Green Chemistry

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View Article Online
DOI: 10.1039/C6GC02423H

Journal Name

ARTICLE

Intramolecular 5-*exo*, 7-*endo*-dig Transition Metal-Free Cyclization Sequence of (2-Alkynylphenyl) Benzyl Ethers: Synthesis of Seven-Membered Fused Benzo[*b*]furans

Received 00th
Accepted 00th
DOI: 10.1039/x0xx00000x

www.rsc.org/

Rafaela Gai,[a] Roberto do Carmo Pinheiro,[a] José S. S. Neto,[a] Bernardo A. Iglesias,[b] Thiago V. Acunha,[b] Davi F. Back[b] and Gilson Zeni*[,a]

Base-promoted cyclization of (2-alkynylphenyl) benzyl ethers was studied in details. The effects of solvent, base, temperature, reaction time and amount of base on the efficacy of the cyclization reaction was analyzed and a new base-solvent system (*tert*-BuOK/DMSO) for effective cyclization of (2-alkynylphenyl) benzyl ethers was reported. The results showed that the cyclization reactions proceeded cleanly and smoothly under mild reaction conditions, employing a *tert*-BuOK as base, DMSO as solvent, at room temperature in a short reaction time (1 h). Under these conditions, a number of different substituted (2-alkynylphenyl) benzyl ethers were cyclized to the corresponding fused heterocycle cyclohepta[*b*]furans. This one-pot, two-steps procedure occurred regioselectively giving only the cyclohepta[*b*]furans as the unique regioisomer via an initial intramolecular 5-*exo*-dig mode followed by an intramolecular 7-*endo*-dig mode. The cyclohepta[*b*]furan derivatives absorbed in the UV region (300-350 nm range) with molar absorptivity coefficient values attributed to spin and symmetry allowed π-π* electronic transitions. An emission located in the purple region (380-440 nm range), with a Stokes shift between 65-100 nm is probably associated to the charge transfer character of the excited state. The electrochemical analysis (CV) of the cyclohepta[*b*]furans showed an oxidation and reduction process, probably due to the presence of the selenium atom and π-anion radical species.

Introduction

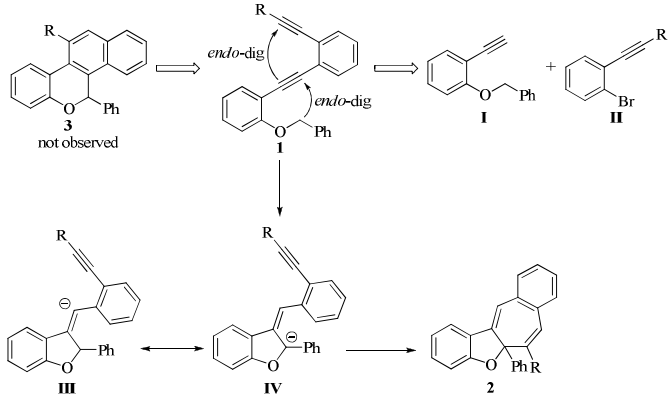
The derivatives of fused heterocycles are valued not only for their rich and varied chemistry but also for many important biological properties.[1] In contrast to the numerous studies developed for the chemistry and preparation of fused five- and six-membered heterocycles, the preparation of seven-membered derivatives is limited and generally involves a multistep synthesis.[2] However, the discovery of several new families of cyclohepta[*b*]furan ring containing different biological activities has generated an interest in the development of new methodologies for the synthesis of these heterocycles.[3] Representative examples of different biological activities include antimicrobial,[4] cytotoxic,[5] antiulcer,[6] and anti-inflammatory activities.[7] Cyclohepta[*b*]furans isolated from natural sources also have a broad spectrum of biological activities, for example, interleukin-8 receptor antagonist,[8] inhibitory activity against PI3K[9] and neuroprotective effects.[10] Besides, substituted cyclohepta[*b*]furans are interesting building blocks and important synthetic intermediates. For example, studies have shown that they have been used as substrate for [8+2] cycloaddition reactions.[11] These higher order conjugate additions have been extensively used to directly entry to a large number of fused-polycyclic compounds, which are part of numerous natural and non-natural compounds. Cyclohepta[*b*]furans have multi-π-bonds and the structural rigidity that leads to fast multistep electron transfer as well as to physicochemical features, such as radical spin-trapping therapeutic agents,[12] near-infrared dark quenchers,[13] color-tags for the chromophore-supported purification technique[14] and electrochromic materials.[15] Up to now, the most useful methodology described to the preparation of these heterocycles is the transition-metal-mediated cycloaddition reactions. In spite of these methods, the cycloaddition reactions,[16] ring expansion reactions,[17] ring-closing metathesis[18] and domino cyclization reactions[19] have emerged as powerful tools to the preparation of wide range of seven-membered heterocycles. Recently, there has been enormous interest in the development of new methods avoiding the use of transition metals.[20] A green alternative to transition metals in intramolecular cyclization is the base-promoted annulations of unsaturated substrates.[21] This methodology has significant advantages over others, particularly in terms of functional group tolerance, high levels of chemo-, regio-, and stereoselectivity. In addition, the base-promoted annulation has emerged as a powerful tool in organic synthesis due to the

[a]*Laboratório de Síntese, Reatividade, Avaliação Farmacológica e Toxicológica de Organocalcogênios CCNE, UFSM, Santa Maria, Rio Grande do Sul, Brazil 97105-900.* E-mail: gzeni@ufsm.br; Fax: (+55)55-3220-8978; Tel: (+55)55-3220-9611.

[b]*Laboratório de Materiais Inorgânicos, Departamento de Química, UFSM, Santa Maria, Rio Grande do Sul, Brazil 97105-900.*

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

reduction of generation of chemical wastes, reaction time, solvent, and energy, demonstrating the clear economic impacts and environmental benefits. In this paper, our aim was to develop conditions for the base promoted annulation of (2-alkynylphenyl) benzyl ethers **1**, bearing a nucleophilic center an appropriate distance to the alkyne, for the selective synthesis of naphtha chromenes **3** (Scheme 1). These cascade annulation reactions generally proceed through double intramolecular *endo*-dig cyclization mode.[22] However, after initial reactions to determine the feasibility of this project, we found that the product obtained was the cyclohepta[*b*]furans **2**. The reactions probably proceed via an intramolecular *exo*-dig/*endo*-dig sequence (Scheme 1). Thus, in order to develop a versatile method for the preparation of cyclohepta[*b*]furans **2**, we performed a systematic study of the base-promoted cyclization reaction of (2-alkynylphenyl) benzyl ethers **1** varying different reaction parameters and these results will presented below.

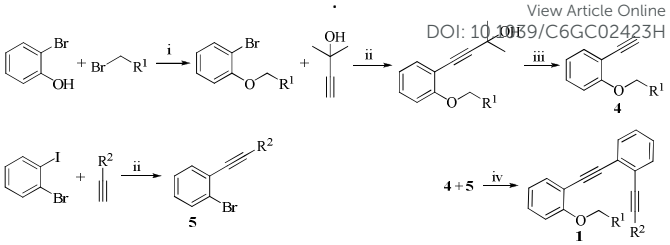


Scheme 1

Results and Discussion

General Conditions

The starting material (2-alkynylphenyl) benzyl ethers **1** was prepared by Sonogashira reaction involving terminal alkynes **4** reacting with aryl bromides **5** (Scheme 2).[24] The terminal alkynes **4** were synthesized by the reaction of 2-bromophenol with corresponding benzyl bromides followed by Sonogashira[25] and retro-Favorskii[26] reactions, respectively. The aryl bromides **5** were prepared reacting 2-bromoiodo-benzene with terminal alkynes via Sonogashira reaction.[27] In order to optimize the reaction conditions, we initiated our study by using (2-alkynylphenyl) benzyl ether **1a** (0.25 mmol), screening the action of bases, solvents, temperature and reaction time and the results are summarized in Table 1.



