New approaches to heterocycles and carbocycles

by

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For the Major Program

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-2-ALKEN-1-ONES AND NUCLEOPHILES

LIST OF ABBREVIATIONS

aq	aqueous
Bu	butyl
t-Bu	*tert*-butyl
cat.	catalytic
d	doublet
dba	dibenzylideneacetone
dd	doublet of doublets
DDQ	2,3-dichloro-5,6-dicyanoquinone
DMF	*N*,*N*-dimethylformamide
dt	doublet of triplets
eq	equation
equiv	equivalent
Et	ethyl
h	hour
HRMS	high resolution mass spectrometry
Hz	Hertz
IR	infrared
m	multiplet
Me	methyl
mL	milliliter
mol	mole
mp	melting point

MS	mass spectrometry
n	normal
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
PMB	*p*-methoxybenzyl
q	quartet
s	singlet
t	triplet
satd	saturated
t	triplet
TBAC	tetra-*n*-butylammonium chloride
tert	tertiary
TLC	thin layer chromatography
TMS	trimethylsilyl
tt	triplet of triplets

ABSTRACT

The electrophilic cyclization of functionally-substituted alkynes is a very promising route to an extraordinary range of medicinally interesting, functionally-substituted heterocycles and carbocycles. For instance, a variety of substituted isocoumarins and α-pyrones are readily prepared in excellent yields under very mild reaction conditions by the reaction of o-(1-alkynyl)benzoates and (Z)-2-alken-4-ynoates with ICl, I_2, PhSeCl, p-$O_2NC_6H_4SCl$, and HI. This methodology accommodates various alkynyl esters and has been successfully extended to the synthesis of polycyclic aromatic and biaryl compounds.

Electrophilic cyclization of o-(1-alkynyl)benzamides with ICl, I_2, and NBS, affords a variety of substituted isoindolin-1-ones in good to excellent yields. In a few cases, substituted isoquinolin-1-ones were obtained as the major product instead. This methodology accommodates various alkynyl amides and functional groups, and has been successfully extended to heterocyclic starting materials. This chemistry has been successfully applied to the formal synthesis of a biologically interesting alkaloid cepharanone B.

A variety of substituted polycyclic aromatics are readily prepared in good to excellent yields under very mild reaction conditions by the reaction of 2-(1-alkynyl)biphenyls with ICl, I_2, NBS, and p-$O_2NC_6H_4SCl$. This methodology readily accommodates various functional groups and has been successfully extended to systems containing a variety of polycyclic and heterocyclic rings.

The coupling of 2-(1-alkynyl)-2-alken-1-ones with nucleophiles, either catalyzed by $AuCl_3$ or induced by an electrophile, provides highly substituted furans in good to excellent yields under very mild reaction conditions. Various nucleophiles, including functionalized

alcohols, H_2O, carboxylic acids, 1,3-diketones and electron-rich arenes, and a range of cyclic and acyclic 2-(1-alkynyl)-2-alken-1-ones readily participate in these cyclizations. Iodine, NIS, and PhSeCl have proven successful as electrophiles in this process. The resulting iodine-containing furans can be readily elaborated to more complex products using known organopalladium chemistry.

GENERAL INTRODUCTION

Electrophilic cyclization of functionally-substituted alkynes has been little studied, although it would appear to be a very promising route to an extraordinary range of medicinally interesting, functionally-substituted heterocycles and carbocycles. Previous work by Cacchi, Flynn, Swager, Barluenga, Rossi and Larock has shown that iodine and other electrophiles can be used for the synthesis of benzo[*b*]furans, benzo[*b*]thiophenes, indoles and isoquinolines. This highly efficient new approach to heterocycles and carbocycles has several very attractive features: (1) the reaction conditions are very mild; (2) the starting materials are readily available or easily prepared with lots of functionality; (3) the iodine functionality introduced into the heterocycle or carbocycle facilitate further elaboration by Pd-catalyzed chemistry.

Our interest in electrophilic cyclization led us to further explore the generality of this synthesis approach. First of all, we have discovered that the electrophilic cyclization of *o*-(1-alkynyl)benzoates and (*Z*)-2-alken-4-ynoates readily affords isocoumarins and α-pyrones. We have also discovered that isoindolin-1-ones and isoquinolin-1-ones can be prepared by the reaction of *o*-(1-alkynyl)benzamides with electrophiles. We have extensively studied the reaction of 2-(1-alkynyl)biaryls with various electrophiles and been able to greatly expand the scope of acetylenic arenes and electrophiles that can be employed in this electrophilic cyclization. Furthermore, we have developed process involving sequential nucleophilic domino attack to transform 2-(1-alkynyl)-2-alken-1-ones into highly substituted furans, either through a AuCl$_3$-catalyzed cyclization or through an electrophile-induced cyclization.

Dissertation Organization

This dissertation is divided into four chapters. Each of these chapters is written up following the guidelines for a full paper in the *Journal of Organic Chemistry*.

Chapter 1 describes the synthesis of substituted isocoumarins and α-pyrones by the reaction of o-(1-alkynyl)benzoates and (Z)-2-alken-4-ynoates with ICl, I_2, PhSeCl, p-$O_2NC_6H_4SCl$, and HI. The general scope of this methodology and its application in preparing polycyclic aromatics and biaryl compounds are examined in detail.

Chapter 2 presents the synthesis of isoindolin-1-ones by the electrophilic cyclization of o-(1-alkynyl)benzamides. In a few cases, substituted isoquinolin-1-ones are obtained as the major product instead. This chemistry has been applied to the formal synthesis of a biologically interesting alkaloid cepharanone B.

Chapter 3 serves to expand the scope and synthetic utility of electrophilic cyclization of acetylenic arenes. The regioselectivity and general scope of this methodology for preparing carbocyclic and heterocyclic aromatics is examined in detail in terms of electronic and steric effects.

Chapter 4 examines a process involving sequential nucleophilic domino attack to transform 2-(1-alkynyl)-2-alken-1-ones into highly substituted furans, either through a $AuCl_3$-catalyzed cyclization or through an electrophile-induced cyclization. This methodology makes use of $AuCl_3$ or electrophiles to generate key carbocation intermediates, which undergo intermolecular nucleophilic attack with various nucleophiles.

The ^1H and ^{13}C NMR spectra for the starting materials and the electrophilic cyclization products in Chapters 1 and 2 can be found in the supporting information of our

previously published papers. The NMR spectra for the new compounds in Chapter 3 and 4

will hopefully be found in our future papers on this work.

CHAPTER 1. SYNTHESIS OF ISOCOUMARINS

AND α-PYRONES VIA ELECTROPHILIC CYCLIZATION

Based on a paper published in the *Journal of Organic Chemistry*

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Abstract

A variety of substituted isocoumarins and α-pyrones are readily prepared in excellent yields under very mild reaction conditions by the reaction of *o*-(1-alkynyl)benzoates and (*Z*)-2-alken-4-ynoates with ICl, I_2, PhSeCl, *p*-$O_2NC_6H_4SCl$, and HI. This methodology accommodates various alkynyl esters and has been successfully extended to the synthesis of polycyclic aromatic and biaryl compounds.

Introduction

Isocoumarins[1] and α-pyrones[2] represent two important classes of naturally occurring lactones, which are structural subunits in numerous natural products that exhibit a wide range of biological activities, such as antimicrobial,[3] androgen-like,[4] phytotoxic,[5] antifungal[6] and pheromonal[7] effects. Recently, low molecular weight α-pyrones have been shown to be potent HIV-1 protease inhibitors.[8]

Considerable efforts have been directed towards the synthesis of isocoumarins[9] and

α-pyrones[10] either by traditional approaches or by organometallic approaches. Isocoumarins

have been prepared by the *ortho*-thallation of benzoic acids and subsequent palladium-

catalyzed olefination using simple olefins, as well as allylic and vinylic halides or esters.[9c]

Unsubstituted or 3-substituted isocoumarins and pyrones have been prepared by the

palladium-catalyzed coupling of 2-halobenzoate esters, 2-halobenzoic acids or 2-

halobenzonitriles with alkenes,[11] vinylic stannanes[12] or terminal alkynes[13] and subsequent

cyclization or by π-allylnickel cross-coupling and palladium-catalyzed cyclization.[9a]

Isocoumarins and α-pyrones have also been prepared by the palladium-catalyzed annulation

of internal alkynes.[14]

Previous workers have reported the synthesis of isocoumarins[15] and 5,6-disubstituted

2(2*H*)-pyranones[16] by the iodolactonization of 2-(1-alkynyl)benzoic acids and 5-substituted

(*Z*)-2-alken-4-ynoic acids respectively (eq 1). These acids have always produced a mixture

of 5- and 6-membered ring products.

$$\text{(1)}$$
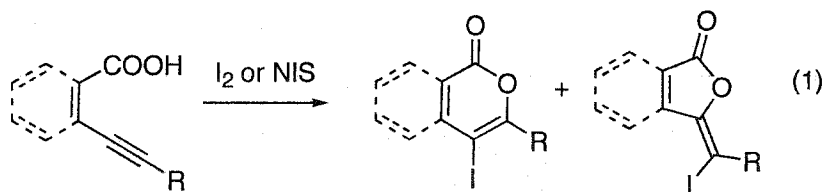
Oliver and Gandour have reported the bromolactonization of alkyl 2-(2-

phenylethynyl)benzoates (eq 2).[17] Unfortunately, only two examples were reported and the

scope of this cyclization has not been examined.

$$\text{(2)}$$
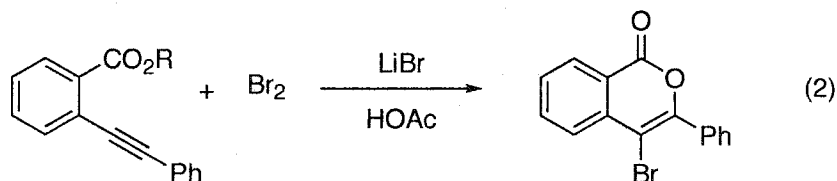
During the course of our investigation of the electrophilic cyclization of analogous esters,[18] Rossi et al reported the synthesis of isocoumarins and α-pyrones by iodocyclization of the corresponding acetylenic esters.[19] They report that the reactions of four 2-alken-4-ynoate methyl esters with I_2 in CH_2Cl_2 generally afford mixtures of the corresponding iodo-pyrones and -furanones, but that the reaction with ICl in CH_2Cl_2 produces predominantly the 6-membered ring lactones, albeit in only 51-72% yields. Analogous reactions of four methyl 2-(arylethynyl)benzoates with I_2 in MeCN produce excellent yields of pure 4-iodoisocoumarins in two cases, but mixtures of 5- and 6-membered ring lactones in 26 and 83% overall yields in the other two cases. The use of ICl in CH_2Cl_2 afforded an 81% yield of an essentially pure isocoumarin in one example, but only a 47% yield of a 55:45 mixture of 6- and 5-membered ring products in another. Herein, we wish to report the successful electrophilic cyclization of analogous esters for the synthesis of isocoumarins and α-pyrones. This chemistry generally produces excellent yields of a single regioisomeric 6-membered ring lactone and can be extended to electrophiles other than I_2 and ICl. In a couple of cases, 5-membered ring lactones are cleanly produced.

Results and Discussion

A two step approach to isocoumarins and α-pyrones has been examined involving (i) preparation of o-(1-alkynyl)benzoates and (Z)-2-alken-4-ynoates by a Sonagashira coupling reaction,[20] and (ii) electrophilic cyclization (Scheme 1).

SCHEME 1

$$E^+ = ICl, I_2, p\text{-}O_2NC_6H_4SCl, PhSeCl, HI$$
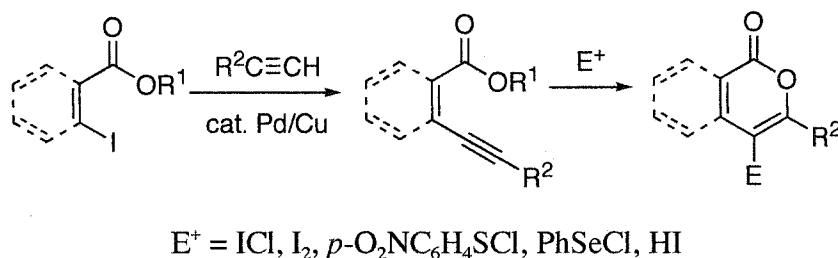
The *o*-(1-alkynyl)benzoates and (*Z*)-2-alken-4-ynoates required for our approach are readily prepared by Sonogashira coupling[20] of the corresponding iodo compounds with terminal alkynes using 2% $PdCl_2(PPh_3)_2$ and 1% CuI in Et_3N solvent at 55 °C. The yields of this process range from 80% to 100% and this procedure should readily accommodate considerable functionality.

To explore the scope of this electrophilic cyclization strategy, the reactions of alkynyl ester **1** with different electrophiles (ICl, I_2, p-$O_2NC_6H_4SCl$, PhSeCl and HI) in CH_2Cl_2 at room temperature have been studied (Table 1, entries 1-5). Excellent ≥ 90% yields of a single regioisomeric isocoumarin have been obtained in all cases. Of all of the electrophilic reagents examined, ICl gave the fastest reaction, followed by I_2, p-$O_2NC_6H_4SCl$ and PhSeCl, while the reaction of HI took 96 h.

Both ICl and I_2 are efficient and quite general for the preparation of isocoumarins. Most of the functional groups that we have studied so far have tolerated the reaction conditions, and yields above 90% have been obtained in most cases (entries 1, 2, 6-8 and 13-14). Aryl- (entries 1 and 2) and long chain alkyl-substituted alkynes (entries 6 and 7) are readily accommodated, and the presence of an olefin (entry 8) or an alcohol group (entry 10) presents no difficulties. However, alkynes bearing a H or Si(*i*-Pr)$_3$ group (entries 11 and 12) have afforded exclusively the 5-membered ring products as determined by the carbonyl

TABLE 1. Synthesis of Substituted Isocoumarins and α-Pyrones (Scheme 1)[a]

entry	alkynyl ester	electrophile		time (h)	product(s)		% isolated yield
1		1	ICl	0.5		2	90
2		1	I_2	1		2	93
3		1	$p\text{-}O_2NC_6H_4SCl$	1		3	90
4		1	PhSeCl	1		4	95
5		1	HI	96		5	92

8
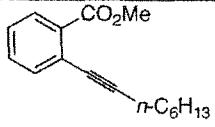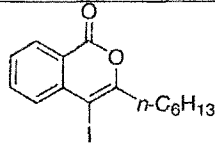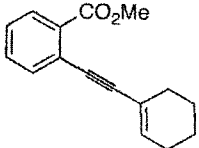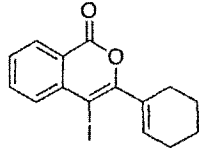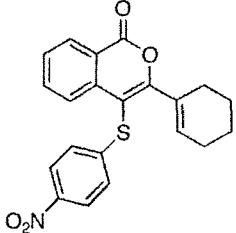
TABLE 1. (continued)

entry	alkynyl ester		electrophile	time (h)	product(s)		% isolated yield
6	CO₂Me, n-C₆H₁₃	6	ICl	0.5	n-C₆H₁₃	7	85
7		6	I₂	1		7	90
8	CO₂Me	8	ICl	0.5		9	98
9		8	p-O₂NC₆H₄SCl	1		10	70

TABLE 1. (continued)

entry	alkynyl ester		electrophile	time (h)	product(s)		% isolated yield
10		**11**	ICl	0.5		**12**	51
11		**13**	ICl	0.5		**14**	63
12		**15**	ICl	0.5		**16**	96
13		**17**	ICl	0.5		**18**	100[b]

TABLE 1. (continued)
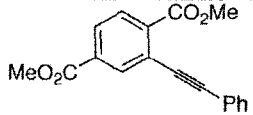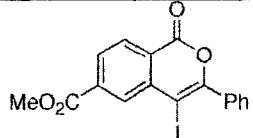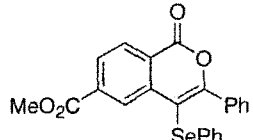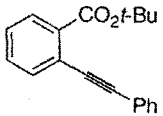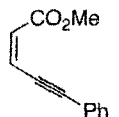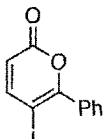
entry	alkynyl ester		electrophile	time (h)	product(s)		% isolated yield
14		**19**	ICl	0.5		**20**	88
15		**19**	PhSeCl	1		**21**	73
16		**22**	ICl	0.5		**2**	100
17		**23**	ICl	0.5		**24**	94

TABLE 1. (continued)
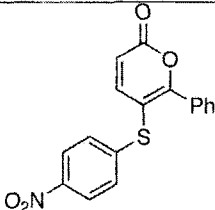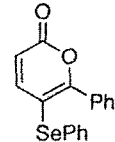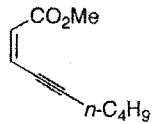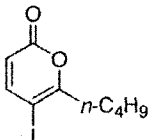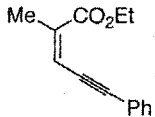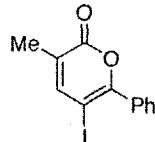
entry	alkynyl ester	electrophile		time (h)	product(s)		% isolated yield
18		**23**	p-O$_2$NC$_6$H$_4$SCl	1		**25**	80
19		**23**	PhSeCl	1		**26**	97
20		**27**	ICl	0.5		**28**	80
21		**29**	ICl	0.5		**30**	~59[c]
22		**29**	I$_2$	1		**30**	84

TABLE 1. (continued)
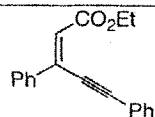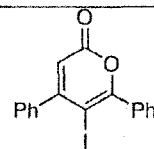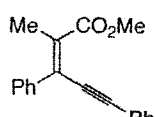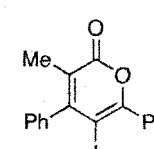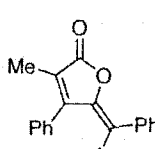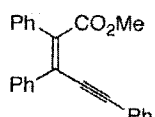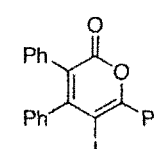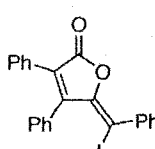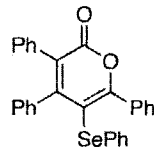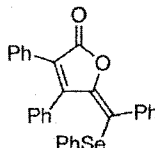
entry	alkynyl ester		electrophile	time (h)	product(s)			% isolated yield
23	Ph CO₂Et / Ph (**31**)	**31**	ICl	0.5	Ph Ph I pyranone (**32**)	**32**		84
24	Me CO₂Me / Ph Ph (**33**)	**33**	I₂	1	Me Ph Ph I (**34**)	**34**	Me Ph Ph I furanone (**35**)	17 + 76
25	Ph CO₂Me / Ph Ph (**36**)	**36**	I₂	1	Ph Ph Ph I (**37**)	**37**	Ph Ph Ph I (**38**)	6 + 71
26		**36**	ICl	0.5	(**37**)	**37**	(**38**)	17 + 55
27		**36**	PhSeCl	1	Ph Ph Ph SePh (**39**)	**39**	Ph Ph Ph PhSe (**40**)	30 + 41

13
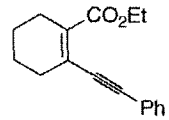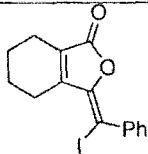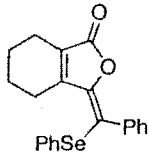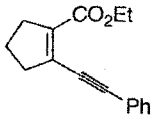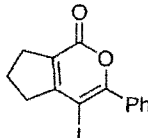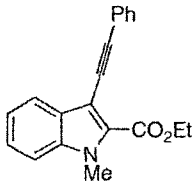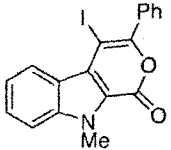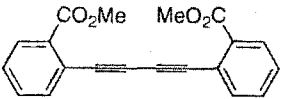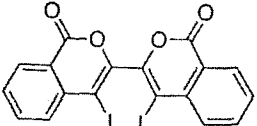
TABLE 1. (continued)

entry	alkynyl ester		electrophile	time (h)	product(s)		% isolated yield
28		**41**	ICl	0.5		**42**	55
29		**41**	PhSeCl	1		**43**	60
30		**44**	ICl	0.5		**45**	0
31		**44**	I$_2$	16		**45**	85
32		**46**	ICl	0.5		**47**	0

TABLE 1. (continued)

entry	alkynyl ester		electrophile	time (h)	product(s)		% isolated yield
33		**46**	I_2	60		**47**	84
34		**48**	ICl	0.5		**49**	90[b]

[a] All reactions were run under the following conditions, unless otherwise specified: 0.30 mmol of the o-(1-alkynyl)benzoate or (Z)-2-alken-4-ynoate in 3 mL of CH_2Cl_2 was placed in a 4-dram vial under N_2 and 1.2 equivs of electrophile in 0.4 mL of CH_2Cl_2 was added at room temperature. [b] The reaction was run at $-78\ ^\circ C$. [c] This product could not be obtained completely pure.

stretch in their IR spectra.[9i] Compound **14** has also been reported earlier by Rossi.[9b] This is

apparently due to the limited stability of the resulting cationic intermediate[19b] (entry 11) and

the steric bulk of the Si(i-Pr)$_3$ group (entry 12) respectively (see the later mechanistic

discussion). Isocoumarins bearing electron-donating or electron-withdrawing substituents in

the 4- and/or 5-positions of the aromatic ring have also been synthesized in excellent yields

(entries 13 and 14). These cyclizations are not limited to simple methyl esters. The

corresponding *tert*-butyl ester **22** has been cyclized by ICl in a quantitative yield (entry 16).

We next examined the possibility of preparing α-pyrones by this same methodology.

(Z)-2-Alken-4-ynoates bearing both an aryl group (**23**) and an alkyl group (**27**) on the

acetylene moiety have reacted with ICl, p-O$_2$NC$_6$H$_4$SCl or PhSeCl to produce the

corresponding α-pyrones **24, 25, 26** and **28** in excellent yields (entries 17-20). Ethyl (Z)-2-

methyl-5-phenyl-2-alken-4-ynoate (**29**) reacts with ICl to afford a 59% yield of the desired 5-

iodo-α-pyrone **30,** along with an inseparable by-product (entry 21). Fortunately, when using

I$_2$, the iodocyclization product **30** is obtained as the only product in an 84% yield (entry 22).

Ethyl (Z)-3,5-diphenyl-2-alken-4-ynoate (**31**) also gives a single pyrone product **32** in an

84% yield (entry 23). However, when 2,3-disubstituted (Z)-2-alken-4-ynoates are employed,

mixtures of 5- and 6-membered ring products are obtained no matter whether I$_2$, ICl or

PhSeCl is employed as the electrophile (entries 24-27). Thus, it appears that steric effects

play an important role in the regioselectivity of cyclization. The more bulky the substituents

are in positions 2 and 3 of the (Z)-2-alken-4-ynoates, the lower the yield of the 6-membered

ring product (compare entries 23 and 26, and 24 and 25). The bulkier substituents on the (Z)-

2-alken-4-ynoates apparently force the oxygen of the carbonyl group closer to C-4 of the

alkenynoate ester resulting in the 5-membered ring product (see the later mechanistic

discussion). The nature of the electrophile plays an important role in these cyclization

reactions. Compared with I_2, the stronger electrophilic reagent ICl affords a higher yield of

the 6-membered ring product (compare entries 25 and 26), although the 5-membered ring

lactone still predominates.

Ring-containing esters can also be used in this iodocyclization process (entries 28-

33). The 6-membered ring ester **41** gives a 55% yield of the 5-membered ring product **42**

when using ICl (entry 28), and a 60% yield of the 5-membered ring product **43** when using

PhSeCl (entry 29). We believe that the 6-membered cyclohexenyl ring in **41** forces the

oxygen of the carbonyl group closer to C-4 of the alkenynoate ester resulting in 5-membered

ring formation (see the later mechanistic discussion). Interestingly, the 5-membered ring-

containing esters **44** and **46** give only products of addition of ICl across the carbon-carbon

triple bond. However, by using I_2 instead of ICl, both substrates **44** and **46** afford the desired

bicyclic α-pyrones **45** and **47** respectively as the only products in excellent yields (entries 31

and 33). Note that these two iodocyclization reactions take a much longer time to reach

completion. A reasonable explanation is that the reaction is slowed down because the

oxygen of the carbonyl group is oriented away from the carbon-carbon triple bond (see the

later mechanistic discussion).

A biisocoumarin has also been prepared by this cyclization methodology as shown in

entry 34. When using ICl or I_2 at room temperature, a mixture of the desired biisocoumarin

49 and an inseparable by-product were obtained. However, using ICl at -78 °C afforded the

biisocoumarin **49** as the only product in a 90 % yield.

Our iodocyclization results are generally consistent with those reported by Rossi.[19]

For instance, in our work, when using ICl or I_2 as the electrophile and CH_2Cl_2 as the solvent,

the reactions generally afford 6-membered ring lactones, except for alkynes **13**, **15** and **41**, where 5-membered ring lactones are formed exclusively and alkynes **33** and **36**, where mixtures of 5- and 6-membered ring lactones are produced. Rossi has usually obtained a mixture of 5- and 6-membered ring products from the cyclization of esters when using solvents other than CH_2Cl_2 and claimed that the solvent employed effects the regioselectivity of iodocyclization.[19a] When using ICl and CH_2Cl_2, Rossi obtained almost exclusively the 6-membered ring lactone from the cyclization of ester **1**, and in some other cases, small amounts of 5-membered ring lactones were detected. Rossi obtained a mixture of (*E*)- and (*Z*)-5-membered ring lactone **14** when using alkyne **13**.[19b] However, in our case, only (*E*)-**14** was obtained. We would like to point out that our reaction times (0.5-1 h) are much shorter than Rossi's (3-3.5 h), which might be the reason why we get higher yields and better stereoselectivity.

Surprisingly, the nature of the R^1 group on the ester had very little effect on the reaction rate or the product yield. Even a *tert*-butyl ester **22** cyclized in approximately the same time and yield as the corresponding methyl ester **1** (compare entries 1 and 16). Based on this observation, we propose the following mechanism for this electrophilic cyclization (Scheme 2). Nucleophilic attack by the oxygen of the carbonyl group on the carbon-carbon triple bond activated by coordination to I^+ is followed by either S_N2 attack of the chloride on the R^1 group when R^1 = Me or perhaps S_N1 cleavage of the R^1 group in the case of the *t*-butyl ester.

SCHEME 2
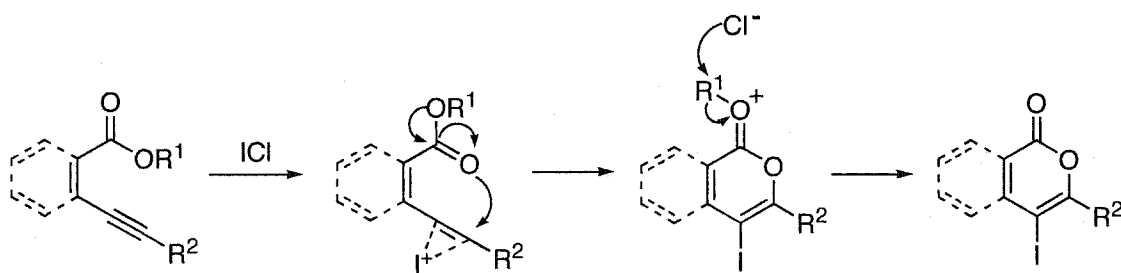
An interesting feature of this process is the fact that the iodoisocoumarins and iodo-2(2H)-pyrones generated can be further elaborated using various palladium-catalyzed processes. For example, the Sonagashira (eq 3),[20] Heck (eq 4),[21] and Suzuki reactions (eqs 5 and 6)[22] afford the corresponding products **50-53** respectively in good yields.

$$1.2\ H\!-\!\!\!\equiv\!\!\!-Ph$$
$$2\ \%\ PdCl_2(PPh_3)_2$$
$$1\ \%\ CuI,\ Et_3N,\ 55\ ^{\circ}C$$

73%　　(3)

50

$$4.0\ H_2C{=}CHCO_2Et$$
$$2\ \%\ Pd(OAc)_2$$
$$NaHCO_3,\ DMF,\ 85\ ^{\circ}C$$

60%　　(4)

51

$$1.2\ NaBPh_4$$
$$5\ \%\ Pd(PPh_3)_4$$
$$LiCl,\ DMF,\ 85\ ^{\circ}C$$

58%　　(5)

52

$$\text{(structure)} \xrightarrow[\substack{5\ \%\ \text{PdCl}_2(\text{PhCN})_2,\ \text{KF} \\ 4:1\ \text{DMF/H}_2\text{O},\ 100\ ^\circ\text{C}}]{2.0\ \text{PhB(OH)}_2} \text{(structure)} \quad 90\% \qquad (6)$$

53
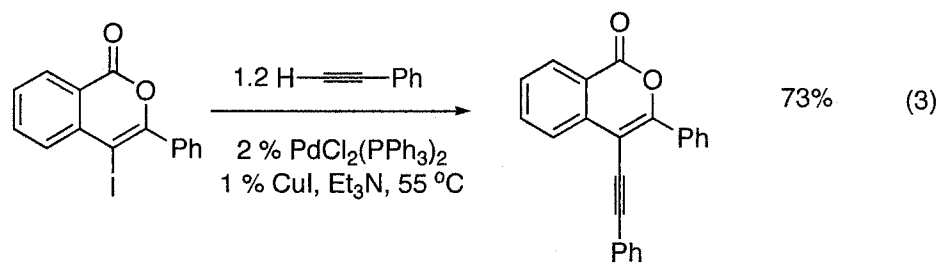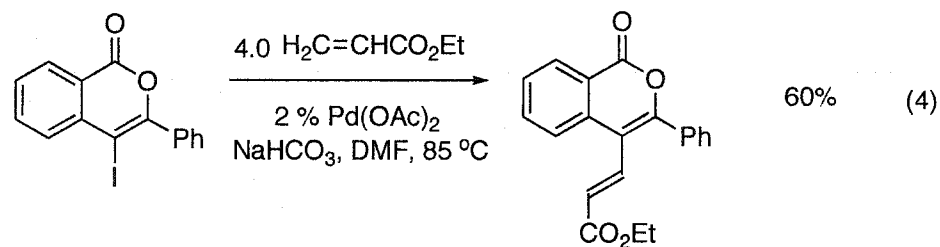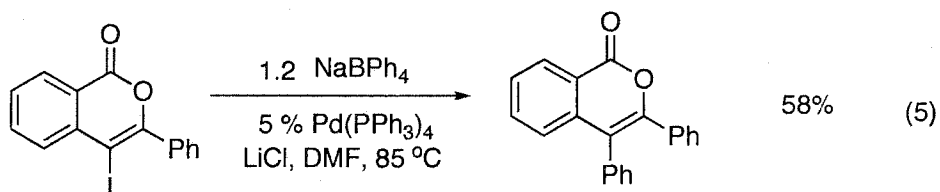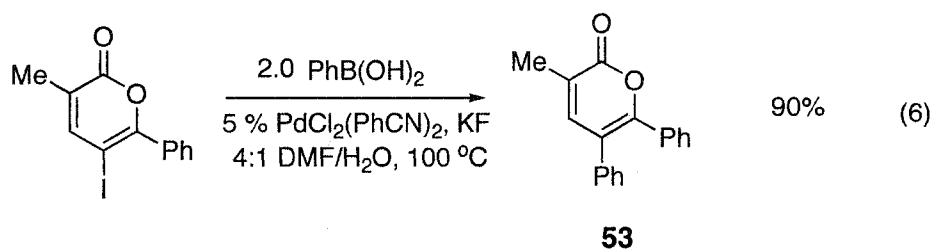
Conclusions

Efficient syntheses of a wide variety of substituted isocoumarins and α-pyrones have been developed under very mild reaction conditions. This methodology accommodates a variety of alkynyl esters with various functional groups and affords the anticipated substituted isocoumarins and α-pyrones in excellent yields. In a few cases, 5-membered ring lactones or mixtures of 5- and 6-membered ring lactones are formed. The resulting iodine-containing products are readily elaborate to more complex products using known organopalladium chemistry. Although Rossi et al[19] have reported several reactions of alkynyl esters with ICl or I_2, we have extended the above chemistry to the synthesis of polycyclic aromatic and biisocoumarins and generally obtained cleaner reactions. We have also shown that electrophiles other than I_2 and ICl, namely HI, PhSeCl and p-$O_2$$NC_6$$H_4$SCl, can be used in this chemistry.

Experimental Section

General. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise

noted. The following starting materials were made according to literature procedures: methyl 4,5-dimethoxy-2-iodobenzoate,[12] *tert*-butyl 2-iodobenzoate,[12] methyl (*Z*)-3-iodo-2-propenoate,[12] methyl 2-trifluoromethanesulfonyloxy-1-cyclohexenecarboxylate,[25] ethyl 2-trifluoromethanesulfonyloxy-1-cyclopentenecarboxylate,[26] ethyl (*Z*)-3-iodo-3-phenyl-2-propenoate,[12] methyl (*Z*)-3-iodo-2-methyl-3-phenyl-2-propenoate,[12] methyl (*Z*)-3-iodo-2,3-diphenyl-2-propenoate,[12] ethyl 3-iodoindole-2-carboxylate,[26] methyl 2-ethynylbenzoate,[27] and dimethyl 2,2'-(1,3-butadiyne-1,4-diyl)bisbenzoate.[27]

General procedure for preparation of the ester alkynes. To a solution of the corresponding aryl or vinylic iodide or triflate (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4 mL) were added $PdCl_2(PPh_3)_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was heated under an N_2 atm at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding ester alkyne.

Methyl 2-(phenylethynyl)benzoate (1). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 235 mg (99%) of the product as a yellow liquid with spectral properties identical to those previously reported.[23]

Methyl 2-(1-octynyl)benzoate (6). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 168.4 mg (69%) of the product as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 0.88-0.93 (m, 3H), 1.30-1.34 (m, 4H), 1.47-1.50 (m, 2H), 1.58-1.66 (m, 1H), 2.47 (t, *J* = 6.9 Hz, 2H), 3.91 (s, 3H), 7.30 (dt, *J* = 1.5, 7.8 Hz, 1H), 7.41 (dt, *J* = 1.5, 7.5 Hz, 1H), 7.51 (dd, *J* = 1.2, 7.8 Hz, 1H), 7.88 (dd, *J* = 1.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 16.6, 20.0,

22.8, 28.8, 28.9, 31.6, 52.2, 79.4, 96.2, 124.7, 127.3, 130.3, 131.7, 132.1, 134.4, 167.2; IR

(neat, cm^{-1}) 2953, 2933, 2857, 1734, 1717; HRMS Calcd for C$_{16}$H$_{20}$O$_2$: 244.1463. Found:

244.1467.

Methyl 2-(1-cyclohexenylethynyl)benzoate (8). Purification by flash

chromatography (20:1 hexane/EtOAc) afforded 221.7 mg (92%) of the product as a clear

liquid with spectral properties identical to those previously reported.[28]

Methyl 2-(5-hydroxy-1-pentynyl)benzoate (11). Purification by flash

chromatography (1:1.5 hexane/EtOAc) afforded 186.1 mg (85%) of the product as a clear

liquid with spectral properties identical to those previously reported:[29] ^{13}C NMR (CDCl$_3$) δ

16.7, 31.2, 52.4, 61.7, 80.0, 95.4, 124.5, 127.5, 130.4, 131.8, 131.9, 134.3, 167.1.

Methyl 2-[tris(1-methylethyl)silylethynyl]benzoate (15). Purification by flash

chromatography (20:1 hexane/EtOAc) afforded 307.9 mg (97%) of the product as a light

yellow liquid: ^{1}H NMR (CDCl$_3$) δ 1.14 (d, $J = 4.5$ Hz, 21H), 3.91 (s, 3H), 7.35 (t, $J = 7.5$

Hz, 1H), 7.43 (t, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 6.6$ Hz, 1H), 7.88 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR

(CDCl$_3$) δ 11.5, 18.3, 52.3, 96.5, 105.3, 123.6, 128.2, 130.3, 131.5, 132.8, 135.1, 167.3; IR

(neat, cm^{-1}) 2944, 2865, 1736, 1720; HRMS Calcd for for C$_{19}$H$_{28}$O$_2$Si: 316.1858. Found:

316.1864.

Methyl 4,5-dimethoxy-2-(phenylethynyl)benzoate (17). Purification by flash

chromatography (6:1 hexane/EtOAc) afforded 151 mg (51%) of the product as a white solid:

mp 115-117 °C; ^{1}H NMR (CDCl$_3$) δ 3.95 and 3.96 (9H), 7.08 (s, 1H), 7.34-7.36 (m, 3H),

7.51 (s, 1H), 7.56-7.59 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 52.3, 56.3, 56.4, 88.8, 93.2, 113.1,

115.9, 117.7, 123.7, 124.7, 128.5, 128.6, 131.8, 148.8, 151.8, 166.5; IR (neat, cm^{-1}) 2950,

2850, 1724, 1701; HRMS Calcd for C$_{18}$H$_{16}$O$_4$: 296.1048. Found: 296.1054.

Dimethyl (phenylethynyl)terephthalate (19). Purification by flash chromatography

(7:1 hexane/EtOAc) afforded 265 mg (90%) of the product as a white solid: mp 91-93 °C; [1]H

NMR (CDCl$_3$) δ 3.96 (s, 3H), 3.99 (s, 3H), 7.35-7.39 (m, 3H), 7.55-7.61 (m, 2H), 8.01-8.02

(m, 2H), 8.30 (t, J = 1.0 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 52.71, 52.81, 87.6, 95.5, 123.2, 124.3,

128.6, 128.8, 129.1, 130.8, 132.0, 133.2, 135.2, 135.6, 165.9, 166.3; IR (neat, cm^{-1}) 1727;

HRMS Calcd for C$_{18}$H$_{14}$O$_4$: 294.0892. Found: 294.0900.

***tert*-Butyl 2-(phenylethynyl)benzoate (22).** Purification by flash chromatography

(30:1 hexane/EtOAc) afforded 272.1 mg (98%) of the product as a light yellow liquid: [1]H

NMR (CDCl$_3$) δ 1.62 (s, 12H), 7.34-7.39 (m, 4H), 7.45 (t, J = 7.5 Hz, 1H), 7.55-7.58 (m,

2H), 7.62 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 28.4, 81.9, 88.7,

93.9, 123.20, 123.21, 123.7, 128.1, 128.6, 130.2, 131.2, 131.8, 134.1, 134.3, 166.1; IR (neat,

cm^{-1}) 3062, 2979, 2931, 1706; HRMS Calcd for C$_{19}$H$_{18}$O$_2$: 278.1306. Found: 278.1309.

Methyl (Z)-5-phenyl-2-penten-4-ynoate (23). Purification by flash chromatography

(15:1 hexane/EtOAc) afforded 165 mg (89%) of the product as a yellow liquid with spectral

properties identical to those previously reported:[23] ^{13}C NMR (CDCl$_3$) δ 51.7, 86.5, 101.6,

122.8, 123.4, 127.9, 128.6, 129.4, 132.3, 165.4.

Methyl (Z)-2-nonen-4-ynoate (27). Purification by flash chromatography (15:1

hexane/EtOAc) afforded 134.5 mg (81%) of the product as a yellow liquid with spectral

properties identical to those previously reported:[23] ^{13}C NMR (CDCl$_3$) δ 13.8, 19.9, 22.1,

30.6, 51.5, 77.8, 104.6, 124.5, 127.1, 165.5.

Ethyl (Z)-2-methyl-5-phenyl-2-penten-4-ynoate (29). Purification by flash

chromatography (15:1 hexane/EtOAc) afforded 207 mg (97%) of the product as a yellow

liquid: ^{1}H NMR (CDCl$_3$) δ 1.30 (t, J = 7.2 Hz, 3H), 2.13 (d, J = 1.2 Hz, 3H), 4.23 (q, J = 7.2

Hz, 2H), 6.03 (d, J = 1.8 Hz, 1H), 7.32-7.36 (m, 3H), 7.50-7.56 (m, 2H); ^{13}C NMR (CDCl$_3$) δ

14.6, 25.5, 60.3, 88.6, 100.4, 123.0, 124.6, 128.6, 129.4, 132.2, 134.8, 165.3; IR (neat, cm^{-1})

1721; HRMS Calcd for C$_{14}$H$_{14}$O$_2$: 214.0994. Found: 214.0998.

Ethyl (Z)-3,5-biphenyl-2-penten-4-ynoate (31). Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 241 mg (92%) of the product as a yellow

liquid: ^{1}H NMR (CDCl$_3$) δ 1.36 (t, J = 7.2 Hz, 3H), 4.31 (q, J = 7.2 Hz, 2H), 6.60 (s, 1H),

7.35-7.45 (m, 6H), 7.62-7.65 (m, 2H), 7.78-7.82 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 14.6, 60.6,

87.1, 102.3, 122.9, 123.0, 127.4, 128.6, 128.9, 129.5, 130.1, 132.3, 136.6, 137.4, 165.6; IR

(neat, cm^{-1}) 1717; HRMS Calcd for C$_{19}$H$_{16}$O$_2$: 276.1150. Found: 276.1157.

Methyl (Z)-2-methyl-3,5-biphenyl-2-penten-4-ynoate (33). Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 256 mg (93%) of the product as a yellow

liquid: ^{1}H NMR (CDCl$_3$) δ 2.02 (s, 3H), 3.89 (s, 3H), 7.28-7.49 (m, 10H); ^{13}C NMR (CDCl$_3$)

δ 17.5, 52.2, 89.8, 97.7, 123.5, 128.3, 128.5, 128.6, 128.8, 128.9, 130.0, 131.9, 134.6, 138.8,

169.0; IR (neat, cm^{-1}) 1707, 1720; HRMS Calcd for C$_{19}$H$_{16}$O$_2$: 276.1150. Found: 276.1157.

Methyl (Z)-2,3,5-triphenyl-2-penten-4-ynoate (36). Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 249 mg (74%) of the product as a yellow

liquid: ^{1}H NMR (CDCl$_3$) δ 3.90 (s, 3H), 7.13-7.23 (m, 8H), 7.26-7.38 (m, 5H), 7.48-7.54 (m,

2H); ^{13}C NMR (CDCl$_3$) δ 52.7, 89.5, 97.8, 123.1, 128.0, 128.2, 128.28, 128.34, 128.4, 128.6,

129.1, 129.9, 130.0, 132.0, 135.5, 137.4, 139.6, 169.1; IR (neat, cm^{-1}) 1724; HRMS Calcd for

C$_{24}$H$_{18}$O$_2$: 338.1307. Found: 338.1312.

Ethyl 2-(phenylethynyl)cyclohex-1-enecarboxylate (41). Purification by flash

chromatography (15:1 hexane/EtOAc) afforded 252 mg (99%) of the product as a yellow

liquid: ^{1}H NMR (CDCl$_3$) δ 1.29-1.34 (m, 3H), 1.66 (d, J = 2.7 Hz, 4H), 2.42 (d, J = 2.7 Hz,

4H), 4.20-4.29 (m, 2H), 7.29-7.36 (m, 3H), 7.44-7.47 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 14.6,

21.9, 22.1, 26.6, 32.6, 60.7, 89.7, 96.3, 123.7, 128.3, 128.5, 128.6, 131.8, 134.7, 167.7; IR

(neat, cm^{-1}) 1698; HRMS Calcd for C$_{17}$H$_{18}$O$_2$: 254.1307. Found: 254.1310.

