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Selectivity in Garratt−Braverman Cyclization of Aryl-/Heteroaryl-Substituted Unsymmetrical Bis-Propargyl Systems: Formal Synthesis of 7′-Desmethylkealiiquinone

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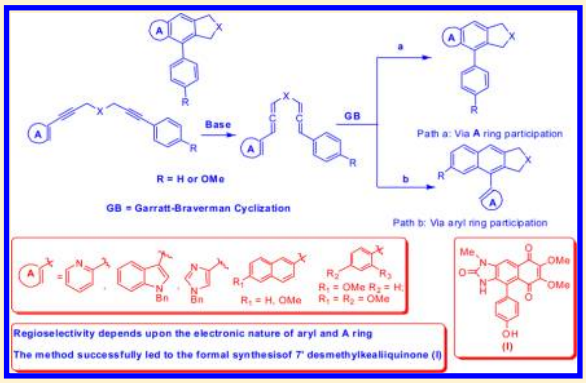
Supporting Information

ABSTRACT: Unsymmetrical bis-propargyl ethers and sulfonamides containing various combinations of aryl/heteroaryl substituents at the acetylene termini were synthesized, and their reactivity under basic conditions was studied. Moderate to high (chemo)selectivity was observed, which followed a trend opposite to that reported earlier for the corresponding sufones. The major products obtained in most cases (except with indole) were formed via participation of the heteroaryl ring or the less electron rich aryl ring. The selectivity observed in imidazole-based systems was exploited to complete a formal total synthesis of 7′-desmethylkealiiquinone, an analogue of the marine alkaloid kealiiquinone.



INTRODUCTION

Garratt−Braverman (GB) cyclization[1a−k] is the rearrangement of aryl-substituted bis-allenic sulfone/sulfides, ethers, and amines/sulfonamides leading to aromatic systems. The reaction involves formation of two C−C bonds, believed to pass through a biradical intermediate, and belongs to the class of cyclo-aromatization reactions.[11] The reactive bis-allenic system is made in situ from the corresponding bis-propargyl counterparts via a base-mediated isomerization. The GB reaction of unsymmetrical bis-propargyl sulfones, ethers, and sulfonamides can follow two pathways, involving either of the two aryl rings at the termini. It was earlier shown[2] by our group that the GB reaction of such sulfones can be made chemoselective by suitable perturbation of the electronic character of the terminal aryl groups (Scheme 1). The reaction follows a pathway in which the aryl group with greater electron-donating ability preferentially participates in the rearrangement. The rationale behind such selectivity was the greater nucleophilic character of the benzylic radical attached to the aryl ring having electron-donating properties. This interpretation was also supported by theoretical calculations. Unlike sulfones, there has been no systematic study of selectivity of GB cyclization involving bis-propargyl ethers or sulfonamides. Moreover, the effect of replacing one of the aryl groups with a heterocyclic ring such as pyridine, indole, or imidazole or an electronically different aryl ring such as naphthyl or methoxyphenyl also has not been evaluated (Scheme 2). Such a study, especially for heteroaryl systems, is relevant, as natural products of the kealiinine family[3] are imidazolyl fused benzenoid systems with a pendant aryl ring (Figure 1). This skeleton, at least in principle, may be obtainable via the GB reaction of a suitably heteroaryl substituted bis-propargyl system, provided proper selectivity is achieved during GB cyclization. It may be mentioned here that the selectivity issue addressed in the present cases is close to chemoselectivity rather than regioselectivity. The two different aryl rings or the aryl and heteroaryl rings on the two arms of the bis-propargyl system may be considered as representing two different functionalities, and thus chemoselectivity is involved in the two possible GB pathways and is used henceforth.[4]

RESULTS AND DISCUSSION

With this in mind, we proceeded with the synthesis of target bis-propargyl ethers and sulfonamides; key synthetic steps involved Sonogashira coupling[5] and O- or N-propargylation.[6] As an example, ether **1a** was prepared via a NaH-mediated O-alkylation of the alcohol **4a** with the propargyl bromide **7**. The alcohol **4a** was prepared by a Sonogashira reaction between *N*-benzyl-3-iodoindole (**6a**) and propargyl alcohol, while the bromide **7** was obtained via a similar reaction of iodobenzene with propargyl alcohol followed by bromination via mesylation and displacement with LiBr. O-alkylation of **4a** with the bromide **7** was achieved using NaH in THF at 0 °C (Scheme 3).

In order to follow the outcome of the Garratt−Braverman rearrangement, these bis-propargyl ethers/sulfonamides were treated with base (KO^{t}Bu/DBN/DBU depending upon the substrate) in toluene at reflux. The ratio of the products, as determined from the ^{1}H NMR spectrum of the crude reaction mixture by comparing the ratio of integrations for characteristic

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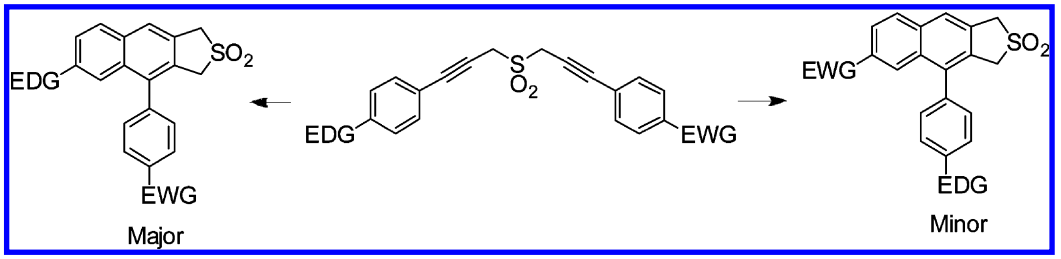
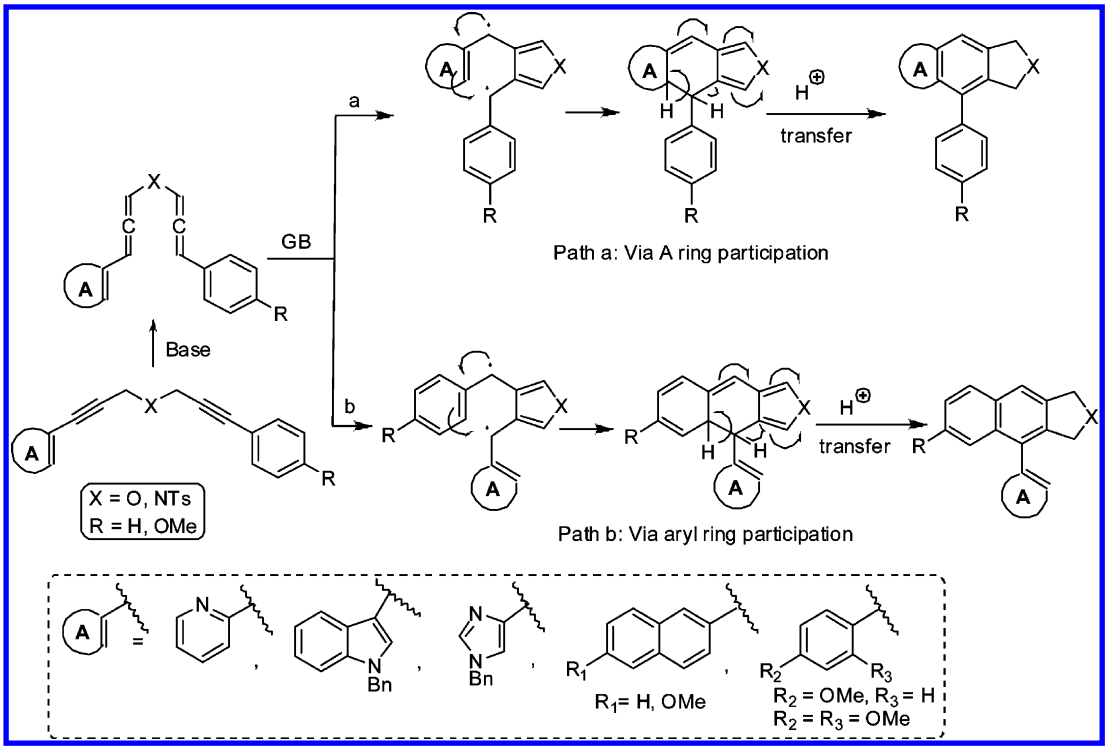
Scheme 1. GB Reaction of Sulfone



Scheme 2. GB Reaction of Mixed Propargyl Systems



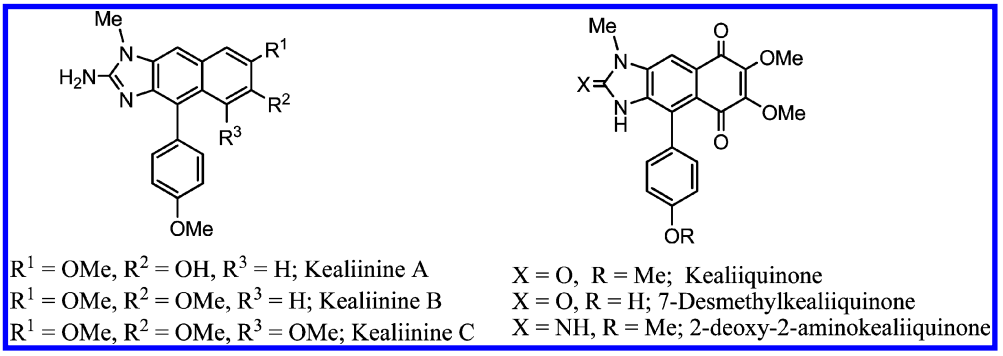


Figure 1. Kealiinine and kealiiquinone alkaloids and analogues.

signals for the two isomers, showed varying degrees of selectivity with a definite trend. In some cases, the selectivity was very high and we failed to see the peaks of the other isomer in the NMR spectrum. The results of the GB reaction for all of the substrates are shown in Table 1. As the molecular masses are the same for the starting material as well as for the products and ^{1}H NMR provides very little discriminatory information, the structures of the products were confirmed on the basis of ^{13}C NMR spectra. For a representative example, the structure elucidation of product **12a** was based upon 13 aryl C−H signals observed in the DEPT-135 spectrum. The alternate structure **9a** would have shown 11 aryl C−H signals (Scheme 4). ^{1}H NMR in d_6-acetone also clearly showed the presence of two one-proton singlets, which is possible only for structure **12a** (for the spectrum see the Supporting Information)

The greater participation of the imidazole nucleus during the GB reaction encouraged us to proceed with the synthesis of a key intermediate, namely the dialdehyde **31** (in an overall yield of 63% starting from **6c**), used en route to the marine alkaloid analogue 7′-desmethylkealiiquinone (**32**). In an earlier report,[7]

