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Sonogashira coupling and cyclization reactions on alumina: a route to aryl alkynes, 2-substituted-benzo[*b*]furans and 2-substituted-indoles

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Abstract—A solventless, microwave-enhanced Sonogashira coupling reaction of aromatic iodides with terminal alkynes on potassium fluoride doped alumina in the presence of palladium powder, cuprous iodide, and triphenylphosphine has been developed. The reaction can be utilized to prepare aryl alkynes in excellent yields. The coupling of *o*-iodophenol with terminal alkynes leads to the formation 2-substituted-benzo[*b*]furans. Whereas the coupling of *o*-iodoanilines with terminal alkynes generates indole products. An in situ desilylation reaction was also developed.

1. Introduction

The Sonogashira coupling reaction of terminal alkynes with aryl halides provides an efficient route to aryl alkynes.[1] Numerous applications to natural product syntheses have been reported, including the construction of complex enediyne antibiotics.[2] The reaction is generally carried out in an organic solvent such as an amine, benzene, THF or DMF along with a complex palladium catalyst which is soluble in these solvents. The prerequisite palladium reagents tend to be expensive and the solvents can pose recyclability (waste handing) problems. In addition, amines such as piperidine, diethylamine and triethylamine are required in most Sonogashira reaction and they add to the environmental burden.

We have found alumina to be a particularly useful reagent in organic synthesis because it can be modified in a variety of ways which enhance its reactivity. Alumina also obviates a number of environmental problems.[3] For example, using a commercially available alumina potassium fluoride mixture to which we added palladium powder, we were able to carry out Suzuki and Sonogashira coupling reactions on a variety of aromatic moieties without the use of a solvent.[4]

Microwave irradiation of organic reactions has gained in popularity since it was found to accelerate a wide variety of transformations.[5] In recent years, a number of reports have appeared in which reactants are coated on to surfaces which themselves absorb little or no microwave energy. In these instances, the reactive species absorb the microwave energy but the temperature of the reaction mixture tends to rise only modestly. This results in relatively large energy savings as well as making it possible to carry out reactions in simple glassware, such as open beakers and flasks.[6]

We now report the details of our study of a solventless, microwave-enhanced, Sonagashira coupling reaction of aromatic iodides with terminal alkynes carried out on potassium fluoride doped alumina in the presence of palladium powder, cuprous iodide, and triphenylphosphine. The reaction produces aryl alkynes in good to excellent yields. We also examined a more direct reaction sequence involving an in situ desilylation followed by Sonogashira coupling of aromatic iodides with 1-substituted-2-(trimethylsilyl)acetylenes. We then examined an in situ cyclization reaction involving the Sonogashira reaction of *o*-iodophenol with terminal alkynes (with and without prior desilylation) which provides a new route to 2-substituted-benzo[*b*]furans. The in situ cyclization was also carried out utilizing *o*-iodoanilines which generates indoles.

2. Results and discussion

A number of reaction parameters (base concentration, temperature, and reaction time) were evaluated in an effort to maximize the yields of the Sonogashira coupling reaction of terminal alkynes with aromatic iodides. The results are summarized in Table 1. Iodobenzene and 1-decyne were chosen as model compounds for the initial study.

Keywords: arylalkynes; solventless coupling; microwave; alumina; indoles; benzofuran.

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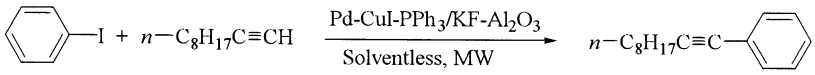
Table 1. The optimization of Sonogashira coupling reaction conditions



Entry	Base (40% by weight)	Pd (mg)	PPh_3 (mg)	CuI (mg)	Reaction time (min.)	Yield (%)[a]
a	K_2CO_3	40	180	70	2.5	20
b	KF	40	180	70	2.5	95
c	NaF	40	180	70	2.5	5
d	K_3PO_4	40	180	70	2.5	0
e	KOH	40	180	70	2.5	72
f	KF	0	180	70	2.5	0
g	KF	10	180	70	2.5	67
h	KF	20	180	70	2.5	87
i	KF	30	180	70	2.5	94
j	KF	40	180	70	2.5	94
k	KF	50	180	70	2.5	93
l	KF	40	0	70	2.5	0
m	KF	40	70	70	2.5	89
n	KF	40	140	70	2.5	94
o	KF	40	180	70	2.5	94
p	KF	40	230	70	2.5	94
q	KF	40	180	0	2.5	0
r	KF	40	180	20	2.5	53
s	KF	40	180	40	2.5	83
t	KF	40	180	60	2.5	93
u	KF	40	180	70	2.5	93
v	KF	40	180	80	2.5	93
w	KF	40	180	90	2.5	93
x	KF	40	180	70	1	28
y	KF	40	180	70	2	89
z	KF	40	180	70	2.5	95
aa	KF	40	180	70	2.75	95
ab	KF	40	180	70	3	95
ac	KF	40	180	70	4	90

Reaction conditions: iodobenzene (1.00 mmol), 1-decyne (1.05 mmol), base (40% by weight)/Al_2O_3 (1.00 g), 1000 watt microwave oven (Sharp R-4A38) used at 100% power.
[a] Isolated yields.

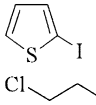
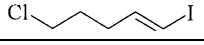
The Sonogashira reaction requires the presence of a base. Of the bases we tested (entries a–e, Table 1), potassium fluoride was the most effective. In addition, KF/Al_2O_3 is commercially available. The palladium powder, triphenylphosphine and cuprous iodide are all essential to the reaction. No reaction occurs in the absence of palladium powder, triphenylphosphine or cuprous iodide (entries f, l, and q, Table 1). The most effective reaction conditions were found to be Pd (40 mg, 99.9+% submicron powder), CuI (70 mg), PPh_3 (180 mg), KF/Al_2O_3 (40% by weight, 1.0 g), terminal alkyne (1.05 mmol) and aryl iodide (1.00 mmol) under microwave irradiation at 100% power for 2.5 min. These conditions were utilized throughout the remainder of the study.

2.1. Sonogashira coupling reaction of organic halides with alkynes

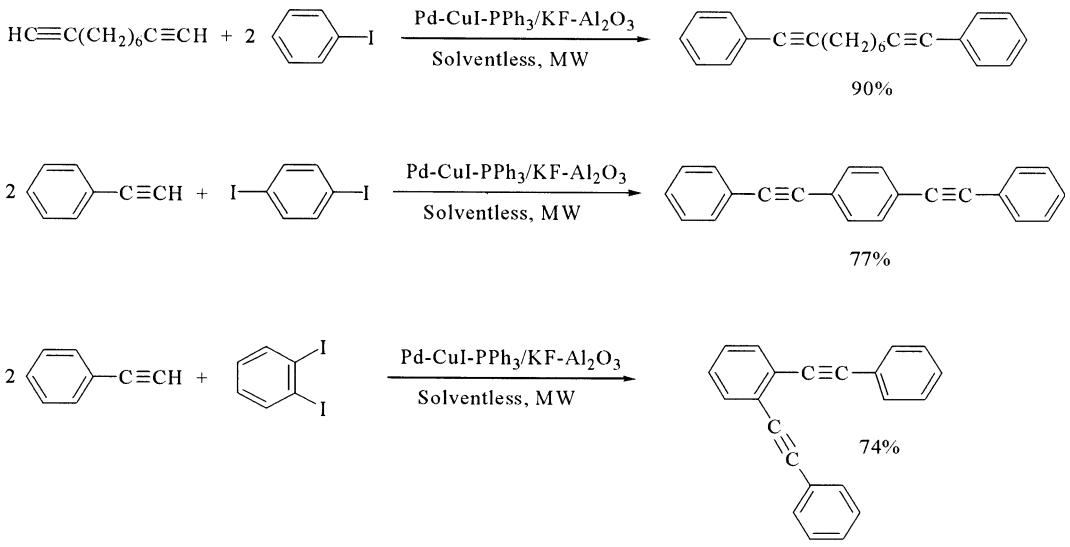
A variety of aromatic terminal alkynes and aliphatic terminal alkynes were successfully coupled with aromatic iodides in excellent yields (Table 2).

