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Substituent effect on anionic cycloaromatization of 2-(2-substituted ethynyl)benzonitriles and related molecules

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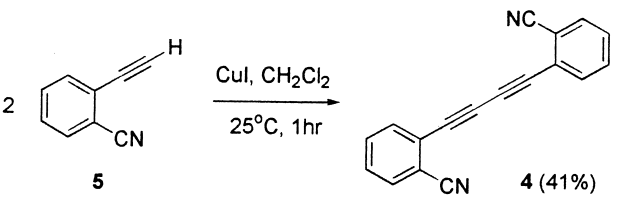
Abstract—Methanolysis of 2-(2-substituted ethynyl)benzonitriles based on the nature of substituents gave 5-*exo* product, isoindolones and 6-*endo* product, isoquinolones, respectively. When a bulky substituent, such as *tert*-butyl group, was employed in this cyclization reaction, a 5-*exo* adduct was obtained. Phenyl and thienyl groups which can stabilize the α-anion affect the cyclization reaction to produce the 5-*exo* adducts. Pyridinyl and pyrazinyl groups can also stabilize the α-anion, but the formation of a more stable intermediate by coordination of sodium with nitrogen atom leads to the 6-*endo* products.

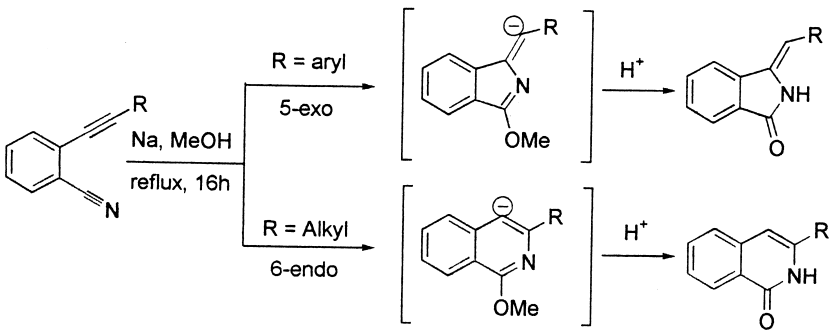
Recently, we reported the anionic cyclization reaction of 2-(2-substituted ethynyl)benzonitriles.[1] When the substituent is an alkyl group, an isoquinolone product was obtained. This cyclization favoring 6-*endo* pathway rather than 5-*exo* is due to the formation of an aromatic ring which lowers the transition state energy. However, when the substituent is changed to an aryl group, an isoindolone was produced. In this case, 5-*exo* transition state has the lower energy due to the ability of the aryl group to stabilize the α-anion (Scheme 1). In order to have more understanding about the substituent effect on this cyclization pathway, more analogs of 2-(2-substituted ethynyl)benzonitriles were prepared by considering both the steric and α-anion stabilization effects and the results are reported.

2-(2-Substituted ethynyl)benzonitriles **1a**–**g** were prepared by palladium catalyzed coupling reaction[2] of 2-iodobenzonitrile (**2**) with alkynes **3a**–**g** in 47–88% yields, respectively. The results are summarized in Scheme 2. Compound **4** was obtained by copper-catalyzed homo-coupling[3] of 2-ethynylbenzonitrile **5** in 41% yield (Eq. (1)).



(1)

Compounds **1a**–**g** were treated with sodium methoxide in refluxing methanol for 16 h to give isoindolones **6** and isoquinolones **7** in different ratios. The results are summarized in Table 1. As we reported earlier,



Scheme 1.

Keywords: cyclization; diynes.

