196.0085.

4-Chloro-2-(cyclohex-1-enyl)furan (3e): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3e** was obtained as a yellow oil. R_f = 0.77. ^{1}H NMR ([D$_6$]-acetone, 300 MHz): δ 1.58–1.76 (m, 4 H), 2.14–2.28 (m, 4 H), 6.27–6.31 (m, 1 H), 6.34 (s, 1 H), 7.58 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]-acetone, 75 MHz): δ = 22.7 (CH_2), 22.9 (CH_2), 25.2 (CH_2), 25.7 (CH_2), 105.8 (CH), 117.3 (C_{quat}), 124.6 (CH), 127.6 (C_{quat}), 138.3 (CH), 156.7 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 184 (32) [^{37}Cl – M$^+$], 182 (100) [^{35}Cl – M$^+$], 169 (10) [^{37}Cl – M$^+$ – CH$_3$], 167 (23) [^{35}Cl – M$^+$ – CH$_3$], 156 (13) [^{37}Cl – M$^+$ – C$_2$H$_4$], 154 (45) [^{35}Cl – M$^+$ – C$_2$H$_4$], 147 (45) [M$^+$ – Cl]. IR (KBr): $\tilde{\nu}$ 2932 cm^{-1}, 2860, 2662, 1778, 1720, 1569, 1448, 1338, 1252, 1120, 942, 786, 737, 589. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 270 nm (7300), 284 (500). HRMS calcd. for $C_{10}H_{11}{}^{37}ClO$: 184.0469; found 184.0463. HRMS calcd. for $C_{10}H_{11}{}^{35}ClO$: 182.0498; found 182.0501.

3-Chloro-2-ethyl-5-phenylfuran (3f): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3f** was obtained as a yellow oil, R_f = 0.87. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 1.29 (t, J = 7.6 Hz, 3 H), 2.74 (q, J = 7.6 Hz, 2 H), 6.60 (s, 1 H), 7.24–7.32 (m, 1 H), 7.35–7.42 (m, 2 H), 7.58–7.64 (m, 2 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 12.4 (CH_3), 19.5 (CH_2), 107.0 (CH), 112.2 (C_{quat}), 123.8 (CH), 128.0 (CH), 129.1 (CH), 130.7 (C_{quat}), 151.7 (C_{quat}), 152.5 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 208 (16) [^{37}Cl – M$^+$], 206 (44) [^{35}Cl – M$^+$], 193 (33) [^{37}Cl – M$^+$ – CH$_3$], 191 (100) [^{37}Cl – M$^+$ – CH$_3$]. IR (neat): $\tilde{\nu}$ 1597 cm^{-1}, 1556, 1488, 1449, 1290, 1099, 1039, 926, 796, 757, 689. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 292 nm (19000), 308 (11470). HRMS calcd. for $C_{12}H_{11}{}^{37}ClO$: 208.0469; found 208.0462. HRMS calcd. for $C_{12}H_{11}{}^{35}ClO$: 206.0498; found 206.0479.

3-Chloro-2-ethyl-5-(thiophen-2-yl)furan (3g): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3g** was obtained as a yellow oil, R_f = 0.72. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 1.25 (t, J = 7.6 Hz, 3 H), 2.69 (q, J = 7.6 Hz, 2 H), 6.44 (s, 1 H), 7.03 (dd, J = 5.1 Hz, J = 3.7 Hz, 1 H), 7.22 (dd, J = 3.7 Hz, J = 1.1 Hz, 1 H), 7.25 (dd, J = 5.1 Hz, J = 1.1 Hz, 1 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 12.3 (CH_3), 19.4 (CH_2), 106.7 (CH), 112.0 (C_{quat}), 123.1 (CH), 124.8 (CH), 128.1 (CH), 133.4 (C_{quat}), 147.4 (C_{quat}), 152.1 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 214 (23) [^{37}Cl – M$^+$], 212 (69) [^{35}Cl – M$^+$], 199 (33) [^{37}Cl – M$^+$ – CH$_3$], 197 (100) [^{35}Cl – M$^+$ – CH$_3$]. IR (neat): $\tilde{\nu}$ 1614 cm^{-1}, 1426, 1095, 1025, 992, 848, 786, 695. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 244 nm (4200), 310 (14800), 330 (7400). HRMS calcd. for $C_{10}H_9{}^{37}ClOS$: 214.0033; found 214.0005. HRMS calcd. for $C_{10}H_9{}^{35}ClOS$: 212.0063; found 212.0036.

