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Sequential Silver-Catalyzed Oxidative Cyclization Reactions of Unprotected 2-Alkynylanilines to Anthranils

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Abstract: The full details of the original Ag-catalyzed domino oxidative cyclization reactions of unprotected 2-alkynylanilines with Oxone are described. The influences of several parameters including the substrate features, oxidant, reaction conditions, and catalyst on the reaction outcome were explored. A plausible mechanism is provided for the unusual silver-catalyzed oxidative cyclization reactions of 2-alkynylanilines to anthranils.

Introduction

The development of new reactions using readily available starting materials with high product selectivity is a significant challenge in current research.[1] It is of particular interest for the synthesis of sets of heterocyclic compounds from the same set of substrates.[2] In this context, the sequential transformations of 2-ethynylaniline derivatives represent an important strategy for the generation of a variety of functionalized heterocyclic compounds. 2-Alkynylaniline derivatives are usually employed as versatile building blocks to assemble indole scaffolds through their cycloisomerization and transition-metal-catalyzed sequential cyclization and subsequent functionalization. Palladium,[3] rhodium,[4] copper,[5] silver,[6] and gold[7] catalysts have been employed widely for the development of a variety of methods for the synthesis of polysubstituted indoles. Benzo(dipyrrole) systems were formed by double cyclizations of the appropriate 2-alkynylaniline starting materials.[8] A straightforward procedure has been developed for the synthesis of 1,2-disubstituted indoles from 2-alkynylanilines and diaryliodonium salts under metal-free conditions.[9] The intramolecular cascade cyclization reactions of anilines bearing diyne moieties led to the formation of indole-derived polycyclic heterocycles.[10] The complex $[Cp^*IrCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl) catalyzed the cyclization of 2-ethynylanilines to 2,2′-biindoles.[11] Conversely, the dimerization of 2-ethynylanilines promoted by $InBr_3$,[12] heterodimetallic $CpRu(PPh_3)Cl(\mu\text{-dppm})AuI$ [Cp = cyclopentadienyl, dppm = 1,1-bis(diphenylphosphino)methane],[13] or dinuclear $Au_2(BIPHEP)(NTf_2)_2$ [BIPHEP = (biphenyl-2,2′-diyl)bis(diphenylphosphine), NTf_2 = bis(trifluoromethylsulfonyl)imide] catalysts led to multifunctional quinolines.[14] 4-Alkyl-2,3-disubstituted quinolines were obtained in good yields through reactions between 2-alkynylanilines and activated ketones such as β-keto esters promoted by *p*-toluenesulfonic acid.[15] A diversity-orientated approach to complex pyrrolo[1,2-*a*]quinoline derivatives was achieved through the sequential iron-catalyzed three-component coupling of 2-alkynylanilines, nitroalkenes, and 1,3-dicarbonyl compounds and a gold(III)-catalyzed intramolecular hydroarylation reaction.[16] An $Sc(OTf)_3$-catalyzed (OTf = trifluoromethanesulfonate) cascade Prins-type cyclization reaction of 2-alkynylanilines bearing a hydroxy or amine functionality with aldehydes efficiently gave 1,2-dihydroquinoline derivatives with an extra fused ring under mild reaction conditions.[17] 3-Aryl- and 3-alkyl-4(1*H*)-cinnolones were isolated in one step from 2-aryl- or 2-alkyl(ethynyl)anilines by reactions with sodium nitrite and dilute hydrochloric acid through Richter cyclization.[18] Moreover, a $BF_3{\cdot}OEt_2$-promoted cascade reaction of 2-alkynylanilines with nitriles in the presence of *tert*-butyl nitrite provided efficient and general access to a variety of 4-amidocinnolines.[19] A variety of sequential cyclization reactions under oxidative conditions accomplished the synthesis of 2-substituted 3-arylindoles,[20] 2,3′-[21] and 3,3′-biindoles,[22] 1,2,3,4-tetrahydropyrrolo[3,2-*b*]indoles,[23] indoloisoquinolinones,[24] and 5,10-dihydroindolo[3,2-*b*]indole scaffolds.[25]

Despite the relevance of N–O bonds in biologically active heterocycles, methods involving direct N–O bond formation to build up the oxazole heterocycle are quite rare.[26] Recently, we described an efficient approach to the synthesis of 2,1-benzisoxazoles through the chemoselective oxidation of (2-aminoacyl)benzenes with Oxone to achieve the direct N–O bond formation of the target heterocyclic derivatives (Scheme 1a).[27] Moreover, as part of our ongoing interest in the synthesis of heterocyclic scaffolds from readily accessible starting materials

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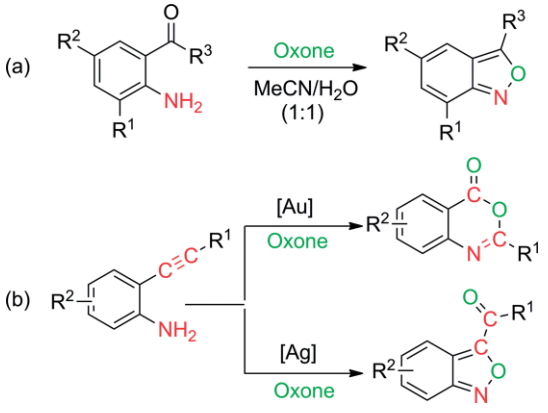
through atom-economical methodologies,[20,28] we reported preliminary results on the development of a divergent sequential cyclization reaction of 2-alkynylanilines involving N–O/O–C bond formation to form (aryl)(benzo[*c*]isoxazol-3-yl)methanone derivatives through a suitable choice of the catalyst and reaction conditions (Scheme 1b).[29] 2-Alkynylanilines were transformed to 2-arylbenzoxazinone derivatives in the presence of a gold catalyst through the expected cycloisomerization to 2-substituted indoles[30] followed by the Oxone-promoted oxidation of 2-arylindoles to 2-arylbenzoxazinones.[31] By switching from gold to silver catalysts, we observed an unprecedented domino oxidative cyclization of unprotected 2-alkynylanilines to benzisoxazoles.

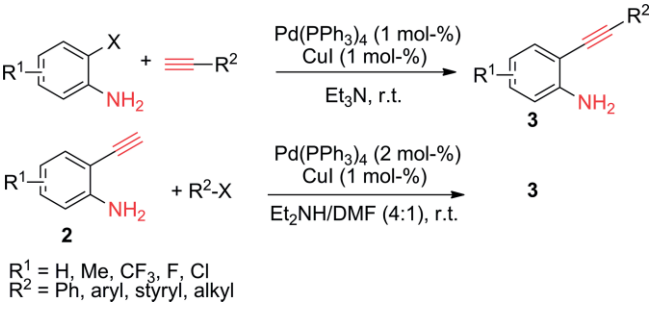


Scheme 1. Synthesis of 2,1-benzisoxazole derivatives through oxidative cyclization reactions.

Herein, we would like to present the full details of the results we have obtained as well as the study of the scope and limitations of the unusual silver-catalyzed oxidative cyclization of 2-alkynylanilines to 2,1-benzisoxazoles.

Results and Discussion

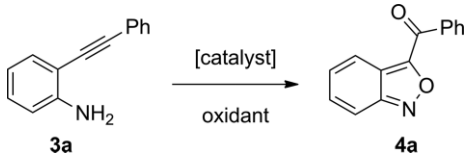
The starting 2-alkynylaniline building blocks **3** can be prepared readily in high yields through the Sonogashira cross-coupling reactions of commercially available 2-haloanilines with terminal alkynes or aryl and vinyl halides with 1-ethynylanilines **2** (Scheme 2).[32]



Scheme 2. Synthesis of 2-alkynylanilines.

