Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 62 (2006) 3843–3855

Coupling and cycloaddition of ynamides: homo- and Negishi coupling of tosylynamides and intramolecular [4+2] cycloaddition of *N*-(*o*-ethynyl)phenyl ynamides and arylynamides

María Fernanda Martínez-Esperón, David Rodríguez, Luis Castedo and Carlos Saá*

Departamento de Química Orgánica y Unidad Asociada al CSIC, Facultad de Química, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain

Received 14 November 2005; accepted 26 November 2005

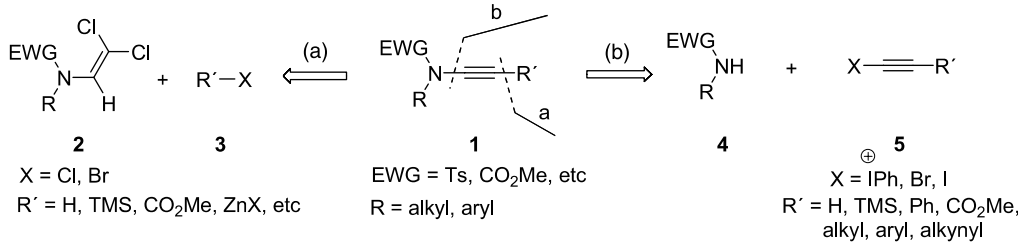
Available online 28 February 2006

Abstract—*N*,*N*′-aryl- and *N*,*N*′-alkyl-buta-1,3-diyne-1,4-ditosylamides have been synthesized for the first time, in good to excellent yields, by copper-catalyzed dimerization of the corresponding *N*-aryl or *N*-alkyl tosylynamides. Negishi coupling of *N*-ethynylzinc tosylamides derivatives with (hetero)aryl iodides in the presence of Pd_2dba_3 and triphenylphosphine affords *N*-aryl and *N*-alkyl arylynamides in yields of up to 90%. Intramolecular [4+2] cycloaddition reactions of *N*-ethynylphenyl ynamides and arylynamides allow the synthesis of carbazoles and benzannulated and heteroannulated carbazoles in moderate-to-good yields.

1. Introduction

Ynamides **1** have emerged as potentially more useful than other ynamines for organic synthesis because of their superior thermal stability.[1,2,3] Typically, ynamides withstand aqueous work-up and chromatographic purification on silica gel, and are often crystalline solids that are stable in air. These features have allowed their recent use in an array of procedures such as Pauson–Khand reactions,[4] hydroboration,[5] Rh(I)- and Ru(II)-catalyzed [2+2+2] cycloadditions,[6] Ni(0)- and Rh(I)-catalyzed [4+2] cycloadditions,[7] ring-closing metatheses,[8] radical cyclizations,[9] Pt-catalyzed cycloisomerizations,[10] Heck reactions[11] and pericyclic reactions.[12]

Although not all possible ynamides are currently accessible, many can be obtained by subjecting to elimination reactions dichloroenamides **2** (Scheme 1, route a) or by direct alkynylation of amide derivatives **4** (route b). Brückner's elimination protocol,[13] based on Viehe's pioneer work,[14] is really a tandem process, a base-promoted elimination followed by lithium–halogen exchange.[15,16] Direct alkynylation was initially developed by Stang[2d] and Feldman[17] to prepare 'push–pull'-type ynamines (R′=CO_2R, SO_2Ar, etc), and consists in the reaction of metalated amides with alkynyl(phenyl)iodonium salts **5** (X=IPh).[18] Though extended by Witulski and Rainier to the preparation of ynamides **1** in which R′=H, TMS, or phenyl,[4,6] this approach is of limited use for synthesis of alkyl ynamides (R′= alkyl), and also gives relatively low yields with some amide substrates.[1a] A second direct alkynylation approach, based on the methods developed by Buchwald and Hartwig for nitrogen–carbon bond formation,[19] involves the



Scheme 1. General approaches to ynamides.

Keywords: Alkynylation; Carbazoles; Coupling; Cycloaddition; Ynamides.
* Corresponding author. Fax: +34 981 595 012; e-mail: qocsaa@usc.es

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.11.082

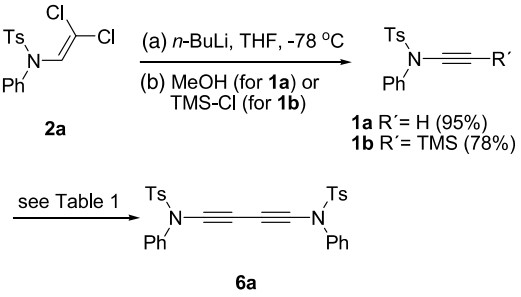
Cu(I)-catalyzed cross-coupling of amide derivatives **4** with readily available alkynyl halides **5** (X=Br, I).[20] This latter strategy was first developed by Hsung[21] and Danheiser,[22] for acyclic and cyclic carbamates, and cyclic ureas and was extended to sulfonamides and heteroaromatic substrates by Hsung[23] (using $CuSO_4$ as catalyst) and Sato.[24] Another straightforward protocol for the synthesis of ynamides involves base-induced isomerization of propargylic amides.[25]

In the course of our research on the synthesis of heterocyclic compounds we required several *N*-aryl ynamides (**1**; R= aryl, R′=H or protecting group) and arylynamides (**1**; R, R′=aryl).[26] To our surprise, only one such compound had previously been synthesized.[23] Here we describe the preparation of *N*-aryl and *N*-alkyl tosylynamides by Brückner's method; their homocoupling reactions; the preparation of *N*-aryl and *N*-alkyl arylynamides by Negishi coupling between the corresponding *N*-ethynylzinc tosylamides and appropriate aryl iodides, the preparation of *N*-ethynylphenyl ynamides and arylynamides by combinations of Sonogashira reactions[27] and Stang's[18] ethynyl(phenyl)iodonium salt approach; and the intramolecular [4+2] cycloaddition reactions of *N*-ethynylphenyl ynamides and arylynamides, which afford carbazoles and benzannulated and heteroannulated carbazoles.

2. Results and discussion

2.1. Preparation and homocoupling of *N*-aryl and *N*-alkyl tosylynamides[16a]

Our interest in the metal-catalyzed cyclization of diynes[28] led us to search the literature for methods for homodimerization of ynamides.[29] Finding none, we decided to evaluate the performance of common alkyne dimerization methods[30] when applied to selected ynamides, starting with aniline ynamides. Aniline ynamide **1a** was prepared as per Brückner[13a] by sequential treatment of the dichlorovinylamide **2a** with *n*-butyllithium and methanol (Scheme 2); similarly, trimethylsilyl ynamide **1b** was obtained in 78% yield by trapping the lithium acetylide with trimethylsilyl chloride.



Scheme 2. Preparation of *N*-phenyltosylynamides **1a**,**b**.

In our first attempt to dimerize ynamide **1a** (Table 1, entry 1) we used a palladium catalyst that had proved useful for other alkyne dimerizations in our laboratory.[31] However, in the presence of this catalyst **1a** gave a mixture from which the dimer **6a** could only be isolated in 40% yield, and similar results were obtained with other terminal alkynes.[32] We then tried copper catalysts.

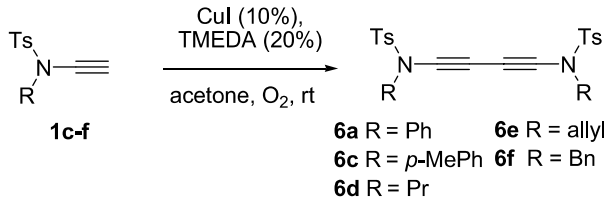
Table 1. Dimerization of *N*-phenyl tosylynamides **1a** and **1b**

Entry	Ynamide	Conditions[a]	Time	Yield **6a** (%)
1	**1a**	$PdCl_2(PPh_3)_2$, CuI, I_2, *i*-Pr_2NH, THF, rt	1 min	See text
2	**1a**	CuCl, TMEDA, acetone, O_2, rt	3 h	63
3	**1a**	$Cu(OAc)_2$, Py, rt	0.5 h	See text
4	**1a**	CuI, TMEDA, acetone, O_2, rt	3 h	91
5	**1a**	CuI, TMEDA, acetone, O_2, rt	1 h	88
6	**1b**	CuCl, DMF, 60 °C	0.5 h	88

[a] Amounts of catalyst: entry 1, 5% $PdCl_2(PPh_3)_2$, 5% CuI; entries 2 and 4, 10% CuX, 20% TMEDA; entry 3, 250% $Cu(OAc)_2$; entry 5, 50% CuI, 100% TMEDA; entry 6, 100% CuCl.

Classical Hay[33] conditions (CuCl, TMEDA, acetone, O_2) afforded dimer **6a** in 63% isolated yield as an air-stable white solid (entry 2). Copper(II) acetate in pyridine (entry 3) also brought about fast, clean conversion of the starting material (as shown by TLC monitoring), but the reaction product could not be isolated due to its decomposition in the presence of Cu_2SO_4 (5%) or HCl (5%) during work-up.[34] By contrast, the conditions reported by Pericàs[35] for the synthesis of 1,4-dialkoxy-1,3-butadiynes, which use 10% CuI instead of CuCl, afforded **6a** in 91% yield (entry 4). Furthermore, increasing the amount of catalyst to 50% shortened the reaction time to 1 h with minimal reduction of yield (entry 5). Trimethylsilyl ynamide **1b** was efficiently dimerized in DMF at 60 °C in the presence of CuCl (entry 6).[36]

We next applied the Pericàs conditions to ynamides **1c–f** (Scheme 3), all of which were prepared following Brückner's procedure.[13a] All these substrates afforded high yields of the corresponding Glaser adduct **6** (Table 2).



Scheme 3. Homocoupling of *N*-aryl and *N*-alkyl tosylynamides **1c–f**.

Table 2. Dimerization of *N*-substituted tosylynamides **1a**,**c**,**d**,**e** and **f**[a]

Entry	Ynamide, R	Product, yield (%)
1	**1a**, Ph	**6a**, 91
2	**1c**, *p*-MePh	**6c**, 84
3	**1d**, Pr	**6d**, 100
4	**1e**, Allyl	**6e**, 86
5	**1f**, Bn	**6f**, 91

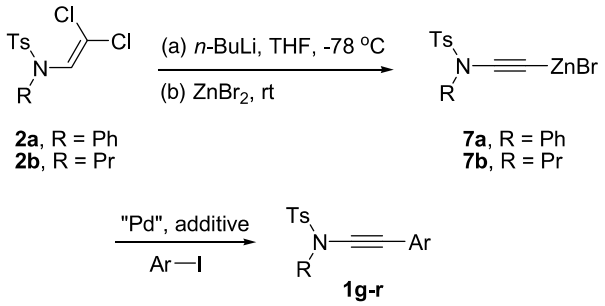
[a] Conditions: CuI (10%), TMEDA (20%), acetone, O_2, rt, 3 h.

All the *N*,*N*′-substituted-buta-1,3-diyne-1,4-ditosylamides **6** were isolated as air-stable white solids that withstood aqueous work-up procedures and chromatographic purification on silica gel. They have been stored at rt for weeks with no appreciable decomposition. Note that dimer **6f**, obtained in 91% yield from benzyl ynamide **1f**, can be

considered as masked 1,3-butadiyne-1,4-diamine, the tosyl and benzyl groups being easily removable under standard conditions.[37]

2.2. Synthesis of *N*-aryl and *N*-alkyl arylynamides by Negishi coupling[16b]

In our first experiments on using the Negishi approach[38] to obtain arylynamides, sequential treatment of *N*-phenyl ynamide **1a** with *n*-BuLi and $ZnBr_2$, followed by addition of $PdCl_2(PPh_3)_2$ and iodobenzene, led only to a low yield of dimer **6a**. When Pd_2dba_3 was used as palladium source, the cross-coupled product was obtained as well as **6a**, but the yield was very poor and the catalyst was contaminated by the starting ynamide. Finally, however, complete formation of zinc acetylide **7a** was achieved by treating the precursor of **1a**, dichlorovinylamide **2a**, with 2 equiv of *n*-BuLi followed by $ZnBr_2$ (Scheme 4).