Ethyl 2-(phenylethynyl)cyclopent-1-enecarboxylate (44). Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 238 mg (99%) of the product as a white

solid: mp 69-71 °C; ^{1}H NMR (CDCl$_3$) δ 1.34 (t, J = 7.2 Hz, 3H), 1.96 (quintet, J = 7.5 Hz,

2H), 2.75 (t, J = 7.5 Hz, 4H), 4.26 (q, J = 7.2 Hz, 2H), 7.31-7.36 (m, 3H), 7.49-7.52 (m, 2H);

^{13}C NMR (CDCl$_3$) δ 14.6, 22.5, 33.6, 39.6, 60.6, 86.0, 99.7, 123.3, 128.6, 129.0, 132.0,

134.4, 138.4, 164.9; IR (neat, cm^{-1}) 1687; HRMS Calcd for C$_{16}$H$_{16}$O$_2$: 240.1150. Found:

240.1156.

Ethyl 1-methyl-3-(phenylethynyl)indole-2-carboxylate (46). Purification by flash

chromatography (7:1 hexane/EtOAc) afforded 300 mg (99%) of the product as a white solid:

mp 85-86 °C; ^{1}H NMR (CDCl$_3$) δ 1.50 (t, J = 7.2 Hz, 3H), 4.09 (s, 3H), 4.48 (q, J = 7.2 Hz,

2H), 7.21-7.45 (m, 6H), 7.56-7.63 (m, 2H), 7.90 (d, J = 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ

14.7, 32.5, 61.3, 83.2, 95.6, 105.0, 110.6, 121.6, 121.9, 124.4, 126.1, 128.2, 128.3, 128.6,

129.2, 131.6, 138.6, 162.0; IR (neat, cm^{-1}) 1703; HRMS Calcd for C$_{20}$H$_{17}$O$_2$N: 303.1259.

Found: 303.1265.

General procedure for the electrophilic cyclization of ester alkynes by ICl. The

ester alkyne (0.30 mmol) in 3 ml of CH$_2$Cl$_2$ was placed in a 4 dram vial and flushed with N$_2$.

The ICl (1.2 equiv) in 0.5 ml of CH$_2$Cl$_2$ was added dropwise to the vial by a syringe. The

reaction was stirred at room temperature for 30 min unless otherwise indicated. The reaction

mixture was then diluted with 50 ml of ether, washed with 25 ml of satd aq Na$_2$S$_2$O$_3$, dried

(MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

4-Iodo-3-phenylisocoumarin (2). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 94.6 mg (90%) of the product as a white solid with spectral properties identical to those previously reported[17a]: mp 137-138 °C (lit.[17a] mp 136-138 °C).

3-*n*-Hexyl-4-iodoisocoumarin (7). Purification by flash chromatography (15:1 hexane/EtOAC) afforded 91.1 mg (85%) of the product as a clear liquid: ^{1}H NMR (CDCl$_3$) δ 0.87-0.91 (m, 3H), 1.29-1.44 (m, 7H), 1.71-1.76 (m, 2H), 2.91 (t, $J = 7.8$ Hz, 2H), 7.47-7.53 (m, 1H), 7.71-7.76 (m, 2H), 8.22 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 14.2, 16.6, 22.7, 27.4, 29.0, 31.7, 37.5, 76.3, 120.1, 128.7, 129.8, 130.6, 135.8, 138.2, 158.4, 162.1; IR (neat, cm^{-1}) 2955, 2929, 2858, 1736; HRMS Calcd for C$_{15}$H$_{17}$O$_2$I: 356.0273. Found: 356.0277.

3-(1-Cyclohexenyl)-4-iodoisocoumarin (9). Purification by flash chromatography (20:1 hexane/EtOAc) afforded 103.1 mg (98%) of the product as a white solid: mp 87-88 °C; ^{1}H NMR (CDCl$_3$) δ 1.67-1.80 (m, 4H), 2.21-2.35 (m, 4H), 6.15-6.17 (m, 1H), 7.51 (t, $J = 8.1$ Hz, 1H), 7.76-7.82 (m, 2H), 8.24 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 21.7, 22.4, 25.2, 26.6, 75.2, 120.4, 128.9, 129.8, 131.5, 134.1, 135.2, 135.7, 138.5, 157.4, 162.1; IR (neat, cm^{-} ^{1}) 2932, 1735; HRMS Calcd for C$_{15}$H$_{13}$O$_2$I: 351.9960. Found: 351.9966.

3-(3-Hydroxy-1-propyl)-4-iodoisocoumarin (12). Purification by flash chromatography (1:1 hexane/EtOAc) afforded 50.1 mg (51%) of the product as a white solid: mp 86-88 °C; ^{1}H NMR (CDCl$_3$) δ 1.78 (s, 1H), 1.98-2.03 (m, 2H), 3.05 (t, $J = 8.1$ Hz, 2H), 3.76 (t, $J = 6.3$ Hz, 2H), 7.48-7.54 (m, 1H), 7.73-7.77 (m, 2H), 8.20 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 30.3, 34.1, 61.9, 120.1, 128.9, 129.9, 130.6, 135.9, 138.0, 145.3, 157.6,

162.0; IR (neat, cm^{-1}) 3428, 2933, 2877, 1734; HRMS Calcd for $C_{12}H_{11}O_3I$: 329.9753.

Found: 329.9756.

(3E)-3-(Iodomethylene)-2-benzofuran-1(3H)-one (14). Purification by flash

chromatography (7:1 hexane/EtOAc) afforded 51 mg (63%) of the product as a white solid:

mp 80-82 °C; ^{1}H NMR (CDCl$_3$) δ 6.56 (s, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.80 (t, J = 7.8 Hz,

1H), 7.95 (d, J = 7.8 Hz, 1H), 8.71 (d, J = 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 57.9, 124.4,

126.1, 126.7, 131.4, 134.7, 138.0, 149.2, 165.8; IR (neat, cm^{-1}) 1777; HRMS Calcd for

$C_9H_5O_2I$: 271.9334. Found: 271.9341.

(3E)-3-[Iodo(triisopropylsilyl)methylene]-2-benzofuran-1(3H)-one (16).

Purification by flash chromatography (20:1 hexane/EtOAc) afforded 123.6 mg (96%) of the

product as a white solid: mp 117-120 °C; ^{1}H NMR (CDCl$_3$) δ 1.17 (d, J = 7.5 Hz, 18H),

1.64-1.74 (m, 3H), 7.65 (t, J = 7.5 Hz, 1H), 7.79 (t, J = 7.2 Hz, 1H), 7.95 (d, J = 7.5 Hz, 1H),

9.18 (d, J = 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 13.6, 18.9, 84.8, 125.8, 126.5, 127.1, 131.1,

134.3, 139.2, 153.1, 165.9; IR (neat, cm^{-1}) 2946, 2866, 1784; HRMS Calcd for $C_{18}H_{25}O_2ISi$:

428.0668. Found: 428.0676.

4-Iodo-6,7-dimethoxy-3-phenylisocoumarin (18). Purification by flash

chromatography (2:1 hexane/EtOAc) afforded 124.2 mg (100%) of the product as a white

solid: mp 178-179 °C; ^{1}H NMR (CDCl$_3$) δ 4.01 (s, 3H), 4.07 (s, 3H), 7.30 (s, 1H), 7.45-7.47

(m, 3H), 7.67-7.70 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 56.6, 56.8, 76.4, 109.7, 113.1, 113.2, 128.2,

130.2, 130.3, 134.1, 135.5, 150.5, 154.1, 155.8, 161.7; IR (neat, cm^{-1}) 2963, 1733; HRMS

Calcd for $C_{17}H_{13}O_4I$: 407.9858. Found: 407.9865. Anal. Calcd for $C_{17}H_{13}O_4I$: C, 50.00; H,

3.21. Found: C, 50.12; H, 2.79.

Methyl 4-iodo-3-phenyl-6-isocoumarincarboxylate (20). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 107 mg (88%) of the product as a white solid:

mp 164-166 °C; ^{1}H NMR (CDCl$_3$) δ 4.03 (s, 3H), 7.48-7.50 (m, 3H), 7.69-7.72 (m, 2H), 8.18

(d, J = 8.1 Hz, 1H), 8.38 (d, J = 8.1 Hz, 1H), 8.56 (d, J = 1.2 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ

53.1, 76.0, 123.4, 128.4, 129.7, 130.2, 130.4, 130.7, 133.3, 135.2, 136.8, 138.7, 155.7, 161.1,

165.7; IR (neat, cm^{-1}) 1727; HRMS Calcd for C$_{17}$H$_{11}$O$_4$I: 405.9702. Found: 405.9710.

Anal. Calcd for C$_{17}$H$_{11}$O$_4$I: C, 50.27; H, 2.73. Found: C, 50.11; H, 2.34.

5-Iodo-6-phenyl-2(2H)-pyranone (24). Purification by flash chromatography (6:1

hexane/EtOAc) afforded 83.6 mg (94%) of the product as a white solid with spectral

properties identical to those previously reported:[14] mp 100-101 °C (lit.[14] mp 101-103 °C).

6-n-Butyl-5-iodo-2(2H)-pyranone (28). Purification by flash chromatography (7:1

hexane/EtOAC) afforded 66.6 mg (80%) of the product as a clear liquid with spectral

properties identical to those previously reported:[14] ^{13}C NMR (CDCl$_3$) δ 13.9, 22.4, 29.2,

36.6, 67.8, 114.9, 152.0, 161.6, 166.0.

5-Iodo-4,6-diphenyl-2(2H)-pyranone (32). Purification by flash chromatography

(6:1 hexane/EtOAc) afforded 94 mg (84%) of the product as a white solid: mp 185-186 °C;

^{1}H NMR (CDCl$_3$) δ 6.30 (s, 1H), 7.20-7.39 (m, 2H), 7.42-7.51 (m, 6H), 7.69-7.78 (m, 2H);

^{13}C NMR (CDCl$_3$) δ 113.2, 128.3, 128.4, 128.5, 129.7, 129.9, 130.9, 135.1, 140.5, 161.3,

161.4, 162.0; IR (neat, cm^{-1}) 1709; HRMS Calcd for C$_{17}$H$_{11}$O$_2$I: 373.9804. Found:

373.9812.

5-Iodo-3,4,6-triphenyl-2(2H)-pyranone (37). Purification by flash chromatography

(10:1 hexane/EtOAc) afforded 23 mg (17%) of the product as a yellow solid: mp 180-182

°C; ^{1}H NMR (CDCl$_3$) δ 7.04-7.18 (m, 7H), 7.23-7.28 (m, 3H), 7.46-7.51 (m, 3H), 7.76-7.81

(m, 2H); ^{13}C NMR (CDCl$_3$) δ 125.7, 127.97, 127.99, 128.1, 128.4, 128.6, 129.1, 130.1, 130.5, 130.8, 134.1, 135.2, 140.7, 157.1, 160.1, 161.8; IR (neat, cm^{-1}) 1718; HRMS Calcd for C$_{23}$H$_{15}$O$_2$I: 450.0117. Found: 450.0124.

(5E)-5-[Iodo(phenyl)methylene]-3,4-diphenylfuran-2(5H)-one (38). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 74 mg (55%) of the product as a yellow solid: mp 138-140 °C; ^{1}H NMR (CDCl$_3$) δ 7.22-7.27 (m, 3H), 7.28-7.33 (m, 1H), 7.33-7.42 (m, 6H), 7.45-7.53 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 84.9, 128.2, 128.4, 129.3, 129.36, 129.4, 129.5, 129.7, 130.1, 130.2, 130.7, 132.0, 141.5, 146.2, 149.9, 167.4; IR (neat, cm^{-1}) 1764; HRMS Calcd for C$_{23}$H$_{15}$O$_2$I: 450.0117. Found: 450.0123. Anal. Calcd for C$_{23}$H$_{15}$O$_2$I: C, 61.35; H, 3.36. Found: C, 61.20; H, 2.97.

(3E)-3-[Iodo(phenyl)methylene]-4,5,6,7-tetrahydro-2-benzofuran-1(3H)-one (42). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 58 mg (55%) of the product as a pale pink solid: mp 134-135 °C; ^{1}H NMR (CDCl$_3$) δ 1.71-1.87 (m, 4H), 2.28-2.32 (m, 2H), 2.94-3.00 (m, 2H), 7.26-7.37 (m, 3H), 7.45-7.48 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 21.0, 21.4, 22.6, 27.8, 81.0, 128.2, 129.2, 130.3, 131.8, 140.5, 148.1, 151.3, 168.5; IR (neat, cm^{-1}) 1763; HRMS Calcd for C$_{16}$H$_{16}$O$_2$: 240.1150. Found: 240.1156.

4,4'-Diiodo-1H,1H'-3,3'-biisocoumarin (49). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 147 mg (90%) of the product as a yellow solid: mp >260 °C; ^{1}H NMR (CDCl$_3$) δ 7.67-7.71 (m, 2H), 7.82-7.91 (m, 4H), 8.35 (dd, J = 0.9, 8.1 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 82.3, 121.5, 130.4, 131.0, 131.8, 136.2, 136.7, 148.9, 160.6; IR (neat, cm^{-1}) 1723; HRMS Calcd for C$_{18}$H$_8$O$_4$I$_2$: 541.8512. Found: 541.8525.

General procedure for the electrophilic cyclization of ester alkynes by I$_2$. The ester alkyne (0.30 mmol), I$_2$ (1.2 equiv) and CH$_2$Cl$_2$ (3 ml) were placed in a 4 dram vial and

flushed with N_2. The reaction mixture was stirred at room temperature for 1 h unless otherwise indicated. The reaction mixture was then diluted with 50 ml of ether, washed with 25 ml of satd aq $Na_2S_2O_3$, dried ($MgSO_4$) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

5-Iodo-3-methyl-6-phenyl-2(2*H*)-pyranone (30). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 79 mg (84%) of the product as a white solid: mp 116-118 °C; ^{1}H NMR (CDCl$_3$) δ 2.37 (d, $J = 0.9$ Hz, 3H), 6.26 (d, $J = 0.9$ Hz, 1H), 7.44-7.48 (m, 3H), 7.62-7.68 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 29.2, 112.4, 128.4, 129.8, 130.8, 134.8, 158.6, 161.1, 161.3; IR (neat, cm^{-1}) 1726; HRMS Calcd for $C_{12}H_9O_2I$: 311.9647. Found: 311.9651.

5-Iodo-3-methyl-4,6-diphenyl-2(2*H*)-pyranone (34). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 19 mg (17%) of the product as a white solid: ^{1}H NMR (CDCl$_3$) δ 1.97 (s, 3H), 7.13-7.16 (m, 2H), 7.42-7.53 (m, 6H), 7.68-7.72 (m, 2H); IR (neat, cm^{-1}) 1721; HRMS Calcd for $C_{18}H_{13}O_2I$: 387.9960. Found: 387.9964.

(5*E*)-5-[Iodo(phenyl)methylene]-3-methyl-4-phenylfuran-2-(5*H*)-one (35). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 88 mg (76%) of the product as a yellow solid: mp 120-121 °C; ^{1}H NMR (CDCl$_3$) δ 1.83 (s, 3H), 7.23-7.38 (m, 5H), 7.44-7.55 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 10.2, 82.9, 128.2, 129.1, 129.2, 129.5, 130.3, 131.1, 132.0, 141.0, 146.4, 151.8, 169.1; IR (neat, cm^{-1}) 1762; HRMS Calcd for $C_{18}H_{13}O_2I$: 387.9960. Found: 387.9970.

4-Iodo-3-phenyl-6,7-dihydrocyclopenta[*c*]pyran-1-5(*H*)-one (45). Purification by flash chromatography (5:1 hexane/EtOAc) afforded 86 mg (85%) of the product as a white solid: mp 134-135 °C; ^{1}H NMR (CDCl$_3$) δ 2.07-2.18 (m, 2H), 2.92-3.05 (m, 4H), 7.42-7.47

(m, 3H), 7.68-7.72 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 21.7, 31.7, 40.7, 70.3, 125.6, 128.3, 129.8, 130.6, 134.0, 159.8, 160.6, 163.1; IR (neat, cm^{-1}) 1723; HRMS Calcd for C$_{14}$H$_{11}$O$_2$I: 337.9804. Found: 337.9808. Anal. Calcd for C$_{14}$H$_{11}$O$_2$I: C, 49.73; H, 3.28. Found: C, 49.62; H, 2.81.

4-Iodo-9-methyl-3-phenylpyrano[3,4-*b*]indol-1(9*H*)-one (47). 3.0 Equiv of I$_2$ was used. Purification by flash chromatography (2:1 hexane/CH$_2$Cl$_2$) afforded 101 mg (84%) of the product as a white solid: mp 241-242 °C; ^{1}H NMR (CDCl$_3$) δ 4.27 (s, 3H), 7.36 (t, *J* = 8.1 Hz, 1H), 7.45-7.52 (m, 4H), 7.56-7.62 (m, 1H), 7.69-7.73 (m, 2H), 8.93 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 31.6, 65.9, 77.5, 110.8, 120.9, 121.2, 122.8, 122.9, 125.9, 128.2, 128.3, 130.0, 130.5, 135.0, 141.6, 152.5, 156.8; IR (neat, cm^{-1}) 1707; HRMS Calcd for C$_{18}$H$_{12}$O$_2$IN: 400.9913. Found: 400.9919.

General procedure for the electrophilic cyclization of ester alkynes by PhSeCl or *p*-O$_2$NC$_6$H$_4$SCl. The ester alkyne (0.30 mmol), PhSeCl or *p*-O$_2$NC$_6$H$_4$SCl (1.5 equiv) and CH$_2$Cl$_2$ (3 ml) were placed in a 4 dram vial and flushed with N$_2$. The reaction mixture was stirred at room temperature for 1 h unless otherwise indicated. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

4-(*p*-Nitrophenylsulfenyl)-3-phenylisocoumarin (3). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 101 mg (90%) of the product as a white solid: mp 220-221 °C; ^{1}H NMR (CDCl$_3$) δ 7.20-7.26 (m, 2H), 7.38-7.47 (m, 3H), 7.57-7.68 (m, 3H), 7.71-7.84 (m, 2H), 8.10 (d, *J* = 8.7 Hz, 2H), 8.41 (dd, *J* = 7.8, 0.6 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 104.7, 121.1, 124.7, 125.5, 125.7, 128.4, 129.4, 129.5, 130.5, 131.0, 132.5, 136.0,

137.2, 145.9, 146.6, 161.1, 161.5; IR (neat, cm^{-1}) 1739; ^{1}HRMS Calcd for $C_{21}H_{13}O_4S$:

375.0565. Found: 375.0569.

3-(1-Cyclohexenyl)-4-(p-nitrophenylsulfenyl)isocoumarin (10). Purification by

flash chromatography (7:1 hexane/EtOAc) afforded 79.2 mg (70%) of the product as a white

solid: mp 222-224 °C; ^{1}H NMR (CDCl$_3$) δ 1.60-1.76 (m, 4H), 2.13-2.18 (m, 2H), 2.31-2.36

(m, 2H), 6.15-6.18 (m, 1H), 7.18 (dt, J = 9.0, 2.7 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.65-7.75

(m, 2H), 8.07 (dt, J = 9.0, 2.4 Hz, 2H), 8.34 (d, J = 7.5 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 21.6,

22.4, 25.6, 27.2, 103.3, 120.9, 124.6, 125.4, 125.6, 129.0, 130.3, 131.2, 135.0, 135.7, 137.4,

145.7, 147.2, 161.4, 164.1; IR (neat, cm^{-1}) 1741, 1517, 1338; HRMS Calcd for $C_{21}H_{17}NO_4S$:

379.0878. Found: 379.0886.

5-(p-Nitrophenylsulfenyl)-6-phenyl-2($2H$)-pyranone (25). Purification by flash

chromatography (2:1 hexane/EtOAc) afforded 77.6 mg (80%) of the product as a yellow

solid: mp 158-159 °C; ^{1}H NMR (CDCl$_3$) δ 6.39 (d, J = 9.6 Hz, 1H), 7.23-7.28 (m, 2H), 7.36-

7.51 (m, 4H), 7.70-7.74 (m, 2H), 8.13-8.18 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 105.7, 115.9,

124.8, 126.5, 128.6, 129.2, 131.3, 131.7, 145.8, 146.2, 150.1, 160.3, 166.3; IR (neat, cm^{-1})

1744, 1513, 1339; HRMS Calcd for $C_{17}H_{11}NO_4S$: 325.0409. Found: 325.0416.

3-Phenyl-4-(phenylselenyl)isocoumarin (4). Purification by flash chromatography

(7:1 hexane/EtOAc) to afford 124 mg (95%) of the product as a white solid: mp 137-139 °C;

^{1}H NMR (CDCl$_3$) δ 7.12-7.22 (m, 5H), 7.38-7.48 (m, 3H), 7.54 (t, J = 7.5 Hz, 1H), 7.65-7.74

(m, 3H), 8.05 (d, J = 8.1 Hz, 1H), 8.37 (dd, J = 8.1, 1.2 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 105.0,

121.1, 126.7, 128.1, 128.5, 129.0, 129.1, 129.7, 129.9, 130.0, 130.4, 132.1, 134.3, 135.6,

138.7, 159.8, 162.0; IR (neat, cm^{-1}) 1739; ^{1}HRMS Calcd for $C_{21}H_{14}O_2Se$: 378.0160. Found:

378.0167.

Methyl 3-phenyl-4-phenylselenyl-6-isocoumarincarboxylate (21). Purification by

flash chromatography (4:1 hexane/EtOAc) afforded 95 mg (73%) of the product as a white

solid: mp 137-139 °C; ^{1}H NMR (CDCl$_3$) δ 3.93 (s, 3H), 7.16-7.26 (m, 5H), 7.39-7.47 (m,

3H), 7.66 (dd, J = 7.5, 1.5 Hz, 2H), 8.13 (dd, J = 8.1, 1.5 Hz, 1H), 8.41 (d, J = 8.1 Hz, 1H),

8.75 (d, J = 0.9 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 53.0, 105.4, 124.0, 127.1, 128.1, 129.2, 129.8,

129.9, 130.0, 13.1, 130.3, 130.6, 131.5, 133.9, 136.4, 139.0, 160.2, 161.3, 165.9; IR (neat,

cm^{-1}) 1728, 1739; HRMS Calcd for C$_{23}$H$_{16}$O$_2$Se: 436.0214. Found: 436.0220.

6-Phenyl-5-phenylselenyl-2(2*H*)-pyranone (26). Purification by flash

chromatography (6:1 hexane/EtOAc) afforded 95.3 mg (97%) of the product as a yellow oil:

^{1}H NMR (CDCl$_3$) δ 6.20 (d, J = 9.6 Hz, 1H), 7.28-7.32 (m, 3H), 7.33-7.40 (m, 3H), 7.43-7.49

(m, 3H), 7.68-7.71 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 105.2, 115.2, 128.2, 128.4, 129.4, 130.0,

130.2, 131.0, 132.5, 132.8, 150.3, 161.4, 162.0; IR (neat, cm^{-1}) 1738; HRMS Calcd for

C$_{16}$H$_{12}$O$_2$Se: 328.0003. Found: 328.0009.

3,4,6-Triphenyl-5-phenylselenyl-2(2*H*)-pyranone (39). Purification by flash

chromatography (8:1 hexane/EtOAc) and recrystallization (hexane/EtOAc) afforded 44 mg

(30%) of the product as a yellow solid: mp 140-141 °C; ^{1}H NMR (CDCl$_3$) δ 6.79-6.82 (m,

2H), 6.86-6.89 (m, 2H), 6.98-7.26 (m, 11H), 7.34-7.46 (m, 3H), 7.73-7.78 (m, 2H); ^{13}C NMR

(CDCl$_3$) δ 108.6, 126.2, 127.0, 127.3, 127.8, 127.9, 128.1, 129.1, 129.4, 130.0, 130.7, 131.1,

132.2, 134.0, 134.1, 137.6, 158.0, 162.0, 163.9; IR (neat, cm^{-1}) 1718; HRMS Calcd for

C$_{29}$H$_{20}$O$_2$Se: 480.0630. Found: 480.0642.

(5*E*)-5-[Phenyl(phenylselenyl)methylene]-3,4-diphenylfuran-2(5*H*)-one (40).

Purification by flash chromatography (8:1 hexane/EtOAc) afforded 60.0 mg (41%) of the

product as a yellow solid: mp 192-193 °C; ^{1}H NMR (CDCl$_3$) δ 6.57-6.61 (m, 2H), 6.62-6.73

(m, 5H), 6.83 (t, J = 7.6 Hz, 2H), 6.90-6.97 (m, 3H), 7.06 (t, J = 7.2 Hz, 1H), 7.16-7.23 (m,

5H), 7.23-7.25 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 126.8, 127.1, 127.5, 127.8, 127.9, 128.1, 128.3,

128.4, 128.6, 128.8, 129.3, 129.4, 129.6, 130.8, 131.1, 132.9, 136.6, 142.8, 147.6, 167.9; IR

(neat, cm^{-1}) 1756, 1724; HRMS Calcd for C$_{29}$H$_{20}$O$_2$Se: 480.0631. Found: 480.0639.

(3*E*)-3-[Phenyl(phenylselenyl)methylene]-4,5,6,7-tetrahydro-2-benzofuran-

1(3*H*)-one (43). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 68.2

mg (60%) of the product as a pale yellow solid: mp 172-173 °C; ^{1}H NMR (CDCl$_3$) δ 1.41-

1.47 (m, 2H), 1.56-1.64 (m, 4H), 2.25-2.30 (m, 2H), 6.97-7.04 (m, 4H), 7.07-7.15 (m, 4H),

7.25-7.28 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 20.8, 21.4, 22.1, 24.2, 122.3, 126.9, 127.9, 128.4,

128.6, 128.7, 128.8, 130.5, 134.5, 137.0, 144.2, 149.7, 169.2; IR (neat, cm^{-1}) 1760, 1717;

HRMS Calcd for C$_{29}$H$_{20}$O$_2$Se: 382.0473. Found: 382.0481.

3-Phenylisocoumarin (5). The ester alkyne (0.30 mmol), 40% HI (2.0 equiv) and

CH$_2$Cl$_2$ (3 ml) were placed in a 4 dram vial and flushed with N$_2$. The reaction mixture was

stirred at room temperature for 96 h. The reaction mixture was then diluted with 50 ml of

ether, washed with 25 mL of satd aq NaHCO$_3$, 25 mL of H$_2$O, dried (MgSO$_4$) and filtered.

The solvent was evaporated under reduced pressure and isolated by chromatography on silica

gel (10:1 hexane/EtOAc) to afford 63 mg (92%) of the product as a white solid with spectral

properties identical to those previously reported:[29] mp 87-89 °C (lit.[29] mp 90-91 °C).

3-Phenyl-4-(phenylethynyl)isocoumarin (50). This compound was prepared using

the same procedure used for the preparation of the earlier ester alkynes. Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 238 mg (73%) of the product as a white

solid: mp 145-146 °C; ^{1}H NMR (CDCl$_3$) δ 7.38-7.40 (m, 3H), 7.48-7.62 (m, 6H), 7.83-7.89

(m, 1H), 8.12 (d, J = 8.1 Hz, 1H), 8.22-8.25 (m, 2H), 8.35 (d, J = 7.8 Hz, 1H); ^{13}C NMR

(CDCl$_3$) δ 82.9, 97.7, 99.9, 119.9, 123.0, 125.6, 128.4, 128.7, 128.92, 128.97, 129.0, 129.7, 130.6, 131.5, 132.6, 135.4, 137.2, 156.9, 161.2; IR (neat, cm^{-1}) 1743; HRMS Calcd for C$_{23}$H$_{14}$O$_2$: 322.0993. Found: 322.0997.

Ethyl (*E*)-3-(3-phenylisocoumarin-4-yl)-2-propenoate (51). To a solution of 4-iodo-3-phenylisocoumarin (0.25 mmol) and ethyl acrylate (1.0 mmol, 4.0 equiv) in DMF (1 ml) were added Pd(OAc)$_2$ (2.8 mg, 5 mol %), *n*-Bu$_4$NCl (0.25 mmol, 1 equiv) and Na$_2$CO$_3$ (0.625 mmol, 2.5 equiv). The resulting mixture was heated under an N$_2$ atmosphere at 85 °C for 30 h. The mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 mL of satd aq NaCl, dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford 47.2 mg (60 %) of the product as a white solid: mp 106-109 °C; ^{1}H NMR (CDCl$_3$) δ 1.32 (t, *J* = 7.2 Hz, 3H), 4.26 (q, *J* = 7.2 Hz, 2H), 6.25 (d, *J* = 16.5 Hz, 1H), 7.45-7.47 (m, 3H), 7.59-7.70 (m, 4H), 7.80-7.85 (m, 2H), 8.41 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 14.5, 61.0, 111.1, 120.7, 124.3, 126.0, 128.6, 128.8, 129.9, 130.4, 130.5, 132.5, 135.2, 136.2, 138.3, 153.8, 161.5, 166.3; IR (neat, cm^{-1}) 1740, 1716; HRMS Calcd for C$_{20}$H$_{16}$O$_4$: 320.1048. Found: 320.1053.

3,4-Diphenylisocoumarin (52). To a solution of 4-iodo-3-phenylisocoumarin (0.25 mmol) and NaBPh$_4$ (0.3 mmol, 1.2 equiv) in DMF (1 ml) were added Pd(OAc)$_2$ (2.8 mg, 5 mol %) and LiCl (0.25 mmol, 1 equiv). The resulting mixture was heated under an N$_2$ atmosphere at 85 °C for 20 h. The mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 ml of satd aq NaCl, dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 12:1 hexane/EtOAc and recrystallized from hexane/EtOAc to afford 44.0 mg (58 %) of the

product as a white solid with spectral properties identical to those previously reported:[12] mp

170-171 °C (lit.[12] mp 169-171 °C).

3-Methyl-5,6-diphenyl-2(2H)-pyranone (53). To a solution of 5-iodo-3-methyl-6-

phenyl-2(2H)-pyranone (0.25 mmol) and phenylboronic acid (0.5 mmol, 2.0 equiv) in 10 mL

of DMF/H$_2$O (V/V = 4/1) were added PdCl$_2$(PhCN)$_2$ (1.9 mg, 2 mol %) and KF (0.5 mmol,

2.0 equiv). The resulting mixture was heated under an N$_2$ atmosphere at 100 °C for 2 h. The

mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 ml

of satd aq NaCl, dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced

pressure. The reaction mixture was chromatographed using 4:1 hexane/EtOAc to afford 41

mg (90 %) of the product as a white solid: mp 122-124 °C; ^{1}H NMR (CDCl$_3$) δ 1.96 (d, J =

1.2 Hz, 3H), 6.25 (d, J = 0.9 Hz, 1H), 7.12-7.18 (m, 4H), 7.20-7.28 (m, 3H), 7.32-7.37 (m,

3H); ^{13}C NMR (CDCl$_3$) δ 22.1, 112.8, 119.9, 128.1, 128.3, 129.2, 129.4, 129.7, 130.8, 132.6,

134.9, 157.3, 157.4, 162.2; IR (neat, cm^{-1}) 1727; HRMS Calcd for C$_{18}$H$_{14}$O$_2$: 262.0994.

Found: 262.0996.

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CHAPTER 2. A REGIO- AND STEREOSELECTIVE

SYNTHESIS OF ISOINDOLIN-1-ONES VIA ELECTROPHILIC CYCLIZATION

Based on a paper to be published in the *Journal of Organic Chemistry*

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Abstract

A variety of substituted isoindolin-1-ones are readily prepared in good to excellent yields under very mild reaction conditions by the reaction of *o*-(1-alkynyl)benzamides with ICl, I_2, and NBS. In a few cases, substituted isoquinolin-1-ones were obtained as the major product instead. This methodology accommodates various alkynyl amides and functional groups, and has been successfully extended to heterocyclic starting materials. This chemistry has been successfully applied to the synthesis of a biologically interesting alkaloid, cepharanone B.

Introduction

The isoindolin-1-one ring system represents a key structural subunit in numerous natural and synthetic products that exhibit a wide range of biological activities, including antihypertensive,[1] antiinflammatory,[2] antiulcer[3] and antileukemic[4] properties. For example, magallanesine (**I**), an isoindolobenzazocine, has been isolated from various Berberis species

(Scheme 1).[5] Aristolactams (**II**) are found exclusively among the plants of the family

Aristolochiaceae.[6] The current interest elicited by these fused phenanthrene lactams arises

from their varied pharmaceutical and biological activities reported in folk medicine[7] and as

immunostimulant and anticancer agents.[6]

SCHEME 1
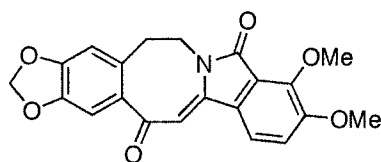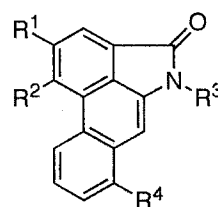
Magallanesine (**I**)   Aristolactams (**II**)

Considerable efforts have been directed towards the synthesis of isoindolinones

(phthalimidines). Isoindolinones have been prepared via Grignard[8] or lithiation[9] procedures,

as well as by Wittig,[10] Diels-Alder,[4,11] rearrangement[12] and photochemical reactions.[13] The

reduction of *N*-substituted phthalimides[14] and the condensation of phthalaldehyde[15] also

afford isoindolinones. Besides the classical methods, metal-catalyzed syntheses of

isoindolinones have also been reported. Cobalt and rhodium carbonyl complexes can be used

as the catalysts to synthesis isoindolinones.[16] Several examples of palladium catalysis have

appeared.[17] Recently, the intramolecular cyclization of alkynamides has been reported to

produce isoindolinones.[18]

We and others have developed methods for the synthesis of benzo[*b*]thiophenes,[19]

isoquinolines and naphthyridines,[20] isocoumarins and α-pyrones,[21] benzofurans,[22] furans,[23]

indoles,[24] furopyridines,[25] cyclic carbonates,[26] 2,3-dihydropyrroles and pyrroles,[27] pyrilium

salts[28] and bicyclic β-lactams[29] via electrophilic cyclization of functionally-substituted

alkynes. In a continuation of our studies, we have investigated the possibility of using electrophilic cyclization for the synthesis of isoindolinones and isoquinolinones. Herein, we report the successful electrophilic cyclization of o-(1-alkynyl)benzamides for the synthesis of isoindolinones. This chemistry generally produces good to excellent yields of the 5-membered ring lactams with good regioselectivity.

Results and Discussion

A two step approach to isoindolinones has been examined involving (i) preparation of o-(1-alkynyl)benzamides by a Sonagashira coupling reaction,[30] and (ii) electrophilic cyclization (Scheme 2).

SCHEME 2

$$E^+ = ICl, I_2, NBS, p\text{-}O_2NC_6H_4SCl, PhSeCl$$
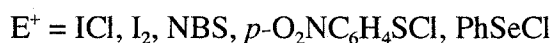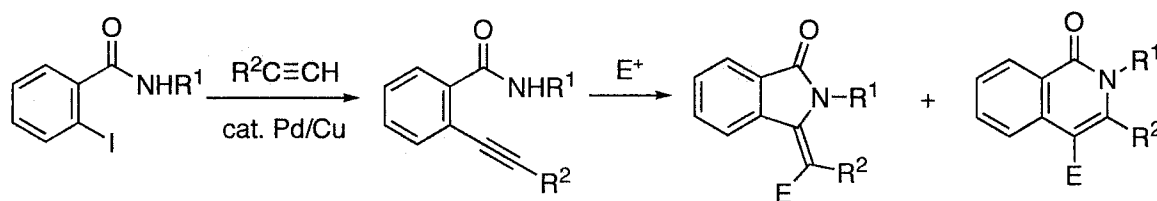
The o-(1-alkynyl)benzamides required for our approach are readily prepared by Sonogashira coupling[30] of the corresponding iodobenzamides with terminal alkynes using 2% $PdCl_2(PPh_3)_2$ and 1% CuI in Et_3N solvent at 55 °C. The yields of this process range from 74 to 99% and this procedure should readily accommodate considerable functionality.

The reaction of o-(1-alkynyl)benzamide **1** with electrophiles was chosen as a model system for optimization of this electrophilic cyclization process (eq 1). The results are summarized in Table 1.
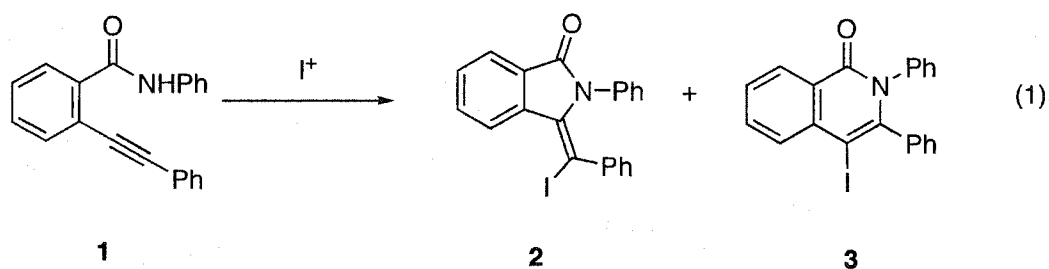
$$(1)$$

TABLE 1. Iodocyclization of o-(1-Alkynyl)benzamide 1 (eq 1)[a]

entry	electrophile	base	solvent	time (h)	% yield of 2	% yield of 3
1[b]	ICl	-	CH_2Cl_2	0.5	54	40
2	I_2	-	CH_2Cl_2	1	60	20
3	I_2	-	CH_3CN	1	75	14
4	I_2	$NaHCO_3$	CH_3CN	1	86	10
5	I_2	$NaHCO_3$	MeOH	1	85	8

[a] All reactions were run under the following conditions, unless otherwise indicated: 0.30 mmol of 1, 0.90 mmol of electrophile and 0.90 mmol of base in 3 mL of solvent were stirred at room temperature under Ar for the specified period of time. [b] 0.36 Mmol of electrophile was employed.

Benzamide 1 reacts at room temperature in CH_2Cl_2 to afforded a mixture of lactams 2 and 3 (Table 1, entry 1). Compared with the stronger electophile ICl, the weaker electrophile I_2 shows better regioselectivity (compare entries 1 and 2). The regioselectivity of this process also depends on the solvent employed in the reaction. Using CH_3CN as the solvent afforded better regioselectivity and a higher yield than CH_2Cl_2 (compare entries 2 and 3). The yield and selectivity can be further improved by adding $NaHCO_3$ to neutralize the acid generated in the reaction (compare entries 3 and 4). A similar yield and regioselectivity were also obtained when using MeOH as the solvent (entry 5). Thus, we have chosen the following reaction conditions A for the synthesis of isoindolin-1-ones: 0.30 mmol of the o-(1-alkynyl)benzamide, 3 equiv of I_2 and 3 equiv of $NaHCO_3$ in 3 mL of CH_3CN stirred at room temperature for 1 h. We have also employed reaction conditions B on occasion: 0.30

mmol of the *o*-(1-alkynyl)benzamide and 1.2 equiv of ICl in 3 mL of CH_2Cl_2 stirred at room temperature for 0.5 h. The reaction of amide 1 with bis(collidine)iodonium hexafluorophosphate in CH_2Cl_2 afforded only very slow reactions and a mixture of 5- and 6-membered ring lactams with the former predominating.

To explore the scope of this electrophilic cyclization strategy, the reactions of alkynyl amide 1 with different electrophiles (ICl, I_2, NBS, *p*-$O_2NC_6H_4SCl$, and PhSeCl) at room temperature have been studied (Table 2, entries 1-5). When using ICl, I_2, and NBS as the electrophilic reagents, a mixture of 5- and 6-membered ring products has been obtained. In all cases, the 5-membered ring product predominates. However, ICl generally affords larger amounts of the 6-membered ring lactam. When using *p*-$O_2NC_6H_4SCl$ and PhSeCl, the reaction proceeds smoothly. Unfortunately, the 5-membered ring products could not be isolated, because they appear to decompose easily. Only small amounts of the 6-membered ring products could be isolated.

The effect of ICl and I_2 on the regiochemistry of ring closure of several different amide moities has been examined (compare entries 1 and 2, 7 and 8, and 9 and 10). Although the results vary somewhat with the nature of the substituent on the nitrogen, I_2 exhibits much better regioselectivity than ICl in all cases examined. A small amount of the 6-membered ring product is always observed. However, when using I_2 and non-substituted or disubstituted amides, none of the desired cyclization products could be obtained (entries 11 and 12).