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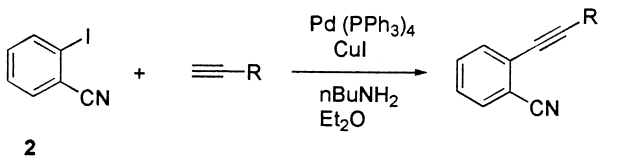


3a, R = Ph — **1a**[1] (54%)

3b, R = thienyl — **1b** (62%)

3c R = t-butyl — **1c** (52%)

3d R = triisopropylsilyl — **1d** (57%)

3e R = cyclohexenyl — **1e** (47%)

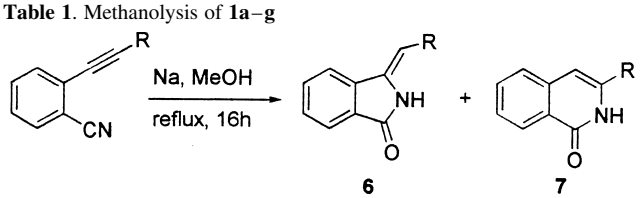
3f R = pyridinyl — **1f** (88%)

3g R = pyrazinyl — **1g** (51%)

Scheme 2.

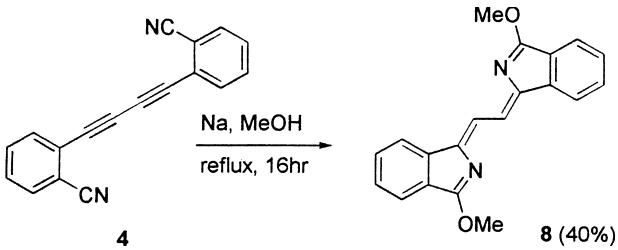
methanolysis of **1a** gave isoindolone **6a** in 48% yield as the major product.[1] When the phenyl substituent was replaced by thienyl, cyclization of **1b** gave **6b** in 82% yield, again it favors the 5-*exo*-pathway. For a bulky substituent, such as *tert*-butyl group, cyclization of **1c** favors the 5-*exo* transition state and gives the isoindolone **6c** in 48% yield and the 6-*endo* product **7c** in only 8% yield. Triisopropylsilyl group and *tert*-butyl have less α-anion stabilization compared to phenyl group. Therefore, cyclization of **1d** also gave isoquinolone **7d** in 42% yield. Compared to phenyl substituent, cyclohexenyl group has similar α-anion stabilization ability but less steric hinderence. Cyclization of **1e** gave the 6-*endo* product **7e** as the major product. When the substituent was switched to 2-pyridinyl, we observed an interesting result. Methanolysis of **1f** gave mainly the 6-*endo* product **7f** in 88% yield. A similar result was obtained on the methanolysis of **1g** to give **7g** in 70% yield.

Table 1. Methanolysis of **1a**–**g**

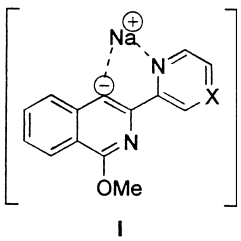


R	Products (yields, %)	
1a R=Ph	**6a**[1] (48)	
1b R=thienyl	**6b** (82)	
1c R=*t*-butyl	**6c** (48)	**7c**[6] (8)
1d R=triisopropylsilyl	**6d**[7] (14), R=H	**7d**[8] (42), R=H
1e R=cyclohexenyl	**6e** (11)	**7e** (35)
1f R=pyridinyl		**7f**[9] (88)
1g R=pyrazinyl		**7g** (70)

We believe that the unusual selectivity for 2-pyridinyl and pyrazinyl is because of the coordination of metal with nitrogen atom to form a stable intermediate **I**. This coordination effect could overcome both the steric effect and the α-anion stabilization ability which favored the formation of the 5-*exo* adduct. Methanolysis of **4** gave a symmetrical bis-isoindole **8** in 40% yield (Eq. (2)). The structure of compound was unambiguously determined by X-ray crystallography.[4] (Fig. 1) This result indicates that cyclization favors 5-*exo*-pathway due to the good stabilization ability of α-anion by sp carbon on the acetylene.