Scheme 4. Preparation of *N*-aryl and *N*-alkyl arylynamides **1g–r** by Negishi coupling.

With zinc acetylide **7a** in hand we explored its palladium-catalyzed coupling with *p*-iodoanisole. $PdCl_2(PPh_3)_2$ and $Pd(PPh_3)_4$ showed no catalytic activity (Table 3, entries 1 and 2) and, when used alone, Pd_2dba_3 produced only small amounts of the desired coupled ynamide **1g** (entry 3).[39] However, when 20 mol% of PPh_3 was added the yield increased to 48% and was accompanied by an 18% yield of the dimer **6g** (entry 4). Using triphenylarsine or P(*o*-Tol)$_3$ instead of PPh_3 gave lower yields of **1g** with or without increased production of dimer **6g** (entries 5 and 6), and there was no reaction when PPh_3 was added without palladium (entry 7). The lithium analogue of **7a** slowly decomposed under the reaction conditions, affording only small amounts of **6g**.[39]

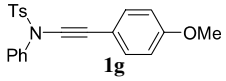
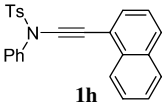
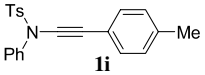
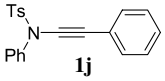
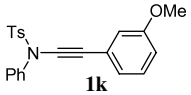
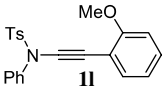
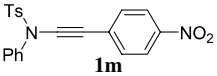
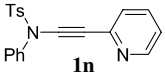
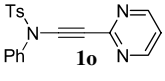
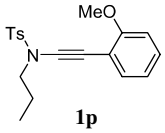
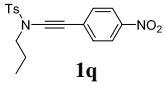
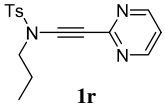
Table 3. Optimization of Negishi coupling of alkynylzinc **7a** and *p*-iodoanisole[a]

Entry	Catalyst (5%)	Additive (20%)	**1g** (%)	**6g** (%)[b]
1	$PdCl_2(PPh_3)_2$	None	0	ND
2	Pd $(PPh_3)_4$	None	0	ND
3	Pd_2dba_3	None	<5	ND
4	Pd_2dba_3	PPh_3	48	18
5	Pd_2dba_3	$AsPh_3$	38	18
6	Pd_2dba_3	P(*o*-Tol)$_3$	35	33
7	None	PPh_3	0	0
8[c]	Pd_2dba_3	PPh_3	0	ND

[a] Catalyst amount=5%, additive amount=20%; rt, 2 h.
[b] ND=not determined.
[c] Reaction with the lithium analogue of zinc acetylide **7a**.

The optimized conditions (5% Pd_2dba_3, 20% PPh_3) were then employed for the synthesis of the new *N*-phenyl aryl and heteroarylynamides **1h–o** (Table 4). The 1-naphthyl, 4-methylphenyl and phenyl derivatives **1h–j**, were obtained in quite good yields (entries 2–4). The *m*-anisole derivative **1k** was obtained in the same yield as its *para* analogue **1g** had been (entries 1 and 5), and the yield of the *ortho* analogue **1l** was only 25% (entry 6). As expected, however, coupling partners with an electron-withdrawing group (entry 7) or with electronegative heteroatoms (entries 8 and 9) afforded higher yields (81–92% after purification). Finally, the *N*-propyl arylynamides **1p–r** were also synthesized, in yields very similar to those of their *N*-phenyl counterparts **1l**, **1m** and **1o** (Table 4, entries 10–12).

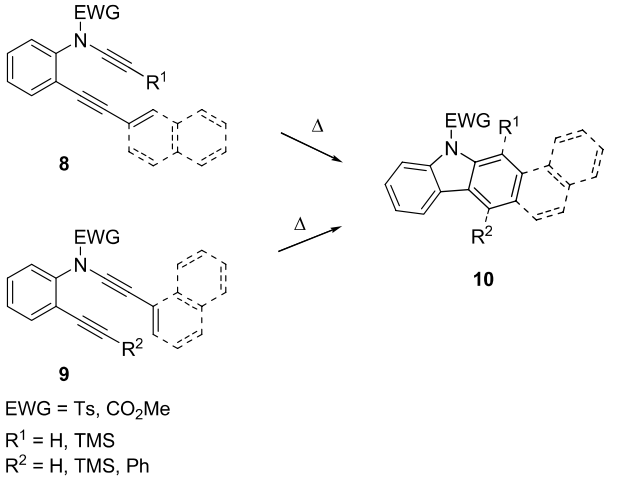
Table 4. Synthesis of arylynamides **1g–r** by Negishi cross-coupling

Entry	Vinyl-amide	I-Ar	Ynamide	Yield (%)[a]
1	**2a**	I-benzene	 **1g**	48
2	**2a**	2-I-naphthalene	 **1h**	63
3	**2a**	4-I-toluene	 **1i**	68
4	**2a**	4-I-anisole	 **1j**	69
5	**2a**	3-I-anisole	 **1k**	48
6	**2a**	2-I-anisole	 **1l**	25
7	**2a**	4-I-nitrobenzene	 **1m**	83
8	**2a**	2-I-pyridine	 **1n**	92
9	**2a**	2-I-pyrimidine	 **1o**	81
10	**2b**	2-I-anisole	 **1p**	24
11	**2b**	4-I-nitrobenzene	 **1q**	81
12	**2b**	2-I-pyrimidine	 **1r**	85

[a] Isolated yields of products purified by column chromatography.

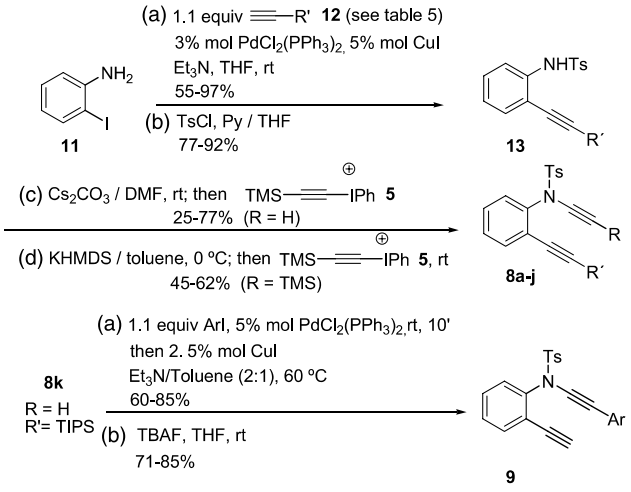
2.3. Intramolecular [4+2] cycloadditions of *N*-aryl ynamides 8 and *N*-aryl arylynamides 9[26]

In this section we report our approach to the synthesis of carbazoles[40] and benzannulated carbazoles **10** by means of intramolecular dehydro Diels–Alder (IDDA) reactions,[41] specifically, the intramolecular [4+2] cycloaddition of *N*-aryl ynamides **8** and *N*-aryl arylynamides **9** (Scheme 5).[42] Carbazoles constitute an important class of alkaloid displaying a wide variety of biological activities,[43] and their derivatives are also widely used as building blocks for new organic materials.[44]



Scheme 5. Carbazoles by intramolecular [4+2] cycloaddition of *N*-aryl ynamides **8** and *N*-aryl arylynamides **9**.

N-Aryl ynamides **8** and *N*-aryl arylynamides **9** were prepared in three and five steps, respectively, starting from commercially available *o*-iodoaniline (**11**) (Scheme 6). Sonogashira reactions between **11** and terminal alkynes **12**, followed by N-tosylation,[45] gave alkynes **13** (which were also obtained by Sonogashira reactions of tosylated **11** with **12**), and N-ethynylation of alkynes **13** with (trimethylsilyl)ethynyliodonium salt **5** then gave the desired *N*-aryl ynamides **8** (Table 5), generally, in good overall yields. Using Cs_2CO_3 as the base in the last step afforded terminal acetylenes **8** (R=H), using KHMDS retained the TMS group.[6c] *N*-aryl arylynamides **9** were synthesized in good yields by Sonogashira cross-coupling of aryl iodides with ynamide **8k**[27] (R=H, R′=TIPS) followed by desilylation.



Scheme 6. Preparation of *N*-aryl ynamides **8** and *N*-aryl arylynamides **9**.

Heating ynamides **8** in toluene at 150 °C (conditions A) generally gave poor to moderate yields of the desired intramolecular [4+2] cycloaddition.[41] Not unexpectedly, in most cases better results were obtained in a mixture of toluene and Et_3N (Table 5, conditions B).[41b,d] For example, for ynamide **8a** the change of medium raised the yield of 2-methylcarbazole **10a** from a poor 16% to an acceptable 40% (Table 5, entry 1). Remarkably, however, access to the interesting tetrahydro-5*H*-benzo[*b*]carbazole nucleus **10b** was achieved in 55% yield using toluene alone (entry 2).[46] This nucleus was also obtained using a carbamate instead of a tosylamide as substrate (**10c**, entry 3). Thus our metal-free IDDA approach to carbazoles nicely complements the intermolecular Rh(I)-catalyzed [2+2+2] cycloaddition of ynamides with alkynes,[6c] which is unable to create fused cyclohexyl rings.

Benzannulated carbazole ring systems are found only rarely in nature but are of considerable interest because of their potential antitumoral and other pharmacological properties,[40] and as building blocks for organic materials.[44] Several synthetic approaches to benzo[*b*]carbazoles (2-deazaellipticines) have been developed over the past half century,[40] including benzannulation of indoles,[47] Fischer indolization of phenylhydrazones,[48] Diels–Alder reactions of pyrano[3,4-*b*]indol-3-ones,[49] 4*H*-furo[3,4-*b*]indoles[50] and 2,4-dihydropyrrolo[3,4-*b*]indoles,[51] and cycloaromatization of *N*-[2-(1-alkynyl)phenyl]keteneimines;[52] yields have varied between 22 and 98%. The main failing of these methods is their lack of flexibility, since they almost exclusively allow the synthesis of the parent benzo[*b*]carbazole nucleus but not that of benz[*b*]annulated analogues. In this work, the 30% yield of benzo[*b*]carbazole **10d** that was obtained by heating **8d** in toluene was surprisingly reduced to 12–15% in basic or protic media (Table 5, entry 4).[41] Indeed, when a mixture of toluene and AcOH was used, hydrolysis of the ynamide group occurred giving **14d** in 68% yield (Fig. 1). However, the carbamate substrate **8e** gave more satisfactory yields of up to 50% (entry 5). Gratifyingly, unlike the methods mentioned above, the ynamide IDDA approach allowed uneventful preparation of benz[*b*]annulated carbazoles with additional benzene rings: heating ynamides **8f–h** in conditions B gave the known naphtho[1,2-*b*]carbazole[47d] **10f** in 90% yield (entry 6) and the hitherto unknown naphtho[2,1-*b*]carbazole **10g** (30% yield, entry 7) and dibenzo[*a*,*c*]carbazole **10h** (58% yield, entry 8).

