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Synthesis and Reactions of Benzannulated Spiroaminals: Tetrahydrospirobiquinolines

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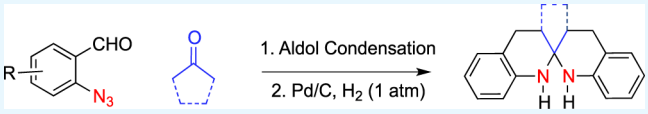
Supporting Information

ABSTRACT: An efficient two-step synthesis of symmetrical and unsymmetrical tetrahydrospirobiquinolines from *o*-azidobenzaldehydes is reported. A novel series of tetrahydrospirobiquinolines was prepared by sequential double-aldol condensation with acetone, cyclopentanone, and cyclohexanone to form the corresponding *o*,*o*′-diazido-dibenzylidene-acetone, -cyclopentanone, and -cyclohexanone derivatives, respectively, and hydrogenation−spirocyclization. The spirodiamines were further derivatized by electrophilic aromatic bromination, Suzuki coupling, and *N*-alkylation, all of which proceeded with preservation of the spirocyclic core.



INTRODUCTION

Access to a broad range of structurally diverse nitrogen heterocycles is important in probing and understanding biological functions and may lead to the discovery of new medicines and agricultural chemicals. Fused-ring nitrogen heterocycles are considered privileged scaffolds in both medicinal chemistry and agrochemistry.[1] There is a need to expand the structural classes of amines, especially to those that are C-(sp^3)-rich, to enhance the structural complexity and for better interaction with biological targets.[2] Whereas spiroketals, including benzannulated systems,[3−7] are common scaffolds in biologically active heterocyclic compounds and spirocyclic compounds with a single oxygen and single aminonitrogen attached to the spirane center are known,[8,9] spirodiamines, which contain two amino-groups at that center, are far less well studied.[10−13] The spirodiamine core is known in several natural products, including (−)-isochizogamine (**1**),[14−16] isoschizogaline (**2**),[17] (+)-melodinine-E (**3**),[18−20] and the immunosuppressant (±)-spiroreticulatine (**4**) (Figure 1).[21]

Following earlier work,[13] we reported a concise synthesis method of spirodiamine **6** from the crossed Claisen condensation of lactam **5** and decarboxylative spirocyclization.[10] In these studies, we demonstrated that spirodiamine **6** underwent metal complexation or a reaction with electrophiles, with either preservation of the spirocyclic core or ring opening and derivatization of 4-aminobutyl-1-tetrahydropyridine core **7** (Figure 2).[10]

In contrast, the synthesis and reactions of benzannulated spirodiamines have not been reported. Inspired by the ubiquitous biological activity of tetrahydroisoquinoline derivatives, we considered that the tetrahydrospirobiquinoline scaffold may provide access to novel pharmacophores and ligands for metal complexation. Indeed, benzannulated spiroketals, **13**, (Figure 3) have been well studied and synthesized most notably by Ding, Wang, and Zhou.[22−25]

RESULTS AND DISCUSSION

By analogy with benzannulated spiroketals, we envisaged that increasing the rigidity of the diaza scaffold of spirodiamine **6** would displace the spirodiamine **6** to aminoimine **7** equilibrium toward the spirane tautomer. We therefore sought to synthesize a range of tetrahydrospirobiquinolines, **14**, from the double-aldol condensation of *o*-azidobenzaldehydes with ketones to provide the corresponding diazido-dibenzylidene-ketones, followed by reductive cyclization (Figure 3). Initial studies were directed toward the synthesis of tetrahydrospirobiquinoline **14a**. *o*-Azidobenzaldehyde **15a** was allowed to react with acetone in the presence of aqueous sodium hydroxide to afford dienone **17a** (94% yield). Subsequent hydrogenation over palladium on carbon gave tetrahydrospirobiquinoline **14a** (Scheme 1), the structure of which was confirmed by two-dimensional NMR spectroscopy and X-ray crystal structure determination.

A two-step reaction was used for the synthesis of a range of tetrahydrospirobiquinolines from the corresponding aromatic aldehydes and acetones,[26,27] including extended aromatic systems; electron-rich and electron-poor systems; as well as ortho-, meta-, and para-substituted examples, **14b−g** (Table 1). The yields show little deviation, with the exceptions of *p*-Cl (**14g**, entry 6), for which some dechlorination was observed, and *o*-Me (**14d**, entry 4), for which steric congestion is greater.