3-Chloro-2-ethyl-5-styrylfuran (3h): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **3h** was obtained as a yellow oil, R_f = 0.70. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 1.29 (t, J = 7.6 Hz, 3 H), 2.69 (q, J = 7.6 Hz, 2 H), 6.29 (s, 1 H), 6.79 (d, J = 16.5 Hz, 1 H), 6.99 (d, J = 16.5 Hz, 1 H), 7.21–7.27 (m, 1 H), 7.30–7.38 (m, 2 H), 7.42–7.48 (m, 2 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 12.3 (CH_3), 19.5 (CH_2), 110.2 (CH), 112.1 (C_{quat}), 116.2 (CH), 126.7 (CH), 127.4 (CH), 128.1 (CH), 129.1 (CH), 137.1 (C_{quat}), 151.0 (C_{quat}), 152.6 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 234 (28) [^{37}Cl – M$^+$], 232 (83) [^{35}Cl – M$^+$], 219 (35) [^{37}Cl – M$^+$ – CH$_3$], 217 (100) [^{35}Cl – M$^+$ – CH$_3$]. IR (neat): $\tilde{\nu}$ 2976 cm^{-1}, 2938, 1597, 1494, 1447, 1280, 1119, 1028, 955, 787, 748, 692, 579. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 314 nm (13700), 328 (13000), 346 (18600). HRMS calcd. for $C_{14}H_{13}{}^{37}ClO$: 234.0625; found 234.0617. HRMS calcd. for $C_{14}H_{13}{}^{35}ClO$: 232.0655; found 232.0664.

General Procedure for the Three-Component Synthesis of Iodofurans 4: In a screw-cap pressure vessel $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol) and CuI (7 mg, 0.04 mmol) were dissolved in 5 mL of degassed THF. Then the acyl chloride **1** (1.00 mmol), THP-protected propargyl alcohol **2** (1.00 mmol), as well as triethylamine (0.14 mL, 1.00 mmol) were successively added to the solution (for experimental details see Table 7). The reaction mixture was stirred for 2 h at room temperature until the conversion was complete (monitored by TLC). Then, sodium iodide (750 mg, 5.00 mmol), *p*-toluenesulfonic acid monohydrate (209 mg, 1.10 mmol) and 3 mL of methanol were

Table 7. Experimental details of the synthesis of iodofuran **4**.

Entry	Acyl chloride **1**	Alkyne **2**	Iodofuran **4** (yield)
1	141 mg (1.00 mmol) of **1a**	141 mg (1.00 mmol) of **2a**	170 mg (63%) of **4a**
2	171 mg (1.00 mmol) of **1b**	141 mg (1.00 mmol) of **2a**	190 mg (63%) of **4b**
3	186 mg (1.00 mmol) of **1c**	141 mg (1.00 mmol) of **2b**	128 mg (40%) of **4c**
4	167 mg (1.00 mmol) of **1g**	141 mg (1.00 mmol) of **2b**	180 mg (61%) of **4d**
5	141 mg (1.00 mmol) of **1a**	168 mg (1.00 mmol) of **2b**	215 mg (72%) of **4e**
6	147 mg (1.00 mmol) of **1f**	168 mg (1.00 mmol) of **2b**	150 mg (49%) of **4f**
7	141 mg (1.00 mmol) of **1a**	247 mg (1.00 mmol) of **2c**	147 mg (39%) of **4g**
8	107 mg (1.00 mmol) of **1h**	247 mg (1.00 mmol) of **2c**	101 mg (29%) of **4h**

added, and the reaction mixture was stirred at room temp. for 2 h. After complete conversion of ynone to furan (TLC), the reaction mixture was diluted with a saturated solution of $NaHCO_3$ (10 mL) and Na_2SO_3 (10 mL), and extracted with dichloromethane (5 × 20 mL). The combined organic layers were dried with sodium sulfate and the solvents evaporated in vacuo. The residue was chromatographed on the neutral aluminium oxide (hexane/ethyl acetate) to give the analytically pure 3(4)-iodofurans **4** as oils or solids (crystallization from hexane).