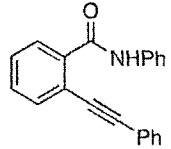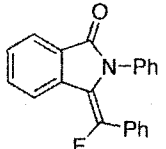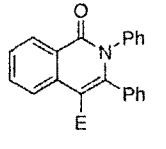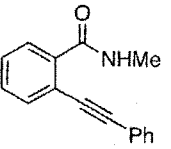**TABLE 2.** Electrophilic Cyclization of Alkynyl Carboxamides
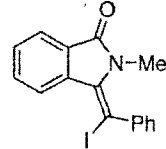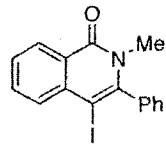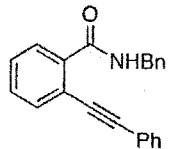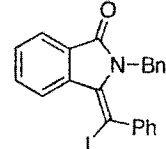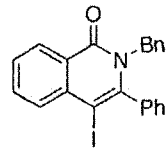
entry	substrate		electrophile	time (h)	products				% isolated yield
								E	
1		**1**	ICl[b]	0.5	**2**	**3**	I		54 + 40
2			I₂	1	**2**	**3**	I		86 + 10
3			NBS[b]	1	**4**	**5**	Br		82 + 17
4			PhSeCl[b]	0.5	**6**	**7**	PhSeCl		0 + 12
5			p-O₂NC₆H₄SCl[b]		**8**	**9**	p-O₂NC₆H₄SCl		0 + 7
7		**10**	ICl[b]	0.5	**11**	**12**			57 + 17
8			I₂	1					80 + 6
9		**13**	ICl[b]	0.5	**14**	**15**			60 + 30
10			I₂	1					85 + 8

TABLE 2. (continued)

entry	substrate	electrophile	time (h)	products		% isolated yield
11	**16**	I$_2$	1	**17**	**18**	0 + 0
12	**19**	I$_2$	1	**20**	**21**	0 + 0
13	**22**	I$_2$	1	**23**	**24**	90 + 9
14	**25**	I$_2$	1	**26**	**27**	77 + 7

TABLE 2. (continued)

entry	substrate	electrophile	time (h)	products	% isolated yield
15	28	I₂	1	29 / 30	31 + 68
16	28	ICl[b]	0.5	29 / 30	8 + 74
17	31	I₂	1	32 / 33	80 + 6
18	34	I₂	1	35 / 36	0 + 0
19	37	I₂	12	38 / 39	41 + 16
20	37	I₂	3	38 / 39	63 + 15
21	37	ICl[b]	0.5	38 / 39	16 + 53

48
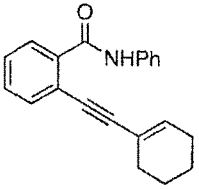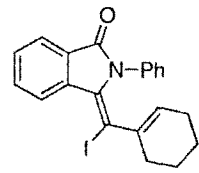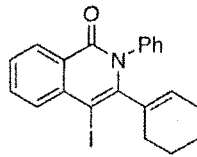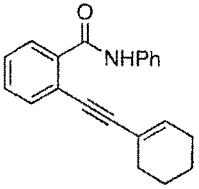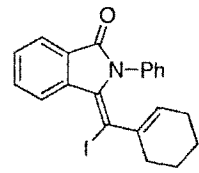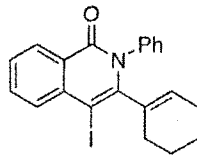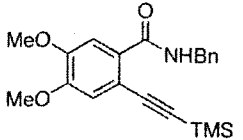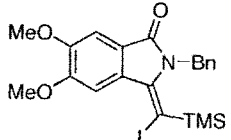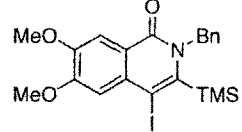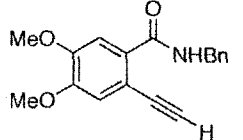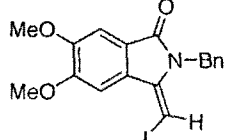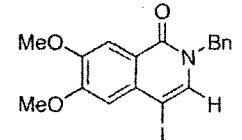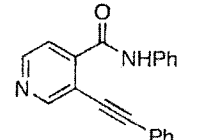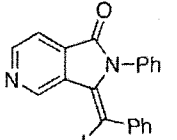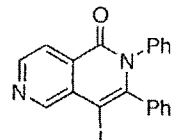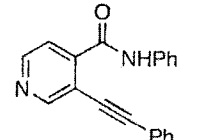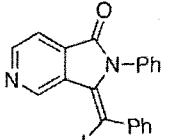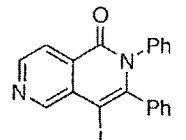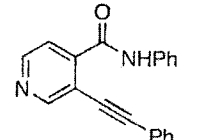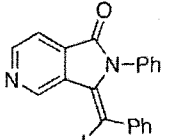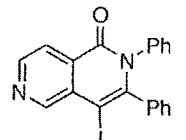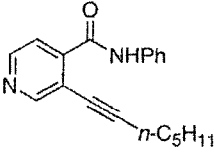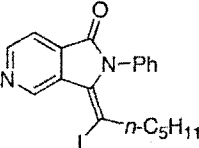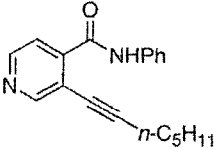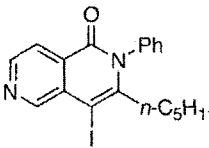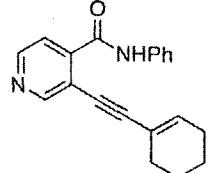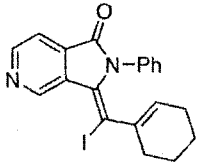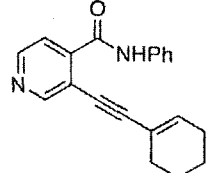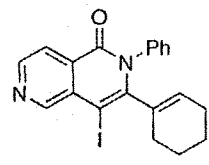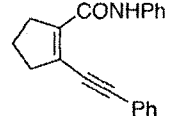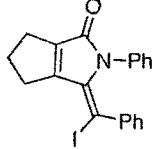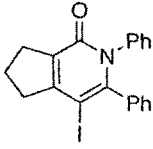
TABLE 2. (continued)

entry	substrate	electrophile	time (h)	products		% isolated yield
22	**40**	I$_2$	1	**41**	**42**	55 + 17
23		ICl[b]	0.5			22 + 40
24	**43**	I$_2$	1	**44**	**45**	0 + 61
25		ICl[b]	0.5			0 + 60
26	**46**	I$_2$	1	**47**	**48**	~15 + 58

[a] All reactions were run under the following conditions, unless otherwise specified: 0.3 mmol of the alkynamide, 3 equiv of the electrophile and 3 equiv of NaHCO$_3$ in 3 mL of CH$_3$CN at room temperature for 1 h. [b] 0.3 Mmol of the alkynamide and 1.2 equiv of the electrophile in 3 mL of CH$_2$Cl$_2$ at room temperature for 0.5 h.

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A wide variety of alkynylarenecarboxamides have been examined in this cyclization process. First of all, using *N*-phenyl carboxamides, we have examined the effect of various substituents on the remote end of the alkyne moiety (entries 13-16). Aryl- (entries 1 and 2) and a long chain alkyl-substituted alkyne **22** (entry 13) afford similar results. Even the TMS-substituted alkyne **25** underwent smooth iodocyclization with I_2 (entry 14). The isoindolinone **26** was obtained in 77% yield, along with a small amount of the corresponding diiodoisoquinolinone **27**. Obviously, the silyl group in the isoquinolinone has undergone iododesilylation either prior to or soon after cyclization. Surprisingly, the presence of an olefin (entries 15 and 16) affords the 6-membered ring isoquinolinone **30** as the major product, no matter whether ICl or I_2 is used. The 6-membered ring lactam is formed fairly cleanly when using ICl (entry 16).

The effect of substitution on the aromatic ring has also been examined. Isoindolinone **32** bearing two electron-donating methoxy substituents on the aromatic ring and a silyl moiety has been obtained in a good yield (entry 17). However, the corresponding alkyne in which the silyl group has been replaced by a hydrogen failed to give any recognizable products (entry 18).

This electrophilic cyclization is not limited to simple benzene-containing aromatics. The pyridine-containing substrates **37**, **40** and **43** have also been observed to give good yields of cyclization products (entries 19-25). A comparison of entry 19 with entry 20 indicates that a higher yield of the 5-membered ring product **38** can actually be obtained using a shorter reaction time. It appears that this isoindolinone is somewhat unstable under the reaction conditions. Interestingly, using ICl produces the 6-membered ring product **39** as the major product, while I_2 affords the 5-membered ring product as the major isomer (compare entries

20 and 21). The alkyl-substituted alkyne **40** reacts in a similar fashion affording the 5-membered ring lactam **41** as the major product when using I_2 and generating the 6-membered ring product **42** as the major product when ICl is used as the electrophile (entries 22 and 23). Introduction of a vinylic moiety directly on the alkyne leads to exclusive 6-membered ring formation no matter whether I_2 or ICl is employed (entries 24 and 25).

We have also briefly examined the cyclization of a ring-containing alkenynamide **46**. The 5-membered ring substrate **46** reacts with I_2 to afford a mixture of lactams **47** and **48** in which the 6-membered ring product **48** predominates presumably due to ring strain (entry 26).

The isoindolinones have been distinguished from the isoquinolinones on the basis of their IR spectra. The 5-membered ring products generally exhibit a carbonyl absorption band at 1710-1680 cm^{-1}, while in the 6-membered ring products the carbonyl absorption is observed at 1640-1650 cm^{-1}. The (*E*)-stereochemistry of isoindolinone **32** has been assigned using a NOESY experiment. This compound exhibits a cross-peak between the CH_2 of the benzyl group and the CH_3 of the TMS group. The stereochemistry of the other isoindolinones is assigned by analogy to lactam **32**.

We propose the following mechanism for this electrophilic cyclization (Scheme 3). Nucleophilic attack by the nitrogen of the amide group on the carbon-carbon triple bond activated by coordination to I$^+$ is followed by deprotonation to afford the cyclized products.

SCHEME 3
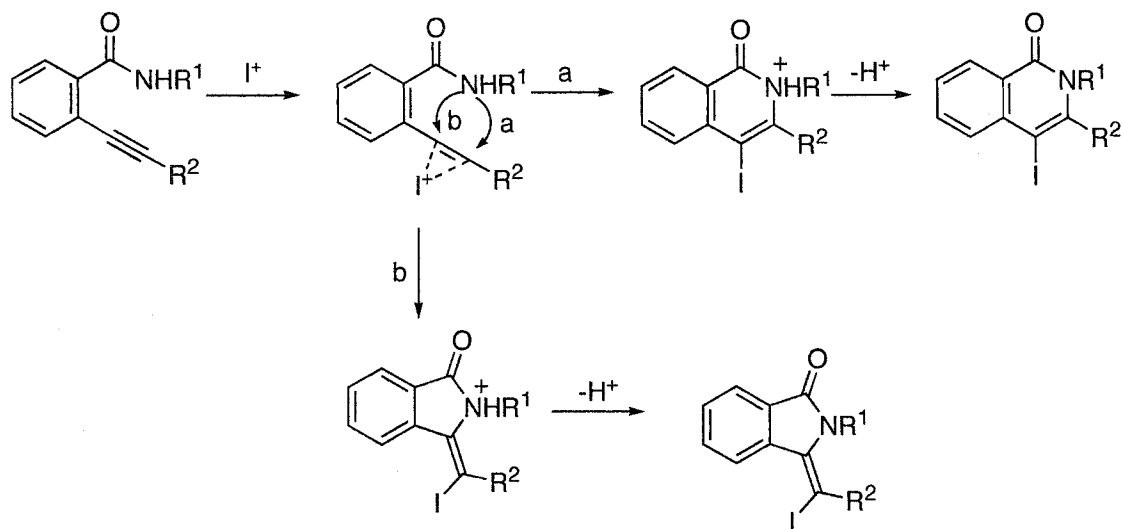
An interesting feature of this process is the fact that the isoindolinones and isoquinolinones produced by iodocyclization can be further elaborated using various palladium-catalyzed processes. For example, the Sonagashira reaction[30] of lactam **2** affords the coupling product **49** in an excellent yield (eq 2).

$$(2)$$
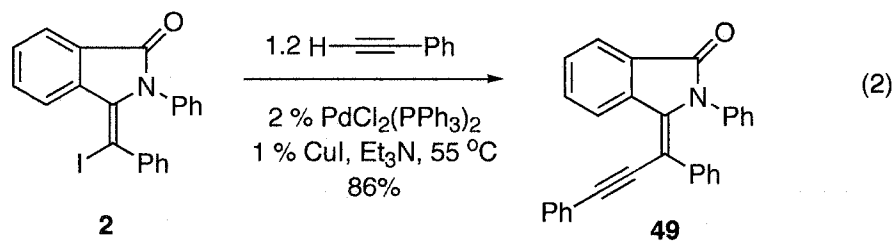
To further demonstrate the versatility of this electrophilic cyclization chemistry, we have applied this methodology to the synthesis of the biologically interesting alkaloid cepharanone B. Cepharanone B displays many pharmacological activities, including fertility-regulating,[31] cyclooxygenase inhibitory[32] and cytotoxic activity.[33] Although the synthesis of cepharanone B has been achieved previously,[34] our approach may provide a useful alternative to existing methodology.

The construction of the isoindolinone unit of lactam **53** has been accomplished by using our iodocyclization chemistry (Scheme 4). The requisite starting alkyne **52** is easily prepared using straight forward methodology and the Sonogashira reaction of aryl iodide **51** and trimethylsilyl acetylene. The iodocyclization of amide **52** afforded an 80% yield of vinylic iodide **53**. Desilylation and Suzuki cross-coupling with 2-bromophenylboronic acid afforded the (*Z*)-arylmethylene-1*H*-isoindolin-1-one **54** in good yield, whose stereochemistry was confirmed by comparison with previously reported ^{1}H and ^{13}C NMR spectra.[3] Initially we tried to obtain the fused aristolactam via organopalladium chemistry. Unfortunately, none of the desired aristolactam could be obtained. However, this key intermediate **54** can readily be converted to the desired cepharanone B in two steps through a previously reported procedure involving free radical chemistry.[3]

SCHEME 4
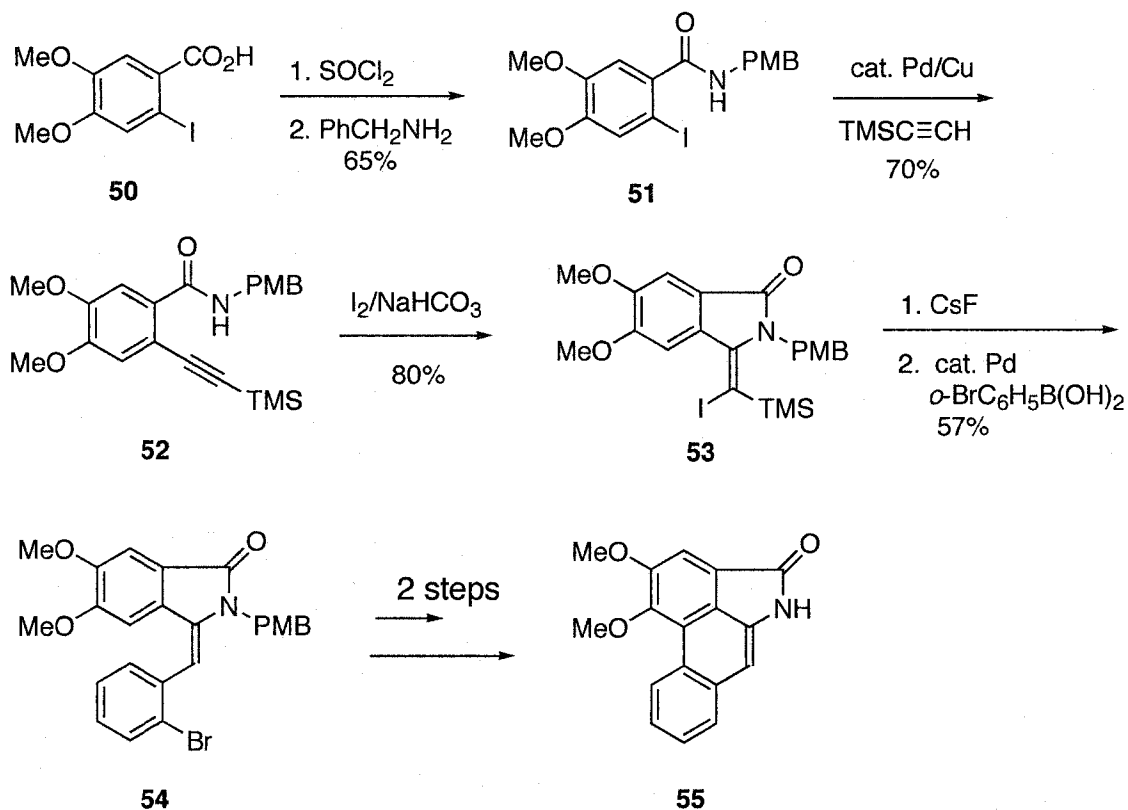
Conclusions

An efficient, regio- and stereoselective synthesis of indolinones from o-(1-

alkynyl)benzamides under very mild reaction conditions has been developed. A wide variety

of alkynyl amides bearing various functional groups readily undergo cyclization using I_2 and

ICl. The resulting iodine-containing products are readily elaborated to more complex

products using known organopalladium chemistry. This methodology has also been

successfully applied to the synthesis of the biologically interesting alkaloid cepharanone B.

Experimental Section

General. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise noted. The following starting materials were made according to literature procedures: 2-iodobenzamide,[17e] N-methyl-2-iodobenzamide,[17e] N-benzyl-2-iodobenzamide,[17e] N-phenyl-2-iodobenzamide,[17e] N-p-anisyl-2-iodo-4,5-dimethoxybenzamide,[17e] 3-iodoisonicotinanilide[35] and ethyl 2-(phenylethynyl)cyclopent-1-enecarboxylate.[21f]

General procedure for preparation of the o-(1-alkynyl)benzamides. To a solution of the corresponding organic iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et$_3$N (4 ml) were added PdCl$_2$(PPh$_3$)$_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was then heated under an N$_2$ atm at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding o-(1-alkynyl)benzamide.

N-Phenyl 2-(phenylethynyl)benzamide (1). Purification by flash chromatography (5:1 hexane/EtOAc) afforded 218 mg (74 %) of the product as a white solid with spectral properties identical to those previously reported:[17e] mp 150-152 °C (lit.[17e] mp 151-153 °C).

N-Methyl 2-(phenylethynyl)benzamide (10). Purification by flash chromatography (1:1 hexane/EtOAc) afforded 235 mg (100 %) of the product as a white solid with spectral properties identical to those previously reported:[17e] mp 105-106 °C (lit.[17e] mp 103-105 °C).

N-Benzyl 2-(phenylethynyl)benzamide (13). Purification by flash chromatography

(3:1 hexane/EtOAc) afforded 280 mg (90 %) of the product as a white solid: mp 99-101 °C;

^{1}H NMR (CDCl$_3$) δ 4.71 (d, *J* = 5.1 Hz, 2H), 7.11-7.15 (m, 2H), 7.22-7.39 (m, 8H), 7.44-7.49

(m, 2H), 7.58-7.61 (m, 1H), 7.80 (s, 1H), 8.13-8.17 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 44.8, 87.7,

96.0, 119.8, 127.8, 128.4, 128.6, 129.0, 129.1, 129.2, 130.5, 130.8, 131.6, 133.8, 135.3,

138.1, 166.3 (one carbon missing due to overlap); IR (neat, cm^{-1}) 3310, 3061, 1636; HRMS

Calcd for C$_{22}$H$_{17}$NO: 311.1310. Found: 311.1317.

2-(Phenylethynyl)benzamide (16). Purification by flash chromatography (1:1

hexane/EtOAc) afforded 206 mg (93 %) of the product as a colorless solid with spectral

properties identical to those previously reported:[17e] mp 159-161 °C (lit.[17e] mp 158-160 °C).

N-Phenyl 2-(1-decynyl)benzamide (22). Purification by flash chromatography (7:1

hexane/EtOAc) afforded 200 mg (60 %) of the product as a colorless oil: ^{1}H NMR (CDCl$_3$) δ

0.89 (t, *J* = 6.7 Hz, 3H), 1.24-1.30 (m, 8H), 1.38-1.44 (m, 2H), 1.55-1.64 (m, 2H), 2.51 (t, *J* =

7.2 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.34-7.43 (m, 4H), 7.49-7.53 (m, 1H), 7.68 (d, *J* = 7.5

Hz, 2H), 8.09-8.13 (m, 1H), 9.42 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 14.4, 20.0, 22.9, 28.8, 29.27,

29.32, 29.35, 32.1, 79.5, 98.8, 120.3, 120.5, 124.6, 128.6, 129.3, 130.4, 131.0, 134.0, 135.6,

138.4, 164.6; IR (neat, cm^{-1}) 3345, 3061, 2956, 1673; HRMS Calcd for C$_{23}$H$_{27}$NO: 333.2093.

Found: 333.2098.

N-Phenyl 2-(trimethylsilylethynyl)benzamide (25). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 142 mg (48 %) of the product as a colorless

solid with spectral properties identical to those previously reported:[17e] mp 97-96 °C (lit.[17e] mp

95-96 °C).

N-Phenyl 2-(cyclohex-1-en-1-ylethynyl)benzamide (28). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 263 mg (88 %) of the product as a yellow

solid: mp 99-100 °C; ^{1}H NMR (CDCl$_3$) δ 1.60-1.69 (m, 4H), 2.14-2.20 (m, 4H), 6.28 (q, J =

2.1 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 7.33-7.44 (m, 4H), 7.50-7.54 (m, 1H), 7.70 (d, J = 7.8

Hz, 2H), 8.10-8.14 (m, 1H), 9.34 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 21.6, 22.4, 26.1, 29.2, 85.1,

99.1, 120.3, 120.3, 124.6, 128.8, 129.3, 130.6, 131.0, 133.7, 135.5, 137.7, 138.3, 164.5 (one

carbon missing due to overlap); IR (neat, cm^{-1}) 3308, 2930, 1671, 1653; HRMS Calcd for

C$_{21}$H$_{19}$NO: 301.1467. Found: 301.1472.

N-Benzyl 4,5-dimethoxy-2-(trimethylsilylethynyl)benzamide (31). Purification by

flash chromatography (7:1 hexane/EtOAc) afforded 332 mg (90 %) of the product as a white

solid: mp 95-96 °C; ^{1}H NMR (CDCl$_3$) δ 0.09 (s, 9H), 3.90 (s, 3H), 3.94 (s, 3H), 4.67 (d, J =

5.7 Hz, 2H), 6.93 (s, 1H), 7.25-7.38 (m, 5H), 7.77 (s, 1H), 8.40 (s, 1H); ^{13}C NMR (CDCl$_3$) δ

0.03, 44.6, 56.5, 56.6, 101.3, 104.4, 112.5, 113.3, 116.0, 127.9, 128.3, 128.8, 129.2, 138.7,

150.1, 150.9, 165.6; IR (neat, cm^{-1}) 3386, 2959, 1654; HRMS Calcd for C$_{21}$H$_{25}$NO$_3$:

367.1604. Found: 367.1612.

N-Phenyl 3-(phenylethynyl)isonicotinamide (37). Purification by flash

chromatography (1:1 hexane/EtOAc) afforded 289 mg (98 %) of the product as a yellow

solid: mp 149-150 °C; ^{1}H NMR (CDCl$_3$) δ 7.19 (t, J = 7.4 Hz, 1H), 7.30-7.44 (m, 5H), 7.51-

7.55 (m, 2H), 7.63-7.67 (m, 2H), 7.96 (d, J = 5.1 Hz, 1H), 8.69 (d, J = 5.1 Hz, 1H), 8.89 (s,

1H), 9.34 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 84.5, 99.8, 115.8, 120.4, 121.3, 123.3, 125.3, 129.0,

129.5, 130.1, 132.0, 137.6, 142.2, 149.9, 154.2, 162.4; IR (neat, cm^{-1}) 3308, 3041, 1661;

HRMS Calcd for C$_{20}$H$_{14}$N$_2$O: 298.1106. Found: 298.1111.

N-Phenyl-3-(1-heptynyl)isonicotinamide (40). Purification by flash

chromatography (1:1 hexane/EtOAc) afforded 119 mg (41 %) of the product as a white solid:

mp 91-92 °C; ^{1}H NMR (CDCl$_3$) δ 0.87 (t, J = 6.9 Hz, 3H), 1.26-1.45 (m, 4H), 1.44-1.68 (m,

2H), 2.57 (t, J = 7.2 Hz, 2H), 7.19 (t, J = 7.5 Hz, 3H), 7.39 (t, J = 8.4 Hz, 2H), 7.63-7.67 (m,

2H), 7.97 (d, J = 5.1 Hz, 1H), 8.65 (d, J = 5.4 Hz, 1H), 8.77 (s, 1H), 9.46 (s, 1H); ^{13}C NMR

(CDCl$_3$) δ 14.1, 20.0, 22.4, 28.3, 31.4, 76.6, 102.2, 116.3, 120.4, 123.2, 125.3, 129.5, 137.6,

141.7, 149.3, 154.6, 162.3; IR (neat, cm^{-1}) 3258, 3041, 1670; HRMS Calcd for C$_{19}$H$_{20}$N$_2$O:

292.1576. Found: 292.1579.

N-Phenyl-3-(cyclohex-1-en-1-ylethynyl)isonicotinamide (43). Purification by flash

chromatography (1:1 hexane/EtOAc) afforded 269 mg (89 %) of the product as a white solid:

mp 130-131 °C; ^{1}H NMR (CDCl$_3$) δ 1.61-1.71 (m, 4H), 2.17-2.22 (m, 4H), 6.36 (q, J = 1.8

Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 8.1 Hz, 2H), 7.67 (d, J = 7.5 Hz, 2H), 7.97 (d, J

= 5.1 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.77 (s, 1H), 9.42 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 21.5,

22.3, 26.1, 29.0, 82.1, 102.1, 116.3, 119.8, 120.4, 123.3, 125.2, 129.4, 137.6, 139.1, 141.4,

149.4, 154.2, 162.3; IR (neat, cm^{-1}) 3302, 3046, 1656, 1599; HRMS Calcd for C$_{20}$H$_{18}$N$_2$O:

302.1419. Found: 302.1423.

N-Phenyl-2-(phenylethynyl)cyclopent-1-ene-1-carboxamide (46). Ethyl 2-

(phenylethynyl)cyclopent-1-enecarboxylate (238 mg, 1.0 mmol) was dissolved in THF (4 ml)

and the resulting solution was added to an aqueous 1.0 M LiOH solution (3.0 ml, 3.0 mmol).

The resulting mixture was stirred at 55 °C for 24 h and then concentrated under reduced

pressure. The residue was diluted with water (10 ml) and washed with Et$_2$O (3 × 10 ml).

The aqueous phase was cooled to 0 °C, acidified with cold 10% H$_2$SO$_4$ and extracted with

Et$_2$O (3 × 25 ml). The organic extract was dried over MgSO$_4$ and concentrated under reduced pressure to give the corresponding acid as a colorless solid.

The acid was dissolved in (COCl)$_2$ (5 ml) and stirred at room temperature overnight. The excess (COCl)$_2$ was removed under reduced pressure and the residue was diluted with THF (2 ml). The resulting solution was added slowly to a mixture of aniline (1.0 equiv) and pyridine (1 equiv) in THF (2 ml) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and diluted with Et$_2$O (20 ml), washed with 5 % HCl (8 ml) and 10 % Na$_2$CO$_3$ (8 ml), dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by flash chromatography (5:1 hexane/EtOAc) to afford 193 mg (67 %) of the product as a yellow solid: mp 132-133 °C; ^{1}H NMR (CDCl$_3$) δ 1.92-2.03 (m, 2H), 2.82-2.94 (m, 4H), 7.07 (t, J = 7.5 Hz, 1H), 7.28-7.43 (m, 5H), 7.50-7.54 (m, 2H), 7.61 (d, J = 7.8 Hz, 2H), 9.16 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 22.0, 34.1, 39.8, 85.1, 101.3, 119.7, 121.9, 124.3, 126.7, 129.0, 129.3, 129.8, 131.8, 138.4, 144.0, 162.5; IR (neat, cm^{-1}) 3368, 3057, 1666, 1597; HRMS Calcd for C$_{20}$H$_{17}$NO: 287.1310. Found: 287.1316.

(3E)-3-(1,3-Diphenylprop-2-ynylidene)-2-phenylisoindolin-1-one (49).

Purification by flash chromatography (7:1 hexane/EtOAc) afforded 343 mg (86 %) of the product as a yellow solid: mp 129-131 °C; ^{1}H NMR (CDCl$_3$) δ 7.26 (t, J = 10.5 Hz, 1H), 7.31-7.49 (m, 10H), 7.57-7.72 (m, 4H), 7.94-7.98 (m, 2H), 8.08 (d, J = 7.5 Hz, 1H), 8.66 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 87.7, 97.3, 102.0, 123.4, 123.9, 124.3, 124.4, 125.4, 128.3, 128.4, 128.8, 128.9, 129.0, 129.4, 130.5, 130.9, 131.8, 132.7, 135.3, 136.4, 145.6, 152.2, 152.9; IR (neat, cm^{-1}) 3056, 1689, 1588; HRMS Calcd for C$_{29}$H$_{19}$NO: 397.1467. Found: 397.1472.

General procedure for electrophilic cyclization of the alkynylarenecarboxamides

by ICl. The alkynylarenecarboxamide (0.30 mmol) in 3 ml of CH_2Cl_2 was placed in a 2

dram vial and flushed with N_2. The ICl (1.2 equiv) in 0.5 ml of CH_2Cl_2 was added dropwise

to the vial by a syringe. The reaction was stirred at room temperature for 30 min unless

otherwise indicated. The reaction mixture was then diluted with ether (50 ml), washed with

satd aq $Na_2S_2O_3$ (25 ml), dried ($MgSO_4$) and filtered. The solvent was evaporated under

reduced pressure and the product was isolated by chromatography on a silica gel column.

4-Iodo-2,3-diphenylisoquinolin-1(2*H*)-one (3). Purification by flash

chromatography (10:1 hexane/EtOAc) afforded 50.5 mg (40%) of the product as a light

yellow solid: mp 131-132 °C; ^{1}H NMR ($CDCl_3$) δ 7.06 (t, *J* = 7.3 Hz, 1H), 7.20-7.33 (m,

4H), 7.39-7.41 (m, 3H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.59-7.67 (m, 3H), 7.76 (d, *J* = 7.5 Hz, 1H),

8.40 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 123.1, 124.0, 124.1, 127.7, 128.2, 128.9, 129.4,

130.1, 130.2, 131.5, 133.2, 135.0, 135.6, 146.1, 148.7, 153.4; IR (neat, cm^{-1}) 1645; HRMS

Calcd for $C_{21}H_{14}INO$: 423.0120. Found: 423.0129.

2-Benzyl-4-iodo-3-phenylisoquinolin-1(2*H*)-one (15). Purification by flash

chromatography (7:1 hexane/EtOAc) afforded 64 mg (30 %) of the product as a yellow oil:

^{1}H NMR ($CDCl_3$) δ 4.70 (s, 2H), 7.25-7.28 (m, 1H), 7.32-7.50 (m, 8H), 7.58-7.72 (m, 4H),

8.32 (dd, *J* = 1.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 50.4, 75.8, 124.1, 126.7, 127.0, 127.9,

128.3, 128.5, 129.2, 130.0, 130.1, 131.3, 132.6, 134.1, 136.3, 141.0, 150.1, 153.6; IR (neat,

cm^{-1}) 3061, 2923, 1663, 1601; HRMS Calcd for $C_{22}H_{16}INO$: 437.0277. Found: 437.0281.

3-(Cyclohex-1-en-1-yl)-4-iodo-2-phenylisoquinolin-1(2*H*)-one (30). Purification by

flash chromatography (7:1 hexane/EtOAc) afforded 94 mg (74 %) of the product as a yellow

oil: ^{1}H NMR ($CDCl_3$) δ 1.60-1.70 (m, 4H), 2.14-2.21 (m, 4H), 6.14 (q, *J* = 1.8, 1H), 7.12 (tt,

J = 1.2, 7.5 Hz, 1H), 7.19 (dd, J = 1.2, 7.5 Hz, 2H), 7.31-7.45 (m, 3H), 7.59 (dt, J = 1.2, 7.8

Hz, 1H), 7.67 (dd, J = 0.6, 8.1 Hz, 1H), 8.33 (dd, J = 0.9, 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ

21.7, 22.5, 25.2, 26.6, 74.1, 123.1, 124.0, 127.5, 128.8, 128.9, 131.5, 133.1, 133.9, 135.1,

135.3, 146.3, 149.1, 155.8 (one carbon missing due to overlap); IR (neat, cm^{-1}) 3063, 2933,

1652, 1592; HRMS Calcd for C$_{21}$H$_{18}$INO: 427.0433. Found: 427.0439.

4-Iodo-2,3-diphenyl-2,6-naphthyridin-1(2*H*)-one (39). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 45 mg (53 %) of the product as a yellow solid:

mp 164-165 °C; ^{1}H NMR (CDCl$_3$) δ 7.12 (tt, J = 1.5, 7.5 Hz, 1H), 7.22-7.34 (m, 4H), 7.39-

7.46 (m, 3H), 7.59-7.63 (m, 2H), 8.11 (s, 1H), 8.77 (s, 1H), 9.08 (s, 1H); ^{13}C NMR (CDCl$_3$) δ

70.3, 123.3, 125.1, 128.3, 129.0, 130.1, 130.2, 130.5, 130.9, 134.8, 145.0, 146.6, 150.0,

153.7, 154.6 (one carbon missing due to overlap); IR (neat, cm^{-1}) 3061, 2930, 1669, 1651;

HRMS Calcd for C$_{20}$H$_{13}$IN$_2$O: 424.0073. Found: 424.0081.

4-Iodo-3-pentyl-2-phenyl-2,6-naphthyridin-1(2*H*)-one (42). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 51 mg (40 %) of the product as a yellow oil:

^{1}H NMR (CDCl$_3$) δ 0.84-0.89 (m, 3H), 1.27-1.33 (m, 4H), 1.55-1.61 (m, 2H), 2.74 (t, J = 7.5

Hz, 2H), 7.11-7.20 (m, 3H), 7.36 (dt, J = 1.8, 7.5 Hz, 2H), 8.00 (d, J = 5.1 Hz, 1H), 8.66 (d, J

= 5.1 Hz, 1H), 8.87 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 14.1, 22.5, 26.8, 31.2, 36.6, 70.1, 119.0,

122.9, 124.8, 128.5, 129.0, 130.4, 145.4, 147.1, 149.5, 152.5, 158.1; IR (neat, cm^{-1}) 2956,

2928, 1661, 1608; HRMS Calcd for C$_{19}$H$_{19}$IN$_2$O: 418.0542. Found: 418.0551.

3-(Cyclohex-1-en-1-yl)-4-iodo-2-phenyl-2,6-naphthyridin-1(2*H*)-one (45).

Purification by flash chromatography (7:1 hexane/EtOAc) afforded 51 mg (60 %) of the

product as a yellow solid: mp 111-112 °C; ^{1}H NMR (CDCl$_3$) δ 1.60-1.71 (m, 4H), 2.11-2.21

(m, 4H), 6.18 (q, J = 2.1 Hz, 1H), 7.13 (tt, J = 1.2, 7.5 Hz, 1H), 7.19-7.23 (m, 2H), 7.32-7.38

(m, 2H), 8.02 (dd, J = 0.6, 5.1 Hz, 1H), 8.66 (d, J = 5.1 Hz, 1H), 8.95 (s, 1H); ^{13}C NMR

(CDCl$_3$) δ 21.7, 22.4, 25.2, 26.4, 68.4, 119.0, 123.2, 124.9, 128.9, 129.1, 130.7, 133.2, 136.2,

145.2, 147.0, 149.6, 153.7, 157.1; IR (neat, cm^{-1}) 2930, 1652, 1592; HRMS Calcd for

C$_{20}$H$_{17}$IN$_2$O: 428.0386. Found: 428.0393.

General procedure for electrophilic cyclization of the alkynylarenecarboxamides

by I$_2$. The alkynylarenecarboxamide (0.30 mmol), I$_2$ (3.0 equiv), NaHCO$_3$ (3.0 equiv) and

CH$_3$CN (3 ml) were placed in a 4 dram vial and flushed with N$_2$. The reaction mixture was

stirred at room temperature for 1 h unless otherwise indicated. The reaction mixture was

then diluted with ether (50 ml), washed with satd aq Na$_2$S$_2$O$_3$ (25 ml), dried (MgSO$_4$) and

filtered. The solvent was evaporated under reduced pressure and the product was isolated by

chromatography on a silica gel column.

(3E)-3-[Iodo(phenyl)methylene]-2-phenylisoindolin-1-one (2). Purification by

flash chromatography (7:1 hexane/EtOAc) afforded 110 mg (86 %) of the product as a white

solid: mp 97-99 °C; ^{1}H NMR (CDCl$_3$) δ 7.09 (t, J = 6.6 Hz, 1H), 7.22-7.36 (m, 7H), 7.59-

7.73 (m, 4H), 8.05 (d, J = 7.5 Hz, 1H), 8.86 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 124.1,

125.07, 125.1, 125.4, 128.1, 128.7, 130.5, 130.9, 132.0, 132.8, 135.8, 140.6, 145.0, 147.8,

152.0 (one carbon missing due to overlap); IR (neat, cm^{-1}) 1684; HRMS Calcd for

C$_{21}$H$_{14}$INO: 423.0120. Found: 423.0129.

(3E)-3-[Iodo(phenyl)methylene]-2-methylisoindolin-1-one (11). Purification by

flash chromatography (7:1 hexane/EtOAc) afforded 86 mg (80%) of the product as a yellow

solid: mp 122-125 °C; ^{1}H NMR (CDCl$_3$) δ 3.16 (s, 3H), 7.28 (t, J = 7.2 Hz, 1H), 7.39 (t, J =

7.5 Hz, 2H), 7.52-7.67 (m, 4H), 7.85 (d, J = 7.5 Hz, 1H), 8.83 (d, J = 7.8 Hz, 1H); ^{13}C NMR

(CDCl$_3$) δ 35.2, 73.5, 123.2, 125.2, 128.2, 128.5, 130.4, 130.8, 131.4, 132.0, 136.2, 140.9,

147.5, 154.9; IR (neat, cm^{-1}) 1714; HRMS Calcd for C$_{16}$H$_{12}$INO: 360.9964. Found: 360.9968.

(3*E*)-2-Benzyl-3-[iodo(phenyl)methylene]isoindolin-1-one (14). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 107 mg (85 %) of the product as a yellow solid: mp 70-72 °C; ^{1}H NMR (CDCl$_3$) δ 4.64 (s, 2H), 7.23-7.34 (m, 6H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.55-7.66 (m, 4H), 7.95 (d, *J* = 7.5 Hz, 1H), 8.83 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 52.1, 73.7, 123.6, 125.2, 126.9, 128.2, 128.3, 128.58, 128.59, 130.4, 130.8, 131.6, 132.1, 136.2, 140.2, 141.0, 147.5, 154.5; IR (neat, cm^{-1}) 3058, 3027, 1694, 1612; HRMS Calcd for C$_{22}$H$_{16}$INO: 437.0277. Found: 437.0283.

(3*E*)-3-(1-Iodononylidene)-2-phenylisoindolin-1-one (23). Purification by flash chromatography (12:1 hexane/EtOAc) afforded 123 mg (90 %) of the product as a yellow liquid: ^{1}H NMR (CDCl$_3$) δ 0.87-0.92 (m, 3H), 1.22-1.32 (m, 10H), 1.59-1.65 (m, 2H), 2.90 (t, *J* = 7.5, 2H), 7.15-7.21 (m, 1H), 7.35-7.46 (m, 4H), 7.55-7.66 (m, 2H), 8.02 (dd, *J* = 0.9, 7.2 Hz, 1H), 8.69 (dd, *J* = 0.9, 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 14.4, 22.9, 28.7, 29.3, 29.5, 29.6, 32.1, 39.9, 82.8, 124.0, 124.3, 124.4, 125.0, 128.9, 130.3, 131.9, 132.6, 135.7, 145.8, 147.4, 152.6; IR (neat, cm^{-1}) 3056, 2924, 1693, 1590; HRMS Calcd for C$_{23}$H$_{26}$IN$_2$O: 459.1059. Found: 459.1068.

(3*E*)-3-[Iodo(trimethylsilyl)methylene]-2-phenylisoindolin-1-one (26). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 95 mg (77 %) of the product as a yellow solid: mp 91-92 °C; ^{1}H NMR (CDCl$_3$) δ 0.18 (t, *J* = 3.6 Hz, 9H), 7.10-7.20 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.60-7.67 (m, 2H), 8.02 (d, *J* = 8.1 Hz, 1H), 8.96 (td, *J* = 0.9, 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 0.0, 80.2, 122.3, 123.4, 123.9, 125.4, 128.3, 130.4, 131.5, 132.0,

136.2, 146.1, 152.8, 154.8; IR (neat, cm^{-1}) 1694, 1591, 1486; HRMS Calcd for CHINO:

419.0202. Found: 419.0213.

(3*E*)-3-[Cyclohex-1-en-1-yl(iodo)methylene]-2-phenylisoindolin-1-one (29).

Purification by flash chromatography (7:1 hexane/EtOAc) afforded 41 mg (31 %) of the

product as a yellow liquid: ^{1}H NMR (CDCl$_3$) δ 1.71-1.89 (m, 5H), 2.14-2.34 (m, 5H), 6.11

(q, *J* = 1.8 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 8.1 Hz, 2H), 7.48-7.53 (m, 2H), 7.66

(dd, *J* = 0.9, 8.1 Hz, 2H), 7.76-7.80 (m, 1H), 7.94-7.98 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 22.1,

22.8, 26.1, 28.0, 81.8, 122.7, 124.1, 125.3, 125.6, 129.0, 129.9, 130.9, 132.2, 132.9, 133.9,

136.8, 145.0, 149.8, 152.2; IR (neat, cm^{-1}) 2928, 1690, 1591; HRMS Calcd for C$_{21}$H$_{18}$INO:

427.0433. Found: 427.0439.

(3*E*)- 2-Benzyl 3-[iodo(trimethylsilyl)methylene]-5,6-dimethoxyisoindolin-1-one

(32). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 119 mg (80 %) of

the product as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 0.37 (s, 9H), 3.94 (s, 3H), 3.98 (s, 3H),

4.78 (s, 2H), 7.24 (t, *J* = 3.0 Hz, 1H), 7.29-7.31 (m, 1H), 7.32-7.35 (m, 2H), 7.38-7.41 (m,

2H), 8.41 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 0.7, 52.2, 56.4, 56.5, 76.8, 104.1, 107.5, 125.8, 126.9,

127.8, 128.5, 130.3, 140.1, 151.82, 151.85, 154.5, 155.2; IR (neat, cm^{-1}) 2956, 1699, 1589,

1495; HRMS Calcd for C$_{21}$H$_{24}$INO$_3$: 493.0570. Found: 493.0580.

(3*E*)-3-[Iodo(phenyl)methylene]-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridin-

1-one (38). Purification by flash chromatography (4:1 hexane/EtOAc) afforded 79 mg (63

%) of the product as a yellow solid: mp 165-167 °C (decompose); ^{1}H NMR (CDCl$_3$) δ 7.14

(t, *J* = 5.4 Hz, 1H), 7.23-7.41 (m, 7H), 7.59-7.63 (m, 2H), 7.90 (d, *J* = 4.5 Hz, 1H), 8.86 (s,

1H), 10.0 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 77.8, 117.2, 125.4, 126.4, 128.2, 128.9, 129.1, 130.4,

139.9, 140.0, 144.1, 147.0, 147.1, 150.2, 150.7; IR (neat, cm^{-1}) 3020, 1687, 1424; HRMS

Calcd for C$_{20}$H$_{13}$IN$_2$O: 424.0073. Found: 424.0081.

(3E)-3-(1-Iodohexylidene)-2-phenyl-2,3-dihydro-1H-pyrrolo[3,4-c]pyridin-1-one

(41). Purification by flash chromatography (4:1 hexane/EtOAc) afforded 68.4 mg (55 %) of

the product as a yellow solid: mp 100-101 °C; ^{1}H NMR (CDCl$_3$) δ 0.86-0.91 (t, J = 6.9 Hz,

3H), 1.30-1.35 (m, 4H), 1.60-1.66 (m, 2H), 2.90 (t, J = 7.5 Hz, 2H), 7.20 (t, J = 6.9 Hz, 1H),

7.36-7.46 (m, 4H), 7.86 (d, J = 5.1 Hz, 1H), 8.81 (d, J = 5.1 Hz, 1H), 10.0 (s, 1H); ^{13}C NMR

(CDCl$_3$) δ 14.2, 22.6, 28.9, 30.8, 39.7, 85.2, 117.1, 124.6, 125.9, 129.0, 130.9, 139.9, 144.8,

146.4, 146.7, 150.2, 150.8; IR (neat, cm^{-1}) 2980, 1683, 1422; HRMS Calcd for C$_{19}$H$_{19}$IN$_2$O:

418.0542. Found: 418.0552.

4-Iodo-2,3-diphenyl-2,5,6,7-tetrahydro-$1H$-cyclopenta[c]pyridin-1-one (48) .

Purification by flash chromatography (5:1 hexane/EtOAc) afforded 71 mg (58 %) of the

product as a yellow solid: mp 148-150 °C; ^{1}H NMR (CDCl$_3$) δ 2.12 (q, J = 7.5 Hz, 2H),

2.85-2.92 (m, 2H), 3.02-3.08 (m, 2H), 7.01 (td, J = 1.2, 7.2 Hz, 1H), 7.15 (dd, J = 1.2, 8.4

Hz, 2H), 7.26 (dt, J = 1.8, 6.9 Hz, 2H), 7.33-7.39 (m, 3H), 7.57-7.62 (m, 2H); ^{13}C NMR

(CDCl$_3$) δ 21.7, 32.9, 40.3, 69.7, 123.1, 123.6, 128.2, 128.7, 129.4, 129.6, 130.2, 134.2,

146.4, 149.4, 152.9, 156.1; IR (neat, cm^{-1}) 2954, 1650, 1635, 1487; HRMS Calcd for

C$_{20}$H$_{16}$INO: 413.0277. Found: 413.0285.

General procedure for electrophilic cyclization of the o-(1-alkynyl)benzamides

by NBS. The alkynylamide (0.30 mmol), NBS (1.5 equiv) and CH$_2$Cl$_2$ (3 ml) were placed in

a 2 dram vial and flushed with N$_2$. The reaction mixture was stirred at room temperature for

1 h unless otherwise indicated. The solvent was evaporated under reduced pressure and the

product was isolated by chromatography on a silica gel column.