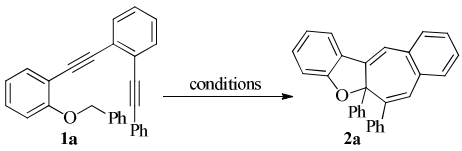
R^1 = C_6H_5, 2-Me-C_6H_4, 3-Me-C_6H_4, 4-Me-C_6H_4, 3-MeO-C_6H_4, 4-Cl-C_6H_4, 4-F-C_6H_4.
R^2 = C_6H_5, 2-Me-C_6H_4, 3-Me-C_6H_4, 4-Me-C_6H_4, 2-MeO-C_6H_4, 3-MeO-C_6H_4, 4-MeO-C_6H_4, 4-Cl-C_6H_4, 4-F-C_6H_4, 3-CF_3-C_6H_4, 2-thienyl, 1-naphthyl, 2-naphthyl.

i) CH_3CN, K_2CO_3 (5 equiv), reflux, 12 h; ii) $PdCl_2(PPh_3)_2$ (2 mol%), CuI (1 mol%), Et_3N, r.t., 10 h; iii) toluene, NaOH (3.0 equiv), reflux, 5 h; iv) $PdCl_2(PPh_3)_2$ (2 mol%), CuI (1 mol%), Et_3N, reflux, 12 h.

Scheme 2

Due to the fact that the acidity of the *t*-BuOH is similar to that of DMSO,[23] the system DMSO/*tert*-BuOK would facilitate the formation and stabilization of the anion intermediates. For this reason, we began our investigation using *tert*-BuOK as base and DMSO as solvent. The results show that the use of a catalytic amount of *tert*-BuOK did not convert the (2-alkynylphenyl) benzyl ether **1a** in the desired product even under extended reaction time (24 h) and high temperature (100 °C) (Table 1, entries 1 and 2). The increase of *tert*-BuOK amount to 2.0 equiv led to a significant increase of **2a** yield, reaching 88%, in a short reaction time (Table 1, entry 3). We subsequently examined the effect of solvent on the cyclization of (2-alkynylphenyl) benzyl ether **1a**. The type of solvent had significant effect and almost all of the solvents tested, except DMF, did not afford the product (Table 1, entries 5-10). The use of protic solvent would quench the anions preventing the conversion of the (2-alkynylphenyl) benzyl ether **1a**. To check this hypothesis we carried out an experiment using *tert*-BuOH as solvent. With this reaction conditions, there was no formation of cyclohepta[*b*]furan **2a** and the (2-alkynylphenyl) benzyl ether **1a** was completely recovered (Table 1, entry 11). This is also assumed by us as an additional evidence for the anionic pathway (see mechanism discussion). It was found that various bases, such as Cs_2CO_3, NaOH, DBU, NaH, and KOH, were not effective to mediate the cyclization of 2-alkynylphenyl) benzyl ether **1a**, although KOH gave moderated yield of cyclohepta[*b*]furan **2a** at a high temperature (Table 1, entries 12-16). The amount of base was then optimized; the yields were not significantly changed by decreasing from 2.0 to 0.5 equiv amount (Table 1, entries 17 and 18). For economic reason, 0.5 equiv of *tert*-BuOK was adopted for further studies. At various interval times, during the optimization reactions, samples of the reaction mixture were analyzed by TLC, which showed that 1 h was the reaction time necessary to the complete consume of starting material. In accordance with these results, we concluded that the optimum set of conditions for the cyclization reaction of (2-alkynylphenyl) benzyl ether **1a** were the addition of *tert*-BuOK (50 mol%) to a solution of (2-alkynylphenyl) benzyl ether **1a** (0.25 mmol) in DMSO (2.0 mL) at room temperature for 1 h. To demonstrate the generality of the methodology, various (2-alkynylphenyl) benzyl ethers **1** were cyclized using the optimized reaction conditions and the results are listed in Table 2.

Table 1. Effect of different reaction parameters on the preparation of cyclohepta[*b*]furan **2a**[a]



entry	base (equiv)	solvent	time (h)	yield (%)[b]
1	*tert*-BuOK (0.2)	DMSO	24	N.R.[c]
2	*tert*-BuOK (0.2)	DMSO	24	N.R.[c,d]
3	*tert* -BuOK (2)	DMSO	1	88
4	*tert* -BuOK (2)	DMF	1	83
5	*tert*-BuOK (2)	THF	24	N.R.
6	*tert*-BuOK (2)	dioxane	24	N.R.
7	*tert*-BuOK (2)	CH_2Cl_2	24	N.R.
8	*tert*-BuOK (2)	CH_3CN	24	N.R.
9	*tert*-BuOK (2)	toluene	24	N.R.
10	*tert*-BuOK (2)	DMA	24	N.R.
11	*tert*-BuOK (2)	*tert*-BuOH	24	N.R.
12	Cs_2CO_3 (2)	DMSO	24	N.R.
13	NaOH (2)	DMSO	24	N.R.
14	DBU (2)	DMSO	24	N.R.
15	NaH (2)	DMSO	24	N.R.
16	KOH (4)	DMSO	11	45[d]
17	*tert*-BuOK (1)	DMSO	1	89
18	*tert*-BuOK (0.5)	DMSO	1	90

[a]The reaction was performed by the addition of *tert*-BuOK to a solution of (2-alkynylphenyl) benzyl ether **1a** (0.25 mmol) in DMSO (2.0 mL) under argon atmosphere, at room temperature for the time indicated.
[b]Yields of purified products.
[c]The substrate **1a** was not consumed.
[d]The reaction was performed at 100 °C.