4-Iodo-2-phenylfuran (4a): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4a** was obtained as a colorless solid, R_f = 0.75, m.p. 64 °C (ref.[14] 64–65 °C). ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 7.02 (d, J = 0.7 Hz, 1 H), 7.28–7.37 (m, 1 H), 7.40–7.48 (m, 2 H), 7.70–7.74 (m, 2 H), 7.75 (d, ^4J = 0.7 Hz, 1 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 66.5 (C_{quat}), 112.9 (CH), 124.5 (CH), 128.9 (CH), 129.6 (CH), 130.4 (C_{quat}), 146.4 (CH), 156.2 (C_{quat}) ppm.

4-Iodo-2-(4-methoxyphenyl)furan (4b): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4b** was obtained as a colorless solid, R_f = 0.60, m.p. 84–85 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 3.83 (s, 3 H), 6.84 (s, 1 H), 6.99 (d, J = 8.8 Hz, 2 H), 7.65 (d, J = 8.8 Hz, 2 H), 7.67 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 55.7 (CH_3), 66.5 (C_{quat}), 111.3 (CH), 115.2 (CH), 123.4 (C_{quat}), 126.2 (CH), 145.7 (CH), 156.6 (C_{quat}), 160.7 (C_{quat}) ppm. MS (EI +Q1): m/z (%) = 300 (100) [M$^+$], 285 (12) [M$^+$ – CH_3], 173 (20) [M$^+$ – I], 145 (25) [M$^+$ – COI]. IR (KBr): $\tilde{\nu}$ 3107 cm^{-1}, 2958, 1612, 1513, 1485, 1291, 1255, 1181, 1103, 1036, 910, 833, 795, 588. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 288 nm (27200), 306 (15700). $C_{11}H_9IO_2$ (300.1): calcd. C 44.03, H 3.02; found C 44.42, H 3.24.

4-Iodo-2-(4-nitrophenyl)furan (4c): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 4:1), **4c** was obtained as yellow crystals, R_f = 0.78, m.p. 160 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 7.35 (s, 1 H), 7.90 (d, ^4J = 0.7 Hz, 1 H), 7.97 (d, J = 9.2 Hz, 2 H), 8.31 (d, J = 9.2 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 67.1 (C_{quat}), 116.8 (CH), 125.0 (CH), 125.2 (CH), 135.9 (C_{quat}), 147.8 (C_{quat}), 148.4 (CH), 154.0 (C_{quat}) ppm. MS (EI+): m/z (%) = 315 (100) [M$^+$], 285 (100) [M$^+$ – NO]. IR (KBr): $\tilde{\nu}$ 3135 cm^{-1}, 1600, 1569, 1514, 1336, 1279, 1143, 1111, 1098, 1023, 913, 854, 827, 816, 773, 752, 692, 587, 515. UV/Vis (CH_2Cl_2): λ_{max} = 244 nm (9200), 350 (18000). $C_{10}H_6INO_3$ (315.1): calcd. C 38.12, H 1.92, N 4.45; found C 38.22, H 2.09, N 4.38.

3-Iodo-2-styrylfuran (4d): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4d** was obtained as a colorless solid, R_f = 0.73, m.p. 79 °C. ^{1}H NMR ([D$_6$]-acetone, 300 MHz): δ = 6.65 (s, 1 H), 7.05 (d, J = 16.5 Hz, 1 H), 7.12 (d, J = 16.5 Hz, 1 H), 7.24–7.31 (m, 1 H), 7.33–7.41 (m, 2 H), 7.54–7.59 (m, 2 H) 7.68 (s, 1 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 66.3 (C_{quat}), 115.8 (CH), 116.2 (CH), 127.1 (CH), 127.3 (CH), 128.7 (CH), 129.3 (CH), 129.5 (CH), 137.4 (C_{quat}), 146.3 (CH), 155.7 (C_{quat}) ppm. MS (EI +Q1): m/z (%) = 296 (100) [M$^+$], 169 (22) [M$^+$ – I], 141 (70) [M$^+$ – COI]. IR (KBr): $\tilde{\nu}$ 3140 cm^{-1}, 3125, 3083, 3059, 3036, 1630, 1446, 1247, 957, 928, 911, 799, 747, 692, 586. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 310 nm (27900), 322 (33000), 336 (22900). $C_{12}H_9IO$ (296.1): calcd. C 48.68, H 3.06; found C 48.93, H 3.23.