(3*E*)-3-[Bromo(phenyl)methylene]-2-phenylisoindolin-1-one (4). Purification by

flash chromatography (5:1 hexane/EtOAc) afforded 93.2 mg (82%) of the product as a white

solid: mp 90-92 °C; ^{1}H NMR (CDCl$_3$) δ 7.13 (t, J = 7.2 Hz, 1H), 7.26-7.41 (m, 7H), 7.60-

7.75 (m, 4H), 8.06 (d, J = 6.6 Hz, 1H), 8.64 (d, J = 8.1 Hz, 1H); IR (neat, cm^{-1}) 1690; HRMS

Calcd for C$_{16}$H$_{12}$BrNO: 375.0259. Found: 375.0266.

Synthesis of cepharanone B.

2-Iodo-4,5-dimethoxy-*N*-(4-methoxybenzyl)benzamide (51). 2-Iodo-4,5-

dimethoxybenzoic acid (3.7 g, 12mmol) and SOCl$_2$ (18 ml) were refluxed at 80 °C for 0.5 h.

Excess SOCl$_2$ was removed under reduced pressure and a solution of pyridine (3 equiv) in

THF (30 ml) was added to the residue. The resulting mixture was cooled to 0 °C and a

solution of 4-methoxybenzylamine (1.0 equiv) in THF (10 ml) was added dropwise. The

resulting reaction mixture was stirred at 0 °C for 0.5 h, followed by stirring at room

temperature for 3 h. The mixture was then diluted with CHCl$_3$ (100 ml), washed with 2N

HCl (25 ml) and satd NaHCO$_3$ (25 ml), dried (MgSO$_4$) and filtered. The solvent was

evaporated under reduced pressure and the product was isolated by flash chromatography

(1:2 hexane/EtOAc) to afford 3.24 g (65 %) of the product as white solid: mp 159-160 °C;

^{1}H NMR (CDCl$_3$) δ 3.77-3.81 (m, 3H), 3.83-3.88 (m, 6H), 4.51-4.56 (m, 2H), 6.23 (s, 1H),

6.83-6.89 (m, 2H), 6.96 (s, 1H), 7.16 (s, 1H), 7.29-7.32 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 44.0,

55.5, 56.3, 56.5, 81.2, 112.1, 114.3, 122.2, 129.8, 129.9, 134.4, 149.3, 150.6, 159.3, 168.8;

IR (neat, cm^{-1}) 3300, 2964, 1638, 1498; HRMS Calcd for C$_{17}$H$_{18}$INO$_4$: 427.0281. Found:

427.0291.

***N*-(4-Methoxybenzyl)-4,5-dimethoxy-2-[(trimethylsilyl)ethynyl]benzamide (52).**

This compound was prepared by following the general procedure for preparation of the *o*-(1-

alkynyl)benzamides. Purification by flash chromatography (3:2 hexane/EtOAc) afforded 277

mg (70 %) of the product as a white solid: mp 107-108 °C; ^{1}H NMR (CDCl$_3$) δ 0.10 (s, 9H),

3.79 (s, 3H), 3.92 (s, 3H), 3.95 (s, 3H), 4.60 (d, J = 5.4 Hz, 2H), 6.86 (dd, J = 1.8, 6.9 Hz,

2H), 6.93 (s, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.77 (s, 1H), 8.32 (s, 1H); ^{13}C NMR (CDCl$_3$) δ

0.0, 44.1, 55.8, 56.5, 56.6, 101.2, 104.4, 112.4, 113.3, 114.6, 116.0, 128.8, 129.6, 130.8,

150.1, 150.8, 159.5, 165.5; IR (neat, cm^{-1}) 3387, 2958, 1653, 1511; HRMS Calcd for

C$_{22}$H$_{27}$NO$_4$Si: 397.1709. Found: 397.1713.

(3E)-3-[Iodo(trimethylsilyl)methylene]-5,6-dimethoxy-2-(4-

methoxybenzyl)isoindolin-1-one (53). This compound was prepared by following the

general procedure for the electrophilic cyclization of alkynylarenecarboxamides by I$_2$.

Purification by flash chromatography (1:1 hexane/EtOAc) afforded 126 mg (80 %) of the

product as a white solid: mp 122-123 °C; ^{1}H NMR (CDCl$_3$) δ 0.39 (s, 9H), 3.79 (s, 3H), 3.95

(s, 3H), 3.99 (s, 3H), 4.72 (s, 2H), 6.88 (dd, J = 1.8, 6.9 Hz, 2H), 7.30-7.34 (m, 3H), 8.42 (s,

1H); ^{13}C NMR (CDCl$_3$) δ 0.0, 50.9, 54.7, 55.7, 55.8, 103.5, 106.8, 113.3, 125.2, 128.4, 129.6,

131.6, 151.2, 153.6, 154.6, 158.0 (two carbons missing due to overlap); IR (neat, cm^{-1}) 3002,

2955, 1698, 1512; HRMS Calcd for C$_{22}$H$_{26}$INO$_4$Si: 523.0676. Found: 523.0686.

(3E)-3-(2-Bromobenzylidene)-5,6-dimethoxy-2-(4-methoxybenzyl)isoindolin-1-

one (54). Compound **53** (366 mg, 0.7 mmol), KF (43 mg, 1.05 equiv) and H$_2$O (14 mg) were

dissolved in DMF (4.5 ml) and the resulting reaction mixture was stirred at room temperature

for 0.5 h. The mixture was then diluted with Et$_2$O (100 ml), washed with H$_2$O (3 × 25 ml),

dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure and this

crude intermediate was used in the next step without any further purification.

The intermediate, 2-bromophenylboronic acid (168.5 mg, 1.2 equiv), PPh$_3$ (18.4 mg), CsF (257 mg, 2.4 equiv) and DMF (3.7 ml) were added to a 2-dram vial and the resulting mixture was then stirred under an N$_2$ atm at room temperature for 30 h. The reaction mixture was diluted with CHCl$_3$ (100 ml), washed with satd aq NH$_4$Cl (25 ml), dried (MgSO$_4$) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by flash chromatography (1:1 hexane/EtOAc) affording 190 mg (57 %) of the product as a yellow solid: mp 122-124 °C; ^{1}H NMR (CDCl$_3$) δ 3.60 (s, 3H), 3.80 (s, 3H), 3.91 (s, 3H), 4.81 (s, 2H), 6.52 (s, 1H), 6.61 (s, 1H), 6.91 (d, J = 8.4 Hz, 2H), 7.22-7.28 (m, 2H), 7.34-7.41 (m, 3H), 7.61 (d, J = 6.9 Hz, 1H), 7.71 (dd, J = 0.9, 8.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 51.4, 55.5, 56.0, 56.6, 104.2, 104.3, 105.1, 114.1, 125.3, 125.5, 127.2, 128.7, 129.4, 129.6, 131.7, 132.7, 133.4, 135.1, 150.6, 151.8, 152.3, 158.8 (one carbon missing due to overlap); IR (neat, cm^{-1}) 3004, 2932, 1698, 1497; HRMS Calcd for C$_{25}$H$_{22}$BrNO$_4$: 479.0732. Found: 479.0741.

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CHAPTER 3. SYNTHESIS OF POLYCYCLIC AROMATICS AND HETEROAROMATICS VIA ELECTROPHILIC CYCLIZATION

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Abstract

A variety of substituted polycyclic aromatics are readily prepared in good to excellent yields under very mild reaction conditions by the reaction of 2-(1-alkynyl)biphenyls with ICl, I_2, NBS, and p-$O_2NC_6H_4SCl$. This methodology readily accommodates various functional groups and has been successfully extended to systems containing a variety of polycyclic and heterocyclic rings.

Introduction

The electrophilic cyclization of alkenes has been studied extensively, and utilized as a key step in a variety of syntheses,[1] particularly the biomimic cyclization of polyenes.[2] Various electrophiles have been reported to effect C-C bond formation in such ring closures.[1-3] Relatively little attention has been paid to the electrophile-induced carbocyclization of alkynes. Nevertheless, the electrophilic addition to carbon-carbon triple bonds can generate cationic species capable of undergoing intramolecular cyclization onto an aromatic ring.[4] Thus, Barluenga first used $I(py)_2BF_4$, a highly electrophilic source of

iodonium ions, in the presence of a very strong acid to cyclize 1,4-diphenyl-1-butyne to the

corresponding iododihydronapthalene (eq 1).[5] Swager employed this same reagent system
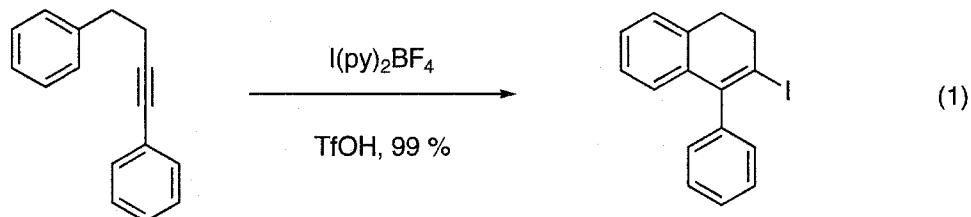
to prepare fused polycyclic aromatics (eq 2).[6] Unfortunately, the presence of a *p*-alkoxy

group on the phenylethynyl moiety was apparently critical to the success of that

methodology. No other applications of this type of carbocyclization have been reported

despite its tremendous synthetic potential.
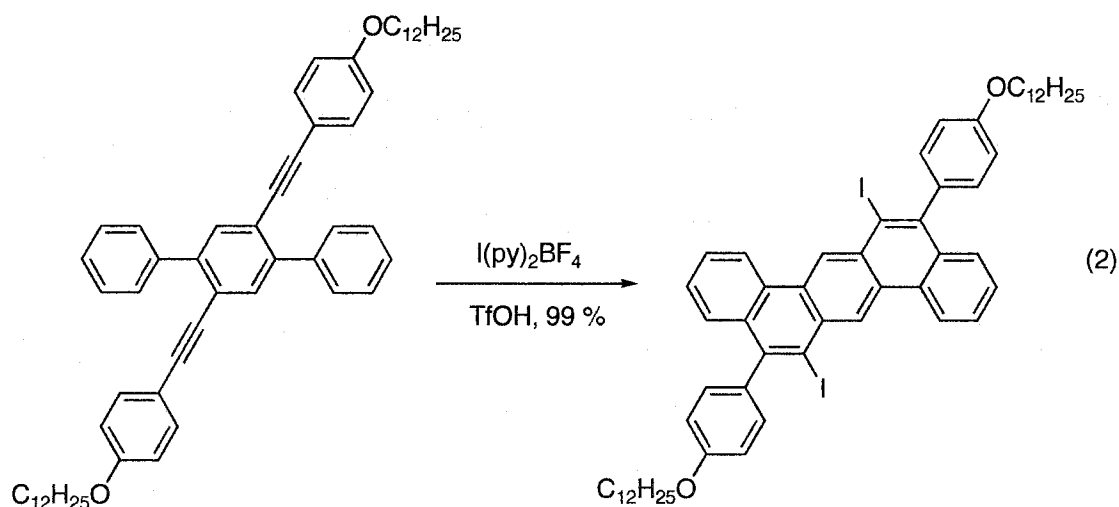
Polycyclic aromatics are critical to advances in a number of areas of chemical

research. For example, polycyclic aromatic iodides are very useful starting materials in

organic synthetic methodology, particularly palladium-catalyzed annulation,[7] cyclization[8] and

carbonylation processes.[9] Polycyclic aromatics can also be used as rigid molecular platforms

in various areas of chemical research, such as host-guest chemistry,[10] liquid crystal

chemistry[11] and biochemical studies of synthetic peptides.[12] Furthermore, these rigid

conjugated materials can serve as key components in many advanced technologies utilizing nonlinear optical,[13] photo- and electroluminescent,[14] and molecule-based sensory devices.[15] They can transfer an applied bias or optical input to a desired response through their highly conjugated π electron systems. Polycyclic aromatics obviously possess the degree of conjugation and rigidity necessary to eliminate conformational disorder which lowers the effective conjugation.[16]

We and others have developed methods for the synthesis of benzo[*b*]thiophenes,[17] isoquinolines and naphthyridines,[18] isocoumarins and α-pyrones,[19] benzofurans,[20] furans,[21] indoles,[22] furopyridines,[23] cyclic carbonates,[24] 2,3-dihydropyrroles and pyrroles,[25] pyrilium salts[26], bicyclic β-lactams[27], isochromenes[28], phosphaisocoumarins[29] and isoindolin-1-ones[30] via electrophilic cyclization of functionally-substituted alkynes. This successful electrophilic cyclization strategy has encouraged us to develop a more general methodology for the synthesis of polycyclic aromatics.[31] Herein, we report the successful electrophilic cyclization of arene-containing acetylenes to polycyclic aromatics. This chemistry generally produces good to excellent yields of polycyclic aromatics under very mild reaction conditions, accommodates various functional groups, and has been successfully extended to systems containing a variety of polycyclic and heterocyclic rings.

Results and Discussion

A two step approach to polycyclic aromatics has been examined involving (i) preparation of 2-(1-alkynyl)biaryls by the Sonagashira coupling reaction,[32] and (ii) electrophilic cyclization (Scheme 1).

SCHEME 1

$E^+ = ICl, I_2, NBS, p\text{-}O_2NC_6H_4SCl, PhSeCl$
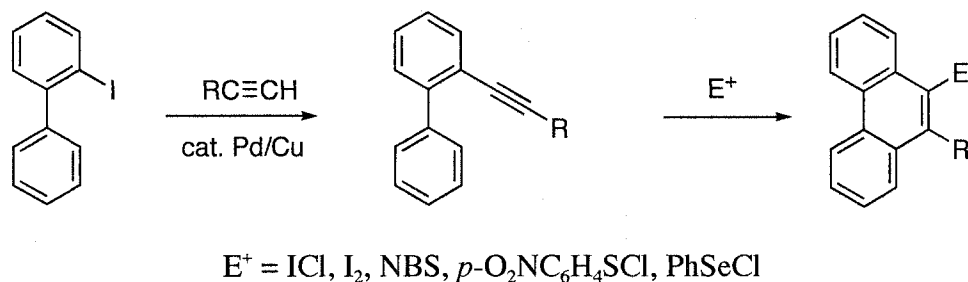
The 2-(1-alkynyl)biaryls required for our approach are readily prepared by

Sonogashira coupling[29] of the corresponding 2-iodobiaryls with terminal alkynes using 2%

$PdCl_2(PPh_3)_2$ and 1% CuI in Et_3N solvent at 55 °C. The yields of this process range from 55

to 99% and this procedure readily accommodates considerable functionality.

To explore the scope of our electrophilic cyclization strategy, the reactions of alkynyl

biphenyl **1** with various electrophiles (ICl, I_2, NBS, $p\text{-}O_2NC_6H_4SCl$ and PhSeCl) in CH_2Cl_2 at

room temperature have been studied (Table 1, entries 1-5). Excellent 99% and 92% yields of

the expected iodo- and sulfur-containing phenanthrenes have been obtained in only 30 min

when ICl and $p\text{-}O_2NC_6H_4SCl$ were used as electrophiles respectively (entries 1 and 4). I_2 can

also be employed as the electrophile, but the reaction took 24 h at room temperature to afford

the corresponding product in only an 80% yield (entry 2). It should be noted that $NaHCO_3$ is

indispensable in this reaction. Otherwise, an inseparable mixture of unidentified products

were obtained. NBS itself did not react with 2-(1-phenylethynyl)biphenyl (**1**). Interestingly,

a mixture of NBS and silica gel provided the cyclized bromine-containing product **3** in an

86% yield after 6 d. Unfortunately, none of the desired selenium-containing product was

observed when using PhSeCl. Only 1,2-adducts formed by PhSeCl addition to the carbon-

carbon triple bond were obtained.

TABLE 1. Synthesis of Polycyclic Aromatics via Electrophilic Cyclization[a]
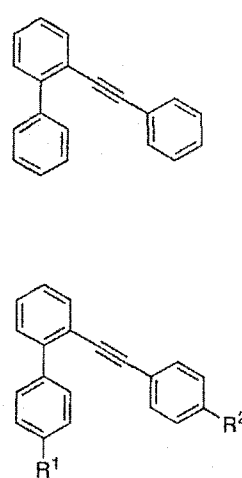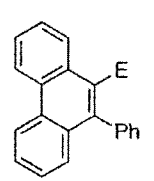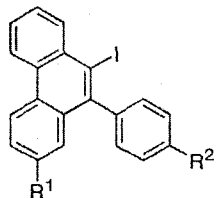
entry	alkyne		electrophile	time (h)	product(s)			% isolated yield
1			ICl	0.5		E = I	2	99[b]
2			I_2/NaHCO$_3$	24		E = I	2	80[b,c]
3		1	NBS	144		E = Br	3	86[b,d]
4			p-O$_2$NC$_6$H$_4$SCl	0.5		E = p-O$_2$NC$_6$H$_4$S	4	92[b]
5			PhSeCl	0.5		E = PhSe	5	0[b]

	R^1	R^2						
6	H	OMe	6	0.5			7	99
7	H	Me	8	0.5			9	98
8	H	CO$_2$Et	10	3			11	99

For entries 6–8 the electrophile is ICl.

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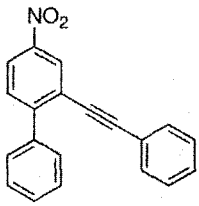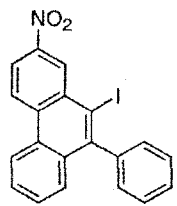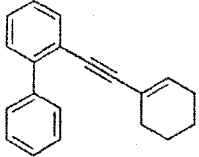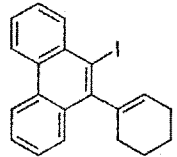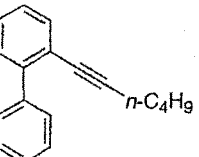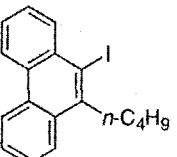
TABLE 1. (continued)

entry	alkyne			electrophile	time (h)	product(s)		% isolated yield
9	H	NO$_2$	**12**		3		**13**	57[c]
10	CHO	H	**14**		1		**15**	71[f]
11	NO$_2$	H	**16**		3		**17**	55[g]
12			**18**	ICl	0.5		**19**	88
13			**20**	ICl	3		**21**	70
14			**22**	ICl	0.5		**23**	0[h]

TABLE 1. (continued)
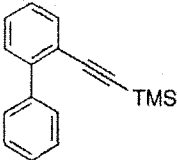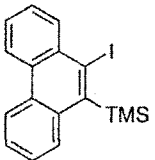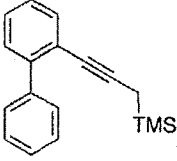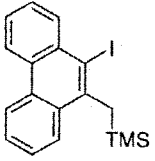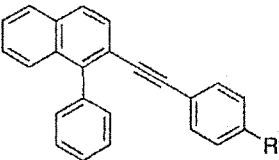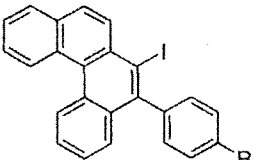
entry	alkyne	electrophile	time (h)	product(s)		% isolated yield
15		**24** ICl	0.5		**25**	0[h]
16		**26** ICl	0.5		**27**	50
		ICl	0.5			
17	R = H	**28**			**29**	48
18	R = OMe	**30**			**31**	97

TABLE 1. (continued)
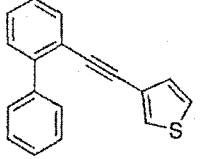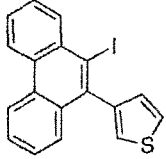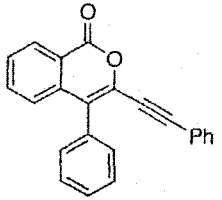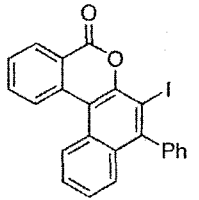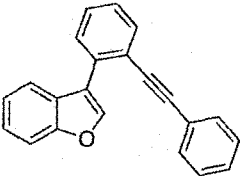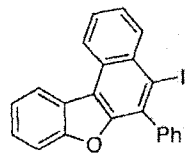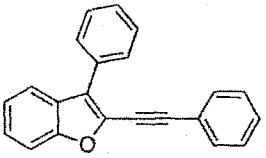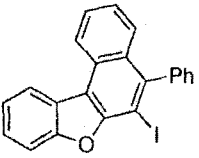
entry	alkyne	electrophile		time (h)	product(s)		% isolated yield
19		**32**	ICl	0.5		**33**	96
20		**34**	ICl	0.5		**35**	65
21		**36**	ICl	0.5		**37**	91
22		**38**	ICl	0.5		**39**	0[h]
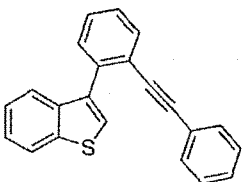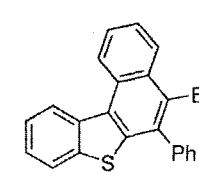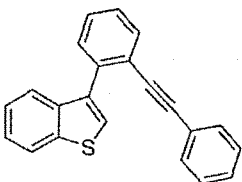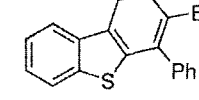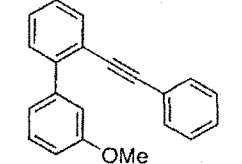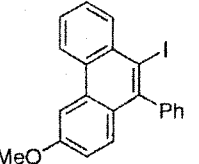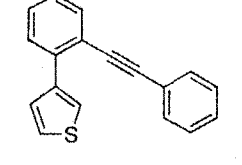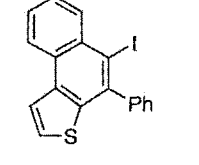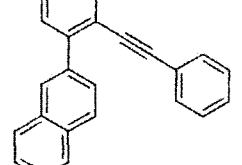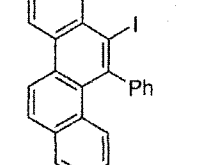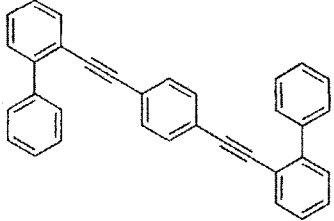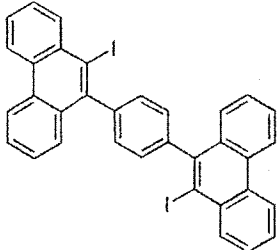
TABLE 1. (continued)

entry	alkyne		electrophile	time (h)	product(s)			% isolated yield
23			NBS	72		E = Br	**41**	88[b,d]
24		**40**	*p*-O$_2$NC$_6$H$_4$SCl	0.5		E = *p*-O$_2$NC$_6$H$_4$S	**42**	91[b]
25		**43**	ICl	0.5		**44**	**45**	66 + 20
26		**46**	ICl	0.5		**47**	**48**	50 + 37
27		**49**	ICl	0.5		**50**	**51**	76 + 14

81

TABLE 1. (continued)

entry	alkyne	electrophile	time (h)	product(s)	% isolated yield
28	52	ICl	0.5	53	90

^a All reactions were run under the following conditions, unless otherwise specified: 0.30 mmol of the acetylene in 3 mL of CH_2Cl_2 was placed in a 4-dram vial under N_2 and 1.2 equiv of electrophile was added at –78 °C. ^b The reaction was run at room temperature. ^c 3.0 Equiv of electrophile and 3.0 equiv of $NaHCO_3$ were used. ^d Silica gel (50 mg) was added. ^e Contains a 42% yield of addition products. ^f Contains a 17% yield of alkyne addition products. ^g Contains a 31% yield of alkyne addition products. ^h Only alkyne addition products were obtained.

We next examined the reaction of 2-(*p*-methoxyphenylethynyl)biphenyl (**6**) and ICl

(Table 1, entry 6). We first examined the reaction of **1** with 1.2 equiv of ICl in CH_2Cl_2 at

room temperature. This reaction afforded a mixture of the corresponding iodocyclization

product **7** and a side-product, which is believed to be 10-iodo-9-(3-iodo-4-

methoxyphenyl)phenanthrene. Fortunately, when the same reaction was carried out at -78

°C, the desired 10-iodo-9-(*p*-methoxyphenyl)phenanthrene (**7**) was the only product formed

in a 99% yield. Thus, our standard reaction conditions employ 0.30 mmol of acetylene, 1.2

equiv of ICl in CH_2Cl_2 at -78 °C.

By employing this standard protocol, the reaction of 2-(*p*-tolylethynyl)biphenyl (**8**)

with ICl afforded the desired 10-iodophenanthrene **9** in a 98 % yield (entry 7). The presence

of a modest electron-withdrawing group, like a *p*-CO_2Et group, on the phenylethynyl moiety,

as in **10**, still provided the cyclization product **11** in a quantitative yield (entry 8).

Surprisingly, even the presence of a strong electron-withdrawing *p*-NO_2 group on the

phenylethynyl moiety (**12**) afforded the corresponding cyclization product **13** in a 57% yield,

along with a 42% combined yield of side-products presumed to be 1,2-adducts formed by ICl

addition to the carbon-carbon triple bond (entry 9). Thus, the *p*-alkoxy group on the

phenylethynyl moiety, which was critical to the success of Swager's cyclization

methodology, is obviously not necessary in our chemistry. A notable feature in this

chemistry is the preference for the 6-endo-dig cyclization to give phenanthrenes over the

alternative 5-exo mode of cyclization.

Encouraged by our success with the above substrates, we next investigated the

cyclization of analogous acetylenes in which various substituents have been attached to the

arene undergoing substitution. Treatment of *p*-[2-(phenylethynyl)phenyl]benzaldehyde (**14**)

with ICl under our standard reaction conditions afforded cyclization product **15** in a 71%

yield. A 17% yield of products from ICl addition to the alkyne was also obtained (entry 10).

Substrate **16** containing a strong electron-withdrawing p-NO_2 group afforded the desired

iodophenanthrene **17** in a 55% yield, along with a 31% yield of ICl alkyne adducts (entry

11). The lower yields for these substrates in which the aromatic ring undergoing cyclization

is electron-poor, is consistent with our proposed mechanism (see the later mechanistic

discussion). Substrate **18**, which also contains a nitro group, undergoes cyclization smoothly

to produce the desired product **19** in an 88 % yield (compare entries 11 and 12). Obviously,

moving the nitro group from the ring undergoing substitution to the central arene facilitates

electrophilic aromatic substitution.

To further investigate the scope of this methodology, we have examined the effect of

various substituents on the remote end of the alkyne moiety. An olefin-substituted alkyne **20**

is readily accommodated (entries 13). However, the reaction of alkynes bearing a saturated

alkyl or TMS group with ICl under our standard reaction conditions failed to produce the

desired phenanthrene products (entries 14 and 15). Interestingly, the (trimethylsilyl)methyl-

substituted alkyne **26** underwent smooth iodocyclization to afford the desired phenanthrene

27 in a 50 % yield. This favorable result can be attributed to the fact that a silyl group can

stabilize a carbocation located in the β position,[33] which favors cyclization onto the

neighboring phenyl group (see the later mechanistic discussion). The desilylation of product

27 will afford a 9-alkyl-substituted phenanthrene, which means that 9-alkyl phenanthrenes

can be prepared by this electrophilic cyclization method in two steps.

This cyclization chemistry has been successfully extended to other biaryl systems.

For instance, 1-phenyl-2-(phenylethynyl)naphthalene (**28**) afforded the cyclization product

29 in a 48% yield (entry 17). Changing the phenyl group of the phenylethynyl moiety to a *p*-methoxyphenyl group dramatically increased the yield to 97% (compare entries 17 and 18). The thiophene-containing acetylene **32** afforded the expected cyclization product **33** in a 96% yield (entry19), despite our concern that electrophilic substitution in the very reactive thiophene ring might prove competitive. Obviously it isn't. In a similar manner, the isocoumarin-containing alkyne **34** provided a 65% yield of the corresponding polycycle **35**. Treatment of the benzofuran-containing acetylene **36** with ICl afforded the cyclization product **37** in a 91% yield (entry 21). Again, direct substitution of the electron-rich benzofuran does not appear to be competitive with iodocyclization. However, the benzofuran-containing acetylene **38** failed to afford the desired product (entry 22). This may be the result of inductive electron-withdrawal by the oxygen moiety disfavoring cation formation or it may be the unfavorable geometry present when the alkyne and arene undergoing substitution are placed on an unsaturated five-membered ring, rather than the more usual six-membered benzene ring. Treatment of the benzothiophene-containing acetylene **40** with NBS and *p*-O$_2$NC$_6$H$_4$SCl afforded the anticipated cyclization products **41** and **42** in 88% and 91% yields respectively, with no indication of any products being formed by direct substitution of the benzothiophene (entries 23 and 24).

The regioselectivity in this electrophilic cyclization chemistry has also been investigated. The iodocyclization of biphenyl **43** afforded approximately a 3:1 regiochemical mixture of **44** and **45**, with cyclization to the less hindered position being favored (entry 25). In the cyclization of thiophene **46**, electronic effects control the regioselectivity, affording product **47** as the major isomer by cyclization to the more electron-rich α-position of the thiophene (entry 26). However, substantial amounts of the product of substitution in the 4-

position are also observed. The iodocyclization of the naphthalene-containing acetylene **49**

afforded approximately a 5:1 regiochemical mixture of **50** and **51** in an excellent overall

yield (entry 27). The predominant isomer is **50**, which arises by cyclization onto the 1-

position of the naphthalene moiety. Clearly, electronic effects favor cyclization to **50** over

cyclization to the less hindered 3-position of the naphthalene, which affords **51**.

The facility with which this carbocyclization process occurs encouraged us to attempt

a double cyclization. The double cyclization of diyne **52** afforded the desired product **53** in a

90% yield (entry 28).

We propose a mechanism for this electrophilic cyclization chemistry that involves (1)

formation of an electrophile acetylene complex, (2) electrophilic attack of this intermediate

on the neighboring aromatic ring of the biaryl moiety, and (3) deprotonation to generate the

desired polycyclic aromatic (Scheme 2).

Scheme 2
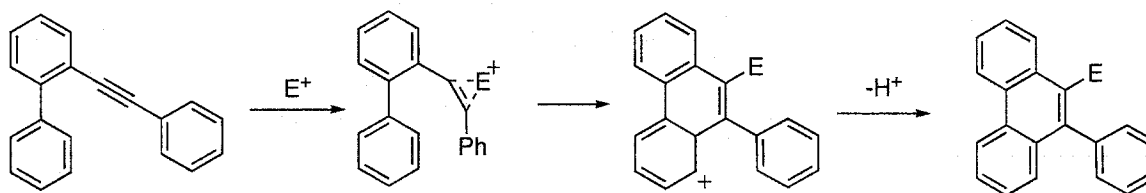
An interesting feature of this chemistry is the fact that the polycyclic aromatic iodides

produced can be further elaborated using a variety of palladium-catalyzed processes. For

example, palladium-catalyzed Sonogashira coupling,[32] alkyne annulation,[7]

cyclocarbonylation[9] and the Heck reaction[34] have afforded the corresponding products **54-57**

in 53%, 83%, 98% and 98% yields, respectively (Scheme 3). The Sonogashira reaction

nicely provides products which can again be subjected to electrophilic cyclization to generate

still further aromatic rings in an iterative process.

SCHEME 3
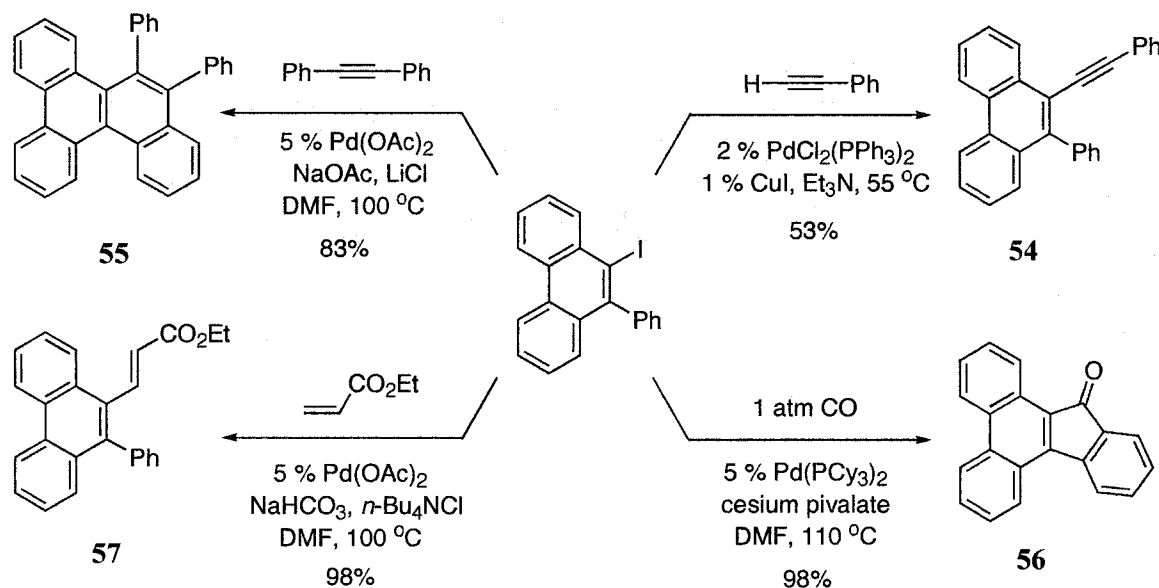
Conclusions

In conclusion, an efficient synthesis of polycyclic aromatics under very mild reaction conditions has been developed. This methodology accommodates various functional groups and affords the anticipated substituted polycyclic aromatics in good to excellent yields. It can be applied to the synthesis of simple polycyclic aromatic hydrocarbons and heterocyclic systems. Finally, the resulting iodine-containing products can be readily elaborated to more complex products using known organopalladium chemistry.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO4 solution [3 g of KMnO$_4$ + 20 g of K$_2$CO$_3$ + 5 mL of NaOH (5%) + 300

mL of H_2O]. All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise noted. 3-(2-Iodophenyl)benzofuran,[9f] 2'-iodobiphenyl-4-carbaldehyde,[9a] 2-(2-iodophenyl)naphthalene,[35] 2-ethynylbiphenyl[36] and 2-(phenylethynyl)phenylboronic acid[37] were prepared according to previous literature procedures.

General procedure for preparation of the 2-(arylethynyl)biphenyls. To a solution of the corresponding aryl iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4 mL), were added $PdCl_2(PPh_3)_2$ (14 mg, 2 mol %) and CuI (2 mg, 1 mol %). The resulting mixture was then heated under an N_2 atmosphere at 55 °C for 3 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding product.

2-Phenylethynylbiphenyl (1). 2-Iodobiphenyl and phenylacetylene were employed. Purification by flash chromatography (30:1 hexane/EtOAc) afforded 254 mg (100%) of the product as a clear liquid with spectral properties identical to those previously reported.[39]

2-[(4-Methoxyphenyl)ethynyl]biphenyl (6). 2-Ethynylbiphenyl and 4-iodoanisole were employed. Purification by flash chromatography (30:1 hexane/EtOAc) afforded 211 mg (74%) of the product as a clear liquid: ^1H NMR ($CDCl_3$) δ 3.80 (s, 3H), 6.84 (dd, $J = 2.4$, 6.9 Hz, 2H), 7.30 (dd, $J = 2.1$, 6.9 Hz, 2H), 7.34-7.50 (m, 6H), 7.64-7.73 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 55.5, 88.4, 92.5, 114.2, 115.9, 122.2, 127.3, 127.6, 128.1, 128.4, 129.6, 129.7, 132.9, 133.1, 140.9, 143.9, 159.8; IR (neat, cm^{-1}) 3059, 3017, 2214, 1605; HRMS Calcd for $C_{21}H_{16}O$: 284.1201. Found: 284.1205.

2-[(4-Methylphenyl)ethynyl]biphenyl (8). 2-Ethynylbiphenyl and 4-iodotoluene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 204 mg (76%) of the product as a clear liquid: ^{1}H NMR (CDCl$_3$) δ 2.35 (s, 3H), 7.11 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.31-7.50 (m, 6H), 7.63-7.71 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 21.7, 89.0, 92.7, 120.6, 122.0, 127.3, 127.7, 128.1, 128.6, 129.3, 129.6, 129.7, 131.5, 133.0, 138.5, 140.9, 144.0; IR (neat, cm^{-1}) 3058, 3025, 2919, 2215; HRMS Calcd for C$_{21}$H$_{16}$: 268.1252. Found: 268.1257.

Ethyl 4-(biphen-2-ylethynyl)benzoate (10). 2-Ethynylbiphenyl and ethyl 4-iodobenzoate were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 274 mg (84%) of the product as a white solid: mp 58-60 °C; ^{1}H NMR (CDCl$_3$) δ 1.38 (t, J = 6.9 Hz, 3H), 4.36 (q, J = 7.2 Hz, 2H), 7.32-7.48 (m, 8H), 7.64-7.66 (m, 3H), 7.96 (d, J = 8.4 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 14.6, 61.3, 91.7, 92.6, 121.3, 127.4, 127.9, 128.2, 128.3, 129.3, 129.63, 129.64, 129.8, 129.9, 131.4, 133.2, 140.6, 144.5, 166.3; IR (neat, cm^{-1}) 3263, 1718; HRMS Calcd for C$_{23}$H$_{18}$O$_2$: 326.1307. Found: 326.1312.

2-(4-Nitrophenylethynyl)biphenyl (12). 2-Ethynylbiphenyl and 1-iodo-4-nitrobenzene were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 269 mg (90%) of the product as a yellow solid: mp 100-101 °C; ^{1}H NMR (CDCl$_3$) δ 7.38-7.50 (m, 8H), 7.62-7.68 (m, 3H), 8.16 (d, J = 7.6 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 90.6, 95.2, 120.7, 123.8, 127.5, 128.0, 128.2, 129.6, 129.8, 129.9, 130.6, 132.2, 133.3, 140.5, 144.8; IR (neat, cm^{-1}) 3062, 2215, 1593, 1516; HRMS Calcd for C$_{20}$H$_{12}$NO$_2$: 299.0946. Found: 299.0950.

2'-(Phenylethynyl)biphenyl-4-carbaldehyde (14). 2'-Iodobiphenyl-4-carbaldehyde and phenylacetylene were employed. Purification by flash chromatography (4:1

hexane/EtOAc) afforded 273 mg (97%) of the product as a white solid: mp 90-93 °C; ^{1}H

NMR (CDCl$_3$) δ 7.27-7.32 (m, 5H), 7.38-7.43 (m, 3H), 7.66-7.68 (m, 1H), 7.83 (d, J = 6.0

Hz, 2H), 7.96 (d, J = 6.3 Hz, 2H), 10.08 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 88.7, 92.9, 121.7,

123.1, 128.1, 128.4, 128.5, 128.8, 129.4, 130.2, 131.4, 133.2, 135.4, 142.4, 146.9, 192.2

(missing one sp^2 carbon due to overlap); IR (neat, cm^{-1}) 3058, 1701, 1605; HRMS Calcd for

C$_{21}$H$_{14}$O: 282.1045. Found: 282.1049.

4-Nitro-2'-(phenylethynyl)biphenyl (16). Pd(dba)$_2$ (28.8 mg, 5 mol %), PPh$_3$ (26.0

mg, 10 mol %), CsF (304 mg, 2.0 mmol), 2-(phenylethynyl)phenylboronic acid (0.266 g, 1.2

mmol) and 1-iodo-4-nitrobenzene (0.249 g, 1.0 mmol) in DME (5 mL) were heated under an

N$_2$ atmosphere at 80 °C for 7 h. The mixture was allowed to cool to room temperature,

diluted with diethyl ether (50 mL), washed with satd aq NH$_4$Cl. The organic layer was dried

(MgSO$_4$), filtered, and the solvent was removed under reduced pressure. The residue was

purified by column chromatography (7:1 hexane/EtOAc) on silica gel to afford 251 mg

(84%) of compound **16** as a yellow solid: mp 95-97 °C; ^{1}H NMR (CDCl$_3$) δ 7.31 (s, 5H),

7.41-7.45 (m, 3H), 7.68-7.70 (m, 1H), 7.83 (d, J = 6.6 Hz, 2H), 8.31 (d, J = 6.6 Hz, 2H); ^{13}C

NMR (CDCl$_3$) δ 88.3, 93.2, 121.7, 122.9, 123.3, 128.5, 128.6, 128.8, 129.4, 130.3, 131.4,

133.3, 141.3, 147.3 (missing two sp^2 carbons due to overlap); IR (neat, cm^{-1}) 3062, 1599,

1516; HRMS Calcd for C$_{20}$H$_{13}$NO$_2$: 299.0946. Found: 299.0950.

2-(Phenylethynyl)-4-nitrobiphenyl (18). 2-Iodo-4-nitrobiphenyl and

phenylacetylene were employed. Purification by flash chromatography (10:1 hexane/EtOAc)

afforded 254 mg (85%) of the product as a yellow solid: mp 129-130 °C; ^{1}H NMR (CDCl$_3$) δ

7.31-7.38 (m, 5H), 7.48-7.55 (m, 3H), 7.58 (d, J = 8.7 Hz, 1H), 7.67-7.71 (m, 2H), 8.21 (dd,

J = 8.7, 2.4 Hz, 1H), 8.50 (d, J = 2.4 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 87.4, 94.7, 122.6, 123.2,

123.5, 128.0, 128.5, 128.7, 129.1, 129.2, 129.4, 130.6, 131.8, 138.7, 147.0, 150.0; IR (neat,

cm^{-1}) 3630, 1514, 1343; HRMS Calcd for $C_{20}H_{13}NO_2$: 299.0946. Found: 299.0950.

2-(Cyclohex-1-en-1ylethynyl)biphenyl (20). 2-Iodobiphenyl and 1-

ethynylcyclohexene were employed. Purification by flash chromatography (40:1

hexane/EtOAc) afforded 146 mg (70%) of the product as a clear liquid: ^1H NMR (CDCl$_3$) δ

1.53-1.65 (m, 4H), 2.07-2.13 (m, 4H), 6.03-6.06 (m, 1H), 7.26-7.47 (m, 6H), 7.53-7.57 (m,

1H), 7.62-7.66 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 21.8, 22.5, 26.0, 29.0, 86.9, 94.4, 121.2, 122.3,

127.2, 127.5, 128.0, 128.2, 129.59, 129.61, 133.0, 135.1, 140.9, 143.7; IR (neat, cm^{-1}) 3059,

3023, 2931, 2199, 1475; HRMS Calcd for $C_{20}H_{18}$: 258.1409. Found: 258.1412.

[3-(Biphenyl-2-yl)prop-2-ynyl](trimethyl)silane (26). 2-Iodobiphenyl and prop-2-

ynyl(trimethyl)silane were employed. Purification by flash chromatography (30:1

hexane/EtOAc) afforded 128 mg (49%) of the product as a clear liquid: ^1H NMR (CDCl$_3$) δ

0.00 (s, 9H), 1.59 (s, 2H), 7.24-7.34 (m, 4H), 7.37-7.41 (m, 2H), 7.48-7.51 (m, 1H), 7.54-

7.58 (m, 2H); ^{13}C NMR (CDCl$_3$) δ -1.9, 8.3, 78.9, 91.5, 123.2, 126.9, 127.1, 127.2, 127.9,

129.3, 129.5, 133.2, 141.2, 143.4; IR (neat, cm^{-1}) 3060, 2955, 2205, 1476, 1249; HRMS

Calcd for $C_{18}H_{20}Si$: 264.1334. Found: 264.1339.

