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1-Phenyl-1,2-benziodoxol-3-(1*H*)-one as Synthon for Phthalide Synthesis *via* Pd-Free, Base-Free, Sonogashira-Type Coupling Cyclization

Ahmad A. Almasalma,[a] and Esteban Mejía*[a]

Abstract: Hypervalent iodine (III) five-membered heterocycles have found broad application as atom-transfer reagents for organic synthesis. Among them, 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one is known as a traditional benzyne precursor, but no further synthetic applications have been reported. Herein, we report the first synthetic application of 1-phenylbenzidoxole to the synthesis of Phthalides using only Cu^{I} as catalyst. High selectivity and yield were achieved under mild reaction conditions with good functional group tolerance. During our investigations, the efficiency of different Cu^{I} and Cu^{II} catalysts under various reaction conditions were studied. The nature of the leaving group, the substituents on the substrate and temperature, play an important role on both yield and selectivity. Moreover, a plausible mechanistic pathway for this transformation was proposed based on our observations and previous literature reports.

Introduction

Thanks to their cyclic nature, hypervalent iodine (III) five-membered heterocycles (benziodoxoles and benziodoxolones) have considerably higher thermal stability than their acyclic counterparts, thanks to the bridging of the equatorial and the apical positions at the hypervalent iodine center.[1] This enhanced stability made possible the preparation of otherwise elusive hypervalent iodine derivatives with, fluoride,[2] chloride,[3] Bromide,[4] peroxide,[5] azido,[6] cyano,[7] methoxy,[8] alkynyl[9] and trifluoromethyl[10] substituents, which in some cases, notably ethynyl (EBX)[11] and trifluoromethy (Togni's reagent),I[12] made their way into the organic chemist's tool-box as powerfull atom-transfer reagents.[13] 1-Phenylbenziodoxole (**1**)[14] is known mostly as a benzyne precursor under heating (scheme 1).[15] Reactions of 1-arylbenziodoxoles with nucleophiles proceed solely by substitution at the *ipso*-carbon of the aromatic benziodoxolone ring, giving aryl iodides and the corresponding *ortho*-substituted benzoic acids as major products (scheme 1).[14, 16] Beyond that, the chemistry of these compounds has not been further developed, and their utilization as synthons in organic synthesis has not been exploited.

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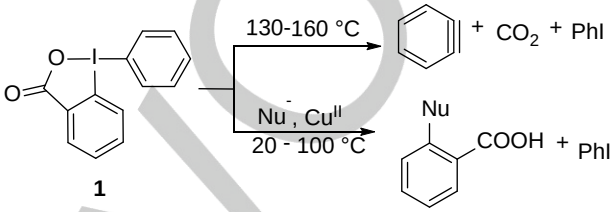


Scheme 1. Reactivity of 1-phenyl-1,2-benziodoxol-3-(1H)-one.

Phthalides are frequently found in naturally occurring products, exhibiting a broad spectrum of biological activity,[17] and are also used as a versatile building blocks in organic synthesis.[18] Some examples of bio-active phtalides (Figure 1) are *n*-butylphthalide (**2**), which is currently in the market as an antiplatelet drug for ischemia-cerebralapoplexy,[19] Mycophenolic acid (**3**), which is in clinical trials for the prevention and reversal of transplant rejection and anti-cancer treatments,[20] and the benzalphtalide derivative **4** which has anti-HIV activity.[21] Most of the recent studies deal with 3-substituted phthalides due to their wide range of pharmacological applications. The isolation of these compounds from natural sources is not cost effective, hence, their laboratory synthesis by either chemical or biochemical means has been an active research area.[22]

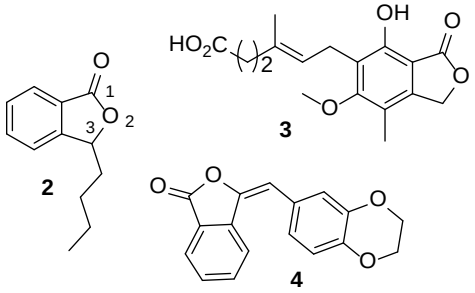
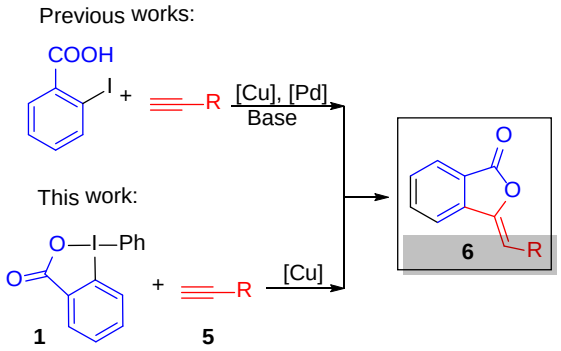


Figure 1. Some bio-active phthalide derivatives.

Traditionally, phthalides can be prepared by the reaction of phthalic anhydride with acetic anhydride or acetic acid at high temperatures,[23] and by condensation of phthalide phosphate with aldehydes.[24] An attractive method for the synthesis of phthalides and isocoumarins is the metal-catalyzed 5-exo-dig or 6-endo-dig cyclization of 2-alkynylbenzoic acid/esters which are available [25] or synthesized *in situ*.[26] One of these approaches, the Sonogashira-type coupling cyclization reaction, although having high substrate scopes, requires the use of

superstoichiometric amounts of bases.[27] The latter feature,[25b] limits the substrate scope, especially in total synthesis, since it requires additional protecting/de-protecting steps.[28]

By reacting 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) with phenylacetylene (**5a**) using only Cu^{I} as catalyst, we have serendipitously discovered the direct, regioselective synthesis of phtalides **6**, in a Pd-free Sonogashira-like coupling reaction. The reaction proceeds under mild conditions and does not require the addition of a base. Coupling reactions of this type are scarce in the literature,[29] and to the best of our knowledge, this is the first report of a Sonogashira-type coupling cyclization reaction which requires neither Pd nor base.[30] Herein, we also report the first synthetic application of 1-arylbenziodoxoles, namely for the preparation of phthalides (Scheme 2) under mild conditions with an excellent functional-group tolerance and high yield.

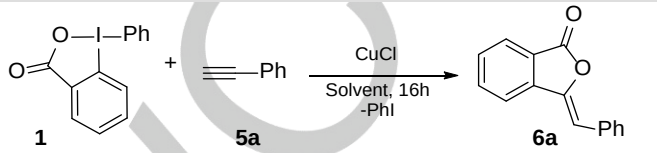


Scheme 2. Phthalide syntheses by Sonogashira-type coupling cyclizations.