To investigate the concept of divergent synthesis through catalyst control, we chose 2-(phenylethynyl)aniline (**3a**) as a

Table 1. Optimization of the conditions for the synthesis of **4a**.[a]



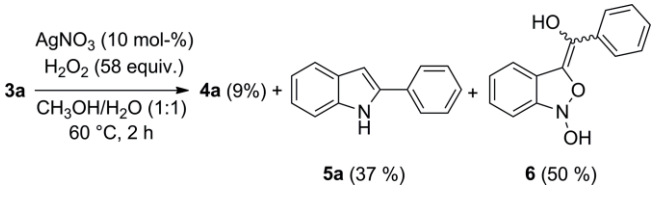
3a **4a**

Entry	Catalyst	Solvent	Oxidant/time [h]	Yield [%] of **4a**[b]
1	$AgNO_3$	CH_3CN	O_2/5[c]	– (95)[d]
2	$AgNO_3$	CH_3CN	*m*-CPBA (1.2 equiv.)/6	– (87)[d]
3	$AgNO_3$	CH_3CN	*N*-oxide[e] (1.0 equiv.)/5	– (92)[d]
4	$AgNO_3$	CH_3CN/H_2O (1:1)	H_2O_2 (4.0 equiv.)/6	– (36)[d,f,g]
5	$AgNO_3$	CH_3CN/H_2O (1:1)	H_2O_2 (58.0 equiv.)/2[g]	– (60)[d,g]
6	$AgNO_3$	CH_3OH/H_2O	H_2O_2 (58.0 equiv.)/2	9[g]
7	$AgNO_3$	CH_3CN	H_2O_2 (58.0 equiv.)/6[h]	28 (35)[d,g]
8	$AgNO_3$	CH_3CN	Oxone (1.0 equiv.)/7	15
9	$AgNO_3$	CH_3OH	Oxone (2.0 equiv.)/6	7
10	$AgNO_3$	CH_3CN/H_2O (10:1)	Oxone (1.0 equiv.)/23	44
11	$AgNO_3$	CH_3CN/H_2O (1:1)	Oxone (1.0 equiv.)/6	50
12	AgOTf	CH_3CN	Oxone (1.0 equiv.)/24	26
13	Ag_2CO_3	CH_3CN/H_2O (10:1)	Oxone (1.0 equiv.)/24	40
14	Ag_2CO_3	CH_3CN/H_2O (1:1)	Oxone (1.0 equiv.)/4	46
15	$AgNO_3$	CH_3CN/H_2O (1:1)	Oxone (2.0 equiv.)/6	69
16	$AgNO_3$	CH_3CN/H_2O (1:1)	Oxone (2.0 equiv.)/2	86[h]
17	$AgNO_3$	CH_3CN/ H_2O (1:1)	Oxone (2.0 equiv.)/4	65[i]
18	$AgNO_3$	CH_3CN/H_2O (1:1)	Oxone (2.0 equiv.)/24	62[j]
19	–	CH_3CN/H_2O (1:1)	Oxone (2.0 equiv.)/24	29

[a] Unless otherwise noted, all reaction were performed with 0.6 mmol of **3a** and 10 mol-% of catalyst at 80 °C. [b] Isolated yield. [c] p_{O_2} = 1 atm. [d] The value in parentheses indicates the yield [%] of recovered **3a**. [e] 2,6-Lutidine *N*-oxide. [f] 2-Phenylindole was isolated in 50 % yield. [g] Hydrogen peroxide–urea adduct. [h] 60 °C. [i] 40 °C. [j] Room temperature.

model substrate to investigate the oxidative cyclization sequences of 2-unprotected 2-alkynylanilines with a variety of oxidants under silver catalysis (Table 1). We previously observed the formation of (benzo[*c*]isoxazol-3-yl)(phenyl)methanone (**4a**) by using silver catalysts instead of gold ones for the reaction of **3a** with Oxone.[29] The formation of the 2,1-benzoisoxazole derivatives could come from a different cascade process involving oxidative steps before the cycloisomerization of the 2-alkynylaniline **3a** to the corresponding 2-phenylindole (**5a**). A brief screening of oxidants revealed the unique behavior of Oxone toward the chemoselective silver-catalyzed oxidation/annulation cascade process to give **4a**.

We failed to obtain the targeted (benzo[*c*]isoxazol-3-yl)-(phenyl)methanone (**4a**) with molecular oxygen as the oxidant (Table 1, Entry 1). Although *m*-chloroperbenzoic acid (*m*-CPBA) was reported as an efficient promoter of the oxidation of aliphatic amines to give the corresponding oximes through the sequential formation of the hydroxylamine/nitroso intermediate,[33] under our conditions, **3a** was recovered in 87 % after 6 h (Table 1, Entry 2). Similarly, the starting aniline **3a** remained unchanged when 2,6-lutidine *N*-oxide was used (Table 1, Entry 3). The use of *N*-oxides as external oxidants allows the assembly of functionalized carbocycles and heterocycles in a remarkably efficient manner.[34] When 30 % H_2O_2, 50 % H_2O_2, and urea–hydrogen peroxide adduct were employed as oxidants (Table 1, Entries 4–7), the product **4a** was isolated only in poor yields. The silver-catalyzed intramolecular hydroamination[35] of **3a** to form **5a** occurred when the reaction was performed at 60 °C in a methanol/H_2O (1:1) mixture in the presence of a large excess of H_2O_2 (50 % H_2O_2 in water; Table 1, Entry 6). Both the temperature[35c] and the reaction medium might play a key role in the promotion of the silver-catalyzed intramolecular hydroamination of unprotected 2-alkynylanilines. The unusual product of peroxidation, 3-[(hydroxy)(phenyl)methylene]-indolin-1-ol (**6**), was also isolated in 50 % yield (Scheme 3).[36] The anthranil derivative **4a** was isolated in 28 % yield when the reaction was performed in CH_3CN at 60 °C in the presence of a large excess of urea–hydrogen peroxide adduct (Table 1, Entry 7). Next, various parameters were modified to address the selective oxidative cyclization reaction toward the formation of the anthranil derivative in the presence of Oxone as the oxidant. Solvents such as CH_3CN and CH_3OH led only to a small amount of the desired **4a** (Table 1, Entries 8 and 9). The amount of H_2O as an additive exerted a great influence on the reaction outcome by assisting the dissolution of Oxone in the reaction medium (Table 1, Entry 10). The influence of the temperature, amount of Oxone, and silver catalyst were investigated briefly.