Since the solid-state reactions utilize larger quantities of palladium than the corresponding solution reactions,[1] we examined the recyclability of the solid-state catalyst. After carrying out a reaction and isolating the product, additional potassium fluoride and triphenylphosphine were added to the palladium on alumina and the reaction repeated. Only

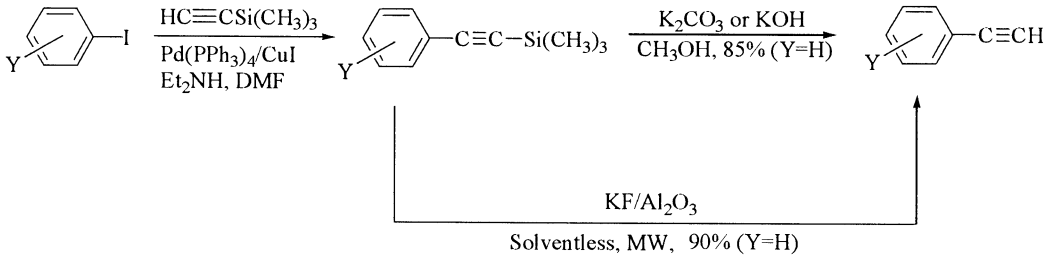
Table 2. Sonogashira coupling reaction of organic halides with terminal alkynes

Entry	R^1X	R^2	Yield (%)[a]
a	C_6H_5I	n-C_8H_{17}	94
b	C_6H_5I	n-C_6H_{13}	84
c	C_6H_5I	C_6H_5	91
d	p-$CH_3C_6H_4I$	n-C_8H_{17}	97
e	p-$CH_3OC_6H_4I$	n-C_8H_{17}	93
f	o-FC_6H_4I	n-C_8H_{17}	84
g	m-FC_6H_4I	n-C_8H_{17}	96
h	p-$CH_3COC_6H_4I$	C_6H_5	82
i	p-$NO_2C_6H_4I$	C_6H_5	67
j	o-$(CH_3)_2NC_6H_4I$	C_6H_5	82
k	C_6H_5I	p-$CH_3C_6H_4$	96
l	C_6H_5I	o-ClC_6H_4	94
m	C_6H_5I	p-FC_6H_4	98
n	C_6H_5I	o-FC_6H_4	91
o	C_6H_5I	p-$CH_3COC_6H_4$	93
p	C_6H_5I	p-BrC_6H_4	88
q		C_6H_5	82
r		C_6H_5	84

Reaction conditions: organic halide (1.00 mmol), alkyne (1.05 mmol), 40% KF/Al_2O_3 (1.00 g), microwave (Sharp R-4A38) time of 2.5 min.
[a] Isolated yields.



Scheme 1. *bis*-Sonogashira reactions.



Scheme 2. Desilylation reactions.

minor decreases in reaction yields were observed through seven repetitive cycles.

Internal alkynes were not reactive. Aryl bromides, aryl chlorides, aryl fluorides and aryl triflates were also not reactive and were recovered unchanged. Aryl diazo salts did not react but simply decomposed under the reaction conditions. Substitutent effects were also examined. The results indicate that the reaction is relatively insensitive to the electronic characteristics of a substituent as well as its location.

We found that 1,9-decadiyne reacts with iodobenzene (excess) to afford the *bis*-Sonogashira coupling product in excellent yield. Phenylacetylene (excess) reacts with both 1,4-diiodobenzene and 1,2-diiodobenzene to generate the corresponding dialkyne in good yields (Scheme 1).

2.2. The Sonogashira coupling of aromatic iodides with 1-substituted-2-(trimethylsilyl)acetylenes

During the study, we generally prepared the aryl terminal alkynes from the corresponding trimethylsilyl reagents using potassium carbonate and potassium fluoride (Scheme 2) in methanol solution.[7] It occurred to us that the potassium fluoride/alumina surface might be an effective desilylating reagent. We then found that phenylacetylene can be prepared from 1-phenyl-2-(trimethylsilyl)acetylene in 90% yield under solvent free conditions. This result led us to use trimethylsilyl derivatives of aryl terminal alkynes in a new one-pot Sonogashira coupling reaction. The trimethylsilylated alkynes react readily with iodobenzene, *p*-methyliodobenzene, *p*-acetyliodobenzene and 2-iodothiophene, respectively, to afford the corresponding coupling products in excellent yields. The results are summarized in Table 3.

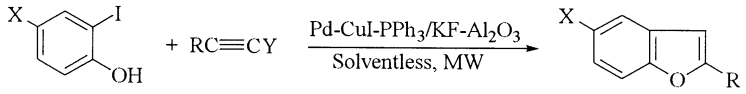
Table 3. Sonogashira coupling reaction of aromatic iodides with 1-substituted-2-(trimethylsilyl)acetylene

$R^1X + R^2C{\equiv}CSi(CH_3)_3 \xrightarrow[\text{Solventless, MW}]{\text{Pd-CuI-PPh}_3/KF\text{-}Al_2O_3} R^2C{\equiv}CR^1$

Entry	R^1X	R^2	Yield (%)[a]
a	C_6H_5I	C_6H_5	90
b	*p*-$CH_3C_6H_4I$	C_6H_5	89
c	C_6H_5I	*p*-$CH_3C_6H_4$	91
d	*p*-$CH_3C_6H_4I$	*p*-$CH_3C_6H_4$	92
e	*p*-$CH_3COC_6H_4I$	*p*-$CH_3COC_6H_4$	78
f	*p*-$CH_3C_6H_4I$	*p*-$CH_3COC_6H_4$	86
g	C_6H_5I	*n*-C_8H_{17}	91
h		*n*-C_8H_{17}	86

Reaction conditions: organic halide (1.00 mmol), alkyne (1.05 mmol), 40% KF/Al_2O_3 (1.00 g), microwave (Sharp R-4A38) time of 2.5 min.
[a] Isolated yields.

Table 4. Sonogashira coupling–cyclization of *o*-iodophenol with terminal alkynes



Entry	X	R	Y	Yield (%)[a]
a	H	C_6H_5	H	54
b	H	C_6H_5	Si $(CH_3)_3$	50
c	H	*p*-$CH_3C_6H_4$	H	53
d	H	*o*-FC_6H_4	H	54
e	H	*p*-BrC_6H_4	H	33
f	H	*n*-C_8H_{17}	H	35
g	H	*n*-C_6H_{13}	H	37
h	CH_3	*p*-$CH_3C_6H_4$	Si $(CH_3)_3$	51
i	CH_3CO	C_6H_5	Si $(CH_3)_3$	49

Reaction conditions: alkyne (1.05 mmol), *o*-iodophenol (1.00 mmol), 40% KF/Al_2O_3 (1.00 g), microwave (Sharp R-4A38) time of 2.5 min.
[a] Isolated yields.

2.3. The formation of 2-substituted-benzo[*b*]furans via the Sonogashira coupling–cyclization of *o*-iodophenol with terminal alkynes

Benzo[*b*]furans and their derivatives have received much attention in recent years because of their occurrence in natural substances and their physiological activity.[8] They are widely used as anti-tumor agents,[9] as ligands of the adenosine A_1 receptor,[10] and as calcium entry blockers.[11] The general routes to benzo[*b*]furans are reductive cyclization of ketoesters by low-valent titanium,[12] photochemically induced rearrangement of phosphate esters,[13] palladium catalyzed Suzuki coupling of appropriate boronic acids with organic halides or triflates[14] and palladium catalyzed Sonogashira coupling followed by cyclization of *o*-iodophenol and terminal alkynes.[15] We investigated the Sonogashira coupling–cyclization of *o*-iodophenol with terminal alkynes to generate 2-substituted-benzo[*b*]furans in the presence of Pd–CuI–Ph_3P–KF/Al_2O_3 under solvent free conditions and microwave irradiation. The results are summarized in Table 4. The yields are moderate to good. In all cases the starting materials were completely utilized and the products were free of volatile contaminants. Presumably, polymerization reactions account for material loss.

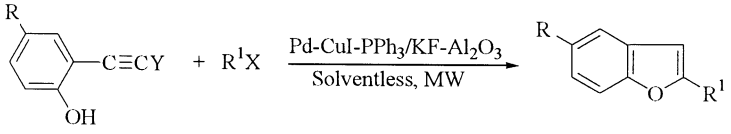
It is noteworthy that 1-substituted-2-(trimethylsilyl)acetylene also reacts with *o*-iodophenol, *p*-methyl-*o*-iodophenol and *p*-acetyl-*o*-iodophenol, respectively, to generate the corresponding 2,5-disubstituted-benzo[*b*]furans in a one-pot reaction through sequential desilylation, coupling and cyclization reactions.

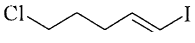
2.4. The synthesis of 2-substituted-benzo[*b*]furans via the Sonogashira coupling–cyclization of *o*-ethynylphenol or *o*-((trimethylsilyl)ethynyl)phenol with aromatic iodides

According to a retro-synthetic analysis, 2-substituted-benzo[*b*]furans could also be synthesized from *o*-ethynylphenol or *o*-((trimethylsilyl)ethynyl)phenol via a reaction with aromatic or vinyl iodides.

The results of a study of the Sonogashira coupling–cyclization reaction of *o*-ethynylphenol (or desilylation–coupling–cyclization of *o*-((trimethylsilyl)ethynyl)phenol with

Table 5. Sonogashira coupling–cyclization of *o*-ethynylphenol or desilylation–coupling–cyclization of *o*-[(trimethylsilyl)ethynyl]phenol with organic iodides



Entry	R	Y	R^1X	Yield (%)[a]
a	H	H	C_6H_5I	56
b	H	Si $(CH_3)_3$	C_6H_5I	49
c	H	Si $(CH_3)_3$	*m*-FC_6H_4I	47
d	H	Si $(CH_3)_3$		50
e	H	Si $(CH_3)_3$	*p*-$CH_3OC_6H_4I$	44
f	H	Si $(CH_3)_3$	*p*-$CH_3COC_6H_4I$	42
g	H	Si $(CH_3)_3$		31
h	CH_3	Si $(CH_3)_3$	*p*-$CH_3C_6H_4I$	48
i	CH_3	H	*p*-$CH_3C_6H_4I$	53
j	CH_3CO	Si $(CH_3)_3$	C_6H_5I	46
k	CH_3CO	H	C_6H_5I	50

Reaction conditions: alkyne (1.05 mmol), organic iodide (1.00 mmol), 40% KF/Al_2O_3 (1.00 g), microwave (Sharp R-4A38) time of 2.5 min.
[a] Isolated yields.

aromatic or vinyl iodides are listed in Table 5. As noted earlier, the products were formed free of volatile contaminants. Less than quantitative yields are presumably due to polymerization reactions. *o*-Ethynylphenol and *o*-((trimethylsilyl)ethynyl)phenol react with aromatic or vinyl iodides to readily afford the desired 2-substituted-benzo[*b*]furans in a one-pot reaction.