Scope of the Reaction

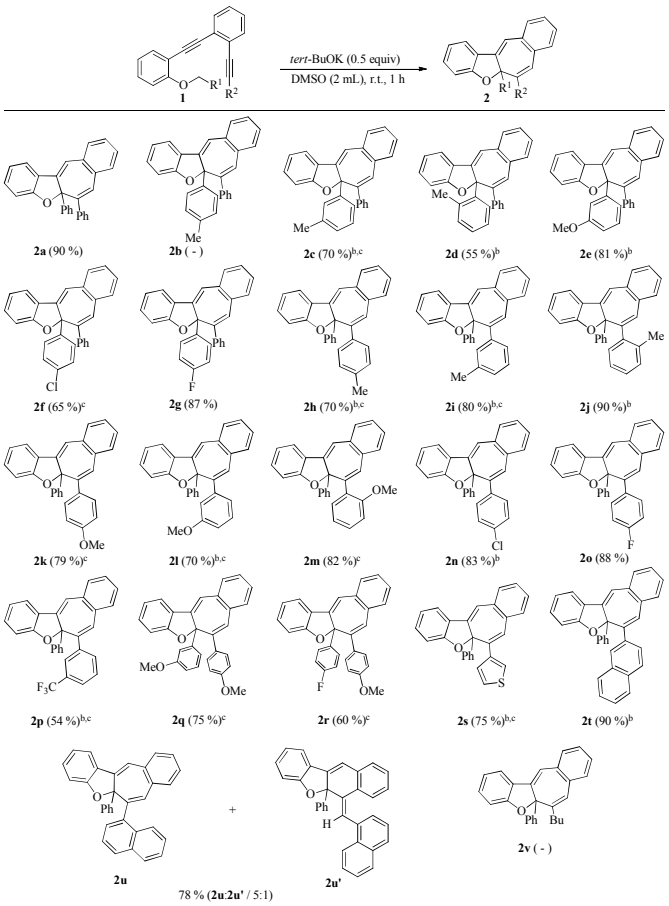
Because the yields varied with both electronic and steric effects, any clear relationship between the structure of the (2-alkynylphenyl) benzyl ether **1a** and the reaction yield could not be established. However, some results deserve a detailed analysis; for example, in respect to the effect of the substituent on the benzyloxy function we observed that the aryl group having no substitution gave the highest yield for cyclohepta[*b*]furan **2a**. The electron-donating groups in the aromatic rings of benzyloxy function were compatible with the reaction conditions, giving the corresponding cyclohepta[*b*]furans **2c-2f** in moderated to good yields, although additional reaction time and an increase in temperature were required. An exception to this behavior was observed for cyclohepta[*b*]furan **2b**, which was not obtained, even though we made several modifications in the standard reaction conditions. In this example, only unreacted starting material was observed. The cyclization conditions also worked well with electron-withdrawing groups at the aromatic rings of benzyloxy affording the corresponding products **2f** and **2g** in 65 and 87% yields, respectively. We also studied the introduction of substituents on the alkyne terminus. We observed that both electron-rich and electron-deficient aryl groups directly bonded to alkyne afforded the products in high yields, even though the aryl containing a CF_3, a strong electron-withdrawing substituent, gave only moderated 54% yield (Table 2, cyclohepta[*b*]furans **2h-2p**). Furthermore, the experiments showed that the cyclization reactions were not influenced by effects of adding substituents on the two aromatic systems given that the expected products were obtained in similar good yields (Table 1, cyclohepta[*b*]furans **2q-2t**). An exception to the other results was observed for the case of (2-alkynylphenyl) benzyl ether having a 1-naphthyl group bonded to alkyne. The reaction of this substrate with standard conditions gave a mixture of cyclohepta[*b*]furan **2u** and the product formed via a double *exo*-dig cyclization **2u'**. In this case, the formation of **2u'** may be attributed to the steric hindrance offered by the 1-naphthyl substituent to the nucleophilic attack at the C1 of alkynes. Concerning the substrate having an alkyl group attached to the carbon-carbon triple bond, we did not observe the formation of cyclohepta[*b*]furan **2v**. In this case, only the starting material was recovered even under various reaction conditions (Table 2, cyclohepta[*b*]furan **2v**). This lower reactivity is probably due to the absence of pi (π) bonds next to the alkyne, which becomes the carbon-carbon triple bond less reactive towards nucleophilic attack.

Mechanism Proposal

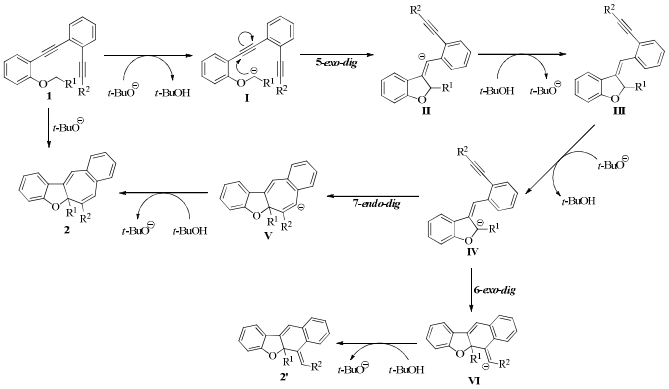
We assumed that the cyclization proceeds through; a) the formation of benzyl anion **I** via abstraction of benzylic hydrogen from (2-alkynylphenyl) benzyl ethers **1** by *tert*-BuOK; b) the intramolecular anionic addition to the carbon-carbon triple bond gives the vinyl anion **II**, via a 5-*exo*-dig mode; c) protonation of the vinyl anion by *tert*-BuOH, generated in situ, affords the benzofuran intermediary **III** that upon further deprotonation gives **IV**. Next, in the second cyclization step, the 6-*exo*-dig mode competes with 7-*endo*-dig mode, therefore a mixture of cyclohepta[*b*]furans **2** and dihydrobenzo-naphthofuran **2'** would be produced (Scheme 3). The nucleophilic attack of benzyl anion at the carbon-carbon bonds of alkyne produces the anion **V**. The protonation/deprotonation sequence gives the cyclized cyclohepta[*b*]furans **2**. There is no way to isolate any intermediates, such as bezofuran **II** and **IV**; however, we presented herein some results of the experiments performed to support this hypothesis. When (2-alkynylphenyl) benzyl ether **1a** reacted under optimized reaction, in the dark, to prevent the light-induced formation of the radical, or in the presence of TEMPO a radical inhibitor, the cyclohepta[*b*]furan **2a** was obtained in 85% and 89% yields, respectively (Schemes 4 and 5). This indicates that the pathway does not follow the typical radical mechanism. When the same reaction was carried out using hydrated THF or a protic solvent instead of anhydrous THF, no cyclohepta[*b*]furan **2a** was detected and the (2-alkynylphenyl) benzyl ether **1a** was completely

recovered. This suggests that water and protic solvent may quench the anions formed, hindering the reaction. In this context, our cyclization methodology showed to be regioselective, providing the desired cyclohepta[*b*]furan **2** via an intramolecular 5-*exo*-dig mode followed by a 7-*endo*-dig mode.

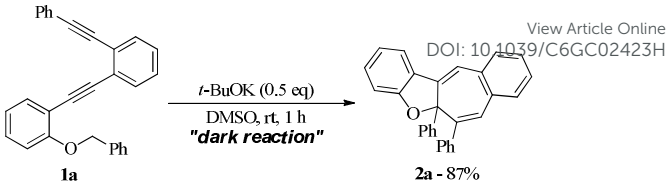
Table 2. Synthesis of cyclohepta[*b*]furans **2**[a]



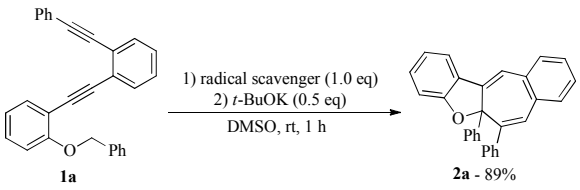
[a]The reaction was performed in the presence of (2-alkynylphenyl) benzyl ethers **1** (0.25 mmol) and *tert*-BuOK (50 mol%) in DMSO (2.0 mL) under an argon atmosphere at room temperature for 1 h.
[b]The reaction was performed with *tert*-BuOK (1.0 equiv).
[c]The reaction was performed at 100 °C.



Scheme 3



Scheme 4



Scheme 5

The formation of six-membered ring via intramolecular 6-*endo*-dig mode, in the first cyclization, or six-membered ring via a 6-*exo*-dig process, in the second cyclization, was not observed in any case. This high regioselectivity can be explained by the stability of the new sigma-bond system formed, the formation of the more stable vinyl carbanion from original alkyl anion and due to the carbon, the nucleophilic cyclization normally goes on via 5-*exo*-dig over 6-*endo* closure in the substrate with these interatomic distances.[28] In the second cyclization step, the 7-*endo*-dig mode was preferred over 6-*exo*-dig, albeit the both processes are acceptable according to the Baldwin rule.[28] It is reasonable to assume that steric and electronic factors over the competitive cyclization modes are involved in this reaction.[29]

Characterization of Cyclohepta[*b*]furan Derivatives

In our methodology, except for the reaction of (2-alkynylphenyl) benzyl ether having a 2-naphthyl group bonded to alkyne, which gave a mixture of isomer derivatives, only the product resulting from 5-*exo*-dig/7-*endo*-dig intramolecular sequence was obtained. The presence of a unique isomer was confirmed by spectral ^{13}C NMR data from crude reaction mixture to avoid error in the detection isomer peaks by ^{1}H NMR. The structures of all products **2** were unambiguously elucidated by their NMR data and confirmed by single crystal X-ray diffraction for compound **2f** (Figure 1, CCDC 1485830), **2g** (CCDC 1485827, Figure S1 Supporting Information) and **2m** (CCDC 1485825, Figure S1 Supporting Information).