Results and Discussion

The starting material, 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) was synthesized following published procedures.[14] Phenylacetylene **5a** was chosen as the model substrate. The reaction between **1** and **5a** in the presence of CuCl (20 mol-%) in CH_3CN at 80 °C produced only phthalide **6a** (yield >99 %) within 2 hours (table 1 entry 1). Using a lower amount of catalyst (10 mol-%) the desired compound was obtained overnight (16 h) with a lower yield (78 %) together with 1,4-diphenylbutadiyne, product of the homocoupling of **5a**. (table 1 entry 2). The yield was not improved after 24 hours under these conditions. An even lower yield (72 %) resulted when the equivalent amount of **1a** was increased (table 1, entry 3). The observed oxidative dimerization reaction of phenylacetylene (**5a**), presumably promoted by the hypervalent iodine (*vide infra*), was also observed at 40 °C with 10 mol-% of the catalyst (table 1, entry 4). Further increase of the equivalents of **1** decreased the yield even further (table 1, entry 5). Reactions at room temperature yield only to traces of the product in either DCM, DMSO or acetonitrile (table 1, entry 6, 7 and 8). Interestingly, by increasing the reaction temperature to 100 °C, the corresponding isocoumarin **7a** was produced in small amount (6 %) together with phthalide **6a**, still as the major product (63 % table 1, entry 9). Almost no changes in the reaction selectivity were observed with 20 mol-% of catalyst (**6a** 64 %, **7a** 4 %, entry 10, table 1). Interestingly, this selectivity is complementary to the reported by Lee and co-workers, who selectively obtained the corresponding 6-membered regioisomers (isocoumarin **7a**) at similar reaction temperatures.[27] Further lowering the amount of catalysts to 5 mol-% only results in 28 % yield (table 1, entry 11).

Table 1. Screening of reaction conditions for the synthesis of phthalides *via* coupling cyclization of 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) with phenylacetylene (**5**)



Entry	CuCl (mol-%)	Ratio **1**:**5a**	Temp. (°C)	Solvent	Yield (%)[a]
1[b]	20	1.5 : 1	80	CH_3CN	>99 (95)[c]
2[e]	10	1.5 : 1	80	CH_3CN	78
3[e]	10	2 : 1	80	CH_3CN	72
4	10	1.5 : 1	40	DCM	70
5	10	1 : 1	40	DCM	63
6	10	1 : 1	25	DCM	3
7	10	1 : 1	25	DMSO	5
8	10	1 : 1	25	CH_3CN	n.d.[d]
9	10	1 : 1	100	DMSO	63
10	20	1 : 1	100	DMSO	64
11	5	1 : 1	40	DCM	28

[a] Determined by GC (see supporting information for details) [b] Reaction time 2 hours. [c] Isolated yield in parentheses. [d] Not detected, [e] Reaction time 5 hours.

After screening the catalyst load, solvent, and temperature, we chose the reaction conditions in entry 4 (table 1) as starting point for the screening of the influence of the copper source (table 2). Changing the chloride counter-ion for bromine or iodine resulted in a decrease of the yield of **6a** (table 2, entry 2 and 3). A similar drop in the yield was observed when nitrate was employed (table 2, entry 4). Conversely, the use of $Cu(NCMe)_4PF_6$ led to the highest yield (72 %, table 2, entry 5), so it was selected for the subsequent studies. Interestingly, we did not observe any conversion using Cu^{II} as catalyst (table 2, entry 6).

Table 2. Screening of copper sources and solvents[a]

Entry	Copper source	Solvent	Yield (%)[b]

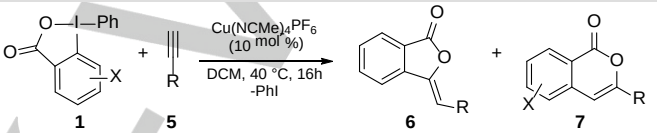
1[c]	CuCl	DCM	70
2	CuBr	DCM	50
3	CuI	DCM	60
4	$CuNO_3(PPh_3)_2$	DCM	53
5	$Cu(NCMe)_4PF_6$	DCM	72
6	$Cu(OTf)_2$	DCM	n.d.[d]
7	$Cu(NCMe)_4PF_6$	DMSO	35
8	$Cu(NCMe)_4PF_6$	CH_3CN	20
9	$Cu(NCMe)_4PF_6$	DMF	28[e]
10	$Cu(NCMe)_4PF_6$	THF	n.d. [d]
11	$Cu(NCMe)_4PF_6$	DCM	5[f]

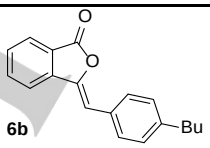
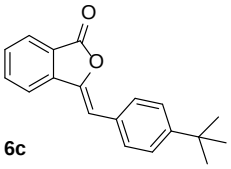
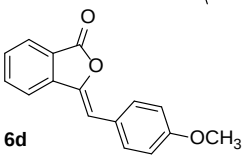
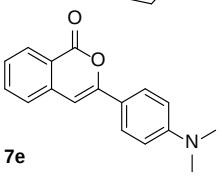
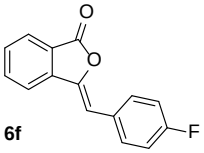
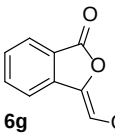
[a] Reaction conditions:**1** 0.66 mmol, **5a** 0.44 mmol, catalyst 0.04 mmol, dry solvent, argon atmosphere, 16 hours [b] Determined by GC (see supporting information for details. [c] Table 1, entry 4. [d] Not detected. [e] Isocumarine (**7a**, 5 %) was also detected. [f] addition of 1,10-phenantroline (10 mol-%)

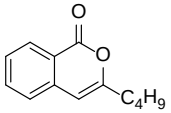
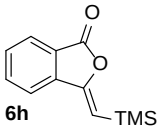
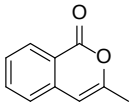
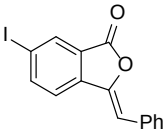
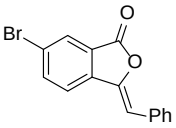
From the tested solvents, 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) was only soluble in DCM at room temperature, being this also the solvent in which better yields were obtained. When the reaction was performed in DMF, isocoumarin **7** was produced (5 %) along with the desired phthalide **6** (28 %, table 2, entry 9). No product was detected using THF (table 2, entry 10), perhaps due to catalysts poisoning by the highly coordinating solvent. Similarly, addition of 1,10-phenanthroline (10 mol-%) as ligand resulted in a dramatic yield drop, perhaps due to a blocking of the catalytic centers (table 2, entry 11). In the absence of the copper catalyst no product was observed, even after 24 hours at 90 °C. This rules out the possible cross-coupling and cyclization triggered by the mere thermal decomposition of the hypervalent iodine reagent.