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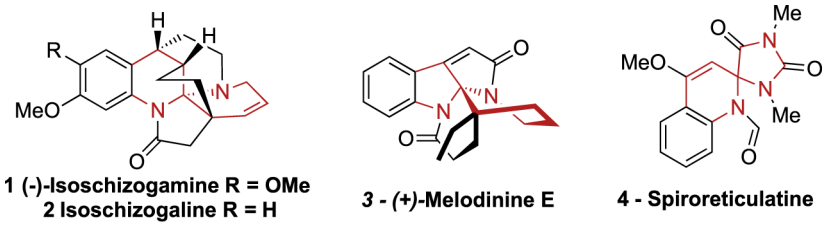


Figure 1. Spiroaminal natural products.[14−21]

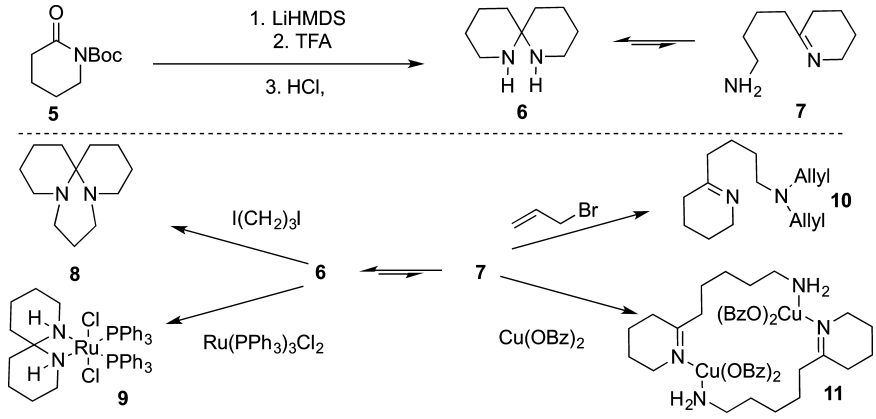


Figure 2. Synthesis and reactions of 1,7-diazaspiro[5.5]undecane.[10]

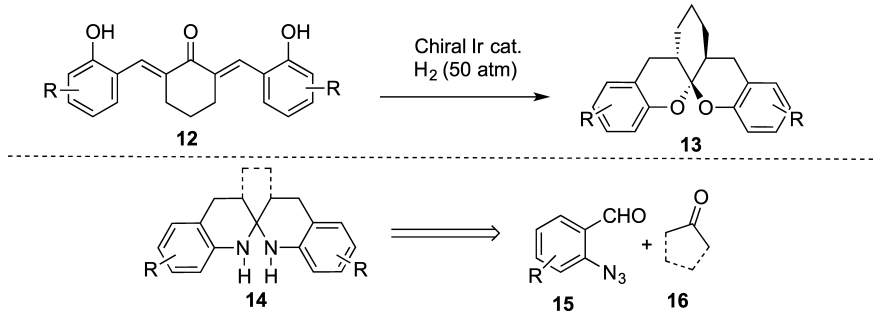
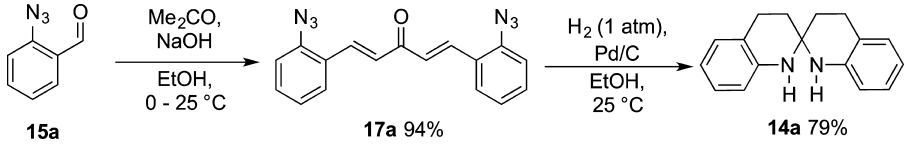


Figure 3. Top: Ding−Wang synthesis of benzannulated spiroketals. Bottom: Proposed synthesis of tetrahydrospirobiquinoline **14**.

Scheme 1. Synthesis of 3,3′,4,4′-Tetrahydro-1*H*,1′*H*-2,2′-spirobi[quinoline] 14a



Furthermore, cyclopentanone and cyclohexanone can readily replace acetone to produce pentacyclic tetrahydrospirobiquinolines **18** and **19**, both as single diastereoisomers, as determined by both ^{1}H and ^{13}C NMR spectroscopy (Scheme 2). These are consistent with the symmetrical trans product for cyclopentanone derivative **18** and desymmetrized cis product **19**. These relative stereochemistries were confirmed in both cases by X-ray crystallography after tetrabromination (see Supporting Information).