We then investigated the application of this coupling–cyclization reaction to the synthesis of indoles. The reactions of *o*-iodoaniline, *o*-iodoacetanilide, *o*-iodotrifluoroacetanilide, and *N*-(*o*-iodophenyl)methanesulfonamide with terminal alkynes were investigated. The results of the study are presented in Scheme 3. In the presence of Pd–CuI–PPh_3/KF–Al_2O_3, and under solvent free conditions and microwave irradiation, only the coupling product was obtained (83%) when *o*-iodoaniline was allowed to react with phenylacetylene. When excess *o*-iodoaniline (2 equiv.) was used, a mixture of coupling and coupling-cyclization products was obtained. Additional Pd(II) increased the formation of the indole product which parallels results obtained in solution.[16] When *o*-iodoacetanilide was used in place of *o*-iodoaniline, only the indole product formed (41%). The use of (*o*-iodophenyl)-methanesulfonamide resulted in the exclusive formation of the indole in good yield.

We then examined the reaction of *o*-ethynylaniline with aromatic iodides. *o*-Ethynylaniline was synthesized via the Sonogashira coupling reaction of *o*-iodoaniline with (trimethylsilyl)acetylene, followed by desilylation under solvent free conditions and microwave irradiation on potassium fluoride doped alumina. Reactions were also carried out using *o*-ethynylacetanilide, *o*-ethynyltrifluoroacetanilide, and *N*-(*o*-ethynylphenyl)methanesulfonamide.

In the presence of Pd–CuI–PPh_3/KF–Al_2O_3, under solvent free conditions and microwave irradiation, a mixture of *o*-ethynylaniline and iodobenzene yielded both the coupling and coupling–cyclization products in the ratio of 93:7.

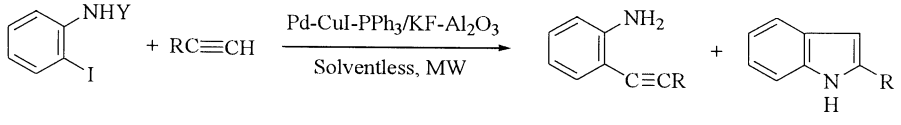
When additional Pd(II) was added to the reaction mixture, the percentabe of indole product was increased. When *o*-ethynylacetanilide was used in place of *o*-ethynylaniline, only the coupling–deprotection–cyclization product was formed. *N*-(*o*-Ethynylphenyl)methanesulfonamide also generated the indole product exclusively, whereas, *o*-ethynyltrifluoroacetanilide yielded a mixture of coupling and coupling–deprotection–cyclization products.

3. Experimental

Melting points were recorded on a MEL-TEMP melting point apparatus and are uncorrected. All ^1H- and ^{13}C NMR spectra were recorded on a 250 MHz Bruker AC 250 spectrometer. Chemical shift are given as δ value with reference to tetramethylsilane (TMS) as an internal standard. GC MS data were obtained using a Hewlett-Packard 6890 series GC equipped with a 5973 mass selective detector. Microanalyses were performed by Atlantic Microlabs, Norcross, GA. A commercially available Sharp Model R-4A38, 1000 watts microwave oven was utilized at 30–100% power in this study. Palladium (99.9+% as submicron powder) and KF/Al_2O_3 (40% by weight) were purchased from Aldrich Chemical Co. Other reagents were analytical grade and used as received. Products were purified by flash chromatography on 230–400 mesh ASTM 60 Å silica gel, SiO_2.

3.1. General procedure: Sonogashira reaction of aryl iodide with terminal alkynes

Aryl iodide (1.00 mmol) and terminal alkyne (1.05 mmol) were added to a mixture of KF/Al_2O_3 (1.00 g, 40% by weight), palladium powder (0.040 g, 0.376 mmol, 99.9+% as a submicron powder), cuprous iodide (0.070 g, 0.368 mmol) and triphenylphosphine (0.180 g, 0.686 mmol) contained in a clean, dry, 25 mL round-bottomed flask. The mixture was then fitted with a septum (punctured by an 18 gauge needle to serve as a pressure release valve), placed in the microwave oven and irradiated at 100% power for 2.5 min. CAUTION!: The microwave irradiation should not be attempted in the absence of alumina which apparently acts as a temperature moderator. Without alumina, the liquid reactants can react uncontrollably in the presence of metallic palladium (DANGER). After cooling, hexane (5 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The mixture was vacuum filtered using a sintered glass funnel and the



		Overall Yield (%)	Ratio		
Y=H	R=C_6H_5	83	100	:	0
Y=H (2 eq.)	R=C_6H_5 (1 eq.)	84	54	:	46
Y=H	R=C_6H_5 [addition of Pd(II)]	67	18	:	82
Y=$COCH_3$	R=C_6H_5	41	0	:	100
Y=$COCF_3$	R=C_6H_5	68	38	:	62
Y=SO_2CH_3	R=C_6H_5	80	0	:	100
Y= H	R=*p*-$CH_3C_6H_4$	87	100	:	0
Y=$COCF_3$	R=*p*-$CH_3C_6H_4$	70	43	:	57

Scheme 3. The synthesis of indoles.

product was purified by flash chromatography to yield the desired aryl alkyne.

3.1.1. 1-Phenyl-1-decyne. Oil[17]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40–7.36 (m, 2H), 7.28–7.22 (m, 3H), 2.38 (t, J=6.96 Hz, 2H), 1.64–1.53 (m, 2H), 1.45–1.28 (m, 10H), 0.88 (t, J=6.54 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.5, 128.1, 127.3, 124.2, 90.3, 80.6, 31.9, 29.2, 29.2, 28.9, 28.8, 22.7, 19.4, 14.1; MS *m/z* (relative intensity) 214 (M^+, 13), 171 (3), 157 (17), 143 (60), 129 (66), 115 (100), 91 (41).

3.1.2. 1-Phenyl-1-octyne. Oil[18]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40–7.37 (m, 2H), 7.30–7.23 (m, 3H), 2.39 (t, J=6.97 Hz, 2H), 1.65–1.54 (m, 2H), 1.50–1.26 (m, 6H), 0.90 (t, J=6.68 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.5, 128.1, 127.4, 124.2, 90.4, 80.6, 31.4, 28.7, 28.6, 22.6, 19.4, 14.0; MS *m/z* (relative intensity) 186 (M^+, 26), 157 (15), 143 (55), 129 (54), 115 (100), 91 (31).

3.1.3. Diphenylacetylene. Mp 59–61°C (lit.[19] 60–62°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.54–7.50 (m, 4H), 7.32–7.28 (m, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.6, 128.3, 128.2, 123.3, 89.4; MS *m/z* (relative intensity) 178 (M^+, 100), 152 (14), 126 (7), 89 (13).

3.1.4. 1-(4-Methylphenyl)-1-decyne. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.27 (d, J=8.00 Hz, 2H), 7.04 (d, J=7.93 Hz, 2H), 2.38 (t, J=7.56 Hz, 2H), 2.29 (s, 3H), 1.63–1.52 (m, 2H), 1.45–1.28 (m, 10H), 0.88 (t, J=6.46 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 137.2, 131.4, 128.8, 121.1, 89.5, 80.6, 31.9, 29.2, 29.1, 28.9, 28.8, 22.7, 21.3, 19.4, 14.0; MS *m/z* (relative intensity) 228 (M^+, 16), 185 (3), 171 (13), 157 (36), 143 (32), 131 (100), 115 (24), 91 (11). Anal. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59. Found: C, 89.43; H, 10.66.

3.1.5. 1-(4-Methoxyphenyl)-1-decyne. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.32 (d, J=8.72 Hz, 2H), 6.80 (d, J=8.73 Hz, 2H), 3.78 (s, 3H), 2.37 (t, J=6.99 Hz, 2H), 1.64–1.53 (m, 2H), 1.46–1.28 (m, 10H), 0.88 (t, J=6.00 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 159.0, 132.8, 116.3, 113.8, 88.7, 80.2, 55.2, 31.8, 29.2, 29.1, 28.9, 22.2, 19.4, 14.1; MS *m/z* (relative intensity) 244 (M^+, 19), 201 (4), 188 (22), 173 (29), 159 (25), 147 (100), 121 (33), 115 (21), 91 (15). Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.51; H, 9.92.

3.1.6. 1-(2-Fluorophenyl)-1-decyne. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41–7.34 (m, 1H), 7.25–7.16 (m, 1H), 7.05–6.96 (m, 2H), 2.43 (t, J=6.98 Hz, 2H), 1.66–1.55 (m, 2H), 1.52–1.28 (m, 10H), 0.88 (t, J=6.51 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.4 (d, J=248.4 Hz), 133.5, 129.0 (d, J=7.6 Hz), 123.7 (d, J=3.4 Hz), 115.3 (d, J=21.4 Hz), 112.6 (d, J=15.5 Hz), 95.9 (d, J=3.0 Hz), 73.9, 31.9, 29.2, 29.1, 28.9, 28.6, 22.7, 19.6, 14.1; MS *m/z* (relative intensity) 232 (M^+, 58), 175 (37), 161 (71), 147 (64), 133 (100), 109 (55). Anal. Calcd for $C_{16}H_{21}F$: C, 82.71; H, 9.11. Found: C, 82.83; H, 9.17.