2-Ethyl-3-iodo-5-phenylfuran (4e): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4e** was obtained as a light yellow oil, R_f = 0.87. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 1.26 (t, ^3J = 7.7 Hz, 3 H), 2.76 (q, ^4J = 7.7 Hz, 2 H), 6.89 (s, 1 H), 7.26–7.32 (m, 1 H), 7.38–7.45 (m, 2 H), 7.66–7.71 (m, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 12.8 (CH_3), 21.6 (CH_2), 63.9 (C_{quat}), 113.6 (CH), 124.2 (CH), 128.5 (CH), 129.7 (CH), 131.0 (C_{quat}), 154.4 (C_{quat}), 158.1 (C_{quat}) ppm. MS (EI+): m/z (%) = 298 (94) [M$^+$], 283 (100) [M$^+$ – CH_3], 105 (22) [$C_6H_5CO^+$], 77 (13) [$C_6H_5^+$]. IR (KBr): $\tilde{\nu}$ 2973 cm^{-1}, 1550, 1487, 1444, 1281, 1142, 1065, 1008, 754, 686. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 294 nm (15300), 308 (10400). HRMS calcd. for $C_{12}H_{11}IO$: 297.9855; found 297.9861.

2-Ethyl-3-iodo-5-(thiophen-2-yl)furan (4f): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4f** was obtained as a light yellow oil, R_f = 0.72. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 1.23 (t, ^3J = 7.5 Hz, 3 H), 2.73 (q, ^3J = 7.5 Hz, 2 H), 6.70 (s, 1 H), 7.09 (dd, J = 3.5, 5.0 Hz, 1 H), 7.33 (dd, J = 1.1, 3.7 Hz, 1 H), 7.44 (dd, J = 1.1, 5.1 Hz, 1 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 12.8 (CH_3), 21.6 (CH_2), 63.7 (C_{quat}), 113.2 (CH), 123.9 (CH), 125.7 (CH), 128.7 (CH), 133.4 (C_{quat}), 150.2 (C_{quat}), 157.7 (C_{quat}) ppm. MS (EI+): m/z (%) = 304 (92) [M$^+$], 289 (100) [M$^+$ – CH_3], 177 (2) [M$^+$ – I], 111 (25) [$C_4H_3SCO^+$]. IR (KBr): $\tilde{\nu}$ 3117 cm^{-1}, 2973, 1426, 1131, 1063, 1016, 1007, 1001, 988, 950, 847, 824, 791, 696. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 302 nm (15200), 312 (16200), 330 (9200). HRMS calcd. for $C_{10}H_9IOS$: 303.9419; found 303.9412.

3-Iodo-2-(4-methoxyphenyl)-5-phenylfuran (4g): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4g** was obtained as colorless crystals, R_f = 0.50, m.p. 116 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 3.87 (s, 3 H), 7.08 (d, J = 8.8 Hz, 2 H), 7.11 (s, 1 H), 7.30–7.37 (m, 1 H, 7.42–7.49 (m, 2 H), 7.78–7.83 (m, 2 H), 8.04 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 55.7 (CH_3), 62.1 (C_{quat}), 114.9 (CH), 116.7 (CH), 123.7 (C_{quat}), 124.5 (CH), 128.5 (CH), 128.8 (CH), 129.7 (CH), 130.6 (C_{quat}), 150.2 (C_{quat}), 154.4 (C_{quat}), 160.8 (C_{quat}) ppm. MS (EI +Q1): m/z (%) = 376 (100) [M$^+$], 361 (22) [M$^+$ – CH_3], 221 (48) [M$^+$ – I – CH_3 – CH], 105 (18) [$C_6H_5CO^+$], 77 (12) [$C_6H_5^+$]. IR (KBr): $\tilde{\nu}$ 1607 cm^{-1}, 1541, 1494, 1440, 1294, 1254, 1180, 1069, 1055, 1026, 945, 831, 797, 760, 688, 663. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 238 nm (14500), 252 (12000), 328 (24600), 350 (13000). $C_{17}H_{13}IO_2$ (376.2): calcd. C 54.28, H 3.48; found C 54.35, H 3.49.