With the optimal conditions in hand, we investigated the scope and limitations of the reaction (table 3). Different Arylalkynes, having electron-donating groups at the *para* position yield phthalides as the major product, accompanied by the corresponding isocoumarins as a minor product (**6b-d**). Reaction with 4-(dimethylamino)phenylacetylene (table 3, entry 4). yield preferably to the corresponding isocumarine **7e**, as confirmed by single-crystal X-ray analysis (see Figure S36 in the supporting information). Conversely, the electron-poor 4'-fluorophenylacetylene produced the corresponding phthalide **6f** as a sole product (Table 3, entry 5). In addition to aryl alkynes, aliphatic alkynes showed to be reactive under these reaction conditions, delivering the desired phthalide (**6g**) only in moderate yield accompanied by the corresponding isocoumarin (**7g**). By increasing the catalyst load (20 mol-%) and the reaction temperature (up to 80 °C), **7g** was obtained as the major product (table 3, entry 7,). It is noteworthy that only Z isomers were observed in all cases (as confirmed by comparison with literature reports). Reaction with the common C2 synthon ethynyltrimethylsilane under optimal reaction conditions yield selectively to the corresponding phthalide **6h**, alas, with moderate yield (table 3, entry 8). Contrariwise, under the same conditions, no reaction was observed with substrates devoid of an acetylenic proton, like 1-(Trimethylsilyl)propyne and 1-(phenyl)propyne. In the former case, increasing of both the load of the catalyst and the amount of **1** resulted in a desilylation-annulation reaction, yielding to the isocoumarin **7i** (table 3, entry 9).[31] Two more 1-phenylbeziodoxole derivatives bearing iodo (17) and bromo (18) substituents were synthesized and its reactivity was tested under the previously described reaction conditions (Table 3, entries 10 and 11). Unfortunately, these halogenated substrates did not undergo coupling cyclization with **5**.

Table 3. Substrate scope investigation

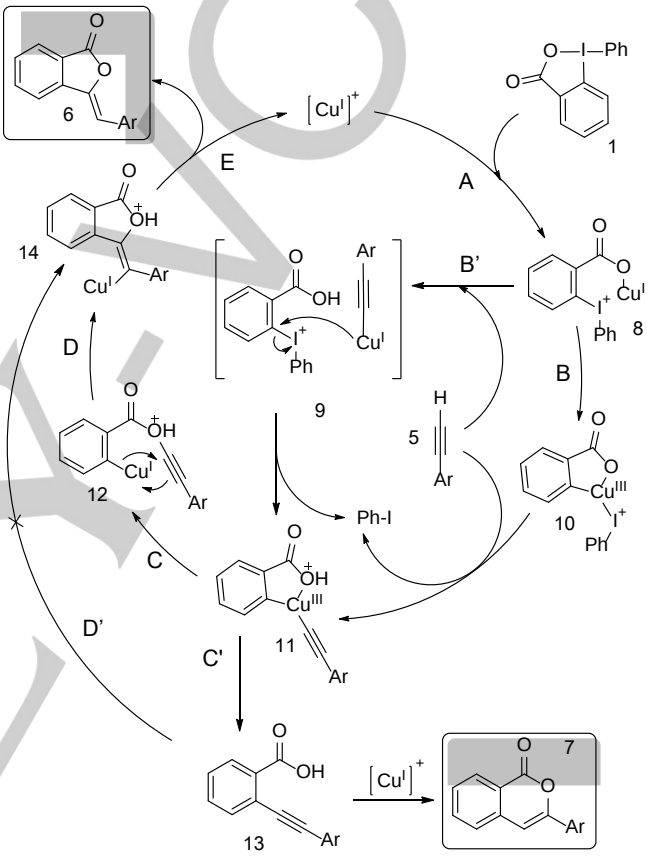


Entry	Major product	Yield (%)[a]	Ratio **6**:**7**
1[c]	 **6b**	66	93:7
2	 **6c**	63	92:8
3	 **6d**	63	92:8
4	 **7e**	82	35:65
5	 **6f**	55	100:0
6	 **6g**	66	50:50

7[b]	 **7g**	90	35:65
8	 **6h**	26	100:0
9[b]	 **7i**	17	100:0
10		n.d[C]	-
11		n.d[C]	-

[a] Isolated yields of the regioisomer mixture; the isomeric ratios **6**:**7** were determined by GC and GC-MS (see supporting information for details) [b] 20 mol-% of catalyst; 5 hours, CH_3CN as solvent at 80 °C. [C] not detected.

Considering our observations and previous literature reports, a plausible reaction mechanism was proposed (scheme 3). It has been established that the benziodoxolone ring (i.e. in the Togni's reagent) can be activated by the presence of Lewis acids through coordination of the metal with the carboxyl group.[12b, 32] Hence, the catalytic cycle shall start with the coordination between the Cu^{I} and **1** (scheme 3, step A), to produce an activated copper(I) dialkylodonium salt (**8**). The substrate activation can be followed either by deprotonation of **5** by the carboxylate group acting as an internal base (step B'). It guards close resemblance to the Pd-free Sonogashira reaction reported by Rothenberg *et al*., where a single equivalent of a carboxylate was added as external base.[29b] This leads to the formation of the corresponding Cu^{I}-cuprate and carboxylic acid (**9**). Alternatively, intermediate **8** can undergo oxidative addition to form a Cu^{III}-aryl intermediate (**10**, step B), analogously to the reaction of 1-Hydroxy-1,2-benziodoxol-3(1*H*)-one with a Pd catalyst in the Suzuki-Miyaura cross-coupling reported by Xia and Chen.[33] A highly electrophilic d^8-species (**11**) results from either oxidative addition of the reactive couple **9** or by deprotonation/ligand exchange from **10** and **5**. From **11**, two intermediates can be formed (**12** and **13**), depending on the ligands involved in the subsequent reductive elimination (RE) step. On the one hand, if the RE involves the alkynyl ligand together with the aryl moiety, **13** will be obtained (path C'). On the other hand, if the RE takes place between the alkynyl and the alkoxy ligands (path C), an aryl cuprate ester intermediate would be formed (**12**) which, upon intramolecular migratory insertion of the alkyne into the Ar-Cu bond, yields to the phthalide precursor **14** (path D). It has been proposed that under basic conditions[29a] the *O*-alkynyl carboxylate intermediate (**13**) in the presence of Cu^{I} yields to **14** through a 5-*exo-dig* cyclization (path D''). To prove this hypothesis, we synthesized **13** (Ar = Ph) following reported procedures[34] and subjected it to our reaction conditions. Interestingly, the cyclization of **13** lead exclusively to isocoumarin **7** in a quantitative yield, which indicates the crucial role of the five-member ring intermediate **11** in determining the regioselectivity of the resulting product.



Scheme 3. Proposed reaction mechanism.

To assess the influence of the iodoaryl leaving group on the reaction outcome, two new derivatives of 1,2-benziodoxol-3(1*H*)-one were synthesized: **15**, substituted with 1,3,5-trifluoro-2-iodobenzene and **16**, with 1-iodo-4-methoxybenzene groups, respectively. For both compounds, single crystals of X-ray diffraction quality were obtained (figure 2). Selected bond distances are presented in table 4.