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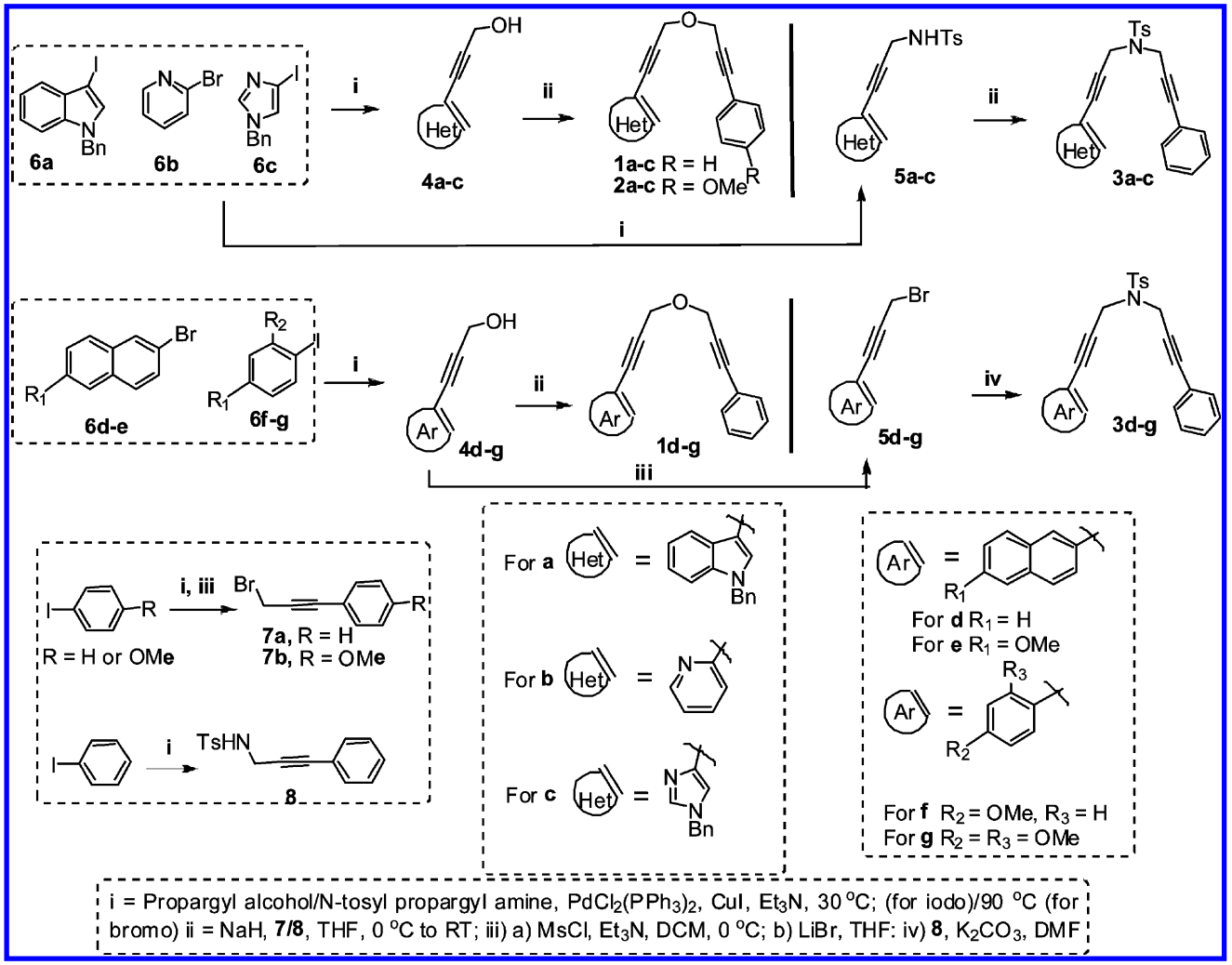
Scheme 3. Synthesis of Target Bis-Propargyl Systems



the dialdehyde was obtained by an intramolecular Diels–Alder reaction of the propargyl ester followed by reduction of the lactone and subsequent oxidation. We recognized that the same dialdehyde could be prepared by the HNO_3-mediated oxidation of the phthalan **30**,[8] obtainable in one step via the GB cyclization of **29** (Scheme 5). The latter was synthesized from *N*-benzyl-4-iodoimidazole (**6c**) via oxidation to imidazolone **28** following the literature procedure of Lovely et al.[9] followed by a Sonogashira coupling. Here because of the greater electron-withdrawing character of imidazolone, only the desired isomer was obtained during GB cyclization in excellent yield. To our delight, the phthalan could be oxidized directly to the dialdehyde **31** by a carefully controlled oxidation with nitric acid. The product matched that reported in the literature in all respects (the two ^{13}C NMR spectra are shown in Figure 2).[7]

The rationale behind the observed selectivity for the GB cyclization was based upon the relative nucleophilic character of the two radicals in the diradical intermediate. We realized a basic difference between the sulfone and the ether. Since the sulfone is an electron-accepting group, captodative stabilization[10] (**16**; Figure 3) will increase the nucleophilicity of the radical adjacent to the donor ring. In the case of ether, the situation is reverse. The vinyl ether functionality now acts as a donor and the more nucleophilic radical will be that adjacent to the electron-withdrawing aryl/heteroaryl group, as that will lead to captodative stabilization (**19**; Figure 3). Thus, in this case, we expect a greater participation of the electron-withdrawing aryl group in the formation of the product.

The experimental results are also in conformity with the above rationale. For example, in the case of pyridine-substituted systems, the radical adjacent to the pyridine ring is expected to have greater negative character, as it is more stabilized by the pyridine nucleus in comparison to the phenyl or 4-methoxyphenyl group (Figure 4). In the case of a competition between indole and phenyl, the former (being a better electron donor) destabilizes the anion adjacent to it. Hence, the major product was formed via the involvement of the aryl ring. The results obtained for the naphthyl or methoxyphenyl systems could also be explained similarly. For the GB reaction of the imidazole-based bis-propargyl ether, the reason for the preferential participation of the imidazole ring is not clear. It may be due to the involvement of the lone pair on the benzyl-attached nitrogen N(1) preferentially delocalizing with C2=N(3) (shown in structure **26**), which reduces the electron-donating capability of the imidazole ring in comparison to the aryl ring.[11] Replacing the imidazole with a more electron withdrawing imidazolone ring as in **29** led to the formation of only the product **30**, involving the sole participation of the imidazolone ring, thus supporting our explanation. The sulfonamides, expectedly, showed a selectivity trend similar to

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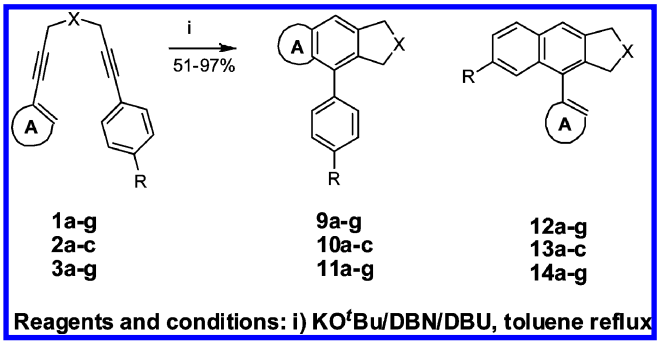
Table 1. Results of GB Cyclization



SM	X	A	R	reaction conditions	yield (%)	product ratio
1a	O	1-benzyl-3-indolyl	H	110 °C, 5 h, KO^{t}Bu	83	only **12a**
2a	O	1-benzyl-3-indolyl	OMe	110 °C, 6 h, KO^{t}Bu	80	1:4 **10a**:**13a**
1b	O	2-pyridyl	H	110 °C, 2 h, KO^{t}Bu	94	only **9b**
2b	O	2-pyridyl	OMe	110 °C, 3 h, KO^{t}Bu	97	only **10b**
1c	O	1-benzyl-4-imidazolyl	H	110 °C, 11 h, KO^{t}Bu	55	2:1 **9c**:**12c**
2c	O	1-benzyl-4-imidazolyl	OMe	110 °C, 9 h, KO^{t}Bu	60	only **10c**
1d	O	2-naphthyl	H	60 °C, 1 h, KO^{t}Bu	97	1.6:1 **9d**:**12d**
1e	O	6-methoxynaphthyl	H	60 °C, 1 h, KO^{t}Bu	94	1:1.25 **9e**:**12e**
1f	O	4-methoxyphenyl	H	110 °C, 30 min, KO^{t}Bu	95	1:8 **9f**:**12f**
1g	O	2,4-dimethoxyphenyl	H	80 °C, 2 h, KO^{t}Bu	94	1:8 **9g**:**12g**
3a	NTs	1-benzyl-3-indolyl	H	110 °C, 24 h, DBN	65	1:4 **11a**:**14a**
3b	NTs	2-pyridyl	H	110 °C, 18 h, DBN	71	only **11b**
3c	NTs	1-benzyl-4-imidazolyl	H	110 °C, 26 h, DBN	51	only **11c**
3d	NTs	2-naphthyl	H	120 °C, 12 h, DBU	80	1.91:1 **11d**:**14d**
3e	NTs	6-methoxynaphthyl	H	120 °C, 12 h, DBU	75	2.43:1 **11e**:**14e**
3f	NTs	4-methoxyphenyl	H	120 °C, 12 h, DBU	73	1:4.88 **11f**:**14f**
3g	NTs	2,4-dimethoxyphenyl	H	120 °C, 12 h, DBU	76	1:3.95 **11g**:**14g**

that of the ethers. However, the selectivity trend is less in case of the bis-aryl sulfonamides and in some cases the selectivity is opposite to what has been observed for the corresponding ether (for **3e** and **1e**). The differential aromaticity (between naphthalene and benzene systems) may be a factor here but needs further exploration.

It should be pointed out here that Kudoh et al.[12,13] in a recent paper has proposed an anionic [4 + 2] (Diels–Alder) mechanism involving a monoallene for the rearrangement of bis-propargyl ethers to arylnaphthalenes. Although their proposal was mainly based on the reactivity of a disubstituted substrate capable of isomerization to monoallene only, nevertheless, these authors have extended this anionic mechanism to ethers that also have the possibility of isomerization to bis-allene. We have considered this mechanism and realized that our observed selectivity can also be explained on the basis of this anionic DA reaction involving monoallene, which will be formed more easily from the propargyl arm attached to the more electron-withdrawing aryl/heteroaryl ring, which thus preferentially participates (Scheme 6). We are presently carrying out computations to evaluate the energetics for both mechanisms along with the effect of spin traps on the kinetics of the reaction. The results will be reported in due course.

In conclusion, we have demonstrated the selective nature of GB reactions of various bis-propargyl ethers and amines containing combinations of heteroaryl and aryl substituents at the acetylene ends. A general guideline for achieving the selectivity for these systems has been formulated. As a followup of the results, we have achieved the formal synthesis of 7′-desmethylkealiiquinone, a marine imidazolone natural product analogue. Our future research is aimed toward distinguishing the two mechanisms, namely diradicals vs anionic DA, as well as the synthesis of other natural products of the kealiinine and kealiiquinone family, including a study of their biological activities.

■ EXPERIMENTAL SECTION

All ^{1}H and ^{13}C NMR spectra were respectively recorded at 400 and 100 MHz in $CDCl_3$ unless mentioned otherwise. ESI-MS and HRMS were obtained using a LCT mass spectrometer; solutions of the compounds were injected directly into the spectrometer via a Rheodyne injector equipped with a 10 μL loop. A 20 micro LC syringe pump delivered the solution to the vaporization nozzle of the electrospray ion source at a flow rate of 3 μL min^{-1}. Nitrogen was used both as a drying gas and for nebulization with flow rates of approximately 3 L min^{-1} and 100 mL min^{-1}, respectively. Pressure in the analyzer region was usually about 3 × 10^{-5} Torr. IR spectra were recorded as thin films, and bands are expressed in cm^{-1}. In all purifications by silica gel chromatography, ethyl acetate/hexane (68 °C) was used as the eluent.