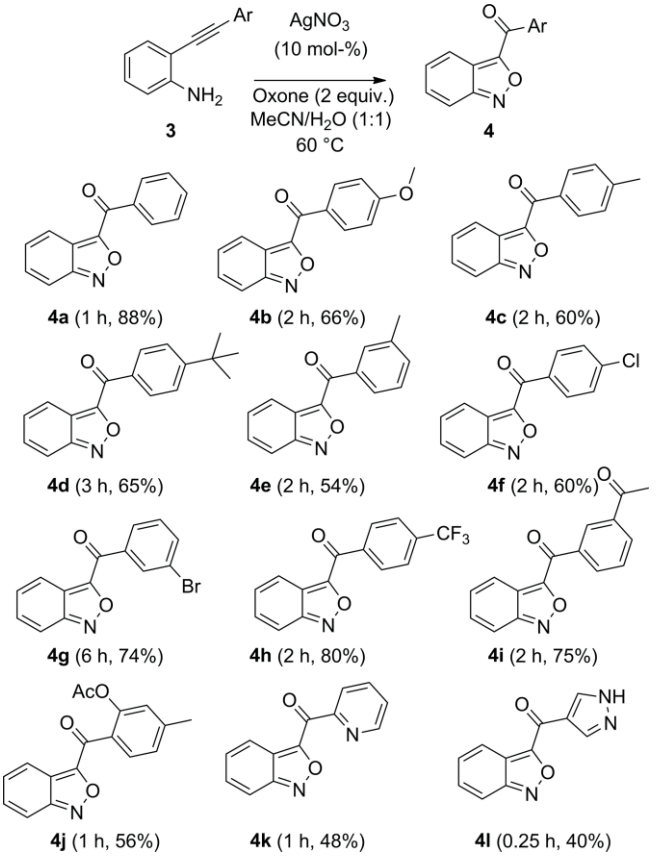
Scheme 3. Unprecedented silver-catalyzed cyclizative peroxidation reaction of 2-(phenylethynyl)aniline (**3a**) with H_2O_2.

Among the different silver catalysts tested, AgOTf and Ag_2CO_3 were less efficient than $AgNO_3$ (Table 1, Entries 11–14).

Compound **4a** was isolated in 50 % yield when the $AgNO_3$-catalyzed reaction of **3a** (1 equiv.) was performed with Oxone as the oxidant (1 equiv.) in CH_3CN/H_2O (1:1) at 80 °C (Table 1, Entry 11). The yield of **4a** increased to 69 % when 2 equiv. of Oxone were used under the same reaction conditions (Table 1, Entry 15). The reaction temperature was also decreased to 60 °C, 40 °C, and room temperature, and the best result (86 % yield) was observed at 60 °C (Table 1, Entries 16–18). Finally, a control experiment demonstrated that **4a** was isolated only in a low yield without the silver catalyst (Table 1, Entry 19).

Subsequently, the scope and limitations of the sequential silver-catalyzed oxidative reaction of 2-alkynylanilines **3** with Oxone were investigated under the best conditions (Table 1, Entry 16).

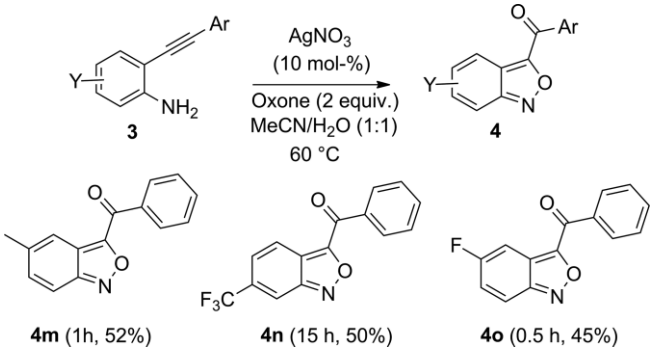
Substrates bearing both electron-rich and electron-poor aromatic groups on the terminal triple bond could be converted into the corresponding benzisoxazoles **4a**–**4j** in moderate to good yields (Scheme 4). Pleasingly, halo substituents such as Cl and Br were well tolerated and could provide the possibility for further elaboration. Acetyl and acetate moieties were also preserved during the domino processes to form functionalized anthranils **4i** and **4j** in 75 and 56 % isolated yield, respectively. In addition to aryl-substituted anilines, substrates bearing heteroaryl moieties afforded the corresponding anthranil deriv-



Scheme 4. Substrate scope for the [Ag]-catalyzed oxidative cyclization with Oxone.

atives **4k**–**4l** in moderate yields. It is worth noting that the previously reported $AuBr_3$-catalyzed cyclization of 2-(arylalkynyl)-nitrobenzenes led to a mixture of isatogens (main product) and anthranils (minor product).[37]

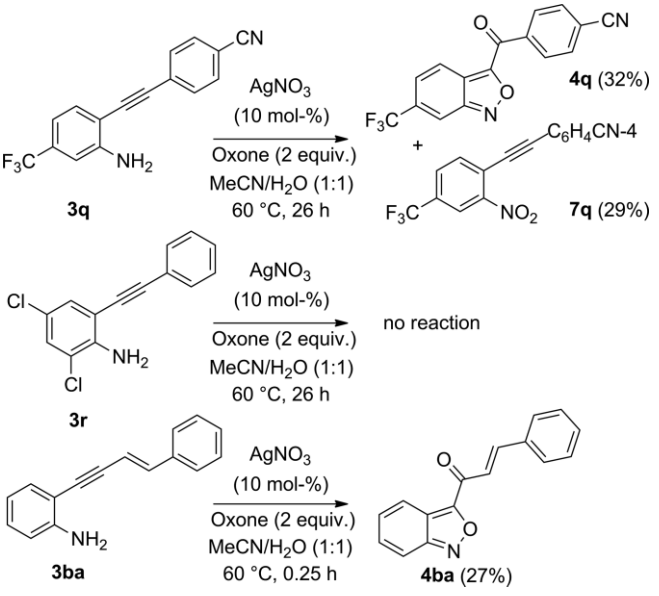
The aniline moiety could also be functionalized (Scheme 5). A methyl group on the aniline moiety (Y) was tolerated, and the corresponding product **4m** was isolated in 52 % yield. Similar modest yields were obtained in the presence of electron-withdrawing substituents. The trifluoromethyl derivative **4n** and the fluoro derivative **4o** were isolated in 50 and 45 % yield, respectively.



Scheme 5. Substrate scope for the [Ag]-catalyzed oxidative cyclization with Oxone.

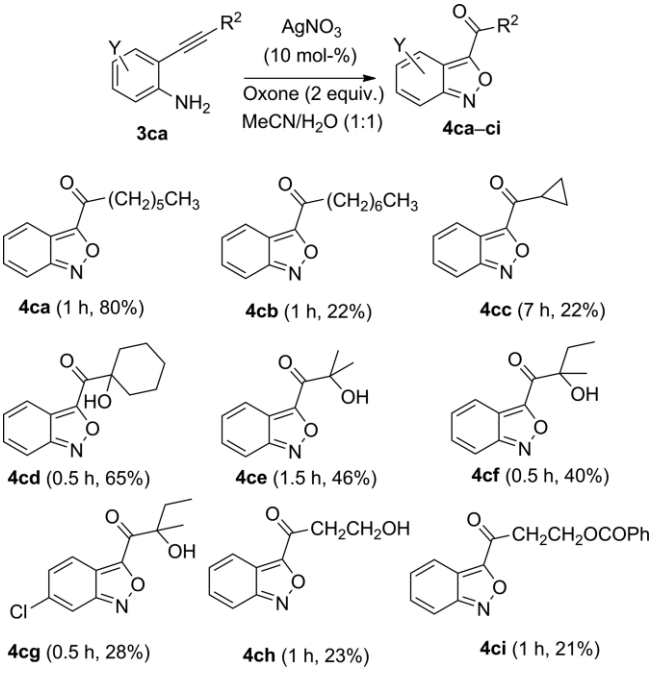
Worse results were observed with the 2-alkynyl derivative **3q** bearing a 4-cyano-substituted phenylalkynyl moiety. The presence of two electron-withdrawing groups hampered the domino oxidation/cyclization process and gave rise to a mixture of the desired compound **4q** and the corresponding noncyclic nitro derivative 4-{[2-nitro-4-(trifluoromethyl)phenyl]ethynyl}-benzonitrile (**7q**) in 32 and 29 % isolated yield, respectively (Scheme 6). The *ortho*-disubstituted chloro derivative **3r** remained unaffected, and no traces of **4r** were detected (Scheme 6), presumably because the chloro substituent at the *ortho* position of aniline prevents oxidation, as reported previously.[38]