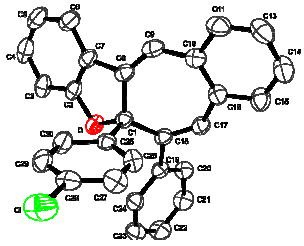


Figure 1. The molecular structure with the atom-labeling scheme of the compound **2f** with 50% thermal ellipsoids (using ORTEP software) (CCDC 1485830)

UV-Vis and Emission Fluorescence Analysis of Cyclohepta[*b*]furan Derivatives 2a-2t

The comparative absorption spectra of compounds **2a-2t**, using $CHCl_3$ as solvent, are shown in Figure 2 and the optical properties are listed in Table 3. The cyclohepta[*b*]furan derivatives showed absorption maxima located around 250-400 nm range, at the UV region. The values for the molar absorptivity coefficient (ε) for these compounds indicate that spin and symmetry allowed electronic transitions, which could be related to π-π* and n→π* transitions (Figure 2). We did not observe significant changes on the absorption maxima location associated with different substituent groups in the cyclohepta[*b*]furan compounds. The fluorescence emission spectra of some cyclohepta[*b*]furans are illustrated in Figure 3. The emission curves were obtained exciting the compounds at the absorption maxima wavelength at λ_{exc} = 350 nm. Cyclohepta[*b*]furan compounds presented fluorescence emission in the purple region (380-450 nm range). As already observed in the ground state, they presented comparable location to the emission maxima, which indicates that the different organic moieties in the cyclohepta[*b*]heterocycles did not play a fundamental role on the excited state of these compounds. In addition, the fluorescent emission of cyclohepta[*b*]furans containing methoxyl substituent (**2k** and **2q**) can be attributed to the electronic nature of this electron donor group (Figure 3). These results probably can be attributed to the nature of the π-π* electronic transition, indicating that these compounds allow better electronic delocalization in the excited state. The Stokes shifts observed in the excited state can indicate that cyclohepta[*b*]furans present some charge separation, in special compounds **2e** and **2k** (both with CH_3O group). These results could be assigned to an intramolecular charge transfer character in the excited state (Table 3). Moreover, they showed good fluorescence quantum yields if compared to that of the DPA standard or cyclohepta[*b*]furan compounds with donating substituents in *meta* or *ortho* position (Table 3). This suggests that the presence of both oxygen atoms and electronic donating groups enhance significantly the fluorescent emission in these cyclohepta[*b*]furan derivatives. Evidence also was found to correlate the higher fluorescence quantum yields with the heterocyclic ring planarities.

Cyclic Voltammetry Analysis of Cyclohepta[*b*]furans 2a-2t

In order to better evaluate the redox properties of cyclohepta[*b*]furans CV experiments were performed to verify the redox potential values of compounds, in dry dichloromethane solutions (Table 4). In general, at -2.00 to +2.00 V potential range, the cyclic voltammograms of cyclofuran-derivatives displayed one reversible reduction peak (E_{pc}) between -0.90 V to -1.30 V versus SHE redox couple (Figure 4). This reduction process can be attributed to a C-O bond cleavage located in the furan unit, which form an anion radical type species. Moving to the positive region, all derivatives exhibit irreversible oxidation waves in the anodic range (E_{pa}) at +1.20 V to +1.80 V (Table 4).

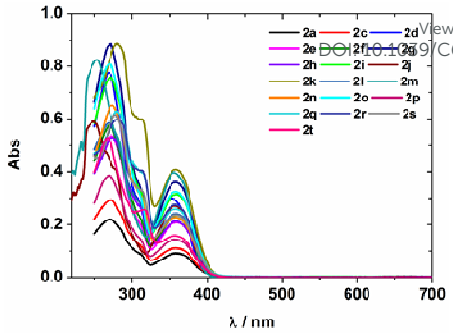


Figure 2. Comparative electronic UV-Vis absorption spectra of cyclohepta[*b*]furan compounds **2a-2t**, containing different substituted groups in chloroform solution

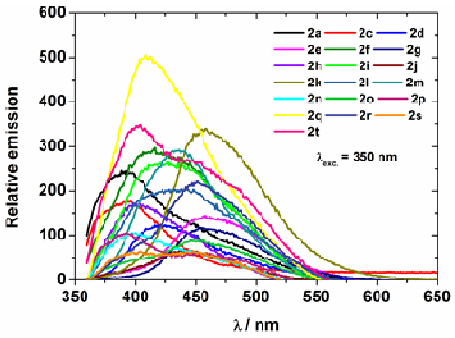


Figure 3. Emission fluorescence spectra of compounds **2a-2t**, in $CHCl_3$ solution

The oxidation peaks observed in these compounds can be assigned to the cation radical species of cyclohepta[*b*]furans in solution. Analyzing the donor/acceptor groups in these derivatives, we observed that they did not influence the changes in the redox potential (Supplementary Information, Figure S2 and S3). An exception was the derivatives **2q** and **2r**, which had lower oxidation potentials when to compare to those of the other compounds (Table 4). This may be related to the electronic properties of the molecule.

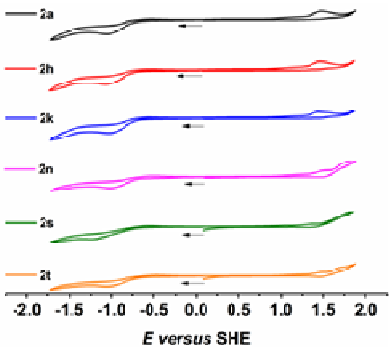


Figure 4. Comparative cyclic voltammogram of compounds **2a**, **2h**, **2k**, **2n**, **2s** and **2t**, in dichloromethane containing 0.1 M $TBAPF_6$, as support electrolyte, using scan rate at 100 mV/s, respectively.

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Table 3. UV-vis and emission data analysis of cyclohepta[*b*]furans **2a-2t**

compound	UV-vis, nm (ε; $M^{-1}cm^{-1}$)[a]	emission (nm)[b]	ϕ_{fl}[c]	Stokes shifts (nm)[d]	$E_{0\text{-}0}$ (eV)[e]
2a	272 (3.469); 360 (1.435)	391	0.135	31	3.444
2c	272 (5.437); 358 (1.485)	395	0.230	37	3.445
2d	269 (7.513); 352 (2.891)	421	0.321	69	3.271
2e	273 (6.940); 359 (1.064)	459	0.308	100	3.229
2f	270 (6.956); 358 (1.067)	415	0.129	56	3.387
2g	271 (4.373); 358 (1.784)	455	0.275	97	3.171
2h	274 (6.333); 359 (1.040)	402	0.290	43	3.378
2i	271 (3.633); 359 (1.507)	425	0.143	66	3.324
2j	248 (6.954); 357 (1.323)	432	0.100	75	3.289
2k	280 (4.487); 358 (2.079)	460	0.187	102	3.155
2l	269 (5.988); 358 (1.226)	431	0.247	73	3.342
2m	253 (4.195); 355 (2.018)	435	0.214	80	3.246
2n	274 (9.871); 358 (2.787)	400	0.060	42	3.406
2o	270 (4.007); 359 (1.605)	453	0.059	94	3.342
2p	270 (7.955); 357 (2.143)	394	0.046	37	3.425
2q	280 (3.122); 357 (1.287)	409	0.255	52	3.333
2r	281 (3.177); 357 (1.461)	450	0.115	93	3.246
2s	276 (3.053); 358 (1.136)	403	0.079	45	3.406
2t	267 (6.507); 358 (2.169)	404	0.144	46	3.425

[a]Measured in $CHCl_3$. [b]Measured in $CHCl_3$ solution at 298K ($\lambda_{exc.}$ = 350 nm). [c]9,10-Diphenylanthracene (DPA) in $CHCl_3$ as standard (ϕ_{fl} = 0.65). [d]Stokes Shift equation: $\Delta\lambda' = \lambda_{em} - \lambda_{abs}$ ($\Delta\lambda' = 1/\lambda_{abs} - 1/\lambda_{em} \times 10^7$ cm^{-1}). [e]$E_{0\text{-}0} = 1240 / \lambda$ (in eV).