General Procedure for the Sonogashira Coupling. To a degassed solution of the respective iodo and bromo aromatic compounds **6a–g** (2 mmol), CuI (20 mol %), and propargyl alcohol or propargylamine-*p*-toluenesulfonamide (1.2 equiv) in 20 mL of triethylamine was added 3 mol % of $Pd(PPh_3)_2Cl_2$, and the mixture was stirred for 3 h at room temperature. The reaction mixture was then poured into ethyl acetate (15 mL), and the organic layer was washed with saturated NH_4Cl solution and brine (30 mL each) and dried over anhydrous Na_2SO_4. Evaporation of the solvent left an oily residue, from which the product was isolated by column chromatography (silica gel, hexane/ethyl acetate mixture as eluent).

General Procedure for the O- and N-Propargylation. To an ice-cold solution of the alcohol or propargylamine-*p*-toluenesulfona-

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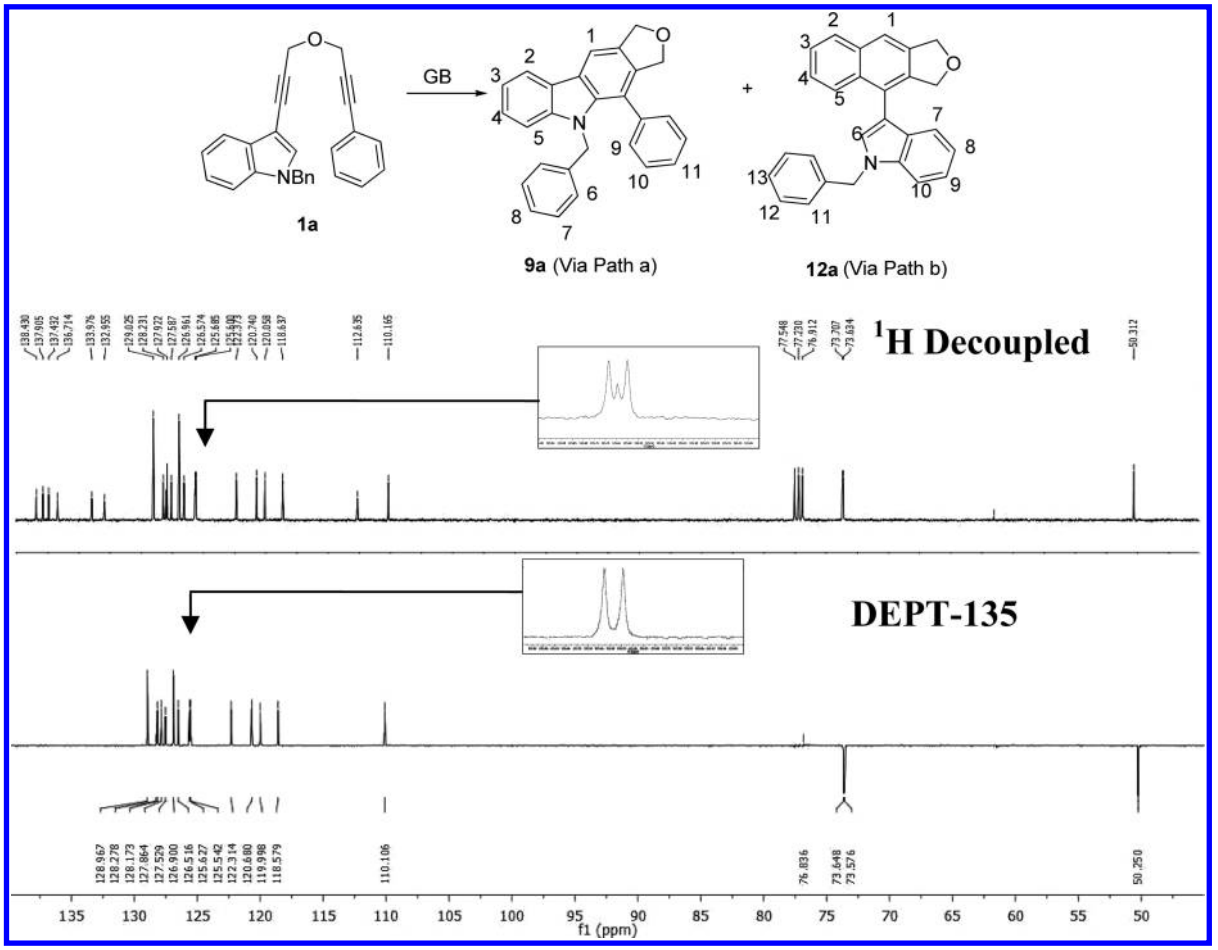
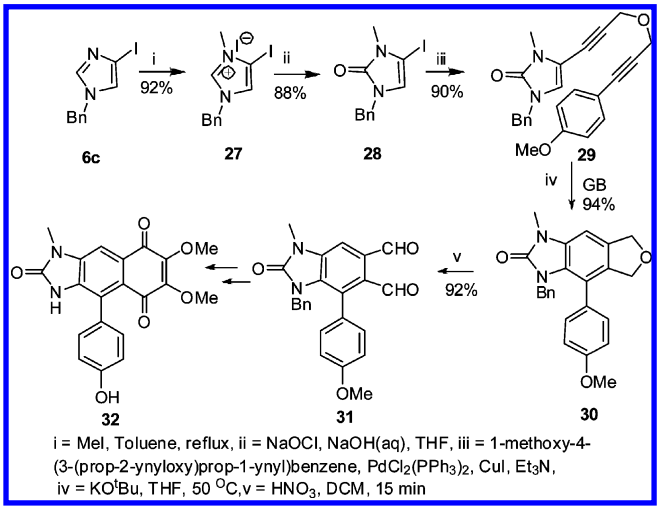
Scheme 4. Expected ^{13}C NMR Signals of Products



Scheme 5. Formal Total Synthesis of 7′-Desmethylkealiiquinone



mide derivatives (1 mmol) in dry THF or dry DMF (5 mL) was added NaH (2 equiv, 60% suspension in mineral oil) or dry K_2CO_3 (2 equiv), and the mixture was stirred. With the temperature maintained in ice, 1.1 equiv of the respective propargyl bromide (**7**, **8**, **5d–g**) was added dropwise as a solution in THF or DMF (1 mL) and the reaction mixture was stirred at room temperature for 1 h. It was then quenched by slow addition of NH_4Cl solution (2 mL) and then partitioned between water and ethyl acetate (3 × 20 mL). The organic layer was evaporated and dried (Na_2SO_4). Silica gel column chromatography furnished the desired product with ethyl acetate/hexane as eluent.

1-Benzyl-3-(3-(3-phenylprop-2-ynyloxy)prop-1-ynyl)-1H-indole (***1a***)*:* state, light yellow oil; R_f = 0.3 (hexane/EtOAc 9/1); yield 292 mg, 78%; IR (neat) ν_{max} 2952, 2360, 2331, 1641, 1490, 1279, 1258, 1081, 749 cm^{-1}; δ_H 7.79–7.77 (m, 1 H), 7.50–7.47 (m, 2 H), 7.35–7.25 (m, 8 H), 7.23–7.18 (m, 2 H) 7.14–7.11 (m, 2 H), 5.29 (s, 2 H), 4.64 (s, 2 H), 4.60 (s, 2 H); δ_C 136.5, 135.7 132.2, 131.8, 129.4, 128.8, 128.4, 128.2, 127.9, 126.9, 122.8, 122.6, 120.6, 120.2, 110.0, 96.9, 86.6, 86.0, 84.7, 80.5, 57.8, 57.1, 50.3; HRMS calcd for $C_{27}H_{21}NO$ + H^+ 376.1701, found 376.1699.

1-Benzyl-3-(3-(3-(4-methoxyphenyl)prop-2-ynyloxy)prop-1-ynyl)-1H-indole (***2a***)*:* state, yellow sticky mass; R_f = 0.4 (hexane/EtOAc 10/1); yield 307 mg, 76%; IR (neat) ν_{max} 2958, 2360, 2331, 1606, 1464, 1273, 1249, 1077, 764 cm^{-1}; δ_H 7.80–7.75 (m, 1 H), 7.44–7.42 (m, 2 H), 7.35 (s, 1 H), 7.32–7.28 (m, 4 H), 7.24–7.20 (m, 2 H), 7.14–7.12 (m, 2 H), 6.86–6.84 (m, 2 H), 5.28 (s, 2 H), 4.63 (s, 2 H), 4.58 (s, 2 H), 3.81 (s, 3 H); δ_C 159.7, 136.5, 135.7,133.3, 132.2, 129.4, 128.9, 127.9, 126.9, 122.8, 120.6, 120.2, 114.7, 113.9, 110.0, 97.0, 86.5, 86.2, 83.0, 80.5, 57.8, 57.2, 55.3, 50.3; HRMS calcd for $C_{28}H_{23}NO_2$ + H^+ 406.1807, found 406.1811.

2-(3-(3-Phenylprop-2-ynyloxy)prop-1-ynyl)pyridine (***1b***)*:* state, brown solid; R_f = 0.4 (hexane/EtOAc 1/1); mp 118–120 °C; yield 224 mg, 91%; IR (neat) ν_{max} 2952, 2355, 2090, 1766, 1633, 1461, 1276, 1050, 764 cm^{-1}; δ_H 8.56–8.53 (m, 1 H), 7.63–7.58 (m, 1 H), 7.44–7.40 (m, 3 H), 7.30–7.25 (m, 3H), 7.22–7.18 (m, 1 H), 4.55 (d, J = 2.0 Hz, 2 H), 4.53 (d, J = 2.0 Hz, 2 H); δ_C 150.0, 142.7, 136.2, 131.8, 128.6, 128.3, 127.2, 123.1, 122.5, 87.0, 86.1, 84.6, 84.3, 57.6, 57.1; HRMS calcd for $C_{17}H_{13}NO$ + H^+ 248.1075, found 248.1077.