1-Phenyl-2-(phenylethynyl)naphthalene (28). 2-Iodo-1-phenylnaphthalene and

phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc)

afforded 301 mg (99%) of the product as a yellow oil: ^1H NMR (CDCl$_3$) δ 7.16-7.21 (m,

2H), 7.23-7.27 (m, 3H), 7.38-7.44 (m, 1H), 7.47-7.55 (m, 5H), 7.65-7.70 (m, 2H), 7.82-7.89

(m, 2H); ^{13}C NMR (CDCl$_3$) δ 90.2, 93.4, 120.4, 123.7, 126.6, 126.7, 126.9, 127.68, 127.7,

128.18, 128.22, 128.23, 128.4, 128.6, 130.9, 131.6, 132.4, 133.4, 139.2, 143.3; IR (neat, cm^{-1}) 3056, 1950, 1598, 1505, 1490; HRMS Calcd for $C_{24}H_{16}$: 304.1252. Found: 304.1257.

2-[(4-Methoxyphenyl)ethynyl]-1-phenylnaphthalene (30). 2-Iodo-1-

phenylnaphthalene and *p*-methoxyphenyl acetylene were employed. Purification by flash

chromatography (20:1 hexane/EtOAc) afforded 276 mg (82%) of the product as a white

solid: mp 109-111 °C; ^{1}H NMR (CDCl$_3$) δ 3.81 (s, 3H), 6.82 (dd, *J* = 2.1, 6.9 Hz, 2H), 7.17

(dd, *J* = 2.1, 6.9 Hz, 2H), 7.34-7.57 (m, 7H), 7.68-7.74 (m, 2H), 7.84-7.92 (m, 2H); ^{13}C NMR

(CDCl$_3$) δ 55.4, 88.9, 93.5, 114.1, 115.7, 120.7, 126.4, 126.6, 126.8, 127.60, 127.62, 128.1,

128.2, 128.4, 130.9, 132.4, 133.0, 133.1, 139.3, 142.8, 159.7; IR (neat, cm^{-1}) 3055, 2956,

2836, 2207, 1605, 1511; HRMS Calcd for C$_{25}$H$_{18}$O: 334.1358. Found: 334.1365.

2-(Biphen-2-ylethynyl)thiophene (32). 2-Ethynylbiphenyl and 2-iodothiophene

were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 221

mg (85%) of the product as a light yellow liquid: ^{1}H NMR (CDCl$_3$) δ 6.98-7.00 (m, 1H),

7.15-7.17 (m, 1H), 7.25-7.27 (m, 1H), 7.37-7.55 (m, 6H), 7.66-7.75 (m, 3H); ^{13}C NMR

(CDCl$_3$) δ 85.9, 93.5, 121.6, 123.8, 127.3, 127.4, 127.5, 127.8, 128.3, 129.0, 129.6, 129.8,

131.8, 132.8, 140.7, 144.0; IR (neat, cm^{-1}) 3063, 2204, 1478; HRMS Calcd for C$_{18}$H$_{12}$S:

260.0660. Found: 260.0663.

4-Phenyl-3-(phenylethynyl)isocoumarin (34). 3-Iodo-4-phenylisocoumarin was

prepared by the following procedure. To a solution of 4-phenyl-3-

(trimethylsilyl)isocoumarin[38] (0.441 g, 1.5 mmol) and I$_2$ (1.14 g, 4.5 mmol) in CH$_3$CN (15

mL) under N$_2$, was added AgOTf (0.78 g, 3.0 mmol) in CH$_3$CN (5 mL) at room temperature.

The reaction mixture was stirred at 55 °C for 5 days. The mixture was allowed to cool to

room temperature, diluted with diethyl ether (100 mL) and filtered. The filtrate was washed

with satd aq Na$_2$S$_2$O$_3$ (25 mL) and the organic layer dried (MgSO$_4$), and filtered. The solvent

was evaporated under reduced pressure and the product was purified by chromatography on a

silica gel column to afford 501 mg (96%) of the product as a white solid: mp 170-171 °C;

^{1}H NMR (CDCl$_3$) δ 6.98 (d, J = 12.0 Hz, 1H), 7.27 (dd, J = 2.0, 7.6 Hz, 2H), 7.50-7.63 (m,

5H), 8.31 (dd, J = 0.8, 8.0 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 107.9, 119.6, 125.6, 127.4, 128.7,

128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2; IR (neat, cm^{-1}) 1736; HRMS Calcd for

C$_{15}$H$_9$O$_2$I: 347.9647. Found: 347.9652.

3-Iodo-4-phenylisocoumarin and phenylacetylene were employed in the above

Sonogashira coupling reaction. Purification by flash chromatography (7:1 hexane/EtOAc)

afforded 148 mg (46%) of the desired product **34** as a light yellow solid: mp 164-166 °C; ^{1}H

NMR (CDCl$_3$) δ 7.19-7.32 (m, 6H), 7.46-7.58 (m, 6H), 7.63-7.69 (m, 1H), 8.38 (d, J = 6.9

Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 82.5, 96.9, 121.5, 121.6, 124.3, 125.7, 128.6, 128.83, 128.84,

129.1, 129.6, 130.2, 130.9, 131.8, 133.6, 135.0, 136.4, 137.7, 161.8; IR (neat, cm^{-1}) 2212,

1729, 1610, 1602; HRMS Calcd for C$_{23}$H$_{14}$O$_2$: 322.0094. Found: 322.0100.

3-[2-(Phenylethynyl)phenyl]benzofuran (36). 3-(2-Iodophenyl)benzofuran[9f] and

phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc)

afforded 253 mg (86%) of the product as a light yellow liquid: ^{1}H NMR (CDCl$_3$) δ 7.22-7.45

(m, 9H), 7.57-7.64 (m, 2H), 7.69-7.78 (m, 2H), 8.07 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 89.4, 93.3,

111.9, 120.7, 121.3, 122.5, 123.0, 123.4, 124.6, 127.3, 127.6, 128.5, 128.8, 129.6, 131.6,

133.4, 134.0, 135.4, 143.8, 155.5; IR (neat, cm^{-1}) 3058, 1601; HRMS Calcd for C$_{22}$H$_{14}$O:

294.1045. Found: 294.1047.

3-[2-(Phenylethynyl)phenyl]-benzothiophene (40). To a solution of 2-bromophenyl

phenyl acetylene (1.5 mmol, 386 mg) and 1-benzothien-3-ylboronic acid (320 mg, 1.2 equiv)

in 7.5 mL of DME were added Pd(dba)$_2$ (43.2 mg, 5 mol %), PPh$_3$ (39 mg, 10 mol %) and

CsF (456 mg, 2.0 equiv). The resulting mixture was heated under an N$_2$ atmosphere at 100

°C for 24 h. The mixture was cooled to room temperature and diluted with 70 mL of ether, washed with 25 mL of satd NaCl, dried ($MgSO_4$) and filtered. The solvent was evaporated under reduced pressure and the residue was chromatographed using 50:1 hexane/EtOAc to afford 145 mg (31%) of the product as a yellow oil: ^1H NMR ($CDCl_3$) δ 7.02-7.08 (m, 2H), 7.18-7.24 (m, 3H), 7.36-7.48 (m, 4H), 7.52-7.56 (m, 1H), 7.63 (s, 1H), 7.70-7.74 (m, 1H), 7.76-7.80 (m, 1H), 7.94-7.98 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 89.3, 93.3, 122.9, 123.3, 123.4, 123.8, 124.3, 124.5, 125.6, 127.8, 128.3, 128.4, 128.5, 130.3, 131.5, 132.9, 136.5, 138.3, 138.7, 140.2; IR (neat, cm^{-1}) 3057, 1597, 1492, 1441; HRMS Calcd for $C_{22}H_{14}S$: 310.0816. Found: 310.0821.

3'-Methoxy-2-(phenylethynyl)biphenyl (43). This alkyne was prepared from 2-(phenylethynyl)phenylboronic acid and 1-methoxy-3-iodobenzene by following the same procedure as compound **40** at 80 °C. 2-(Phenylethynyl)phenylboronic acid (133 mg, 0.6 mmol), 3-iodoanisole (126 mg, 0.9 equiv), Pd(dba)$_2$ (14.4 mg, 0.05 equiv), PPh$_3$ (13 mg, 0.1 equiv), CsF (182 mg, 2.0 equiv) and DME (2.5 mL) afforded, after purification by flash column chromatography (silica gel, 20:1 hexane/EtOAc), 76 mg (50%) of the indicated compound **43** as light a yellow oil: ^1H NMR ($CDCl_3$) δ 3.86 (s, 3H), 6.97-7.00 (m, 1H), 7.26-7.33 (m, 5H), 7.36-7.49 (m, 6H), 7.67-7.71 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 55.5, 89.6, 92.7, 113.7, 115.0, 121.8, 122.2, 123.7, 127.4, 128.4, 128.5, 128.8, 129.2, 129.7, 131.7, 133.2, 142.2, 144.0, 159.4; IR (neat, cm^{-1}) 3058, 3023, 2955, 2936, 2833, 1599, 1581, 1490; HRMS Calcd for $C_{21}H_{16}O$: 284.1201. Found: 284.1206

3-[2-(Phenylethynyl)phenyl]thiophene (46). This alkyne was prepared from 2-bromophenyl phenyl acetylene and 3-thiopheneboronic acid by following the same procedure as compound **40** at 90 °C. 2-bromophenyl phenyl acetylene (257 mg, 1 mmol), 3-

thiopheneboronic acid (154 mg, 1.2 equiv), Pd(dba)$_2$ (24 mg, 0.05 equiv), PPh$_3$ (22 mg, 0.1

equiv), CsF (304 mg, 2.0 equiv) and DME (4 mL) afforded, after purification by flash

column chromatography (silica gel, 20:1 hexane/EtOAc), 235 mg (90%) of the indicated

compound **46** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 7.26-7.39 (m, 6H), 7.42-7.44 (m,

2H), 7.48-7.50 (m, 1H), 7.53 (dd, J = 0.9, 3.9 Hz, 1H), 7.61-7.64 (m, 1H), 7.70 (dd, J = 0.9,

2.1 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 89.7, 92.7, 121.2, 123.5, 123.7, 124.8, 127.0, 128.3, 128.4,

128.6, 128.7, 129.1, 131.5, 133.3, 138.2, 141.0; IR (neat, cm^{-1}) 3103, 3058, 3028, 1597,

1492, 1442; HRMS Calcd for C$_{18}$H$_{12}$S: 260.0660. Found: 260.0663.

2-[2-(Phenylethynyl)phenyl]naphthalene (49). 2-(2-Iodophenyl)naphthalene[35] and

phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc)

afforded 292 mg (96%) of the product as a light yellow liquid: ^{1}H NMR (CDCl$_3$) δ 7.24-7.58

(m, 10H), 7.70-7.72 (m, 1H), 7.86-7.97 (m, 4H), 8.17 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 89.7,

92.7, 122.0, 123.6, 126.2, 126.3, 127.4, 127.5, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9,

130.0, 131.6, 132.9, 133.3, 133.5, 138.3, 144.0 (one carbon was missed due to overlap); IR

(neat, cm^{-1}) 3055, 1600, 1493; HRMS Calcd for C$_{24}$H$_{16}$: 304.1252. Found: 304.1256.

1,4-Bis(biphen-2-ylethynyl)benzene (52). 2-Ethynylbiphenyl and 1,4-

diiodobenzene were employed. Purification by flash chromatography (20:1 hexane/EtOAc)

afforded 103 mg (80%) of the product as a white solid: mp 163-164 °C; ^{1}H NMR (CDCl$_3$) δ

7.23 (s, 2H), 7.34-7.49 (m, 6H), 7.63-7.68 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 91.5, 92.2, 121.6,

123.3, 127.3, 127.8, 128.1, 128.9, 129.6, 129.7, 131.4, 133.1, 140.7, 144.2; IR (neat, cm^{-1})

3062, 1512; HRMS Calcd for C$_{24}$H$_{16}$: 304.1252. Found: 304.1256.

9-Phenyl-10-(phenylethynyl)phenanthrene (54). 9-Iodo-10-phenylphenanthrene

(2) and phenylacetylene were employed. Purification by flash chromatography (40:1

hexane/EtOAc) afforded 188 mg (53%) of the product as a white solid: mp 143-144 °C; [1]H

NMR (CDCl$_3$) δ 7.24-7.30 (m, 5H), 7.50-7.77 (m, 10H), 8.63-8.79 (m, 3H); ^{13}C NMR

(CDCl$_3$) δ 88.0, 98.5, 119.3, 122.8, 122.9, 123.7, 127.0, 127.3, 127.4, 127.5, 127.6, 127.7,

128.0, 128.3, 128.4, 128.5, 130.0, 130.5, 130.9, 131.0, 131.6, 131.7, 140.0, 143.2; IR (neat,

cm^{-1}) 3061, 1599; HRMS Calcd for C$_{24}$H$_{16}$: 304.1252. Found: 304.1256.

General procedure for the electrophilic cyclization of 2-(arylethynyl)biphenyls

by ICl. To a solution of 2-(arylethynyl)biphenyl (0.30 mmol) in CH$_2$Cl$_2$ (3 mL) under N$_2$

was added ICl (1.2 equiv) in CH$_2$Cl$_2$ (0.5 mL) at -78 °C. The reaction mixture was stirred at

-78 °C for 1 h unless otherwise indicated. The reaction mixture was then diluted with diethyl

ether (50 mL), washed with 25 mL of satd aq Na$_2$S$_2$O$_3$, dried (MgSO$_4$), and filtered. The

solvent was evaporated under reduced pressure and the product was purified by

chromatography on a silica gel column.

9-Iodo-10-phenylphenanthrene (2). Purification by flash chromatography (40:1

hexane/EtOAc) afforded 112 mg (99%) of the product as a white solid with a melting point

and spectral properties identical to those previously reported.[9a]

9-Iodo-10-(4-methoxyphenyl)phenanthrene (7). Purification by flash

chromatography (30:1 hexane/EtOAc) afforded 122 mg (99%) of the product as a white

solid: mp 170-171 °C; ^{1}H NMR (CDCl$_3$) δ 3.94 (s, 3H), 7.09 (dd, J = 2.1, 6.6 Hz, 2H), 7.21

(dd, J = 2.1, 6.6 Hz, 2H), 7.40-7.49 (m, 2H), 7.64-7.72 (m, 3H), 8.45-8.49 (m, 1H), 8.67-8.78

(m, 2H); ^{13}C NMR (CDCl$_3$) δ 55.6, 107.7, 114.0, 122.8, 122.9, 127.2, 127.3, 127.7, 128.3,

129.0, 130.5, 130.8, 131.3, 132.7, 132.9, 135.0, 138.2, 145.3, 159.4; IR (neat, cm^{-1}) 3066,

3024, 2834, 1610; HRMS Calcd for C$_{21}$H$_{15}$IO: 410.0168. Found: 410.0172.

9-Iodo-10-(4-methylphenyl)phenanthrene (9). Purification by flash

chromatography (30:1 hexane/EtOAc) afforded 116 mg (98%) of the product as a yellow

solid: m 179-181 °C; ^{1}H NMR (CDCl$_3$) δ 2.52 (s, 3H), 7.18 (dd, J = 1.5, 6.3 Hz, 2H), 7.36-

7.44 (m, 4H), 7.64-7.76 (m, 3H), 8.46-8.49 (m, 1H), 8.66-8.78 (m, 2H); ^{13}C NMR (CDCl$_3$) δ

21.7, 107.0, 122.8, 122.9, 127.2, 127.3, 127.7, 128.3, 129.0, 129.4, 130.0, 130.5, 130.8,

132.8, 134.9, 137.8, 142.7, 145.6 (missing one sp^2 carbon due to overlap); IR (neat, cm^{-1})

3067, 3020, 2917; HRMS Calcd for C$_{21}$H$_{15}$I: 394.0219. Found: 394.0226.

Ethyl 4-(10-iodo-9-phenanthryl)benzoate (11). The reaction mixture was stirred at

room temperature for 1 h. Purification by flash chromatography (15:1 hexane/EtOAc)

afforded 136 mg (100%) of the product as a white solid: mp 152-153 °C; ^{1}H NMR (CDCl$_3$) δ

1.46 (t, J = 7.2 Hz, 3H), 4.47 (q, J = 7.2 Hz, 2H), 7.30-7.45 (m, 4H), 7.66-7.75 (m, 3H), 8.26

(dd, J = 1.8, 6.6 Hz, 2H), 8.45-8.49 (m, 1H), 8.68-8.78 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 14.6,

61.4, 106.0, 122.9, 123.0, 127.4, 127.5, 128.0, 128.4, 128.5, 130.1, 130.3, 130.4, 130.5,

130.8, 132.1, 132.5, 134.9, 144.6, 150.0, 166.7; IR (neat, cm^{-1}) 3069, 2979, 1714; HRMS

Calcd for C$_{23}$H$_{17}$IO$_2$: 452.0273. Found: 452.0278.

9-Iodo-10-(4-nitrophenyl)phenanthrene (13). Purification by flash chromatography

(7:1 hexane/EtOAc) afforded an inseparable mixture of the desired compound **10** (57%) and

ICl alkyne adducts (42%) (yields were calculated by ^{1}H NMR spectroscopic analysis).

Recrystallization from hexanes/ethyl acetate afforded 31 mg (30%) of the desired product **10**

as a yellow solid: mp 205-206 °C; ^{1}H NMR (CDCl$_3$) δ 7.23-7.26 (m, 1H), 7.43-7.51 (m,

3H), 7.68-7.77 (m, 3H), 8.43-8.46 (m, 3H), 8.70-8.79 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 105.9,

123.0, 123.2, 124.2, 127.6, 127.8, 128.0, 128.4, 128.6, 130.6, 130.9, 131.5, 131.7, 132.2,

134.9, 143.2, 147.8, 152.1; IR (neat, cm⁻¹) 3070, 1599, 1516; HRMS Calcd for $C_{20}H_{12}INO_2$: 424.9913. Found: 424.9919.

9-Iodo-10-phenylphenanthrene-2-carbaldehyde (15). Purification by flash chromatography (5:1 hexane/EtOAc) afforded an inseparable mixture of the desired compound **12** (71%) and ICl alkyne adducts (17%) (yields were calculated by ¹H NMR spectroscopic analysis). Recrystallization from hexanes/ethyl acetate afforded 49 mg (40%) of the desired product **12** as a white solid: mp 121-123 °C; ¹H NMR (CDCl₃) δ 7.30-7.33 (m, 2H), 7.58-7.61 (m, 3H), 7.76-7.79 (m, 2H), 7.88 (s, 1H), 8.16 (dd, J = 1.5, 8.4 Hz, 1H), 8.50-8.53 (m, 1H), 8.71-8.74 (m, 1H), 8.84 (d, J = 8.7 Hz, 1H), 9.96 (s, 1H); ¹³C NMR (CDCl₃) δ 108.3, 123.8, 124.0, 124.9, 128.3, 128.6, 129.0, 129.8, 130.0, 130.2, 132.2, 133.8, 133.9, 134.5, 134.8, 135.2, 144.7, 145.7, 192.2; IR (neat, cm⁻¹) 3059, 3024, 1694, 1606; HRMS Calcd for $C_{21}H_{13}IO$: 408.0011. Found: 408.0018.

9-Iodo-2-nitro-10-phenylphenanthrene (17). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 70 mg (55%) of the product as a yellow solid: mp 193-194 °C; ¹H NMR (CDCl₃) δ 7.23-7.30 (m, 2H), 7.59-7.62 (m, 3H), 7.79-7.82 (m, 2H), 8.30 (s, 1H), 8.40-8.44 (m, 1H), 8.52-8.55 (m, 1H), 8.66-8.74 (m, 1H), 8.81-8.89 (m, 1H); ¹³C NMR (CDCl₃) δ 109.4, 120.9, 123.9, 124.4, 124.6, 128.7, 128.9, 129.1, 129.4, 130.0, 130.3, 132.0, 134.0, 134.4, 135.4, 144.1, 145.6, 146.4; IR (neat, cm⁻¹) 3083, 1536, 1513; HRMS Calcd for $C_{20}H_{12}INO_2$: 424.9913. Found: 424.9919. Anal. Calcd for $C_{20}H_{12}INO_2$: C, 56.48; H, 2.84; N, 3.29. Found: C, 56.14; H, 2.56; N, 3.17.

10-Iodo-2-nitro-9-phenylphenanthrene (19). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 112 mg (88%) of the product as a yellow solid: mp 182-183 °C; ¹H NMR (CDCl₃) δ 7.25-7.30 (m, 2H), 7.44-7.62 (m, 5H), 7.75 (dt, J = 1.2, 7.8 Hz, 1H),

8.45 (td, J = 2.7, 9.0 Hz, 1H), 8.73 (d, J = 8.4 Hz, 1H), 8.81 (dd, J = 3.3, 9.3 Hz, 1H), 9.42 (t,

J = 2.7 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 105.5, 121.3, 123.8, 124.7, 128.3, 128.5, 128.9, 129.28,

129.33, 129.4, 129.8, 131.1, 132.9, 133.8, 134.8, 144.8, 147.2, 148.0; IR (neat, cm^{-1}) 3080,

3059, 3025, 1577, 1515, 1345; HRMS Calcd for C$_{20}$H$_{12}$INO$_2$: 424.9913. Found: 424.9921.

9-(Cyclohex-1-en-1-yl)-10-iodophenanthrene (21). Purification by flash

chromatography (50:1 hexane/EtOAc) afforded 79 mg (70%) of the product as a colorless

oil: ^{1}H NMR (CDCl$_3$) δ 1.85-2.01 (m, 4H), 2.19-2.26 (m, 1H), 3.35-2.48 (m, 3H), 5.71-5.74

(m, 1H), 7.54-7.60 (m, 1H), 7.62-7.70 (m, 3H), 8.06 (dd, J = 0.9, 8.1 Hz, 1H), 8.41-8.46 (m,

1H), 8.61-8.64 (m, 1H), 8.69 (d, J = 8.7 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 22.3, 23.2, 25.7, 29.5,

105.4, 122.8, 123.0, 127.2, 127.28, 127.33, 128.0, 128.2, 129.2, 130.5, 130.7, 131.4, 132.8,

134.5, 142.4, 147.2; IR (neat, cm^{-1}) 3067, 3025, 2926, 1562, 1482, 1445; HRMS Calcd for

C$_{20}$H$_{17}$I: 384.0375. Found: 384.0380.

[(10-Iodo-9-phenanthryl)methyl](trimethyl)silane (27). Purification by flash

chromatography (50:1 hexane/EtOAc) afforded 54 mg (50%) of the product as a white solid:

mp 70-72 °C; ^{1}H NMR (CDCl$_3$) δ 0.11 (s, 9H), 3.24 (s, 2H), 7.56-7.71 (m, 4H), 8.09 (dd, J =

0.8, 8.1 Hz, 1H), 8.39-8.42 (m, 1H), 8.58-8.62 (m, 1H), 8.70-8.73 (m, 1H); ^{13}C NMR

(CDCl$_3$) δ 0.00, 31.1, 106.0, 122.2, 122.9, 125.9, 126.54, 126.57, 126.64, 127.5, 129.2,

130.1, 130.7, 133.0, 134.2, 141.8; IR (neat, cm^{-1}) 3068, 2951, 1562, 1485, 1445; HRMS

Calcd for C$_{18}$H$_{19}$ISi: 390.0301. Found: 390.0310.

6-Iodo-5-phenylbenzo[c]phenanthrene (29). Purification by flash chromatography

(3:1 hexane/CH$_2$Cl$_2$) afforded 61 mg (48%) of the product as a white solid: mp 159-160 °C;

^{1}H NMR (CDCl$_3$) δ 7.32-7.36 (m, 2H), 7.44-7.47 (m, 1H), 7.52-7.60 (m, 4H), 7.62-7.70 (m,

3H), 7.95 (d, J = 9.0 Hz, 1H), 8.03-8.07 (m, 1H), 8.43 (m, J = 9.0 Hz, 1H), 9.04 (d, J = 8.1

Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 106.4, 126.4, 126.6, 126.7, 126.8, 128.1, 128.3, 128.4, 128.6,

128.67, 128.71, 128.8, 129.0, 129.6, 130.1, 130.3, 131.2, 132.2, 133.4, 133.8, 145.2, 145.4;

IR (neat, cm^{-1}) 3057, 1599, 1503, 1488; HRMS Calcd for C$_{24}$H$_{15}$I: 430.0219. Found:

430.0228.

5-(4-Methoxyphenyl)-6-iodobenzo[*c*]phenanthrene (31). Purification by flash

chromatography (20:1 hexane/ EtOAc) afforded 134 mg (97%) of the product as a green

solid: mp 186-187 °C; ^{1}H NMR (CDCl$_3$) δ 3.94 (s, 3H), 7.10 (d, J = 4.5 Hz, 2H), 7.23-7.26

(m, 2H), 7.42-7.47 (m, 1H), 7.57-7.69 (m, 4H), 7.94 (d, J = 9.0 Hz, 1H), 8.02-8.06 (m, 1H),

8.42 (d, J = 9.0 Hz, 1H), 9.01-9.05 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 55.6, 107.3, 114.1, 126.4,

126.6, 126.7, 126.8, 128.41, 128.44, 128.61, 128.64, 128.8, 129.0, 129.7, 130.2, 131.3, 131.5,

132.4, 133.75, 133.80, 138.0, 145.0, 159.4; IR (neat, cm^{-1}) 3065, 2961, 2838, 1607, 1510,

1247; HRMS Calcd for C$_{25}$H$_{17}$IO: 460.0324. Found: 460.0334

9-Iodo-10-(2-thiophenyl)phenanthrene (33). Purification by flash chromatography

(30:1 hexane/EtOAc) afforded 111 mg (96%) of the product as a white solid: mp 140-142

°C; ^{1}H NMR (CDCl$_3$) δ 7.06-7.08 (m, 1H), 7.23-7.26 (m, 1H), 7.45-7.76 (m, 6H), 8.44-8.49

(m, 1H), 8.66-8.75 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 110.5, 122.7, 122.9, 126.5, 127.2, 127.5,

128.2, 128.4, 128.7, 128.8, 130.3, 131.1, 132.6, 133.2, 135.3, 138.4, 146.5; IR (neat, cm^{-1})

2925, 1464, 1216; HRMS Calcd for C$_{18}$H$_{11}$IS: 385.9626. Found: 385.9631.

7-Iodo-8-phenyl-5*H*-dibenzo[*c*,*f*]chromen-5-one (35). Purification by flash

chromatography (3:1 hexane/EtOAc) afforded 87 mg (65%) of the product as a white solid:

mp 205-207 °C; ^{1}H NMR (CDCl$_3$) δ 7.25-7.29 (m, 2H), 7.36-7.42 (m, 1H), 7.51-7.70 (m,

6H), 8.92 (t, J = 7.8 Hz, 1H), 8.53 (d, J = 7.2 Hz, 1H), 8.62 (d, J = 7.6 Hz, 1H), 8.75 (d, J =

7.0 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 92.8, 113.3, 122.9, 125.4, 126.1, 127.1, 127.9, 128.5,

128.8, 128.91, 128.93, 129.5, 129.9, 130.9, 131.7, 134.6, 135.0, 143.2, 148.0, 149.0, 160.9;

IR (neat, cm^{-1}) 3431, 1744; HRMS Calcd for $C_{23}H_{13}IO_3$: 447.9960. Found: 447.9967.

5-Iodo-6-phenylbenzo[*b*]naphtho[1,2-*d*]furan (37). The reaction mixture was

stirred at -78 °C for 5 h. Purification by flash chromatography (50:1 hexane/EtOAc)

afforded 113 mg (91%) of the product as a light yellow liquid: ^{1}H NMR (CDCl$_3$) δ 7.45-7.69

(m, 9H), 7.77 (t, *J* = 7.8 Hz, 1H), 8.41-8.44 (m, 1H), 8.54 (d, *J* = 8.7 Hz, 1H), 8.64 (d, *J* = 8.1

Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 105.0, 112.6, 118.2, 122.4, 123.7, 124.0, 124.7, 126.6, 126.8,

128.0, 128.6, 128.7, 128.9, 130.5, 131.9, 134.3, 135.1, 140.6, 152.2, 156.1; IR (neat, cm^{-1})

3058, 2961; HRMS Calcd for $C_{22}H_{13}IO$: 420.0011. Found: 420.0021.

9-Iodo-3-methoxy-10-phenylphenanthrene (44). Purification by flash

chromatography (30:1 hexane/ EtOAc) afforded 83 mg (66%) of the product as a white solid:

mp 136-138 °C; ^{1}H NMR (CDCl$_3$) δ 4.02 (s, 3H), 7.05 (dd, *J* = 2.5, 9.3 Hz, 1H), 7.26-7.35

(m, 3H), 7.51-7.58 (m, 3H), 7.68-7.71 (m, 2H), 8.09 (d, *J* = 2.4 Hz, 1H), 8.43-8.47 (m, 1H),

8.59-8.62 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 55.7, 103.3, 104.3, 117.0, 122.9, 127.3, 127.5, 128.0,

128.4, 128.7, 130.2, 130.4, 130.5, 132.0, 133.0, 134.9, 145.3, 145.7, 158.9; IR (neat, cm^{-1})

3056, 3025, 2957, 2933, 2834, 1613, 1576, 1519; HRMS Calcd for $C_{21}H_{15}IO$: 410.0168.

Found: 410.0175.

9-Iodo-1-methoxy-10-phenylphenanthrene (45). Purification by flash

chromatography (30:1 hexane/ EtOAc) afforded 26 mg (20%) of the product as a light yellow

oil: ^{1}H NMR (CDCl$_3$) δ 3.34 (s, 3H), 6.94 (d, *J* = 7.8 Hz, 1H), 7.18-7.21 (m, 2H), 7.37-7.46

(m, 3H), 7.58-7.69 (m, 3H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.48-8.52 (m, 1H), 8.64-8.67 (m, 1H);

^{13}C NMR (CDCl$_3$) δ 56.2, 109.5, 110.0, 115.8, 123.4, 123.5, 126.5, 127.4, 127.6, 128.0,

128.5, 129.0, 130.4, 132.7, 133.0, 135.3, 142.9, 151.1, 156.6; IR (neat, cm^{-1}) 3056, 3021,

2929, 1601, 1575, 1455; HRMS Calcd for $C_{21}H_{15}IO$: 410.0168. Found: 410.0172.

5-Iodo-4-phenylnaphtho[2,1-*b*]thiophene (47). Purification by flash

chromatography (20:1 hexane/ EtOAc) afforded 58 mg (50%) of the product as a light yellow

solid: mp 98-99 °C; ^{1}H NMR (CDCl$_3$) δ 7.41-7.44 (m, 2H), 7.54-7.58 (m, 4H), 7.63-7.68 (m,

2H), 8.01 (d, *J* = 5.4 Hz, 1H), 8.30-8.35 (m, 1H), 8.43-8.49 (m, 1H); ^{13}C NMR (CDCl$_3$) δ

101.18, 122.2, 124.2, 127.3, 127.4, 127.9, 128.8, 128.9, 129.0, 129.6, 132.8, 134.4, 136.3,

139.7, 141.2, 144.8; IR (neat, cm^{-1}) 3102, 3059, 3025, 1551, 1492, 1442; HRMS Calcd for

$C_{18}H_{11}IS$: 385.9626. Found: 385.9633.

5-Iodo-4-phenylnaphtho[1,2-*c*]thiophene (48). Purification by flash

chromatography (20:1 hexane/ EtOAc) afforded 43 mg (37%) of the product as a white solid:

mp 149-150 °C; ^{1}H NMR (CDCl$_3$) δ 7.36-7.40 (m, 2H), 7.52-7.67 (m, 6H), 7.81 (s, 1H),

8.12-8.17 (m, 1H), 8.40-8.44 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 101.1, 121.4, 124.0, 127.6, 127.7,

128.1, 129.0, 129.4, 132.9, 133.8, 134.5, 135.2, 138.2, 140.4, 144.1 (one sp^2 carbon missing

due to overlap); IR (neat, cm^{-1}) 3057, 3022, 1554, 1496; HRMS Calcd for $C_{18}H_{11}IS$:

385.9626. Found: 385.9632.

6-Iodo-5-phenylchrysene (50). Purification by flash chromatography (40:1

hexane/EtOAc) afforded 98 mg (76%) of the product as a light yellow solid: mp 168-169 °C;

^{1}H NMR (CDCl$_3$) δ 7.07 (t, *J* = 6.9 Hz, 1H), 7.33-7.57 (m, 7H), 7.71-7.76 (m, 2H), 8.89 (d, *J*

= 6.5 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 8.56-8.60 (m, 1H), 8.78 (d, *J* = 7.0 Hz, 2H); ^{13}C

NMR (CDCl$_3$) δ 111.5, 121.3, 123.7, 125.4, 126.1, 127.7, 128.2, 128.4, 128.6, 128.9, 129.0,

129.2, 129.3, 130.4, 130.7, 130.8, 131.1, 133.5, 133.8, 135.3, 144.3, 150.0; IR (neat, cm^{-1})

2922; HRMS Calcd for $C_{24}H_{15}I$: 430.0219. Found: 430.0025.

5-Iodo-6-phenylchrysene (51). Purification by flash chromatography (40:1 hexane/EtOAc) afforded 18 mg (14%) of the product as a white solid: mp 174-176 °C; ^{1}H NMR (CDCl$_3$) δ 7.12 (t, J = 7.2 Hz, 1H), 7.30-7.33 (m, 3H), 7.49-7.61 (m, 5H), 7.70-7.78 (m, 2H), 8.39 (d, J = 7.2 Hz, 1H), 8.55-8.68 (m, 2H), 8.87 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 111.7, 121.8, 123.5, 124.9, 126.0, 127.0, 128.0, 128.1, 128.3, 128.8, 129.1, 129.2, 129.8, 130.2, 130.8, 131.0, 131.8, 132.9, 133.7, 135.4, 143.8, 149.6; IR (neat, cm^{-1}) 3057, 2920; HRMS Calcd for C$_{24}$H$_{15}$I: 430.0219. Found: 430.0025.

1,4-Bis(10-iodophenanthr-9-yl)benzene (53). Filtration afforded 184 mg (90%) of the product as a white solid: mp 328-331 °C; ^{1}H NMR (CDCl$_3$) 7.50-7.79 (m, 14H), 8.54-8.57 (m, 2H), 8.74-8.83 (m, 4H); the ^{13}C NMR and IR spectra could not be obtained due to the poor solubility of this compound in common organic solvents. HRMS Calcd for C$_{34}$H$_{20}$I$_2$: 681.9655. Found: 681.9667. Anal. Calcd for C$_{34}$H$_{20}$I$_2$: C, 59.85; H, 2.95. Found: C, 59.43; H, 2.52.

General procedure for the electrophilic cyclization of 2-(1-alkynyl)biphenyls by I$_2$. To a solution of 2-(1-alkynyl)biphenyl (0.30 mmol) in CH$_2$Cl$_2$ (3 mL) was added I$_2$ (3.0 equiv) and NaHCO$_3$ (3.0 equiv) at room temperature. The reaction mixture was stirred at room temperature for 24 h unless otherwise indicated. The reaction mixture was then diluted with diethyl ether (50 mL), washed with satd aq Na$_2$S$_2$O$_3$ (25 mL), dried (MgSO$_4$), and filtered. The solvent was evaporated under reduced pressure and the product was purified by chromatography on a silica gel column.

9-Iodo-10-phenylphenanthrene (2). Purification by flash chromatography (50:1 hexane/EtOAc) afforded 92 mg (80%) of the product as a white solid with a melting point and spectral properties identical to those previously reported.[9a]

General procedure for the electrophilic cyclization of 2-(1-alkynyl)biphenyls by

NBS. To a solution of 2-(1-alkynyl)biphenyl (0.30 mmol) in CH_2Cl_2 (3 mL) was added NBS

(1.2 equiv) and silica gel (50 mg) at room temperature. The reaction mixture was stirred at

room tempature for 144 h unless otherwise indicated. The reaction mixture was then diluted

with diethyl ether (50 mL), washed with satd aq $Na_2S_2O_3$ (25 mL), dried ($MgSO_4$), and

filtered. The solvent was evaporated under reduced pressure and the product was purified by

chromatography on a silica gel column.

9-Bromo-10-phenylphenanthrene (3). Purification by flash chromatography (40:1

hexane/EtOAc) afforded 86 mg (86%) of the product as a white solid: mp 108-109 °C; ^{1}H

NMR (CDCl$_3$) δ 7.34-7.38 (m, 2H), 7.41-7.47 (m, 2H), 7.50-7.60 (m, 3H), 7.64-7.77 (m,

3H), 8.53-8.57 (m, 1H), 8.72-8.77 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 122.9, 123.8, 127.1, 127.3,

127.7, 127.9, 128.0, 128.2, 128.7, 129.2, 129.3, 130.2, 130.7, 131.2, 132.9, 139.9, 141.3; IR

(neat, cm^{-1}) 3070, 3058, 3027, 1583, 1567, 1484; HRMS Calcd for $C_{20}H_{15}Br$: 332.0201.

Found: 332.0209.

5-Bromo-6-phenylbenzo[*b*]naphtha[1,2-*d*]thiophene (41). Purification by flash

chromatography (40:1 hexane/EtOAc) afforded 102 mg (88%) of the product as a yellow oil:

^{1}H NMR (CDCl$_3$) δ 7.46-7.53 (m, 3H), 7.54-7.63 (m, 4H), 7.68-7.74 (m, 1H), 7.78-7.83 (m,

1H), 7.88 (dd, J = 7.8, 0.6 Hz, 1H), 8.64 (dd, J = 8.4, 1.2 Hz, 1H), 8.86 (d, J = 8.1 Hz, 1H),

9.07 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 122.7, 123.3, 123.6, 125.1, 125.3, 125.8, 126.5,

127.9, 128.9, 129.0, 129.70, 129.74, 130.9, 131.0, 136.4, 136.6, 140.6, 141.0, 141.4; IR

(neat, cm^{-1}) 3059, 2921, 1558, 1494, 1442; HRMS Calcd for $C_{22}H_{13}BrS$: 387.9921. Found:

387.9930.

General procedure for the electrophilic cyclization of 2-(1-alkynyl)biphenyls by

p-O$_2$NC$_6$H$_4$SCl. To a solution of 2-(1-alkynyl)biphenyl (0.30 mmol) in CH$_2$Cl$_2$ (3 mL) was

added p-O$_2$NC$_6$H$_4$SCl (1.2 equiv) at room temperature. The reaction mixture was stirred for

0.5 h unless otherwise indicated. The reaction mixture was then diluted with diethyl ether

(50 mL), washed with satd aq NH$_4$Cl (25 mL), dried (MgSO$_4$), and filtered. The solvent was

evaporated under reduced pressure and the product was purified by chromatography on a

silica gel column.

9-(4-Nitrophenylsulfenyl)-10-phenylphenanthrene (4). Purification by flash

chromatography (30:1 hexane/EtOAc) afforded 112 mg (92%) of the product as a yellow

solid: mp 192-193 °C; ^{1}H NMR (CDCl$_3$) δ 6.94-6.98 (m, 2H), 7.20-7.24 (m, 2H), 7.39-7.47

(m, 3H), 7.50-7.54 (m, 2H), 7.71-7.64 (m, 1H), 7.72-7.79 (m, 2H), 7.93 (dt, J = 9.3, 2.1 Hz,

2H), 8.46 (dd, J = 8.4, 0.9 Hz, 1H), 8.83 (d, J = 8.4 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 123.0,

123.4, 124.1, 125.0, 125.9, 127.3, 127.4, 127.8, 128.1, 128.3, 128.4, 128.6, 129.2, 129.4,

131.3, 131.6, 131.7, 132.3, 139.9, 145.1, 148.0, 149.2; IR (neat, cm^{-1}) 3066, 3024, 2834,

1610; HRMS Calcd for C$_{26}$H$_7$NO$_2$S: 407.0980. Found: 407.0989.

5-(4-Nitrophenylthio)-6-phenylbenzo[b]naphtha[1,2-d]thiophene (42).

Purification by flash chromatography (9:1 hexane/EtOAc) afforded 101 mg (91%) of the

product as a yellow solid: mp > 215 °C (decomposed); ^{1}H NMR (CDCl$_3$) δ 6.93-6.97 (m,

2H), 7.34-7.38 (m, 2H), 7.43-7.57 (m, 4H), 7.61-7.68 (m, 2H), 7.79-7.85 (m, 1H), 7.92-7.95

(m, 3H), 8.63 (dd, J = 8.7, 0.9 Hz, 1H), 8.94 (d, J = 8.4 Hz, 1H), 9.17 (d, J = 5.4 Hz, 1H); ^{13}C

NMR (CDCl$_3$) δ 123.4, 124.2, 125.5, 125.6, 126.0, 126.5, 126.9, 128.03, 128.04, 128.7,

129.0, 129.0, 131.2, 131.7, 132.8, 136.6, 139.9, 141.3, 141.4, 143.3, 145.2, 149.1 (two sp^2

carbons missing due to overlap); IR (neat, cm^{-1}) 3060, 2924, 1579, 1513, 1336; HRMS Calcd

for C$_{28}$H$_{17}$NO$_2$S$_2$: 463.0701 Found: 463.0713.

9,10-Diphenylbenzo[g]chrysene (55). Pd(OAc)$_2$ (2.8 mg, 5 mol %), NaOAc (41 mg,

0.5 mmol), LiCl (31.5 mg, 0.75 mmol), DMF (5 mL), 9-iodo-10-phenylphenanthrene (95

mg, 0.25 mmol) and diphenylacetylene (44.5 mg, 0.25 mmol) were placed in a vial. The

resulting mixture was heated under an N$_2$ atmosphere at 100 °C for 5 d. The mixture was

allowed to cool to room temperature, diluted with diethyl ether (50 mL), washed with satd aq

NH$_4$Cl (25 mL), dried (MgSO$_4$), and filtered. The solvent was removed under reduced

pressure and the residue was purified by column chromatography (100:1 hexane/EtOAc) on

silica gel to afford 89 mg (83%) of the product as a white solid: mp 228-230 °C; ^{1}H NMR

(CDCl$_3$) δ 7.04-7.10 (m, 6H), 7.17-7.30 (m, 5H), 7.40-7.51 (m, 2H), 7.57-7.80 (m, 5H), 8.58

(d, J = 7.6 Hz, 1H), 8.69 (d, J = 7.0 Hz, 1H), 8.83 (t, J = 6.8 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ

123.2, 123.8, 125.7, 125.8, 126.27, 126.29, 126.41, 126.66, 126.69, 127.0, 127.1, 127.8,

128.03, 128.06, 128.07, 129.0, 129.5, 129.7, 130.05, 130.08, 130.87, 130.98, 131.4, 131.7,

132.1, 132.5, 136.1, 138.5, 139.7, 143.0; IR (neat, cm^{-1}) 3062, 2925; HRMS Calcd for

C$_{34}$H$_{22}$: 430.1722. Found: 430.1729.