Both substrates were subjected to optimized cyclization conditions taking aliquots periodically. The same procedure was applied to **1**. The resulting plot of phthalide (**6a**) production versus time (Figure 3) shows how it is clearly (although slightly) accelerated compared to **1** when the electron-enriched *p*-methoxy derivative **16** is used. Conversely, a dramatic decrease in the reaction rate is observed for the electron-poor **15**.

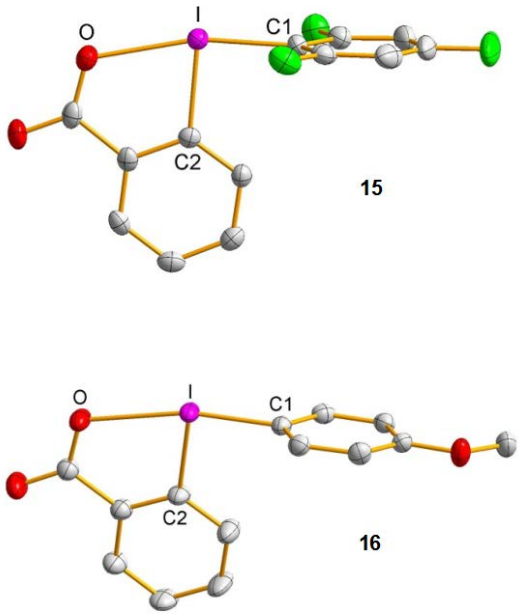


Figure 2. X-ray molecular structure of compounds **15** and **16**. Hydrogen atoms are omitted for clarity. Compound **16** presents two molecules in the asymmetric cell together with two water molecules (omitted for clarity). The thermal ellipsoids correspond to 50 % probability. For selected bond distances see table 4. CCDC deposition numbers: 1558837 (**15**); 1558836 (**16**)

Table 4. selected bond distances in Å for compounds **1**, **15** and **16**

Bond	**1**[a]	**15**	**16**
I-O	2.4787 (52)	2.371 (22)	2.5188 (17)
I-C1	2.1063 (53)	2.1199 (32)	2.098 (2)
I-C2	2.1187 (35)	2.1248 (28)	2.131 (2)

[a] Taken from reference [35]

This marked difference in reactivity between the three benziodoxole analogues **1**,[35] **15** and **16**, follows the same trend as the lengths of their reactive I-O bond. Compound **15** has the shortest (hence strongest) bond in the series probably making the Cu-O bond formation difficult, while **16**, possessing the longest I-O bond, is more prone to dissociate, resulting in an enhanced reactivity compared to **15**. To explain this issue, further kinetic and mechanistic insights are necessary.

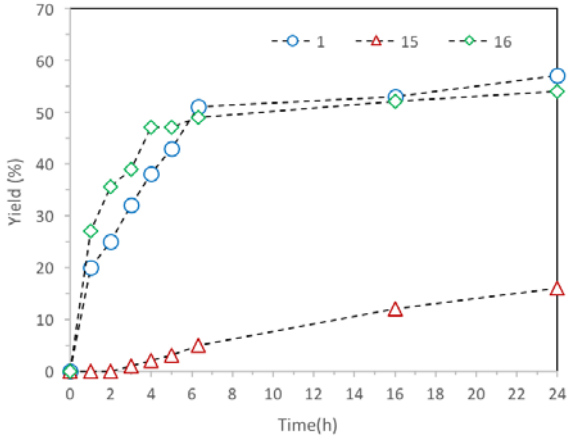


Figure 3. Plot of phthalide (**6a**) production versus time for the different 1-alkyl-benziodoxolone derivatives.

Conclusions

In summary, we have developed new method to synthesize different types of phthalide compounds directly from 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one under mild reaction conditions with good selectivity and yield. Importantly, this investigation explores and exploits for the first time the latent reactivity of 1-alkyl-beziodoxolones. The regioselectivity of this transformation was affected by temperature and the nature of acetylene coupling partner. The advantages of this method over the reported alternatives are that neither palladium, nor super-stoichiometric amounts of base are required, increasing the scope of the reaction. Moreover, we studied the effect of the iodoalkyl leaving group on the reaction rate and proposed a plausible reaction mechanism. Kinetic experiments as well as deeper mechanistic studies are currently ongoing in our laboratories. We hope that the present contribution serves as a starting point for the usage of 1-alkyl-benziodoxolones as building blocks in organic transformations.

Experimental Section

General Remarks

Chemicals, reagents, and solvents were purchased from commercial suppliers and used without further purification. Thin-layer chromatography (TLC) was performed on silica HSGF254 plates. Melting points were determined with a digital melting-point apparatus. ^{1}H and ^{13}C NMR spectra were obtained from a solution in $CDCl_3$ using a 400/101 MHz ($^{1}H/^{13}C$) or 300/75 MHz ($^{1}H/^{13}C$) spectrometer. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. High-resolution mass-spectrometry (HRMS) analyses were carried out on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry

General Procedure for Synthesis of Phthalides (6)

To a dried two-neck round-bottom flask flushed with Argon and equipped with a reflux condenser, 0.66 mmol of 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) were added, followed by addition of the corresponding acetylene derivative (**5**) (0.4 mmol), $Cu(NCMe)_4PF_6$ (0.04 mmol) and 2 ml of dried DCM were added. The suspension was stirred for 16h at 40°C. After cooling, the mixture was poured into DCM (50 mL) and filtrated over Celite. Evaporation of the solvent under reduced pressure provided the crude product, which was purified by column chromatography (EtOAc/hexane 15 %) or recrystallized from hexane to afford the final product.

(Z)-3-Benzylideneisobenzofuran-1(3H)-one (6a)[36]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (214 mg, 0.66 mmol), and phenylacetylene (**5a**) (45 mg, 0.44 mmol) afforded the desired product as a pale yellow solid; yield 68 mg (0.3 mmol, 70%) mp 82–85°C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 7.7 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.59 – 7.51 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.32 (m, 1H), 6.44 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.23, 144.73, 140.77, 134.63, 133.23, 130.28, 129.94, 128.93, 128.58, 125.75, 123.57, 119.97, 107.22, HR-MS (ESI-TOF):*m/z*=223.0754, calcd. for $C_{15}H_{10}O_2[M+H]^+$ 223.0755.