2-(3-(3-(4-Methoxyphenyl)prop-2-ynyloxy)prop-1-ynyl)pyridine (***2b***)*:* state, brown semisolid; R_f = 0.4 (hexane/EtOAc 1/1); yield 217 mg, 88%; IR (neat) ν_{max} 2950, 2361, 2331, 1644, 1460, 1273, 1249,

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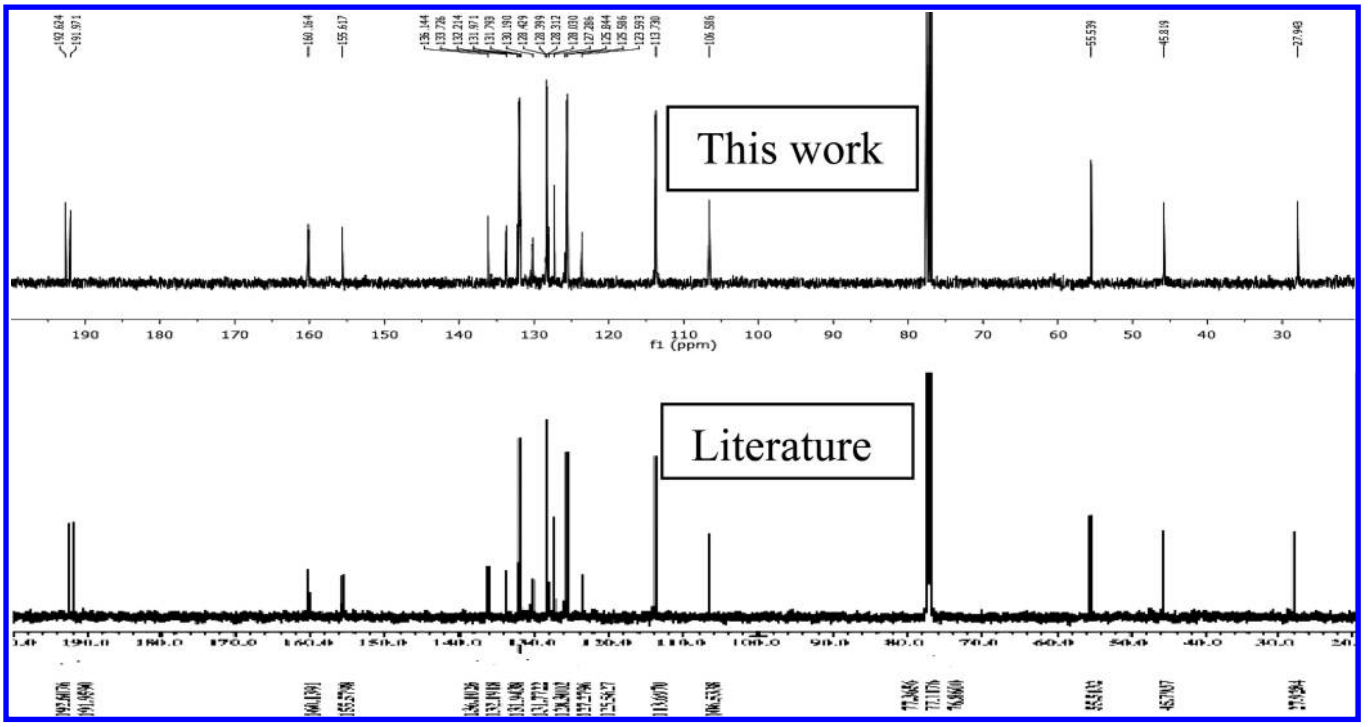


Figure 2. ^{13}C NMR spectra of the dialdehyde **31** (prepared via the route described here and reported).

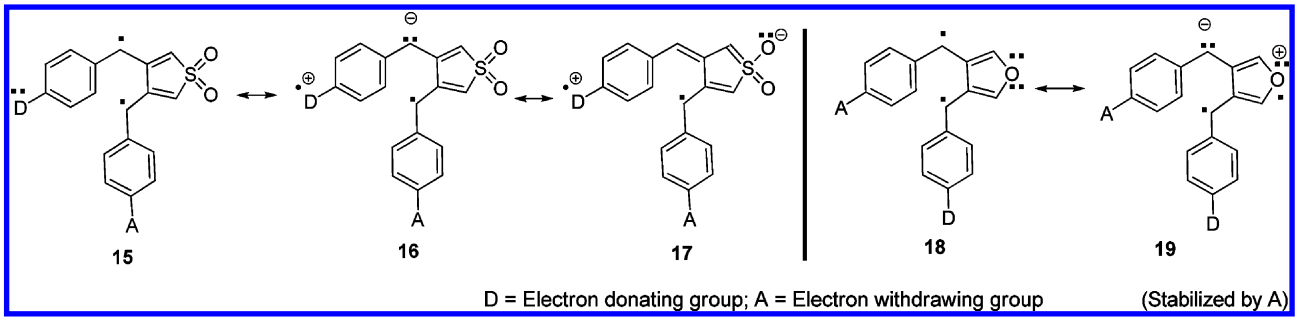


Figure 3. Captodative stabilization of the nucleophilic radical.

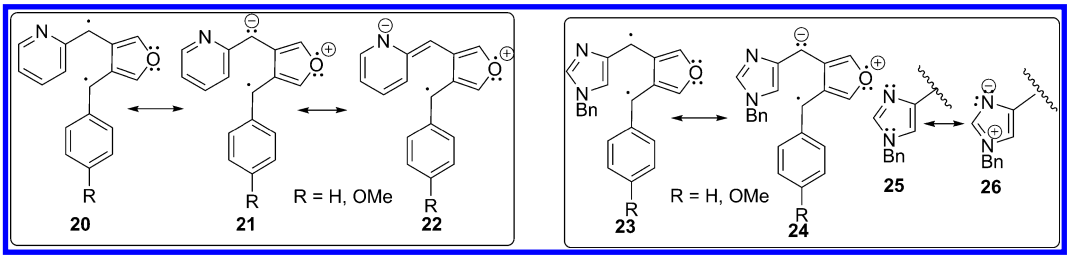
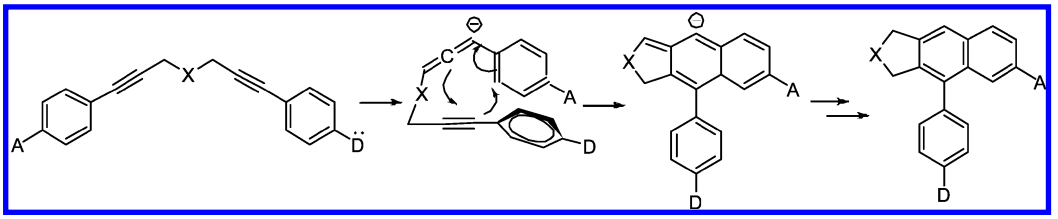


Figure 4. Radical stabilization for pyridine and imidazole systems.

Scheme 6. Explanation of Selectivity Based on Anionic Diels–Alder Mechanism As Proposed by Kudoh et al.[12]



764 cm^{-1}; δ_H 8.56–8.54 (m, 1 H), 7.64–7.59 (m, 1 H), 7.43–7.40 (m, 1 H), 7.39–7.35 (m, 2 H), 7.22–7.19 (m, 1 H), 6.82–6.79 (m, 2 H), 4.54 (m, 2 H), 4.52 (m, 2 H), 3.76 (m, 3 H); δ_C 159.9, 150.1, 142.8, 136.2, 133.4, 127.3, 123.2, 144.6, 144.0, 87.0, 86.0, 84.8, 82.9, 57.8, 57.1, 55.3; HRMS calcd for $C_{18}H_{15}NO_2$ + H^+ 278.1181, found 278.1187.

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*1-Benzyl-4-(3-(3-phenylprop-2-ynyloxy)prop-1-ynyl)-1H-imidazole (**1c**):* state, yellow viscous liquid; R_f = 0.3 (hexane/EtOAc 8/1); yield 221 mg, 68%; IR (neat) ν_{max} 2976, 2952, 2850, 2360, 2078, 1644, 1487, 1258, 1075, 757 cm^{-1}; δ_H 7.51 (s, 1 H), 7.45−7.43 (m, 2 H), 7.37−7.29 (m, 6 H), 7.17−7.08 (m, 2 H), 6.97 (s, 1 H), 5.08 (s, 2 H), 4.51 (s, 4 H); δ_C 139.0, 137.5, 135.4, 132.0, 129.3, 128.8, 128.6, 128.4, 127.7, 127.6, 125.0, 124.2, 123.8, 122.7, 86.8, 84.8, 84.6, 80.5, 57.5, 57.4, 51.4; HRMS calcd for $C_{22}H_{18}N_2O$ + H^+ 327.1497, found 327.1499.

*1-Benzyl-4-(3-(3-(4-methoxyphenyl)prop-2-ynyloxy)prop-1-ynyl)-1H-imidazole (**2c**):* state, orange liquid; R_f = 0.3 (hexane/EtOAc 8/1); yield 249 mg, 70%; IR (neat) ν_{max} 2978, 2950, 2848, 2362, 2078, 1640, 1487, 1259, 1075, 756 cm^{-1}; δ_H 7.47 (s, 1 H), 7.37−7.35 (m, 5 H), 7.18−7.14 (m, 2 H), 7.08 (s, 1 H), 6.82 (d, J = 8.8 Hz, 2 H), 5.07 (s, 2 H), 4.50 (s, 2 H), 4.49 (s, 2 H), 3.80 (s, 3 H); δ_C 159.8, 137.4, 133.4, 129.2, 128.7, 128.6, 127.6, 127.5, 114.7, 113.9, 86.7, 84.7, 83.1, 80.4, 57.4, 57.3, 55.3, 51.2; HRMS calcd for $C_{23}H_{20}N_2O_2$ + H^+ 357.1603, found 357.1607.

*2-[3-(3-Phenylprop-2-ynyloxy)prop-1-ynyl]naphthalene (**1d**):* state, brown liquid; R_f = 0.5 (hexane/EtOAc 30/1); yield 180 mg, 61%; IR (neat) ν_{max} 3061, 2926, 2851, 2232, 1723, 1493, 1079, 754 cm^{-1}; δ_H 8.06 (s, 1 H), 7.86−7.81 (m, 3 H), 7.56−7.52 (m, 5 H), 7.37−7.36 (bs, 3 H), 4.65 (s, 2 H), 4.64 (s, 2 H); δ_C (50 MHz): 133.0, 131.9, 128.7, 128.6, 128.5, 128.2, 127.9, 126.9, 126.7, 122.7, 119.9, 87.3, 87.0, 84.9, 84.6, 57.7; HRMS calcd for $C_{22}H_{16}O$ + Na^+ 319.1099, found 319.1099.

*2-Methoxy-6-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]-naphthalene (**1e**):* state, gummy liquid; R_f = 0.5 (hexane/EtOAc 20/1); yield 195 mg, 60%; IR (neat) ν_{max} 3066, 2971, 2851, 2223, 1628, 1488, 1079, 759 cm^{-1}; δ_H 7.96 (s, 1 H), 7.72−7.69 (m, 2 H), 7.54 (app s, 3 H), 7.37−7.35 (comp, 3 H), 7.19 (d, J = 8.0 Hz, 1 H), 7.12 (s, 1 H), 4.64 (s, 4 H), 3.92 (s, 3 H); δ_C (50 MHz): 158.5, 134.4, 131.9, 131.8, 129.4, 129.1, 128.6, 128.4, 126.9, 122.6, 119.5, 117.4, 105.8, 87.5, 86.9, 84.6, 84.1, 57.7, 57.5, 55.4; HRMS calcd for $C_{23}H_{18}O_2$ + Na^+ 349.1204, found 349.1205.

*1-Methoxy-4-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzene (**1f**):* state, yellow viscous liquid; R_f = 0.5 (hexane/EtOAc 20/1); yield 165 mg, 60%; IR (neat) ν_{max} 3061, 2972, 2851, 2232, 1620, 1482, 1049, 754 cm^{-1}; δ_H 7.51−7.50 (bm, 2 H), 7.44 (d, J = 8.4 Hz, 2 H), 7.34 (bs, 3 H), 6.86 (d, J = 8.4 Hz, 2 H), 4.57(s, 4 H), 3.79 (s, 3 H); δ_C 159.9, 138.3, 133.4, 131.9, 128.4, 122.6, 116.5, 114.7, 114.0, 86.8, 84.7, 83.2, 57.6, 57.4, 55.3; HRMS calcd for $C_{19}H_{16}O_2$ + Na^+ 299.1048, found 299.1049.