The origins of these diastereoselectivities were probed using dispersion-corrected density functional theory calculations (B3LYP+D3BJ/Def2-TZVPP/SCRF = ethanol)[28] of relative free energies ($\Delta\Delta G_{298}$), with the assumption of fast equilibria between amine−imine and spirodiamine. The dipole moments computed for the former class were uniformly higher (3.8−4.9 D) than those for the latter (1.1−1.7 D). The equilibrium free energies did not provide sufficient support for the observed diastereoselectivity. We speculate that the stabilities of the two intermediate ketones are predominant factors in the overall stereochemical control. On the basis of the known preferential formation of *cis*-2,5-dibenzyl-cyclopentanone and *cis*-2,6-dibenzyl-cyclohexanone on the palladium-catalyzed hydrogenation of the corresponding 2,5- or 2,6-benzylidene ketones and the facile cis to trans isomerization of the former, equivalent cis to trans isomerization took place prior to spirocyclization with spirane **18** but not with spirane **19**.[29,30] Alternatively, the opposite diastereoisomers do not spirocyclize and exist as amine−imine isomers, which were not isolated chromatographically due to their higher polarities. Attempts were made to isolate these compounds as well as to cyclize

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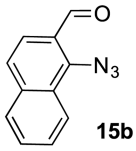
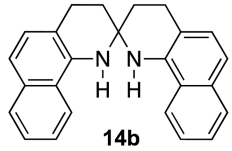
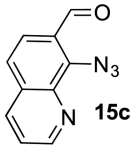
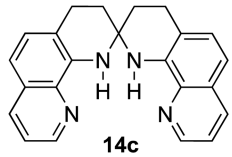
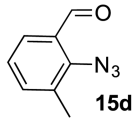
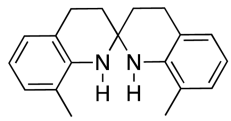
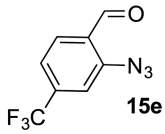
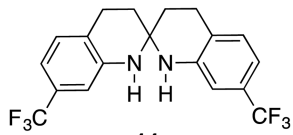
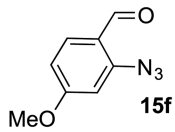
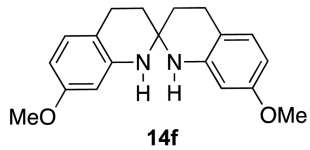
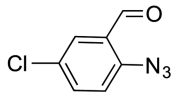
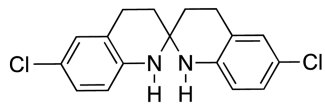
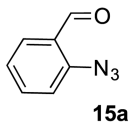
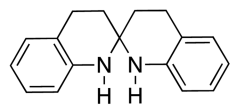
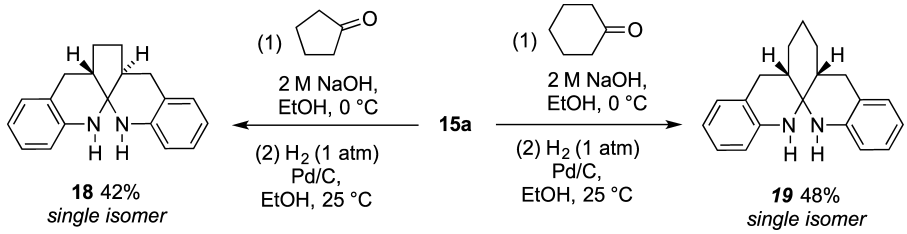
Table 1. Substrate Scope[a]

Entry	Aldehyde	Product	Yield (%)[b]
1	 **15b**	 **14b**	67
2	 **15c**	 **14c**	75
3	 **15d**	 **14d**	53
4	 **15e**	 **14e**	82
5	 **15f**	 **14f**	78
6	 **15g**	 **14g**	34
7[c]	 **15a**	 **14a**	69

[a]Reaction conditions: (i) *o*-azido-benzaldehyde derivative **15** (2 mmol), Me_2CO (1 mmol), 2 M NaOH (5 mmol), EtOH, 0−25 °C, 4 h; (ii) 10% Pd/C (10 wt %), H_2 (1 atm), EtOH, 25 °C, 16 h. [b]Isolated yield over two steps. [c]Aldehyde, 40 mmol scale.

Scheme 2. Synthesis of Pentacyclic Tetrahydrospirobiquinolines 18 and 19



them upon treatment with a variety of Lewis and Brønsted acids;[24] however, this was unsuccessful. Further investigations into these systems are ongoing in our laboratory.