(2)



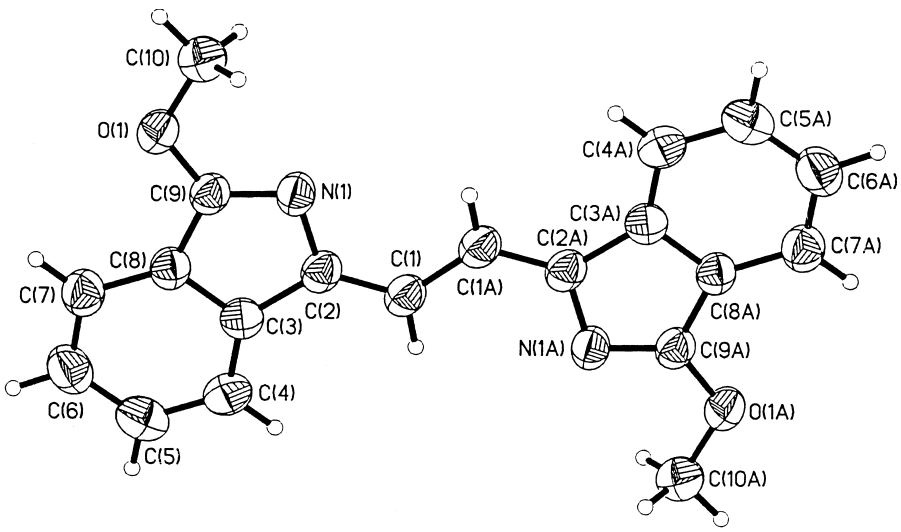
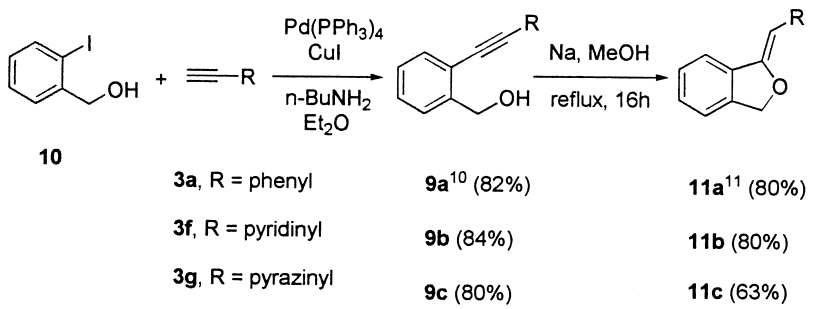


Figure 1. X-Ray structure of **8**.



Scheme 3.

Further interesting results were observed on the cyclization of 2-(substituted ethynyl)benzyl alcohols **9a–c**. These compounds were prepared by palladium catalyzed coupling reaction of 2-iodobenzyl alcohol **10** with alkynes **3a** and **3f–g**. Methanolysis of **9a–c** under the same reaction conditions gave the 5-*exo* products **11a–c** in all cases regardless of whether there is a coordination effect or not (Scheme 3).

In conclusion, intramolecular nucleophilic addition to triple bond usually proceeds via a 5-*exo*-dig transition state.[5] In this study, we found that methanolysis of 2-(2-substituted ethynyl)benzonitriles gave 6-*endo* product isoquinolones and 5-*exo* product isoindolones based on the nature of the substituents. The driving force to form the 6-*endo* product is the formation of an aromatic ring. However, steric, electronic and coordination effects also have strong impact on this cyclization reaction. When a bulky substituent, such as *tert*-butyl group, was employed in this cyclization reaction, a 5-*exo* adduct was obtained. Phenyl and thienyl groups which can stabilize the α-anion will affect the cyclization reaction to produce the 5-*exo* adducts. Pyridinyl and pyrazinyl groups can also stabilize the α-anion, but the formation of a more stable intermediate by coordination of sodium with nitrogen atom leads to the 6-*endo* products.

1. Experimental

1.1. General procedure of the coupling reaction of 2-substituted ethyne with 2-iodobenzonitrile (method A)

A degassed solution of 2-iodobenzonitrile (12 mmol) in dry ether (30 mL) containing $Pd(PPh_3)_4$ (0.8 mmol) and CuI (3.2 mmol) was added to a solution of acetylene (24 mmol) containing *n*-butylamine (34 mmol). The resulting solution was stirred for 6 h at 25°C, quenched with saturated aqueous NH_4Cl and Na_2CO_3 solutions and extracted with EtOAc. The organic layer was separated and dried over $MgSO_4$. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography to give the products.