*2,4-Dimethoxy-1-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]-benzene (**1g**):* state, Yellow liquid; R_f = 0.5 (hexane/EtOAc 20/1); yield 199 mg, 65%; %; IR (neat) ν_{max} 3016, 2931, 2851, 2227, 1613, 1508, 1079, 764 cm^{-1}; δ_H 7.47−7.45 (m, 2 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.32−7.30 (m, 2 H), 6.45 (app d, J = 4.0 Hz, 1 H), 6.43 (s, 1 H), 4.58 (s, 2 H), 4.56 (s, 2 H), 3.86 (s, 3 H), 3.81 (s, 3 H); δ_C 161.6, 161.5, 134.8, 131.9, 128.4, 122.8, 104.9, 104.4, 98.6, 87.1, 86.7, 84.9, 83.4, 57.9, 57.4, 55.9, 55.6; HRMS calcd for $C_{20}H_{18}O_3$ + Na^+ 329.1154, found 329.1154.

*N-(3-(1-Benzyl-1H-indol-3-yl)prop-2-ynyl)-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3a**):* state, light yellow semisolid; R_f = 0.3 (hexane/EtOAc 1/1); yield 324 mg, 61%; IR (neat) ν_{max} 2958, 2952, 2358, 2084, 1637, 1460, 1276, 1080, 764 cm^{-1}; δ_H 7.81 (d, J = 7.6 Hz, 2 H), 7.52 (d, J = 7.6 Hz, 1 H), 7.31−7.27 (m, 4 H), 7.26−7.20 (m, 8 H), 7.17−7.10 (m, 4 H), 5.25 (s, 2 H), 4.52 (s, 2 H), 4.50 (s, 2 H), 2.22 (s, 3 H); δ_C 143.7, 136.5, 135.7, 135.6, 132.0, 131.7, 129.7, 129.6, 129.3, 128.9, 128.4, 128.2, 128.0, 126.9, 122.9, 122.4, 120.6, 120.1, 115.7, 110.1, 96.8, 85.7, 83.3, 82.0, 79.6, 50.3, 38.0, 37.4, 21.4; MS: m/z = 529 [MH^+]. HRMS calcd for $C_{34}H_{28}N_2O_2S$ + H^+ 529.1950, found 529.1956.

*4-Methyl-N-(3-phenylprop-2-ynyl)-N-(3-(pyridin-2-yl)prop-2-ynyl)benzenesulfonamide (**3b**):* state, brown gummy liquid; R_f = 0.5 (hexane/EtOAc 1/1); yield 260 mg, 65%; IR (neat) ν_{max} 2956, 2361, 1644, 1463, 1259, 1079, 762 cm^{-1}; δ_H 8.51 (d, J = 4.0 Hz, 1 H), 7.77 (d, J = 7.6 Hz, 2 H), 7.57 (t, J = 7.6 Hz, 1 H), 7.28−7.20 (m, 5 H), 7.18−7.13 (m, 4 H), 4.46 (s, 2 H), 4.44 (s, 2 H), 2.26 (s, 3 H); δ_C 150.0, 144.1, 142.4, 136.3, 135.5, 131.8, 129.8, 128.7, 128.3, 128.1, 127.4, 123.4, 122.3, 86.2, 85.0, 82.3, 81.6, 37.8, 37.4, 21.5; HRMS calcd for $C_{24}H_{20}N_2O_2S$ + H^+ 401.1324, found 401.1324.

*N-(3-(1-Benzyl-1H-imidazol-4-yl)prop-2-ynyl)-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3c**):* state, dark red gummy oil; R_f = 0.3 (hexane/EtOAc 3:2); yield 239 mg, 50%; IR (neat) ν_{max} 2958, 2856, 2360, 1635, 1457, 1279, 1159, 764 cm^{-1}; δ_H 7.75 (d, J = 8.0 Hz, 2 H), 7.45 (s, 2 H), 7.35−7.34 (m, 3 H), 7.23−7.19 (m, 5 H), 7.15−7.12 (m, 3 H), 6.89 (s, 1 H), 5.02 (s, 2 H), 4.41 (s, 2 H), 4.36 (s, 2 H), 2.24 (s, 3 H); δ_C 143.9, 137.5, 135.7, 135.5, 132.3, 132.2, 131.9, 129.8, 129.4, 128.8, 128.7, 128.6, 128.3, 128.2, 127.7, 86.0, 82.1, 81.8, 79.6, 51.4, 37.7, 37.5, 21.6; HRMS calcd for $C_{29}H_{25}N_3O_2S$ + H^+ 480.1746, found 480.1751.

*4-Methyl-N-(3-naphthalen-2-ylprop-2-ynyl)-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3d**):* state, yellow solid; R_f = 0.5 (hexane/EtOAc 5/1); yield 314 mg, 70%; IR (neat) ν_{max} 3061, 2926, 2856, 2237, 1603, 1493, 1363, 1169, 754 cm^{-1}; δ_H 7.87−7.81 (m, 4 H), 7.33 (app d, J = 4.0 Hz, 2 H), 7.52−7.50 (m, 2 H), 7.28−7.26 (m, 7 H), 7.15 (app d, J = 4.0 Hz, 1 H), 4.53 (s, 2 H), 4.52 (s, 2 H), 2.31 (s, 3 H); δ_C 143.9, 135.4, 132.9, 132.8, 131.8, 131.7, 131,6, 129.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.5, 126.9, 126.7, 122.2, 119.5, 86.3, 85.9, 82.0, 81.8, 37.8, 37.7, 21.5; HRMS calcd for $C_{29}H_{23}NO_2S$ + Na^+ 472.1347, found 472.1348.

*N-[3-(6-Methoxynaphthalen-2-yl)prop-2-ynyl]-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3e**):* state, gummy oil; R_f = 0.5 (hexane/EtOAc 5/1); yield 350 mg, 73%; IR (neat) ν_{max} 3051, 2966, 2926, 2856, 2232, 1633, 1488, 1348, 1163, 1094, 759 cm^{-1}; δ_H 7.82 (d, J = 8.0 Hz, 2 H), 7.64−7.60 (m, 3 H), 7.30−7.24 (m, 8 H), 7.21−7.09 (m, 1 H), 7.08 (s, 1 H), 4.48 (s, 4 H), 3.92 (s, 3 H), 2.30 (s, 3 H); δ_C 158.5, 143.9, 135.5, 134.3, 131.8, 131.6, 129.8, 129.7, 129.3, 128.9, 128.6, 128.3, 128.2, 128.1, 127.6, 126.7, 122.3, 119.6, 117.2, 105.8, 86.4, 85.9, 81.9, 81.3, 55.4, 37.8, 37.7, 21.6; HRMS calcd for $C_{30}H_{25}NO_3S$ + Na^+ 502.1453, found 502.1453.

*N-[3-(2,4-Dimethoxyphenyl)prop-2-ynyl]-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3g**):* state, viscous liquid; R_f = 0.5 (hexane/EtOAc 5/1); yield 298 mg, 65%; %; IR (neat) ν_{max} 3052, 2961, 2926, 2854, 2231, 1635, 1470, 1349, 1161, 1094, 754 cm^{-1}; δ_H 7.79 (d, J = 8.0 Hz, 2 H), 7.26−7.17 (comp, 6 H), 7.06 (d, J = 8.0 Hz, 2 H), 6.37 (app d, J = 8.0 Hz, 2 H), 4.46 (s, 4 H), 3.80 (s, 6 H), 2.30 (s, 3 H); δ_C 161.4, 143.7, 137.5, 135.6, 134.4, 131.7, 130.3, 129.5, 128.4, 128.2, 128.0, 122.4, 104.7, 104.1, 98.3, 85.6, 84.2, 82.4, 81.9, 55.8, 55.5, 37.9, 37.3, 21.5; HRMS calcd for $C_{27}H_{25}NO_4S$ + Na^+ 482.1402, found 482.1402.

*N-[3-(4-Methoxyphenyl)prop-2-ynyl]-4-methyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide (**3f**):* state, gummy liquid; R_f = 0.5 (hexane/EtOAc 5/1); yield 300 mg, 69%; IR (neat) ν_{max} 3061, 2926, 2851, 2242, 1603, 1463, 1348, 1158, 1089, 749 cm^{-1}; δ_H 7.81 (d, J = 8 Hz, 2 H), 7.28−7.21 (comp, 7 H), 7.18 (d, J = 8.0 Hz, 2 H), 6.80 (d, J = 8.0 Hz, 2 H), 4.46 (s, 2 H), 4.44 (s, 2 H), 3.82 (s, 3 H), 2.35 (s, 3 H); δ_C (50 MHz): 159.9, 143.9, 135.6, 133.3, 131.8, 129.7, 128.6, 128.3, 128.1, 122.4, 114.4, 113.9. 85.9, 81.9, 80.4, 55.4, 37.7, 37.6, 21.5; HRMS calcd for $C_{26}H_{23}NO_3S$ + Na^+ 452.1296, found 452.1297.

General Procedure for the GB Rearrangement of the Bis-Propargyl Ether and Sulfonamide. To an ice-cold solution of the ether (0.3 mmol) or amine (0.3 mmol) in dry toluene (10 mL) was added 2 equiv of KO^{t}Bu (for the ether) or DBN/DBU (for the amine). After removal of the ice bath, the reaction mixture was warmed to room temperature and heated gradually to reflux for 5−6 h in a preheated oil bath at 110 °C. The solvent was then evaporated, and the crude mass was purified via silica gel column filtration with hexane/ethyl acetate as eluent.

*1-Benzyl-3-(1,3-dihydronaphtho[2,3-c]furan-4-yl)-1H-indole (**12a**).* state, colorless liquid; R_f = 0.3 (hexane/EtOAc 9/1); yield 93 mg, 83%; IR (neat) ν_{max} 2957, 2921, 2850, 2310, 2342, 1630, 1218, 1052, 772 cm^{-1}; δ_H 7.98 (d, J = 8.8 Hz, 1 H), 7.94 (d, J = 8.8 Hz, 1 H), 7.74 (s, 1 H), 7.52 (dt, J = 8.0, 1.6 Hz, 1 H), 7.45 (d, J = 8.0 Hz, 1 H), 7.43−7.34 (m, 6 H), 7.31 (dt, J = 7.4, 1.2 Hz, 1H), 7.24 (dd, J = 6.8 Hz, 1 H), 7.22 (s, 1 H), 7.15 (dt, J = 8.0, 1.2 Hz, 1 H), 5.44 (s, 2 H), 5.38 (s, 2 H), 5.15 (dd, J = 12.8, 10.4 Hz, 2 H); δ_C 138.4, 137.9, 137.4, 136.7, 133.9, 132.9, 129.0, 128.2, 127.9, 127.5, 126.9, 126.5, 122.3,

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120.7, 120.0, 118.6, 112.6, 110.1, 73.7, 73.6, 61.5, 50.3; HRMS calcd for $C_{27}H_{21}NO + H^+$ 376.1701, found 376.1663.