To expand on the potential number of derivatives accessible by the method, unsymmetrical systems were also studied. Application of the known sequential condensation reaction of acetone with two different *o*-azido-benzaldehyde derivatives, **20** and **22**,[31] hydrogenation, and spirocyclization gave tetrahydrospirobiquinolines **24a** and **24b** (Scheme 3).

Reaction of tetrahydrospirobiquinoline **14a** with varying equivalents of *N*-bromosuccinimide (NBS) gave brominated products **25** and **26** in 56 and 74% yields, respectively.

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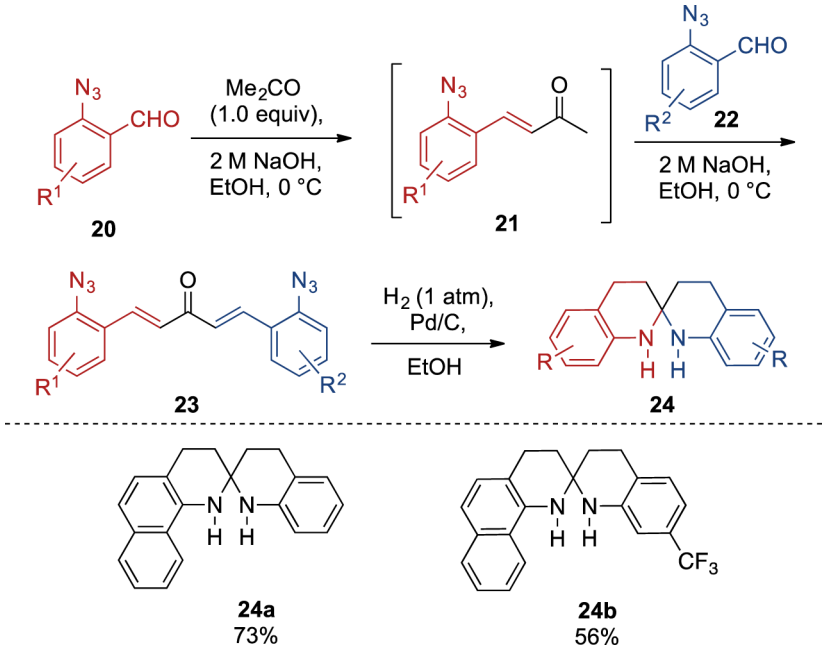
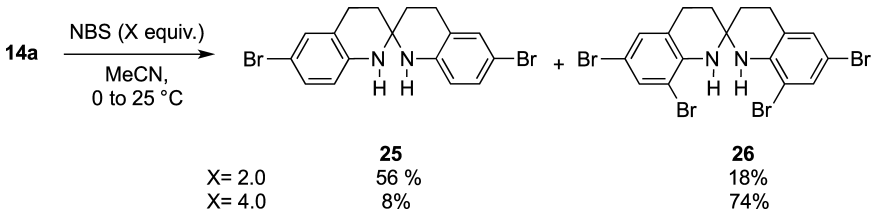
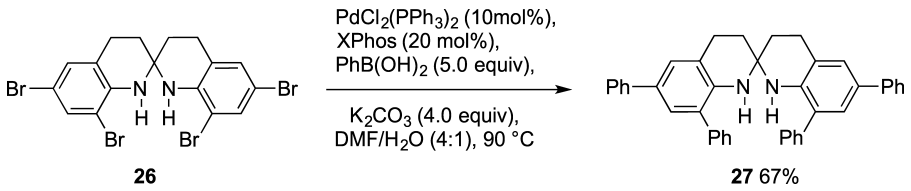
Scheme 3. Synthesis of Unsymmetrical Tetrahydrospirobiquinolines 24a and 24b



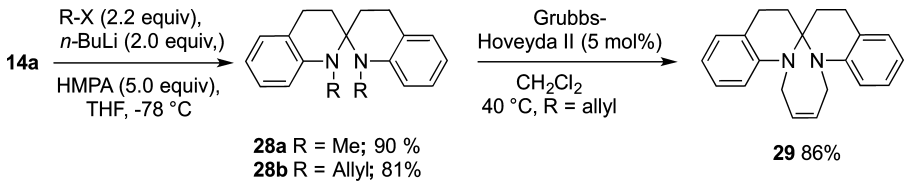
Scheme 4. Bromination of Tetrahydrospirobiquinoline 14a with NBS



Scheme 5. Suzuki–Miyuara Cross-Coupling of Tetrahydrospirobiquinoline 26



Scheme 6. Alkylation of Tetrahydrospirobiquinoline 14a and Ring-Closing Metathesis of 28b



Dibromination first occurs para to the nitrogen to yield the dibromo analogue **25**; then, it occurs ortho to the nitrogen to yield the tetrabromo analogue **26** (Scheme 4), with both structures being confirmed by X-ray crystal structure determinations.