The reactivities of other functionalized alkynylanilines, such as 2-alkynylanilines bearing vinyl or alkyl R^2 groups, were then investigated (Schemes 6 and 7). The reaction of the enyne derivative **3ba** bearing a vinyl group on the terminal triple bond gave (*E*)-1-(benzo[*c*]isoxazol-3-yl)-3-phenylprop-2-en-1-one (**4ba**) only in poor yield. A very good yield was obtained for the synthesis of **4ca**, whereas disappointing results were observed for the preparations of anthranils **4cb**–**4cc** (Scheme 7). In all examined cases, full conversion of the starting materials occurred. Very likely, further oxidation through the reaction of the more reactive alkyl ketone moiety with Oxone generates dioxirane derivatives, which are responsible for degradation processes.[39] The presence of an alcohol moiety was also compatible with the reaction conditions to some extent. The hydroxyanthranil derivatives **4cd**–**4ch** were isolated in low to moderate yields depending on the features of the starting propargylic alcohol derivative (Scheme 7). In the presence of tertiary propargylic alcohols, the corresponding α-hydroxy ketones[40] were isolated in satisfactory synthetic yields. Although



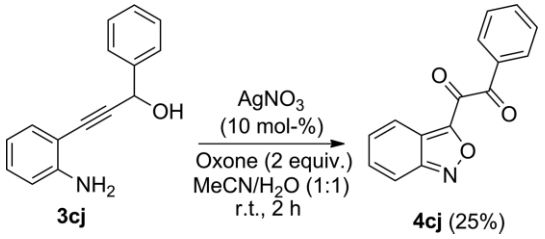
Scheme 6. Substrate scope for the [Ag]-catalyzed oxidative cyclization with Oxone.

the yield was low, the anthranil derivative **4ch** bearing an unprotected alcohol group was isolated in a yield comparable to that of the benzoate derivative **4ci**.



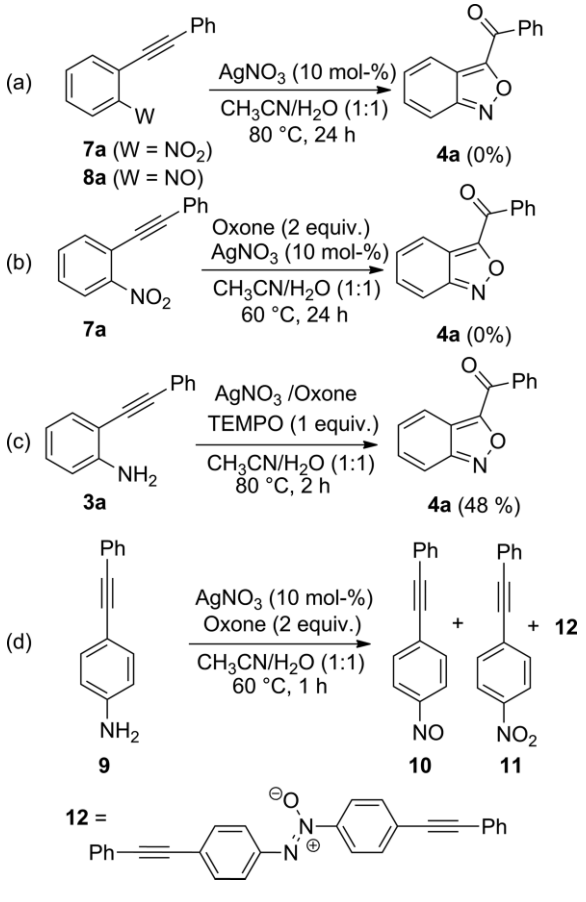
Scheme 7. Substrate scope for the [Ag]-catalyzed oxidative cyclization with Oxone.

Conversely, only 1-(benzo[*c*]isoxazol-3-yl)-2-phenylethane-1,2-dione (**4cj**) was isolated from 3-(2-aminophenyl)-1-phenylprop-2-yn-1-ol (**3cj**; Scheme 8). Benzylic alcohols are more prone to oxidation by Oxone.[41] Therefore, the further oxidative cleavage[42] of the 1,2-dione **4cj** that occurs under our reactions conditions limits its synthetic utility.



Scheme 8. Substrate scope for the [Ag]-catalyzed oxidative cyclization with Oxone.

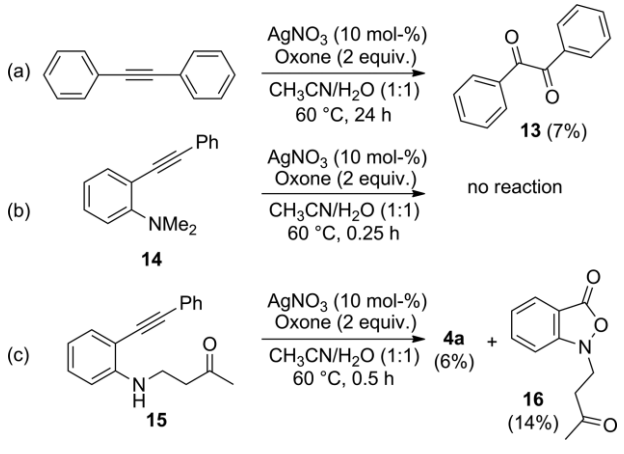
Mechanistically, the silver-catalyzed domino oxidative cyclization of 2-alkynylanilines **3** is intricate, as the obtained anthranil skeleton may come from different pathways. The faster oxidation of the amino group[43] of the 2-alkynylanilines **3** by Oxone seems to override the hydroamination step under silver catalysis in CH_3CN/H_2O (1:1).[35] The nitro or nitroso compounds derived from **4** could be ruled out as intermediates for the formation of anthranils in our domino process. Indeed, attempts to employ 1-[2-(2-nitrophenyl)ethynyl]benzene (**7a**) and the nitroso adduct **8a** as the precursors of the corresponding anthranil derivative **4a** in the presence of the silver catalyst were unfruitful (Scheme 9a).



Scheme 9. Mechanistic investigations.

Anthranils **4** were obtained through the Au-[37,44] or Ir-catalyzed[45] reactions of 2-(alkylalkynyl)nitrobenzenes, the iodine-mediated cycloisomerizations of nitroheterocyclic adducts,[46] or as byproducts in the specific case of Hg-catalyzed or Oxone-mediated oxidation of nitrobenzenyl-substituted alkynes.[47] Moreover, **7a** was recovered unchanged under the optimized reaction conditions for the silver-catalyzed oxidative cyclization of **3a** with Oxone (Scheme 9b). The oxidation of 2,4′-(ethyne-1,2-diyl)bis(nitrobenzene) by Oxone in trifluoroacetic acid (TFA) furnished benzo[*c*]isoxazol-3-yl(4-nitrophenyl)methanone as the major product.[48] The addition of (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) had a slight influence but did not interrupt the reaction, and this suggests that radical intermediates are not involved in the process (Scheme 9c).[49] It is noticeable that the C–C triple bond of the isomeric 4-(phenylethynyl)aniline (**9**) remained unaltered under the standard reaction conditions. 1-[2-(4-Nitrosophenyl)ethynyl]benzene (**10**, 19 % yield), 1-[2-(4-nitrophenyl)ethynyl]benzene (**11**, 27 % yield), and (*Z*)-1,2-bis-[4-(phenylethynyl)phenyl]diazene 1-oxide (**12**, 12 % yield) were isolated (Scheme 9d).[50]