We then investigated whether benzo[*c*]carbazoles might be prepared through rearrangement of the cyclic allene intermediate that would be formed in the course of the IDDA reaction of silylynamide **8i**.[53] Unfortunately, all attempts at IDDA reaction of **8i** led to its decomposition (entry 9), even when we tried to trap the putative initial cyclic allene in the presence of MeOH (entry 9). By contrast, silylynamide **8j**, in which the terminal phenyl of **8i** was replaced by a cyclohexenyl ring, smoothly cyclized in very good yields to the 6-(trimethylsilyl)tetrahydrobenzo[*b*]carbazole **10j** (entry 10).

Table 5. Results of intramolecular [4+2] cycloaddition of ynamides **8**

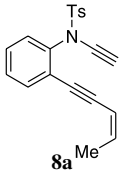
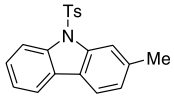
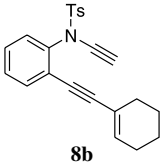
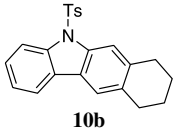
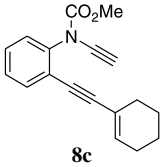
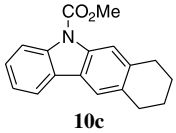
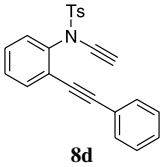
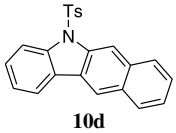
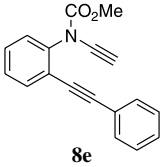
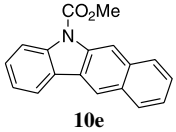
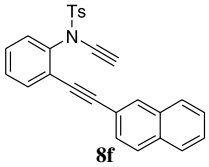
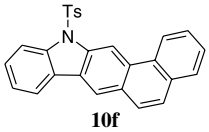
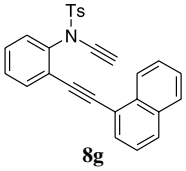
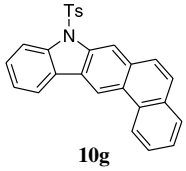
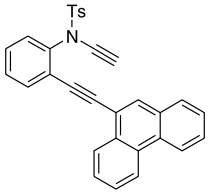
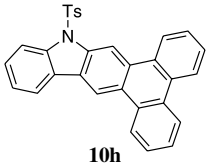
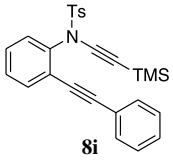
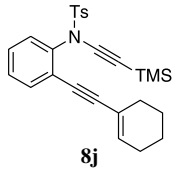
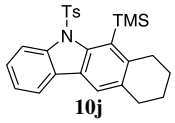
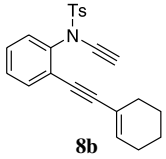
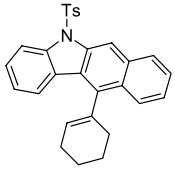
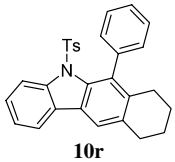
Entry	Ynamide	Carbazole	Yield (%)
1	 **8a**	 **10a**	16,[a] 40[b]
2	 **8b**	 **10b**	55[a]
3	 **8c**	 **10c**	35,[a] 43[b]
4	 **8d**	 **10d**	30,[a] 12,[b] 15[c]
5	 **8e**	 **10e**	42,[a] 50[b]
6	 **8f**	 **10f**	21,[a] 90[b]
7	 **8g**	 **10g**	10,[a] 30[b]
8	 **8h**	 **10h**	27,[a] 58[b]
9	 **8i**	decomp.[a,c]	

Table 5 (*continued*)

Entry	Ynamide	Carbazole	Yield (%)
10	 **8j**	 **10j**	72,[b] 85[c]
11[d]	 **8b**	 **10q** +  **10r**	8+16

[a] Experimental conditions. A: **8** (0.01 M), toluene (typically, 6 mL), 150 °C, sealed tube (normal).
[b] Conditions B: conditions A plus 0.5 mL of Et_3N.
[c] Conditions C: conditions A plus 0.5 mL of MeOH or ^{i}PrOH.
[d] PhI (1.1 equiv), 5% $Pd(PPh_3)_4$, 2% CuI, 2:1 Et_3N/toluene, 60 °C.

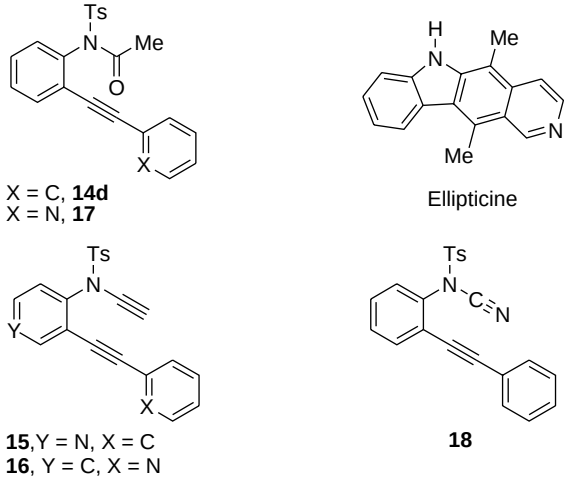


Figure 1.

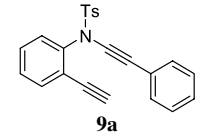
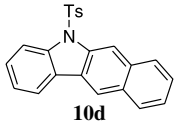
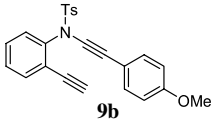
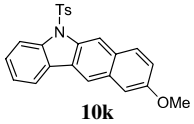
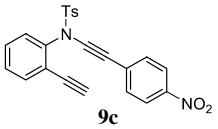
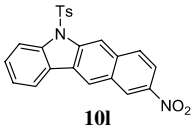
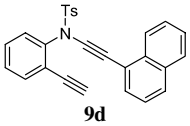
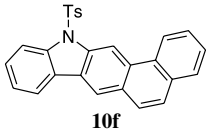
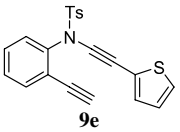
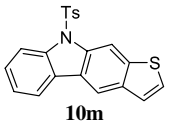
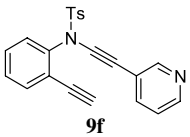
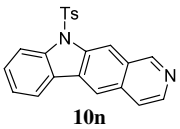
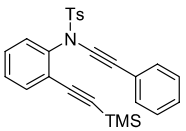
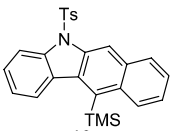
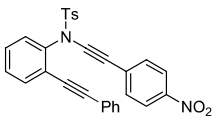
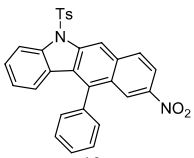
We were also unsuccessful in our attempts to prepare pyrido[4,3-*b*]benzo[*f*]indoles, pyrido[3,2-*b*]carbazoles or indolo[2,3-*b*]quinolines, which we sought as isomers of the skeleton of the interesting antitumoral agent ellipticine (Fig. 1).[40] Heating **15**[54] or **16** in toluene at 150 °C led to their decomposition, giving at best traces of the desired cyclized products; heating **16** in the presence of AcOH resulted in its 85% conversion into the hydrolysis product **17**; and heating cyanamide **18**[55] had no effect, a result that contrasts with the exceptionally easy photocyclizations of the related aryldiimides.[56]

When we investigated the intramolecular [4+2] cycloaddition reactions of arylynamides **9** we found that in toluene/Et_3N a much better yield of the benzo[*b*]carbazole **10d** was obtained from **9a** than from **8d**, 50% (Table 6, entry 1) as against 12% (Table 5, entry 4). This exemplifies a trend noted by Danheiser,[22b] that conjugated enynamides (in our case, **9a**) give better results than ynamides lacking such conjugation, such as **8d**, and in the case of **8d** may be due to the cyclic allene intermediate undergoing ring-opening reactions.[41,57] However, naphthylynamide **9d** gave a lower yield of naphthocarbazole **10f** than did **8f**, 73% (Table 6, entry 4) as against 90% (Table 5, entry 7). Surprisingly, the yields of the IDDA reactions of arylynamides **9** did not seem to be influenced by the electronic nature of the arylynamide moiety (Table 6, entries 2 and 3).

Unlike ynamides **15** and **16**, heteroarylynamides **9e** and **9f** responded to IDDA conditions, giving moderate yields of thienocarbazole **10m** and pyridocarbazole **10n** (Table 6, entries 5 and 6).[58] Also, the silylated benzo[*b*]carbazole **10o** was obtained in 31% yield from phenylynamide **9g** (Table 6, entry 7), silylynamide **8i** had failed to react (Table 5, entry 9).

Finally, we examined the regioselectivity of the dehydro Diels–Alder reaction by installing a second phenyl ring in the aryl *N*-substituent of the starting arylynamide: heating **9h** gave the 2-nitro-11-phenylbenzo[*b*]carbazole **10p** regioselectively,[59] (though in rather poor yield), showing that the cycloaddition occurred selectively on the conjugated arenynamide moiety (Table 6, entry 8). Interestingly, however when ynamide **8b** was subjected to Sonogashira conditions in the presence of iodobenzene, two carbazoles were isolated, 11-cyclohexenylbenzo[*b*]carbazole **10q** in 8% yield and 6-phenyltetrahydrobenzo[*b*]carbazole **10r** in 16% yield, suggesting that after initial phenylation of **8b**[27] the two possible cycloadditions had occurred in roughly 1:2 ratio (Table 5, entry 11).

Table 6. Results of intramolecular [4+2] cycloaddition of arylynamides **9**

Entry	Arylynamide	Carbazole	Yield (%)[a]
1	 **9a**	 **10d**	50
2	 **9b**	 **10k**	50
3	 **9c**	 **10l**	60
4	 **9d**	 **10f**	73
5	 **9e**	 **10m**	34
6	 **9f**	 **10n**	21
7	 **9g**	 **10o**	31
8	 **9h**	 **10p**	16

[a] Experimental conditions: **9** (0.01 M), toluene (typically, 6 mL) plus 0.5 mL of Et_3N, 150 °C, sealed tube.

3. Conclusions

The catalytic system CuI/TMEDA promotes dimerization of *N*-aryl- and *N*-alkyl tosylynamides in high yield. The resulting *N*,*N*′-substituted-buta-1,3-diyne-1,4-ditosylamides are air-stable solids. The use of these diynes in metal-catalyzed cyclization reactions is currently being explored in our laboratories.

Negishi coupling allows one-pot synthesis of *N*-aryl and *N*-alkyl arylynamides starting from readily available dichlorovinylamides, and intramolecular [4+2] cycloaddition reactions of *N*-ethynylphenyl ynamides and arylynamides afford carbazoles and benzannulated and heteroannulated carbazoles in relatively good yields. These results open new perspectives for the application of ynamides in the field of poly- and heterocyclic aromatic chemistry.

4. Experimental

4.1. General

All reactions were carried out under argon atmosphere with magnetic stirring. The solvents were purified and dried using standard procedures. All reagents were purchased and used without further purification. Melting points were measured using a Koefler melting point apparatus, and are uncorrected. ^1H and ^{13}C NMR spectra were obtained on a Brucker DPX-250 (250 and 63 MHz), AMX-300 (300 and 75 MHz) and Brucker WM-500 (500 and 125 MHz) spectrometers using $CDCl_3$ as solvent with tetramethylsilane as internal standard. Mass spectra were recorded on either a Hewlett-Packard HP5988A and Micromass Autospec MS (EI and HRMS) or an Applied 'API 4000' (ESI). Microanalyses were performed on a Thermo Finnigan Flash 112 at the University of Santiago de Compostela, Spain. Column chromatography was carried out using Merck 230–400 mesh ASTM silica gel.