Table 4. Electrochemical data of cyclohepta[*b*]furans **2a-2t**

compound	E_1[a]	E_2[a]	E_3[b]	HOMO (eV)[c]	LUMO (eV)[d]	Δ*E* (eV)
2a	+1.477 V	-----	-1.045 V	-6.277	-2.833	3.444
2c	+1.186 V	+1.489 V	-0.994 V	-5.986	-2.541	3.445
2d	+1.150 V	+1.471 V	-1.022 V	-5.950	-2.679	3.271
2e	+1.379 V	+1.661 V	-1.148 V	-6.179	-2.950	3.229
2f	+1.489 V	+1.769 V	-1.023 V	-6.289	-2.902	3.387
2g	+1.456 V	+1.739 V	-1.048 V	-6.256	-3.085	3.171
2h	+1.468 V	-----	-1.062 V	-6.268	-2.890	3.378
2i	+1.137 V	+1.481 V	-1.041 V	-5.937	-2.613	3.324
2j	+1.164 V	+1.453 V	-1.022 V	-5.964	-2.675	3.289
2k	+1.434 V	-----	-1.026 V	-6.234	-3.079	3.155
2l	+1.432 V	+1.675 V	-1.200 V	-6.232	-2.890	3.342
2m	+1.560 V	-----	-1.126 V	-6.360	-3.114	3.246
2n	+1.492 V	+1.768 V	-1.007 V	-6.292	-2.886	3.406
2o	+1.360 V	+1.654 V	-1.099 V	-6.160	-2.818	3.342
2p	+1.456 V	+1.761 V	-1.171 V	-6.256	-2.831	3.425

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DOI: 10.1039/C6GC02423H

2q	+0.698 V	+1.155 V	-1.054 V	-5.498	-2.165	3.333
2r	+0.675 V	-0.309 V	-0.913 V	-5.475	-2.229	3.246
2s	+1.338 V	-----	-1.228 V	-6.138	-2.732	3.406
2t	+1.469 V	+1.704 V	-1.046 V	-6.269	-2.844	3.425

[a]E_{pa} = Anodic peak (*versus* SHE). [b]E_{pc} = Cathodic peak (*versus* SHE). [c]E_{HOMO} = -[4.8 + E_{1ox} (*versus* SHE)]eV. [d]E_{LUMO} = [E_{HOMO} + $E_{0\text{-}0}$]. [e]ΔE = E_{LUMO} - E_{HOMO}.

Conclusions

To summarize, we showed that the (2-alkynylphenyl) benzyl ethers **1** react with *tert*-BuOK in DMSO to give the corresponding cyclohepta[*b*]furans **2**, via a sequential regioselective 5-*exo*-dig mode followed by a 7-*endo*-dig mode. A systematic study to determine the best reaction conditions of the cyclization system revealed that the amount of base and solvent played an essential role in this reaction. The reaction afforded cyclohepta[*b*]furans in moderate to good yields and various functional groups were readily accommodated in the final structure. We consider that this method has significant advantages, such as a short reaction time, the reactions were carried out under room temperature and given that *tert*-BuOK is easily available commercially, less expensive and relative non-toxic, our method could be considered an economic and eco-friendly protocol. Another feature of this protocol is the atom economy because two new carbon-carbon bonds were formed in a one-pot procedure, which is an important concept of green chemistry philosophy. The cyclohepta[*b*]furans **2** was identified by their NMR data and the structures were confirmed by single crystal X-ray diffraction. Furthermore, the cyclohepta[*b*]furan derivatives absorbed the UV region (π-π* and n→π* transitions) and present fluorescence emission in the purple region (380-450 nm range) as well as redox potentials which can be attributed to the anion/cation radical species.

Experimental Section

General Methods

Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained on a NMR spectrometer at 400 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (*J*) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained on a 400 NMR spectrometer at 100 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet), dt (double triplet), td (triple doublet) and m (multiplet). High resolution mass spectra were recorded on a mass spectrometer using electrospray ionization (ESI). Column chromatography was performed using Silica Gel (230-400 mesh) following the methods described by Still. Thin layer chromatography (TLC) was performed using Gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. The following solvents were dried and purified by distillation from the reagents indicated: tetrahydrofuran from sodium with a benzophenone ketyl indicator. All other solvents were ACS or HPLC grade unless otherwise noted. Air- and moisture-sensitive reactions were conducted in flame-dried or oven dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry nitrogen or argon. Reagents and solvents were handled using standard syringe techniques. Spectroscopic grade solvents (Sigma-Aldrich) were used for fluorescence and UV-Vis measurements. UV-Vis electronic absorption spectra in solution were performed on a UV-2600 spectrophotometer at a concentration of 1.0 x 10^{-4} - 1.0 x 10^{-5} M range. Steady state fluorescence spectra were taken with an Cary Eclipse spectrofluorometer. The maximum absorption wavelength was used as excitation wavelength for fluorescence measurements. The quantum yield of fluorescence (ϕ_F) was measured at 25 °C using spectroscopic grade solvents within solutions with absorbance intensity lower than A = 0.2. 9,10-Diphenylanthracene (DPA, Aldrich) in $CHCl_3$ was used as fluorescence quantum yield standard (ϕ_F = 0.65). Cyclic voltammograms were recorded on potenciostat/galvanostat system at room temperature under argon atmosphere, using dry dichloromethane solution (Sigma-Aldrich). Electrochemical grade tetrabutylammonium hexafluorophosphate ($TBAPF_6$, Sigma-Aldrich) was used as supporting electrolyte. These experiments were carried out by employing a standard three component system: a glassy carbon working electrode; a platinum wire auxiliary electrode and a platinum wire pseudo-reference electrode. To monitor the reference electrode, the Fc/Fc^+ couple was used as an internal reference. All measurements were performed at room temperature (25 °C).

General Procedure

General Procedure for the Preparation of *H*-benzo[4,5]cyclohepta[1,2-*b*]benzofurans Derivatives 2a-u

To a tube, under argon, containing the substrate **1** (0.25 mmol) and DMSO (2 mL), was added *t*-BuOK. The reaction mixture was allowed to stir for 1 h. After this time, the mixture was diluted with ethyl acetate (20 mL) and washed saturated solution of NH_4Cl (2 x 20 mL). The organic phase was separated, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography on silica gel.