Ethyl (2E)-3-(10-phenyl-9-phenanthryl)acrylate (57). To a solution of 9-iodo-10-

phenylphenanthrene (0.20 mmol) and ethyl acrylate (1.0 mmol, 5.0 equiv) in DMF (0.8 mL)

were added Pd(OAc)$_2$ (2.2 mg, 5 mol %), n-Bu$_4$NCl (0.20 mmol, 1 equiv) and NaHCO$_3$ (0.5

mmol, 2.5 equiv). The resulting mixture was heated under a N$_2$ atmosphere at 100 °C for 3

d. The mixture was cooled to room temperature and diluted with 70 mL of ether, washed

with 25 mL of satd aq NaCl, dried (MgSO$_4$) and filtered. The solvent was evaporated under

reduced pressure. The residue was chromatographed using 7:1 hexane/EtOAc to afford 69.0

mg (98%) of the product as a yellow solid: mp 135-136 °C; ^{1}H NMR (CDCl$_3$) δ 1.28 (t, J = 7.1 Hz, 3H), 4.20 (q, J = 6.9 Hz, 2H), 6.02 (d, J = 16.2 Hz, 1H), 7.26-7.31 (m, 2H), 7.44-7.55 (m, 5H), 7.62-7.75 (m, 3H), 7.88 (d, J = 16.2 Hz, 1H), 8.23 (dd, J = 1.2, 8.1 Hz, 1H), 8.73-8.81 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 14.5, 60.7, 122.7, 123.2, 126.1, 126.5, 127.0, 127.1, 127.31, 127.34, 127.8, 128.3, 128.6, 129.9, 130.2, 130.4, 130.6, 130.9, 131.7, 138.3, 139.0, 143.5, 166.6; IR (neat, cm^{-1}) 3066, 2982, 1712, 1642, 1488; HRMS Calcd for C$_{25}$H$_{20}$O$_2$: 352.1463. Found: 352.1469.

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CHAPTER 4. SYNTHESIS OF HIGHLY SUBSTITUTED FURANS BY THE ELECTROPHILE-INDUCED COUPLING OF 2-(1-ALKYNYL)-2-ALKEN-1-ONES AND NUCLEOPHILES

Based on a paper to be submitted to the *Journal of American Chemical Society*

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Abstract

The coupling of 2-(1-alkynyl)-2-alken-1-ones with nucleophiles, either catalyzed by $AuCl_3$ or induced by an electrophile, provides highly substituted furans in good to excellent yields under very mild reaction conditions. Various nucleophiles, including functionalized alcohols, H_2O, carboxylic acids, 1,3-diketones and electron-rich arenes, and a range of cyclic and acyclic 2-(1-alkynyl)-2-alken-1-ones readily participate in these cyclizations. Iodine, NIS, and PhSeCl have proven successful as electrophiles in this process. The resulting iodine-containing furans can be readily elaborated to more complex products using known organopalladium chemistry.

Introduction

Furans, one of the most important five-membered ring heterocycles,[1] can be found in many naturally-occurring compounds arising from plants and marine organisms.[2] For example, in a number of biologically significant natural products, such as pinguisone,[3]

furodysinin,[4] and methyl vouacapenate,[5] a 2,3-disubstituted furan ring constitutes a distinctive structural feature. Furans are used as commercial pharmaceutical agents, flavor and fragrance compounds, insecticides, and antileukemic agents.[6] Polysubstituted furans can also be employed as building blocks for the total synthesis of complicated naturally-occurring metabolites,[7] and as versatile starting materials for the preparation of a variety of heterocyclic and acyclic compounds.[8]

Their important biological activity and great utility have encouraged the search for ever newer, more efficient methods for the synthesis of furans.[9] The vast majority of the previous routes to furans have involved the chemical modification of acyclic precursors. A particularly effective approach to the synthesis of functionalized furans is through the transition metal-catalyzed cyclization of an alkynyl or allenyl ketone,[10] alcohol,[11] or epoxide,[12] or electrophilic cyclization of alk-3-yne-1,2-diols,[13] 2,4-dialkenyl-1,3-dicarbonyl compounds[14] or 2-alkynyl carbonyl compounds.[15] No attention has been paid to 2-(1-alkynyl)-2-alken-1-ones as possible furan precursors, although they are more readily accessible and more easily manipulated than are alkynyl or allenyl ketones.[16] The utilization of 2-(1-alkynyl)-2-alken-1-ones for transition metal-catalyzed or electrophilic cyclization should significantly expand the range of suitable starting materials for the synthesis of functionally-substituted furans.

Recently, we have communicated a $AuCl_3$-catalyzed synthesis of substituted furans from 2-(1-alkynyl)-2-alken-1-ones, which produces highly substituted furans in good to excellent yields (eq. 1).[17] Now, we wish to report a detailed study of the $AuCl_3$-

$$\text{[structure]} \xrightarrow[\text{CH}_2\text{Cl}_2, \text{ r.t.}]{1.5 \text{ NuH}, 1\% \text{ AuCl}_3} \text{[furan structure]} \quad (1)$$
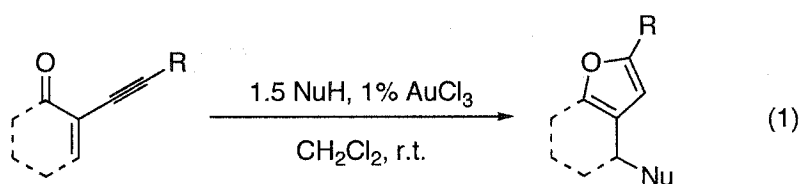
catalyzed synthesis of substituted furans, together with a novel electrophile-induced three-

component reaction, which produces tetrasubstituted furans in good to excellent yields (eq.

2). These unique cyclizations are particularly attractive, because *sequential nucleophilic*

$$\text{[structure]} \xrightarrow[\text{CH}_3\text{CN, NaHCO}_3, \text{ r.t.}]{\text{NuH, E}^+} \text{[furan structure]} \quad (2)$$
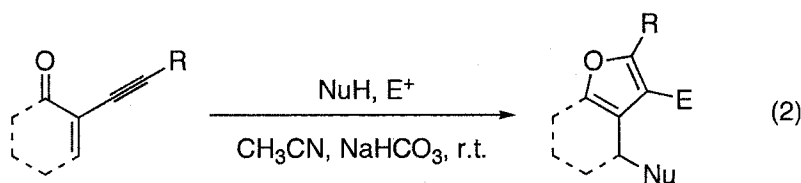
domino attack onto an alkyne affords multiply-substituted furans through simultaneous

formation of a C-O bond and a remote carbon-nucleophile bond. One of the advantages of

this approach to furans, is that the regioselective introduction of substituents about the furan

ring comes down to the appropriate choice of the 2-(1-alkynyl)-2-alken-1-one and

nucleophile, which allows for considerable versatility (Scheme 1). Furthermore, the

electrophile-induced cyclization provides a general and efficient approach to the

regioselective synthesis of tetrasubstituted furans, which is still today a challenge in organic

synthesis.

SCHEME 1

$$R^1\text{-COCH}_3 + R^2\text{CHO} \longrightarrow \text{[structure]} \xrightarrow[\text{base}]{X_2} \text{[structure]} \xrightarrow[\text{cat. Pd/Cu}]{\text{H}\text{---}\text{R}^3} \text{[structure]}$$

X = I, Br
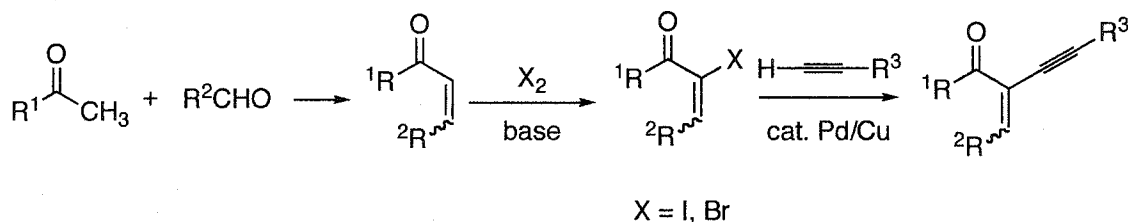
Results and Discussion

Our preliminary studies have been carried out on the transition metal-catalyzed coupling of 2-phenylethynyl-2-cyclohexen-1-one (**1**) and methanol to afford furan **2** (Table 1). As we previously communicated, silver, copper, gold and mercury salts afford good yields of furan **2** (Table 1, entries 1-4).[17] Among these salts, $AuCl_3$ is the most efficient catalyst based on reaction time and yield. This is consistent with previous work on the cyclization of 3-alkyn-1-ones to furans.[10i] $Pd(OAc)_2$ provided a low yield, mainly due to the facile reduction of Pd(II) to Pd(0) in the presence of the alcohol (Table 1, entry 5).[18] The addition of 2 equivs of PPh_3 to $Pd(OAc)_2$ did stabilize the Pd(II) salt, but slowed the reactions. $PtCl_2$, $Cu(NO_3)_2$ and $RuCl_3$ (Table 1, entries 6-8) are not efficient catalysts, in part due to their poor solubility in dichloromethane. $PtCl_2(PPh_3)_2$ does have good solubility, but shows poor catalytic activity (Table 1, entry 9). $RhCl_3$ is barely active in this reaction (Table 1, entry 10). Thus, $AuCl_3$ was chosen as the catalyst for the cyclization of a number of other substrates. When the reaction of **1** was performed in the absence of $AuCl_3$ or in the presence of a catalytic amount of HBF_4 instead of $AuCl_3$, no cyclization product **2** was obtained at all (Table 1, entry 11). These blank tests clearly indicate that $AuCl_3$ is required for the reaction to proceed.

To expand the scope of our Au-catalyzed process, we have examined the use of other electrophiles. Our study of the electrophile-induced cyclization has also been carried out on 2-phenylethynyl-2-cyclohexen-1-one (**1**) and methanol in the presence of $NaHCO_3$. Initially, when I_2 was employed as the electrophile, and methanol was utilized as both the solvent and

TABLE 1. Catalytic Cyclization and Coupling of 2-Phenylethynyl-2-cyclohexen-1-one (**1**) and Methanol[a]
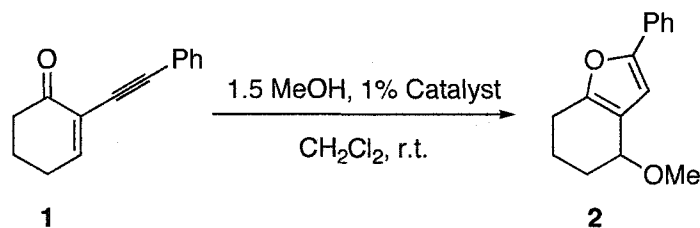
entry	catalyst	time (h)	% yield of **2**[b]	% recovery of **1**
1	AgO_2CCF_3	10	87	0
2	$Cu(O_3SCF_3)_2$	9	81	0
3	**$AuCl_3$**	**0.5**	**90**	**0**
4	$Hg(O_2CCF_3)_2$	8	86	0
5	$Pd(OAc)_2$	6	30[c]	65
6	$PtCl_2$	24	10	81
7	$Cu(NO_3)_2 \cdot 2.5H_2O$	24	27	68
8	$RuCl_3 \cdot 3H_2O$	24	0	95
9	$PtCl_2(PPh_3)_2$	24	18	71
10	$RhCl_3$	24	8	90
11	HBF_4	1	0	0

[a] Reaction conditions: **1** (0.1 mmol), catalyst (0.001 mmol) and MeOH (0.15 mmol) in CH_2Cl_2 (0.5 mL) at room temperature. [b] Determined by ^{1}H NMR spectroscopic analysis. [c] Pd black appeared.

the nucleophile, the reaction afforded the desired 3-iodofuran **3** in a 70% yield (Table 2, entry 1). To make the reaction more useful, 3 equiv of MeOH were used as the nucleophile together with acetonitrile as the solvent (Table 2, entry 2). Unfortunately, in addition to the desired 3-iodofuran **3** (50%), compound **7** (see eq. 3), which is obviously formed by nucleophilic attack of iodide on the anticipated carbocation intermediate (see the later discussion of the mechanism), was isolated in a 17% yield. This implied that I_2 could serve *as both an electrophile and nucleophile* in the reaction. Indeed, when the reaction was carried out in CH_3CN without any MeOH, compound **7** was isolated in a 41% yield (eq. 3).

Thus, to totally trap the carbocation intermediate, an excess of MeOH is required. We were

happy to see that when 8 equiv of MeOH was employed, the desired 3-iodofuran **3** was

obtained in an 80% yield, without any of compound **7** being formed (Table 2, entry 3). NIS

and PhSeCl can also be employed as electrophiles in this process, *albeit* in lower yields

(Table 2, entries 4 and 6). The electrophile p-$O_2NC_6H_4SCl$ afforded an inseparable mixture

of the desired furan product and p-$O_2NC_6H_4SOMe$ in low yield (Table 2, entry 7).

Unfortunately, NBS did not afford any furan product (Table 2, entry 5).

TABLE 2. Electrophile-Induced Cyclization and Coupling of 2-Phenylethynyl-2-cyclohexen-1-one (**1**) and Methanol[a]
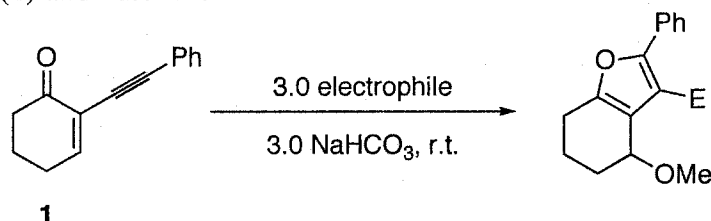
entry	electrophile	nucleophile	solvent	product		% yield[b]
1	I_2	MeOH	MeOH	E = I	**3**	70
2	I_2	3.0 MeOH	CH_3CN		**3**	50[c]
3	I_2	8.0 MeOH	CH_3CN		**3**	80
4	NIS	3.0 MeOH	CH_2Cl_2		**3**	60
5	NBS	3.0 MeOH	CH_2Cl_2	E = Br	**4**	0
6	PhSeCl	3.0 MeOH	CH_2Cl_2	E = PhSe	**5**	45
7	p-$O_2NC_6H_4SCl$	3.0 MeOH	CH_2Cl_2	E = p-$O_2NC_6H_4S$	**6**	~20[d]

[a] Reaction conditions: a solution of 0.2 mmol of **1**, 3 equiv of electrophile, the nucleophile indicated and 3 equiv of $NaHCO_3$ in 2 mL of solvent was stirred at room temperature for 1 h. [b] Isolated yield. [c] Compound **7** was also isolated in a 17% yield. [d] An inseparable mixture with p-$O_2NC_6H_4SOMe$ was obtained. The yield was determined by ^{1}H NMR spectroscopic analysis.

$$\text{1} \xrightarrow[\text{3.0 NaHCO}_3, \text{ r.t.}]{\text{3.0 I}_2} \text{7}$$

(3)

41%
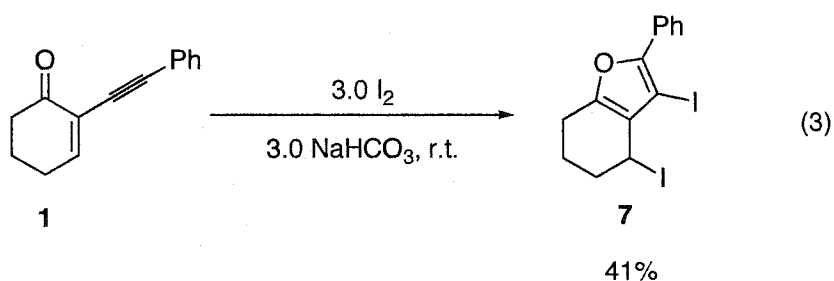
With the optimized reaction conditions in hand, the effect on the yield of the

substituents on the alkyne was examined next (Table 3, entries 1-11). Alkynes bearing either

electron-rich or electron-poor aryl groups are readily accommodated in both the $AuCl_3$-

catalyzed and I_2-induced cyclizations (entries 3-7). The presence of a vinylic group presents

no difficulties in the $AuCl_3$-catalyzed cyclization (entry 8), but afforded only a modest 46%

yield upon reaction with I_2/MeOH (entry 9). Interestingly, while the TMS-substituted alkyne

did not afford any furan product in the $AuCl_3$-catalyzed cyclization (entry 10), a good yield

of 2,3-diiodofuran **21** was obtained in the electrophile-induced cyclization (entry 11).

Obviously, iododesilylation of the TMS group takes place either prior to or soon after

cyclization. Alkynes bearing H and alkyl groups have thus far failed to provide any of the

desired products, using either $AuCl_3$ or I_2.

TABLE 3. Cyclization and Coupling of 2-(1-Alkynyl)-2-alken-1-ones and Various Nucleophiles[a]

entry	substrate	NuH	product(s)	E =		% yield
1	R = Ph (**1**)	MeOH		H	**2**	88
2				I	**3**	80
3	R = p-MeOC$_6$H$_4$ (**8**)			H	**9**	88
4				I	**10**	83
5	R = p-EtO$_2$CC$_6$H$_4$ (**11**)			H	**12**	91

TABLE 3. (continued)
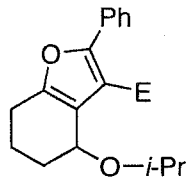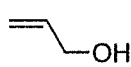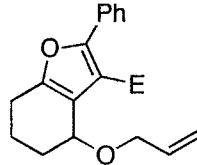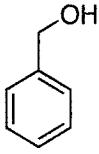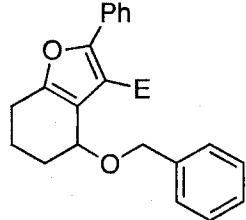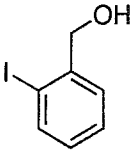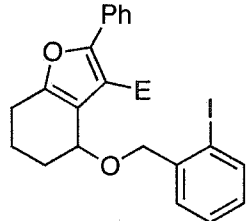
entry	substrate	NuH	product(s)	E =		% yield
6				I	**13**	83
7	R = p-O$_2$NC$_6$H$_4$ (**14**)	MeOH		H	**15**	99
8	R = 1-cyclohexenyl (**16**)			H	**17**	80
9				I	**18**	46
10	R = TMS (**19**)			H	**20**	0
11			R = I	I	**21**	66
	R = Ph (**1**)	i-PrOH				
12				I	**22**	73
13				H	**23**	71
14				I	**24**	57
15				H	**25**	75
16				I	**26**	60
17				H	**27**	87

TABLE 3. (continued)

entry	substrate	NuH	product(s)	E =		% yield
18				I	**28**	77
19				H	**29**	75
20				H	**30**	63
21		H₂O		I	**31**	77
22				H	**32**	0
23		CH₃CO₂H		I	**33**	66
24				H	**34**	0
25				I	**35**	0

TABLE 3. (continued)
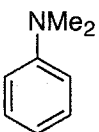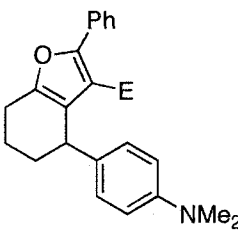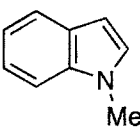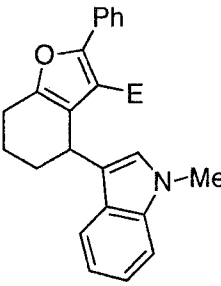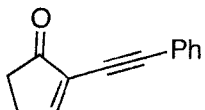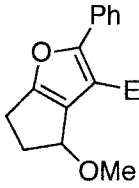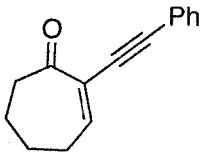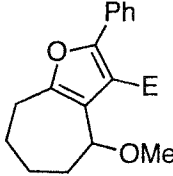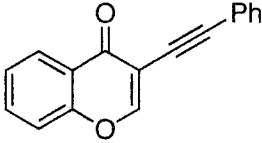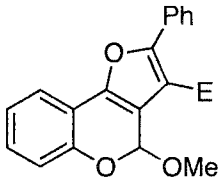
entry	substrate	NuH	product(s)	E =		% yield
26				H	**36**	81
27				I	**37**	0
28				H	**38**	52
29				I	**39**	0
30				H	**40**	90
31		**41**	MeOH	I	**42**	74[b]
32				H	**43**	0
33		**44**		I	**45**	76
34				H	**46**	82
		47				
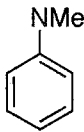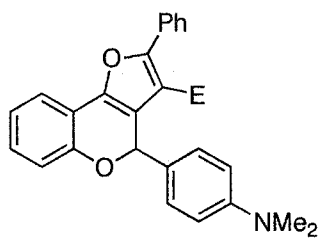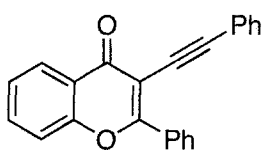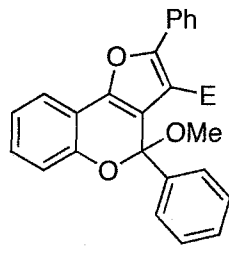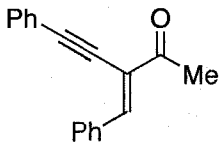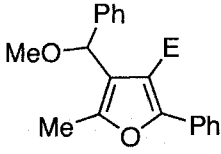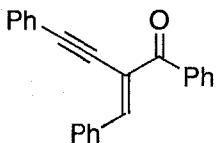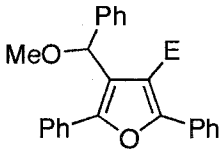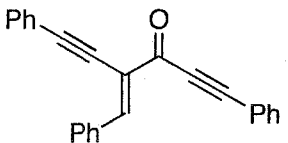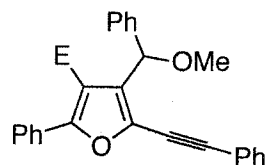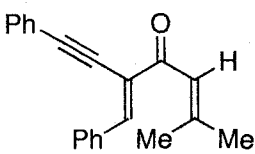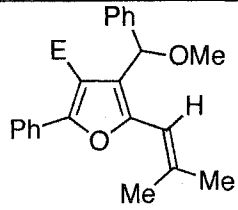
TABLE 3. (continued)

entry	substrate	NuH	product(s)	E =		% yield
35				I	**48**	87[c]
36				H	**49**	62
37				I	**50**	80[c]
38				I	**52**	61[c]
39				H	**53**	0
40				I	**55**	72[d]
41				H	**56**	60[e,f]
42				I	**58**	71[d]
43				H	**59**	89[b,e]
44				I	**61**	0
45				H	**62**	63

TABLE 3. (continued)

entry	substrate	NuH	product(s)	E =	% yield
		63 MeOH			
46				I	**64** 0
47				H	**65** 63[b,e]

[a] For E = H, the following procedure was employed unless otherwise specified: a solution of 0.2 mmol of 2-(1-alkynyl)-2-alken-1-one, 1 mol % of $AuCl_3$ and 1.5 equiv of nucleophile in 1 mL of CH_2Cl_2 was stirred at room temperature for 1 h. For E = I, the following procedure was employed unless otherwise specified: a solution of 0.2 mmol of 2-(1-alkynyl)-2-alken-1-one, 3 equiv of I_2, 8 equiv of nucleophile and 3 equiv of $NaHCO_3$ in 2 mL of CH_3CN was stirred at room temperature for 1 h. [b] The reaction took 4 h. [c]1.5 Equiv of nucleophile was used and CH_2Cl_2 was employed as the solvent. [d] The reaction took 50 h. [e] 2 Mol % of $AuCl_3$ was used. [f] The reaction took 24 h.

An unprecedented set of nucleophiles can be employed in these cyclizations (Table 3, entries 12-30). Not only simple alcohols, like methanol and 2-propanol (Table 3, entries 12 and 13), but also labile alcohols, like allyl alcohol, benzylic alcohols, 3-phenyl-2-propyn-1-ol and a protected D-pyranose are effective nucleophiles in these cyclizations (Table 3, entries 14-20). Even though H_2O and acetic acid did not afford furan products in the $AuCl_3$-catalyzed process, they work well in the I_2-induced cyclization (Table 3, entries 21-24). It should be noted that the hydration of alkynes catalyzed by gold(I) and gold(III) has been reported previously,[19] which may explain the failure of H_2O in the $AuCl_3$-catalyzed cyclization, even though we did not observe any hydration products. Since iodide itself can serve as a nucleophile, weak nucleophiles, like 1,3-cyclohexanedione, and electron-rich arenes did not afford coupling products in the I_2-induced process (Table 3, entries 25, 27 and 29). On the other hand, these weak nucleophiles work very well in the $AuCl_3$-catalyzed cyclization. Thus, the reaction of 1,3-cyclohexanedione afforded a high yield of the ether **36** in which the new bond has been formed between the β-carbon of the α,β-unsaturated ketone

and the enol oxygen of the diketone (Table 3, entry 26). Electron-rich arenes, such as *N,N*-dimethylaniline and *N*-methylindole, can also be easily introduced completely regioselectively into furan products as carbon-based nucleophiles (Table 3, entries 28 and 30). *N,N*-Dialkylanilines can also be employed as benzene surrogates, since the direct deamination of *N,N*-dialkylanilines has recently been reported.[20] Overall, the $AuCl_3$ and I_2 induced cyclizations compliment each other, and together they provide a general and efficient route to highly substituted furans.

A range of 2-(1-alkynyl)-2-alken-1-ones readily participate in these cyclizations (Table 3, entries 31-47). In addition to the successful cyclization of 2-(1-alkynyl)cyclohexenones **1** and **66** (Scheme 3), 2-phenylethynyl-2-cyclopenten-1-one (**41**) afforded iodofuran **42** (74%) after an unusually long reaction time, but this alkyne was not reactive at all in the $AuCl_3$-catalyzed cyclization (Table 3, entries 31 and 32). A possible explanation is that the reaction is slowed down because the carbonyl group is oriented away from the carbon-carbon triple bond. 2-Phenylethynyl-2-cyclohepten-1-one (**44**) (Table 3, entries 33 and 34) and chromone **47** (Table 3, entries 35-37) undergo smooth cyclizations. Interestingly, since the carbocation intermediates in the chromones are resonance-stabilized by a neighboring oxygen (Scheme 2), *N,N*-dimethylaniline now proves to be an effective carbon-based nucleophile in the I_2-induced cyclization (Table 3, entry 37). Even sterically hindered chromone **51** afforded 3-iodofuran **52** in a good yield (Table 3, entry 38). Furthermore, acyclic 2-alken-1-ones also afford highly substituted furans in both the $AuCl_3$- and I_2-induced cyclizations (Table 3, entries 40-43). Note that the acyclic substrates readily accommodate additional carbon-carbon double or triple bonds in the $AuCl_3$-catalyzed

cyclizations, but not in the I_2-induced cyclizations (Table 3, entries 44–47). Again, these two

cyclizations compliment to each other.

SCHEME 2
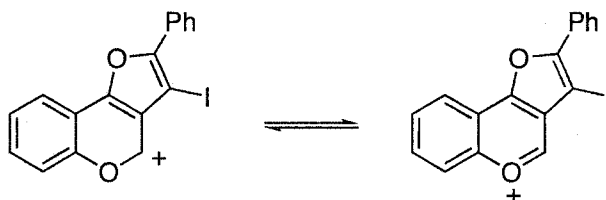
We have also examined the stereochemistry of nucleophilic attack on the enone **66**

(Scheme 3). This enone affords a mixture of *cis-* and *trans-*products in both cyclizations,

SCHEME 3
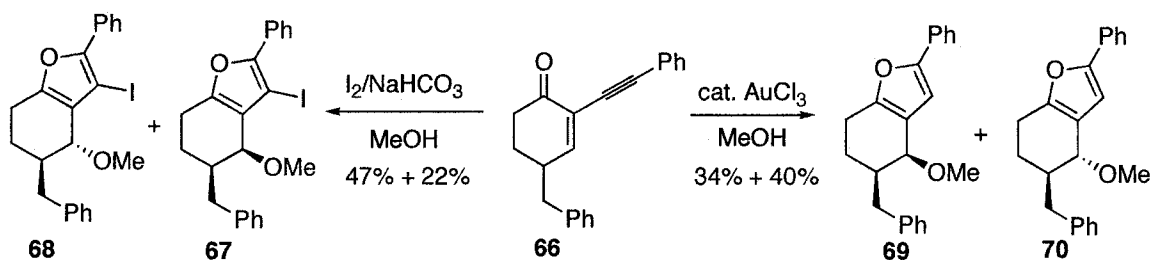
with the latter predominating. Interestingly, when pure isomer **69** or **70** was subjected to our

standard $AuCl_3$-catalyzed cyclization conditions, they were both readily isomerized to a

51:49 *cis/trans* mixture of **69** and **70** (eq. 3).[21] Thus, the ratio of stereoisomers **69** and **70**

reported in Scheme 3 appears to roughly reflect the thermodynamic stability of the products.

On the other hand, no isomerization of **67** and **68** was observed when they were subjected to

our standard I_2-induced cyclization conditions.

$$51 : 49$$
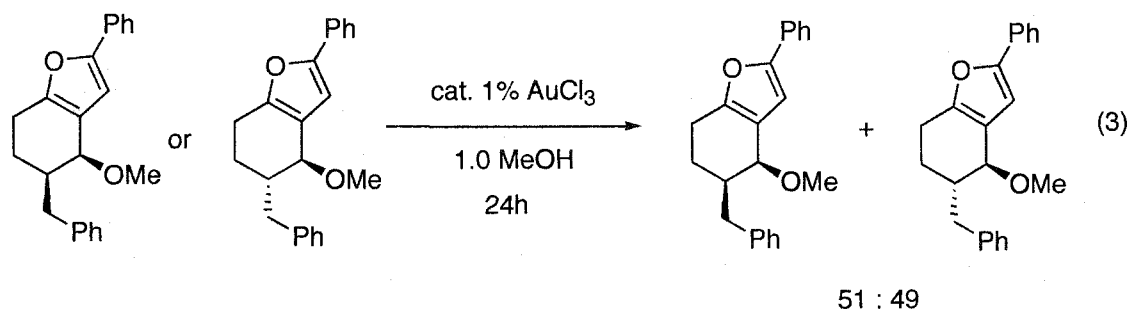
This isomerization may occur through either Lewis acid-promoted ionization of the methyl ether to the corresponding cyclohexyl carbocation or electrophilic aromatic substitution of **69** or **70** by $AuCl_3$ to provide a furyl-gold species,[10i] which reverts back to starting material **66**, followed by $AuCl_3$-catalyzed recyclization of **66** to afford an equilibrium mixture of isomers (Scheme 4).

SCHEME 4
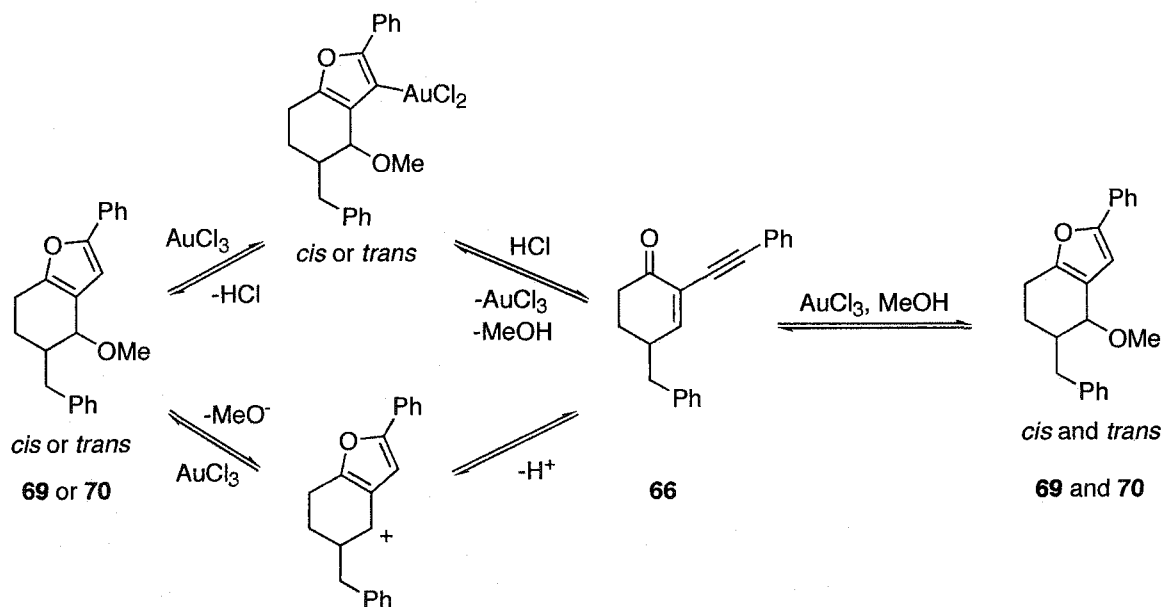
At least two mechanisms are plausible for the gold-catalyzed cyclization (Scheme 5). In one (Cycle A), gold functions as both a Lewis acid and a transition metal.[22] $AuCl_3$ first acts as a Lewis acid, forming a complex with the carbonyl oxygen. This facilitates 1,4-addition of the nucleophile to the carbon-carbon double bond to produce **72**.[23] Subsequent

coordination of the alkynyl moiety of the alkenynone **72** to AuCl$_3$ induces a cyclization of the carbonyl oxygen onto the triple bond, followed by elimination of a proton, and protonation of the resulting organogold intermediate to afford furan **2** with simultaneous regeneration of the AuCl$_3$ catalyst. An alternative mechanism in which AuCl$_3$ functions simply as a transition metal is also possible (Scheme 5, Cycle B).[10i] Coordination of the triple bond of **1** to AuCl$_3$ enhances the electrophilicity of the triple bond. Subsequent nucleophilic attack of the carbonyl oxygen on the electron-deficient triple bond generates carbocation **76**. Intermolecular nucleophilic attack on the carbocation and subsequent protonation of the carbon-gold bond afford furan **2** and regenerate the catalyst AuCl$_3$. The mechanism illustrated in Cycle B appears more likely, since 1% AuCl$_3$ fails to catalyze the 1,4-addition of methanol to 2-cyclohexenone or methyl vinyl ketone under our standard reaction conditions.

SCHEME 5

Cycle A

Cycle B

AuCl₃
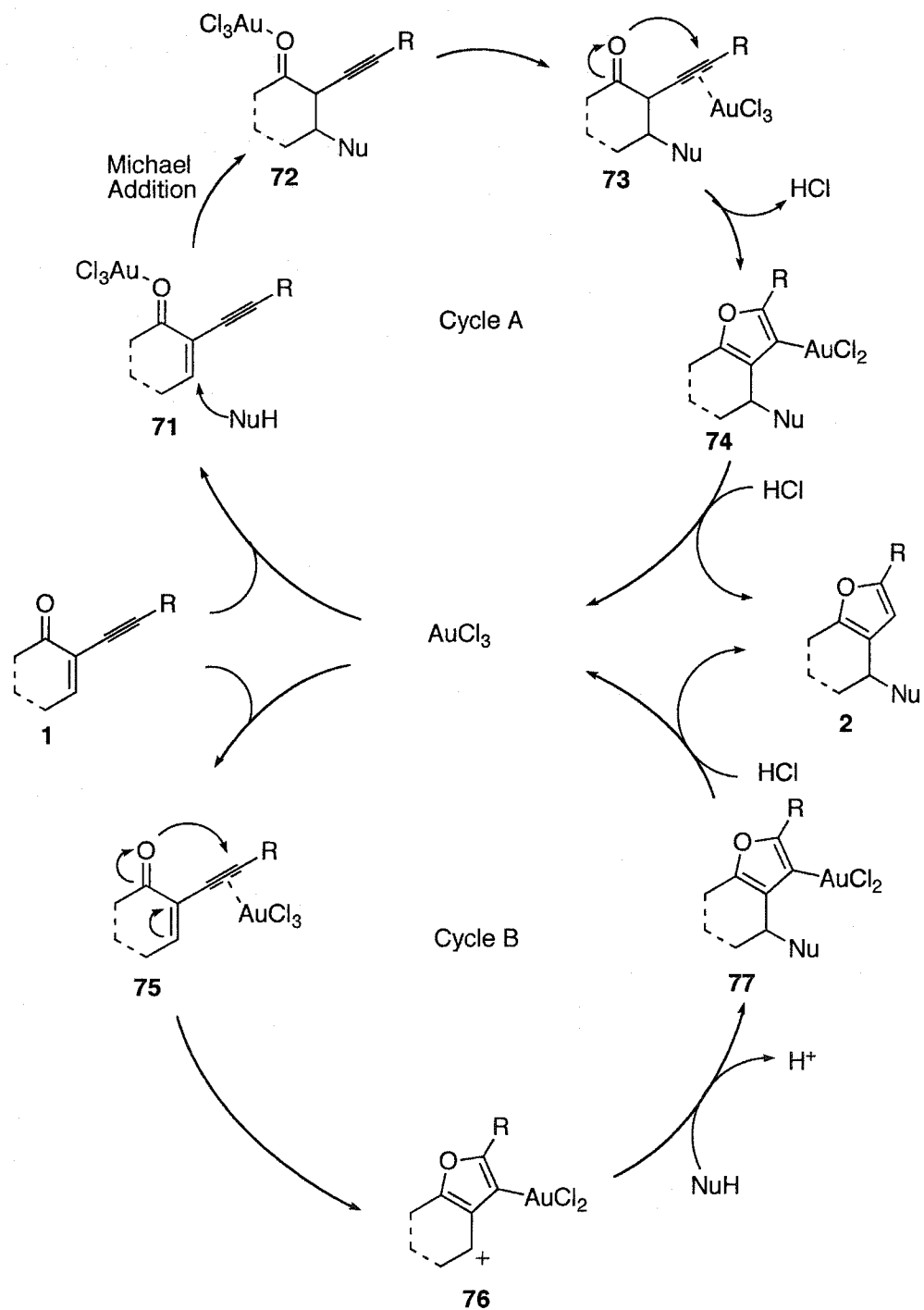
An experiment using fully deuterated methanol as the nucleophile, although it cannot

distinguish between Cycle A and Cycle B in Scheme 5, produced furan **78** with 70%

deuterium incorporation into the furan (eq. 4). The proton-containing furan product is apparently formed by inadvertent introduction of water into the deuterated methanol and/or the solvent. Using 3.0 equiv of fully deuterated methanol improved the deuterium incorporation in the furan to 85%.

$$1 \quad \xrightarrow[\substack{CH_2Cl_2, \; r.t. \\ 86\%}]{1.5 \; CD_3OD, \; 1\% \; AuCl_3} \quad 78 \tag{4}$$
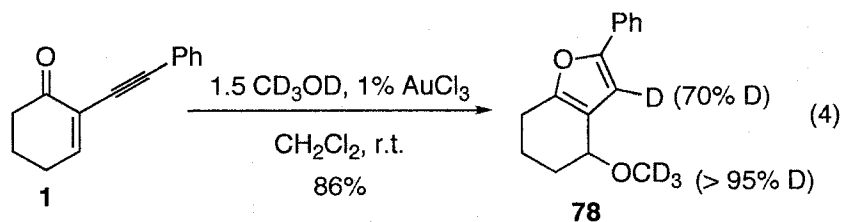
The mechanism of the I_2-induced cyclization is presumably similar to that shown in Cycle B (Scheme 4). Coordination of the electrophile to the triple bond promotes nucleophilic attack of the carbonyl oxygen on the triple bond, generating a carbocation intermediate, which then undergoes nucleophilic attack to afford the furan product.

We have also investigated further transformations of the furan products (Scheme 6). For example, palladium-catalyzed intramolecular arylation,[24] intramolecular hydroarylation,[25] intramolecular Heck reaction[26] and carbonylation[27] have afforded the anticipated products in good yields. Benzofuran 84 can also be prepared through the DDQ-promoted dehydrogenation of 2,[28] thus providing a regioselective method for the preparation of 4-substituted benzofurans.

SCHEME 6
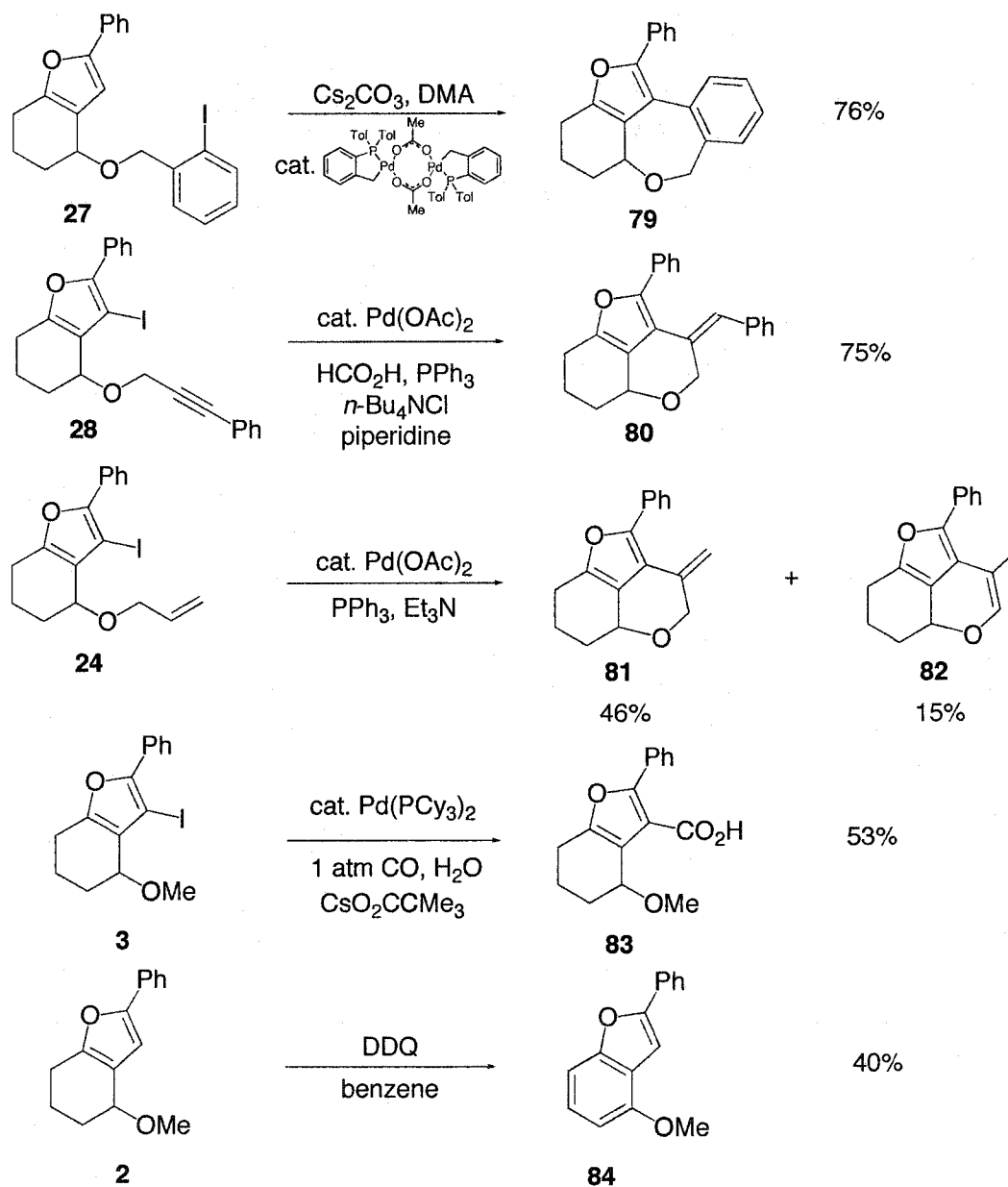
Conclusions

An efficient synthesis of highly substituted furans has been developed through the

cyclization of 2-(1-alkynyl)-2-alken-1-ones in the presence of various nucleophiles. If $AuCl_3$

is used as a catalyst, a proton is introduced into the 3 position of the furan. An iodide is

readily introduced into the 3 position by using I_2 as the electrophile. Selenium and sulfur

electrophiles can also be utilized, but the yields are low. An unprecedented range of electrophiles can be employed in these processes, which are often complementary. This methodology accommodates various functional groups and affords the anticipated furans in good to excellent yields under very mild reaction conditions. The resulting iodine-containing products can be readily elaborated to more complex products using known organopalladium chemistry.