4.2. Typical procedure for the homocoupling of tosylynamides

4.2.1. *N*,*N*′-1,3-Butadiyn-1,4-diyl-*N*,*N*′-diphenyl ditosylamide 6a. TMEDA (5 μL, 0.033 mmol) was added to a suspension of CuI (3 mg, 0.017 mmol) in dry acetone (4 mL) under O_2 atmosphere, at rt. After 15 min, a solution of **1a** (45 mg, 0.177 mmol) in acetone (4 mL) was added and the mixture was vigorously stirred until TLC showed complete comsuption of the starting material (3 h). After removal of the solvent, the crude residue was purified by column chromatography on silica gel using a mixture of hexanes/EtOAc 1:3 as eluent, yielding 41 mg (91%) of **6a** as white prisms, mp 157–159 °C (dec). ^1H NMR (250 MHz, $CDCl_3$) δ: 7.62–7.56 (m, 4H, ArH), 7.36–7.26 (m, 10H, ArH), 7.25–7.17 (m, 4H, ArH), 2.44 (s, 6H, 2×CH_3). ^{13}C NMR+DEPT (62.83 MHz, $CDCl_3$) δ: 145.3 (2×C), 138.2 (2×C), 133.1 (2×C), 129.7 (4×CH), 129.2 (4×CH), 128.7 (2×CH), 128.1 (4×CH), 126.4 (4×CH), 75.7 (2×C), 58.5 (2×C), 21.7 (2×CH_3). MS (70 eV) *m*/*z* (%): 545 (M^+-CH_3, 29), 369 (57), 322 (55), 278 (97), 247 (63), 218 (82), 139 (100), 91 (60). Elemental analysis calcd (%) for $C_{30}H_{24}N_2O_4S_2$: C 66.65, H 4.47, N 5.18, S 11.86; found: C 66.21, H 4.21, N 5.27, S 11.67.

4.2.2. *N*,*N*′-1,3-Butadiyn-1,4-diyl-*N*,*N*′-di-4-methylphenyl ditosylamide 6c. Brown powder, mp 125 °C (dec). ^1H NMR ($CDCl_3$) δ: 7.59 (d, J=8.2 Hz, 4H, ArH), 7.29 (d, J=8.2 Hz, 4H, ArH), 7.12 (d, J=8.5 Hz, 4H, ArH), 7.05 (d, J=8.5 Hz, 4H, ArH), 2.44 (s, 6H, CH_3), 2.34 (s, 6H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 145.2 (2×C), 138.8 (2×C), 135.5 (2×C), 133.0 (2×C), 129.8 (4×CH), 128.0 (4×CH), 126.3 (4×CH), 75.8 (2×C), 58.2 (2×C), 21.6 (2×CH_3), 21.0 (2×CH_3).

4.2.3. *N*,*N*′-1,3-Butadiyn-1,4-diyl-*N*,*N*′-dipropyl ditosylamide 6d. White powder, mp 90–92 °C. ^1H NMR ($CDCl_3$) δ: 7.79 (d, J=8.2 Hz, 4H, ArH), 7.37 (d, J=8.2 Hz, 4H,

ArH), 3.31 (t, J=7.2 Hz, 4H, CH_2), 2.47 (s, 6H, CH_3), 1.71–1.60 (m, 4H, CH_2), 0.89 (t, J=7.4 Hz, 6H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (2×C), 134.5 (2×C), 128.8 (4×CH), 127.4 (4×CH), 75.1 (2×C), 59.3 (2×C), 53.2 (2×CH_2), 21.5 (2×CH_3), 21.1 (2×CH_2), 10.6 (2×CH_3). MS (70 eV) m/z (%): 472 (M^+, 8), 248 (85), 206 (88), 162 (100).

4.2.4. *N*,*N*′-1,3-Butadiyn-1,4-diyl-*N*,*N*′-di-2-propenyl ditosylamide 6e. White powder, mp 109–111 °C. ^{1}H NMR ($CDCl_3$) δ: 7.79 (d, J=8.3 Hz, 4H, ArH), 7.36 (d, J=8.3 Hz, 4H, ArH), 5.49–5.63 (m, 2H, C*H*=CH_2), 5.24 (t, J=8.6 Hz, 4H, CH=CH_2), 4.00 (d, J=6.3 Hz, 4H, CH_2), 2.47 (s, 6H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 145.0 (2×C), 134.5 (2×C), 130.3 (2×CH), 129.8 (4×CH), 127.6 (4×CH), 120.4 (2×CH_2), 75.2 (2×C), 59.5 (2×C), 54.3 (2×CH_2), 21.6 (2×CH_3).

4.2.5. *N*,*N*′-1,3-Butadiyn-1,4-diyl-*N*,*N*′-dibenzyl ditosylamide 6f. White needles, mp 153 °C (dec). ^{1}H NMR ($CDCl_3$) δ: 7.68 (d, J=8.4 Hz, 4H, ArH), 7.30–7.21 (m, 14H, ArH), 4.52 (s, 4H, CH_2), 2.45 (s, 6H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (2×C), 134.6 (2×C), 134.1 (2×C), 129.8 (4×CH), 128.5 (4×CH), 128.4 (4×CH), 128.3 (2×CH), 127.6 (4×CH), 75.9 (2×C), 60.0 (2×C), 55.8 (2×CH_2), 21.7 (2×CH_3). MS (70 eV) m/z (%): 568 (M^+, 22), 413 (100), 139 (62).

4.3. Typical procedure for the preparation of arylynamides by Negishi coupling of zinc acetylides and aromatic iodides

4.3.1. *N*-Phenyl-*N*-(pyrimidin-2-yl)ethynyl tosylamide 1o. *n*-BuLi (0.56 mL, 1.6 M in hexanes) was slowly added to a solution of **2a** (0.15 g, 0.43 mmol) in dry THF (8 mL) cooled at −78 °C and the mixture was stirred for 5 min. A solution of $ZnBr_2$ (0.31 mL, 1.5 M in THF) was added via syringe and, after stirring for 20 additional minutes at rt, the reaction mixture was transferred via cannula to a solution of Pd_2dba_3 (22 mg, 0.02 mmol), PPh_3 (22 mg, 0.09 mmol) and 2-iodopyrimidine (0.11 g, 0.51 mmol) in dry THF (4 mL). After 3 h TLC showed complete consumption of the intermediate acetylide. The volatiles were removed and the resulting residue was solved in EtOAc (20 mL) and washed with brine (2×20 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude residue was purified by column chromatography on silica gel using hexane/EtOAc 1:2 as eluent to yield **1o** (0.12 g, 81%) as colorless prisms, mp 107–109 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.68–8.63 (m, 2H, ArH), 7.75–7.67 (m, 2H, ArH), 7.38–7.24 (m, 7H, ArH), 7.19–7.12 (m, 1H, ArH), 2.43 (s, 3H, CH_3). ^{13}C NMR+DEPT (62.83 MHz, $CDCl_3$) δ: 157.0 (2×CH), 153.2 (C), 145.3 (C), 137.7 (C), 132.8 (C), 129.6 (2×CH), 129.2 (2×CH), 128.7 (CH), 128.2 (2× CH), 126.5 (2×CH), 119.0 (CH), 82.3 (C), 71.4 (C), 21.6 (CH_3). Elemental analysis calcd (%) for $C_{19}H_{15}N_3O_2S$ (349.41): C 65.31, H 4.33, N 12.03, S 9.18; found: C 65.62, H 4.21, N 11.90, S 9.38.

4.3.2. *N*-(4-Methoxyphenyl)ethynyl-*N*-phenyl tosylamide 1g. White powder, mp 106–108 °C. ^{1}H NMR ($CDCl_3$) δ: 7.62 (d, J=8.3 Hz, 2H, ArH), 7.35–7.26 (m, 9H, ArH), 6.83 (d, J=8.3 Hz, 2H, ArH), 3.80 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 159.6 (C), 144.8 (C), 139.1 (C), 133.4 (CH), 133.0 (C), 129.4 (2×CH), 129.0 (2×CH), 128.3 (2×CH), 128.1 (2×CH), 126.2 (2×CH), 114.5 (C), 113.9 (2×CH), 81.5 (C), 70.2 (C), 55.3 (OCH_3), 21.7 (CH_3). MS (70 eV) m/z (%): 377 (M^+, 71), 222 (100), 119 (20).

4.3.3. *N*-(1-Naphthyl)ethynyl-*N*-phenyl tosylamide 1h. Clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.87–7.83 (m, 1H, ArH), 7.80 (d, J=7.5 Hz, 1H, ArH), 7.69 (d, J=8.4 Hz, 2H, ArH), 7.60 (dd, J=7.2, 1.2 Hz, 1H, ArH), 7.56–7.52 (m, 2H, ArH), 7.43–7.38 (m, 7H, ArH), 7.28 (d, J=8.4 Hz, 2H, ArH), 2.43 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 145.0 (C), 143.3 (C), 149.0 (C), 133.2 (C), 133.1 (C), 133.0 (C), 129.8 (CH), 129.6 (2×CH), 129.2 (2×CH), 128.9 (CH), 128.4 (CH), 128.3 (2×CH), 128.2 (CH), 126.7 (CH), 126.3 (CH), 126.2 (2×CH), 126.2 (CH), 125.2 (CH), 80.0 (C), 69.0 (C), 21.7 (CH_3). MS (70 eV) m/z (%): 397 (M^+, 15), 242 (100), 139 (13).

4.3.4. *N*-(4-Methylphenyl)ethynyl-*N*-phenyl tosylamide 1i. Pale brown powder, mp 113–115 °C. ^{1}H NMR ($CDCl_3$) δ: 7.61 (d, J=8.3 Hz, 2H, ArH), 7.32–7.25 (m, 9H, ArH), 7.10 (d, J=8.0 Hz, 2H, ArH), 2.43 (s, 3H, CH_3), 2.33 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 139.0 (C), 138.1 (C), 132.9 (C), 131.5 (2×CH), 129.4 (2×CH), 129.0 (3×CH), 128.2 (2×CH), 128.1 (2×CH), 126.2 (2×CH), 119.4 (C), 82.2 (C), 70.5 (C), 21.7 (CH_3), 21.4 (CH_3). MS (70 eV) m/z (%): 361 (M^+, 96), 297 (10), 206 (100).

4.3.5. *N*-Phenyl-*N*-(phenyl)ethynyl tosylamide 1j. Pale brown powder, mp 68–70 °C. ^{1}H NMR ($CDCl_3$) δ: 7.64 (d, J=7.9 Hz, 2H, ArH), 7.43–7.39 (m, 4H, ArH), 7.34–7.29 (m, 8H, ArH), 2.44 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 138.8 (C), 132.8 (C), 131.3 (2×CH), 129.4 (2×CH), 129.0 (2×CH), 128.9 (CH), 128.3 (2×CH), 128.2 (2×CH), 127.9 (CH), 126.2 (2×CH), 122.5 (C), 82.9 (C), 70.4 (C), 21.6 (CH_3). MS (70 eV) m/z (%): 347 (M^+, 22), 192 (100), 89 (18).