Characterization

6-diphenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2a): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.086 g (90 %), mp 76-79 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52-7.50 (m, 1H), 7.48-7.40 (m, 2H), 7.30-7.23 (m, 7H), 7.20 (s, 1H), 7.17-7.02 (m, 6H), 6.93-6.90 (m, 2H), 6.71 (d, *J* = 8.0 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 142.6, 140.9, 140.6, 140.4, 135.0, 134.1, 131.3, 130.6, 129.9, 129.4, 129.3, 128.1, 127.9, 127.5, 127.3, 126.8, 126.2, 126.1, 126.0, 121.0, 120.7, 116.5, 110.5, 91.5. MS (EI, 70 eV; *m/z* (relative intensity)): 385 ([M + 1], 8), 384 (28), 307 (100), 276 (10), 205 (3), 169 (3), 153 (11), 138 (4). HRMS (ESI-TOF) *m/z* calcd for $C_{29}H_{21}O$ [M + H]$^+$: 385.1592. Found: 385.1602.

6-phenyl-5a-(*m*-tolyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2c): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.069 g (70 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56-7.52 (m, 1H), 7.49-7.42 (m, 2H), 7.36-7.25 (m, 5H), 7.22 (s, 1H), 7.20-7.07 (m, 5H), 6.99-6.91 (m, 3H), 6.90-6.86 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 142.6, 140.9, 140.7, 140.3, 137.5, 135.1, 134.2, 131.2, 130.6, 129.9, 129.4, 129.3, 128.9, 127.7, 127.5, 127.2, 126.9, 126.7, 126.2, 126.1, 123.4, 121.0, 120.7, 116.4, 110.5, 91.5, 21.4. MS (EI, 70 eV; *m/z* (relative intensity)): 400 ([M + 2], 3), 399 ([M + 1], 19), 398 (60), 383 (4), 321 (68), 307 (100), 276 (11), 205 (4), 160 (10), 138 (4). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O$ [M + H]$^+$: 399.1749. Found: 399.1752.

6-phenyl-5a-(*o*-tolyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2d): Isolated by column chromatography (hexane as eluent) as a yellow viscous oil. Yield: 0.054 g (55 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51-7.42 (m, 4H), 7.35-7.21 (m, 5H), 7.20-7.02 (m, 4H), 6.99-6.87 (m, 4H), 6.85-6.79 (m, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 2.19 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.9, 141.8, 141.7, 139.9, 138.2, 135.3, 135.2, 134.3, 132.2, 130.6, 130.2, 129.4, 129.1, 129.0, 128.7, 128.2, 127.5, 127.2, 126.4, 126.3, 125.8, 124.6, 121.1, 120.5, 114.6, 109.9, 92.7, 21.7. MS (EI, 70 eV; *m/z* (relative intensity)): 400 ([M + 2], 3), 399 ([M + 1], 33), 398 (100), 383 (7), 321 (24), 307 (67), 276 (17), 205 (11), 176 (12). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O$ [M + H]$^+$: 399.1749. Found: 399.1755.

5a-(3-methoxyphenyl)-6-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2e): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.083 g (81 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.5 Hz, 1H), 7.48-7.42 (m, 2H), 7.35-7.26 (m, 5H), 7.21 (s, 1H), 7.20-7.11 (m, 3H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.96-6.92 (m, 2H), 6.90 (ddd, *J* = 7.8 Hz, *J* = 1.7 Hz, *J* = 1.1 Hz, 1H), 6.86-6.83 (m, 1H), 6.77-6.73 (m, 1H), 6.62 (ddd, *J* = 8.0 Hz, *J* = 3.0 Hz, *J* = 1.0 Hz, 1H), 3.52 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$. 100 MHz): δ 161.2, 159.2, 142.3, 142.2, 140.9, 140.7, 135.0, 134.1, 131.3, 130.6, 130.0, 129.5, 129.3, 128.9, 127.5, 127.3, 126.8, 126.2, 126.0, 121.0, 120.8, 118.5, 116.6, 113.6, 112.1, 110.5, 91.2, 55.0. MS (EI, 70 eV; *m/z* (relative intensity)): 415 ([M + 1], 14), 414 (42), 337 (58), 321 (10), 307 (100), 276 (10), 207 (4), 163 (6), 138 (4). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O_2$ [M + H]$^+$: 415.1698. Found: 415.1704.

5a-(4-chlorophenyl)-6-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2f): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.068 g (65 %), mp 174-176 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.6 Hz, 1H), 7.46-7.40 (m, 2H), 7.38-7.11 (m, 11H), 7.03 (d, *J* = 9.0 Hz, 2H), 6.98-6.92 (m, 2H), 6.77-6.72 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.1, 142.3, 140.6, 140.3, 139.1, 134.9, 134.0, 133.9, 131.3, 130.8, 130.0, 129.5, 129.3, 128.1, 127.8, 127.6, 127.4, 127.0, 126.4, 125.9, 121.2, 120.8, 116.7, 110.5, 90.8. MS (EI, 70 eV; *m/z* (relative intensity)): 420 ([M + 2], 13), 419 ([M + 1], 13), 418 (38), 383 (3), 341 (72), 307 (100), 276 (22), 207 (8), 152 (16). HRMS (ESI-TOF) *m/z* calcd for $C_{29}H_{20}ClO$ [M + H]$^+$: 419.1203. Found: 419.1210.

5a-(4-fluorophenyl)-6-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2g): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.087 g (87 %), mp 183-185 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.5 Hz, 1H), 7.47-7.42 (m, 2H), 7.36-7.25 (m, 7H), 7.23 (s, 1H), 7.21-7.11 (m, 3H), 6.97-6.92 (m, 2H), 6.78-6.69 (m, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.3 (d, *J* = 247.0 Hz), 161.0, 142.5, 140.7, 140.3, 136.3 (d, *J* = 3.0 Hz), 134.8, 134.0, 131.2, 130.7, 129.8, 129.4, 129.3, 128.2 (d, *J* = 8.0 Hz), 127.6, 127.4, 126.9, 126.3, 125.8, 121.1, 120.7, 116.5, 114.7 (d, *J* = 21.0 Hz), 110.5, 90.8. MS (EI, 70 eV; *m/z* (relative intensity)): 403 ([M + 1], 20), 402 (61), 325 (100), 307 (95), 276 (12), 205 (5), 162 (11), 153 (12). HRMS (ESI-TOF) *m/z* calcd for $C_{29}H_{20}FO$ [M + H]$^+$: 403.1498. Found: 403.1503.

5a-phenyl-6-(*p*-tolyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2h): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.069 g (70 %), mp 170-173 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.33-7.24 (m, 4H), 7.23 (s, 1H), 7.21-7.01 (m, 8H), 6.99-6.90 (m, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 142.5, 140.7, 140.4, 137.8, 137.0, 135.0, 134.0, 131.2, 130.5, 129.8, 129.2, 128.9, 128.2, 128.0, 127.8, 126.6, 126.2, 126.1, 120.9, 120.6, 116.5, 110.5, 91.5, 21.1. MS (EI, 70 eV; *m/z* (relative intensity)): 399 ([M+1], 10), 398 (47), 321 (100), 307 (72), 276 (14), 253 (16), 207 (15), 177 (9). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O$ [M + H]$^+$: 399.1749. Found: 399.1758.

5a-phenyl-6-(*m*-tolyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2i): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.080 g (80 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57-7.47 (m, 1H), 7.36-6.99 (m, 15H), 6.97-6.89 (m, 2H), 6.77-6.71 (m, 1H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 142.7, 140.9, 140.5, 140.4, 137.1, 135.0, 134.1, 131.2, 130.6, 129.9, 129.8, 129.2, 128.1, 128.0, 127.9, 127.4, 126.7, 126.6, 126.3, 126.1, 126.0, 121.0, 120.7, 116.4, 110.5, 91.5, 21.4. MS (EI, 70 eV; *m/z* (relative intensity)): 399 ([M + 1], 13), 398 (47), 321 (100), 307 (83), 276 (15), 207 (11), 163 (6), 153 (8). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O$ [M + H]$^+$: 399.1749. Found: 399.1755.