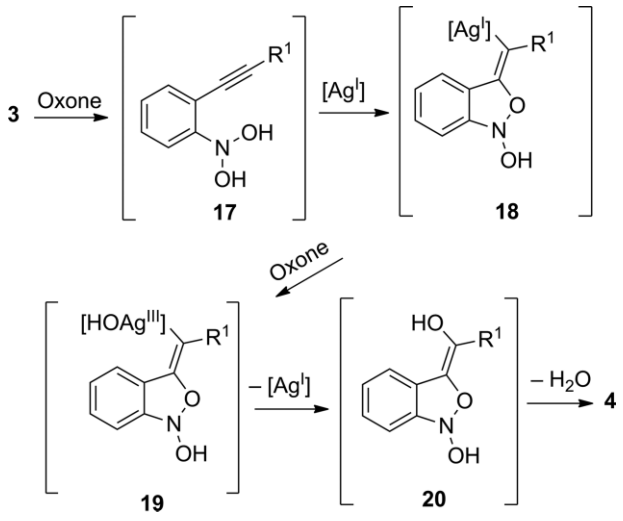
Although the Oxone-promoted oxidation of diarylalkynes to 1,2-diketones in TFA has been described,[48] 1,2-diphenylethane-1,2-dione (**13**) was isolated only in traces (7 %) when diphenylacetylene was treated with Oxone under our reaction conditions (diphenylacetylene was recovered in 76 % yield). Moreover, a rapid complete decomposition was observed for *N*,*N*′-dimethyl-2-(2-phenylethynyl)benzeneamine (**14**), and 4-{[2-(phenylethynyl)phenyl]amino}butan-2-one (**15**) gave a complex mixture. The isolation of derivatives **4a** (6 % yield) and **16** (14 % yield) in this latter case confirmed that the presence of an *o*-amino group in the 2-alkynylanilines plays a key role in the formation of the anthranil derivative (Scheme 10).



Scheme 10. Mechanistic investigations.

On the basis of the results of our control experiments, a plausible mechanism is outlined in Scheme 11. The Oxone-mediated oxidation of the starting 2-alkynylaniline **3** should generate the dihydroxylamine intermediate **17**. The intramolecular nucleophilic attack of the hydroxy group on the activated triple bond would result in the *anti*-vinylsilver(I) species **18** selectively through a 5-*exo*-*dig* annulation process.[51] The Ag^I/Ag^{III} redox cycle should determine the C–O bond formation to give the enol derivative **20**, which would lead to the anthranil after dehydration (Scheme 11). Direct evidence for C–O bond formation through a reductive elimination step at a monometallic silver

center has been described recently.[52] Moreover, Ag^{III} intermediates[53] were proposed in the synthesis of 2-aryl-2*H*-benzotriazoles from azobenzenes.[54]



Scheme 11. Proposed mechanism.

Conclusions

The scope and limitations of the original Ag-catalyzed domino oxidative cycloisomerization reactions of unprotected 2-alkynylanilines to afford anthranils were investigated thoroughly. Under the optimized reaction conditions, the methodology with Oxone as the oxidant without any acids or bases was compatible with many 2-[(hetero)arylethynyl]anilines bearing various electron-donating and electron-withdrawing groups on the aromatic moiety. The influence of the features of the substituents of the aniline aromatic ring on the product selectivity was highlighted. Alkenyl- and alkyl-substituted starting alkynes gave intriguing results. The results of control experiments suggest the involvement of an Ag^{I}/Ag^{III} catalytic cycle in the unusual oxidative cyclization of 2-alkynylanilines.

Experimental Section

General Methods: All reactions were performed with magnetic stirring and monitored by TLC with silica gel 60A (Fluorochem). The IR spectra were recorded with samples as KBr pellets or neat in NaCl with a Perkin–Elmer Spectrum Two FTIR spectrometer. The ^{1}H NMR spectra were recorded at 400 MHz with a Bruker Avance III spectrometer. The chemical shifts [ppm] were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ or to [D_6]dimethyl sulfoxide ([D_6]DMSO) as an internal standard (δ = 2.49 ppm). The ^{13}C NMR spectra were recorded with the same spectrometer at 100.6 MHz and were calibrated with $CDCl_3$ (δ = 77.00 ppm) or [D_6]DMSO (δ = 30.50 ppm). Mass spectrometry was performed with an AB SCIEX TOF/TOF 5800 MALDI-TOF spectrometer. Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and used as purchased. The reaction products were purified by flash chromatography with silica gel (60–200 μm) by elution with *n*-hexane/EtOAc mixtures. All 2-alkynylanilines **3** (except **3ba** and **3gc**), **14**, and **15** were described previously and prepared according to literature procedures. Compounds **4a**–**4c**, **4e**–**4n**, **4q**, **4ca**, **4cc**, **5**, **7q**, **9**, and **13** are known products and were identified by comparison of the reported physical and spectroscopic data.

Typical Procedure for the Synthesis of the 2-Alkynylanilines. (*E*)-2-(4-Phenylbut-3-en-1-yn-1-yl)aniline (3ba): A mixture of 2-ethynylaniline (0.300 g, 2.56 mmol), β-bromostyrene (0.702 g, 3.84 mmol), $Pd(PPh_3)_4$ (0.059 g, 0.051 mmol), CuI (0.005 g, 0.025 mmol), and diethylamine (4 mL) in *N*,*N*-dimethylformamide (DMF; 1 mL) was stirred at room temperature under nitrogen for 4 h. Then, 1 M HCl (200 mL) and $CHCl_3$ (200 mL) were added. The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The purification of the residue by flash chromatography (eluent: hexane/EtOAc, 95:5) afforded **3ba** (0.404 g, 72 % yield). IR (KBr): $\tilde{\nu}$ = 2182, 1607, 743, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 8.03 (d, *J* = 15.9 Hz, 1 H), 7.82 (d, *J* = 15.9 Hz, 1 H), 7.77 (dd, *J* = 1.1, *J* = 0.8 Hz, 1 H), 7.76–7.73 (m, 2 H), 7.48–7.46 (m, 3 H), 7.43 (ddd, *J* = 9.1, *J* = 6.4 Hz, *J* = 1.0 Hz, 1 H), 7.30 (ddd, *J* = 8.8, *J* = 6.4 Hz, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 178.3 (C=O), 160.7 (C), 157.7 (C), 146.1 (CH), 134.4 (C), 131.4 (CH), 131.3 (CH), 129.1 (2CH), 129.0 (2CH), 128.4 (CH), 127.3 (C), 121.7 (CH), 121.3 (CH), 116.0 (CH) ppm. HRMS (ESI+): calcd. for $C_{16}H_{12}NO_2$ [M + H]$^+$ 250.0868; found 250.0872.