4.3.6. *N*-(3-Methoxyphenyl)ethynyl-*N*-phenyl tosylamide 1k. Clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.62 (d, J=8.4 Hz, 2H, ArH), 7.34–7.27 (m, 7H, ArH), 7.20 (t, J=7.9 Hz, 1H, ArH), 6.98 (d, J=7.6 Hz, 1H, ArH), 6.91 (dd, J=2.6, 1.1 Hz, 1H, ArH), 6.84 (ddd, J=8.3, 2.6, 1.0 Hz, 1H, ArH), 3.79 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 159.3 (C), 145.0 (C), 138.9 (C), 133.0 (C), 129.5 (2×CH), 129.3 (CH), 129.5 (2×CH), 128.3 (2×CH), 128.28 (CH), 126.3 (2×CH), 123.9 (CH), 123.6 (C), 116.3 (CH), 114.4 (CH), 82.8 (C), 70.5 (C), 55.3 (OCH_3), 21.7 (CH_3). MS (70 eV) m/z (%): 377 (M^+, 100), 222 (61), 119 (27).

4.3.7. *N*-(2-Methoxyphenyl)ethynyl-*N*-phenyl tosylamide 1l. Clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.69 (d, J=8.3 Hz, 2H, ArH), 7.38–7.23 (m, 9H, ArH), 6.91–6.85 (m, 2H, ArH), 3.87 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 160.0 (C), 144.7 (C), 139.1 (C), 133.1 (CH), 133.0 (C), 129.3 (2×CH), 128.9 (2×CH), 128.4 (2×CH), 128.0 (2×CH), 126.1 (2×CH), 120.4 (CH), 112.0 (C), 110.7 (CH), 86.6 (C), 67.0 (CH_3), 21.7 (CH_3). MS (70 eV) m/z (%): 377 (M^+, 24), 222 (100), 119 (27).

4.3.8. *N*-(4-Nitrophenyl)ethynyl-*N*-phenyl tosylamide 1m. Pale brown needles, mp 129–131 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.17 (d, J=8.7 Hz, 2H, ArH), 7.62 (d, J=8.2 Hz, 2H, ArH), 7.48 (d, J=8.7 Hz, 2H, ArH), 7.39–7.26 (m, 7H, ArH), 2.45 (s, 3H, CH_3). ^{13}C NMR/DEPT (62.83 MHz, $CDCl_3$) δ: 146.3 (C), 145.4 (C), 138.1 (C), 132.7 (C), 131.0 (2×CH), 130.0 (C), 129.7 (2×CH), 129.3 (2×CH), 128.7 (CH), 128.1 (2×CH), 126.3 (2×CH), 123.5 (2×CH), 89.7 (C), 69.8 (C), 21.7 (CH_3). MS (70 eV) *m*/*z* (%): 392 (M^+, 14), 237 (74), 91 (100).

4.3.9. *N*-Phenyl-*N*-(pyridin-2-yl)ethynyl tosylamide 1n. Clear oil. ^{1}H NMR (DMSO) δ: 8.55–8.51 (m, 1H, ArH), 7.79 (dt, J=7.9, 1.8 Hz, 1H, ArH), 7.67–7.60 (m, 2H, ArH), 7.52–7.42 (m, 6H, ArH), 7.36 8 (ddd, J=7.6, 4.8, 1.2 Hz, 1H, ArH), 7.30–7.25 (m, 2H, ArH), 2.42 (s, 3H, CH_3). ^{13}C NMR/DEPT (DMSO) δ: 150.0 (CH), 145.8 (C), 141.9 (C), 137.7 (CH), 136.7 (CH), 132.0 (C), 130.1 (2×CH), 129.7 (2×CH), 129.0 (C), 127.8 (2×CH), 126.5 (CH), 126.0 (2×CH), 123.0 (CH), 82.2 (C), 70.5 (C), 21.1 (CH_3). MS (70 eV) *m*/*z* (%): 348 (M^+, 14), 283 (100), 193 (10).

4.3.10. *N*-(4-Nitrophenylethynyl)-*N*-propyl tosylamide 1q. Clear oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.15 (d, J=8.7 Hz, 2H, ArH), 7.83 (d, J=8.0 Hz, 2H, ArH), 7.40 (d, J=8.7 Hz, 2H, ArH), 7.37 (d, J=8.0 Hz, 2H, ArH), 3.41 (t, J=7.2 Hz, 2H, CH_2N), 2.46 (s, 3H, CH_3), 1.78–1.70 (m, 2H, CH_2), 0.96 (t, J=7.4 Hz, 2H, CH_3). ^{13}C NMR/DEPT (62.83 MHz, $CDCl_3$) δ: 146.1 (C), 145.0 (C), 134.3 (C), 130.7 (2×CH), 130.3 (C), 129.9 (2×CH), 127.4 (2×CH), 123.5 (2×CH), 88.4 (C), 70.4 (C), 53.0 (CH_2), 21.6 (CH_3), 21.3 (CH_2), 10.7 (CH_3). MS (70 eV) *m*/*z* (%): 358 (M^+, 7), 150 (37), 91 (100).

4.4. Typical procedure for the preparation of ynamides 8

To a stirred solution of *N*-tosylaniline **13** (1 mmol) (or the corresponding carbamate) in dry DMF (20 mL) at rt was added Cs_2CO_3 (1.3 equiv). After 30 min, a solution of **5** (1.3 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise. Stirring was continued until starting materials disappeared (TLC monitoring, typically 5 h). Then, ether was added (10 mL) and the combined organic layers were extracted with water and brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. Purification of the residue by flash chromatography on silica gel using a gradient mixture of EtOAc/hexanes as eluent afforded ynamides **8** in good yields.

Ynamides **15** and **16** have been prepared following the same procedure.

4.4.1. *N*-Ethynyl-*N*-2-[(*Z*)-pent-3-en-1-ynyl]phenyl tosylamide 8a. Obtained in 68% yield as a clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.71 (d, J=8.3 Hz, 2H, ArH), 7.47–7.44 (m, 1H, ArH), 7.35–7.21 (m, 5H, ArH), 6.07–5.94 (m, 1H, C=CH), 5.47 (dd, J=10.7, 1.6 Hz, 1H, C=CH), 3.83 (s, 1H, C≡CH), 2.41 (s, 3H, CH_3), 1.90 (dd, J=6.9, 1.6 Hz, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 139.4 (CH), 137.8 (C), 134.2 (C), 133.4 (CH), 129.5 (2×CH), 129.1 (2×CH), 128.7 (CH), 128.3 (2×CH), 123.5 (C), 110.4 (C), 109.7 (CH), 92.2 (C), 89.0 (C), 75.8 (CH), 58.6 (C), 21.6 (CH_3), 16.2 (CH_3). MS (70 eV) *m*/*z* (%): 335 (M^+, 2), 156 (31), 123 (51), 91 (100). HRMS ($C_{20}H_{17}NO_2S$): calcd: 335.0980, found: 335.0979.

4.4.2. *N*-Ethynyl-*N*-2-[2-cyclohexen-1-ynyl]phenyl tosylamide 8b. Obtained in 80% yield as a clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.55 (d, J=8.2 Hz, 2H, ArH), 7.28–7.24 (m, 1H, ArH), 7.14–7.11 (m, 5H, ArH), 5.92 (br s, 1H, ArH), 2.70 (s, 1H, CCH), 2.27 (s, 3H, CH_3), 1.95–1.89 (m, 4H, CH_2), 1.46–1.44 (m, 4H, CH_2). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.6 (C), 137.8 (C), 135.8 (CH), 134.4 (C), 133.0 (CH), 129.4 (CH), 129.2 (2×CH), 128.9 (CH), 128.3 (CH), 128.2 (2×CH), 123.3 (C), 120.4 (C), 97.3 (C), 82.1 (C), 75.7 (CH), 58.7 (C), 28.5 (CH_2), 25.7 (CH_2), 22.1 (CH_2), 21.5 (CH_3), 21.4 (CH_2). MS (70 eV) *m*/*z* (%): 375 (M^+, 17), 180 (74), 123 (100). HRMS ($C_{23}H_{21}NO_2S$): calcd: 375.1293, found: 375.1290.

4.4.3. Methyl *N*-ethynyl-*N*-2-[2-cyclohexen-1-ynyl]-phenyl carbamate 8c. Clear oil, 10% yield. ^{1}H NMR ($CDCl_3$) δ: 7.45 (dd, J=6.5, 2.4 Hz, 1H, ArH), 7.41–7.24 (m, 3H, ArH), 6.22 (br s, 1H, ArH), 3.82 (s, 3H, CH_3), 2.82 (s, 1H, C≡CH), 2.21–2.18 (m, 4H, CH_2), 1.71–1.60 (m, 4H, CH_2). ^{13}C NMR/DEPT ($CDCl_3$) δ: 139.5 (C), 136.1 (CH), 132.4 (CH), 128.6 (CH), 128.3 (CH), 126.9 (CH), 122.4 (C), 120.4 (C), 97.3 (C), 81.9 (C), 76.3 (CH), 57.5 (C), 54.4 (CH_3), 29.0 (CH_2), 25.9 (CH_2), 22.3 (CH_2), 21.5 (CH_2).

4.4.4. *N*-Ethynyl-*N*-2-(2-phenylethynyl)phenyl tosylamide 8d. Obtained in 77% yield as a clear oil. ^{1}H NMR ($CDCl_3$) δ: 7.68 (d, J=7.8 Hz, 2H, ArH), 7.51–7.30 (m, 9H, ArH), 7.07 (d, J=7.8 Hz, 2H, ArH), 2.94 (s, 1H, C≡CH), 2.15 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 138.0 (C), 134.2 (C), 133.1 (CH), 131.4 (2×CH), 129.7 (CH), 129.5 (2×CH), 129.1 (CH), 128.9 (CH), 128.4 (CH), 128.1 (2×CH), 127.9 (2×CH), 122.6 (C), 122.5 (C), 95.3 (C), 84.6 (C), 75.6 (CH), 59.1 (C), 21.3 (CH_3). MS (FAB) m/z: 372 (M^++1, 3), 231 (61), 154 (79), 137 (100). HRMS FAB ($C_{23}H_{17}NO_2S$): calcd: (M+1) 372.1058, found: 372.1052.

4.4.5. Methyl *N*-ethynyl-*N*-2-(2-phenylethynyl)phenyl carbamate 8e. White solid, 20% yield, mp 111–112 °C. ^{1}H NMR ($CDCl_3$) δ: 7.61 (dd, J=7.6, 1.7 Hz, 1H, ArH), 7.57–7.54 (m, 2H, ArH), 7.44–7.39 (m, 2H, ArH), 7.38–7.34 (m, 4H, ArH), 3.85 (s, 3H, CH_3), 2.88 (s, 1H, C≡CH). ^{13}C NMR/DEPT ($CDCl_3$) δ: 139.9 (C), 132.7 (CH), 131.7 (2×CH), 129.3 (CH), 128.7 (CH), 128.5 (CH), 128.3 (2×CH), 127.2 (CH), 122.7 (C), 121.9 (C), 95.3 (C), 84.6 (C), 76.3 (CH), 57.7 (C), 54.5 (CH_3).

4.4.6. *N*-Ethynyl-*N*-2-[2-(naphthalen-2-yl)ethynyl]-phenyl tosylamide 8f. Clear oil, 31% yield. ^{1}H NMR ($CDCl_3$) δ: 7.80–7.71 (m, 6H, ArH), 7.54–7.37 (m, 7H, ArH), 7.05 (d, J=8.2 Hz, 2H, ArH), 2.98 (s, 1H, C≡CH), 2.01 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 138.3 (C), 134.5 (C), 133.3 (CH), 132.9 (C), 132.7 (C), 131.5 (CH), 130.0 (CH), 129.6 (CH), 129.5 (2×CH), 129.2 (CH), 129.0 (CH), 128.3 (2×CH), 128.2 (CH), 127.7 (CH), 127.6 (CH), 126.8 (CH), 126.6 (CH), 122.6 (C), 120.1 (C), 95.8 (C), 85.2 (C), 75.9 (CH), 59.2 (C), 21.3 (CH_3). MS (FAB) *m*/*z* (%): 422 (M^++1, 13), 397 (74), 243 (100).