5a-phenyl-6-(*o*-tolyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2j): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.089 g (90 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (d, J = 7.6 Hz, 1H), 7.40-7.10 (m, 12H), 7.09-6.98 (m, 3H), 6.91 (td, J = 7.6 Hz, J = 0.7 Hz, 1H), 6.74-6.67 (m, 2H), 1.96 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.5, 142.0, 140.9, 140.5, 140.0, 137.1, 134.8, 134.4, 131.3, 130.7, 130.2, 129.8, 129.5, 128.9, 127.9, 127.8, 127.2, 126.9, 126.3, 126.1, 125.9, 124.9, 121.0, 120.8, 117.0, 110.5, 91.7, 20.2. MS (EI, 70 eV; *m/z* (relative intensity)): 400 ([M + 2], 3), 399 ([M + 1], 19), 398 (59), 321 (100), 307 (39), 276 (10), 205 (3), 169 (6), 138 (4). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O$ $[M + H]^+$: 399.1749. Found: 399.1753.

6-(4-methoxyphenyl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2k): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.081 g (79 %), mp 163-166 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 8.7 Hz, 2H), 7.34-7.22 (m, 4H), 7.20 (s, 1H), 7.18-7.00 (m, 6H), 6.95-6.88 (m, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.74 (d, J = 8.0 Hz, 1H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.2, 159.0, 142.4, 140.5, 140.3, 135.1, 134.0, 133.2, 131.2, 130.6, 130.5, 129.8, 128.5, 128.0, 127.9, 126.5, 126.2, 126.1, 126.0, 121.0, 120.7, 116.5, 113.0, 110.4, 91.6, 55.2. MS (EI, 70 eV; *m/z* (relative intensity)): 415 ([M + 1], 15), 414 (48), 337 (100), 307 (65), 293 (19), 276 (8), 207 (7), 163 (7). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O_2$ $[M + H]^+$: 415.1698. Found: 415.1708.

6-(3-methoxyphenyl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2l): Isolated by column chromatography (hexane as eluent) as a yellow viscous oil. Yield: 0.072 g (70 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56-7.50 (m, 1H), 7.34-7.02 (m, 13H), 7.00-6.97 (m, 1H), 6.96-6.90 (m, 2H), 6.85 (ddd, J = 8.2 Hz, J = 2.6 Hz, J = 1.0 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 3.73 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 159.0, 142.7, 142.1, 140.8, 140.5, 134.9, 134.3, 131.4, 130.7, 130.0, 129.4, 128.5, 128.1, 128.0, 126.9, 126.3, 126.2, 126.1, 122.1, 121.1, 120.8, 116.6, 115.1, 113.1, 110.6, 91.5, 55.3. MS (EI, 70 eV; *m/z* (relative intensity)): 415 ([M + 1], 18), 414 (65), 337 (99), 307 (100), 293 (17), 276 (11), 207 (13), 163 (9). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O_2$ $[M + H]^+$: 415.1698. Found: 415.1703.

6-(2-methoxyphenyl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2m): Isolated by column chromatography (hexane as eluent) as a white solid. Yield: 0.084 g (82 %), mp 138-140 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (d, J = 7.3 Hz, 1H), 7.42 (s_l, 1H), 7.36-7.23 (m, 5H), 7.21 (d, J = 7.5 Hz, 1H), 7.18-6.88 (m, 8H), 6.79 (s, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 3.19 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.4, 157.8, 142.9, 139.9, 139.2, 134.8, 134.7, 130.7, 130.6, 130.5, 130.3, 129.7, 128.8, 128.2, 127.6, 127.5, 126.4, 126.3, 125.8, 120.6, 120.4, 120.1, 115.9, 110.1, 109.8, 91.4, 54.6. MS (EI, 70 eV; *m/z* (relative intensity)): 416 ([M + 2], 4), 415 ([M + 1], 23), 414 (69), 337 (100), 321 (52), 307 (60), 292 (8), 276 (8), 207 (6), 168 (9). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{23}O_2$ $[M + H]^+$: 415.1698. Found: 415.1700.

6-(4-chlorophenyl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2n): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.086 g (83 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55-7.51 (m, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.34-7.23 (m, 6H), 7.22-7.00 (m, 7H), 6.94 (td, J = 7.5 Hz, J = 0.9 Hz, 1H), 6.91 (s, 1H), 6.77-6.72 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.1, 142.5, 140.2, 139.5, 138.9, 134.7, 134.1, 133.3, 131.3, 130.7, 130.6, 129.9, 129.6, 128.2, 128.0, 127.7, 127.0, 126.3, 126.1, 126.0, 121.2, 120.8, 116.6, 110.5, 91.2. MS (EI, 70 eV; *m/z* (relative intensity)): 420 ([M + 2], 18), 419 ([M + 1], 18), 418 (56), 341 (100), 307 (85), 276 (27), 205 (9), 176 (12), 153 (25). HRMS (ESI-TOF) *m/z* calcd for $C_{29}H_{20}ClO$ $[M + H]^+$: 419.1203. Found: 419.1225.

6-(4-fluorophenyl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2o): Isolated by column chromatography (hexane as eluent) as a yellow viscous oil. Yield: 0.088 g (88 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (ddd, J = 7.6 Hz, J = 1.3 Hz, J = 0.6 Hz, 1H), 7.45-7.38 (m, 2H), 7.33-7.24 (m, 4H), 7.22 (s, 1H), 7.21-7.12 (m, 3H), 7.11-7.04 (m, 3H), 7.03-6.91 (m, 3H), 6.91 (s, 1H), 6.75-6.72 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.2 (d, J = 247.0 Hz), 161.1, 142.5, 140.2, 139.6, 136.5 (d, J = 3.0 Hz), 134.8, 134.1, 131.3, 131.0 (d, J = 8.0 Hz), 130.7, 129.9, 129.3, 128.2, 128.0, 126.9, 126.2, 126.1, 126.0, 121.1, 120.7, 116.6, 114.4 (d, J = 21.0 Hz), 110.4, 91.3. MS (EI, 70 eV; *m/z* (relative intensity)): 403 ([M + 1], 16), 402 (50), 325 (100), 307 (58), 276 (8), 205 (5), 176 (4), 153 (13). HRMS (ESI-TOF) *m/z* calcd for $C_{29}H_{20}FO$ $[M + H]^+$: 403.1498. Found: 403.1503.

5a-phenyl-6-(3-(trifluoromethyl)phenyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2p): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.061 g (54 %), mp 59-61 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71 (s, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.46-7.37 (m, 1H), 7.36-7.02 (m, 11H), 7.01-6.90 (m, 2H), 6.73 (d, J = 8.0 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.1, 142.8, 141.3, 140.2, 139.5, 134.7, 134.5, 132.9, 131.4, 130.9, 130.3 (quart, J = 32.0 Hz), 130.2, 130.0, 128.3, 128.0, 127.9, 127.2, 126.3, 126.2 (2C), 126.0, 124.3 (quart, J = 272.0 Hz), 124.0 (quart, J = 4.0 Hz), 121.3, 120.8, 116.7, 110.6, 91.2. MS (EI, 70 eV; *m/z* (relative intensity)): 453 ([M + 1], 14), 452 (45), 375 (100), 307 (69), 276 (11), 205 (5), 176 (5), 153 (20). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{20}F_3O$ $[M + H]^+$: 453.1466. Found: 453.1471.