3.1.7. 1-(3-Fluorophenyl)-1-decyne. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.23–7.05 (m, 3H), 6.99–6.92 (m, 1H), 2.38 (t, J=7.00 Hz, 2H), 1.62–1.54 (m, 2H), 1.46–1.29 (m, 10H), 0.89 (t, J=5.98 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.4 (d, J=244.4 Hz), 129.6 (d, J=9.1 Hz), 127.4, 126.0 (d, J=9.4 Hz), 118.3 (d, J=21.7 Hz), 114.7 (d, J=20.9 Hz), 91.6, 79.5, 31.8, 29.2, 29.1, 28.9, 28.6, 22.7, 19.4, 14.1; MS *m/z* (relative intensity) 232 (M^+, 14), 175 (26), 161 (59), 147 (74), 133 (100), 109 (58). Anal. Calcd for $C_{16}H_{21}F$: C, 82.71; H, 9.11. Found: C, 82.63; H, 9.17.

3.1.8. (4-Acetylphenyl)phenylacetylene. Mp 95–96°C (lit.[20] 94–96°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.91 (d, J=8.42 Hz, 2H), 7.58 (d, J=8.41 Hz, 2H), 7.54–7.52 (m, 2H), 7.36–7.33 (m, 3H), 2.57 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 197.1, 136.1, 131.7, 131.6, 128.7, 128.4, 128.2, 128.1, 122.6, 92.6, 88.6, 26.5; MS *m/z* (relative intensity) 220 (M^+, 60), 205 (100), 176 (48), 151 (18), 102 (10), 88 (19).

3.1.9. (4-Nitrophenyl)phenylacetylene. Mp 120–122°C (lit.[21] 120–121°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.19 (d, J=8.83 Hz, 2H), 7.64 (d, J=8.73 Hz, 2H), 7.57–7.53 (m, 2H), 7.39–7.37 (m, 3H), 2.57 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 146.9, 132.2, 131.8, 130.2, 129.2, 128.5, 123.6, 122.0, 94.7, 87.5; MS *m/z* (relative intensity) 223 (M^+, 100), 193 (40), 176 (80), 165 (33), 151 (40), 139 (8), 126 (14).

3.1.10. *N*,*N*-Dimethyl-2-(phenylethynyl)benzeneamine. Mp 46–47°C (lit.[22] 45–48°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.54–7.46 (m, 3H), 7.34–7.17 (m, 4H), 6.89–6.82 (m, 2H), 2.96 (s, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.6, 134.2, 131.1, 129.1, 128.2, 127.9, 123.8, 120.3, 116.8, 114.9, 94.6, 88.9, 43.3; MS *m/z* (relative intensity) 220 (M^+, 100), 204 (22), 178 (15), 144 (68).

3.1.11. Phenyl-*p*-tolylacetylene. Mp 71–73°C (lit.[23] 72–73°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.41 (d, J=7.81 Hz, 2H), 7.29–7.26 (m, 3H), 7.10 (d, J=7.84 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 138.3, 131.5, 129.0, 128.2, 128.0, 123.4, 120.2, 89.6, 88.7, 21.4; MS *m/z* (relative intensity) 192 (M^+, 100), 165 (15), 139 (4), 115 (6), 94 (10).

3.1.12. (2-Chlorophenyl)phenylacetylene. Oil[24]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.58–7.50 (m, 3H), 7.40–7.30 (m, 4H), 7.20–7.16 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 135.8, 133.1, 131.7, 129.2, 128.6, 128.3, 126.4, 123.1, 122.8, 94.5, 86.2; MS *m/z* (relative intensity) 214, 212 (M^+, 32, 100), 176 (44), 151 (14), 106 (15), 88 (20).

3.1.13. (4-Fluorophenyl)phenylacetylene. Mp 108–110°C (lit.[25] 108–109°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.53–7.47 (m, 4H), 7.35–7.31 (m, 3H), 7.06–6.99 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.5 (d, J=248.1 Hz), 133.5 (d, J=8.9 Hz), 131.5, 128.3, 123.1, 119.3 (d, J=5.6 Hz), 115.6 (d, J=22.4 Hz), 89.0, 88.3; MS *m/z* (relative intensity) 196 (M^+, 100), 175 (7), 144 (5), 98 (15).

3.1.14. (2-Fluorophenyl)phenylacetylene. Mp 46–48°C (lit.[26] 46–47°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.56–7.46 (m, 3H), 7.32–7.21 (m, 4H), 7.10–7.02 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 162.6 (d, J=250.1 Hz), 133.4, 131.6, 129.9 (d, J=7.7 Hz), 128.5, 128.3, 123.9 (d, J=2.6 Hz),

122.9, 115.4 (d, J=20.8 Hz), 111.9 (d, J=15.3 Hz), 94.4, 82.7; MS m/z (relative intensity) 196 (M^+, 100), 175 (8), 170 (11), 144 (5), 98 (17), 85 (12).

3.1.15. (4-Bromophenyl)phenylacetylene. Mp 83–84°C (lit.[25] 82–84°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.53–7.44 (m, 4H), 7.38–7.32 (m, 5H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 133.0, 131.6, 128.5, 128.4, 122.9, 122.5, 122.2, 90.5, 88.3. MS m/z (relative intensity) 258, 256 (M^+, 97, 100), 176 (88), 151 (37), 128 (17), 88 (61).

3.1.16. 2-Phenylethynylthiophene. Mp 51–53°C (lit.[27] 51–52°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.51–7.47 (m, 2H), 7.31–7.22 (m, 5H), 6.98–6.94 (m, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.8, 131.4, 128.3, 127.2, 127.0, 123.3, 122.9, 93.0, 82.6; MS m/z (relative intensity) 184 (M^+, 100), 152 (17), 139 (21), 92 (9).

3.1.17. 7-Chloro-1-phenyl-3-hepten-1-yne. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.44–7.40 (m, 2H), 7.31–7.27 (m, 3H), 6.23–6.11 (m, 1H), 5.74 (d, J=16.89 Hz, 1H), 3.52 (t, J=6.79 Hz, 2H), 2.35–2.26 (m, 2H), 1.92–1.81 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 142.5, 131.4, 128.2, 128.0, 123.3, 111.0, 88.4, 87.8, 44.0, 31.4, 30.1; MS m/z (relative intensity) 206, 204 (M^+, 14, 42), 155 (55), 141 (100), 128 (22), 115 (73), 91 (29). Anal. Calcd for $C_{13}H_{13}Cl$: C, 76.28; H, 6.40. Found: C, 76.12; H, 6.50.

3.1.18. 1,10-Diphenyl-1,9-decadiyne. The titled compound was prepared as general procedure of Sonogashira reaction from iodobenzene (2.00 mmol) and 1,9-decadiyne (1.00 mmol) by using KF/Al_2O_3 (2.00 g, 40% by weight), palladium powder (0.080 g, 0.752 mmol, 99.9+% as submicron powder), cuprous iodide (0.140 g, 0.736 mmol) and triphenylphosphine (0.360 g, 1.372 mmol). Oil[28]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41–7.38 (m, 2×2H), 7.31–7.23 (m, 2×3H), 2.40 (t, J=6.76 Hz, 2×2H), 1.61–1.48 (m, 4×2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.5, 128.1, 127.4, 126.6, 90.2, 80.7, 28.6, 28.3, 19.3; MS m/z (relative intensity) 286 (M^+, 7), 258 (11), 243 (10), 229 (10), 215 (10), 178 (8), 167 (17), 153 (9), 141 (20), 128 (41), 115 (100), 91 (43).

3.1.19. 1,4-Di(phenylethynyl)benzene. The titled compound was generated as general procedure of Sonogashira reaction from 1,4-diiodobenzene (1.00 mmol) and phenylethyne (2.00 mmol) by using KF/Al_2O_3 (2.00 g, 40% by weight), palladium powder (0.080 g, 0.752 mmol, 99.9+% as submicron powder), cuprous iodide (0.140 g, 0.736 mmol) and triphenylphosphine (0.360 g, 1.372 mmol). Mp 177–179°C (lit.[29] 178–179°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.55–7.50 (m, 8H), 7.35–7.33 (m, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.6, 131.5, 128.4, 128.4, 123.1, 123.0, 91.2, 89.1; MS m/z (relative intensity) 278 (M^+, 100), 250 (4), 224 (4), 200 (4), 139 (33).

3.1.20. 1,2-Di(phenylethynyl)benzene. The titled compound was synthesized as described for 1, 4-di(phenylethynyl)benzene from 1,2-diiodobenzene (1.00 mmol) and phenylethyne (2.00 mmol). Mp 47–48°C (lit.[30] 48°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.58–7.52 (m, 6H), 7.32–7.24 (m, 8H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 131.7, 131.6, 128.3, 128.0, 125.8, 123.3, 93.6, 88.3; MS m/z (relative intensity) 278 (M^+, 70), 250 (5), 207 (100), 191 (11), 138 (36).

3.1.21. Phenylacetylene. 1-Phenyl-2-(trimethylsilyl)-acetylene (0.870 g, 5.00 mmol) was added to KF/Al_2O_3 (3.00 g, 40% by weight) contained in a 25 mL round-bottomed flask. The mixture was stirred at room temperature to ensure efficient mixing. The flask was then fitted with a septum, placed in the microwave oven and irradiated at 30% power for 3 min. After cooling, hexane (10 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The mixture was vacuum filtered and the product purified by flash chromatography (hexane as eluent agent) to yield 0.460 g (90% yield) of phenylacetylene. Oil[31]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.49–7.45 (m, 2H), 7.27–7.24 (m, 3H), 3.04 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 132.0, 128.7, 128.2, 122.1, 83.6, 77.2; MS m/z (relative intensity) 102 (M^+, 100), 76 (26), 63 (6), 50 (12).