Bromide **26** was converted to tetraphenyl-derivative **27** (67%) by Suzuki–Miyaura coupling with phenylboronic acid (Scheme 5). Most importantly, this demonstrates the robustness of the benzannulated spirodiamine core, which tolerates palladium-mediated cross-coupling. The structure of spirane-diamine **27** was confirmed by X-ray crystal structure determination.

We also investigated derivatization by substitution at the nitrogen of the spirane center. Unsurprisingly, a combination of electronics and steric congestion of the aniline nitrogens mandated forcing conditions for alkylation reactions. Thus, alkylation of tetrahydrospirobiquinoline **14a** with *n*-butyllithium in tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) and iodomethane gave dimethyl derivative **28a** (90%), and allyl bromide afforded the diallyl derivative **28b** (81%), again with preservation of the spirocyclic framework

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(Scheme 6). This is in contrast to allylation of spirodiamine **6**, which results in reaction of the amino group of aminoimine tautomer **7** (Figure 2).[10] Diallyl tetrahydrospirobiquinoline **28b** smoothly underwent ring-closing metathesis, giving pentacyclic tetrahydrospirobiquinoline **29**. The structure of spirane-diamine **29** was confirmed by X-ray crystal structure determination.

CONCLUSIONS

We have developed a chemically robust and straightforward procedure for the synthesis of tetrahydrospirobiquinoline derivatives, a class of understudied heterocyclic compounds. Further syntheses and applications of spirodiamines, including tetrahydrospirobiquinolines, will be reported in due course.

EXPERIMENTAL SECTION

General Remarks. All reactions were carried out in oven-dried glassware under atmospheric conditions using commercially supplied solvents and reagents, unless otherwise stated. Large-scale hydrogenations were carried out in a Parr hydrogenator. Column chromatography was carried out on silica gel using flash chromatography techniques, unless otherwise stated (eluents are given in parentheses). Analytical thin-layer chromatography (TLC) was performed on precoated silica gel F254 aluminum plates, with visualization under UV light or by staining with an acidic vanillin dip. Melting points were measured with a hot-stage apparatus and are uncorrected. IR spectra were recorded on neat films. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 101 MHz, respectively, with chemical shifts (δ) quoted in ppm, relative to $CHCl_3$ (^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm).

Safety Note. Although low-molecular-weight azides are potentially hazardous, we have had no issues with any of the intermediates in terms of their thermal stability or uncontrolled decomposition. However, it is advised that these compounds be handled carefully, behind a blast shield. When carrying out S_NAr reactions with sodium azide, it is advised that the solutions be kept basic, with the addition of 20 mol % Et_3 N or an equivalent of 2,6-lutidine, with constant sparging with argon to clear the headspace, as published by Zhou et al.[35]

*1-Azido-2-naphthaldehyde (**15b**).* 1-Azido-2-naphthaldehyde (**15b**) was synthesized using a modified version of the procedure followed by Boswell and Licause.[32] 1-Fluoro-2-naphthaldehyde[33] (2.42 g, 13.9 mmol, 1.0 equiv) in anhydrous dimethylformamide (DMF) (21 mL) was cooled to 0 °C under argon. NaN_3 (1.80 g, 27.7 mmol, 2.0 equiv) was added in one portion, and the resultant solution was heated to 60 °C with constant sparging with argon for 2 h. Following this, the mixture was cooled to room temperature, diluted with H_2O (50 mL), and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed sequentially with 5% aqueous LiCl (3 × 50 mL) and brine (1 × 50 mL) and dried ($MgSO_4$). The solvent was rotary-evaporated to give azide **15b** as a yellow crystalline solid, without the need for further purification (2.42 g, 87%): melting point (mp) 50−51 °C (PhMe) (lit. mp 50−52 °C), which showed spectroscopic data matching that previously reported.[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.41−8.33 (m, 1H), 7.92−7.84 (m, 2H), 7.77 (d, J = 8.6 Hz, 1H), 7.71−7.61 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.8, 140.4, 137.1, 129.8, 128.70, 128.1, 127.7, 126.5, 125.5, 125.0, 124.0; high-resolution mass spectrometry (HRMS) (EI), calcd for $C_{11}H_7N_3O$ (M^+): 197.0589; found: 197.0582; microanalysis, calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31; found: C, 66.78; H, 3.39; N, 21.12.