3-Iodo-5-isopropyl-2-(4-methoxyphenyl)furan (4h): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **4h** was obtained as a colorless oil, R_f = 0.61. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 1.27 (d, J = 7.0 Hz, 6 H), 2.99 (dsept, J = 1.1, 7.0 Hz, 1 H), 3.85 (s, 3 H), 6.27 (d, J = 1.1 Hz, 1 H), 7.03 (d, J = 9.2 Hz, 2 H), 7.88 (d, J = 9.2 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 21.0 (CH_3), 28.4 (CH), 55.5 (CH_3), 60.2 (C_{quat}), 114.4 (CH), 114.6 (CH), 124.0 (C_{quat}), 128.1 (CH), 153.7 (C_{quat}), 160.3 (C_{quat}), 162.5 (C_{quat}) ppm. MS (EI+): m/z (%) = 342 (88) [M$^+$], 327 (100) [M$^+$ – CH_3]. IR (KBr): $\tilde{\nu}$ 2964 cm^{-1}, 1607, 1550, 1492, 1280, 1247, 1176, 1032, 941, 826. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 286 nm (19300), 296 (17600), 314 (8820). HRMS calcd. for $C_{14}H_{15}IO_2$: 342.0117; found 342.0125.

General Procedure for the Three-Component Synthesis of Chloroiodofurans 5: In a screw-cap pressure vessel $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol), and CuI (7 mg, 0.04 mmol) were dissolved in 5 mL of degassed THF. Then acyl chloride **1** (1.00 mmol), THP-protected propargyl alcohol **2** (1.00 mmol) as well as triethylamine (0.14 mL, 1.00 mmol) were successively added to the solution (for experimental details see Table 8). The reaction mixture was stirred for 2 h at room temperature until the conversion was complete (monitored by TLC). Then, sodium chloride (293 mg, 5.0 mmol), iodine monochloride (244 mg, 1.5 mmol or 406 mg, 2.5 mmol) and *p*-tolylsulfonic acid monohydrate (209 mg, 1.1 mmol) and 3 mL of methanol

Table 8. Experimental details of the synthesis of chloro-iodofurans **5**.

Entry	Acyl chloride **1**	Alkyne **2**	Chloro-iodofuran **5** (yield)
1	141 mg (1.00 mmol) of **1a**	141 mg (1.00 mmol) of **2a**	160 mg (52%) of **5a**
2	171 mg (1.00 mmol) of **1b**	141 mg (1.00 mmol) of **2a**	140 mg (42%) of **5b**
3	186 mg (1.00 mmol) of **1c**	141 mg (1.00 mmol) of **2a**	107 mg (31%) of **5c**
4	147 mg (1.00 mmol) of **1f**	141 mg (1.00 mmol) of **2a**	98 mg (31%) of **5d**
5	171 mg (1.00 mmol) of **1b**	168 mg (1.00 mmol) of **2b**	232 mg (64%) of **5e**
6	167 mg (1.00 mmol) of **1g**	168 mg (1.00 mmol) of **2b**	205 mg (57%) of **5f**
7	171 mg (1.00 mmol) of **1b**	247 mg (1.00 mmol) of **2c**	226 mg (51%) of **5g**

were added, and the reaction mixture was stirred at room temperature for 4 h. After complete conversion of ynone to furan (TLC), the reaction mixture was diluted with saturated solution of $NaHCO_3$ (20 mL) and Na_2SO_3 (20 mL), and extracted with dichloromethane (5 × 20 mL). The combined organic layers were dried with sodium sulfate and the solvents evaporated in vacuo. The residue was chromatographed on neutral aluminium oxide (hexane/ethyl acetate) to give the analytically pure chloro-iodofurans **5** as oils or solids (crystallization from hexane).