(Z)-3-(4-Butylbenzylidene)isobenzofuran-1(3H)-one (6b)[27]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (276 mg, 0.85 mmol), and 1-butyl-4-ethynylbenzene (**5b**) (98 mg, 0.57 mmol) afforded a mixture of the phthalide **6b** and isocoumarin **7b** in the ratio of 93:7 as white solid; yield 105 mg(0.37 mmol, 66%); mp 152- 154 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.74 (dd, *J* = 15.1, 7.7 Hz, 4H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 6.40 (s, 1H), 2.70 – 2.57 (m, 2H), 1.62 (p, *J* = 7.8, 7.4 Hz, 2H), 1.38 (h, *J* = 7.3 Hz, 2H), 0.94 (d, *J* = 14.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.28, 144.05, 143.78, 140.80, 134.50, 130.60, 130.22, 129.61, 128.98, 125.60, 123.36, 119.79, 107.34, 77.58, 77.16, 76.74, 35.64, 33.54, 22.47, 14.06. HR-MS (ESI-TOF): *m/z*=279.1379, calcd. for $C_{19}H_{18}O_2$ $[M+H]^+$ 279.1378.

3-(4-(tert-butyl)benzylidene)isobenzofuran-1(3H)-one (6c)[29a]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (230 mg, 0.71 mmol), and 1-(tert-butyl)-4-ethynylbenzene (**5c**) (75 mg, 0.47 mmol) afforded a mixture of the phthalide **6c** and isocoumarin **7c** in the ratio of 92:8 as white solid; yield 83 mg(0.3 mmol, 63%); mp 96- 98 °C; 1H NMR (400 MHz, Chloroform-d) δ 7.91 (d, J = 7.7 Hz, 1H), 7.77 (dd, J = 16.1, 8.2 Hz, 3H), 7.69 (t, J = 7.9 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.43 (d, J = 8.5 Hz, 2H), 6.41 (s, 1H), 1.35 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 167.21, 151.82, 144.18, 140.75, 134.47, 130.39, 130.02, 129.67, 129.61, 125.86, 125.81, 125.55, 123.37, 119.81, 107.12, 34.83, 31.28. ; HR-MS (ESI-TOF): *m/z*=279.1379, calcd. for $C_{19}H_{18}O_2$ $[M+H]^+$ 279.1382.

(Z)-3-(4-Methoxybenzylidene)isobenzofuran-1(3H)-one (6d)[37]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (331 mg, 1.0 mmol), and 1-ethynyl -4- methoxybenzene (**5d**) (90 mg, 0.68) afforded the desired phthalide **6d** and the corresponding isocoumarin **7d** in a ratio of 92:8 as a white solid; yield 108 mg (0.42 mmol, 63%); mp 108–110 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.55 – 7.47 (m, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.38 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.41, 159.92, 143.20, 140.92, 134.49, 131.83, 129.42, 126.01, 125.65, 123.22, 119.64, 114.41, 107.09, 55.47. HR-MS (ESI-TOF): *m/z*=253.0859 calcd. for $C_{16}H_{12}O_3$ $[M+H]^+$ 253.0860.

3-(4-(dimethylamino)phenyl)-1H-isochromen-1-one (7e)[27]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (301 mg, 0,930 mmol), and 4-ethynyl-*N,N´*-dimethylaniline (**5e**) (90 mg, 0.62 mmol) afforded the mixture of phthalide **6e** and isocoumarin **7e** in a ratio of 65:35 as a pale yellow solid; yield 135 mg (0.5 mmol, 82 %); mp 121–124 °C; ^{1}H NMR (300 MHz, Chloroform-d) δ 7.89 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 2.1 Hz, 2H), 7.65 (s, 1H), 7.40 (d, *J* = 8.9 Hz, 2H), 6.70 (d, *J* = 2.3 Hz, 2H), 6.35 (s, 1H), 3.01 (s, 6H); ^{13}C NMR (75 MHz, CDCl3) δ 167.70, 150.37, 141.66, 141.16, 134.77, 131.73, 128.62, 125.47, 122.75, 121.21, 119.29, 112.14, 111.86, 108.20, 40.26; HR-MS (ESI-TOF): *m/z*=266.1175, calcd. for $C_{17}H_{15}NO_2$ $[M+H]^+$ 266.1173.

(Z)-3-(4-Fluorobenzylidene)isobenzofuran-1(3H)-one (6f)[36]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (364 mg, 1.1 mmol), and 1-ethynyl-4-flurobenzene (**5f**) (90 mg, 0.75 mmol) afforded **6f** as a white solid; yield 100 mg (0.41 mmol, 55 %); mp 148- 151 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 7.7 Hz, 1H), 7.84 (dd, *J* = 8.9, 5.5 Hz, 2H), 7.79 – 7.69 (m, 2H), 7.59 – 7.51 (m, 1H), 7.10 (t, *J* = 8.7 Hz, 2H), 6.39 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.11, 164.33, 161.02, 144.38, 144.34, 140.64, 134.69, 132.11, 132.00, 129.98, 129.51, 129.46, 125.79, 123.46, 119.89, 116.15, 115.86, 105.99.HR-MS (ESI-TOF): *m/z* 241.0659, calcd. for $C_{15}H_9FO_2$ $[M+H]^+$ 241.0662

(Z)-3-pentylideneisobenzofuran-1(3H)-one (6g)[38]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (324 mg, 1.0 mmol), and 1-hexyne (**5g**) (75 mg, 0.67 mmol) afforded a mixture of phthalide **6g** and isocoumarin **7g** in a ratio of 50:50 as a colorless oil; yield 89 mg (0.44 mmol, 66%) mp 40-40.5°C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.62 (m, 1H), 7.45 – 7.39 (m, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 6.23 (s, 1H), 2.53 – 2.48 (m, 2H), 1.67 (dt, *J* = 15.3, 7.5 Hz, 2H), 1.38 (dt, *J* = 14.7, 7.5 Hz, 4H), 0.95 – 0.93 (m, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 163.18, 158.38, 134.78, 134.30, 129.54, 127.59, 125.28, 119.71, 102.95, 33.29, 29.05, 22.19, 13.85; HR-MS (ESI-TOF): *m/z*=203.1066, calcd. for $C_{13}H_{14}O_2$ $[M+H]^+$ 203.1067.

(Z)-3-((trimethylsilyl)methylene)isobenzofuran-1(3H)-one (6h)[25a]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (371 mg, 1.15 mmol), and acetylene ethynyltrimethylsilane (**5h**) (75 mg, 0.76 mmol) afforded the phthalide **6h** as a yellow oil; yield 30 mg (0.2 mmol, 26 %); ^{1}H NMR (300 MHz, Chloroform-d) δ 7.89 (d, *J* = 6.8 Hz, 1H), 7.70 (d, *J* = 3.6 Hz, 2H), 7.56 (dd, *J* = 7.7, 3.9 Hz, 1H), 5.65 (s, 1H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, CDCl3) δ 167.54, 156.02, 139.44, 134.43, 130.40, 125.22, 125.10, 120.84, 105.50, -0.27.