*8-Azidoquinoline-7-carbaldehyde (**15c**).* NaN_3 (1.78 g, 27.4 mmol, 3.0 equiv) was added to 8-nitroquinoline-7-carbaldehyde[34] (1.85 g, 9.13 mmol, 1.0 equiv) in anhydrous DMF (14 mL) and Et_3N (260 μL, 1.82 mmol, 0.2 equiv) under an argon atmosphere and heated at 60 °C with sparging with argon. After 1 h, the mixture was allowed to cool, diluted with H_2O (50 mL), and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed sequentially with 5% aqueous LiCl (3 × 50 mL) and brine (1 × 50 mL) and dried ($MgSO_4$). After rotary evaporation, the residue was chromatographed (gradient; pentane/CH_2Cl_2 1:1 to 0:1) to give azide **15c** (785 mg, 43%) as a yellow solid: mp 125−126 °C (CH_2Cl_2); IR ν = 2125, 1675, 1384, 1295, 1256, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.68 (s, 1H), 8.95 (d, J = 4.0 Hz, 1H), 8.18 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 8.6 Hz, 1H), 7.63−7.50 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.3, 148.9, 143.5, 141.8, 136.6, 132.4, 125.7, 124.1, 123.8, 123.7; HRMS (ES+), calcd for $C_{10}H_7N_4O$ ($M + H^+$): 199.0620; found: 199.0628; microanalysis, calcd for $C_{10}H_6N_4O$: C, 60.60; H, 3.05; N, 28.27; found: C, 60.38; H, 3.17; N, 28.09.

General Procedure for the Synthesis of Tetrahydrospirobiquinolines (14a−g). *o*-Azido-benzaldehyde (2.0 mmol, 2.0 equiv) in absolute EtOH (20 mL) was cooled in an ice bath. Me_2CO (73 μL, 1.0 mmol, 1.0 equiv) was added, followed by the addition of 2 M NaOH (2.5 mL, 5.0 mmol, 5.0 equiv) dropwise over 30 s, with stirring. The ice bath was removed, and after 4 h at room temperature, the resultant precipitate was collected by filtration and washed with ice-cold absolute EtOH. The slurry was resuspended in EtOH (20 mL) with 10% Pd/C (10 wt %) and stirred under a hydrogen atmosphere (balloon) for 16 h. The catalyst was removed by filtration, and the solvent was removed by rotary evaporation. The purification for each spirobiquinoline is given separately.

*3,3′,4,4′-Tetrahydro-1H,1′H-2,2′-spirobi[quinoline] (**14a**).* *o*-Azidobenzaldehyde gave spirobiquinoline **14a** (185 mg, 74%) as a colorless crystalline solid. A sample was chromatographed (pentane/CH_2Cl_2 1:1): mp 131−132 °C (CH_2Cl_2); IR ν = 3372, 3047, 2915, 1600, 1488, 1468, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11−6.96 (m, 4H), 6.70 (td, J = 7.4, 1.2 Hz, 2H), 6.48 (dd, J = 7.9, 1.2 Hz, 2H), 4.27 (s, 2H), 2.91 (t, J = 6.8 Hz, 4H), 2.10−1.90 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6 (2C), 129.2 (2C), 127.24 (2C), 120.2 (2C), 117.8 (2C), 114.8 (2C), 63.5, 33.3 (2C), 23.4 (2C); HRMS (ESI), calcd for $C_{17}H_{19}N_2$ ($M + H^+$): 251.1548; found: 251.1546; microanalysis, calcd for $C_{17}H_{18}N_2$: C, 81.56; H, 7.25; N, 11.19; found: C, 81.44; H, 7.37; N, 11.08.