5a-(3-methoxyphenyl)-6-(4-methoxyphenyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2q): Isolated by column chromatography (hexane as eluent) as a yellow solid. Yield: 0.083 g (75 %), mp 156-159 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (ddd, J = 7.6 Hz, J = 1.3 Hz, J = 0.6 Hz, 1H), 7.41 (d, J = 8.9 Hz, 2H), 7.35-7.26 (m, 2H), 7.21 (s, 1H), 7.20-7.10 (m, 3H), 7.02-6.96 (m, 1H), 6.95-6.89 (m, 3H), 6.88-6.82 (m, 3H), 6.78-6.74 (m, 1H), 6.62 (ddd, J = 8.0 Hz, J = 2.6 Hz, J = 1.0 Hz, 1H), 3.80 (s, 3H), 3.53 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.2, 159.1, 159.0, 142.2, 142.1, 140.4, 135.1, 134.0, 133.3, 131.3, 130.6, 130.5, 129.9, 128.9, 128.6, 126.6, 126.2, 126.1, 121.0, 120.7, 118.6, 116.6, 113.5, 113.0, 112.2, 110.4, 91.4, 55.2, 55.0. MS (EI, 70 eV; *m/z* (relative intensity)): 446 ([M + 2], 2), 445 ([M + 1], 16), 444 (50), 429 (2), 413 (3), 337 (100), 321 (6), 293

(15), 265 (4), 163 (4). HRMS (ESI-TOF) *m/z* calcd for $C_{31}H_{25}O_3$ [M + H]$^+$: 445.1804. Found: 445.1810.

5a-(4-fluorophenyl)-6-(4-methoxyphenyl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2r): Isolated by column chromatography (hexane as eluent) as a white yellow solid. Yield: 0.064 g (60 %), mp 75-78 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.5 Hz, 1H), 7.40 (d, *J* = 8.9 Hz, 2H), 7.35-7.09 (m, 8H), 6.94 (td, *J* = 7.6 Hz, *J* = 0.9 Hz, 1H), 6.91 (s, 1H), 6.86 (d, *J* = 8.9 Hz, 2H), 6.78-6.70 (m, 3H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162. 3 (d, *J* = 247. 0 Hz), 161.1, 159.1, 142.5, 140.3, 136.4 (d, *J* = 3.0 Hz), 135.0, 133.9, 133.0, 131.2, 130.7, 130.6, 129.8, 128.5, 128.2 (d, *J* = 8.0 Hz), 126.7, 126.2, 125.9, 121.1, 120.7, 116.5, 114.7 (d, *J* = 22.0 Hz), 113.0, 110.5, 91.0, 55.2. MS (EI, 70 eV; *m/z* (relative intensity)): 434 ([M + 2], 4), 433 ([M + 1], 30), 432 (96), 417 (3), 401 (3), 337 (100), 325 (99), 294 (20), 276 (4), 168 (11). HRMS (ESI-TOF) *m/z* calcd for $C_{30}H_{22}FO_2$ [M + H]$^+$: 433.1604. Found: 433.1609.

5a-phenyl-6-(thiophen-3-yl)-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2s): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.073 g (75 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.6 Hz, 1H), 7.48 (dd, *J* = 3.0 Hz, *J* = 1.3 Hz, 1H), 7.40-7.00 (m, 14H), 6.95 (td, *J* = 7.6 Hz, *J* = 0.9 Hz, 1H), 6.84-6.77 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.0, 142.2, 141.1, 140.2, 135.5, 134.8, 134.3, 131.2, 130.7, 129.8, 129.2, 128.1, 128.0, 127.9, 126.7, 126.3, 126.2, 126.1, 124.2, 124.0, 121.0, 120.7, 116.7, 110.5, 91.5. MS (EI, 70 eV; *m/z* (relative intensity)): 392 ([M + 2], 5), 391 ([M + 1], 17), 390 (54), 357 (6), 313 (100), 285 (7), 252 (7), 205 (4), 153 (5). HRMS (ESI-TOF) *m/z* calcd for $C_{27}H_{19}OS$ [M + H]$^+$: 391.1157. Found: 391.1163.

6-(naphthalen-2-yl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2t): Isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Yield: 0.097 g (90 %). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92-7.88 (m, 1H), 7.84-7.77 (m, 2H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.60 (dd, *J* = 8.6 Hz, *J* = 1.8 Hz, 1H), 7.55 (ddd, *J* = 7.6 Hz, *J* = 1.3 Hz, *J* = 0.5 Hz, 1H), 7.46-7.39 (m, 2H), 7.38-7.27 (m, 4H), 7.25 (s, 1H), 7.19-7.06 (m, 6H), 7.05 (s, 1H), 6.93 (td, *J* = 7.6 Hz, *J* = 0.9 Hz, 1H), 6.71-6.67 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.4, 142.9, 140.9, 140.5, 138.5, 135.1, 134.3, 133.3, 132.8, 131.3, 130.7, 129.9, 129.7, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 126.8, 126.6, 126.4, 126.2, 126.1, 126.0, 125.9, 121.1, 120.8, 116.5, 110.6, 91.7. MS (EI, 70 eV; *m/z* (relative intensity)): 436 ([M + 2], 5), 435 ([M + 1], 30), 434 (87), 357 (100), 307 (88), 276 (7), 178 (19), 163 (10), 77 (6). HRMS (ESI-TOF) *m/z* calcd for $C_{33}H_{23}O$ [M + H]$^+$: 435.1749. Found: 435.1758.

6-(naphthalen-1-yl)-5a-phenyl-5a*H*-benzo[4,5]cyclohepta[1,2-*b*]benzofuran (2u): Compounds **2u** and **2u'** exist as an inseparable mixture (**2u**:**2u'** / 5:1, determined by ^{1}H NMR) isolated by column chromatography (hexane as eluent) as a white yellow viscous oil. Total yield: 0.084 g (78 %). The combined chemical shifts are reported. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02-7.96 (m, 0, 2H), 7.88-7.84 (m, 0.2H), 7.83-7.75 (m, 2.3H), 7.63-7.58 (m, 2H), 7.57-7.54 (m, 1H), 7.52-6.84 (m, 20.7H), 6.67-6.62 (m, 0.2H), 6.39-6.33 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.5, 161.0, 142.1, 140.4, 139.7, 139.3, 139.0, 138.5, 138.1, 134.8, 134.7, 134.5, 133.9, 133.3, 132.9, 132.6, 131.3, 131.1, 130.7, 130.6, 130.3, 130.2, 130.1, 130.0, 128.6, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.1, 127.0, 126.9, 126.8, 126.7, 126.4, 126.2, 126.1, 126.0, 125.9, 125.8, 125.4, 125.3, 124.9, 124.6, 121.1, 121.0, 120.9, 120.7, 117.1, 116.8, 110.6, 110.5, 91.8. MS (EI, 70 eV; *m/z* (relative intensity)): 436 ([M + 2], 4), 435 ([M + 1], 26), 434 (75), 357 (100), 326 (11), 307 (35), 217 (3), 178 (13), 163 (10). HRMS (ESI-TOF) *m/z* calcd for $C_{33}H_{23}O$ [M + H]$^+$: 435.1749. Found: 435.1760.

Acknowledgements

We are grateful to FAPERGS, CAPES and CNPq for financial support. CNPq and CAPES are also acknowledged for the fellowships (R.G. and G. Z.).

Notes and references

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View Article Online
DOI: 10.1039/C6GC02423H

Table of Contents

We present the results on the intramolecular transition metal-free cyclization of (2-alkynylphenyl) benzyl ethers promoted by sodium tert-butoxide.