4-Chloro-3-iodo-2-phenylfuran (5a): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **5a** was obtained as a colorless oil, R_f = 0.75. ^{1}H NMR ([D$_6$]-acetone, 300 MHz): δ = 7.41–7.56 (m, 3 H), 7.97–8.02 (m, 3 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ 67.9 (C_{quat}), 123.5 (C_{quat}), 127.0 (CH), 129.4 (CH), 129.8 (CH), 130.5 (C_{quat}), 139.6 (CH), 153.5 (C_{quat}) ppm. MS (EI+): *m*/*z* (%) = 306 (31) [^{37}Cl – M$^+$], 304 (100) [^{35}Cl – M$^+$], 179 (9) [^{37}Cl – M$^+$ – I], 177 (26) [^{35}Cl – M$^+$ – I]. IR (KBr): $\tilde{\nu}$ 3149 cm^{-1}, 1522, 1480, 1444, 1209, 1147, 1053, 1027, 978, 907, 764, 690, 668, 593. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 276 nm (13700), 288 (12200), 302 (7200). HRMS calcd. for $C_{10}H_6{}^{37}ClIO$: 305.9122; found 305.9127. HRMS calcd. for $C_{10}H_6{}^{35}ClIO$: 303.9152; found 303.9154.

4-Chloro-3-iodo-2-(4-methoxyphenyl)furan (5b): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 15:1), **5b** was obtained as colorless crystals, m.p. 53–54 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 3.68 (s, 3 H), 6.88 (d, *J* = 9.1 Hz, 2 H), 7.73 (s, 1 H), 7.72 (d, *J* = 9.1 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 55.7 (CH_3), 66.3 (C_{quat}), 114.9 (CH), 123.1 (C_{quat}), 123.3 (C_{quat}), 128.7 (CH), 139.0 (CH), 148.1 (C_{quat}), 161.2 (C_{quat}) ppm. MS (EI+): *m*/*z* (%) = 336 (31) [^{37}Cl – M$^+$], 334 (100) [^{35}Cl – M$^+$], 209 (7) [^{37}Cl – M$^+$ – I], 207 (21) [^{35}Cl – M$^+$ – I], 181 (30) [^{37}Cl – M$^+$ – COI], 179 (94) [^{35}Cl – M$^+$ – COI]. IR (KBr): $\tilde{\nu}$ 3101 cm^{-1}, 2973, 2859, 1610, 1528, 1489, 1256, 1179, 1022, 841. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 282 nm (18000). $C_{11}H_8ClIO_2$ (334.54): calcd. C 39.49, H 2.41; found C 39.86, H 2.55.

4-Chloro-3-iodo-2-(4-nitrophenyl)furan (5c): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 6:1 to 4:1), **5c** was obtained as yellow crystals, m.p. 105–106 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.12 (s, 1 H), 8.28 (d, *J* = 9.2 Hz, 2 H), 8.37 (d, *J* = 9.2 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 71.9 (C_{quat}), 124.5 (C_{quat}), 124.7 (CH), 127.3 (CH), 136.0 (C_{quat}), 141.2 (CH), 148.3 (C_{quat}), 151.2 (C_{quat}) ppm. MS (EI+): *m*/*z* (%) = 351 (31) [^{37}Cl – M$^+$], 349 (100) [^{35}Cl – M$^+$], 321 (4) [^{37}Cl – M$^+$ –NO], 319 (12) [^{35}Cl – M$^+$ – NO], 224 (7) [^{37}Cl – M$^+$ – I], 222 (21) [^{35}Cl – M$^+$ – I]. IR (KBr): $\tilde{\nu}$ 1598 cm^{-1}, 1509, 1338, 910, 852. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 240 nm (9900), 350 (18500). $C_{10}H_5ClINO_3$ (349.51): calcd. C 34.37, H 1.44, N 4.01; found C 34.48, H 1.60, N 3.98.