*3,3′,4,4′-Tetrahydro-1H,1′H-2,2′-spirobi[benzo[h]-quinoline] (**14b**).* 1-Azido-2-naphthaldehyde (**15b**) gave spirobiquinoline **14b** as a white amorphous solid (235 mg, 67%). A sample was chromatographed (gradient; pentane/CH_2Cl_2 4:1 to 1:1): mp 169−170 °C (pentane); IR ν = 3373, 3050, 2922, 1574, 1473, 1396, 745 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.74 (m, 2H), 7.72−7.65 (m, 2H), 7.42−7.38 (m, 2H), 7.28−7.23 (m, 4H), 4.92 (s, 2H), 3.20−3.05 (m, 4H), 2.29−2.06 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9 (2C), 133.3 (2C), 128.7 (2C), 128.1 (2C), 125.3 (2C), 125.1 (2C), 123.1 (2C), 119.4 (2C), 117.7 (2C), 114.4 (2C), 64.3, 32.9 (2C), 24.4 (2C); HRMS (ES+), calcd for $C_{25}H_{23}N_2$ ($M + H^+$): 351.1861; found: 351.1872; microanalysis, calcd for $C_{25}H_{22}N_2$: C, 85.68; H, 6.33; N, 7.99; found: C, 85.57; H, 6.40; N, 7.90.

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*3,3′,4,4′-Tetrahydro-1H,1′H-2,2′-spirobi[[1,10]-phenanthroline] (**14c**).* 8-Azidoquinoline-7-carbaldehyde (**15c**) gave spirobiquinoline **14c** (264 mg, 75%) as a yellow solid. A sample was chromatographed (gradient; CH_2Cl_2/MeOH 1:0 to 9:1): mp 153−155 °C (CH_2Cl_2); IR ν = 3402, 3040, 2830, 1508, 1472, 1325, 819, 793 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (dd, J = 4.2, 1.7 Hz, 2H), 8.05 (dd, J = 8.2, 1.7 Hz, 2H), 7.33−7.28 (m, 4H), 7.10 (d, J = 8.2 Hz, 2H), 6.55 (s, 2H), 3.23 (ddd, J = 17.3, 9.1, 5.7 Hz, 2H), 3.11 (dt, J = 17.1, 6.0 Hz, 2H), 2.37−2.27 (m, 2H), 2.16 (ddd, J = 12.7, 9.1, 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3 (2C), 138.7 (2C), 137.6 (2C), 135.9 (2C), 128.7 (2C), 127.6 (2C), 120.8 (2C), 116.0 (2C), 114.2 (2C), 63.0, 33.3 (2C), 24.0 (2C); HRMS (ES+), calcd for $C_{23}H_{20}N_4$ (M + H^+): 353.1766; found: 353.1772; microanalysis, calcd for $C_{23}H_{20}N_4$: C, 78.38; H, 5.72; N, 15.90; found: C, 78.19; H, 5.81; N, 15.73.

*8,8′-Dimethyl-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**14d**).* 2-Azido-6-methylbenzaldehyde[27] (**15d**) gave spirobiquinoline **14d** (147 mg, 53%) as a colorless oil. A sample was chromatographed (pentane/CH_2Cl_2 3:2): IR ν = 3392, 3008, 1658, 1541, 1514, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.00−6.91 (m, 4H), 6.67 (t, J = 7.5 Hz, 2H), 2.91 (t, J = 6.8 Hz, 4H), 2.11 (s, 6H), 2.05 (t, J = 6.8 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7 (2C), 128.4 (2C),127.1 (2C), 121.4 (2C), 119.6 (2C), 117.1 (2C), 64.4, 33.2 (2C), 24.0 (2C), 17.4 (2C); HRMS (ESI), calcd for $C_{19}H_{23}N_2$ (M + H^+): 279.1856; found: 279.1977; microanalysis, calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06; found: C, 82.08; H, 8.05; N, 9.85.

*7,7′-Bis(trifluoromethyl)-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi[quinoline] (**14e**).* 2-Azido-4-(trifluoromethyl)-benzaldehyde[27] (**15e**) gave spirobiquinoline **14e** (316 mg, 82%) as a white solid. A sample was chromatographed (pentane/CH_2Cl_2 4:1): mp 132−133 °C ($CHCl_3$); IR ν = 3401, 2925, 1508, 1467, 1325, 1103, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J = 7.8 Hz, 2H), 6.92 (dd, J = 7.8, 1.7 Hz, 2H), 6.71 (d, J = 1.6 Hz, 2H), 4.40 (s, 2H), 2.98−2.84 (m, 4H), 2.09−1.87 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6 (2C), 129.6 (2C), 123.6 (2C), 114.3 (2C), 114.3 (2C), 111.1 (2C), 111.0 (2C), 63.7, 33.0 (2C), 23.4 (2C); HRMS (ESI), calcd for $C_{19}H_{17}N_2F_6$ (M + H^+): 387.1296; found: 387.1294; microanalysis, calcd for $C_{19}H_{16}N_2F_6$: C, 59.07; H, 4.17; N, 7.25; found: C, 58.93; H, 4.24; N, 7.21.