3-methyl-1H-isochromen-1-one (7i)[39]

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (520 mg, 1.6 mmol), and trimethyl(prop-1-yn-1-yl)silane (**5i**) (90 mg, 0.8 mmol), Cu $(NCCH_3)_4PF_6$ (0.16 mmol) afforded the title compound **7i** as a white solid; mp 75-77 °C; yield 25 mg (0.15 mmol, 17%); ^{1}H NMR (300 MHz, Chloroform-d) δ 8.25 (d, *J* = 8.0 Hz, 1H), 7.75 - 7.62 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 6.26 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 163.14, 154.70, 137.78, 134.88, 129.66, 127.69, 124.99, 120.07, 103.67,19.81.

2-(phenylethynyl)benzoic acid (11, Ar = Ph)

This intermediate was synthesized following the method reported by Gabriele *et al*.[34], ^{1}H NMR (300 MHz, Chloroform-d) δ 8.15 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.70 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.63 - 7.52 (m, 3H), 7.44 (td, *J* = 7.7, 1.4 Hz, 1H), 7.31 (dd, *J* = 5.1, 2.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.45, 134.33, 132.75, 131.90, 131.54, 130.64, 128.78, 128.53, 128.13, 124.50, 123.24, 95.54, 88.14, NMR data matched with the reported values.

3-phenyl-1H-isochromen-1-one (7a)

In a dry two-neck round-bottom flask charged with a magnetic stirrer and flushed with argon, 100 mg (0.45 mmol) of 2-(phenylethynyl) benzoic acid, 17 mg (0.04 mmol) of $Cu(NCMe)_4PF_6$, and 2 ml of dry DCM were added. The mixture was heated at 40 °C for 5 hours. After cooling, the mixture to room temperature, it was poured into DCM (50 mL) and filtrated over Celite. Evaporation of the solvent under reduced pressure provided the crude product, which was purified by column chromatography (EtOAc/hexane 15 %), affording the title compound (**7a**) as a white solid mp 88-90 °C, yield 90 mg (90 %, 0.4 mmol); ^{1}H NMR (400 MHz, Chloroform-d) δ 8.33 - 8.24 (m, 1H), 7.86 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.70 (td, *J* = 7.7, 1.3 Hz, 1H), 7.50 - 7.40 (m, 5H), 6.92 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.28, 153.55, 137.49, 134.88, 131.92, 129.97, 129.58, 128.83, 128.14, 126.02, 125.22, 120.50, 101.82.

General Procedure for Preparation of 1-Arylbenziodoxones (1, 15, 16)

The finely crushed, solid 2-iodobenzoic acid (4.03 mmol) was mixed with powdered Oxone© (potassium peroxymonosulfate) (2.6 mmol) in a 100 mL round-bottom flask and stirred without solvent for 5 min using a magnetic stirrer until a homogeneous mass was formed. Then the reaction mixture was cooled with ice to 5 °C and, under magnetic stirring, concentrated H_2SO_4 (total 3.2 mL) was added *via* syringe in 0.2 mL portions to the reaction mixture. After addition of each portion of H_2SO_4, the reaction mass was mechanically shaken to achieve better mixing; the color of the resulting mass can vary from pale yellow to brown depending on the intensity of mixing. After all H_2SO_4 was added, the magnetic stirring was continued for 30min at room temperature, the mixture was cooled to 5 °C, and CH_2Cl_2 (4 mL) and the corresponding ArH (10 mmol) was added. The magnetic stirring of the resulting mixture was continued at 5 °C for 1 h and then at room temperature for 2 h. The reaction mixture was cooled again to 5 °C and CH_2Cl_2 (10 mL), followed by a saturated aqueous solution of $NaHCO_3$ were added in small portions until pH 8.0. The organic layer was separated, and the aqueous layer was additionally extracted with CH_2Cl_2 (10 mL). The organic extracts were combined and dried with Na_2SO_4, the solvent was evaporated, and the crystalline product was dried in vacuum. Additional purification of products can be performed by crystallization from water.

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (1)

The reaction of 2-iodobenzoic acid 1 (1.00 g, 4.03 mmol), Oxone (1.6g, 2.6 mmol), H_2SO_4 (total 3.2 mL), and benzene (0.8 mL) according to the general procedure afforded 1g (77%) of **1**, isolated as an off-white crystalline solid, mp 221−222 °C; 1H NMR (300 MHz, Chloroform-d) δ 8.24 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.97 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 6.9 Hz, 1H), 7.26 (t, *J* = 6.9 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H); 13C NMR (75 MHz, CDCl3) δ 166.74, 137.21, 133.50, 133.41, 132.48, 132.42, 131.72, 130.45, 126.36, 115.67, 115.37.

1-(2,4,6-trifluorophenyl)-1,2-benziodoxol-3-(1*H*)-one (15)

The reaction of 2-iodobenzoic acid (1.00 g, 4.03 mmol), Oxone© (1.6g, 2.6 mmol), conc. H_2SO_4 (total 3.2 mL), and 1,3,5-trifluorobenzene (0.6 mL) according to the general procedure, afforded 1.1 g (71 %) of **15**, isolated as a white crystalline solid, mp 240 - 242 °C; ^{1}H NMR (300 MHz, Chloroform-d) δ 8.40 (d, *J* = 7.5 Hz, 1H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.06 - 6.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.18, 136.73, 134.58, 133.49, 133.19, 132.81, 131.95, 131.62, 131.31, 127.05, 125.32, 115.59; 19F NMR (282 MHz, Chloroform-d) δ -90.75 - -91.03 (m), -97.02 (p, J = 9.1 Hz).

1-(4-methoxyphenyl)-1,2-benziodoxol-3-(1*H*)-one (16).

The reaction of 2-iodobenzoic acid (1.00 g, 4.03 mmol), Oxone© (1.6 g, 2.6 mmol), H_2SO_4 (total 3.2 mL), and anisole (0.75 mL) according to the general procedure afforded 0.8 g (62 %) of **16**, isolated as brown crystalline solid, mp 212-214 °C; ^{1}H NMR (300 MHz, Chloroform-d) δ 8.37 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.87 (d, *J* = 8.9 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 6.9 Hz, 1H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.75 (d, *J* = 7.8 Hz, 1H), 5.28 (s, 0H), 3.91 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 166.63, 163.09, 139.14, 133.51, 132.71, 130.69, 125.90, 117.79, 116.09, 104.21, 55.78.

5-iodo-1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (17)

The reaction of 2,5 diiodobenzoic acid (0.5 g, 1.33 mmol), Oxone© (0.53g, 0.86 mmol), conc. H_2SO_4 (total 1.6 mL), and benzene (0.4 mL) according to the general procedure, afforded 420 mg (97 %) of **17**, isolated as white solid, mp 224 - 226°C, ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.99 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.67 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 2H), 6.42 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3) δ 142.53, 141.84, 137.26, 133.01, 132.16, 127.84, 115.70, 114.99, 97.60.