4-Chloro-3-iodo-5-(thiophen-2-yl)furan (5d): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 20:1), **5d** was obtained as a colorless oil. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.18 (dd, *J* = 3.7, 5.1 Hz, 1 H), 7.46 (dd, *J* = 1.1, 5.1 Hz, 1 H), 7.56 (s, 1 H), 7.76 (dd, *J* = 1.1, 3.7 Hz, 1 H) ppm. ^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 67.0 (C_{quat}), 123.2 (C_{quat}), 126.0 (CH), 126.5 (CH), 127.8 (CH), 131.8 (C_{quat}), 137.6 (CH), 150.4 (C_{quat}) ppm. MS (EI+): *m*/*z* (%) = 312 (31) [^{37}Cl – M$^+$], 310 (100) [^{35}Cl – M$^+$], 185 (10) [^{37}Cl – M$^+$ – I], 183 (26) [^{35}Cl – M$^+$ – I], 157 (17) [^{37}Cl – M$^+$ – COI], 155 (30) [^{35}Cl – M$^+$ – COI]. IR (KBr): $\tilde{\nu}$ 3148 cm^{-1}, 3106, 1578, 1535, 1421, 1314, 1247, 1038, 970, 746, 589. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 298 nm (14500), 308 (15100), 326 (8900). HRMS calcd. for $C_8H_4{}^{37}ClIOS$: 311.8686; found 311.8716. HRMS calcd. for $C_8H_4ClIO^{35}S$: 309.8716; found 309.8723.

3-Chloro-2-ethyl-4-iodo-5-(4-methoxyphenyl)furan (5e): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **5e** was obtained as a yellow oil, R_f = 0.62. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 1.26 (t, *J* = 7.6 Hz, 3 H), 2.80 (q, *J* = 7.6 Hz, 2 H), 3.86 (s, 3 H), 7.05 (d, *J* = 9.1 Hz, 2 H), 7.90 (d, *J* = 9.1 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 12.2 (CH_3), 20.2 (CH_2), 55.7 (CH_3), 66.2 (C_{quat}), 114.8 (CH), 117.6 (C_{quat}), 123.4 (C_{quat}), 126.7 (C_{quat}), 128.4 (CH), 152.2 (C_{quat}), 161.0 (C_{quat}) ppm. MS (EI+): *m*/*z* (%) = 364 (37) [^{37}Cl – M$^+$], 362 (100) [^{35}Cl – M$^+$], 349 (19) [^{37}Cl – M$^+$ – CH_3], 345 (57) [^{35}Cl – M$^+$ – CH_3], 237 (8) [^{37}Cl – M$^+$ – I], 235 (25) [^{35}Cl – M$^+$ – I]. HRMS calcd. for $C_{13}H_{12}{}^{37}ClIO_2$: 363.9541; found 363.9521. HRMS calcd. for $C_{13}H_{12}{}^{35}ClIO_2$: 361.9571; found 361.9561.

3-Chloro-2-ethyl-4-iodo-5-styrylfuran (5f): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 9:1), **5f** was obtained as a yellow oil, R_f = 0.81. ^{1}H NMR ([D$_6$]-acetone, 300 MHz): δ = 1.27 (t, *J* = 7.7 Hz, 3 H), 2.80 (q, *J* = 7.7 Hz, 2 H), 6.97 (d, *J* = 16.5 Hz, 1 H), 7.18 (d, *J* = 16.5 Hz, 1 H), 7.27–7.34 (m, 1 H), 7.36–7.42 (m, 2 H), 7.59–7.64 (m, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 12.0 (CH_3), 20.2 (CH_2), 72.2 (C_{quat}), 115.4 (CH), 117.4 (C_{quat}), 127.4 (CH), 129.0 (CH), 129.6 (CH), 130.3 (CH), 137.2 (C_{quat}), 152.0 (C_{quat}), 153.3 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 360 (37) [^{37}Cl – M$^+$], 358 (100) [^{35}Cl – M$^+$], 345 (17) [^{37}Cl – M$^+$ – CH_3], 343 (42) [^{35}Cl – M$^+$ – CH_3]. IR (KBr): $\tilde{\nu}$ 2975 cm^{-1}, 2936, 1586, 1493, 1458, 1447, 1319, 1268, 1092, 1062, 990, 954, 749, 691, 595. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 310 nm (15800), 326 (26300), 338 (32100), 356 (23700). HRMS calcd. for $C_{14}H_{12}{}^{37}ClIO$: 359.9591; found 359.9609. HRMS calcd. for $C_{14}H_{12}{}^{35}ClIO$: 357.9621; found 357.9627.