4.4.7. *N*-Ethynyl-*N*-2-[2-(naphthalen-1-yl)ethynyl]phenyl tosylamide 8g. Clear oil, 25% yield. ^{1}H NMR ($CDCl_3$) δ: 8.35–8.31 (m, 1H, ArH), 7.84 (d, J=7.9 Hz, 2H, ArH), 7.69–7.39 (m, 10H, ArH), 6.87 (d, J=7.9 Hz, 2H, ArH), 3.02 (s, 1H, C≡CH), 1.83 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 138.1 (C), 134.3 (C), 133.6 (CH), 132.94 (C), 132.89 (C), 130.7 (CH), 130.1 (CH), 129.4 (2×CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 128.2 (2×CH), 128.0 (CH), 126.7 (CH),126.6 (CH), 126.4 (CH), 125.0 (CH), 122.9 (C), 120.5 (C), 93.4 (C), 89,4 (C), 76.1 (CH), 59.1 (C), 21.1 (CH_3). MS (FAB) *m/z* (%): 422 (M^++1, 5), 301 (13), 282 (100). HRMS FAB ($C_{27}H_{19}NO_2S$): calcd (M+1): 422.1214, found: 422.1212.

4.4.8. *N*-Ethynyl-*N*-2-[2-(phenanthren-10-yl)ethynyl]-phenyl tosylamide 8h. Clear oil, 69% yield. ^{1}H NMR ($CDCl_3$) δ: 8.71–8.67 (m, 3H, ArH), 8.44 (d, J=7.5 Hz, 1H, ArH), 7.87–7.85 (m, 2H, ArH), 7.72–7.63 (m, 6H, ArH), 7.47–7.43 (m, 3H, ArH), 6.86 (d, J=8.0 Hz, 2H, ArH), 3.05 (s, 1H, C≡CH), 1.74 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 138.2 (C), 134.3 (C), 133.6 (CH), 132.2 (CH), 130.9 (C), 130.6 (C), 130.2 (C), 130.0 (CH), 129.7 (C), 129.34 (2×CH), 129.28 (CH), 129.2 (CH), 128.5 (CH), 128.2 (2×CH), 127.6 (CH), 127.3 (CH), 127.0 (CH), 126.9 (2×CH), 122.8 (C), 122.5 (CH), 122.4 (CH), 119.2 (C), 93.6 (C), 89.1 (C), 76.2 (CH), 59.2 (C), 20.9 (CH_3). FAB *m/z* (%): 472 (M^++1, 13), 293 (100), 137 (67). HRMS FAB ($C_{31}H_{21}NO_2S$): calcd (M+1): 472.1371, found: 472.1369.

4.4.9. *N*-(Trimethylsilyl)ethynyl-*N*-2-(2-phenylethynyl)-phenyl tosylamide 8i. To a stirred solution of *N*-tosylaniline **13** (1 mmol) in dry toluene (10 mL) at 0 °C was added KHMDS dropwise (1.2 equiv). After 15 min a solution of **5** (1.4 mmol) in dry CH_2Cl_2 (4 mL) was added and stirring was continued overnight. The reaction mixture was concentrated, dissolved in ether (10 mL), extracted with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. Purification of the residue by flash chromatography on silica gel using a mixture of 10% EtOAc in hexanes as eluent afforded ynamide **8i** as a white powder in 62% yield, mp 124–126 °C. ^{1}H NMR ($CDCl_3$) δ: 7.85 (d, J=8.2 Hz, 2H, ArH), 7.66–7.61 (m, 9H, ArH), 7.24 (d, J=8.2 Hz, 2H, ArH), 2.32 (s, 3H, CH_3), 0.24 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.8 (C), 138.5 (C), 134.4 (C), 133.2 (CH), 131.6 (2×CH), 129.8 (CH), 129.4 (2×CH), 128.9 (2×CH), 128.8 (CH), 128.5 (2×CH), 127.9 (2×CH), 122.7 (C), 122.5 (C), 95.4 (C), 94.3 (C), 85.0 (C), 73.1 (C), 21.4 (CH_3), 0.0 ($Si(CH_3)_3$). MS (70 eV) *m/z* (%): 443 (M^+, 6), 304 (32), 288 (100); HRMS ($C_{26}H_{25}NO_2SSi$): calcd: 443.1375, found: 443.1368.

4.4.10. *N*-(Trimethylsilyl)ethynyl-*N*-2-[2-cyclohexen-1-ynyl]phenyl tosylamide 8j. Clear oil, 45% yield. ^{1}H NMR ($CDCl_3$) δ: 7.71 (d, J=8.4 Hz, 2H, ArH), 7.42–7.40 (m, 1H, ArH), 7.31–727 (m, 5H, ArH), 6.1 (s, 1H, C=CH), 2.43 (s, 3H, CH_3), 2.09–2.08 (br s, 2H, CH_2), 2.02–2.01 (br s, 2H, CH_2), 1.62–1.58 (m, 4H, CH_2), 0.13 (s, 3H, $Si(CH_3)_3$). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.5 (C), 138.2 (C), 135.9 (CH), 134.6 (C), 133.2 (CH), 129.3 (3×CH), 128.9 (CH), 128.7 (2×CH), 128.3 (CH), 123.4 (C), 120.5 (C), 97.4 (C), 94.4 (C), 82.4 (C), 72.8 (C), 28.7 (CH_2), 25.7 (CH_2), 22.2 (CH_2), 21.7 (CH_3), 21.5 (CH_2), 0.0 ($Si(CH_3)_3$).

4.4.11. *N*-Ethynyl-*N*-3-(2-phenylethynyl)pyridyl tosylamide 15. Clear oil, 12% yield. ^{1}H NMR ($CDCl_3$) δ: 8.75 (s, 1H, ArH), 8.59 (d, J=5.3 Hz, 1H, ArH), 7.69 (d, J=8.1 Hz, 2H, ArH), 7.42–7.27 (m, 6H, ArH), 7.13 (d, J=8.1 Hz, 2H, ArH), 2.99 (s, 1H, C≡CH), 2.20 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 154.3 (CH), 149.4 (CH), 145.5 (C), 145.2 (C), 133.9 (C), 131.5 (2×CH), 129.8 (2×CH), 129.1 (CH), 128.2 (2×CH), 128.1 (2×CH), 123.5 (CH), 122.1 (C), 118.7 (C), 98.9 (C), 81.7 (C), 74.4 (CH), 60.6 (C), 21.5 (CH_3). MS (70 eV) *m/z* (%): 372 (M^+, 2), 308 (59), 217 (100). HRMS ($C_{22}H_{16}N_2O_2S$): calcd: 372.0925, found: 372.0932.

4.4.12. *N*-Ethynyl-*N*-2-[2-(pyrid-2-yl)ethynyl)]phenyl tosylamide 16. Clear oil, 50% yield. ^{1}H NMR ($CDCl_3$) δ: 8.58 (d, J=4.4 Hz, 1H, ArH); 7.70 (d, J=8.2 Hz, 2H, ArH), 7.64–7.60 (m, 2H, ArH), 7.40–7.39 (m, 3H, ArH), 7.27–7.22 (m, 1H, ArH), 7.12 (d, J=8.1 Hz, 2H, ArH), 2.94 (s, 1H, C≡CH), 2.22 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 149.7 (CH), 145.0 (C), 142.9 (C), 138.6 (C), 135.8 (CH), 134.1 (C), 133.8 (CH), 129.7 (CH), 129.6 (2×CH+CH), 129.2 (CH), 128.2 (2×CH), 127.5 (CH), 122.9 (CH), 94.1 (C), 84.4 (C), 75.8 (CH), 59.1 (C), 21.5 (CH_3). MS (70 eV) *m/z* (%): 372 (M^+, 100), 217 (36), 190 (14). HRMS ($C_{22}H_{16}N_2O_2S$): calcd: 372.0932, found: 372.0943.

4.5. Typical procedure for the preparation of aryl ynamides 9

A solution of 1 mmol of ynamide **8k**, 1.1 mmol of iodoarene and 0.05 mmol of $Pd(PPh_3)_4$ in 7.5 mL of Et_3N and 3.7 mL of toluene was stirred at rt for 10 min. Then, 0.02 mmol of CuI was added and the reaction mixture was heated at 60 °C until starting material disappeared (TLC monitoring, 4–8 h). The mixture was diluted with EtOAc, filtered through silica, and concentrated to dryness. Purification of the residue by flash chromatography on silica gel using a gradient mixture of EtOAc/hexanes as eluent afforded TIPS-protected arylynamides **9a–f′** in good yields.

Excess of tetrabutylammonium fluoride (1.0 M solution in THF) was added to a solution of TIPS-protected arylynamides **9a–f′** (0.1 mmol) in THF (10 mL), and the resulting mixture was stirred at rt for 10 min. After solvent removal, the residue was dissolved in EtOAc, washed with brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. The residue was purified by flash chromatography on silica gel using a gradient mixture of EtOAc/hexanes as eluent giving arylynamides **9a–f** in good yields.

4.5.1. *N*-2-Ethynylphenyl-*N*-2-phenylethynyl tosylamide 9a. Clear oil, 60% yield (overall). ^{1}H NMR ($CDCl_3$) δ: 7.77 (d, J=8.3 Hz, 2H, ArH), 7.53 (dd, J=6.3, 3.3 Hz, 1H, ArH), 7.41–7.26 (m, 10H, ArH), 3.09 (s, 1H, C≡CH), 2.44 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.9 (C), 139.7 (C), 134.1 (CH+CH), 133.7 (C), 131.3 (2×CH), 129.5 (2×CH), 128.9 (2×CH), 128.4 (2×CH), 128.1 (2×CH), 127.7 (CH), 122.6 (C), 122.0 (C), 83.1 (C), 82.5 (C), 78.7 (CH), 70.1 (C), 21.5 (CH_3). FAB *m/z* (%): 372 (M^++1) (1), 154 (89), 137 (100). HRMS ($C_{23}H_{18}NO_2S$): calcd: 372.1058, found: 372.1064.

4.5.2. *N*-2-Ethynylphenyl-*N*-2-(4-methoxyphenyl)-ethynyl tosylamide 9b. Clear oil, 44% yield (overall). ^{1}H NMR ($CDCl_3$) δ: 7.75 (d, J=8.4 Hz, 2H, ArH), 7.52 (dd, J=6.9, 2.4 Hz, 1H, ArH), 7.39–7.27 (m, 7H, ArH), 6.81 (d, J=8.9 Hz, 2H, ArH), 3.79 (s, 3H, OCH_3), 3.06 (s, 1H, C≡CH), 2.46 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 159.5 (C), 144.8 (C), 140.1 (C), 134.2 (CH), 134.1 (C), 133.5 (2×CH), 129.5 (CH), 129.5 (2×CH), 129.1 (CH), 128.8 (CH), 128.6 (2×CH), 122.2 (C), 114.7 (C), 113,8 (2×CH), 82.9 (C), 81.2 (C), 79.0 (CH), 69.9 (C), 55.2 (CH_3), 27.7 (CH_3).

4.5.3. *N*-2-Ethynylphenyl-*N*-2-(4-nitrophenyl)ethynyl tosylamide 9c. Clear oil, 65% yield (overall). ^{1}H NMR ($CDCl_3$) δ: 8.14 (d, J=8.9 Hz, 2H, ArH), 7.75 (d, J=8.3 Hz, 2H, ArH), 7.55 (dd, J=6.6, 2.7 Hz, 1H, ArH), 7.48–7.34 (m, 7H, ArH), 3.05 (s, 1H, C≡CH), 2.47 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 146.2 (C), 145.4 (C), 138.9 (C), 134.2 (CH), 130.9 (2×CH), 130.2 (C), 129.7 (2×CH), 129.6 (CH), 129.3 (CH), 129.1 (CH), 128.4 (2×CH), 123.4 (2×CH), 121.9 (C), 88.3 (C), 83.3 (CH), 78.4 (C), 70.0 (C), 60.3 (C), 21.6 (CH_3).