1.2. General procedure for methanolysis of 2-(2-substituted ethynyl)benzonitrile (method B)

To a solution of 2-(2-substituted ethynyl)benzonitrile (1 mmol) in 10 mL of methanol was added freshly cut sodium metal (5 mmol), the solution was heated to reflux and stirred for 16 h. After cooling to room temperature, the methanol was removed in vacuo. To the residue, sat. NaCl(aq) was added and extracted with EtOAc. The combined organic layer was dried over anhydrous $MgSO_4$(s). After filtration and removal of solvent, the residue was purified by column chromatography to give the separated products.

1.2.1. 2-(2-Phenylethynyl)benzonitrile (1a).[1] Obtained in 54% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.69–7.55 (m, 5H), 7.43–7.36 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 132.6, 132.3, 131.9, 129.2, 128.4, 128.4, 128.1, 127.2, 122.0, 117.5, 115.3, 96.0, 85.5.

1.2.2. 2-(2-Thienylethynyl)benzonitrile (1b). Obtained in 62% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.68–7.51 (m, 3H), 7.45–7.36 (m, 3H), 7.04 (dd, 1H, *J*=5.2, 3.6 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 133.4, 132.6, 132.2, 131.9, 131.9, 128.7, 128.2, 127.3, 126.9, 121.8, 117.4, 114.8, 111.9, 89.2. MS (EI): 209 (M^+, 100), 219 (13), 194 (12), 97 (17). HRMS (EI) calcd for $C_{13}H_7NS$ 209.0300, found 209.0304.

1.2.3. 2-(2-*tert*-Butylethynyl)benzonitrile (1c). Obtained in 52% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.60 (dd, 1H, *J*=7.6, 0.8 Hz), 7.57–7.46 (m, 2H), 7.30 (td, 1H, *J*=7.6, 0.8 Hz), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 132.4, 132.4, 132.1, 131.9, 128.0, 127.4, 117.6, 115.5, 105.8, 30.6, 28.2. MS (EI): 183 (M^+, 44), 167 (100), 140 (13), 107 (12). HRMS (EI) calcd for $C_{13}H_{13}N$ 183.1048, found 183.1048.

1.2.4. 2-(2-Triisopropylsilylethynyl)benzonitrile (1d). Obtained in 57% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.62 (dd, 1H, *J*=7.6, 1.2 Hz), 7.57–7.30 (m, 3H), 1.51–1.37 (m, 3H), 1.25 (d, 18H, *J*=7.0 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 132.7, 132.5, 132.1, 128.3, 127.2, 117.3, 115.7, 102.3, 98.9, 18.7, 18.6. MS (EI): 283 (M^+, 15), 240 (100), 184 (50), 170 (53), 154 (22). HRMS (EI) calcd for $C_{18}H_{25}SiN$ 283.1757, found 283.1742.

1.2.5. 2-(2-Cyclohexenylethynyl)benzonitrile (1e). Obtained in 47% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.65 (td, 1H, *J*=7.4, 1.2 Hz), 7.51–7.29 (m, 3H), 6.41–6.30 (m, 1H), 2.27–2.12 (m, 4H), 1.70–1.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 138.2, 133.0, 132.8, 132.7, 129.2, 128.1, 120.6, 118.1, 115.5, 98.6, 83.7, 30.8, 29.4, 23.4, 22.6. MS (EI): 207 (M^+, 82), 206 (100), 179 (25), 165 (54), 140 (51), 77 (22). HRMS (EI) calcd for $C_{15}H_{13}N$ 207.1017, found 207.1049.

1.2.6. 2-(2-Pyridinylethynyl)benzonitrile (1f). Obtained in 88% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.64 (dd, 1H J=7.6, 0.8 Hz), 7.73–7.57 (m, 5H), 7.45 (td, 1H, J=7.6, 1.2 Hz), 7.31–7.27 (m, 1H); MS (EI): 204 (M^+, 100), 177 (13), 151 (8). HRMS (EI) calcd for $C_{14}H_8N_2$ 204.0688, found 204.0692.