3-Chloro-4-iodo-2,5-bis(4-methoxyphenyl)furan (5g): According to the general procedure after chromatography on silica gel (hexanes/ethyl acetate, 6:1), **5g** was obtained as colorless crystals, R_f = 0.79, m.p. 129 °C. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 3.86 (s, 3 H), 3.87 (s, 3 H), 7.04–7.11 (m, 4 H), 7.93 (d, *J* = 8.8 Hz, 2 H), 8.03 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 55.6 (CH_3), 55.7 (CH_3), 69.0 (C_{quat}), 114.8 (CH), 115.0 (CH), 116.9 (C_{quat}), 122.1 (C_{quat}), 123.0 (C_{quat}), 147.4 (C_{quat}), 151.2 (C_{quat}), 160.8 (C_{quat}), 161.1 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 442 (28) [^{37}Cl – M$^+$], 440 (100) [^{35}Cl – M$^+$], 427 (5) [^{37}Cl – M$^+$ – CH_3], 425

(18) [$^{35}Cl - M^+ - CH_3$], 313 (1) [$^{35}Cl - M^+ - I$], 285 (24) [$^{37}Cl - M^+ - COI$], 283 (77) [$^{35}Cl - M^+ - COI$], 135 (48) [*p*-$MeOC_6H_4CO^+$]. IR (KBr): $\tilde{\nu}$ 1613 cm^{-1}, 1504, 1495, 1299, 1284, 1250, 1180, 1086, 1029, 940, 828. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 260 nm (23700), 324 (26200). $C_{18}H_{14}ClIO_3$ (440.67): C 49.06, H 3.20; found C 48.74, H 3.30.

3-Chloro-2,4,5-tris(4-methoxyphenyl)furan (7): In a screw-cap pressure vessel $Pd(PPh_3)_2Cl_2$ (35 mg, 0.05 mmol), and 3-chloro-4-iodo-2,5-bis(4-methoxyphenyl)furan (**5g**, 441 mg, 1.00 mmol) were dissolved in a mixture of 5 mL of degassed THF and 5 mL of degassed methanol. Then 4 mL of a sodium carbonate solution (2 M, 8.00 mmol) and (*p*-methoxyphenyl)boronic acid (**6**, 160 mg, 1.05 mmol) were added, and the reaction mixture was heated at 90 °C for 24 h. Then the reaction mixture was diluted with water (20 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic layers were dried with sodium sulfate, evaporated and applied to column chromatography on the neutral aluminium oxide eluting with hexane-ethyl acetate (9:1) to give 226 mg (51%) of **7** as a colorless solid, m.p. 128 °C. ^1H NMR ([D$_6$]DMSO, 300 MHz): δ = 3.74 (s, 3 H), 3.82 (s, 3 H), 3.83 (s, 3 H), 6.92 (d, J = 8.8 Hz, 2 H), 7.06 (d, J = 8.8 Hz, 2 H), 7.10 (d, J = 9.2 Hz, 2 H), 7.30 (d, J = 8.5 Hz, 2 H), 7.39 (d, J = 8.8 Hz, 2 H), 7.92 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ = 55.1 (CH_3), 55.1 (CH_3), 55.2 (CH_3), 111.9 (C_{quat}), 114.2 (CH), 114.38 (CH), 114.4 (CH), 121.2 (C_{quat}), 121.4 (C_{quat}), 122.2 (C_{quat}), 122.5 (C_{quat}), 125.8 (C_{quat}), 126.3 (CH), 126.6 (CH), 131.2 (CH), 145.0 (C_{quat}), 146.5 (C_{quat}), 159.1 (C_{quat}), 159.1 (C_{quat}), 159.1 (C_{quat}) ppm. MS (EI +Q1): *m*/*z* (%) = 422 (22) [$^{37}Cl - M^+$], 420 (100) [$^{35}Cl - M^+$], 407 (5) [$^{37}Cl - M^+ - CH_3$], 405 (18) [$^{35}Cl - M^+ - CH_3$], 135 (17) [$CH_3OC_6H_4CO^+$]. IR (KBr): $\tilde{\nu}$ 1612 cm^{-1}, 1598, 1519, 1505, 1463, 1441, 1298, 1291, 1277, 1251, 1176, 1079, 1032, 945, 833. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 268 nm (22300), 322 (15300), 334 (26300). $C_{25}H_{21}ClO_4$ (420.9): calcd. C 71.34, H 5.03, Cl 8.42; found C 70.96, H 5.05, Cl 8.72.

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