4.5.4. *N*-2-(2-Triisopropylsilylethynyl)phenyl-*N*-2-(naphthalen-1-yl)ethynyl tosylamide 9d′. Clear oil, 62% yield. ^{1}H NMR ($CDCl_3$) δ: 8.26 (d, J=8.0 Hz, 1H, ArH), 7.86–7.72 (m, 4H, ArH), 7.63 (t, J=7.1 Hz, 1H, ArH), 7.52 (d, J=6.0 Hz, 2H, ArH), 7.44–7.17 (m, 6H, ArH), 6.98 (d, J=8.0 Hz, 1H, ArH), 2.45 (s, 3H, CH_3), 1.09 (br s, 21H, $Si(CH(CH_3)_2)_3$). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.8 (C), 144.7 (C), 139.5 (C), 136.6 (C), 134.7 (C), 134.6 (CH), 133.1 (C), 133.06 (C), 129.7 (2×CH), 129.5 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.4 (2×CH), 128.0 (CH), 127.8 (CH), 126.4 (CH), 126.2 (CH), 125.0 (CH), 102.0 (C), 98.1 (C), 87.7 (C), 68.5 (C), 21.6 (CH_3), 18.6 (CH_3), 11.3 (CH).

4.5.5. *N*-2-(2-Triisopropylsilylethynyl)phenyl-*N*-2-(thien-2-yl)ethynyl tosylamide 9e′. Clear oil, 80% yield. ^{1}H NMR ($CDCl_3$) δ: 7.77 (d, J=8.3 Hz, 2H, ArH), 7.58 (dd, J=7.0, 2,0 Hz, 1H, ArH), 7.34–7.22 (m, 5H, ArH), 7.13 (dd, J=3.6, 1.1 Hz, 1H, ArH), 7.04 (dd, J=7.5, 1.7 Hz, 1H, ArH), 6.93 (dd, J=5.2, 3.6 Hz, 1H, ArH), 2.46 (s, 3H, CH_3), 1.16 (br s, 21H, $Si(CH(CH_3)_2)_3$). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.7 (C), 139.4 (C), 134.6 (C), 134.4 (CH), 132.8 (CH), 129.6 (2×CH), 129.0 (CH), 128.9 (CH), 128.3 (2×CH), 127.9 (CH), 127.6 (CH), 126.8 (CH), 124.2 (C), 123.0 (C), 102.0 (C), 97.8 (C), 86.3 (C), 63.2 (C), 21.7 (CH_3), 18.7 (CH_3), 11.3 (CH).

4.5.6. *N*-2-Ethynylphenyl-*N*-2-(pyridin-3-yl)ethynyl tosylamide 9f. Clear oil, 55% yield (overall). ^{1}H NMR ($CDCl_3$) δ: 8.59 (s, 1H, ArH), 8.49 (d, J=4.8 Hz, 1H, ArH), 7.76 (d, J=8.4 Hz, 2H, ArH), 7.66 (dt, J=7.9, 1.7 Hz, 1H, ArH), 7.55 (dd, J=6.9, 2.3 Hz, 1H, ArH), 7.44–7.32 (m, 5H, ArH), 7.22 (dd, J=7.8, 4.8 Hz, 1H, ArH), 3.05 (s, 1H, C≡CH), 2.48 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 152.0 (CH), 148.1 (CH), 145.2 (C), 139.4 (C), 138.2 (CH), 134.3 (2×CH +C), 133.9 (C), 129.6 (2×CH+CH), 129.2 (CH), 129.1 (CH), 128.5 (CH), 122.9 (CH), 122.0 (C), 85.5 (C), 83.2 (CH), 78.6 (C), 67.3 (C), 21.7 (CH_3). FAB *m/z* (%): 373 (M^++1, 100), 218 (90). HRMS ESI-TOF: ($C_{22}H_{17}N_2O_2S$): calcd: 373.1005, found: 373.1013.

4.5.7. *N*-2-(2-Trimethylsilylethynyl)phenyl-*N*-2-phenylethynyl tosylamide 9g. Obtained as a white powder in 80% yield by silylation of **9a**. ^{1}H NMR ($CDCl_3$) δ: 7.75 (d, J=8.3 Hz, 2H, ArH), 7.52–7.50 (m, 1H, ArH), 7.36–7.24 (m, 10H, ArH), 2.45 (s, 3H, CH_3), 0.08 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR/DEPT ($CDCl_3$) δ: 144.7 (C), 139.2 (C), 134.5 (C), 134.1 (CH), 131.0 (2×CH), 129.6 (2×CH), 129.1 (2×CH), 128.7 (CH), 128.5 (2×CH), 128.1 (2×CH), 127.4 (CH), 123.0 (C), 122.8 (C), 101.3 (C), 98.8 (C), 82.5 (C), 70.6 (C), 21.7 (CH_3), −0.4 ($Si(CH_3)_3$). MS (ESI-TOF) *m/z* (%): 466 (M^++Na, 16). HRMS ($C_{26}H_{25}NO_2SSiNa$): calcd: 466.1267, found: 466.1282.

4.5.8. *N*-2-(2-Phenylethynyl)phenyl-*N*-2-(4-nitrophenyl)-ethynyl tosylamide 9h. Clear oil, 46% yield. ^{1}H NMR ($CDCl_3$) δ: 8.10 (d, J=8.5 Hz, 2H, ArH), 7.73 (d, J=8.5 Hz, 2H, ArH), 7.57–7.52 (m, 2H, ArH), 7.46–7.41 (m, 4H, ArH), 7.28–7.10 (m, 7H, ArH), 2.18 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 146.1 (C), 145.3 (C), 138.0 (C), 134.0 (C), 133.4 (CH), 131.3 (2×CH), 130.8 (2×CH), 130.3 (C), 129.9 (CH), 129.7 (2×CH), 129.3 (CH), 129.1 (CH), 128.6 (CH), 128.2 (2×CH), 127.9 (2×CH), 123.5 (2×CH), 122.4 (C), 122.3 (C), 95.6 (C), 88.4 (C), 84.4 (C), 70.6 (C), 21.4 (CH_3). MS (70 eV) *m/z* (%): 492 (M^+, 29), 337 (100), 281 (59). HRMS ($C_{29}H_{20}N_2O_4S$): calcd: 492.1143, found: 492.1127.

Obtained by Negishi coupling of **2** (EWG=Ts, R=2-(2-phenylethynyl)phenyl) with *p*-nitroiodobenzene.

4.5.9. *N*-2-[2-(Pyrid-2-yl)ethynyl)]phenyl tosylacetamide 17. Clear oil, 50% yield. ^{1}H NMR ($CDCl_3$) δ: 8.56 (d, J=4.5 Hz, 1H, ArH), 8.01 (d, J=8.2 Hz, 2H, ArH), 7.75–7.71 (m, 1H, ArH), 7.57–7.47 (m, 4H, ArH), 7.25–7.20 (m, 1H, ArH), 7.14 (d, J=8.2 Hz, 2H, ArH), 6.97 (d, J=7.8 Hz, 1H, ArH), 2.21 (s, 3H, CH_3), 1.98 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 390 (M^+, 1), 348 (70), 283 (100).

4.5.10. *N*-2-(2-Phenylethynyl)phenyl tosylcyanamide 18. White solid, 51% yield. ^{1}H NMR ($CDCl_3$) δ: 7.97 (d, J=8.1 Hz, 2H, ArH), 7.53–7.34 (m, 4H, ArH), 7.21–7.05 (m, 5H, ArH), 6.70 (d, J=8.1 Hz, 2H, ArH), 2.09 (s, 3H, CH_3). ^{13}C NMR/DEPT ($CDCl_3$) δ: 162.0 (C), 145.6 (C), 136.9 (C), 135.1 (C), 132.8 (CH), 131.2 (CH), 131.1 (2×CH), 130.7 (2×CH), 129.7 (CH), 129.3 (CH), 128.9 (2×CH), 128.6 (CH), 127.9 (2×CH), 122.8 (C), 121.5 (C), 95.1 (C), 85.2 (C), 21.4 (CH_3).

Acknowledgements

We thank the Ministerio de Ciencia y Tecnología (Spain), the European Regional Development Fund and the Xunta de Galicia (XUGA) for financial support under projects BQU2002-02135 and PGIDT03PXIC20909PN. M.F. Martínez-Esperón and D. Rodríguez also thank XUGA and the Universidad de Santiago de Compostela for predoctoral and postdoctoral grants, respectively.

References and notes

1. For reviews on ynamides, see: (a) Mulder, J. A.; Kurtz, K. C. M.; Hsung, R. P. *Synlett* **2003**, 1379–1390. (b) Zificsak,