1.2.7. 2-(2-Pyrazinylethynyl)benzonitrile (1g). Obtained in 51% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (d, 1H, J=1.6 Hz), 8.62 (td, 2H, J=8.0, 1.0 Hz), 7.77–7.51 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.2, 144.5, 143.6, 139.3, 132.8, 132.8, 132.5, 129.6, 125.3, 117.0, 115.8, 91.4, 88.5. MS (EI): 205 (M^+, 100), 152 (48), 53 (7). HRMS (EI) calcd for $C_{13}H_7N_3$ 205.0641, found 205.0646.

1.2.8. Bis-(2-ethynylbenzonitrile) (4). To a solution of 2-ethynylbenzonitrile (1 mmol) in 5 ml of DMF was added CuI (1 mmol), the solution was stirred for 2 h. To the solution, sat. NaCl(aq) was added and extracted with EtOAc. The combined organic layer was dried over anhydrous $MgSO_4$(s). After filtration and removal of solvent, the residue was purified by column chromatography to give the product **4** (41%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.71–7.45 (m, 4H). MS (EI): 252 (M^+, 100), 225 (10), 126 (6). HRMS (EI) calcd for $C_{18}H_8N_2$ 252.0688, found 252.0691.

1.2.9. 3-(Phenylmethylene)isoindol-1-one (6a).[1] Obtained in 48% yield as a solid according to method B. Mp=187–188°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (bs, 1H), 7.88 (d, 1H, J=7.6 Hz), 7.79 (d, 1H, J=7.6 Hz), 7.64 (td, 1H, J=7.6, 1.2 Hz), 7.52 (t, 1H, J=7.6 Hz), 7.47–7.41 (m, 4H), 7.33–7.29 (m, 1H), 6.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 169.0, 138.2, 134.9, 133.1, 132.2, 132.2, 129.2, 128.7, 128.5, 127.7, 123.5, 119.8, 105.9.

1.2.10. 3-(Thienylmethylene)isoindol-1-one (6b). Obtained in 82% yield as a solid according to method B. Mp=144–145°C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.06 (bs, 1H), 7.86 (dd, 1H, J=7.4, 1.4 Hz), 7.74 (dd, 1H, J=7.6, 3.0 Hz), 7.66–7.37 (m, 3H), 7.17–7.08 (m, 2H), 6.71 (s, 1H).; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 168.3, 138.0, 132.3, 131.2, 129.0, 128.5, 128.0, 128.0, 127.8, 126.1, 123.8, 119.6, 99.3. MS (EI): 227 (M^+, 100), 198 (14), 183 (12), 97 (17). HRMS (EI) calcd for $C_{13}H_9ONS$ 227.0405, found 227.0410.

1.2.11. 3-(*tert*-Butylmethylene)isoindol-1-one (6c) and 3-(*tert*-butyl)isoquinolin-1-one (7c).[6] Compounds **6c** and **7c** obtained in 56% as a yellow solid according to method B and they were not separated by liquid chromatography, from ^{1}H NMR spectrum, it shows as a mixture of **6c** (48%) and **7c** (8%). The following spectrum belongs to **6c**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.98 (bs, 1H), 7.82 (dd, 1H, J=7.6, 0.8 Hz), 7.63 (dd, 1H, J=7.6, 0.8 Hz), 7.56 (td, 1H, J=7.6, 0.8 Hz), 7.45 (td, 1H, J=7.6, 1.0 Hz), 5.58 (s, 1H), 1.30 (s, 9H). The following peaks of the spectrum belong to **7c**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 10.30 (bs, 0.16H), 6.52 (s, 0.16H), 1.40 (s, 1.44H), the other peaks of aromatic could not be separated from **6c**.