*1-Benzyl-3-(6-methoxy-1,3-dihydronaphtho[2,3-c]furan-4-yl)-1H-indole (**13a**).* state, yellow gummy mass; R_f = 0.2 (hexane/EtOAc 9/1); yield 78 mg, 64%; IR (neat) ν_{max} 2958, 2922, 2851, 2361, 2343, 1628, 1219, 1052, 772 cm^{-1}; δ_H 7.78 (d, J = 9.2 Hz, 1 H), 7.63 (s, 1 H), 7.44 (d, J = 8.4 Hz, 1 H), 7.35−7.31 (m, 3 H), 7.29−7.24 (m, 3 H), 7.22−7.19 (m, 3 H) 7.16−7.09 (m, 2 H), 5.46, 5.43 (Abq, J = 16.0, 4.4 Hz, 2 H), 5.30 (s, 2 H), 5.06 (s, 2 H), 3.60 (s, 3 H); δ_C 157.7, 138.9, 137.6, 136.9, 135.6, 134.1, 129.6, 129.5, 129.1, 128.0, 127.7, 127.5, 127.0, 124.5, 122.4, 120.9, 120.0, 118.5, 118.3, 112.9, 110.2, 105.2, 73.8, 73.7, 55.2, 50.3; HRMS calcd for $C_{28}H_{23}NO_2 + H^+$ 406.1807, found 406.1783.

*9-Benzyl-10-phenyl-3,9-dihydro-1H-2-oxa-9-azacyclopenta[b]-fluorene (**10a**):* state, orange oil; R_f = 0.4 (hexane/EtOAc 9/1); yield 20 mg, 16%; IR (neat) ν_{max} 2956, 2922, 2851, 2360, 2342, 1627, 1508, 1458, 1246, 1176, 1055, 772 cm^{-1}; δ_H 8.12 (d, J = 8.0 Hz, 1 H), 7.96 (s, 1 H), 7.37 (dt, J = 8.4, 1.2 Hz, 1 H), 7.27−7.20 (m, 3 H), 7.13−7.03 (m, 3 H), 7.02−7.00 (m, 2 H) 6.75−6.73 (m, 2 H), 6.56 (d, J = 7.6 Hz, 2 H), 5.33 (s, 2 H), 5.10 (s, 2 H), 4.88 (s, 2 H), 3.82 (s, 3 H); δ_C 159.2, 142.3, 138.5, 138.0, 137.9, 130.5, 130.3, 129.2, 128.3, 126.9, 126.1, 125.7, 124.6, 122.8, 120.0, 119.6, 119.4, 113.8, 11.4, 109.6, 74.2, 73.7, 55.4, 47.8; HRMS calcd for $C_{28}H_{23}NO_2 + H^+$ 406.1807, found 406.1809.

*5-Phenyl-6,8-dihydrofuro[3,4-g]quinoline (**9b**):* state, yellow solid; R_f = 0.4 (hexane/EtOAc 1/1); mp 144−145 °C; yield 70 mg, 94%; IR (neat) ν_{max} 2959, 2922, 2851, 2361, 2343, 1767, 1609, 1508, 1289, 1219, 1168, 1056, 772 cm^{-1}; δ_H 8.85−8.82 (m, 1 H), 8.01−7.97 (m, 1 H), 7.94 (s, 1 H), 7.49−7.40 (m, 3 H), 7.30−7.24 (m, 3 H), 5.29 (s, 2 H), 5.01 (s, 2 H); δ_C 149.7, 148.3, 141.7, 137.4, 136.8, 134.1, 132.5, 129.4, 128.7, 128.0, 126.7, 120.7, 120.1, 73.3, 72.6; HRMS calcd for $C_{17}H_{13}NO + H^+$ 248.1075, found 248.1091.

*5-(4-Methoxyphenyl)-6,8-dihydrofuro[3,4-g]quinoline (**10b**).* state, brown solid; R_f = 0.3 (hexane/EtOAc 1/1); mp 150−152 °C; yield 81 mg, 97%; IR (neat) ν_{max} 2961, 2851, 2360, 1628, 1508, 1458, 1351, 1246, 1219, 1163, 1053, 772 cm^{-1}; δ_H 8.87 (dd, J = 4.0, 1.6 Hz, 1 H), 8.08 (dd, J = 5.4, 1.6 Hz, 1 H), 7.96 (s, 1 H), 7.32 (dd, J = 6.2, 4.0 Hz, 1 H), 7.28−7.24 (m, 2 H), 7.06−7.02 (m, 2 H), 5.33 (s, 2 H), 5.06 (s, 2 H), 3.89 (s, 3 H); δ_C 159.5, 149.8, 148.7, 141.8, 137.6, 134.2, 132.4, 130.7, 129.1, 127.0, 120.7, 120.1, 114.3, 73.4, 72.8, 55.4; HRMS calcd for $C_{18}H_{15}NO_2 + H^+$ 278.1181, found 278.1198.

*1-Benzyl-8-phenyl-3a,5,7,8a-tetrahydro-1H-isobenzofuro[5,6-d]-imidazole (**9c**).* state, whitish gum; R_f = 0.3 (hexane/EtOAc 1/1); yield 36 mg, 37%; IR (neat) ν_{max} 2955, 2921, 2851, 2360, 2342, 1636, 1219, 1055, 772 cm^{-1}; δ_H 7.87 (s, 1 H), 7.64 (s, 1 H), 7.34 (t, J = 7.2 Hz, 1 H), 7.26 (t, J = 7.6 Hz, 2 H), 7.16−7.09 (m, 3 H), 7.04 (d, J = 7.2 Hz, 2 H) 6.47 (d, J = 7.6 Hz, 2 H), 5.24 (s, 2 H), 4.92 (s, 2 H), 4.84 (s, 2 H); HRMS calcd for $C_{22}H_{18}N_2O + H^+$ 327.1497, found 327.1495.

*1-Benzyl-4-(1,3-dihydronaphtho[2,3-c]furan-4-yl)-1H-imidazole (**12c**).* state, white gum; R_f = 0.3 (hexane/EtOAc 1/1); yield, 18%; IR (neat) ν_{max} 2958, 2922, 2851, 2361, 2343, 1628, 1219, 1053, 772 cm^{-1}; δ_H 8.31−8.29 (m, 1 H), 7.87−7.81 (m, 1 H), 7.72 (s, 1 H), 7.62 (s, 1 H), 7.44−7.34 (m, 5 H), 7.28 (s, 2 H), 7.06 (s, 1 H), 5.26 (s, 2 H), 5.24 (s, 2 H), 5.23 (s, 2 H); δ_C 139.1, 138.1, 137.8, 137.5, 136.1, 134.0, 131.6, 129.7, 129.3, 128.7, 128.4, 127.5, 125.9, 125.6, 125.0, 119.2, 119.0, 115.5, 73.9, 73.3, 51.3; HRMS calcd for $C_{22}H_{18}N_2O + H^+$ 327.1497, found 327.1494.

*1-Benzyl-8-(4-methoxyphenyl)-3a,5,7,8a-tetrahydro-1H-isobenzofuro[5,6-d]imidazole (**10c**):* state, yellow oil; R_f = 0.4 (hexane/EtOAc 3:2); yield 64 mg, 60%; IR (neat) ν_{max} 2956, 2922, 2851, 2365, 2344, 1628, 1219, 1053, 772 cm^{-1}; δ_H 7.87 (s, 1 H), 7.63 (s, 1 H), 7.18−7.14 (m, 4 H), 6.97 (d, J = 8.0 Hz, 2 H), 6.79 (d, J = 8.0 Hz, 2 H), 6.55 (d, J = 8.0 Hz, 2 H), 5.25 (s, 2 H), 4.95 (s, 2 H), 4.85 (s, 2 H), 3.84 (s, 3 H); δ_C 159.4, 145.3, 145.0, 136.4, 135.3, 134.1, 130.4, 128.6, 127.9, 127.8, 126.2, 120.2, 113.8, 114.4, 73.9, 73.0, 55.5, 50.1; HRMS calcd for $C_{23}H_{20}N_2O_2 + H^+$ 357.1603, found 357.1633.

*11-Phenyl-8,10-dihydro-9-oxacyclopenta[b]phenanthrene (**9d**, major) and 4-naphthalen-2-yl-1,3-dihydronaphtho[2,3-c]furan (**12d**, minor) (**9d:12d** = 1.6:1):* state, pale yellow sticky mass; R_f = 0.5 (hexane/EtOAc 20/1); yield 86 mg, 97%; IR (neat) ν_{max} 2924, 2854, 1657, 1462, 1051, 753 cm^{-1}; δ_H 8.00−7.68 (comp, 10 H, major + minor), 7.59−7.34 (comp, 13 H, major + minor), 7.12 (td, J = 8.0, 4.0 Hz, 1 H, major), 5.38 (s, 2 H, major), 5.34 (s, 2 H, minor), 5.12, 5.04 (ABq, J = 12.0 Hz, 2 H, minor), 4.96 (s, 2 H, major); δ_C (major + minor) 142.6, 139,7, 137.7, 137.4, 137.2, 135.7, 133.7, 133.6, 133.5, 132.8, 132.5, 131.9, 130.8, 130.1, 129.6, 128.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.7, 127.6, 127.5, 126.5, 126.4, 125.9, 125.8, 125.7, 125.2, 120.3, 74.0,73.9, 73.4, 72.9; HRMS calcd for $C_{22}H_{16}O + Na^+$ 319.1099, found 319.1099.

*4-(6-Methoxynaphthalen-2-yl)-1,3-dihydronaphtho[2,3-c]furan (**12e**, major) and 3-methoxy-11-phenyl-8,10-dihydro-9-oxacyclopenta[b]phenanthrene (**9e**, minor) (**9e:12e** = 1:1.25):* state, yellow gummy mass; R_f = 0.5 (hexane/EtOAc 15/1); yield 92 mg, 94%; IR (neat) ν_{max} 2924, 2852, 1608, 1460, 1049, 751 cm^{-1}; δ_H 7.88 (t, J = 8.0 Hz, 2 H, major), 7.78−7.72 (m, 6 H, minor), 7.65 (d, J = 8.0 Hz, 1 H, minor), 7.55−7.44 (m, 5 H, major, 1 H, minor), 7.38 (d, J = 8.0 Hz, 1 H, minor), 7.33 (d, J = 8.0 Hz, 2 H, major), 7.25 (d, J = 8.0 Hz, 2 H, major), 7.21 (t, J = 4.0 Hz, 1 H, minor), 6.72 (dd, J = 8.0 Hz, 4 Hz, 1 H, minor), 5.35−5.30 (m, 4 H, major + minor), 5.09, 5.02 (ABq, J = 12.0 Hz, 2 H, major), 4.92 (s, 2 H, minor), 3.98 (s, 3 H, major), 3.88 (s, 3 H, minor); δ_C (50 MHz) (major + minor) 158.2, 157.5, 142.7, 137.9, 137.3, 136.6, 134.1, 133.9, 133.5, 132.9, 132.7, 132.2, 129.8, 129.3, 129.1, 128.5, 128.4, 128.3, 127.7, 127.2, 126.0, 125.9, 125.8, 120.5, 119.5, 118.9, 115.3, 109.0, 105.9, 74.1, 73.6, 73.2, 55.6, 55.4; HRMS calcd for $C_{23}H_{18}O_2 + Na^+$ 349.1204, found 349.1204.