C. A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L.-L. *Tetrahedron* **2001**, *57*, 7575–7606.
2. For reviews on ynamines, see: (a) Himbert, G. In *Methoden Der Organischen Chemie (Houben-Weyl)*; Kropf, H., Schaumann, E., Eds.; Georg Thieme: Stuttgart, 1993; pp 3267–3443. (b) Collard-Motte, J.; Janousek, Z. *Top. Curr. Chem.* **1986**, *130*, 89. (c) Ficini, J. *Tetrahedron* **1976**, *32*, 1449–1486. For 'push–pull' ynamines, see: (d) Murch, P.; Williamson, B. L.; Stang, P. J. *Synthesis* **1994**, 1255–1256.
3. For the first ynamides, see: Janousek, Z.; Collard, J.; Viehe, H. G. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 917.
4. (a) Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 489–492. (b) Witulski, B.; Gössmann, M. *Chem. Commun.* **1999**, 1879–1880. (c) Rainier, J. D.; Imbriglio, J. E. *Org. Lett.* **1999**, *1*, 2037–2039. (d) Rainier, J. D.; Imbriglio, J. E. *J. Org. Chem.* **2000**, *65*, 7272–7276. (e) Witulski, B.; Gössmann, M. *Synlett* **2000**, 1793–1797.
5. Witulski, B.; Buschmann, N.; Bergsträsser, U. *Tetrahedron* **2000**, *56*, 8473–8480.
6. (a) Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2426–2430. (b) Witulski, B.; Stengel, T.; Fernández-Hernández, J. M. *Chem. Commun.* **2000**, 1965–1966. (c) Witulski, B.; Alayrac, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3281–3284. For an Ru(II)-catalyzed [2+2] cycloaddition, see: (d) Ridell, N.; Villeneuve, K.; Tam, W. *Org. Lett.* **2005**, *7*, 3681–3684.
7. Witulski, B.; Lumtscher, J.; Bergsträsser, U. *Synlett* **2003**, 708–710.
8. (a) Saito, N.; Sato, Y.; Mori, M. *Org. Lett.* **2002**, *4*, 803–805. (b) Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417–2420.
9. Marion, F.; Courillon, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 5095–5097.
10. Marion, F.; Coulomb, J.; Courillon, C.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2004**, *6*, 1509–1511.
11. Couty, S.; Liégault, B.; Meyer, C.; Cossy, J. *Org. Lett.* **2004**, *6*, 2511–2514.
12. (a) Hsung, R. P.; Zificsak, C.; Wei, L.-L.; Douglas, C. J.; Xiong, H.; Mulder, J. *Org. Lett.* **1999**, *1*, 1237–1240. (b) Mulder, J. A.; Hsung, R. P.; Frederick, M. O.; Tracey, M. R.; Zificsak, C. A. *Org. Lett.* **2002**, *4*, 1383–1386. (c) Frederick, M.; Hsung, R. P.; Lambeth, R. H.; Mulder, J. A.; Tracey, M. R. *Org. Lett.* **2003**, *5*, 2663–2666.
13. (a) Brückner, D. *Synlett* **2000**, 1402–1404. (b) Hoffmann, R. W.; Brückner, D. *New J. Chem.* **2001**, *25*, 369–373.
14. (a) Viehe, H. G. *Chemistry of Acetylenes*; Marcel Dekker: New York, 1969; pp 861–912. For variations of Viehe's original sequence, see: (b) Bloxham, J.; Dell, C. P. *J. Chem. Soc., Perkin Trans. 1* **1993**, 3055–3059. (c) Wei, L.-L.; Mulder, J. A.; Xiong, H.; Zificsak, C. A.; Douglas, C. J.; Hsung, R. P. *Tetrahedron* **2001**, *57*, 459–466.
15. Joshi, R. V.; Xu, Z.-Q.; Ksebati, M. B.; Kessel, D.; Corbett, T. H.; Drach, J. C.; Zemlicka, J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1089–1098.
16. (a) Rodríguez, D.; Castedo, L.; Saá, C. *Synlett* **2004**, 377–379. (b) Rodríguez, D.; Castedo, L.; Saá, C. *Synlett* **2004**, 783–786.
17. Feldman, K. S.; Bruendl, M. M.; Schildknegt, K.; Bohnstedt, A. C. *J. Org. Chem.* **1996**, *61*, 5440–5452.
18. Zhdankin, V. V.; Stang, P. *J. Chem. Rev.* **2002**, *102*, 2523–2584 and references therein.
19. For reviews, see: (a) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131–209. (b) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067. See also: (c) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421–7428.
20. For reviews on halo acetylenes, see: (a) Hopf, H.; Witulski, B. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995; pp 33–66. (b) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: New York, 1988.
21. Frederick, M. O.; Mulder, J. A.; Tracey, M. R.; Hsung, R. P.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 2368–2369.
22. (a) Dunetz, J. R.; Danheiser, R. L. *Org. Lett.* **2003**, *5*, 4011–4014. (b) Dunetz, J. R.; Danheiser, R. L. *J. Am. Chem. Soc.* **2005**, *127*, 5776–5777.
23. Zhang, Y.; Hsung, R.; Tracedy, M. R.; Kurtz, K. C. M.; Vera, E. L. *Org. Lett.* **2004**, *6*, 1151–1154.
24. Hirano, S.; Tanaka, R.; Urabe, H.; Sato, F. *Org. Lett.* **2004**, *6*, 727–729.
25. Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417–2420 and references therein.
26. Martínez-Esperón, M. F.; Rodríguez, D.; Castedo, L.; Saá, C. *Org. Lett.* **2005**, *7*, 2213–2216.
27. Tracey, M. R.; Zhang, Y.; Frederick, M. O.; Mulder, J. A.; Hsung, R. P. *Org. Lett.* **2004**, *6*, 2209–2212.
28. (a) Varela, J. A.; Castedo, L.; Maestro, M.; Mahía, J.; Saá, C. *Chem. Eur. J.* **2001**, *7*, 5203–5213. (b) Varela, J. A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120*, 12147–12148.
29. As well as finding no precedent for the Glaser reaction of ynamides, we found only very few ynamine dimerizations: (a) Ficini, J.; Barbara, C.; d'Angelo, J.; Duréault, A. *Bull. Soc. Chim. Fr.* **1974**, 1535–1537. (b) Mayerle, J. J.; Flandera, M. A. *Acta Crystallogr., Sect. B* **1978**, *34*, 1374–1376. (no experimental details are given).
30. For a recent review of acetylene coupling, see: Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632–2657.
31. Liu, Q.; Burton, D. J. *Tetrahedron Lett.* **1997**, *38*, 4371–4374.
32. Without the cocatalyst CuI, **1a** slowly decomposed, and with CuI and Et_3N alone dimerization was very slow.
33. Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320–3321.
34. Although **6a** decomposed during work-up under acidic conditions followed by removal of the solvent in a rotary evaporator, a pure sample of **6a** was unaffected when dissolved in EtOAc or $CHCl_3$ before mixing with HCl (5%) or NaOH (10%).
35. Valenti, E.; Pericàs, M. A.; Serratosa, F. *J. Am. Chem. Soc.* **1990**, *112*, 7405–7406.
36. Ynamide **1b** reacted much faster (in 0.5 h) than the non-nitrogenated acetylenes used by Mori and co-workers, which took 6–12 h. See (a) Ikegashira, K.; Nishihara, Y.; Hirabayashi, K.; Mori, A.; Hiyama, T. *Chem. Commun.* **1997**, 1039–1040. (b) Nishihara, Y.; Ikegashira, K.; Hirabayashi, K.; Ando, J.-I.; Mori, A.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 1780–1787.
37. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991.
38. For a comprehensive review of palladium-catalysed cross-coupling, see: Negishi, E. In *Handbook of Organopalladium Chemistry for Organic Synthesis*, *Vol. 1*; Wiley-Interscience: New York, 2002; Part III, pp 215–1119.
39. For entries 1 and 2, starting material was almost completely recovered. For entry 3, the reaction transcurred very slow. For entry 8, decomposition was observed.

40. For a recent review of carbazole synthesis, see: Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303–4428 and references therein.
41. (a) Rodríguez, D.; Navarro, A.; Castedo, L.; Domínguez, D.; Saá, C. *Org. Lett.* **2000**, *2*, 1497–1500. (b) Rodríguez, D.; Navarro-Vázquez, A.; Castedo, L.; Domínguez, D.; Saá, C. *Tetrahedron Lett.* **2002**, *43*, 2717–2720. (c) Rodríguez, D.; Navarro-Vázquez, A.; Castedo, L.; Domínguez, D.; Saá, C. *J. Org. Chem.* **2003**, *68*, 1938–1946. (d) Rodríguez, D.; Martínez-Esperón, M. F.; Navarro-Vázquez, A.; Castedo, L.; Domínguez, D.; Saá, C. *J. Org. Chem.* **2004**, *69*, 3842–3848.
42. For a synthesis of indoles by [4+2] cycloaddition of aliphatic ynamides, see Ref. 22b
43. (a) Chakraborty, D. P. In Cordell, G. A., Ed.; The Alkaloids; Academic: New York, 1993; Vol. 44, p 257. (b) Gallagher, P. T.; Science of Synthesis; Thieme: Stuttgart, 2000; Vol. 10; pp 693. (c) Omura, S.; Sasaki, Y.; Iwai, Y.; Takeshima, H. *J. Antibiot.* **1995**, *48*, 535. (d) Knölker, H. J. In Moody, C. J., Ed.; Advances in Nitrogen Heterocycles; JAI: Greenwich, 1995; Vol. 1, p 173.
44. (a) Wakim, S.; Bouchard, J.; Simard, M.; Drolet, N.; Tao, Y.; Leclerc, M. *Chem. Mater.* **2004**, *16*, 4386–4388. (b) Wakim, S.; Bouchard, J.; Blouin, N.; Michaud, A.; Leclerc, M. *Org. Lett.* **2004**, *6*, 3413–3416. (c) Van Dijken, A.; Bastiaansen, J. J. A. M.; Kiggen, N. M. M.; Langeveld, B. M. W.; Rothe, C.; Monkman, A.; Bach, I.; Stössel, P.; Brunner, K. *J. Am. Chem. Soc.* **2004**, *126*, 7718–7727. (d) Justin Thomas, K. R.; Lin, J. T.; Tao, Y.-T.; Ko, C.-W. *J. Am. Chem. Soc.* **2001**, *123*, 9404–9411. (e) Kawamura, Y.; Yanagida, S.; Forrest, S. R. *J. Appl. Phys.* **2002**, *92*, 87–93. (f) Das, R. R.; Lee, C.-L.; Noh, Y.-Y.; Kim, J.-J. *Opt. Mater.* **2002**, *21*, 143–146. (g) Gong, X.; Robinson, M. R.; Ostrowski, J. C.; Moses, D.; Bazan, G. C.; Heeger, A. J. *Adv. Mater.* **2002**, *14*, 581–585.
45. For carbamates **8c** and **8e**, treatment with methyl cloroformate instead tosyl chloride was performed.
46. For an extraordinarily slow Diels–Alder approach to 5,6-dimethyltetrahydro-5*H*-benzo[*b*]carbazole, see: Van Broeck, P. I.; Van Doren, P. E.; Toppet, S. M.; Hoornaert, G. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 415–419.
47. (a) Kano, S.; Sugino, E.; Shibuya, S.; Hibino, S. *J. Org. Chem.* **1981**, *46*, 2979–2981. (b) Bergman, J.; Pelcman, B. *Tetrahedron* **1988**, *44*, 5215–5228. (c) Boogaard, A. T.; Pandit, U. K.; Koomen, G.-J. *Tetrahedron* **1994**, *50*, 4811–4828. (d) Syam Kumar, U. K.; Patra, P. K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1998**, *39*, 2029–2032. (e) Fraser, H. L.; Gribble, G. W. *Can. J. Chem.* **2001**, *79*, 1515–1521.
48. Martarello, L.; Joseph, D.; Kirsch, G. *Heterocycles* **1996**, *43*, 367–379.
49. Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2505–2508.
50. Gribble, G. W.; Keavy, D. J.; Davis, D. A.; Saulnier, M. G.; Pelcman, B.; Barden, T. C.; Sibi, M. P.; Olson, E. R.; BelBruno, J. J. *J. Org. Chem.* **1992**, *57*, 5878–5891 and references therein.
51. (a) Sha, C.-K.; Chuang, K.-S.; Young, J. J.; Wey, S.-J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 977–980. (b) Kreher, R. P.; Dyker, G. Z. *Naturforsch.* **1987**, *42b*, 473.
52. For syntheses of benzo[*b*]carbazoles by related cycloaromatizations of arenyne ketenimines, see: (a) Shi, C.; Wang, K. K. *J. Org. Chem.* **1998**, *63*, 3517–3520. (b) Schmittel, M.; Rodríguez, D.; Steffen, J.-P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2152–2155. For a recent synthesis of benzo[*a*]carbazoles, see: (c) Liu, Z.; Larock, R. C. *Org. Lett.* **2004**, *6*, 3739–3741.
53. TMS-substituted cyclic allenes of the benzo[*b*] series can isomerize to the more stable benzo[*c*] form, see: (a) Rodríguez, D.; Navarro-Vázquez, A.; Castedo, L.; Domínguez, D.; Saá, C. *J. Am. Chem. Soc.* **2001**, *123*, 9178–9179. (b) Rodríguez, D.; Castedo, L.; Domínguez, D.; Saá, C. *Synthesis* **2004**, 761–764.
54. Obtained following the same procedure as for **8** (Scheme 6) but starting with 4-amino-3-bromopyridine.
55. Prepared in 51% yield by treatment of **13d** with BrCN in the presence of KH.
56. Schmittel, M.; Rodríguez, D.; Steffen, J.-P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2152–2155.
57. In fact, careful examination of the IDDA reaction of **8d** showed it to produce both the benzo[*b*]carbazole **10d** and small amounts of an isomer.
58. Although the 2-pyridylynamide (not shown) decomposed under thermal conditions, as also did the 2-pyridyl analogue of **8d** (not shown).
59. Previously misidentified as the other regioisomer in Ref. 26 Table 1, entry 23.