1.2.12. 3-Methyleneisoindol-1-one (6d)[7] **and isoquinolin-1-one (7d).**[8] Compounds **6d** and **7d** were obtained in 56% as a yellow solid according to method B and they were not separated by liquid chromatography. From the ^{1}H NMR spectrum, a mixture of **6d** (14%) and **7d** (42%) were assumed. The following spectrum belongs to **7d**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.80 (bs, 1H), 8.41 (dd, 1H, J=7.6, 0.8 Hz), 7.69 (td, 1H, J=7.6, 0.8 Hz), 7.58 (d, 1H, J=8.0 Hz), 7.52 (td, 1H, J=7.6, 0.8 Hz), 7.18 (d, 1H, J=7.2 Hz), 6.60 (d, 1H, J=7.2 Hz); the following peaks of the spectrum belong to **6d**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (bs, 0.33H), 5.21 (d, 0.33H, J=2.0 Hz), 4.98 (d, 0.33H, J=2.0 Hz), the other peaks of aromatic could not be separated from **7d**.

1.2.13. 3-(2-Cyclohexenylmethylene)isoindol-1-one (6e) and 3-(cyclohexenyl)isoquinolin-1-one (7e). Compound **6e** was obtained in 11% yield and **7e** in 35% yield as a yellow oil according to method B. **6e**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.97 (bs, 1H), 7.87–7.82 (m, 1H), 7.68–7.63 (m, 1H), 7.59–7.54 (m, 1H), 7.48–7.43 (m, 1H), 6.05–6.01 (m, 1H), 5.50 (d, 1H, J=8.0 Hz), 2.39–2.32 (m, 2H), 2.23–2.03 (m, 2H), 1.86–1.62 (m, 4H). MS (EI): 225 (M^+, 10), 212 (100), 184 (56), 147 (68), 141 (90), 130 (47). HRMS (EI) calcd for $C_{15}H_{15}ON$ 225.1154, found 225.1158.

7e: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 9.48 (bs, 1H), 8.34 (d, 1H, J=8.0 Hz), 7.64 (td, 1H, J=7.6, 1.2 Hz), 7.52 (d, 1H, J=7.6 Hz), 7.44 (td, 1H, J=7.6, 1.2 Hz), 7.39–7.35 (m, 1H), 6.51 (s, 1H), 2.42–2.38 (m, 2H), 2.31–2.27 (m, 2H), 1.82–1.77 (m, 2H), 1.72–1.66 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 163.2, 139.3, 138.4, 132.9, 130.3, 127.6, 127.3, 126.4, 126.3, 112.0, 102.9, 29.6, 25.7, 22.3, 21.7. MS (EI): 225 (M^+, 100), 196 (39), 161 (37), 149 (32), 85 (37), 43 (44). HRMS (EI) calcd for $C_{15}H_{15}ON$ 225.1154, found 225.1160.

1.2.14. 3-Pyridinylisoquinolin-1-one (7f).[9] Obtained in 88% yield as a solid according to method B. Mp=143–144°C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 10.65 (bs, 1H), 8.61–8.57 (m, 2H), 8.38 (d, 1H, J=7.6 Hz), 7.89 (dt, 1H, J=7.6, 1.0 Hz), 7.67–7.58 (m, 3H), 6.39 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 169.2, 156.2, 149.6, 138.6, 138.3, 137.1, 132.5, 130.2, 103.0, 124.8, 124.2, 121.5, 120.5, 102.4.

1.2.15. 3-Pyrazinylisoquinolin-1-one (7g). Obtained in 70% yield as a solid according to method B. Mp=186–187°C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 10.56 (bs, 1H), 8.43 (td, 2H, J=7.8, 1.2 Hz), 8.24 (d, 1H, J=8.0 Hz), 7.74–7.63 (m, 2H), 7.56–7.38 (m, 2H), 6.29 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 168.1, 151.2, 144.9, 143.0, 140.9, 139.9, 137.0, 132.1, 129.9, 128.7, 123.3, 120.0, 111.7. MS (EI): 223 (M^+, 94), 222 (100), 195 (12), 130 (9). HRMS (EI) calcd for $C_{13}H_9ON_3$ 223.0747, found 223.0740.