5-bromo-1-Phenyl-1,2-benziodoxol-3-(1*H*)-one (18)

The reaction of 5-bromo-2-iodobenzoic acid (1 g, 3.05 mmol), Oxone© (1.12 g, 6.4 mmol), conc. H_2SO_4 (total 3.2 mL), and benzene (0.8 mL) according to the general procedure, afforded 785 mg (64%) of **18**, isolated as off white solid, mp 234 - 236°C, ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.43 (s, 1H), 8.02 (d, *J* = 9.2 Hz, 2H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.42 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.52 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.35, 136.45, 135.69, 132.88, 132.11, 128.11, 125.90, 115.03, 114.46.

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[1] a) E. W. Shefter, W., *J. Pharm. Sci.* **1965**, *54*, 104-107; b) F. de Nanteuil, Y. Li, M. V. Vita, R. Frei, E. Serrano, S. Racine, J. Waser, *Chimia* **2014**, *68*, 516-521; c) H. Pinto de Magalhaes, H. P. Luthi, A. Togni, *J. Org. Chem.* **2014**, *79*, 8374-8382.

[2] J. P. Claude Y. Legaulta, *Acta Crystallogr., Sect. E: Crystallogr. Commun.* **2012**, *E68*, o1238.

[3] L. J. Andrews, R. M. Keefer, *J. Am. Chem. Soc.* **1959**, *81*, 4218-4223.
[4] D. C. Braddock, G. Cansell, S. A. Hermitage, A. J. P. White, *Chem. Commun.* **2006**, 1442-1444.
[5] M. Ochiai, T. Ito, Y. Masaki, M. Shiro, *J. Am. Chem. Soc.* **1992**, *114*, 6269-6270.
[6] V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, M. S. Formaneck, J. T. Bolz, *Tetrahedron Lett.* **1994**, *35*, 9677-9680.
[7] a) V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, B. Mismash, J. K. Woodward, A. J. Simonsen, *Tetrahedron Lett.* **1995**, *36*, 7975-7978; b) V. Matoušek, E. Pietrasiak, R. Schwenk, A. Togni, *J. Org. Chem.* **2013**, *78*, 6763-6768.
[8] Y. Zong, Y. Rao, *Org. Lett.* **2014**, *16*, 5278-5281.
[9] a) M. Ochiai, Y. Masaki, M. Shiro, *J. Org. Chem.* **1991**, *56*, 5511-5513; b) D. Fernandez Gonzalez, J. P. Brand, J. Waser, *Chem. - Eur. J.* **2010**, *16*, 9457-9461, S9457/9451-S9457/9465; c) J. P. Brand, J. Waser, *Synthesis* **2012**, *44*, 1155-1158.
[10] a) P. Eisenberger, S. Gischig, A. Togni, *Chem. - Eur. J.* **2006**, *12*, 2579-2586; b) K. Niedermann, J. M. Welch, R. Koller, J. Cvengroš, N. Santschi, P. Battaglia, A. Togni, *Tetrahedron* **2010**, *66*, 5753-5761; c) I. K. Patrick Eisenberger, Raffael Koller, Kyrill Stanek, and Antonio Togni, *Org. Synth.* **2011**, *88*, 12; d) V. Matousek, P. Beier, A. Togni, EP2982672A1, ETH Zurich, Switz.; Academy of Sciences of the Czech Republic, V.V.I. . **2016**; e) N. Santschi, A. Togni, *Chimia* **2014**, *68*, 419-424; f) V. Matousek, E. Pietrasiak, R. Schwenk, A. Togni, *J. Org. Chem.* **2013**, *78*, 6763-6768.
[11] a) D. Fernandez Gonzalez, J. P. Brand, R. Mondiere, J. Waser, *Adv. Synth. Catal.* **2013**, *355*, 1631-1639; b) J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem., Int. Ed.* **2009**, *48*, 9346-9349, S9346/9341-S9346/9361; c) J. P. Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. - Eur. J.* **2012**, *18*, 5655-5666, S5655/5651-S5655/5668; d) H. Ghari, Y. Li, R. Roohzadeh, P. Caramenti, J. Waser, A. Ariafard, *Dalton Trans.* **2017**, *46*, 12257-12262; e) R. Frei, M. D. Wodrich, D. P. Hari, P.-A. Borin, C. Chauvier, J. Waser, *J. Am. Chem. Soc.* **2014**, *136*, 16563-16573; f) D. P. Hari, J. Waser, *J. Am. Chem. Soc.* **2016**, *138*, 2190-2193; g) D. P. Hari, J. Waser, *J. Am. Chem. Soc.* **2017**, *139*, 8420-8423; h) J. Waser, *Top. Curr. Chem.* **2016**, *373*, 187-222.
[12] a) J. Charpentier, N. Früh, A. Togni, *Chem. Rev.* **2015**, *115*, 650-682; b) E. Mejia, A. Togni, *ACS Catal.* **2012**, *2*, 521-527; c) D. Katayev, H. Kajita, A. Togni, *Chem. - Eur. J.* **2017**, *23*, 8322; d) R. Koller, A. Togni, *Chim. Oggi* **2010**, *28*, 33-35; e) M. S. Wiehn, E. V. Vinogradova, A. Togni, *J. Fluorine Chem.* **2010**, *131*, 951-957; f) N. Santschi, A. Togni, *J. Org. Chem.* **2011**, *76*, 4189-4193; g) D. Katayev, V. Matousek, R. Koller, A. Togni, *Org. Lett.* **2015**, *17*, 5898-5901; h) V. Matousek, A. Togni, V. Bizet, D. Cahard, *Org. Lett.* **2011**, *13*, 5762-5765; i) N. Früh, J. Charpentier, A. Togni, *Top. Curr. Chem.* **2016**, *373*, 167-186.
[13] a) A. Yoshimura, V. V. Zhdankin, *Chem. Rev.* **2016**, *116*, 3328-3435; b) J. P. Brand, D. F. Gonzalez, S. Nicolai, J. Waser, *Chem. Commun.* **2011**, *47*, 102-115; c) Y. Li, D. P. Hari, M. V. Vita, J. Waser, *Angew. Chem., Int. Ed.* **2016**, *55*, 4436-4454; d) M. V. Vita, J. Waser, *Angew. Chem., Int. Ed.* **2015**, *54*, 5290-5292; e) J. Waser, *Synlett* **2016**, *27*, 2761-2773.
[14] M. S. Yusubov, R. Y. Yusubova, V. N. Nemykin, V. V. Zhdankin, *J. Org. Chem.* **2013**, *78*, 3767-3773.
[15] a) N. Juzo, T. Takayuki, H. Masamatsu, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2907-2908; b) D. Del Mazza, M. G. Reinecke, *J. Org. Chem.* **1988**, *53*, 5799-5806.
[16] R. A. Scherrer, H. R. Beatty, *J. Org. Chem.* **1980**, *45*, 2127-2131.
[17] G. Lin, S. S.-K. Chan, H.-S. Chung, S.-L. Li, in *Studies in Natural Products Chemistry, Vol. Volume 32, Part L* (Ed.: R. Atta ur), Elsevier, **2005**, pp. 611-669.
[18] a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879-933; b) C. D. Donner, *Tetrahedron* **2013**, *69*, 3747-3773.
[19] X. Diao, P. Deng, C. Xie, X. Li, D. Zhong, Y. Zhang, X. Chen, *Drug Metab. Dispos.* **2013**, *41*, 430-444.
[20] a) D. Floryk, E. Huberman, *Cancer Lett.* **2006**, *231*, 20-29; b) A. G. Chapuis, G. Paolo Rizzardi, C. D'Agostino, A. Attinger, C. Knabenhans, S. Fleury, H. Acha-Orbea, G. Pantaleo, *Nat. Med.* **2000**, *6*, 762-768.
[21] L. M. Bedoya, E. del Olmo, R. Sancho, B. Barboza, M. Beltrán, A. E. García-Cadenas, S. Sánchez-Palomino, J. L. López-Pérez, E. Muñoz, A. S. Feliciano, J. Alcamí, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4075-4079.
[22] R. Karmakar, P. Pahari, D. Mal, *Chem. Rev.* **2014**, *114*, 6213-6284.
[23] M. Lácová, J. Chovancová, E. Veverková, Š. Toma, *Tetrahedron* **1996**, *52*, 14995-15006.
[24] S. Shapiro, K. Geiger, J. Youlus, L. Freedman, *J. Org. Chem.* **1961**, *26*, 3580-3582.
[25] a) H. Sashida, A. Kawamukai, *Synthesis* **1999**, *1999*, 1145-1148; b) M. Uchiyama, H. Ozawa, K. Takuma, Y. Matsumoto, M. Yonehara, K. Hiroya, T. Sakamoto, *Org. Lett.* **2006**, *8*, 5517-5520; c) C. Kanazawa, M. Terada, *Tetrahedron Lett.* **2007**, *48*, 933-935; d) D. Rambabu, G. P. Kumar, B. D. Kumar, R. Kapavarapu, M. V. B. Rao, M. Pal, *Tetrahedron Lett.* **2013**, *54*, 2989-2995.
[26] a) N. G. Kundu, M. Pal, *J. Chem. Soc., Chem. Commun.* **1993**, 86-88; b) H.-Y. Liao, C.-H. Cheng, *J. Org. Chem.* **1995**, *60*, 3711-3716; c) L. Zhou, H.-F. Jiang, *Tetrahedron Lett.* **2007**, *48*, 8449-8452; d) S. Inack-Ngi, R. Rahmani, L. Commeiras, G. Chouraqui, J. Thibonnet, A. Duchêne, M. Abarbri, J.-L. Parrain, *Adv. Synth. Catal.* **2009**, *351*, 779-788; e) A. Duchêne, J. Thibonnet, J.-L. Parrain, E. Anselmi, M. Abarbri, *Synthesis* **2007**, *2007*, 597-607.
[27] M. R. Kumar, F. M. Irudayanathan, J. H. Moon, S. Lee, *Adv. Synth. Catal.* **2013**, *355*, 3221-3230.
[28] K. Tatsuta, S. Hosokawa, *Chem. Rev.* **2005**, *105*, 4707-4729.
[29] a) S. Dhara, R. Singha, M. Ghosh, A. Ahmed, Y. Nuree, A. Das, J. K. Ray, *RSC Adv.* **2014**, *4*, 42604-42607; b) M. B. Thathagar, J. Beckers, G. Rothenberg, *Green Chem.* **2004**, *6*, 215-218.
[30] R. Chinchilla, C. Nájera, *Chem. Rev.* **2007**, *107*, 874-922.
[31] R. C. Larock, M. J. Doty, X. Han, *J. Org. Chem.* **1999**, *64*, 8770-8779.
[32] a) S. Fantasia, J. M. Welch, A. Togni, *J. Org. Chem.* **2010**, *75*, 1779-1782; b) R. Shimizu, H. Egami, T. Nagi, J. Chae, Y. Hamashima, M. Sodeoka, *Tetrahedron Lett.* **2010**, *51*, 5947-5949.
[33] M. Xia, Z. Chen, *Synth. Commun.* **2000**, *30*, 63-68.
[34] S. V. Giofre, R. Romeo, R. Mancuso, N. Cicero, N. Corriero, U. Chiacchio, G. Romeo, B. Gabriele, *RSC Adv.* **2016**, *6*, 20777-20780.
[35] R. J. Batchelor, T. Birchall, J. F. Sawyer, *Inorg. Chem.* **1986**, *25*, 1415-1420.
[36] X.-D. Fei, Z.-Y. Ge, T. Tang, Y.-M. Zhu, S.-J. Ji, *J. Org. Chem.* **2012**, *77*, 10321-10328.
[37] E. Marchal, P. Uriac, B. Legouin, L. Toupet, P. v. d. Weghe, *Tetrahedron* **2007**, *63*, 9979-9990.
[38] T. F. Mikhailovskaya, S. F. Vasilevsky, *Russ. Chem. Bull.* **2010**, *59*, 632-636.
[39] M. Zhang, H.-J. Zhang, T. Han, W. Ruan, T.-B. Wen, *J. Org. Chem.* **2015**, *80*, 620-627.