*4-(4-Methoxyphenyl)-1,3-dihydronaphtho[2,3-c]furan (**12f**, major) and 6-methoxy-4-phenyl-1,3-dihydronaphtho[2,3-c]furan (**9f**, minor) (**9f:12f** = 1:8):* state, gummy yellow solid; R_f = 0.5 (hexane/EtOAc 10/1); yield 79 mg, 95%; IR (neat) ν_{max} 2923, 2853, 1634, 1462, 1053, 752 cm^{-1}; δ_H 7.86 (d, J = 8.0 Hz, 1 H, major), 7.72 (d, J = 8.0 Hz, 1 H, major), 7.67 (s, 1 H, major), 7.46 (t, J = 8.0 Hz, 1 H, major), 7.38 (t, J = 8.0 Hz, 1 H, major), 7.29 (d, J = 8.0 Hz, 2 H, major), 7.04 (d, J = 8.0 Hz, 2 H, major), 5.29 (s, 2 H, major), 5.27 (s, 2 H, minor), 5.03 (s, 2 H, major), 5.00 (s, 2 H, minor), 3.90 (s, 6 H, major + minor); δ_C (50 MHz) (major + minor) 159.3, 137.8, 137.2, 133.9, 132.5, 132.3, 130.8, 130.5, 128.3, 125.9, 125.8, 125.7, 118.7, 114.2, 73.6, 73.2, 55.5; HRMS calcd for $C_{19}H_{16}O_2 + Na^+$ 299.1048, found 299.1048.

*4-(2,4-Dimethoxyphenyl)-1,3-dihydronaphtho[2,3-c]furan (**12g**, major) and 6,8-dimethoxy-4-phenyl-1,3-dihydronaphtho[2,3-c]furan (**9g**, minor) (**9g:12g** = 1:8):* state, pale yellow gummy solid; yield 86 mg, 94%; δ_H 7.85 (d, J = 8.0 Hz, 1 H, major), 7.67 (s, 1 H, major), 7.58 (d, J = 12 Hz, 1 H, major), 7.44 (td, J = 8.0, 4.0 Hz, 1 H, major), 7.35 (app td, J = 8.0, 4.0 Hz, 1 H, major), 7.12 (d, J = 8.0 Hz, 1 H, major), 6.64 (m, 1 H, major), 6.61 (d, J = 4.0 Hz, 1 H, major), 6.56 (s, 1 H, minor), 6.52 (s, 1 H, minor), 5.30 (s, 4 H, major + minor), 4.98 (app s, 4 H, major + minor), 3.90 (s, 6 H, major + minor); HRMS calcd for $C_{20}H_{18}O_3 + Na^+$ 329.1154, found 329.1154.

*4-(2,4-Dimethoxyphenyl)-1,3-dihydronaphtho[2,3-c]furan (**12g**):* state, yellow solid; R_f = 0.5 (hexane/EtOAc 10/1); yield 76 mg, 82%; IR (neat) ν_{max} 2924, 2853, 1610, 1461, 1048, 754 cm^{-1}; δ_H (DMSO-d_6): 7.91 (d, J = 8.0 Hz, 1 H), 7.78 (s, 1 H), 7.46−7.33 (m, 3 H), 7.09 (d, J = 8.0 Hz, 1 H), 6.73 (d, J = 2.4 Hz, 1 H), 6.65 (dd, J = 8.2 Hz, 2.4 Hz,1 H), 5.17 (s, 2 H), 4.82, 4.73 (ABq, J = 12.0 Hz, 2 H), 3.83 (s, 3 H), 3.63 (s, 3 H); δ_C (DMSO-d_6) 161.0, 158.1, 137.9, 133.7, 132.3, 131.9, 129.1, 128.6, 126.1, 125.9, 125.7, 119.1, 118.3, 105.8, 99.3, 72.9, 72.4, 55.9, 55.8; HRMS calcd for $C_{20}H_{18}O_3 + Na^+$ 329.1154, found 329.1154.

*4-(1-Benzyl-1H-indol-3-yl)-2-tosyl-2,3-dihydro-1H-benzo[f]-isoindole (**14a**):* state, light yellow sticky mass; R_f = 0.3 (hexane/EtOAc 2/3); yield 83 mg, 52%; IR (neat) ν_{max} 2957, 2921, 2850, 2361, 2342, 1628, 1508, 1458, 1249, 1159, 1054, 772 cm^{-1}; δ_H 7.80 (t, J = 9.6 Hz, 2 H), 7.70 (d, J = 7.2 Hz, 2 H), 7.63 (s, 1 H), 7.45−7.36 (m, 4 H), 7.33−7.21 (m, 7 H), 7.14 (s, 1 H), 7.10−7.06 (m, 2 H); δ_C 143.6, 137.1, 129.7, 128.9, 127.9, 127.8, 127.6, 127.4, 126.9, 126.3, 125.8, 125.7, 122.3, 120.4, 120.3, 119.9, 111.7, 111.1, 53.8, 53.7, 50.2, 21.1; HRMS calcd for $C_{34}H_{28}N_2O_2S + Na^+$ 551.1769, found 551.1768.

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*5-Phenyl-7-tosyl-7,8-dihydro-6H-pyrrolo[3,4-g]quinoline (**11b**):* state, yellow solid; R_f = 0.4 (hexane/EtOAc 3/2); mp 204−206 °C; yield 85 mg, 70%; IR (neat) ν_{max} 2956, 2919, 2361, 2337, 1728, 1463, 1259, 963, 749 cm^{-1}; δ_H 8.84 (s, 1 H), 7.91−7.89 (m, 2 H), 7.74 (d, *J* = 7.6 Hz, 2 H), 7.53−7.47 (m, 3 H), 7.31−7.22 (m, 5 H), 4.82 (s, 2 H), 4.51 (s, 2 H), 2.37 (s, 3 H); δ_C 150.4, 148.4, 144.1, 138.4, 136.4, 134.6, 134.4, 134.3, 134.2, 133.5, 130.1, 129.5, 129.1, 128.5, 127.8, 127.0, 122.4, 121.2, 53.8, 53.1, 21.7; HRMS calcd for $C_{24}H_{20}N_2O_2S$ + H^+ 401.1324, found 401.1351.

*1-Benzyl-8-phenyl-6-tosyl-1,3a,5,6,7,8a-hexahydroimidazo[4,5-f]isoindole (**11c**):* state, brown sticky mass; R_f = 0.2 (hexane/EtOAc 1/1); yield 73 mg, 51%; IR (neat) ν_{max} 2959, 2921, 2851, 2361, 2342, 1701, 1611, 1516, 1465, 1364, 1273, 1219, 1052, 842, 772 cm^{-1}; δ_H 8.13 (d, *J* = 7.2 Hz, 1 H), 7. 78−7.72 (m, 4 H), 7.56 (s, 1 H), 7.45−7.36 (m, 4 H), 7.29−7.26 (m, 4 H), 7.07 (s, 1 H), 5.23 (s, 2 H), 4.76 (s, 2 H), 4.73 (s, 2 H), 2.37 (s, 3 H); δ_C 143.8, 134.7, 134.6, 133.8, 133.7, 130.0, 129.4, 128.7, 128.2, 127.9, 127.7, 126.2, 125.9, 125.8, 120.9, 119.3, 115.5, 54.2, 53.6, 51.4, 21.6; HRMS calcd for $C_{29}H_{25}N_3O_2S$ + H^+ 480.1746, found 480.1735.

*11-Phenyl-9-(toluene-4-sulfonyl)-9,10-dihydro-8H-9-azacyclopenta[b]phenanthrene (**11d**, major) and 4-naphthalen-2-yl-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**14d**, minor) (**11d:14d** = 1.9:1):* state, light brown sticky mass; R_f = 0.5 (hexane/EtOAc 4/1); yield 108 mg, 80%; IR (neat) ν_{max} 2924, 2856, 1598, 1448, 1346, 1163, 1097, 748 cm^{-1}; δ_H 7.99 (t, *J* = 8.0 Hz, 1 H, major), 7.84−7.58 (complex, 20 H, major + minor), 7.56−7.25 (comp, 10 H, major + minor), 7.08 (t, *J* = 8.0 Hz, 1 H, major), 4.87 (s, 2 H, major), 4.84 (s, 2 H, minor), 4.48−4.58 (m, 2 H, minor), 4.44 (s, 2 H, major), 2.40 (s, 6 H, major + minor); δ_C (50 MHz) (major + minor) 143.9, 142.0, 136.3, 135.3, 134.3, 133.8, 133.6, 130.6, 130.0, 128.7, 128.5, 128.4, 128.0, 127.8, 127.7, 127.5, 127.4, 126.7, 126.2, 125.5, 122.1, 120.9, 54.3, 54.1, 53.3, 21.7; HRMS calcd for $C_{29}H_{23}NO_2S$ + Na^+ 472.1347, found 472.1344.

*3-Methoxy-11-phenyl-9-(toluene-4-sulfonyl)-9,10-dihydro-8H-9-azacyclopenta[b]phenanthrene (**11e**, major) and 4-(6-methoxy-naphthalen-2-yl)-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]-isoindole (**14e**, minor) (**11e:14e** = 2.4:1).* state, Gummy solid; yield 108 mg, 75%; δ_H 7.89 (d, *J* = 8.0 Hz, 1 H, minor), 7.85 (d, *J* = 8.0 Hz, 1 H, minor), 7.75 (d, *J* = 8.0 Hz, 2 H, major, 3 H, minor), 7.69−7.62 (m, 3 H, major, 3 H minor), 7.57−7.52 (m, 3 H, major), 7.45 (app d, *J* = 9.6 Hz, 1 H, major, 1 H, minor), 7.37−7.25 (m, 4 H, major, 5 H, minor), 7.19 (d, *J* = 2.4 Hz, 1 H, major), 6.72 (dd, *J* = 8.4 Hz, 2 Hz, 1 H, major), 4.85 (s, 4 H, major + minor), 4.52−4.54 (m, 2 H, minor), 4.43 (s, 2 H, major), 4.02 (s, 3 H, minor), 3.88 (s, 3 H, major), 2.41 (s, 6 H, major + minor); HRMS calcd for $C_{30}H_{25}NO_3S$ + H^+ 480.1633, found 480.1614.

*3-Methoxy-11-phenyl-9-(toluene-4-sulfonyl)-9,10-dihydro-8H-9-azacyclopenta[b]phenanthrene (**11e**):* state, pale yellow solid; R_f = 0.5 (hexane/EtOAc 4/1); yield 76 mg, 52%; IR (neat) ν_{max}, 2922, 2851, 1628, 1480, 1349, 1161, 1092, 750 cm^{-1}; δ_H 7.73 (d, *J* = 8.0 Hz, 2 H), 7.67−7.61 (m, 3 H), 7.56−7.50 (m, 3 H), 7.42 (d, *J* = 9.6 Hz, 1 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.24−7.22 (m, 2 H), 7.17 (d, *J* = 2.8 Hz, 1 H), 6.69 (dd, *J* = 9.6 Hz, 2.8 Hz, 1 H), 4.84 (s, 2 H), 4.40 (s, 2 H), 3.86 (s, 3 H), 2.39 (s, 3 H); δ_C (50 MHz) 157.7, 143.9, 142.1, 136.4, 135.3, 134.6, 133.9, 133.4, 132.9, 130.1, 129.3, 128.6, 128.5, 128.1, 128.0, 127.9, 127.8, 127.6, 124.9, 122.2, 115.5, 109.1, 55.5, 54.4, 54.2, 21.7); HRMS calcd for $C_{30}H_{25}NO_3S$ + H^+ 480.1633, found 480.1614.