Experimental Section

General procedures. All ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO$_4$ solution [3 g of KMnO$_4$ + 20 g of K$_2$CO$_3$ + 5 mL of NaOH (5%) + 300 mL of H$_2$O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

2-Phenylethynyl-2-cyclohexen-1-one (1). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following a procedure from the literature.[16] 2-Iodo-2-cyclohexen-1-one (444 mg, 2.0 mmol), PdCl$_2$(PPh$_3$)$_2$ (70.2 mg, 0.05 equiv), phenylacetylene (408 mg, 2.0 equiv) and CuI (38 mg, 0.1 equiv) were taken up in THF (14 mL) at 0 °C. Diisopropylamine (0.84 mL, 3.0 equiv) was added, and the resulting mixture was stirred at 0 °C for 45 min. The mixture was diluted with Et$_2$O (100 mL), and washed with 1M HCl (50 mL) and brine (20 mL). The organic layer was dried over MgSO$_4$, filtered and concentrated. The residue was purified by flash column chromatography (silica gel, 6:1 hexane/EtOAc) to afford 333 mg (85%) of the indicated compound **1** as light yellow solid:

mp 109-110 °C; ^{1}H NMR (CDCl$_3$) δ 2.03-2.11 (m, 2H), 2.47-2.56 (m, 4H), 7.29-7.38 (m,

4H), 7.47-7.52 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 22.7, 26.8, 38.4, 84.0, 92.3, 123.1, 125.6, 128.4,

128.6, 132.0, 154.4, 195.8; IR (CH$_2$Cl$_2$) 2936, 2917, 1676, 1488, 1355 cm^{-1}; HRMS m/z

196.0893 (calcd for C$_{14}$H$_{12}$O, 196.0888).

2-(4-Methoxyphenyl)ethynyl-2-cyclohexen-1-one (8). This 2-(1-alkynyl)-2-alken-1-

one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following the same procedure as that

used for compound **1**. 2-Iodo-2-cyclohexen-1-one (444 mg, 2.0 mmol), PdCl$_2$(PPh$_3$)$_2$ (70.2

mg, 0.05 equiv), (4-methoxyphenyl)ethyne (529 mg, 2.0 equiv), CuI (38 mg, 0.1 equiv) and

diisopropylamine (0.84 mL, 3.0 equiv) afforded, after purification by flash column

chromatography (silica gel, 3:1 hexane/EtOAc), 301 mg (67%) of the indicated compound **8**

as light yellow solid: mp 70-71 °C; ^{1}H NMR (CDCl$_3$) δ 2.03-2.10 (m, 2H), 2.46-2.55 (m,

4H), 3.80 (s, 3H), 6.83 (dt, J = 8.4, 2.1 Hz, 2H), 7.32 (t, J = 4.5 Hz, 1H), 7.43 (dt, J = 9.0, 2.1

Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 22.7, 26.7, 38.4, 55.5, 82.7, 92.4, 114.1, 115.2, 125.7, 133.5,

153.8, 159.9, 196.0; IR (CH$_2$Cl$_2$) 2952, 1688, 1510, 1249 cm^{-1}; HRMS m/z 226.0996 (calcd

for C$_{15}$H$_{14}$O$_2$, 226.0994).

Ethyl 4-[(6-oxocyclohexenyl)ethynyl]benzoate (11). This 2-(1-alkynyl)-2-alken-1-

one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following the same procedure as that

used for compound **1**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), ethyl 4-

ethynylbenzoate (348 mg, 2.0 equiv), PdCl$_2$(PPh$_3$)$_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1

equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash

column chromatography (silica gel, 3:1 hexane/EtOAc), 160 mg (60%) of the indicated

compound **11** as a yellow solid: mp 116-117 °C; ^{1}H NMR (CDCl$_3$) δ 1.38 (t, J = 6.9 Hz, 3H),

2.05-2.10 (m, 2H), 2.48-2.57 (m, 4H), 4.36 (q, J = 6.9 Hz, 2H), 7.39 (t, J = 4.5 Hz, 1H), 7.54

(dt, J = 8.4, 1.8 Hz, 2H), 7.98 (dt, J = 8.7, 1.8 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 14.5, 22.6, 26.8, 38.3, 61.4, 86.8, 91.5, 125.3, 127.7, 129.6, 130.2, 131.9, 155.3, 166.3, 195.6; IR (CH$_2$Cl$_2$) 2981, 1714, 1682 cm^{-1}; HRMS m/z 268.1103 (calcd for C$_{17}$H$_{16}$O$_3$, 268.1099).

2-(4-Nitrophenyl)ethynyl-2-cyclohexen-1-one (14). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following the same procedure as that used for compound **1**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), (4-nitrophenyl)ethyne (294 mg, 2.0 equiv), PdCl$_2$(PPh$_3$)$_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 2:1 hexane/EtOAc), 168 mg (70%) of the indicated compound **14** as a yellow solid: mp 113-115 °C; ^{1}H NMR (CDCl$_3$) δ 2.06-2.11 (m, 2H), 2.51-2.58 (m, 4H), 4.36 (q, J = 6.9 Hz, 2H), 7.44 (t, J = 4.5 Hz, 1H), 7.62 (d, J = 9.0 Hz, 2H), 8.18 (d, J = 9.0 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 22.5, 26.9, 38.3, 89.3, 90.3, 123.8, 125.0, 130.1, 132.7, 147.3, 156.2, 195.4; IR (CH$_2$Cl$_2$) 3055, 2952, 1682, 1592 cm^{-1}; HRMS m/z 241.0743 (calcd for C$_{14}$H$_{11}$NO$_3$, 241.0739).

2-(Cyclohexenylethynyl)-cyclohexen-1-one (16). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following the same procedure as compound **1**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), 1-ethynylcyclohexene (212 mg, 2.0 equiv), PdCl$_2$(PPh$_3$)$_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 5:1 hexane/EtOAc), 144 mg (72%) of the indicated compound **16** as a yellow solid: mp 46-48 °C; ^{1}H NMR (CDCl$_3$) δ 1.56-1.65 (m, 4H), 1.99-2.18 (m, 6H), 2.41-2.51 (m, 4H), 6.16-6.19 (m, 1H), 7.21 (t, J = 4.5 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 21.7,

22.5, 22.7, 25.9, 26.7, 29.3, 38.4, 81.3, 94.3, 120.6, 125.7, 136.1, 153.4, 196.0; IR (CH_2Cl_2)

3022, 2930, 1689, 1347 cm^{-1}; HRMS m/z 200.1203 (calcd for $C_{14}H_{16}O$, 200.1201).

2-(Trimethylsilyl)ethynyl-2-cyclohexen-1-one (19). This 2-(1-alkynyl)-2-alken-1-

one was prepared from 2-iodo-2-cyclohexen-1-one[29] by following the same procedure as that

used for compound **1**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol),

(trimethylsilyl)ethyne (196 mg, 2.0 equiv), $PdCl_2(PPh_3)_2$ (35.6 mg, 0.05 equiv), CuI (20 mg,

0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash

column chromatography (silica gel, 5:1 hexane/EtOAc), 159 mg (83%) of the indicated

compound **19** as a white solid: mp 100-101 °C; ^{1}H NMR ($CDCl_3$) δ 0.20 (t, J = 3.5 Hz, 9H),

1.98-2.03 (m, 2H), 2.40-2.49 (m, 4H), 7.32 (t, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.0, 22.4,

26.5, 38.1, 97.6, 99.3, 125.4, 155.5, 195.5; IR (CH_2Cl_2) 3042, 2960, 1682, 1349 cm^{-1}; HRMS

m/z 192.0974 (calcd for $C_{11}H_{16}OSi$, 192.0970).

2-Phenylethynyl-2-cyclopenten-1-one (41). This 2-(1-alkynyl)-2-alken-1-one was

prepared from 2-iodo-2-cyclopenten-1-one[29] by following the same procedure as that used for

compound **1**. 2-Iodo-2-cyclopenten-1-one (208 mg, 1.0 mmol), phenylacetylene (204 mg,

2.0 equiv), $PdCl_2(PPh_3)_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine

(0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel,

3:1 hexane/EtOAc), 182 mg (100%) of the indicated compound **41** as a brown solid: mp 65-

66 °C; ^{1}H NMR ($CDCl_3$) δ 2.49-2.53 (m, 2H), 2.74-2.78 (m, 2H), 7.31-7.33 (m, 3H), 7.49-

7.53 (m, 2H), 7.84 (t, J = 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.7, 34.3, 80.1, 96.0, 122.7,

128.5, 129.0, 130.3, 132.1, 165.4, 205.9; IR (CH_2Cl_2) 3061, 2923, 1716, 1488 cm^{-1}; HRMS

m/z 182.0734 (calcd for $C_{13}H_{10}O$, 182.0732).

2-Phenylethynyl-2-cyclohepten-1-one (44). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohepten-1-one[30] by following the same procedure as that used for compound **1**. 2-Iodo-2-cyclohepten-1-one (236 mg, 1.0 mmol), phenylacetylene (204 mg, 2.0 equiv), $PdCl_2(PPh_3)_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 5:1 hexane/EtOAc), 90 mg (43%) of the indicated compound **44** as a yellow oil: ^1H NMR $(CDCl_3)$ δ 1.77-1.86 (m, 4H), 2.47-2.54 (m, 2H), 2.68 (t, J = 6.5 Hz, 2H), 7.14 (t, J = 6.3 Hz, 1H), 7.25-7.31 (m, 3H), 7.44-7.48 (m, 2H); ^{13}C NMR $(CDCl_3)$ δ 21.7, 25.2, 28.7, 42.6, 86.6, 90.4, 123.3, 128.4, 128.5, 128.9, 131.9, 151.2, 201.2; IR (CH_2Cl_2) 3055, 2940, 1679, 1421 cm^{-1}; HRMS m/z 210.1047 (calcd for $C_{15}H_{14}O$, 210.1045).

3-Phenylethynyl-4*H***-benzopyran-4-one (47).** This 2-(1-alkynyl)-2-alken-1-one was prepared from 3-iodo-4*H*-benzopyran-4-one[31] by the following procedure. To a solution of 3-iodo-4*H*-benzopyran-4-one (544 mg, 2.0 mmol) and phenylacelene (245 mg, 1.2 equiv) in Et_3N (20 mL) and DMF (1 mL), were added $PdCl_2(PPh_3)_2$ (14 mg, 1 mol %) and CuI (2.0 mg, 0.5 mol %). The resulting mixture was stirred under an N_2 atm at room temperature overnight. The mixture was diluted with $CHCl_3$ (100 mL) and washed with H_2O (30 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 5:1 hexane/EtOAc) to afford 448 mg (91%) of the indicated compound **47** as a yellow solid: mp 179-181 °C; ^1H NMR $(CDCl_3)$ δ 7.32-7.36 (m, 3H), 7.40-7.49 (m, 2H), 7.55-7.59 (m, 2H), 7.66-7.18 (m, 1H), 8.23 (s, 1H), 8.28 (dd, J = 7.8, 1.6 Hz, 1H); ^{13}C NMR $(CDCl_3)$ δ 79.7, 95.3, 111.6, 118.5, 122.9, 123.8, 126.0, 126.5, 128.5, 128.9, 132.1, 134.2, 156.2, 158.1, 175.6; IR (CH_2Cl_2) 3075, 2916, 1649, 1617, 1464, 1303 cm^{-1}; HRMS m/z 246.0685 (calcd for $C_{17}H_{10}O_2$,

246.0681).

2-Phenyl-3-phenylethynyl-4H-benzopyran-4-one (51). This 2-(1-alkynyl)-2-alken-1-one was prepared from 3-iodo-2-phenyl-4H-benzopyran-4-one[32] by following the same procedure as that used for compound **47**. 3-Iodo-2-phenyl-4H-benzopyran-4-one (696 mg, 2.0 mmol), phenylacetylene (245 mg, 1.2 equiv), Et$_3$N (20 mL), DMF (1 mL) ,PdCl$_2$(PPh$_3$)$_2$ (14 mg, 1 mol %) and CuI (2.0 mg, 0.5 mol %) afforded, after purification by flash column chromatography (silica gel, 4:1 hexane/EtOAc), 516 mg (80%) of the indicated compound **51** as a light yellow solid: mp 155-157 °C; ^{1}H NMR (CDCl$_3$) δ 7.31-7.35 (m, 3H), 7.42-7.59 (m, 7H), 7.68-7.74 (m, 1H), 8.23-8.32 (m, 3H); IR (CH$_2$Cl$_2$) 3071, 1644, 1614, 1463 cm^{-1}; HRMS m/z 322.0997 (calcd for C$_{23}$H$_{14}$O$_2$, 322.0994).

(3E)-3-Benzylidene-5-phenylpent-4-yn-2-one (54). This 2-(1-alkynyl)-2-alken-1-one was prepared from (E)-2-benzylidene-4-phenylbut-3-ynal[33] by following a procedure from the literature.[34] To a solution of (E)-2-benzylidene-4-phenylbut-3-ynal (531 mg, 2.3 mmol) in dry THF (5 mL) cooled to −78 °C, was added MeLi (1.6 M in diethyl ether, 1.5 mL, 2.4 mmol). The reaction was stirred at the same temperature for 30 min and quenched with satd aq NH$_4$Cl (3 mL). The resultant mixture was extracted with Et$_2$O (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was dissolved in dry THF (30 mL). To this solution was added MnO$_2$ (4.0 g, 20 equiv), followed by stirring at room temperature for 12 h. The reaction mixture was filtered through a short pad of Celite with rinsing by EtOAc. The combined organic layer was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 7:1 hexane/EtOAc) to afford 239 mg (42%) of the indicated compound **54** as a light yellow solid: mp 63-64 °C; ^{1}H NMR (CDCl$_3$)

δ 2.63 (s, 3H), 7.39-7.46 (m, 6H), 7.54-7.58 (m, 2H), 7.84 (s, 1H), 8.09-8.12 (m, 2H); ^{13}C

NMR (CDCl$_3$) δ 28.4, 87.3, 99.4, 120.2, 123.1, 128.9, 129.2, 131.0, 131.6, 134.8, 143.2,

196.4; IR (CH$_2$Cl$_2$) 3060, 1694, 1583, 1563, 1489, 1445, 1355, 1248 cm^{-1}; HRMS m/z

246.1049 (calcd for C$_{18}$H$_{14}$O, 246.1045).

(*E*)-2-Benzylidene-1,4-diphenylbut-3-yn-1-one (57). This 2-(1-alkynyl)-2-alken-1-one was

prepared from (*E*)-2-benzylidene-4-phenylbut-3-ynal[33] by following the same procedure as

compound **54**. (*E*)-2-benzylidene-4-phenylbut-3-ynal (531 mg, 2.3 mmol), PhMgBr (1 M in

THF, 3.5 mL, 3.5 mmol) and MnO$_2$ (4.0 g, 20 equiv) afforded, after purification by flash

column chromatography (silica gel, 7:1 hexane/EtOAc), 470 mg (66%) of the indicated

compound **57** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 7.33-7.38 (m, 3H), 7.41-7.53 (m, 7H),

7.57-7.63 (m, 1H), 7.67 (s, 1H), 8.02-8.06 (m, 2H), 8.13-8.17 (m, 2H); ^{13}C NMR (CDCl$_3$) δ

87.5, 101.2, 121.2, 123.1, 128.4, 128.7, 128.9, 129.1, 130.0, 130.7, 130.9, 131.6, 132.8,

135.1, 137.4, 145.4, 193.6; IR (CH$_2$Cl$_2$) 3059, 1663, 1597, 1564, 1490, 1446, 1318, 1264 cm$^-$

^{1}; HRMS m/z 308.1209 (calcd for C$_{23}$H$_{16}$O, 308.1201).

(4*E*)-4-Benzylidene-1,6-diphenylhexa-1,5-diyn-3-one (60). This 2-(1-alkynyl)-2-

alken-1-one was prepared from (*E*)-2-benzylidene-4-phenylbut-3-ynal[33] by following the

same procedure as compound **54**. (*E*)-2-Benzylidene-4-phenylbut-3-ynal (464 mg, 2.0

mmol), a THF solution (9 mL) of PhC≡CLi prepared from phenylacetylene (0.27 mL, 2.4

mmol) and n-BuLi (1.6 M in hexanes, 1.4 mL, 2.2 mmol), and MnO$_2$ (3.46 g, 20 equiv)

afforded, after purification by flash column chromatography (silica gel, 6:1 hexane/EtOAc),

378 mg (58%) of the indicated compound **60** as a yellow solid: mp 126-127 °C; ^{1}H NMR

(CDCl$_3$) δ 7.38-7.50 (m, 9H), 7.58-7.66 (m, 4H), 8.14-8.20 (m, 3H); ^{13}C NMR (CDCl$_3$) δ

85.2, 87.2, 94.4, 100.7, 120.4, 122.1, 123.1, 128.7, 128.9, 129.0, 129.2, 131.0, 131.3, 131.6,

132.0, 133.3, 134.5, 147.0, 176.6; IR (CH_2Cl_2) 3078, 3061, 2201, 1694, 1641, 1595, 1489,

1444, 1277, 1163 cm^{-1}; HRMS m/z 332.1207 (calcd for $C_{25}H_{16}O$, 332.1201).

(3E)-3-Benzylidene-6-methyl-1-phenylhep-5-en-1-yn-4-one (63). This 2-(1-

alkynyl)-2-alken-1-one was prepared from (E)-2-benzylidene-4-phenylbut-3-ynal[33] by

following the same procedure as compound **54**. (E)-2-Benzylidene-4-phenylbut-3-ynal (450

mg, 1.9 mmol), Me_2C=CHMgBr (0.5 M in THF, 4.5 mL, 2.3 mmol) and MnO_2 (3.5 g, 20

equiv) afforded, after purification by flash column chromatography (silica gel, 6:1

hexane/EtOAc), 253 mg (47%) of the indicated compound **63** as a light yellow solid: mp 45-

47 °C; ^{1}H NMR $(CDCl_3)$ δ 2.04 (d, J = 0.9 Hz, 3H), 2.27 (d, J = 0.9 Hz, 3H), 7.03-7.05 (m,

1H), 7.38-7.46 (m, 6H), 7.54-7.58 (m, 2H), 7.86 (s, 1H), 8.08-8.11 (m, 2H); ^{13}C NMR

$(CDCl_3)$ δ 21.6, 28.5, 87.4, 99.6, 121.7, 122.0, 123.3, 128.7, 128.8, 129.0, 130.6, 130.8,

131.6, 135.3, 143.5, 158.7, 187.8; IR (CH_2Cl_2) 3059, 2911, 1669, 1616, 1490, 1445, 1132

cm^{-1}; HRMS m/z 286.1362 (calcd for $C_{21}H_{18}O$, 286.1358).

4-Benzyl-2-(phenylethynyl)cyclohex-2-enone (66). Compound **66** was prepared from

3-ethoxycyclohex-2-enone in four steps. 3-Ethoxycyclohex-2-enone was converted to 6-

benzyl-3-ethoxycyclohex-2-enone by a procedure reported by Piers et al.[35] To a cold (-78

°C), stirred solution of LDA (3 mmol) in dry THF (40 mL) was added dropwise by a syringe

a solution of 3-ethoxycyclohex-2-enone (420 mg, 3.0 mmol) in dry THF (15 mL). The

mixture was warmed to room temperature and stirred for 1 h, then was cooled back down to -

78 °C. To the resulting solution was added dropwise by a syringe the solution of benzyl

bromide (530 mg, 3.0 mmol) in dry THF (15 mL). The mixture was stirred for 1 h at -78 °C,

then warmed slowly to room temperature and stirred for an additional hour. Aqueous NH_3-

NH_4Cl (pH ~8, 30 mL) was added and stirring was continued for 15 min. The phases were

separated and the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined

organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated. The

residue was purified by column chromatography (silica gel, 3:1 hexane/EtOAc) to afford

301.5 mg (55%) of 6-benzyl-3-ethoxycyclohex-2-enone as a clear oil: ^1H NMR ($CDCl_3$) δ

1.35 (t, J = 6.9 Hz, 3H), 1.56-1.67 (m, 1H), 1.85-2.04 (m, 1H), 2.33-2.40 (m, 2H), 2.42-2.54

(m, 2H), 3.38 (dd, J = 13.0, 2.9 Hz, 1H), 3.85-3.93 (m, 2H), 5.37 (s, 1H), 7.16-7.22 (m, 3H),

7.26-7.31 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.4, 25.8, 28.5, 35.9, 47.3, 64.5, 102.5, 126.3,

128.6, 129.4, 140.4, 177.3, 200.6. To a cold (0 °C), stirred solution of 6-benzyl-3-

ethoxycyclohex-2-enone (302 mg, 1.3 mmol) in dry Et_2O (10 mL) was added dropwise by a

syringe a solution of DIBAL-H (1.0 M in hexanes, 2.0 mL, 1.5 equiv). The mixture was

stirred for 30 min and then treated with aq NH_3-NH_4Cl (pH ~8, 0.5 mL). The mixture was

warmed to room temperature and stirred for 1 h, during which it became a thick white slurry.

The mixture was treated with anhydrous $MgSO_4$ (195 mg), stirred for 1 h, and then filtered

through a pad of Celite. The filtrate was concentrated and the residue was dissolved in dry

Et_2O (15 mL). The solution was treated with H_2O (117 mg, 5.0 equiv) and TsOH•H_2O (0.1

equiv), and the mixture was stirred for 1 h. Aq NH_3-NH_4Cl (pH ~8, 10 mL) was added and

the phases were separated. The aqueous phase was extracted with Et_2O (3 x 10 mL). The

combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was

purified by silica gel column chromatography (silica gel, 3:1 hexane/EtOAc) to afford 192

mg (79%) of 4-benzylcyclohex-2-enone as a clear oil: ^1H NMR ($CDCl_3$) δ 1.60-1.76 (m,

1H), 2.00-2.07 (m, 1H), 2.25-2.37 (m, 1H), 2.43-2.52 (m, 1H), 2.66-2.79 (m, 3H), 5.97 (dd, J

= 10.0, 1.2 Hz, 1H), 6.83 (dt, J = 10.0, 1.6 Hz, 1H), 7.17-7.38 (m, 5H). 4-Benzylcyclohex-2-

enone was converted to 4-benzyl-2-iodocyclohex-2-enone by following a procedure from the

literature.[29] To an ice-cold solution of 4-benzylcyclohex-2-enone (191 mg, 1.0 mmol) in

CCl_4 (3 mL) and pyridine (3 mL) was added a solution of I_2 (0.58 g, 2.28 mmol) dissolved in

CCl_4 and pyridine (1:1, 6 mL). After stirring overnight at room temperature, the mixture was

diluted with Et_2O (20 mL) and H_2O (10 mL). The organic layer was separated, and the

aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic layers were

washed with satd aq $Na_2S_2O_3$ (25 ml) and H_2O (20 mL), dried over $MgSO_4$ and concentrated.

The residue was purified by column chromatography (silica gel, 5:1 hexane/EtOAc) to afford

238 mg (76%) of 4-benzyl-2-iodocyclohex-2-enone as a yellow oil: ^1H NMR ($CDCl_3$) δ

1.71-1.80 (m, 1H), 2.03-2.14 (m, 1H), 2.44-2.55 (m, 1H), 2.70-2.85 (m, 4H), 7.17-7.36 (m,

4H), 7.61-7.62 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.9, 36.0, 40.7, 42.8, 104.4, 127.0, 129.0,

129.2, 138.5, 162.7, 192.4. 4-Benzyl-2-iodocyclohex-2-enone was converted to 4-benzyl-2-

(phenylethynyl)cyclohex-2-enone by following the same procedure as compound 1. 4-

Benzyl-2-iodo-2-cyclohepten-1-one (237 mg, 0.76 mmol), phenylacetylene (155 mg, 2.0

equiv), $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.1 equiv) and diisopropylamine (0.32 mL, 3 equiv)

afforded, after purification by column chromatography (silica gel, 4:1 hexane/EtOAc), 193

mg (89%) of the indicated compound **66** as a light yellow oil: ^1H NMR ($CDCl_3$) δ 1.69-1.83

(m, 1H), 2.05-2.12 (m, 1H), 2.36-2.49 (m, 1H), 2.59-2.68 (m, 1H), 2.75-2.86 (m, 3H), 7.21-

7.38 (m, 10H), 7.47-7.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.6, 37.2, 39.1, 41.1, 84.0, 92.7,

123.0, 125.0, 126.9, 128.5, 128.7, 128.9, 129.3, 132.1, 138.8, 157.2, 195.8; IR (CH_2Cl_2)

3059, 3026, 2921, 1690, 1490, 1453, 1094 cm^{-1}; HRMS m/z 286.1362 (calcd for $C_{21}H_{18}O$,

286.1358).

Representative procedure for the $AuCl_3$-catalyzed cyclizations. A solution of $AuCl_3$

(30.3 mg) in MeCN (970 mg) was prepared. To the appropriate 2-(1-alkynyl)-2-alken-1-one

(0.2 mmol) and nucleophile (1.5 equiv) in CH_2Cl_2 (1 mL), was added the above $AuCl_3$

solution (20 mg, 1 mol %). The mixture was stirred at room temperature for 1 h unless

otherwise specified. The solvent was removed under reduced pressure and the residue was

purified by flash chromatography on silica gel.

4-Methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2). Compound **1** (39.2 mg, 0.2

mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction

conditions for 0.5 h. The reaction mixture was chromatographed (silica gel, 9:1

hexane/EtOAc) to afford 40 mg (88%) of the indicated compound **2** as a colorless oil: ^1H

NMR (CDCl$_3$) δ 1.78-1.93 (m, 2H), 1.94-2.14 (m, 2H), 2.62-2.77 (m, 2H), 3.46 (s, 3H), 4.31

(t, J = 3.9 Hz, 1H), 6.67 (s, 1H), 7.20-7.25 (m, 1H), 7.33-7.39 (m, 2H), 7.62-7.65 (m, 2H);

^{13}C NMR (CDCl$_3$) δ 19.1, 23.5, 28.6, 56.4, 72.6, 105.6, 120.2, 123.7, 127.1, 128.8, 131.4,

152.5, 153.1; IR (CH$_2$Cl$_2$) 2940, 2817, 1604, 1486, 1449, 1260, 1095 cm^{-1}; HRMS m/z

228.1154 (calcd for C$_{15}$H$_{16}$O$_2$, 228.1150).

4-Methoxy-2-(4-methoxyphenyl)-4,5,6,7-tetrahydrobenzofuran (9). Compound **8**

(45.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our

standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel,

7:1 hexane/EtOAc) to afford 45.5 mg (88%) of the indicated compound **9** as a colorless oil:

^1H NMR (CDCl$_3$) δ 1.74-1.88 (m, 2H), 1.91-2.11 (m, 2H), 2.53-2.64 (m, 1H), 2.67-2.77 (m,

1H), 3.45 (s, 3H), 3.82 (s, 3H), 4.29 (t, J = 3.9 Hz, 1H), 6.51 (s, 1H), 6.90 (dt, J = 9.0, 3.0

Hz, 2H), 7.56 (dt, J = 9.0, 3.0 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 19.2, 23.5, 28.7, 55.5, 56.4, 72.7,

104.0, 114.3, 120.0, 124.5, 125.1, 152.3, 152.5, 159.0; IR (CH$_2$Cl$_2$) 2943, 1613, 1503, 1463,

1411 cm^{-1}; HRMS m/z 258.1260 (calcd for C$_{16}$H$_{18}$O$_3$, 258.1256).

Ethyl 4-(4-methoxy-4,5,6,7-tetrahydro-1-benzofuran-2-yl)benzoate (12). Compound

11 (53.6 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our

standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel,

3:1 hexane/EtOAc) to afford 54.7 mg (91%) of the indicated compound **12** as a light yellow

oil: ^{1}H NMR (CDCl$_3$) δ 1.39 (t, J = 7.4 Hz, 3H), 1.75-1.88 (m, 2H), 1.91-2.11 (m, 2H), 2.54-

2.66 (m, 1H), 2.68-2.78 (m, 1H), 3.44 (s, 3H), 4.29 (t, J = 3.9 Hz, 1H), 4.37 (q, J = 6.9 Hz,

2H), 6.78 (s, 1H), 7.66 (dd, J = 6.9, 1.8 Hz, 2H), 8.03 (dd, J = 6.9, 1.8 Hz, 2H); ^{13}C NMR

(CDCl$_3$) δ 14.6, 19.0, 23.5, 28.5, 56.4, 61.1, 72.5, 107.8, 120.7, 123.1, 128.6, 130.3, 135.2,

151.5, 154.4, 166.6; IR (CH$_2$Cl$_2$) 2942, 1713, 1607, 1574, 1423 cm^{-1}; HRMS m/z 300.1365

(calcd for C$_{18}$H$_{20}$O$_4$, 300.1362).

4-Methoxy-2-(4-nitrophenyl)-4,5,6,7-tetrahydrobenzofuran (15). Compound **14** (48.3

mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 3:1

hexane/EtOAc) to afford 54.3 mg (99%) of the indicated compound **15** as a yellow oil: ^{1}H

NMR (CDCl$_3$) δ 1.76-1.89 (m, 2H), 1.91-2.11 (m, 2H), 2.54-2.67 (m, 1H), 2.69-2.79 (m,

1H), 3.44 (s, 3H), 4.30 (t, J = 3.6 Hz, 1H), 6.87 (s, 1H), 7.70 (dt, J = 9.0, 2.4 Hz, 2H), 8.19

(dt, J = 9.3, 2.1 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 18.9, 23.5, 28.3, 56.5, 72.4, 109.7, 121.4,

123.6, 124.5, 136.9, 146.2, 150.3, 155.7; IR (CH$_2$Cl$_2$) 2943, 1595, 1514, 1453 cm^{-1}; HRMS

m/z 273.1004 (calcd for C$_{15}$H$_{15}$NO$_4$, 273.1001).

2-Cyclohexenyl-4-methoxy-4,5,6,7-tetrahydrobenzofuran (17). Compound **16** (40 mg,

0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard

reaction condition for 0.5 h. The reaction mixture was chromatographed (silica gel, 9:1

hexane/EtOAc) to afford 37.1 mg (80%) of the indicated compound **17** as a colorless oil: ^{1}H

NMR (CDCl₃) δ 1.59-1.81 (m, 6H), 1.87-2.02 (m, 2H), 2.16-2.25 (m, 4H), 2.47-2.57 (m,

1H), 2.60-2.69 (m, 1H), 3.40 (s, 3H), 4.23 (t, J = 3.9 Hz, 1H),; ¹³C NMR (CDCl₃) δ 19.1,

22.5, 22.6, 23.4, 25.1, 25.4, 28.7, 56.3, 72.7, 104.1, 119.2, 121.5, 127.5, 151.9, 154.1; IR

(CH₂Cl₂) 2934, 2860, 1449, 1095 cm⁻¹.

4-Isopropoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (23). Compound **1** (39.2 mg,

0.2 mmol) was allowed to react with isopropanol (18 mg, 1.5 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1

hexane/EtOAc) to afford 36.1 mg (71%) of the indicated compound **23** as a colorless oil: ¹H

NMR (CDCl₃) δ 1.22-1.26 (m, 6H), 1.77-1.88 (m, 3H), 2.00-2.13 (m, 1H), 2.53-2.64 (m,

1H), 2.68-2.75 (m, 1H), 3.77-3.89 (m, 1H), 4.46 (t, J = 3.8 Hz, 1H), 6.60 (s, 1H), 7.18-7.24

(m, 1H), 7.32-7.38 (m, 2H), 7.61-7.65 (m, 2H); ¹³C NMR (CDCl₃) δ 19.3, 22.9, 23.4, 23.5,

30.0, 68.7, 69.6, 105.3, 121.2, 123.7, 127.0, 128.8, 131.5, 152.5, 152.9; IR (CH₂Cl₂) 2968,

1604, 1487, 1449, 1122, 1066 cm⁻¹; HRMS m/z 256.1467 (calcd for C₁₇H₂₀O₂, 256.1463).

4-Allyloxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (25). Compound **1** (39.2 mg, 0.2

mmol) was allowed to react with allyl alcohol (17.4 mg, 1.5 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 70:1

hexane/EtOAc) to afford 37.8 mg (75%) of the indicated compound **25** as a colorless oil: ¹H

NMR (CDCl₃) δ 1.78-1.88 (m, 2H), 1.92-2.17 (m, 2H), 2.55-2.66 (m, 1H), 2.70-2.79 (m,

1H), 4.12-4.15 (m, 2H), 4.46 (t, J = 3.8 Hz, 1H), 5.22 (dd, J = 10.4, 1.4 Hz, 1H), 5.31-5.39

(m, 1H), 5.93-6.07 (m, 1H), 6.65 (s, 1H), 7.20-7.26 (m, 1H), 7.33-7.39 (m, 2H), 7.62-7.66

(m, 2H); ¹³C NMR (CDCl₃) δ 19.2, 23.5, 29.2, 69.7, 70.7, 105.5, 116.9, 120.4, 123.7, 127.1,

128.8, 131.4, 135.7, 152.5, 153.2; IR (CH₂Cl₂) 3079, 2943, 1633, 1553, 1449 cm⁻¹; HRMS

m/z 254.1311 (calcd for C₁₇H₁₈O₂, 254.1307).

4-[(2-Iodobenzyl)oxy]-2-phenyl-4,5,6,7-tetrahydrobenzofuran (27). Compound **1**

(39.2 mg, 0.2 mmol) was allowed to react with 2-iodobenzyl alcohol (70.2 mg, 1.5 equiv)

under our standard reaction conditions for 1 h. The reaction mixture was chromatographed

(Al_2O_3, 90:1 hexane/EtOAc) to afford 75.1 mg (87%) of the indicated compound **27** as a light

yellow oil: ^1H NMR ($CDCl_3$) δ 1.82-1.95 (m, 2H), 2.04-2.22 (m, 2H), 2.58-2.69 (m, 1H),

2.73-2.80 (m, 1H), 4.59 (t, J = 4.2 Hz, 1H), 4.64 (d, J = 3.9 Hz, 2H), 6.71 (s, 1H), 6.98 (dt, J

= 7.8, 1.7 Hz, 1H), 7.20-7.25 (m, 1H), 7.34-7.39 (m, 3H), 7.52 (dd, J = 7.5, 1.5 Hz, 1H),

7.63-7.67 (m, 2H), 7.84 (dd, J = 7.8, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 19.3, 23.5, 29.1, 71.4,

74.6, 98.3, 105.6, 120.2, 123.7, 127.2, 128.5, 128.8, 129.3, 129.4, 131.4, 139.4, 141.3, 152.6,

153.3; IR (CH_2Cl_2) 3059, 2942, 1604, 1553, 1486 cm^{-1}; HRMS m/z 430.0437 (calcd for

$C_{21}H_{19}IO_2$, 430.0430).

2-Phenyl-4-(3-phenylprop-2-ynyloxy)-4,5,6,7-tetrahydrobenzofuran (29). Compound

1 (39.2 mg, 0.2 mmol) was allowed to react with 3-phenyl-2-propyn-1-ol (39.6 mg, 1.5

equiv) under our standard reaction conditions for 0.5 h. The reaction mixture was

chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 49.4 mg (75%) of the indicated

compound **29** as a light yellow oil: ^1H NMR ($CDCl_3$) δ 1.81-1.92 (m, 2H), 2.02-2.18 (m,

2H), 2.63-2.69 (m, 1H), 2.72-2.80 (m, 1H), 4.51 (s, 2H), 4.76 (t, J = 3.9 Hz, 1H), 6.74 (s,

1H), 7.20-7.26 (m, 1H), 7.32-7.39 (m, 5H), 7.47-7.52 (m, 2H), 7.63-7.66 (m, 2H); ^{13}C NMR

($CDCl_3$) δ 19.1, 23.5, 29.1, 56.5, 69.8, 86.1, 86.4, 105.7, 119.6, 123.0, 123.7, 127.2, 128.6,

128.7, 128.8, 131.3, 132.0, 152.6, 153.5; IR (CH_2Cl_2) 3057, 2940, 2848, 1603, 1488, 1441,

1071 cm^{-1}; HRMS m/z 328.1469 (calcd for $C_{23}H_{20}O_2$, 328.1463).

1,2;3,4-Di-O-isopropylidene-6-O-[(2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl)-β-D-

galactopyranose (30). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with (78 mg,

1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was

chromatographed (silica gel, 4:1 hexane/EtOAc) to afford 55.7 mg (63%) of the indicated

compound **30** (mixture of diastereomers) as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.33-1.38

(m, 6H), 1.47-1.48 (m, 3H), 1.52-1.54 (m, 3H), 1.74-1.88 (m, 2H), 1.92-2.07 (m, 2H), 2.58-

2.64 (m, 1H), 2.67-2.75 (m, 1H), 3.69-3.83 (m, 2H), 3.97-4.04 (m, 1H), 4.30-4.35 (m, 2H),

4.47-4.54 (m, 1H), 4.58-4.63 (m, 1H), two distinct proton signals corresponding to two

diastereomers at δ 5.55 (s) and δ 5.57 (s) (1H), two distinct proton signals corresponding to

two diastereomers at δ 6.69 (s) and δ 6.72 (s) (1H), 7.18-7.23 (m, 1H), 7.32-7.37 (m, 2H),

7.60-7.63 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 19.2, 19.3, 23.45, 23.47, 24.6, 24.7, 25.2, 26.27,

26.29, 26.3, 26.4, 28.9, 29.2, 67.1, 67.3, 67.45, 67.50, 70.8, 70.9, 70.96, 70.99, 71.2, 71.3,

71.8, 72.1, 96.59, 96.64, 105.6, 105.7, 108.7, 108.8, 109.3, 109.4, 120.5, 120.6, 123.6,

127.02, 127.05, 128.78, 128.79, 131.46, 131.47, 152.46, 152.48, 153.06, 153.1 (two carbons

missing due to overlap); IR (CH$_2$Cl$_2$) 2986, 2935, 1604, 1381, 1256, 1211, 1071 cm^{-1}; HRMS

m/z 456.2158 (calcd for C$_{26}$H$_{23}$O$_7$, 456.2148).

3-(2-Phenyl-4,5,6,7-tetrahydro-1-benzofuran-4-yloxy)cyclohex-2-enone (36).

Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with 1,3-cyclohexanedione (33.6 mg,

1.5 equiv) under our standard reaction conditions for 0.5 h. The reaction mixture was

chromatographed (silica gel, 1:1 hexane/EtOAc) to afford 51 mg (81%) of the indicated

compound **36** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.85-1.94 (m, 2H), 1.96-2.10 (m,

4H), 2.35-2.43 (m, 4H), 2.63-2.69 (m, 1H), 2.73-2.81 (m, 1H), 5.25 (t, J = 3.6 Hz, 1H), 5.61

(s, 1H), 6.60 (s, 1H), 7.20-7.26 (m, 1H), 7.32-7.37 (m, 2H), 7.59-7.62 (m, 2H); ^{13}C NMR

(CDCl$_3$) δ 19.0, 21.4, 23.2, 28.4, 29.8, 37.0, 70.2, 103.6, 105.0, 118.1, 123.8, 127.5, 128.9,

130.9, 153.1, 154.1, 177.3, 200.1; IR (CH_2Cl_2) 2947, 1650, 1598, 1379, 1215, 1181 cm^{-1};

HRMS m/z 308.1418 (calcd for $C_{20}H_{20}O_3$, 308.1412).

4-(4-N,N-Dimethylphenyl)-2-phenyl-4,5,6,7-tetrahydrobenzofuran (38). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with N,N-dimethylaniline (36.2 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 33 mg (52%) of the indicated compound **38** as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 1.68-1.88 (m, 2H), 1.98-2.15 (m, 2H), 2.75-2.80 (m, 2H), 2.96 (s, 6H), 3.85 (t, J = 2.3 Hz, 1H), 6.31 (s, 1H), 6.74 (d, J = 9.0 Hz, 2H), 7.11 (d, J = 8.7 Hz, 2H), 7.18-7.26 (m, 1H), 7.32-7.38 (m, 2H), 7.60-7.64 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 21.8, 23.6, 34.1, 39.5, 41.1, 106.3, 113.0, 122.7, 123.5, 126.8, 128.8, 128.9, 131.6, 133.8, 149.5, 151.7, 151.9; IR (CH_2Cl_2) 2933, 2851, 1613, 1519, 1486, 1446, 1346 cm^{-1}; HRMS m/z 317.1786 (calcd for $C_{22}H_{23}NO$, 317.1780).

1-Methyl-3-(2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl)-1H-indole (40). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with 1-methylindole (39.2 mg, 1.5 equiv) under our standard reaction conditions for 1 h. Then, another portion of AuCl$_3$ solution (20 mg, 1 mol%) was added and the reaction mixture was further stirred for 1 h. The reaction mixture was chromatographed (silica gel, 25:1 hexane/EtOAc) to afford 59.2 mg (90%) of the indicated compound **40** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.90-2.03 (m, 3H), 2.13-2.18 (m, 1H), 2.79 (t, J = 5.9 Hz, 2H), 3.74 (s, 3H), 4.28 (t, J = 5.6 Hz, 1H), 6.48 (s, 1H), 6.75 (s, 1H), 7.10-7.16 (m, 1H), 7.18-7.29 (m, 2H), 7.32-7.38 (m, 3H), 7.61-7.66 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 21.3, 23.7, 31.0, 31.6, 32.9, 106.4, 109.5, 118.9, 119.5, 121.8, 122.5, 123.5, 126.8, 127.2, 127.3, 128.8, 131.6, 137.5, 151.5, 151.9 (one sp^2 carbon missing due to

overlap); IR (CH$_2$Cl$_2$) 3053, 2935, 2855, 1602, 1549, 1473, 1327, 1264 cm^{-1}; HRMS m/z 327.1630 (calcd for C$_{23}$H$_{21}$NO, 327.1623).

4-Methoxy-2-phenyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]furan (46). Compound **44** (42 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 39.7 mg (82%) of the indicated compound **9** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.70-1.90 (m, 4H), 1.99-2.14 (m, 2H), 2.84-2.90 (m, 2H), 3.37 (s, 3H), 4.20 (dd, J = 6.3, 2.4 Hz, 1H), 6.59 (s, 1H), 7.17-7.24 (m, 1H), 7.32-7.38 (m, 2H), 7.59-7.63 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 24.4, 26.6, 28.9, 33.3, 56.6, 75.6, 108.4, 123.48, 123.54, 126.9, 128.8, 131.3, 150.3, 154.0; IR (CH$_2$Cl$_2$) 2927, 2845, 1602, 1552, 1486, 1447, 1084 cm^{-1}; HRMS m/z 242.1310 (calcd for C$_{16}$H$_{18}$O$_2$, 242.1307).

4-Methoxy-2-phenyl-4*H*-furo[3,2-*c*]chromene (49). Compound **47** (49.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction condition for 2.5 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 34.5 mg (62%) of the indicated compound **49** as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 3.57 (s, 3H), 6.34 (s, 1H), 6.74 (s, 1H), 7.06-7.12 (m, 2H), 7.21-7.33 (m, 2H), 7.39-7.45 (m, 2H), 7.65 (dd, J = 7.5, 1.7 Hz, 1H), 7.73-7.77 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 55.0, 98.4, 103.7, 115.3, 115.7, 117.0, 120.1, 122.1, 124.1, 128.1, 128.8, 129.0, 130.6, 147.0, 151.2, 154.9; IR (CH$_2$Cl$_2$) 3060, 2956, 2930, 1644, 1499, 1484, 1451, 1308, 1207, 1071 cm^{-1}; HRMS m/z 278.1313 (calcd for C$_{18}$H$_{14}$O$_3$, 278.1307).