1-(2-Amino-4-chlorophenyl)-3-methylpent-1-yn-3-ol (3cg): To a solution of 5-chloro-2-iodoaniline (0.646 g, 2.55 mmol) in Et_3N (5.0 mL) were added $Pd(PPh_3)_2Cl_2$ (0.036 g, 0.051 mmol), CuI (0.010 g, 0.051 mmol), and 3-methylpent-1-yn-3-ol (0.300 g, 3.06 mmol). The mixture was stirred at 30 °C under N_2 for 4 h, and saturated NH_4Cl solution (200 mL) and EtOAc (200 mL) were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The purification of the residue by flash chromatography (eluent: hexane/EtOAc, 60:40) afforded **3cg** (0.562 g, 99 % yield). IR (KBr): $\tilde{\nu}$ = 3387, 3285, 2212, 1419, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (dt, *J* = 8.2, *J* = 0.4 Hz, 1 H), 6.67 (dt, *J* = 2.0, *J* = 0.4 Hz, 1 H), 6.63 (ddd, *J* = 8.2, *J* = 2.0 Hz, *J* = 0.4 Hz, 1 H), 4.26 (br. s, 2 H, NH_2), 2.41 (br. s, 1 H, OH), 1.84–1.74 (m, 2 H, CH_2), 1.57 (s, 3 H, CH_3), 1.09 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 148.7 (C_q), 135.2 (C_q), 133.1 (CH), 118.1 (CH), 114.1 (CH), 106.0 (C_q), 99.1 (C_q), 79.1 (C_q), 69.4 (C–OH), 36.7 (CH_2), 29.5 (CH_3), 9.2 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{12}H_{15}ClNO$ [M + H]$^+$ 224.0842; found 224.0843.

Typical Procedure for the Silver-Catalyzed Oxidative Cyclization of 2-Alkynylanilines 3 with Oxone. (Benzo[*c*]isoxazol-3-yl)[4-(*tert*-butyl)phenyl]methanone (4d): $AgNO_3$ (0.013 g, 0.074 mmol) and Oxone (0.911 g, 1.48 mmol) were added to a solution of 2-{[(4-*tert*-butyl)phenyl]ethynyl}aniline (**3d**; 0.185 g, 0.74 mmol) in CH_3CN/H_2O (2.5 mL:2.5 mL). The mixture was stirred at 60 °C, and the reaction was monitored by TLC. After 3 h, the mixture was cooled, and H_2O (150 mL) and CH_2Cl_2 (150 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography on silica gel (eluent: hexane/EtOAc, 95:5) to give **4d** (0.135 g, 65 % yield). IR (KBr): $\tilde{\nu}$ = 1643, 1292, 895, 758 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.15 (m, 2 H), 8.06 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.66 (ddd, *J* = 9.1, *J* = 1.7 Hz, *J* = 0.8 Hz, 1 H), 7.53–7.49 (m, 2 H), 7.33 (ddd, *J* = 9.1, *J* = 6.4 Hz, *J* = 0.8 Hz, 1 H), 7.19 (ddd, *J* = 8.8, *J* = 6.4 Hz, *J* = 0.7 Hz, 1 H), 1.30 (s, 9 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 181.1 (C=O), 160.8

(C_q), 157.8 (C_q), 157.3 (C_q), 133.5 (C_q), 131.3 (CH), 130.2 (2 CH), 128.3 (CH), 125.8 (2 CH), 121.9 (CH), 121.5 (C_q), 115.9 (CH), 35.3 (C_q), 31.1 (3 CH_3) ppm. HRMS (ESI+): calcd. for $C_{18}H_{17}KNO_2$ $[M + K]^+$ 318.0896; found 318.0898.

(5-Fluorobenzo[*c*]isoxazol-3-yl)(phenyl)methanone (4o): IR (KBr): $\tilde{\nu}$ = 1658, 1267, 809, 712 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.28 (m, 2 H), 7.80 (ddd, *J* = 9.6, *J* = 4.6 Hz, *J* = 0.8 Hz, 1 H), 7.76 (ddd, *J* = 8.2, *J* = 2.3 Hz, *J* = 0.8 Hz, 1 H), 7.71 (tt, *J* = 7.4, *J* = 1.3 Hz, 1 H), 7.63–7.59 (m, 2 H), 7.29 (ddd, *J* = 9.6, *J* = 8.5 Hz, *J* = 2.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 181.2 (C=O), 161.8 (d, *J* = 253.6 Hz, C–F), 160.9 (d, *J* = 11.5 Hz, C_q), 155.4 (C_q), 135.8 (C_q), 133.9 (CH), 130.1 (2 CH), 128.8 (2 CH), 124.8 (d, *J* = 31.7 Hz, CH), 121.8 (d, *J* = 12.6 Hz, C_q), 118.7 (d, *J* = 9.8 Hz, CH), 103.8 (d, *J* = 26.3 Hz, CH) ppm. HRMS (ESI+): calcd. for $C_{14}H_9FNO_2$ $[M + H]^+$ 242.0617; found 242.0610.

1-(2,1-Benzisoxazol-3-yl)-3-phenylprop-2-en-1-one (4ba): IR (KBr): $\tilde{\nu}$ = 1658, 1597, 1155, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 8.03 (d, *J* = 15.9 Hz, 1 H), 7.82 (d, *J* = 15.9 Hz, 1 H), 7.77 (dd, *J* = 1.1, *J* = 0.8 Hz, 1 H), 7.76–7.73 (m, 2 H), 7.48–7.46 (m, 3 H), 7.43 (ddd, *J* = 9.1, *J* = 6.4 Hz, *J* = 1.0 Hz, 1 H), 7.30 (ddd, *J* = 8.8, *J* = 6.4 Hz, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 178.3 (C=O), 160.7 (C_q), 157.7 (C_q), 146.1 (CH), 134.4 (C_q), 131.4 (CH), 131.3 (CH), 129.1 (2 CH), 129.0 (2 CH), 128.4 (CH), 127.3 (C_q), 121.7 (CH), 121.3 (CH), 116.0 (CH) ppm. HRMS (ESI+): calcd. for $C_{16}H_{12}NO_2$ $[M + H]^+$ 250.0868; found 250.0872.

1-(2,1-Benzisoxazol-3-yl)octan-1-one (4cb): IR (KBr): $\tilde{\nu}$ = 1683, 1292, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.65 (ddd, *J* = 9.1, *J* = 1.2 Hz, *J* = 0.8 Hz, 1 H), 7.32 (ddd, *J* = 9.1, *J* = 6.4 Hz, *J* = 1.1 Hz, 1 H), 7.19 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 3.09 (t, *J* = 7.4 Hz, 2 H), 1.80–1.70 (m, 2 H), 1.38–1.18 (m, 8 H), 0.82 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 190.5 (C=O), 159.8 (C_q), 157.6 (C_q), 131.2 (CH), 128.4 (CH), 121.3 (CH), 119.1 (C_q), 115.9 (CH), 40.2 (CH_2), 31.7 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 23.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{15}H_{19}KNO_2$ $[M + K]^+$ 284.1053; found 284.1050.

(2,1-Benzisoxazol-3-yl)(1-hydroxycyclohexyl)methanone (4cd): IR (KBr): $\tilde{\nu}$ = 3468, 1663, 1119, 870, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.76 (ddd, *J* = 9.1, *J* = 1.2 Hz, *J* = 0.8 Hz, 1 H), 7.43 (ddd, *J* = 9.1, *J* = 6.5 Hz, *J* = 1.0 Hz, 1 H), 7.31 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 3.63 (br. s, 1 H, OH), 2.36 (td, *J* = 12.8, *J* = 4.7 Hz, 2 H), 1.91–1.70 (m, 8 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.4 (C=O), 157.8 (C), 157.1 (C), 131.5 (CH), 129.1 (CH), 122.3 (C), 121.6 (CH), 116.0 (CH), 78.4 (COH), 33.8 (2 CH_2), 25.1 (CH_2), 21.2 (2 CH_2) ppm. HRMS (ESI+): calcd. for $C_{14}H_{16}NO_3$ $[M + H]^+$ 246.1130; found 246.1130.