3.2. Recycling of the palladium/alumina catalyst

Reactions were carried out as described in Section 3.1. After filtration of the alkyne products from the surface, the solid support was washed sequentially with methanol (2×5 mL). Potassium fluoride (0.40 g) and triphenylphosphine (0.180 g) were added and the coupling reaction was repeated as described in Section 3.1.

3.3. General procedure for the synthesis of aryl alkynes via the desilylation–coupling reaction of aryl iodide with 1-substituted-2-(trimethylsilyl)acetylene, one-pot reaction

The reaction conditions were identical to those described earlier for the reactions of aryliodides with alkynes. In these reactions, the trimethylsilated alkyne was simply substituted for the alkyne.

3.3.1. 1,2-Di(4-methylphenyl)ethyne. Mp 134–136°C (lit.[29] 134–135°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40 (d, J=8.02 Hz, 2×2H), 7.17 (d, J=7.91 Hz, 2×2H), 2.32 (s, 2×3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 138.1, 131.4, 129.1, 120.4, 88.9, 21.4; MS m/z (relative intensity) 206 (M^+, 100), 191 (18), 176 (4), 165 (9), 139 (7), 115 (6).

3.3.2. 1,2-Di(4-acetylphenyl)ethyne. Mp 198–200°C (lit.[32] 198.5–200°C); ^{1}H NMR (250 Hz, $CDCl_3$) δ 7.95 (d, J=7.87 Hz, 2×2H), 7.63 (d, J=7.86 Hz, 2×2H), 2.62 (s, 2×3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 197.2, 136.6, 131.8, 128.3, 127.4, 91.6, 26.6; MS m/z (relative intensity) 262 (M^+, 46), 247 (100), 204 (20), 189 (12), 176 (35), 116 (29).

3.3.3. 1-(4-*p*-Tolylethynylphenyl)ethanone. Mp 125–126°C (lit.[33] 124–126°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.89 (d, J=8.22 Hz, 2H), 7.56 (d, J=8.32 Hz, 2H), 7.42 (d, J=7.99 Hz, 2H), 7.14 (d, J=7.87 Hz, 2H), 2.56 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 197.1, 139.0, 135.9, 131.6, 131.5, 129.1, 128.3, 128.1, 119.5, 93.0, 88.0, 26.4, 21.4; MS m/z (relative intensity) 234 (M^+, 64), 219 (100), 189 (48), 165 (11), 109 (21), 95 (25).

3.3.4. 2-(1-Decyl)thiophene. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.14–7.09(m, 2H), 6.91 (t, J=4.37 Hz, 1H), 2.40 (t, J=7.01 Hz, 2H), 1.64–1.51 (m, 2H), 1.45–1.28 (m, 10H), 0.88 (t, J=6.34 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 130.8, 126.7, 125.7, 124.3, 94.5, 73.7, 31.8, 29.2, 29.1, 28.9, 28.6, 22.7, 19.7, 14.1; MS *m/z* (relative intensity) 220 (M^+, 13), 177 (5), 163 (15), 149 (27), 123 (100), 97 (30). Anal. Calcd for $C_{14}H_{20}S$: C, 76.30; H, 9.15. Found: C, 76.60; H, 9.19.

3.4. One-pot synthesis of 2-substitutited-benzo[*b*]furans via the coupling–cyclization of *o*-iodophenol with terminal alkynes or 1-substituted-2-(trimethylsilyl)-ethylene with terminal alkynes. General procedure

o-Iodophenol (0.220 g, 1.00 mmol) and terminal alkyne (1.00 mmol) or 1-substituted-2-(trimethylsilyl)ethylene (1.00 mmol) was added to a mixture of of KF/Al_2O_3 (1.00 g, 40% by weight), palladium powder (0.040 g, 0.376 mmol, 99.9+% as submicron powder), cuprous iodide (0.070 g, 0.368 mmol) and triphenylphosphine (0.180 g, 0.686 mmol) contained in a clean, dry, 25 mL round-bottomed flask. The mixture was then fitted with a septum (punctured by an 18 gauge needle), placed in the microwave oven and irradiated at 100% power for 3.5 min. After cooling, hexane (5 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The mixture was vacuum filtered using a sintered glass funnel and the product was purified by flash chromatography (hexane–EtOAc as eluting agent) to afford the desired 2-substituted-benzo[*b*]furan.

3.4.1. 2-Phenylbenzofuran. Mp 118–120°C (lit.[34] 119–120°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.85–7.82 (m, 2H), 7.56–7.19 (m, 7H), 6.96 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 155.9, 154.9, 130.5, 129.2, 128.7, 128.5, 124.9, 124.2, 122.9, 120.9, 111.2, 101.3; MS *m/z* (relative intensity) 194 (M^+, 100), 165 (55), 139 (10), 115 (6), 97 (16), 82 (20).

3.4.2. 2-*p*-Tolylbenzofuran. Mp 126–128°C (lit.[35] 127°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.73 (d, J=8.13 Hz, 2H), 7.55–7.44 (m, 2H), 7.25–7.19 (m, 4H), 6.91 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 156.2, 154.8, 138.5, 129.5, 129.4, 127.8, 124.9, 124.0, 122.8, 120.7, 111.1, 100.5, 21.3; MS *m/z* (relative intensity) 208 (M^+, 100), 178 (18), 165 (18), 152 (8), 139 (5), 104 (13), 89 (19).

3.4.3. 2-(2-Fluorophenyl)benzofuran. Mp 44–45°C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.02–7.95 (m, 1H), 7.58–7.47 (m, 2H), 7.30–7.06 (m, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 159.5 (d, J=250.5 Hz), 154.1, 149.8 (d, J=3.0 Hz), 129.4 (d, J=8.3 Hz), 126.9, 124.7, 124.3, 122.9, 121.3, 118.7 (d, J=11.4 Hz), 115.9 (d, J=22.1 Hz), 111.0, 106.6 (d, J=12.7 Hz); MS *m/z* (relative intensity) 212 (M^+, 100), 183 (55), 157 (8), 133 (5), 106 (18), 91 (13). Anal. Calcd for $C_{14}H_9OF$: C, 79.22; H, 4.28. Found: C, 79.10; H, 4.30.

3.4.4. 2-(4-Bromophenyl)benzofuran. Mp 159–161°C (lit.[36] 160°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.72 (d, J=8.57 Hz, 2H), 7.58–7.50 (m, 4H), 7.33–7.20 (m, 2H), 7.02 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.9, 154.8, 132.0, 129.4, 129.1, 126.4, 124.6, 123.1, 122.5, 121.0, 111.2, 101.8; MS *m/z* (relative intensity) 274, 272 (M^+, 98, 98), 165 (100), 137 (31), 83 (71).

3.4.5. 2-Octylbenzofuran. Oil[37]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.48–7.38 (m, 2H), 7.21–7.12 (m, 2H), 6.35 (s, 1H), 2.74 (t, J=7.51 Hz, 2H), 1.75–1.67 (m, 2H), 1.50–1.27 (m, 10H), 0.88 (t, J=5.92 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 159.8, 154.6, 129.0, 123.0, 122.3, 120.1, 110.7, 101.7, 31.9, 29.3, 29.2, 28.5, 27.7, 22.7, 14.1; MS *m/z* (relative intensity) 230 (M^+, 10), 187 (6), 173 (8), 145 (9), 131 (100), 77 (11).

3.4.6. 2-Hexylbenzofuran. Oil[38]; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.47–7.38 (m, 2H), 7.21–7.12 (m, 2H), 6.34 (s, 1H), 2.74 (t, J=7.54 Hz, 2H), 1.78–1.66 (m, 2H), 1.48–1.27 (m, 6H), 0.89 (t, J=6.52 Hz, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 159.8, 154.6, 129.0, 123.0, 122.3, 120.1, 110.7, 101.7, 31.6, 28.9, 28.5, 27.7, 22.6, 14.1; MS *m/z* (relative intensity) 202 (M^+, 18), 173 (5), 145 (8), 131 (100), 95 (21), 77 (11).

3.4.7. 5-Methyl-2-(4-methylphenyl)benzofuran. Mp 155–157°C (lit.[39] 155–156°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.69 (d, J=7.67 Hz, 2H), 7.35 (d, J=8.33 Hz, 1H), 7.27 (s, 1H), 7.18 (d, J=7.83 Hz, 2H), 7.03 (d, J=8.31 Hz, 1H), 6.80 (s, 1H), 2.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 156.2, 153.2, 138.3, 132.2, 129.4, 127.9, 125.2, 124.8, 120.6, 110.5, 100.3, 21.3; MS *m/z* (relative intensity) 222 (M^+, 100), 207 (4), 178 (27), 165 (8), 152 (10), 110 (29).