Entry for the Table of Contents

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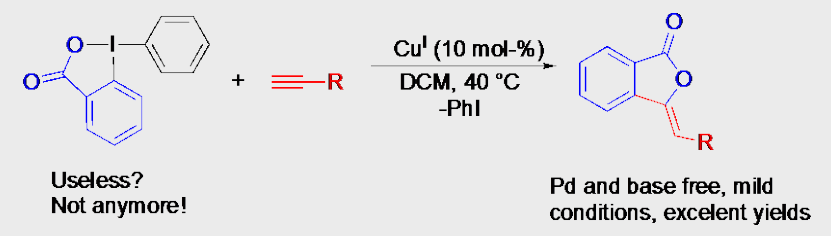

Hypervalent Iodine

*Ahmad A. Almasalma, Esteban Mejía**

Page No. – Page No.

1-Phenyl-1,2-benziodoxol-3-(1*H*)-one as Synthon for Phthalide synthesis via Pd-Free, Base-Free Sonogashira-Type Coupling Cyclization

Herein, we report the first synthetic application of 1-Phenyl-1,2-benziodoxol-3-(1*H*)-one to the synthesis of phthalides using Cu^{I} as catalyst. This unprecedented transformation exploits for the first time the latent reactivity of this somehow neglected kind of hypervalent iodine derivatives. The advantages of this method over the reported alternatives are that neither palladium, nor super-stoichiometric amounts of base are required.