*4-(4-Methoxyphenyl)-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**14f**, major) and 6-methoxy-4-phenyl-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**11f**, minor) (**11f:14f** = 1:4.9):* state, gummy solid; R_f = 0.5 (hexane/EtOAc 4/1); yield 94 mg, 0.73 mmol, 73%; IR (neat) ν_{max} 2924, 2856, 1662, 1465, 1352, 1162, 1093, 755 cm^{-1}; δ_H 7.80 (d, *J* = 8.0 Hz, 1 H, major), 7.75 (d, *J* = 8.0 Hz, 2 H, major), 7.60 (app d, *J* = 8.0 Hz, 2 H, major), 7.43 (t, *J* = 8.0 Hz, 1 H, major), 7.35 (app t, *J* = 8.0 Hz, 1 H, major), 7.30 (d, *J* = 8.0 Hz, 2 H, major), 7.18 (d, *J* = 12.0 Hz, 2 H, major), 7.03 (d, *J* = 12.0 Hz, 2 H, major), 6.85 (d, *J* = 2.4 Hz, 1 H, minor), 4.79 (s, 2 H, major), 4.77 (s, 2 H, minor), 4.50 (s, 2 H, major), 4.46 (s, 2 H, minor), 3.91 (s, 3 H, major), 3.69 (s, 3 H, minor), 2.39 (s, 6 H, major + minor); δ_C (50 MHz) (major + minor) 159.5, 143.9, 134.5, 133.9, 132.3, 130.7, 130.0, 129.5, 129.1, 128.1, 127.9, 126.2, 126.1, 120.6, 114.4, 100.2, 55.6, 53.8, 53.4, 21.7; HRMS calcd for $C_{26}H_{23}NO_3S$ + Na^+ 452.1296, found 452.1293.

*4-(2,4-Dimethoxyphenyl)-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**14g**, major) and 6,8-dimethoxy-4-phenyl-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**11g**, minor) (**11g:14g** = 1:4):* state, sticky mass; yield 105 mg, 76%; δ_H (DMSO-d_6): 7.93 (s, 1 H, minor), 7.85 (d, *J* = 8.0 Hz, 1 H, major), 7.74−7.68 (complex, 5 H, major, 2 H, minor), 7.40−7.24 (complex, 3 H, major, 7 H, minor), 7.01 (d, *J* = 8.0 Hz, 1 H, major), 6.74 (s, 1 H, major), 6.67 (d, *J* = 8.0 Hz, 1 H, major), 6.60 (s, 1 H, minor), 6.33 (s, 1 H, minor), 4.73 (s, 2 H, major), 4.69 (s, 2 H, minor), 4.34−4.19 (m, 4 H, major + minor), 3.92 (s, 3 H, minor), 3.85 (s, 3 H, major), 3.57 (app s, 6 H, major + minor), 2.48 (s, 6 H, major + minor), 2.35 (s, 3 H, minor), 2.32 (s, 3 H, major); HRMS calcd for $C_{27}H_{25}NO_4S$ + Na^+ 482.1402, found 482.1402.

*4-(2,4-Dimethoxyphenyl)-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-benzo[f]isoindole (**14g**):* state, pale yellow solid; R_f = 0.5 (hexane/EtOAc 4/1); yield 83 mg, 60%; IR (neat) ν_{max}, 2922, 2852, 1604, 1461, 1349, 1161, 1032, 754 cm^{-1} δ_H 7.81 (d, *J* = 8.0 Hz, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.72 (d, *J* = 8.0 Hz, 2 H), 7.60 (s, 1 H), 7.50 (d, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H), 7.34−7.28 (m, 2 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.61 (app d, *J* = 7.6 Hz, 2 H), 4,81−4.75 (m, 2 H), 4.46 (s, 2 H), 3.91 (s, 3 H), 3.64 (s, 3 H), 2.38 (s, 3 H); δ_C (50 MHz) 161.2, 158.0, 143.8, 134.8, 134.2, 133.8, 133.7, 132.6, 131.9, 130.8, 129.9, 128.1, 127.9, 126.7, 126.0, 125.9, 120.7, 118.4, 105.0, 99.2, 55.7, 53.9, 53.6, 21.7; HRMS calcd for $C_{27}H_{25}NO_4S$ + Na^+ 482.1402, found 482.1402.

Procedure for the Synthesis of 1-Benzyl-4-iodo-3-methyl-1*H*-imidazol-2(3*H*)-one (28). 1-Benzyl-4-iodoimidazole (**6c**; 85 mg, 0.3 mmol) was taken up in 5 mL of toluene, MeI (1.5 equiv) was added to it, and the mixture was heated to reflux for 3 h. Toluene was then evaporated off, and the yellow gummy mass was triturated with petroleum ether (3 × 5 mL) to free the mass from the excess MeI trapped. The yellow gum **27** (112 mg, 0.27 mmol) was dried and dissolved in 5 mL of THF, 1 mL of 1 M NaOH was added to that solution, and subsequently 500 μL of 5% NaOCl was added slowly. After that the reaction mixture was partitioned between ethyl acetate (2 × 10 mL) and water. The combined organic layers were washed with brine (15 mL) and dried (anhydrous $MgSO_4$). Ethyl acetate was evaporated under vacuum, and the crude product was subjected to chromatography to give the pure product: state, yellow semisolid; R_f = 0.3 (hexane/EtOAc 1/1); yield 76 mg, 81% (based on 0.3 mmol of **6e**); IR (neat) ν_{max} 2952, 2853, 2923, 2856, 2343, 1709, 1674, 1463, 1273, 1077, 750 cm^{-1}; δ_H 7.34−7.30 (m, 3 H), 7.29−7.24 (m, 2 H), 6.29 (s, 1 H), 4.76 (s, 2 H), 3.23 (s, 3 H); δ_C 152.8, 136.4, 128.8, 128.1, 128.0, 116.8, 60.6, 47.5, 31.4; HRMS calcd for $C_{11}H_{11}N_2OI$ + H^+ 314.9994, found 314.9999.

Procedure for the Synthesis of 1-Benzyl-4-(3-(3-(4-methoxyphenyl)prop-2-ynyloxy)prop-1-ynyl)-3-methyl-1*H*-imidazol-2(3*H*)-one (29). **28** (79 mg, 0.25 mmol), CuI (0.2 mol %), and 1-methoxy-4-(3-(prop-2-ynloxy)prop-1-ynyl)benzene (1.2 equiv) were taken u in dry degassed triethylamine (8 mL), to this solution was added $Pd(PPh_3)_2Cl_2$ (0.03 mol %), and the mixture was stirred for 4 h. Triethylamine was evaporated in a rotavap, and the crude mixture was subjected to silica gel column chromatography to give the coupling product: state, yellow liquid; R_f = 0.4 (hexane/EtOAc 1/2); yield 87 mg, 90% (based on 0.25 mmol of **28**); IR (neat) ν_{max} 2952, 2361, 2331, 1710, 1605, 1460, 1249, 1080, 767 cm^{-1}; δ_H 7.34−7.27 (m, 5 H), 7.21−7.19 (m, 3 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 6.38 (s, 1 H), 4.74 (s, 2 H), 4.46 (s, 2 H), 4.42 (s, 2 H), 3.76 (s, 3 H), 3.24 (s, 3 H); δ_C 159.9, 152.3, 136.2, 133.3, 128.9, 128.1, 128.0, 116.1, 114.1, 114.0, 106.8, 90.8, 87.1, 82.6, 82.6, 75.0, 57.6, 57.1, 55.3, 47.3, 28.5; HRMS calcd for $C_{24}H_{22}N_2O_3$ + H^+ 387.1709, found 387.1714.

Procedure for the GB Cyclization of 1-Benzyl-4-(3-(3-(4-methoxyphenyl)prop-2-ynyloxy)prop-1-ynyl)-3-methyl-1*H*-imidazol-2(3*H*)-one (29). To a solution of **29** (77 mg, 0.2 mmol) in 8 mL dry THF was added KO^{t}Bu (2 equiv), and the mixture was heated to 50 °C for 2 h. After the completion of the reaction THF was evaporated off and the crude mixture was purified by silica gel column filtration: state, whitish gum; R_f = 0.3 (hexane/EtOAc 1/5); yield 73 mg, 94% (based on 0.2 mmol of **29**); IR (neat) ν_{max} 2924, 2852, 2359,

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1755, 1705, 1612, 1518, 1494, 1468, 1287, 1053, 1032, 839, 747 cm^{-1}; δ_H 7.07−7.04 (m, 3 H), 6.86−6.83 (m, 3 H), 6.72 (d, J = 8.2 Hz, 2 H), 6.55−6.52 (m, 2 H), 5.16 (s, 2 H). 4.77 (s, 2 H), 4.73 (s, 2 H), 3.79(s, 3 H), 3.48 (s, 3 H); δ_C 159.2, 155.5, 136.9, 132.6, 131.5, 131.0, 130.4, 128.0, 127.3, 126.8, 126.0, 125.9, 118.9, 113.5, 99.4, 74.3, 73.4, 55.3, 45.4, 27.5; HRMS calcd for $C_{24}H_{22}N_2O_3$ + H^+ 387.1709, found 387.1714.

Procedure for the Conversion of Phthalan 30 to Dialdehyde 31. To an ice-cold solution of the phthalan **30** (77 mg, 0.2 mmol) in 2 mL of dry DCM was added slowly a pre cooled solution of HNO_3 (2 equiv) in 1 mL of DCM. After the completion (approximately 15 min) of the reaction, the mixture was diluted with DCM (5 mL) and basic alumina was added. After filtration the solvent was removed in a liquid nitrogen trap. The dialdehyde was obtained pure via crystallization from ethyl acetate/hexane.

*3-Benzyl-4-(4-methoxyphenyl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5,6 dicarbaldehyde (**31**):* state, light yellow solid; mp 151−156 °C (Reported 152−155 °C) yield 74 mg; 92% (based on 0.2 mmol of **30**); δ_H 10.3 (s, 1 H), 9.70 (s, 1 H), 7.12−7.06 (m, 3 H), 6.91 (d, J = 8.4 Hz, 2 H), 6.73 (d, J = 8.6 Hz, 2 H), 6.53 (d, J = 6.4 Hz, 2 H), 4.73 (s, 2 H), 3.82 (s, 3 H), 3.57 (s, 3 H); δ_C 192.6, 191.9, 160.1, 155.6, 136.1, 133.7, 132.2, 131.9, 131.7, 130.1, 128.3, 128.0, 127.2, 125.5, 123.5, 113.7, 106.5, 55.5, 45.8, 27.9; HRMS calcd for $C_{24}H_{20}N_2O_4$ + H^+ 401.1501, found 401.1527.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving ^1H and ^{13}C NMR spectra of GB precursors and products and HRMS spectra of GB products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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