3-[Methoxy(phenyl)methyl]-2-methyl-5-phenylfuran (56). Compound **54** (49.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 24 h. Then, another portion of AuCl$_3$ solution (20 mg, 1 mol %) was

added and the reaction mixture was further stirred for 24 h. The reaction mixture was chromatographed (silica gel, 20:1 hexane/EtOAc) to afford 33.4 mg (60%) of the indicated compound **56** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 2.40 (s, 3H), 3.39 (s, 3H), 5.22 (s, 1H), 6.51 (s, 1H), 7.20-7.44 (m, 7H), 7.58-7.62 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 12.4, 56.8, 78.1, 105.5, 122.6, 123.6, 126.8, 127.1, 127.7, 128.7, 128.8, 131.1, 141.9, 148.9, 152.1; IR (CH$_2$Cl$_2$) 3060, 3029, 2923, 2819, 1601, 1555, 1488, 1450, 1089 cm^{-1}; HRMS m/z 278.1313 (calcd for C$_{19}$H$_{18}$O$_2$, 278.1307).

3-[Methoxy(phenyl)methyl]-2,5-diphenylfuran (59). Compound **57** (61.6 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 4 h (2 mol % of AuCl$_3$ was used). The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 60.4 mg (89%) of the indicated compound **59** as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 3.44 (s, 3H), 5.57 (s, 1H), 6.75 (s, 1H), 7.25-7.54 (m, 11H), 7.72-7.76 (m, 4H); ^{13}C NMR (CDCl$_3$) δ 57.0, 77.9, 107.3, 124.1, 124.2, 126.8, 127.4, 127.8, 128.1, 128.8, 128.9, 129.0, 130.8, 131.1, 141.1, 150.5, 153.1 (one sp^2 carbon missing due to overlap); IR (CH$_2$Cl$_2$) 3060, 2933, 1594, 1493, 1086 cm^{-1}; HRMS m/z 340.1469 (calcd for C$_{24}$H$_{20}$O$_2$, 340.1463).

3-[Methoxy(phenyl)methyl]-5-phenyl-2-(phenylethynyl)furan (62). Compound **60** (66.4 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 15:1 hexane/EtOAc) to afford 48 mg (66%) of the indicated compound **62** as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 3.49 (s, 3H), 5.49 (s, 1H), 6.70 (s, 1H), 7.25-7.33 (m, 2H), 7.36-7.42 (m, 7H), 7.50-7.54 (m, 2H), 7.57-7.61 (m, 2H), 7.68-7.72 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 57.2, 77.9, 79.1, 97.4, 105.4, 122.6, 124.4, 126.7, 127.9, 128.3, 128.73, 128.75, 128.9, 129.0,

130.2, 131.7, 133.8, 134.4, 141.3, 155.1; IR (CH$_2$Cl$_2$) 3061, 3029, 2985, 2930, 2821, 2208,

1600, 1540, 1481, 1450, 1188, 1074 cm^{-1}; HRMS m/z 364.1470 (calcd for C$_{26}$H$_{20}$O$_2$,

364.1463).

3-[Methoxy(phenyl)methyl]-2-(2-methylprop-1-enyl)-5-phenylfuran (65). Compound

63 (57.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our

standard reaction conditions for 3 h. Then, another portion of AuCl$_3$ solution (20 mg, 1 mol

%) was added and the reaction mixture was further stirred for 4 h. The reaction mixture was

chromatographed (silica gel, 25:1 hexane/EtOAc) to afford 40 mg (63%) of the indicated

compound **65** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.98 (d, J = 0.6 Hz, 3H), 2.23 (s,

3H), 3.40, (s, 3H), 5.32 (s, 1H), 6.17 (t, J = 1.4 Hz, 1H), 6.57 (s, 1H), 7.22-7.30 (m, 2H),

7.33-7.44 (m, 6H), 7.60-7.64 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 20.8, 28.0, 57.0, 77.6, 105.9,

111.7, 123.7, 124.0, 126.8, 127.3, 127.7, 128.7, 128.8, 130.9, 136.5, 141.8, 150.3, 152.2; IR

(CH$_2$Cl$_2$) 3079, 3029, 2976, 2925, 2819, 1657, 1605, 1485, 1449, 1173, 1096 cm^{-1}; HRMS

m/z 318.1625 (calcd for C$_{22}$H$_{22}$O$_2$, 318.1620).

***cis*-5-Benzyl-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (69).** Compound **66**

(57.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our

standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel,

12:1 hexane/EtOAc) to afford 25.1 mg (40%) compound **70** alongside 21.6 mg (34%) of the

indicated compound **69** as a light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.61-1.68 (m, 1H), 2.08-

2.11 (m, 1H), 2.29-2.33 (m, 1H), 2.45-2.54 (m, 1H), 2.65-2.70 (m, 2H), 2.78-2.85 (m, 1H),

3.42 (s, 3H), 4.10 (d, J = 4.5 Hz, 1H), 6.67 (s, 1H), 7.19-7.26 (m, 4H), 7.30-7.40 (m, 4H),

7.64-7.68 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 20.9, 23.4, 37.0, 39.9, 55.1, 76.6, 105.9, 119.0,

123.7, 126.3, 127.2, 128.6, 128.9, 129.3, 131.3, 140.7, 152.5, 152.8; IR (CH$_2$Cl$_2$) 3060, 2931,

1602, 1553, 1487, 1450, 1083 cm^{-1}; HRMS m/z 318.1620 (calcd for $C_{22}H_{22}O_2$, 318.1625).

***trans*-5-Benzyl-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (70).** Compound

70 was obtained as a yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.78-1.82 (m, 1H), 1.97-2.06 (m, 2H),

2.64-2.83 (m, 3H), 2.91-2.98 (m, 1H), 3.41 (s, 3H), 3.90 (d, J = 2.7 Hz, 1H), 6.56 (s, 1H),

7.19-7.27 (m, 4H), 7.31-7.39 (m, 4H), 7.60-7.64 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 23.6, 24.0,

37.9, 42.4, 56.6, 72.9, 106.3, 120.1, 123.6, 126.1, 127.1, 128.5, 128.9, 129.5, 131.3, 141.2,

152.4, 153.2; IR (CH$_2$Cl$_2$) 3060, 3026, 2931, 1602, 1553, 1488, 1449, 1109, 1076 cm^{-1};

HRMS m/z 318.1625 (calcd for $C_{22}H_{22}O_2$, 318.1620).

Representative procedure for the iodine-induced cyclizations. To the mixture of

appropriate 2-(1-alkynyl)-2-alken-1-one (0.2 mmol), I$_2$ (3.0 equiv) and NaHCO$_3$ (3.0 equiv),

was added a solution of nucleophile (8.0 equiv) in CH$_3$CN (2.0 mL). The resulting mixture

was stirred at room temperature for 1 h unless otherwise specified. The mixture was diluted

with ether (25 mL), washed with satd Na$_2$S$_2$O$_3$ (15 mL) and dried (MgSO$_4$). The solvent was

removed under reduced pressure and the residue was purified by flash chromatography on

silica gel.

3-Iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (3). Compound 1 (39.2 mg,

0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 10:1

hexane/EtOAc) to afford 56.8 mg (80%) of the indicated compound **3** as a colorless oil: ^{1}H

NMR (CDCl$_3$) δ 1.52-1.65 (m, 1H), 1.83-2.10 (m, 2H), 2.14-2.23 (m, 1H), 2.51-2.63 (m,

1H), 2.69-2.79 (m, 1H), 3.52 (s, 3H), 4.13 (t, J = 2.9 Hz, 1H), 7.27-7.34 (m, 1H), 7.37-7.44

(m, 2H), 7.90-7.98 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 18.5, 23.5, 27.1, 57.3, 65.3, 72.2, 123.7,

126.4, 128.1, 128.5, 130.8, 150.4, 154.1; IR (CH_2Cl_2) 2938, 2817, 1628, 1483, 1414, 1083 cm^{-1}; HRMS m/z 354.0121 (calcd for $C_{15}H_{15}IO_2$, 354.0117).

3,4-Diiodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (7). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react under our standard reaction conditions, in the absence of any nucleophile for 1 h. The reaction mixture was chromatographed (silica gel, 40:1 hexane/EtOAc) to afford 55.0 mg (41%) of the indicated compound **7** as a white solid: mp 160-162 °C; ^{1}H NMR $(CDCl_3)$ δ 1.49-1.60 (m, 1H), 1.86-2.00 (m, 1H), 2.38-2.66 (m, 2H), 2.73-2.84 (m, 2H), 4.56 (s, 1H), 7.26-7.33 (m, 1H), 7.37-7.43 (m, 2H), 7.86-7.90 (m, 2H); ^{13}C NMR $(CDCl_3)$ δ 19.1, 23.5, 27.3, 65.3, 67.9, 123.0, 126.7, 128.1, 128.5, 130.9, 150.4, 155.1; IR (CH_2Cl_2) 3060, 2984, 2941, 1620, 1603, 1483 cm^{-1}.

3-Iodo-4-methoxy-2-(4-methoxyphenyl)-4,5,6,7-tetrahydrobenzofuran (10). Compound **8** (45.2 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 63.9 mg (83%) of the indicated compound **10** as a colorless oil: ^{1}H NMR $(CDCl_3)$ δ 1.58 (tt, J = 3.5, 13.6 Hz, 1H), 1.81-1.92 (m, 1H), 1.94-2.10 (m, 1H), 2.12-2.21 (m, 1H), 2.50-2.61 (m, 1H), 2.67-2.76 (m, 1H), 3.51 (s, 3H), 3.83 (s, 3H), 4.11 (t, J = 3.0 Hz, 1H), 6.94 (dt, J = 9.0, 2.7 Hz, 2H), 7.85 (dt, J = 9.0, 2.7 Hz, 2H); ^{13}C NMR $(CDCl_3)$ δ 18.5, 23.5, 27.1, 55.5, 57.3, 63.8, 72.3, 114.0, 123.4, 123.6, 128.0, 150.6, 153.5, 159.5; IR (CH_2Cl_2) 2939, 2835, 1612, 1495 cm^{-1}; HRMS m/z 384.0229 (calcd for $C_{16}H_{17}IO_3$, 384.0223).

Ethyl 4-(3-iodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran-2-yl)benzoate (13). Compound **11** (53.6 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed

(silica gel, 5:1 hexane/EtOAc) to afford 70.7 mg (83%) of the indicated compound **13** as a

colorless oil: ^{1}H NMR (CDCl$_3$) δ 1.40 (t, J = 7.2 Hz, 3H), 1.62 (tt, J = 3.3, 13.8 Hz, 1H),

1.88-2.10 (m, 2H), 2.14-2.22 (m, 1H), 2.50-2.62 (m, 1H), 2.68-2.79 (m, 1H), 3.51 (s, 3H),

4.12 (t, J = 3.0 Hz, 1H), 4.38 (q, J = 7.2 Hz, 3H), 8.02-8.09 (m, 4H); ^{13}C NMR (CDCl$_3$) δ

14.6, 18.4, 23.5, 26.9, 57.3, 61.2, 67.6, 72.1, 124.4, 125,7, 129.4, 129.9, 134.7, 149.2, 155.1,

166.5; IR (CH$_2$Cl$_2$) 2932, 2817, 1713, 1607, 1276 cm^{-1}; HRMS m/z 426.0336 (calcd for

C$_{18}$H$_{19}$IO$_4$, 426.0328).

2-(Cyclohex-1-enyl)-3-iodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (18).

Compound **16** (40.0 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv)

under our standard reaction conditions for 1 h. The reaction mixture was chromatographed

(silica gel, 11:1 hexane/EtOAc) to afford 33.0 mg (46%) of the indicated compound **18** as a

colorless oil: ^{1}H NMR (CDCl$_3$) δ 1.43-1.75 (m, 5H), 1.77-1.85 (m, 1H), 1.92-2.06 (m, 1H),

2.08-2.22 (m, 3H), 2.40-2.52 (m, 3H), 2.58-2.66 (m, 1H), 3.47 (s, 3H), 4.04 (s, 1H), 6.42-

6.46 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 18.5, 22.1, 22.8, 23.4, 25.6, 26.7, 27.1, 57.2, 63.0, 72.3,

122.8, 127.9, 128.2, 152.4, 152.5; IR (CH$_2$Cl$_2$) 2928, 2858, 1629, 1435, 1346 cm^{-1}; HRMS

m/z 358.0435 (calcd for C$_{15}$H$_{19}$IO$_2$, 358.0430).

2,3-Diiodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (21). Compound **19** (38.4 mg,

0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1

hexane/EtOAc) to afford 47.2 mg (60%) of the indicated compound **21** as a colorless oil: ^{1}H

NMR (CDCl$_3$) δ 1.47-1.60 (m, 1H), 1.72-1.84 (m, 1H), 1.89-2.13 (m, 2H), 2.48-2.59 (m,

1H), 2.64-2.73 (m, 1H), 3.46 (s, 3H), 4.04 (t, J = 3.0 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 18.3,

23.7, 27.2, 57.4, 72.0, 83.1, 96.4, 124.2, 159.8; IR (CH₂Cl₂) 2940, 2817, 1625, 1452, 1410

cm⁻¹; HRMS m/z 403.8777 (calcd for $C_9H_{10}I_2O_2$, 403.8770).

3-Iodo-4-isopropoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (22). Compound **1** (39.2

mg, 0.2 mmol) was allowed to react with isopropanol (96 mg, 8.0 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 12:1

hexane/EtOAc) to afford 55.5 mg (73%) of the indicated compound **22** as a light yellow oil:

¹H NMR (CDCl₃) δ 1.25 (d, J = 6.3 Hz, 3H), 1.36 (d, J = 6.0 Hz, 3H), 1.53-1.63 (m, 1H),

1.82-1.93 (m, 1H), 2.02-2.17 (m, 2H), 2.50-2.62 (m, 1H), 2.69-2.78 (m, 1H), 3.87-3.97 (m,

1H), 4.35 (s, 3H), 7.26-7.33 (m, 1H), 7.37-7.43 (m, 2H), 7.90-7.94 (m, 2H); ¹³C NMR

(CDCl₃) δ 18.3, 23.2, 23.6, 24.2, 28.6, 65.3, 68.7, 70.5, 123.7, 126.6, 128.0, 128.5, 130.9,

150.3, 154.2; IR (CH₂Cl₂) 3058, 2967, 2882, 1625, 1483, 1445 cm⁻¹; HRMS m/z 382.0437

(calcd for $C_{17}H_{19}IO_2$, 382.0430).

4-Allyoxy-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (24). Compound **1** (39.2 mg,

0.2 mmol) was allowed to react with allyl alcohol (139 mg, 8.0 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 100:1

hexane/EtOAc) to afford 43.3 mg (57%) of the indicated compound **24** as a light yellow oil:

¹H NMR (CDCl₃) δ 1.61 (tt, J = 13.5, 3.2 Hz, 1H), 1.83-1.93 (m, 1H), 1.99-2.21 (m, 2H),

2.51-2.63 (m, 1H), 2.70-2.79 (m, 1H), 4.15-4.26 (m, 2H), 4.29-4.32 (m, 1H), 5.20 (dd, J =

10.4, 1.2 Hz, 1H), 5.35 (dd, J = 17.4, 1.4 Hz, 1H), 6.01-6.13 (m, 1H), 7.28-7.33 (m, 1H),

7.38-7.44 (m, 2H), 7.91-7.96 (m, 2H); ¹³C NMR (CDCl₃) δ 18.5, 23.5, 27.8, 65.3, 70.7, 70.9,

117.2, 123.7, 126.5, 128.0, 128.5, 130.8, 135.6, 150.3, 154.2; IR (CH₂Cl₂) 3079, 2940, 2860,

1627, 1603, 1483 cm⁻¹; HRMS m/z 380.0278 (calcd for $C_{17}H_{17}IO_2$, 380.0273).

4-Benzyloxy-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (26). Compound **1** (39.2

mg, 0.2 mmol) was allowed to react with benzyl alcohol (173 mg, 8.0 equiv) under our

standard reaction conditions for 1 h. The reaction mixture was chromatographed (Al_2O_3,

100:1 hexane/EtOAc) to afford 51.5 mg (60%) of the indicated compound **26** as a light

yellow oil: ^1H NMR ($CDCl_3$) δ 1.65 (tt, $J = 13.5$, 3.3 Hz, 1H), 1.85-1.97 (m, 1H), 2.05-2.20

(m, 1H), 2.21-2.29 (m, 1H), 2.53-2.65 (m, 1H), 2.71-2.80 (m, 1H), 4.43 (t, $J = 2.9$ Hz, 1H),

4.73 (s, 1H), 7.25-7.50 (m, 8H), 7.93-7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.6, 23.5, 27.7,

65.4, 71.1, 72.1, 123.8, 126.5, 127.9, 128.1, 128.5, 128.56, 128.58, 130.8, 138.8, 150.3,

154.3; IR (CH_2Cl_2) 3062, 3029, 2940, 1628, 1603, 1484 cm^{-1}; HRMS m/z 419.9653 (calcd for

$C_{21}H_{19}IO_2$, 419.9647).

3-Iodo-2-phenyl-4-(3-phenyl-2-propynyl)oxy-4,5,6,7-tetrahydrobenzofuran (28).

Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with 3-phenyl-2-propyn-1-ol (211

mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was

chromatographed (silica gel, 18:1 hexane/EtOAc) to afford 70.0 mg (77%) of the indicated

compound **28** as a colorless oil: ^1H NMR ($CDCl_3$) δ 1.67 (tt, $J = 13.8$, 3.3 Hz, 1H), 1.86-1.97

(m, 1H), 2.05-2.20 (m, 1H), 2.28-2.37 (m, 1H), 2.53-2.66 (m, 1H), 2.72-2.82 (m, 1H), 4.56

(t, $J = 3.2$ Hz, 1H), 4.61 (d, $J = 5.7$ Hz, 2H), 7.29-7.36 (m, 4H), 7.38-7.45 (m, 2H), 7.47-7.52

(m, 2H), 7.93-7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.5, 23.5, 27.8, 57.7, 65.1, 70.3, 86.3,

86.4, 123.2, 123.5, 126.5, 128.1, 128.55, 128.58, 128.60, 130.8, 132.0, 150.5, 154.6; IR

(CH_2Cl_2) 3057, 2940, 1660, 1626, 1487 cm^{-1}; HRMS m/z 454.0437 (calcd for $C_{23}H_{19}IO_2$,

454.0430).

3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-ol (31). Compound **1** (39.2 mg, 0.2

mmol) was allowed to react with H_2O (28.8 mg, 8.0 equiv) under our standard reaction

conditions for 1 h. The reaction mixture was chromatographed (silica gel, 4:1

hexane/EtOAc) to afford 52.1 mg (77%) of the indicated compound **31** as a white solid: mp

83-84 °C; ^{1}H NMR (CDCl$_3$) δ 1.75-1.96 (m, 3H), 1.99-2.14 (m, 2H), 2.53-2.65 (m, 1H),

2.70-2.79 (m, 1H), 4.70 (q, *J* = 3.9 Hz, 1H), 7.29-7.35 (m, 1H), 7.38-7.45 (m, 2H), 7.92-7.97

(m, 2H); ^{13}C NMR (CDCl$_3$) δ 18.6, 23.5, 31.8, 63.7, 64.1, 125.0, 126.3, 128.2, 128.6, 130.6,

150.3, 153.8; IR (CH$_2$Cl$_2$) 3340, 2940, 1624, 1483, 1442, 1223 cm^{-1}; HRMS *m/z* 339.9970

(calcd for C$_{14}$H$_{13}$IO$_2$, 339.9960).

3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl acetate (33). Compound **1** (39.2

mg, 0.2 mmol) was allowed to react with acetic acid (144 mg, 8.0 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 6:1

hexane/EtOAc) to afford 50.3 mg (66%) of the indicated compound **33** as a light yellow

solid: mp 115-116 °C; ^{1}H NMR (CDCl$_3$) δ 1.82-1.97 (m, 3H), 2.00-2.14 (m, 4H), 2.57-2.65

(m, 1H), 2.76-2.87 (m, 1H), 5.79 (t, *J* = 3.0 Hz, 1H), 7.29-7.35 (m, 1H), 7.38-7.45 (m, 2H),

7.92-7.96 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 19.1, 21.5, 23.3, 29.3, 63.9, 66.3, 121.6, 126.4,

128.3, 128.6, 130.5, 150.7, 155.3, 170.8; IR (CH$_2$Cl$_2$) 2951, 1731, 1628, 1483, 1370 cm^{-1};

HRMS *m/z* 382.0071 (calcd for C$_{16}$H$_{15}$IO$_3$, 382.0066).

3-Iodo-4-methoxy-2-phenyl-5,6-dihydro-4*H*-cyclopentafuran (42). Compound **41**

(36.4 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our

standard reaction conditions for 4 h. The reaction mixture was chromatographed (silica gel,

6:1 hexane/EtOAc) to afford 50.3 mg (74%) of the indicated compound **42** as a light yellow

solid: mp 70-71 °C; ^{1}H NMR (CDCl$_3$) δ 2.36-2.45 (m, 1H), 2.64-2.78 (m, 2H), 2.98-3.06 (m,

1H), 3.47 (s, 3H), 4.65-4.69 (m, 1H), 7.29-7.35 (m, 1H), 7.39-7.45 (m, 2H), 7.92-7.96 (m,

2H); ^{13}C NMR (CDCl$_3$) δ 24.2, 35.2, 56.6, 60.0, 77.7, 126.5, 128.2, 128.6, 131.1, 133.2,

155.7, 162.3; IR (CH$_2$Cl$_2$) 2974, 2931, 2819, 1619, 1601, 1479 cm^{-1}; HRMS m/z 399.9968

(calcd for C$_{14}$H$_{13}$IO$_2$, 399.9960).

3-Iodo-4-methoxy-2-phenyl-5,6,7,8-tetrahydro-4H-cycloheptafuran (45). Compound

44 (42.0 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our

standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel,

9:1 hexane/EtOAc) to afford 56.0 mg (76%) of the indicated compound **45** as a light yellow

oil: ^{1}H NMR (CDCl$_3$) δ 1.50-1.68 (m, 2H), 1.78-1.87 (m, 1H), 1.96-2.11 (m, 2H), 2.35-2.42

(m, 1H), 2.87-2.94 (m, 2H), 3.40 (s, 3H), 4.28 (dd, J = 1.8, 5.1 Hz, 1H), 7.25-7.34 (m, 1H),

7.38-7.44 (m, 2H), 7.91-7.96 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 23.2, 26.4, 28.8, 31.8, 56.6, 70.1,

74.5, 125.0, 126.4, 128.0, 128.5, 130.8, 149.0, 155.3; IR (CH$_2$Cl$_2$) 3055, 2926, 1602, 1485,

1445 cm^{-1}; HRMS m/z 368.0279 (calcd for C$_{16}$H$_{17}$IO$_2$, 368.0273).

3-Iodo-4-methoxy-2-phenyl-4H-furo[3,2-c]chromene (48). Compound **47** (49.2 mg,

0.2 mmol) was allowed to react with MeOH (12.8 mg, 2.0 equiv) under our standard reaction

conditions for 1 h. The reaction mixture was chromatographed (silica gel, 4:1

hexane/EtOAc) to afford 70.1 mg (87%) of the indicated compound **48** as a white solid: mp

74-75 °C; ^{1}H NMR (CDCl$_3$) δ 3.64 (s, 3H), 6.10 (s, 1H), 7.06-7.14 (m, 2H), 7.23-7.29 (m,

1H), 7.36-7.42 (m, 1H), 7.44-7.51 (m, 2H), 7.63 (dd, J = 7.5, 1.4 Hz, 1H), 8.03-8.08 (m, 2H);

^{13}C NMR (CDCl$_3$) δ 55.8, 61.2, 98.9, 114.6, 117.4, 119.4, 120.2, 122.3, 126.7, 128.77,

128.81, 129.5, 130.1, 147.6, 151.6, 152.0; IR (CH$_2$Cl$_2$) 3059, 2927, 2828, 1642, 1497 cm^{-1};

HRMS m/z 403.9918 (calcd for C$_{18}$H$_{13}$IO$_3$, 403.9910).

4-[4-(Dimethylamino)phenyl]-3-iodo-2-phenyl-4H-furo[3,2-c]chromene (50).

Compound **47** (49.2 mg, 0.2 mmol) was allowed to react with N,N-dimethylaniline (36.2 mg,

1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was

chromatographed (silica gel, 8:1 hexane/EtOAc) to afford 78.4 mg (80%) of the indicated

compound **50** as a white solid: mp 157-158 °C; ^{1}H NMR (CDCl$_3$) δ 2.94 (s, 6H), 6.31 (s,

1H), 6.67 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 7.09 (t, J =

7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.34-7.39 (m, 1H), 7.43-7.55 (m, 3H), 8.09 (d, J = 8.7

Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 40.6, 62.7, 79.1, 112.3, 115.6, 117.2, 119.8, 121.4, 121.7,

126.5, 127.0, 128.5, 128.7, 129.35, 129.43, 130.3, 146.3, 151.1, 151.6, 152.7 (one sp^2 carbon

missing due to overlap; IR (CH$_2$Cl$_2$) 2962, 2918, 1612, 1522 cm^{-1}; HRMS m/z 493.0544

(calcd for C$_{25}$H$_{20}$INO$_2$, 493.0539).

3-Iodo-4-methoxy-2,4-diphenyl-4H-furo[3,2-c]chromene (52). Compound **51** (64.4

mg, 0.2 mmol) was allowed to react with MeOH (32.0 mg, 5 equiv) under our standard

reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 3:1

hexane/EtOAc) to afford 58.7 mg (61%) of the indicated compound **52** as a yellow oil: ^{1}H

NMR (CDCl$_3$) δ 3.39 (s, 3H), 7.02-7.09 (m, 2H), 7.23-7.28 (m, 1H), 7.36-7.51 (m, 6H), 7.61-

7.70 (m, 3H), 8.11 (d, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 51.6, 61.7, 105.5, 112.7, 116.1,

117.2, 120.1, 121.5, 127.0, 127.1, 128.2, 128.7, 129.0, 129.05, 129.9, 130.1, 141.4, 148.7,

152.5, 153.1; IR (CH$_2$Cl$_2$) 3061, 3031, 2934, 1636, 1491, 1448 cm^{-1}; HRMS m/z 480.0229

(calcd for C$_{24}$H$_{17}$IO$_3$, 480.0223).

3-Iodo-4-[methoxy(phenyl)methyl]-5-methyl-2-phenylfuran (55). Compound **54** (49.2

mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard

reaction conditions for 50 h. The reaction mixture was chromatographed (silica gel, 12:1

hexane/EtOAc) to afford 58.2 mg (72%) of the indicated compound **55** as a colorless oil: ^{1}H

NMR (CDCl$_3$) δ 2.25 (s, 3H), 3.46 (s, 3H), 5.34 (s, 1H), 7.26-7.47 (m, 8H), 7.94-7.98 (m,

2H); ^{13}C NMR (CDCl$_3$) δ 13.1, 57.2, 67.3, 79.6, 123.3, 126.5, 127.0, 127.7, 128.1, 128.5,

130.6, 140.8, 150.08, 150.13 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3060,

3028, 2925, 1602, 1485 cm^{-1}; HRMS m/z 404.0279 (calcd for $C_{19}H_{17}IO_2$, 404.0273).

3-Iodo-4-[methoxy(phenyl)methyl]-2,5-diphenylfuran (58). Compound **57** (61.6 mg,

0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction

conditions for 50 h. The reaction mixture was chromatographed (silica gel, 12:1

hexane/EtOAc) to afford 66.1 mg (71%) of the indicated compound **58** as a white solid: mp

94-95 °C; ^{1}H NMR (CDCl$_3$) δ 3.43 (s, 3H), 5.75 (s, 1H), 7.25-7.51 (m, 11H), 7.69-7.72 (m,

2H), 8.11-8.15 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 57.1, 68.2, 123.3, 127.0, 127.1, 127.6, 128.4,

128.59, 128.63, 128.65, 128.67, 130.1, 130.4, 140.2, 151.5, 152.1 (one sp^2 carbon missing

due to overlap); IR (CH_2Cl_2) 3059, 3029, 2927, 1602, 1481 cm^{-1}; HRMS m/z 466.0437 (calcd

for $C_{24}H_{19}IO_2$, 466.0430).

cis-**5-Benzyl-3-iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (67).**

Compound **66** (57.2 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv)

under our standard reaction conditions for 1 h. The reaction mixture was chromatographed

(silica gel, 12:1 hexane/EtOAc) to afford 19.8 mg (22%) of the indicated compound **67** as a

light yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.76-1.80 (m, 1H), 1.97-2.04 (m, 2H), 2.51-2.63 (m,

1H), 2.69-2.81 (m, 2H), 2.96-3.03 (m, 1H), 3.63 (s, 3H), 3.98 (s, 1H), 7.21-7.28 (m, 3H),

7.29-7.36 (m, 3H), 7.38-7.43 (m, 2H), 7.91-7.95 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 23.2, 23.6,

38.6, 43.1, 59.4, 66.1, 73.8, 124.9, 126.2, 126.6, 128.1, 128.5, 128.6, 129.5, 130.8, 140.9,

150.6, 154.3; IR (CH_2Cl_2) 3025, 2930, 2818, 1629, 1602, 1484, 1459 cm^{-1}; HRMS m/z

444.0593 (calcd for $C_{22}H_{21}IO_2$, 444.0586).

trans-**5-Benzyl-3-iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (68).** The

reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford, together

with **67**, 42.1 mg (47%) of the indicated compound **68** as a light yellow oil: ^{1}H NMR

(CDCl$_3$) δ 1.71-1.78 (m, 1H), 2.13-2.21 (m, 1H), 2.44-2.59 (m, 3H), 2.67-2.72 (m, 2H), 3.43

(s, 3H), 3.90 (d, J = 0.9 Hz, 1H), 7.18-7.22 (m, 2H), 7.24-7.28 (m, 1H), 7.30-7.37 (m, 3H),

7.39-7.47 (m, 2H), 7.96-8.01 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 19.9, 22.2, 36.2, 38.0, 57.2, 65.9,

76.1, 122.3, 126.4, 128.1, 128.6, 128.7, 129.1, 130.8, 140.5, 150.7, 153.2; IR (CH$_2$Cl$_2$) 3025,

2930, 2821, 1615, 1603, 1484, 1453 cm^{-1}; HRMS m/z 444.0592 (calcd for C$_{22}$H$_{21}$IO$_2$,

444.0586).

Representative procedure for the PhSeCl-induced cyclizations. To the mixture of

appropriate 2-(1-alkynyl)-2-alken-1-one (0.2 mmol), PhSeCl (3.0 equiv) and NaHCO$_3$ (3.0

equiv), was added a solution of nucleophile (10 equiv) in CH$_3$CN (2.0 mL). The resulting

mixture was stirred at room temperature for 1 h unless otherwise specified. The mixture was

diluted with ether (25 mL), washed with brine (15 mL) and dried (MgSO$_4$). The solvent was

removed under reduced pressure and the residue was purified by flash chromatography on

silica gel.

4-Methoxy-2-phenyl-3-phenylseleno-4,5,6,7-tetrahydrobenzofuran (5).

Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with MeOH (64 mg, 10 equiv) under

our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica

gel, 9:1 hexane/EtOAc) to afford 34.2 mg (45%) of the indicated compound **5** as a light

yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.44-1.57 (m, 1H), 1.82-1.91 (m, 1H), 2.00-2.14 (m, 2H),

2.55-2.68 (m, 1H), 2.72-2.82 (m, 1H), 3.31 (s, 3H), 4.13 (t, J = 2.7 Hz, 1H), 7.11-7.24 (m,

3H), 7.26-7.38 (m, 5H), 7.93-7.98 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 18.2, 23.4, 27.3, 57.1, 71.3,

103.6, 124.1, 126.1, 126.6, 128.1, 128.5, 129.2, 129.4, 130.9, 132.8, 153.6, 154.4; IR

(CH_2Cl_2) 3056, 2938, 1603, 1577, 1478 cm^{-1}; HRMS m/z 384.0636 (calcd for $C_{21}H_{20}O_2Se$, 384.0629).

79
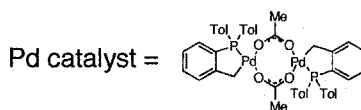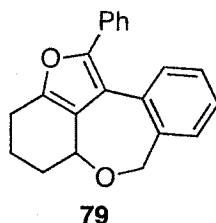
Pd catalyst =

This compound was prepared by following a procedure from the literaure.[24] The Pd catalyst (11.8 mg, 5 mol %), Cs_2CO_3 (195 mg, 0.6 mmol), furan **27** (87.1 mg, 0.20 mmol) and DMA (2.5 mL), were placed in a vial. The resulting mixture was heated under a N_2 atmosphere at 100 °C for 17 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH_4Cl (15 mL), dried ($MgSO_4$), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (9:1 hexane/EtOAc) on silica gel to afford 46.6 mg (76%) of the indicated compound **79** as a white solid: mp 156-157 °C; ^1H NMR ($CDCl_3$) δ 1.81-2.05 (m, 4H), 2.55-2.64 (m, 1H), 2.73-2.80 (m, 1H), 4.49-4.56 (m, 2H), 4.76 (d, J = 9.0 Hz, 1H), 7.24-7.35 (m, 5H), 7.42-7.45 (m, 1H), 7.54-7.56 (m, 1H), 7.69-7.71 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.7, 23.4, 30.8, 68.2, 68.8, 120.5, 121.0, 125.8, 127.6, 127.70, 127.73, 128.7, 128.8, 131.1, 131.5, 134.7, 137.5, 146.0, 152.1; IR (CH_2Cl_2) 3057, 2945, 2856, 1603, 1497 cm^{-1}; HRMS m/z 302.1312 (calcd for $C_{21}H_{18}O_2$, 302.1307).

80
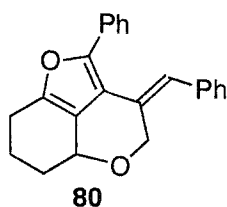
This compound was prepared by following a procedure from the literaure.[25]

Pd(OAc)$_2$ (4.5 mg, 10 mol %), PPh$_3$ (10.5 mg, 20 mol %), n-Bu$_4$NCl (55.3 mg, 0.2 mmol), 88% HCO$_2$H (31.4 mg, 0.6 mmol), piperidine (68.2 mg, 0.8 mmol), furan **28** (90.7 mg, 0.20 mmol) and CH$_3$CN (5 mL), were placed in a vial. The resulting mixture was heated under a N$_2$ atmosphere at 60 °C for 14 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH$_4$Cl (15 mL), dried (MgSO$_4$), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (9:1 hexane/EtOAc) on silica gel to afford 49.2 mg (75%) of the indicated compound **80** as a yellow oil: ^{1}H NMR (CDCl$_3$) δ 1.35-1.48 (m, 1H), 1.78-1.92 (m, 1H), 2.13-2.29 (m, 2H), 2.58-2.77 (m, 2H), 4.48 (dd, J = 2.1, 14.4 Hz, 1H), 4.52-4.59 (m, 1H), 5.03 (dd, J = 1.2, 14.1 Hz, 1H), 7.11-7.15 (m, 2H), 7.19-7.26 (m, 1H), 7.29-7.36 (m, 4H), 7.39-7.55 (m, 2H), 7.76-7.80 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 20.7, 22.9, 29.4, 67.5, 71.9, 114.8, 121.9, 123.4, 127.1, 127.7, 128.2, 128.5, 128.8, 129.4, 132.6, 136.8, 147.9, 148.4; IR (CH$_2$Cl$_2$) 3056, 3021, 2946, 2846, 1673, 1599, 1486 cm^{-1}; HRMS m/z 328.1471 (calcd for C$_{23}$H$_{20}$O$_2$, 328.1463).


81
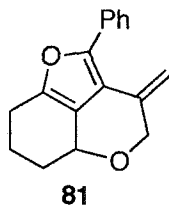
This compound was prepared by following a procedure from the literaure.[26]

Pd(OAc)$_2$ (4.5 mg, 10 mol %), PPh$_3$ (10.5 mg, 20 mol %), Et$_3$N (81 mg, 0.8 mmol) and furan

24 (76.9 mg, 0.20 mmol) in CH$_3$CN (4.5 mL) were refluxed for 3 h. The mixture was

allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq

NH$_4$Cl (15 mL), dried (MgSO$_4$), and filtered. The solvent was removed under reduced

pressure and the residue was purified by column chromatography (12:1 hexane/EtOAc) on

silica gel to afford 23.3 mg (46%) of the indicated compound **81** as a light yellow solid: mp

68-70 °C; ^{1}H NMR (CDCl$_3$) δ 1.34-1.44 (m, 1H), 1.76-1.91 (m, 1H), 2.09-2.25 (m, 2H),

2.56-2.72 (m, 2H), 4.31-4.43 (m, 2H), 4.48-4.53 (m, 1H), 4.89 (s, 1H), 5.66 (s, 1H), 7.26-

7.31 (m, 1H), 7.39 (t, J = 5.9 Hz, 2H), 7.68-7.71 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 20.6, 22.7,

29.2, 72.0, 72.2, 106.8, 113.6, 121.5, 127.3, 128.0, 128.5, 132.0, 135.2, 147.7, 149.0; IR

(CH$_2$Cl$_2$) 3007, 2946, 2848, 1669, 1602, 1443 cm^{-1}; HRMS m/z 252.1154 (calcd for C$_{17}$H$_{16}$O$_2$,
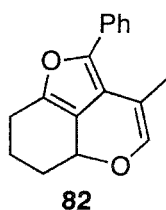
252.1150).

82

The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford,

together with **81**, 7.6 mg (15%) of the indicated compound **82** as a colorless oil: ^{1}H NMR

(CDCl$_3$) δ 1.60-1.69 (m, 1H), 1.79-1.88 (m, 1H), 1.92 (d, J = 1.2 Hz, 3H), 2.14-2.21 (m, 1H),

2.29-2.35 (m, 1H), 2.63-2.68 (m, 2H), 4.87-4.92 (m, 1H), 6.29 (d, J = 1.2 Hz, 1H), 7.27-7.31

(m, 1H), 7.35-7.41 (m, 2H), 7.56-7.60 (m, 2H); IR (CH$_2$Cl$_2$) 3013, 2941, 2851, 1669, 1600,

1445 cm^{-1}; HRMS m/z 252.1154 (calcd for C$_{17}$H$_{16}$O$_2$, 252.1150).

83
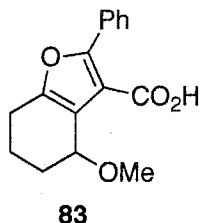
Pd(PCy$_3$)$_2$ (8.4 mg, 10 mol %), CsO$_2$CCMe$_3$ (117 mg, 20 mol %), furan **3** (88.5 mg,

0.25 mmol), H$_2$O (9 mg, 0.5 mmol) and DMF (6 mL) were placed in a vial. The resulting

mixture was heated under a CO atmosphere (1 atm) at 110 °C for 7 h. The mixture was

allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq

NH$_4$Cl (15 mL), dried (MgSO$_4$), and filtered. The solvent was removed under reduced

pressure and the residue was purified by column chromatography (2:1 hexane/EtOAc) on

silica gel to afford 36.2 mg (53%) of the indicated compound **83** as a white solid: mp 159-

160 °C; ^{1}H NMR (CDCl$_3$) δ 1.78-1.90 (m, 2H), 1.97-2.10 (m, 2H), 2.51-2.66 (m, 1H), 2.69-

2.80 (m, 1H), 3.50 (s, 3H), 4.64 (t, J = 3.7 Hz, 1H), 7.36-7.44 (m, 3H), 7.83-7.89 (m, 2H);

^{13}C NMR (CDCl$_3$) δ 18.5, 23.2, 26.8, 56.5, 72.2, 112.8, 118.6, 128.3, 128.8, 129.5, 130.0,

153.5, 157.9, 166.8; IR (CH$_2$Cl$_2$) 3059, 2930, 1711, 1681, 1491 cm^{-1}; HRMS m/z 272.1052

(calcd for C$_{16}$H$_{16}$O$_4$, 272.1049).

84
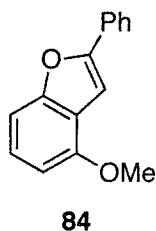
This compound was prepared by following a procedure from the literaure.[28] Furan **2**

(45.6 mg, 0.20 mmol) and DDQ (85 mg, 0.34 mmol) in benzene (6.5 mL) were refluxed for 6

h. The mixture was allowed to cool to room temperature, filtrated, washed with 10 %

Na_2CO_3 (6 mL), dried ($MgSO_4$), and filtered. The solvent was removed under reduced

pressure and the residue was purified by column chromatography (12:1 hexane/EtOAc) on

silica gel to afford 17.7 mg (40%) of the indicated compound **84** as a colorless oil: ^{1}H NMR

($CDCl_3$) δ 3.97 (s, 3H), 6.67 (dd, J = 0.9, 7.5 Hz, 1H), 7.13-7.26 (m, 3H), 7.31-7.36 (m, 1H),

7.41-7.48 (m, 2H), 7.83-7.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 55.8, 99.0, 103.5, 104.7, 119.8,

125.0, 125.2, 128.5, 129.0, 130.8, 153.7, 154.9, 156.3; IR (CH_2Cl_2) 2961, 1607, 1486, 1252

cm^{-1}; HRMS m/z 224.0841 (calcd for $C_{15}H_{12}O_2$, 224.0837).

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GENERAL CONCLUSIONS

In this dissertation, the scope and limitations of several electrophilic cyclization processes have been presented, which result in the synthesis of isocoumarins, α-pyrones, isoindolin-1-ones, polycyclic aromatics and furans.

Chapter 1 describes the synthesis of various isocoumarins and α-pyrones by the electrophilic cyclization of o-(1-alkynyl)benzoates and (Z)-2-alken-4-ynoates. Various electrophiles, including ICl, I_2, PhSeCl, p-$O_2NC_6H_4SCl$ and HI, can be used to introduce a hydrogen or different functional groups into the cyclized products. This chemistry tolerates a wide range of functional groups and has been successfully extended to the synthesis of polycyclic aromatic and biaryl compounds. However, in a few cases, five-membered ring lactones have been produced.

Chapter 2 describes the synthesis of isoindolin-1-ones by the electrophilic cyclization reactions of o-(1-alkynyl)benzamides. This cyclization generally affords a mixture of five- and six-membered ring lactams with the former predominating. In some cases, using different electrophiles can partially control the regioselectivity of this process. This methodology accommodates various alkynyl amides and functional groups, and has been successfully extended to heterocyclic starting materials. This chemistry has been successfully applied to the formal synthesis of a biologically interesting alkaloid cepharanone B.

Chapter 3 describes in detail the synthesis of a variety of substituted polycyclic aromatics by the reaction of 2-(1-alkynyl)biphenyls with electrophiles. The success of this process is dependent upon the substituents on the arenes and the carbon-carbon triple bond. The regioselectivity of this chemistry has also been examined. This methodology readily

accommodates various functional groups and has been successfully extended to systems containing a variety of polycyclic and heterocyclic rings.

Chapter 4 describes a novel coupling of 2-(1-alkynyl)-2-alken-1-ones with nucleophiles, either catalyzed by $AuCl_3$ or induced by an electrophile, to provide highly substituted furans in good to excellent yields under very mild reaction conditions. Various nucleophiles, including functionalized alcohols, H_2O, carboxylic acids, 1,3-diketones and electron-rich arenes, and a range of cyclic and acyclic 2-(1-alkynyl)-2-alken-1-ones readily participate in these cyclizations, which are often complementary. The resulting iodine-containing furans can be readily elaborated to more complex products using known organopalladium chemistry.

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