3.4.8. 5-Acetyl-2-phenylbenzofuran. Mp 162–164°C (lit.[40] 162–163.5°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.95 (d, J=8.48 Hz, 1H), 7.87 (d, J=7.35 Hz, 2H), 7.55 (d, J=8.64 Hz, 1H), 7.50–7.38 (m, 3H), 7.08 (s, 1H), 2.67 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 197.6, 157.6, 157.4, 132.9, 129.8, 129.3, 129.1, 128.9, 125.1, 122.1, 111.1, 101.6, 26.7; MS *m/z* (relative intensity) 236 (M^+, 61), 221 (100), 193 (48), 165 (29), 139 (39), 110 (28), 82 (40).

3.5. Preparation of *o*-((trimethylsilyl)ethynyl)phenol and *o*-ethynylphenol

To a stirred solution of *o*-iodophenol (1.100 g, 5.00 mmol) and Et_3N–Dioxane (8 mL, 1:1 mixture), $PdCl_2(PPh_3)_2$ (0.035 g, 0.050 mmol) and CuI (0.019 g, 0.100 mmol), (trimethylsilyl)acetylene (0.85 mL, 6.00 mmol) was added dropwise at room temperature under nitrogen. The reaction mixture was stirred overnight. Triethylamine, dioxane and unreacted (trimethylsilyl)acetylene were removed under reduced pressure. The product was extracted into Et_2O (3×20 mL) and combined organic phase was washed with H_2O, dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified by column chromatography (silica gel, hexane–ethyl acetate 94/6 (v/v)) to give 0.858 g (90% yield) of *o*-((trimethylsilyl)ethynyl)-phenol. Mp 46–48°C (lit.[7b] 46–47°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.32 (dd, J=6.28, 1.43 Hz, 1H), 7.20 (dt, J=7.00, 1.46 Hz, 1H), 6.93 (d, J=8.22 Hz, 1H), 6.82 (t, J=7.56 Hz, 1H), 5.90 (s, 1H), 0.26 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 157.0, 131.6, 130.6, 120.1, 114.5, 109.5, 102.2, 99.0, −0.1; MS *m/z* (relative intensity) 190 (M^+, 18), 175 (100), 159 (19), 135 (13), 115 (16), 77 (14).

o-((Trimethylsilyl)ethynyl)phenol (0.570 g, 3.00 mmol) was added to KF/Al_2O_3 (2.00 g, 40% by weight) and stirred at room temperature to ensure efficient mixing. The resultant mixture was placed in the microwave oven and irradiated at 30% power for 3 min. After cooling, hexane (10 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The product was purified by chromatography (hexane–ethyl acetate: 85/15) to afford 0.275 g (85% yield) of *o*-ethynylphenol. Oil;[41] ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.38 (d, J=7.51 Hz, 1H), 7.27 (dt, J=7.65, 1.04 Hz, 1H), 6.95 (d, J=8.20 Hz, 1H), 6.87 (t, J=7.48 Hz, 1H), 5.80 (s, br, 1H), 3.46 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 157.4, 132.0, 130.9, 120.3, 114.8, 108.3, 84.3, 78.3; MS *m/z* (relative intensity) 118 (M^+, 100), 89 (44), 63 (21).

3.6. One-pot coupling–cyclization reaction of *o*-ethynylphenol and *o*-((trimethylsilyl)ethynyl)phenol with aryl and vinyl iodides

The general procedure was identical as that described for the synthesis of 2-substituted benzo[*b*]furan from *o*-ethynylphenol or (*o*-((trimethylsilyl)ethynyl)phenol).

3.6.1. 2-(3-Fluorophenyl)benzofuran. Mp 82–84°C (lit.[36] 83°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.62–7.49 (m, 4H), 7.41–7.19 (m, 3H), 7.05–6.98 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 163.1 (d, J=244.4 Hz), 154.9, 154.5, 132.5 (d, J=8.9 Hz), 130.3 (d, J=7.8 Hz), 128.9, 124.7, 123.1, 121.1, 120.5, 115.3 (d, J=21.0 Hz), 111.8 (d, J=24.1 Hz), 111.2, 102.3; MS *m/z* (relative intensity) 212 (M^+, 100), 183 (60), 157 (9), 106 (19), 91 (17).

3.6.2. 2-(2-Thienyl)benzofuran. Mp 94–96°C (lit.[35] 95°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.54–7.46 (m, 3H), 7.32–7.18 (m, 3H), 7.10–7.06 (m, 1H), 6.84 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.5, 151.3, 133.3, 129.1, 127.9, 125.8, 124.6, 124.3, 123.1, 120.7, 111.1, 101.1; MS *m/z* (relative intensity) 200 (M^+, 100), 171 (42), 155 (5), 145 (5), 127 (8), 100 (15).

3.6.3. 2-(4-Methoxyphenyl)benzofuran. Mp 146–147°C (lit.[7b] 145–147°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.86 (d, J=8.59 Hz, 2H), 7.55–7.47 (m, 2H), 7.24–7.20 (m, 2H), 6.95 (d, J=8.60 Hz, 2H), 6.86 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 160.0, 156.0, 154.7, 129.5, 126.4, 123.7, 123.3, 122.8, 120.6, 114.2, 111.0, 99.7, 55.3; MS *m/z* (relative intensity) 224 (M^+, 100), 209 (75), 181 (45), 152 (30), 126 (8), 112 (18).

3.6.4. 2-(4-Acetylphenyl)benzofuran. Mp 168–170°C (lit.[42] 169–170°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.00 (d, J=8.29 Hz, 2H), 7.90 (d, J=8.37 Hz, 2H), 7.60–7.51 (m, 2H), 7.34–7.21 (m, 2H), 7.12 (s, 1H), 2.60 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 197.2, 155.2, 154.5, 136.5, 134.5, 128.9, 125.1, 124.7, 123.2, 121.5, 121.3, 111.3, 103.6, 26.5; MS *m/z* (relative intensity) 236 (M^+, 70), 221 (100), 193 (17), 165 (56), 139 (11), 110 (19), 82 (29).

3.6.5. 2-(5-Chloro-1-pentenyl)benzofuran. Oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.50–7.40 (m, 2H), 7.27–7.14 (m, 2H), 6.48 (s, 1H), 6.43–6.33 (m, 2H), 3.60 (t, J=6.47 Hz, 2H), 2.46–2.38 (m, 2H), 2.03–1.92 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.7, 131.2, 129.0, 124.2, 122.7, 120.7, 120.0, 110.8, 103.3, 44.2, 31.8, 29.9; MS *m/z* (relative intensity) 222, 220 (M^+, 29, 9), 185 (5), 171 (10), 157 (100), 128 (50), 115 (13), 91 (12). Anal. Calcd for $C_{13}H_{13}OCl$: C, 70.75; H, 5.94. Found: C, 71.01; H, 6.30.

3.6.6. Preparation of *o*-iodoacetanilide. To a stirred solution of *o*-iodoaniline (1.10 g, 5.00 mmole) in dry ether (25 mL), Et_3N (0.7 mL) was added and the solution cooled to 0°C. Acetyl chloride (0.51 g, 5.04 mmol) dissolved in 15 mL of ether was added dropwise. After 2 h of stirring at 0°C, the reaction mixture was allowed to reach room temperature and stirred overnight. Filtration, followed by concentration of filtrate, yielded a crude product which was purified by column chromatography (hexane–EtOAc: 50/50) to afford 0.96 g (73%) of a colorless, crystalline *o*-iodoacetanilide. Mp 100°C (lit.[43] 109–111°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.17 (d, J=7.72 Hz, 1H), 7.77 (d, J=7.78 Hz, 1H), 7.46 (s, br, 1H), 7.33 (t, J=7.48 Hz, 1H), 6.84 (t, J=7.41 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 168.2, 138.7, 138.2, 129.2, 126.0, 122.2, 90.1, 24.7; MS *m/z* (relative intensity) 261 (M^+, 10), 219 (50), 134 (100), 92 (60), 65 (38).

3.6.7. Preparation of *o*-iodotrifluoroacetanilide. To a stirred solution of *o*-iodoaniline (1.10 g, 5 mmol) and Et_3N (0.7 mL) in THF (15 mL) at −15°C, $(CF_3CO)_2O$ (1.28 g, 6.00 mmole) dissolved in 10 mL of THF was added dropwise. After 1 h of stirring at −15°C, the reaction mixture was allowed to warm up to room temperature, stirred overnight and then poured into a separatory funnel containing H_2O (25 mL). The product was extracted into Et_2O (3×20 mL), the combined organic layer was then dried ($MgSO_4$), the solvent evaporated, and the product chromatographed (silica gel, hexane–EtOAc: 92/8 (v/v)) to afford 1.42 g (90% yield) of colorless crystalline *o*-iodotrifluoroacetaniline. Mp 101–102°C (lit.[44] 102°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.29 (s, br, 1H), 8.18 (dd, J=8.23, 0.72 Hz, 1H), 7.83 (dd, J=8.93, 0.98 Hz, 1H), 7.40 (t, J=7.79 Hz, 1H), 6.97 (dt, J=8.23, 1.21 Hz, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.8 (q, J=37.8 Hz), 139.2, 135.7, 129.6, 127.9, 122.2, 115.6 (q, J=286.6 Hz), 90.3; MS *m/z* (relative intensity) 315 (M^+, 10), 246 (2), 188 (100), 168 (26), 119 (20), 91 (40).