1.2.16. Bis-(3-methyleneisoindol-1-methyl ether) (8). Obtained in 40% yield as a solid according to method B. Mp=250–251°C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.88 (dt, 2H, J=8.0, 1.0 Hz), 7.59 (s, 2H), 7.55 (dd, 2H, J=7.8, 1.2 Hz), 7.47–7.37 (m, 4H), 4.31 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 131.1, 129.3, 128.1, 127.8, 124.2, 123.5, 120.5, 120.0, 117.3, 56.1. MS (EI): 316 (M^+, 36), 301 (52), 286 (38), 186 (24), 32 (25), 28 (100). HRMS (EI) calcd for $C_{20}H_{16}N_2O_2$ 316.1213, found 316.1202.

1.2.17. 2-(2-Phenylethynyl)benzyl alcohol (9a).[10] Obtained in 82% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.62–7.46 (m, 4H), 7.43–7.21 (m, 5H), 4.91 (s, 2H), 3.00 (bs, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 142.0, 131.5, 131.0, 128.2, 127.9, 126.7, 126.7, 126.4, 122.4, 120.5, 93.7, 86.3, 63.0.

1.2.18. 2-(2-Pyrazinylethynyl)benzyl alcohol (9b). Obtained in 84% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (d, 1H, J=4.4 Hz), 7.32 (td, 1H, J=7.8, 1.2 Hz), 7.60–7.50 (m, 3H), 7.35 (td, 1H, J=7.6, 1.2 Hz), 7.30–7.26 (m, 2H), 4.95 (s, 2H), 2.70 (bs, 1H). MS (EI): 208 (M^+, 53), 179 (100), 152 (11). HRMS (EI) calcd for $C_{14}H_{11}ON$ 209.0841, found 209.0847.

1.2.19. 2-(2-Pyrazinylethynyl)benzyl alcohol (9c). Obtained in 80% yield as an oil according to method A. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.75 (s, 1H), 8.54 (s, 1H), 8.49 (s, 1H), 7.60 (dd, 1H, J=7.6, 1.2 Hz), 7.54 (dd, 1H, J=7.8, 1.0 Hz), 7.42 (td, 1H, J=7.6, 1.2 Hz), 7.30 (td, 1H, J=7.8, 1.0 Hz), 4.95 (s, 2H), 2.60 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 147.6, 144.4, 143.5, 142.9, 132.7, 130.4, 130.0, 127.5, 127.4, 90.8, 90.2, 63.4. MS (EI): 210 (M^+, 49), 181 (100), 127 (11). HRMS (EI) calcd for $C_{13}H_{10}ON_2$ 210.0794, found 210.0795.

1.2.20. 1-(Phenylmethylidene)-1,3-dihydroisobenzofuran (11a).[11] Obtained in 80% yield as an oil according to method B. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.90 (d, 1H, J=7.6 Hz), 7.63 (dd, 1H, J=7.6, 1.0 Hz), 7.53–7.26 (m, 7H), 6.06 (s, 1H), 5.53 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 156.4, 139.2, 136.4, 134.8, 128.7, 128.4, 128.0, 127.8, 125.3, 121.2, 119.9, 96.2, 74.9.

1.2.21. 1-(Pyridinylmethylidene)-1,3-dihydroisobenzofuran (11b). Obtained in 80% yield as an oil according to method B. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.52 (d, 1H, J=4.4 Hz), 8.05 (d, 1H, J=8.0 Hz), 7.63–7.59 (m, 2H), 7.38–7.32 (m, 3H), 6.98 (dd, 1H, J=8.0, 1.0 Hz), 6.22 (s, 1H), 5.52 (s, 2H). MS (EI): 209 (M^+, 70), 180 (81), 152 (11). HRMS (EI) calcd for $C_{14}H_{11}ON$ 209.0841, found 209.0848.

1.2.22. 1-(Pyrazinylmethylidene)-1,3-dihydroisobenzofuran (11c). Obtained in 63% yield as an oil according to method B. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 9.30 (s, 1H), 8.46 (s, 1H), 8.25 (s, 1H), 7.64 (dd, 1H, J=8.0, 1.0 Hz), 7.49–7.37 (m, 3H), 6.14 (1H), 5.59 (s, 2H). MS (EI): 210 (M^+, 100), 180 (32), 127 (10). HRMS (EI) calcd for $C_{13}H_{10}ON_2$ 210.0794, found 210.0786.

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