1-(2,1-Benzisoxazol-3-yl)-2-hydroxy-2-methylpropan-1-one (4ce): IR (KBr): $\tilde{\nu}$ = 3478, 1663, 1287, 1170, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.71 (dt, *J* = 9.1, *J* = 1.0 Hz, 1 H), 7.38 (ddd, *J* = 9.0, *J* = 6.5 Hz, *J* = 1.1 Hz, 1 H), 7.27 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 3.90 (br. s, 1 H, OH), 1.69 (s, 6 H, CH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.2 (C=O), 157.3 (C_q), 157.1 (C_q), 131.5 (CH), 129.2 (CH), 122.2 (C_q), 121.4 (CH), 116.1 (CH), 76.3 (C_q), 26.7 (2 CH_3) ppm. HRMS (ESI+): calcd. for $C_{11}H_{12}NO_3$ $[M + K]^+$ 244.0376; found 244.0377.

1-(2,1-Benzisoxazol-3-yl)-2-hydroxy-2-methylbutan-1-one (4cf): IR (KBr): $\tilde{\nu}$ = 3524, 1668, 1190, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.77 (ddd, *J* = 9.1, *J* = 1.2 Hz, *J* = 0.8 Hz, 1 H), 7.44 (ddd, *J* = 9.1, *J* = 6.5 Hz, *J* = 1.0 Hz, 1 H), 7.33 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 4.00 (br. s, 1 H, OH), 2.39–2.30 (m, 1 H, CH_2), 2.10–2.01 (m, 1 H, CH_2), 1.73 (s, 3 H, CH_3), 0.85 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.7 (C=O), 157.4 (C_q), 157.2 (C_q), 131.5 (CH), 129.3 (CH), 122.0 (C_q), 121.4 (CH), 116.1 (CH), 79.3 (C_q), 32.5 (CH_2), 25.4 (CH_3), 7.8 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{12}H_{14}NO_3$ $[M + H]^+$ 220.0974; found 220.0977.

1-(6-Chloro-2,1-benzisoxazol-3-yl)-2-hydroxy-2-methylbutan-1-one (4cg): IR (KBr): $\tilde{\nu}$ = 3468, 1673, 1297, 1175, 809 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 9.2, *J* = 0.9 Hz, 1 H), 7.77 (dd, *J* = 1.6, *J* = 0.9 Hz, 1 H), 7.25 (dd, *J* = 9.2, *J* = 1.6 Hz, 1 H), 3.90 (br. s, 1 H, OH), 2.31 (td, *J* = 14.6, *J* = 7.4 Hz, 1 H, CH_2), 2.05 (td, *J* = 14.6, *J* = 7.6 Hz, 1 H, CH_2), 1.71 (s, 3 H, CH_3), 0.85 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 193.7 (C=O), 157.9 (C_q), 157.3 (C_q), 138.2 (C_q), 131.2 (CH), 122.7 (CH), 120.3 (C_q), 114.6 (CH), 79.4 (C_q), 32.4 (CH_2), 25.2 (CH_3), 7.8 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{12}H_{13}ClNO_3$ $[M + H]^+$ 254.0584; found 254.0585.

1-(2,1-Benzisoxazol-3-yl)-3-hydroxypropan-1-one (4ch): IR (KBr): $\tilde{\nu}$ = 3433, 1683, 1282, 1114, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.65 (ddd, *J* = 9.1, *J* = 1.2 Hz, *J* = 0.9 Hz, 1 H), 7.33 (ddd, *J* = 9.1, *J* = 6.5 Hz, *J* = 1.1 Hz, 1 H), 7.20 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 4.06 (t, *J* = 5.5 Hz, 2 H, CH_2), 3.37 (t, *J* = 5.5 Hz, 2 H, CH_2), 2.51 (br. s, 1 H, OH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 189.6 (C=O), 159.4 (C_q), 157.6 (C_q), 131.4 (CH), 128.9 (CH), 121.0 (CH), 119.3 (C_q), 116.0 (CH), 57.4 (CH_2), 42.4 (CH_2) ppm. HRMS (ESI+): calcd. for $C_{10}H_9KNO_3$ $[M + K]^+$ 230.0220; found 230.0223.

3-(2,1-Benzisoxazol-3-yl)-3-oxopropyl Benzoate (4ci): IR (KBr): $\tilde{\nu}$ = 1719, 1683, 1282, 753, 707 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 8.01–7.98 (m, 2 H), 7.74 (ddd, *J* = 9.1, *J* = 1.2 Hz, *J* = 0.8 Hz, 1 H), 7.54 (tt, *J* = 7.5, *J* = 1.7 Hz, 1 H), 7.44–7.39 (m, 3 H), 7.29 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 4.84 (t, *J* = 6.2 Hz, 2 H, CH_2), 3.67 (t, *J* = 6.2 Hz, 2 H, CH_2) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 186.8 (C=O), 166.4 (C=O), 159.3 (C_q), 157.6 (C_q), 133.1 (CH), 131.4 (CH), 130.2 (C_q), 129.6 (2 CH), 128.9 (CH), 128.4 (2 CH), 121.4 (C_q), 121.1 (CH), 116.0 (CH), 59.2 (CH_2), 39.2 (CH_2) ppm. HRMS (ESI+): calcd. for $C_{17}H_{13}NNaO_4$ $[M + Na]^+$ 318.0742; found 318.0743.

1-(Benzo[*c*]isoxazol-3-yl)-2-phenylethane-1,2-dione (4cj): IR (KBr): $\tilde{\nu}$ = 1737, 1674, 845 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.06 (m, 2 H), 8.02 (dt, *J* = 8.8, *J* = 1.1 Hz, 1 H), 7.82 (dt, *J* = 9.0, *J* = 1.0 Hz, 1 H), 7.72 (tt, *J* = 7.5, *J* = 1.3 Hz, 1 H), 7.60–7.55 (m, 2 H), 7.47 (ddd, *J* = 9.0, *J* = 6.5 Hz, *J* = 1.0 Hz, 1 H), 7.38 (ddd, *J* = 8.8, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 190.5 (C=O), 181.1 (C=O), 157.5 (C_q), 136.4 (C_q), 135.4 (CH), 134.5 (C_q), 131.5 (CH), 130.3 (2 CH), 129.9 (CH), 129.2 (2 CH), 125.2 (C_q), 120.5 (CH), 116.6 (CH) ppm. HRMS (ESI+): calcd. for $C_{15}H_9KNO_3$ $[M + K]^+$ 290.0220; found 290.0218.

Silver-Catalyzed Oxidative Cyclization of 3a with Hydrogen Peroxide. 3-[(Hydroxy)(phenyl)methylene]-2,1-benzisoxazol-1(3*H*)-ol (6): $AgNO_3$ (0.010 g, 0.058 mmol) and H_2O_2 (2.5 mL, 50 wt.-% in H_2O) were added to a solution of **3a** (0.113 g, 0.58 mmol) in CH_3OH (2.5 mL). The mixture was stirred at 60 °C, and the reaction was monitored by TLC. After 0.5 h, the mixture was cooled, and H_2O (150 mL) and CH_2Cl_2 (150 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography with silica gel (eluent: hexane/EtOAc, 95:5) to give a mixture of (*E*)- and (*Z*)-**6** (0.70 g, 50 % yield). IR (KBr): $\tilde{\nu}$ = 3414, 3125, 1612, 1216, 754, 701 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 12.15 (s, 1 H, NOH), 8.71–8.69 (m, 1 H), 8.06–8.04 (m, 1 H), 7.96–7.93 (m, 2 H), 7.67–7.55 (m, 4 H), 7.22–7.17 (m,1 H), 3.87 (br. s, 1 H, OH) ppm. ^{13}C NMR (100.6 MHz, [D_6]DMSO): δ =

169.90 (C), 169.85 (C), 164.7 (C), 164.6 (C), 141.1 (C), 140.9 (C), 134.50 (C), 134.45 (C), 134.3 (CH), 132.14 (CH), 132.13 (CH), 131.24 (CH), 131.23 (CH), 128.9 (CH), 127.0 (CH), 122.9 (CH), 119.9 (CH), 119.8 (CH), 116.5 (C), 116.4 (C) ppm. HRMS (ESI+): calcd. for $C_{14}H_{11}KNO_3$ $[M + K]^+$ 280.0376; found 280.0368.