3.6.8. Preparation of *N*-(*o*-iodophenyl)methanesulfonamide. To a stirred solution of *o*-iodoaniline (1.10 g, 5 mmol) and 4-dimethylaminopyridine (0.06 g, 0.5 mmol) in pyridine (12 mL), CH_3SO_2Cl (0.69 g, 6.00 mmole) in 4 mL of pyridine was added dropwise at room temperature. The mixture was heated to reflux for 12 h. The cooled reaction mixture was diluted with dichloromethane and then washed with aqueous HCl (5%). The organic layer was dried ($MgSO_4$), the solvent evaporated, and the product purified by column chromatography (hexane–EtOAc: 80/20, silica gel) to yield 0.91 g (61% yield) of *N*-(*o*-iodophenyl)methanesulfonamide. Mp 97–99°C (lit.[45] 96–98°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.82 (d, J=7.78 Hz, 1H), 7.63 (d, J=7.92 Hz, 1H), 7.37 (t, J=7.43 Hz, 1H), 6.93 (t, J=7.44 Hz, 1H), 6.74 (s, br, 1H), 3.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 139.3, 137.5, 129.7, 127.2, 122.5,

92.2, 40.1; MS *m/z* (relative intensity) 297 (M^+, 17), 218 (49), 170 (5), 108 (21), 91 (100).

3.6.9. Preparation of *o*-ethynylaniline. To a stirred solution of *o*-iodoaniline (2.20 g, 10.00 mmol) in DMF (2 mL) and Et_2NH (10 mL) were added $Pd(PPh_3)_4$ (0.080 g, 0.068 mmol) and CuI (0.019 g, 0.010 mmol). Then (trimethylsilyl)acetylene (1.80 mL, 12.7 mmol) was added dropwise at room temperature under nitrogen. The reaction mixture was stirred overnight and then the Et_2NH and unreacted (trimethylsilyl)acetylene were removed under reduced pressure. The product extracted with Et_2O (3×20 mL) and the combined organic phase was washed with H_2O, dried (Na_2SO_4) and concentrated under vacuum. The residue was added to KF/Al_2O_3 (5.00 g, 40% by weight) and stirred at room temperature to ensure efficient mixing. The result mixture was placed in a microwave oven and irradiated at 30% power for 4 min. After cooling, hexane (15 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The product was purified by chromatography (hexane–ethyl acetate: 95/5) to generate 0.940 g (80% yield) of a pale yellow oil[46], *o*-ethynylaniline. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.30 (dd, J=9.10, 1.47 Hz, 1H), 7.08 (dt, J=7.74, 1.41 Hz, 1H), 6.65–6.58 (m, 2H), 4.19 (s, br, 1H), 3.35 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 148.4, 132.3, 129.9, 117.5, 114.1, 106.3, 82.5, 80.5; MS *m/z* (relative intensity) 117 (M^+, 100), 90 (55), 89 (50), 63 (17).

3.6.10. *N*-Acetyl-*o*-ethynylaniline. The titled compound was prepared as described for *o*-iodoacetanilide from *o*-ethynylaniline and AcCl, in 71% yield. Mp 84–85°C (lit.[47] 83–84°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.39 (d, J=8.34 Hz, 1H), 7.93 (s, br, 1H), 7.45 (d, J=7.74 Hz, 1H), 7.35 (t, J=7.94 Hz, 1H), 7.03 (t, J=7.55 Hz, 1H), 3.52 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 168.2, 139.5, 132.1, 130.1, 123.2, 119.3, 110.5, 84.3, 79.1, 24.8; MS *m/z* (relative intensity) 159 (M^+, 33), 117 (100), 90 (49), 63 (15).

3.6.11. *o*-Ethynyltrifluoroacetanilide. The titled compound was prepared as described for *o*-iodotrifluoroacetanlide from *o*-ethynylaniline and $(CF_3CO)_2O$, in 88% yield. Mp 34–35°C (lit.[48] 35–37°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.76 (s, br, 1H), 8.35 (d, J=8.32 Hz, 1H), 7.52 (d, J=7.60 Hz, 1H), 7.43 (t, J=7.87 Hz, 1H), 7.18 (t, J=7.60 Hz, 1H), 3.61 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.5 (q, J=36.6 Hz), 136.8, 132.3, 130.4, 125.4, 119.7, 115.6 (q, J=287.5 Hz), 112.1, 85.7, 77.9; MS *m/z* (relative intensity) 213 (M^+, 92), 144 (18), 116 (100), 89 (54), 69 (23).

3.6.12. *N*-(*o*-Ethynylphenyl)methanesulfonamide. The titled compound was prepared as described for *N*-(*o*-iodophenyl)methanesulfonamide from *o*-ethynylaniline and CH_3SO_2Cl, in 55% yield. Mp 103–105°C (lit.[49]105°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.60 (d, J=8.28 Hz, 1H), 7.50 (d, J=7.70 Hz, 1H), 7.38 (t, J=7.84 Hz, 1H), 7.14 (t, J=7.61 Hz, 1H), 7.01 (s, br, 1H), 3.52 (s, 1H), 3.03 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 138.4, 132.8, 130.4, 124.6, 119.6, 112.9, 84.8, 78.5, 39.6; MS *m/z* (relative intensity) 195 (M^+, 30), 132 (21), 116 (100), 89 (71), 63 (23).

3.7. General procedure for the synthesis of phenylethynylaniline and 2-phenylindole via the reaction of *o*-iodoaniline with terminal alkynes

o-Iodoaniline (0.220 g, 1.00 mmol) and a terminal alkyne (1.00 mmol) were added to a mixture of KF/Al_2O_3 (1.00 g, 40% by weight), palladium powder (0.040 g, 0.376 mmol, 99.9+% as a submicron powder), cuprous iodide (0.070 g, 0.368 mmol) and triphenylphosphine (0.180 g, 0.686 mmol) contained in a clean, dry, 25 mL round-bottomed flask. The mixture was then fitted with a septum (punctured by an 18 gauge needle), placed in the microwave oven and irradiated at 100% power for 3 min. After cooling, hexane (5 mL) was added and the slurry stirred at room temperature to ensure product removal from the surface. The mixture was vacuum filtered using a sintered glass funnel and the product purified by flash chromatography (hexane–EtOAc as eluting agent) to afford the desired phenylethynylaniline or 2-phenylindole.

3.8. General procedure for the synthesis of phenylethynylaniline or 2-phenylindole via the reaction of iodobenzene with *o*-ethynylaniline or *N*-substituted-*o*-ethynylaniline

The procedure paralleled that described for reactions of *o*-iodoaniline and terminal alkyne.

3.8.1. 2-Phenylethynylaniline. Mp 87–88°C (lit.[49] 85–86°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.37–7.28 (m, 4H), 7.13–7.07 (m, 1H), 6.71–6.64 (m, 2H), 4.22 (s, br, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.7, 132.0, 131.3, 129.6, 128.3, 128.1, 123.2, 117.8, 114.2, 107.5, 94.6, 85.9; MS *m/z* (relative intensity) 193 (M^+, 100), 165 (39), 139 (7), 90 (22), 89 (23).

3.8.2. 2-Phenylindole. Mp 189–200°C (lit.[50] 188–189°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.26 (s, br, 1H), 7.64–7.61 (m, 3H), 7.44–7.27 (m, 4H), 7.22–7.09 (m, 2H), 6.82 (s, 1H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 137.9, 136.8, 132.3, 129.2, 129.0, 127.7, 125.1, 122.3, 120.6, 120.2, 110.9, 100.0; MS *m/z* (relative intensity) 193 (M^+, 100), 165 (25), 139 (4), 96 (18), 90 (12), 89 (16).

3.8.3. 2-(4-Methylphenyl)ethynylaniline. Mp 101–102°C (lit.[16] 100–102°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40–7.32 (m, 3H), 7.11–7.05 (m, 3H), 6.70–6.62 (m, 2H), 4.21 (s, br, 2H), 2.31 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.6, 138.2, 131.9, 129.4, 129.0, 120.1, 117.8, 114.2, 108.0, 94.8, 85.2, 21.3; MS *m/z* (relative intensity) 207 (M^+, 100), 192 (5), 178 (14), 165 (13), 139 (4), 115 (8), 102 (18), 89 (26).

3.8.4. 2-*p*-Tolylindole. Mp 213–214°C (lit.[16] 212–214°C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.26 (s, br, 1H), 7.61 (d, J=7.61 Hz, 1H), 7.54 (d, J=8.01 Hz, 2H), 7.36 (d, J=7.87 Hz, 1H), 7.23 (d, J=7.92 Hz, 2H), 7.18–7.07 (m, 2H), 6.77 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 138.1, 137.6, 136.7, 129.7, 129.6, 129.3, 125.1, 122.1, 120.5, 120.2, 110.8, 99.4, 21.2; MS *m/z* (relative intensity) 207 (M^+, 100), 192 (3), 178 (9), 165 (6), 102 (14), 89 (15).

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References

1. (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, *61*, 8551. (c) Ma, S.; Shi, Z.; Yu, Z. *Tetrahedron* **1999**, *55*, 12137. (d) Jones, G. B.; Wright, J. M.; Plourde II, G. W.; Hynd, G.; Huber, R. S.; Mathews, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 1937. (e) Liu, S.-X.; Michel, C.; Schmittel, M. *Org. Lett.* **2000**, *2*, 3959. (f) Shen, W.; Thomas, S. A. *Org. Lett.* **2000**, *2*, 2857.
2. (a) Sonogashira, K. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 3, p. 521. (b) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387. (c) Grissom, J. M.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. (d) De Kort, M.; Correa, V.; Valentijin, A. R. P. M.; Van der Marel, G. A.; Potter, B. V. L.; Taylor, C. W.; Van Boom, J. H. *J. Med. Chem.* **2000**, *43*, 3295. (e) Nazare, M.; Waldmann, H. *Tetrahedron Lett.* **2000**, *41*, 625. (f) Lang, P.; Magnin, G.; Mathis, G.; Burger, A.; Biellmann, J.-F. *J. Org. Chem.* **2000**, *65*, 7825.
3. (a) Kabalka, G. W.; Pagni, R. M. *Tetrahedron* **1997**, *53*, 7999. (b) McGinnis, M. B.; Vagle, K.; Green, J. F.; Tan, L.-C.; Palmer, R.; Siler, J.; Pagni, R. M.; Kabalka, G. W. *J. Org. Chem.* **1996**, *61*, 3496. (c) Sponholtz III, W. R.; Pagni, R. M.; Kabalka, G. W.; Green, J. F.; Tan, L.-C. *J. Org. Chem.* **1991**, *56*, 5700. (d) Pala Wilgus, C.; Downing, S.; Molitor, E.; Bains, S.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1995**, *36*, 3469.
4. (a) Kabalka, G. W.; Pagni, R. M.; Hair, C. M. *Org. Lett.* **1999**, *1*, 1423. (b) Kabalka, G. W.; Pagni, R. M.; Wang, L.; Namboodiri, V.; Hair, C. M. *Green Chem.* **2000**, *2*, 120. (c) Kabalka, G. W.; Wang, L.; Namboodiri, V.; Pagni, R. M. *Tetrahedron Lett.* **2000**, *41*, 5151.
5. (a) Abramovich, R. A. *Org. Prep. Proced. Int.* **1991**, *23*, 683. (b) Blettner, C. G.; Koenig, W. A.; Wilfried, A.; Stenzel, W.; Schotten, T. *J. Org. Chem.* **1999**, *64*, 3885. (c) Bose, D. S.; Jayalakshmi, B. *J. Org. Chem.* **1999**, *64*, 1713.
6. (a) Varma, R. S. *Green Chem.* **1999**, *1*, 43 and references cited therein. (b) Ranu, B. C.; Hajra, A.; Jana, U. *Synlett* **2000**, 75. (c) Erdelyi, M.; Gogull, A. *J. Org. Chem.* **2001**, *66*, 4165. (d) Villemin, D.; Caillot, F. *Tetrahedron Lett.* **2001**, *42*, 639.
7. (a) Austin, W. B.; Bilow, N.; Kellegan, W. J.; Lau, K. S. Y. *J. Org. Chem.* **1981**, *46*, 2280. (b) Arcadi, A.; Cacchi, S.; Rosario, M. D.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280.
8. (a) Kumar, V.; Ackerman, J. A. H.; Alexander, M. D.; Bell, M. R.; Christiansen, R. G.; Dung, J. S.; Jaeger, E. P.; Hermann, Jr., J. L.; Krolski, M. E.; McKloskey, P.; Batzold, F. H.; Juniewicz, P. E.; Reel, J.; Snyder, B. W.; Winneker, R. C. *J. Med. Chem.* **1994**, *37*, 4227. (b) Ohemeng, K. A.; Apollina, M. A.; Nguyen, V. N.; Schwender, C. F.; Singer, M.; Steber, M.; Ansell, J.; Argentieri, D.; Hageman, W. *J. Med. Chem.* **1994**, *37*, 3663.
9. Gangjee, A.; Devraj, R.; McGuire, J. J.; Kisliuk, R. L. *J. Med. Chem.* **1995**, *38*, 3798.
10. Yang, Z.; Liu, H. B.; Lee, C. M.; Chang, H. M.; Wong, H. N. C. *J. Org. Chem.* **1992**, *57*, 7248.
11. (a) Kozikowsky, A. P.; Ma, D.; Du, L.; Lewin, N. E.; Blumberg, P. M. *J. Am. Chem. Soc.* **1995**, *117*, 6666. (b) Gubin, J.; de Vogelaer, H.; Inion, H.; Houben, C.; Lucchetti, J.; Mahaux, J.; Rosseels, G.; Peiren, M.; Clinet, M.; Polster, P.; Chatelain, P. *J. Med. Chem.* **1993**, *36*, 1425.
12. (a) Fürstner, A.; Jumbam, D. N. *Tetrahedron* **1992**, *48*, 5991. (b) Fürstner, A.; Jumbam, D. N.; Weidmann, H. *Tetrahedron Lett.* **1991**, *32*, 6695.
13. (a) Givens, R. S.; Athey, P. S.; Matuszewski, B.; Kueper III, L. W.; Xue, J.-Y.; Fister, T. *J. Am. Chem. Soc.* **1993**, *115*, 6001. (b) Givens, R. S.; Athey, P. S.; Matuszowski, B.; Kueper III, L. W.; Xue, J.-Y. *J. Am. Chem. Soc.* **1992**, *114*, 8708.
14. (a) Jinno, S.; Okita, T.; Inouye, K. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1029. (b) Cockerill, G. S.; Easterfield, H. J.; Percy, J. M. *Tetrahedron Lett.* **1999**, *40*, 2601.
15. (a) Larock, R. C.; Yum, E. K.; Doty, J. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (b) Kundu, N. G.; Pal, M.; Mahanty, J. S.; Dasgupta, S. K. *J. Chem. Soc., Chem. Commun.* **1992**, 41. (c) Arcadi, A.; Marinelli, F.; Cacchi, S. *Synthesis* **1986**, 749. (d) Fancelli, D.; Fagnola, M. C.; Severino, D.; Bedeschi, A. *Tetrahedron Lett.* **1997**, *38*, 2311.
16. Cacchi, S.; Carnicelli, V.; Marinell, F. *J. Organomet. Chem.* **1994**, *475*, 289.
17. Sato, H.; Isono, N.; Miyoshi, I.; Mori, M. *Tetrahedron* **1996**, *52*, 8143.
18. Masuda, Y.; Hoshi, M.; Arase, A. *Chem. Lett.* **1980**, 413.
19. Carpino, L. A.; Chen, H.-W. *J. Am. Chem. Soc.* **1979**, *101*, 390.
20. Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **1999**, *12*, 3305.
21. Hunter, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5765.
22. van Koten, G.; ten Hoedt, R. W. M.; Noltes, J. G. *J. Org. Chem.* **1977**, *42*, 2705.
23. Paquett, L. A.; Wittenbrook, L. S. *J. Am. Chem. Soc.* **1967**, *89*, 4483.
24. Mouries, V.; Waschbusch, R.; Carran, J.; Savignac, P. *Synthesis* **1998**, 271.
25. Rudenko, A. P.; Vasil'ev, A. V. *Russ. J. Org. Chem.* **1995**, *31*, 1360.
26. Martelli, G.; Spagnolo, P.; Tiecco, M. *J. Chem. Soc. B* **1970**, 1413.
27. Rossi, R.; Carpita, A.; Lezzi, A. *Tetrahedron* **1984**, *40*, 2773.
28. Katritzky, A. R.; Wang, J.; Karodia, N.; Li, J. *J. Org. Chem.* **1997**, *62*, 4142.
29. Colvin, E. W.; Hamill, B. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869.
30. Grubbs, R. H.; Kratz, D. *Chem. Ber.* **1993**, *126*, 149.
31. Fujii, A.; Miller, S. I. *J. Am. Chem. Soc.* **1971**, *93*, 3694.
32. Seyferth, D.; Nestle, M. O.; Wehman, A. T. *J. Am. Chem. Soc.* **1975**, *97*, 7417.
33. Vasil'ev, A. V.; Rudenko, A. P. *Russ.J. Org. Chem.* **1997**, *33*, 1555.
34. Buckle, D. R.; Rockell, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2443.
35. Astoin, J.; Demerseman, P.; Riveron, A.; Royer, R. *J. Heterocycl. Chem.* **1977**, *14*, 867.
36. Hellwinkel, D.; Goeke, K. *Synthesis* **1995**, 1135.
37. Katritzky, A. R.; Lan, X.; Zhang, Z. *J. Heterocycl. Chem.* **1993**, *30*, 381.
38. Kitamura, T.; Zheng, L.; Fukuoka, T.; Fujiwara, Y.;

Taniguchi, H.; Sakurai, M.; Tanaka, R. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1511.
39. Kasahara, A.; Izumi, T.; Yodono, M.; Saito, R.; Takeda, T.; Sugawara, T. *Bull. Chem. Soc. Jpn* **1973**, *46*, 1220.
40. Ota, T.; Hasegawa, S.; Inoue, S.; Sato, K. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3029.
41. Alberola, A.; Calvo, B.; Ortega, A. G.; Pedrosa, R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3075.
42. Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Toni, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951.
43. Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652.
44. Tietze, L. F.; Schimpf, R. *Chem. Ber.* **1994**, *127*, 2235.
45. Kizil, M.; Patro, B.; Callagham, O.; Murphy, J. A.; Hursthouse, M. B.; Hibbs, D. *J. Org. Chem.* **1999**, *64*, 7856.
46. Topolski, M. *J. Org. Chem.* **1995**, *60*, 5588.
47. Rudisill, D. E.; Still, J. K. *J. Org. Chem.* **1989**, *54*, 5856.
48. Arcadi, A.; Cacchi, S.; Carnicelli, V.; Marinelli, F. *Tetrahedron* **1994**, *50*, 437.
49. Yasuhara, A.; Kanamori, Y.; Kaneko, M.; Numata, A.; Kondo, Y.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 529.
50. Akazome, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1994**, *59*, 3375.