Silver-Catalyzed Oxidative Reaction of 4-(Phenylethynyl)aniline (9) with Oxone: $AgNO_3$ (0.014 g, 0.083 mmol) and Oxone (1.020 g, 1.66 mmol) were added to a solution of **9** (0.160 g, 0.83 mmol) in CH_3CN/H_2O (2.5/2.5 mL). The mixture was stirred at 60 °C, and the reaction was monitored by TLC. After 1.0 h, the mixture was cooled, and H_2O (150 mL) and CH_2Cl_2 (150 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography on silica gel (eluent: hexane/EtOAc, 90:10) to give **10**–**12**.

1-Nitroso-4-(phenylethynyl)benzene (10): 0.019 g, 19 % yield. IR (KBr): $\tilde{\nu}$ = 2207, 1114, 844, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 2 H), 7.75–7.73 (m, 2 H), 7.60–7.56 (m, 2 H), 7.41–7.37 (m, 3 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.5 (C_q), 132.5 (2 CH), 131.9 (2 CH), 131.0 (C_q), 129.2 (2 CH), 128.5 (2 CH), 122.3 (C_q), 120.9 (CH), 95.5 (C_q), 88.5 (C_q) ppm. HRMS (ESI+): calcd. for $C_{14}H_9NNaO$ $[M + Na]^+$ 230.0582; found 230.0582.

1-Nitro-4-(phenylethynyl)benzene (11): 0.050 g, 27 % yield. IR (KBr): $\tilde{\nu}$ = 2212, 1343, 855, 768 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.23–8.20 (m, 2 H), 7.68–7.64 (m, 2 H), 7.57–7.55 (m, 2 H), 7.41–7.37 (m, 3 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 147.0 (C_q), 132.3 (2 CH), 131.8 (2 CH), 130.3 (C_q), 129.3 (2 CH), 128.5 (2 CH), 123.6 (CH), 122.1 (C_q), 94.7 (C_q), 87.6 (C_q) ppm. HRMS (ESI+): calcd. for $C_{14}H_{10}NO_2$ $[M + K]^+$ 262.0270; found 262.0267.

(*Z*)-1,2-Bis[4-(phenylethynyl)phenyl]diazene 1-Oxide (12): 0.019 g, 12 % yield. IR (KBr): $\tilde{\nu}$ = 2212, 1597, 1261, 1099, 844, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.31 (m, 2 H), 8.24–8.22 (m, 2 H), 7.68–7.63 (m, 4 H), 7.58–7.55 (m, 4 H), 7.39–7.36 (m, 6 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 143.4 (C_q), 138.1 (C_q), 132.00 (2 CH), 131.96 (2 CH), 131.8 (2 CH), 131.7 (2 CH), 128.9 (CH), 128.6 (CH), 128.5 (2 CH), 128.4 (2 CH), 127.1 (C_q), 125.8 (2 CH), 124.7 (C_q), 122.9 (C_q), 122.6 (C_q), 122.4 (2 CH), 92.8 (C_q), 91.7 (C_q), 89.3 (C_q), 88.2 (C_q) ppm. HRMS (ESI+): calcd. for $C_{28}H_{19}N_2O$ $[M + H]^+$ 399.1497; found 399.1497.

Silver-Catalyzed Reaction of Diphenylacetylene with Oxone: $AgNO_3$ (0.014 g, 0.085 mmol) and Oxone (1.046 g, 1.70 mmol) were added to a solution of diphenylacetylene (0.152 g, 0.35 mmol) in CH_3CN/H_2O (2.5/2.5 mL). The mixture was stirred at 60 °C, and the reaction was monitored by TLC. After 24 h, the mixture was cooled, and H_2O (150 mL) and CH_2Cl_2 (150 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography on silica gel (eluent: hexane/EtOAc, 98:2) to give 1,2-diphenylethane-1,2-dione (**13**;[48] 0.012 g, 7 % yield) and recovered starting diphenylacetylene (0.115 g, 76 % yield).

Silver-Catalyzed Oxidative Reaction of 4-{[2-(Phenylethynyl)phenyl]amino}butan-2-one (15) with Oxone: $AgNO_3$ (0.019 g, 0.115 mmol) and Oxone (1.360 g, 2.30 mmol) were added to a solution of **15** (0.283 g, 1.15 mmol) in CH_3CN/H_2O (2.5 mL:2.5 mL). The mixture was stirred at 60 °C, and the reaction was monitored by TLC. After 0.5 h, the mixture was cooled, and H_2O (150 mL) and CH_2Cl_2 (150 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried with sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography withon silica gel (eluent: hexane/EtOAc, 75:25) to give (benzo[*c*]isoxazol-3-yl)(phenyl)methanone (**4a**; 0.015 g, 6 % yield).

1-(3-Oxobutyl)-2,1-benzisoxazol-3(1*H*)-one (16): (0.033 g, 14 % yield): IR (KBr): $\tilde{\nu}$ = 1765, 1709, 1170, 758, 682 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (ddd, *J* = 7.9, *J* = 1.2 Hz, *J* = 0.8 Hz, 1 H), 7.67 (ddd, *J* = 8.3, *J* = 7.2 Hz, *J* = 1.2 Hz, 1 H), 7.27 (ddd, *J* = 7.9, *J* = 6.5 Hz, *J* = 0.8 Hz, 1 H), 7.22 (dt, *J* = 8.3, *J* = 0.8 Hz, 1 H), 3.85 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.93 (tq, *J* = 6.6, *J* = 0.4 Hz, 2 H, CH_2), 2.22 (t, *J* = 0.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 205.9 (C=O), 167.8 (C=O), 157.2 (C), 135.3 (CH), 125.9 (CH), 124.4 (CH), 113.2 (C), 111.9 (CH), 51.0 (CH_2), 39.8 (CH_2), 30.5 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{11}H_{11}KNO_3$ $[M + K]^+$ 244.0376; found 244.0375.

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Silver Catalysis

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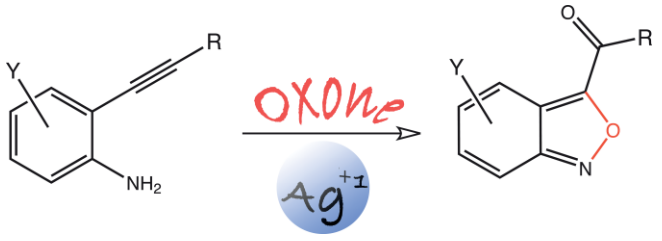
VIP

Sequential Silver-Catalyzed Oxidative Cyclization Reactions of Unprotected 2-Alkynylanilines to Anthranils



The scope and limitations of the unusual silver-catalyzed oxidative cyclizations of 2-alkynylanilines to 2,1-benzisoxazoles are studied.

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