*7,7′-Dimethoxy-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**14f**).* 2-Azido-4-methoxybenzaldehyde[27] (**15f**) gave spirobiquinoline **14f** (241 mg, 77%) as a white solid. A sample was chromatographed (pentane/CH_2Cl_2 1:1): mp 159−161 °C ($CHCl_3$); IR ν = 3382, 2925, 1613, 1479, 1325, 1199, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.94 (d, J = 8.2 Hz, 2H), 6.28 (dd, J = 8.3, 2.5 Hz, 2H), 6.04 (d, J = 2.4 Hz, 2H), 4.27 (s, 2H), 3.73 (s, 6H), 2.83 (t, J = 6.7 Hz, 4H), 1.94 (tt, J = 12.8, 5.8 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2 (2C), 143.5 (2C), 130.0 (2C), 112.7 (2C), 104.0 (2C), 99.9 (2C), 63.3, 55.32 (2C), 33.5 (2C), 22.6 (2C); HRMS (ESI), calcd for $C_{19}H_{23}N_2O_2$ (M + H^+): 311.1760; found: 311.1773; microanalysis, calcd for $C_{17}H_{18}N_2$: C, 73.52; H, 7.14; N, 9.03; found: C, 73.33; H, 6.98; N, 8.80.

*6,6′-Dichloro-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**14g**).* 2-Azido-5-chlorobenzaldehyde[27] (**15g**) gave the spiroquinoline **14g** (108 mg, 34%) as a colorless oil. A sample was chromatographed (pentane/CH_2Cl_2 1:1): IR ν = 3398, 2936, 1480, 1291, 850 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J = 2.4 Hz, 2H), 6.96 (dd, J = 8.4, 2.5 Hz, 2H), 6.40 (d, J = 8.5 Hz, 2H), 4.21 (s, 2H), 2.85 (m, 4H), 2.03−1.84 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1 (2C), 128.9 (2C), 127.2 (2C), 122.4 (2C), 121.7 (2C), 115.8 (2C), 63.7, 32.9 (2C), 23.3 (2C); HRMS (ESI), calcd for $C_{17}H_{18}N_2Cl$ (M + H^+ − Cl^-): 285.1159; found: 285.1164; microanalysis, calcd for $C_{17}H_{16}N_2Cl_2$: C, 63.96; H, 5.05; N, 8.78; found: C, 64.00; H, 5.10; N, 8.71.

*5,5a,6,7,7a,8,13,14-Octahydrocyclopenta[1,2-b:1,5-b′]-diquinoline (**18**).* Using the general procedure above, cyclopentanone (89 μL, 1.0 mmol, 1.0 equiv) was used instead of Me_2CO alongside *o*-azidobenzaldehyde to afford spiroquinoline **18** (115 mg, 42%) as a white solid. A sample was chromatographed (pentane/CH_2Cl_2 1:1): mp 109−111 °C (pentane); IR ν = 3384, 2918, 1605, 1474, 1261, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13−7.00 (m, 5H), 6.71 (td, J = 7.4, 1.2 Hz, 2H), 6.50 (dd, J = 7.8, 1.1 Hz, 2H), 4.12 (s, 2H), 2.90 (dd, J = 15.9, 5.7 Hz, 2H), 2.65 (dd, J = 15.9, 7.2 Hz, 2H), 2.20 (td, J = 7.3, 5.5 Hz, 2H), 2.01−1.88 (m, 2H), 1.51−1.38 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7 (2C), 128.9 (2C), 127.1 (2C), 121.3 (2C), 117.7 (2C), 75.3, 113.6 (2C), 43.8 (2C), 30.1 (2C), 27.78 (2C); HRMS (ESI), calcd for $C_{19}H_{21}N_2$ (M + H^+): 277.1705; found: 277.1710; microanalysis, calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.14; found: C, 82.45; H, 7.35; N, 9.98.

*5a,6,7,8,8a,9,14,15-Octahydro-5H-quinolino[3,2-d]-acridine (**19**).* Using the general procedure above, cyclohexanone (103 μL, 1.00 mmol, 1.0 equiv) was used instead of Me_2CO alongside *o*-azidobenzaldehyde to afford spirobiquinoline **19** (175 mg, 48%) as a white solid. A sample was chromatographed (pentane/CH_2Cl_2 1:1): mp 140−141 °C (pentane); IR ν = 3372, 2928, 1586, 1477, 1251, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.07−7.03 (m, 2H), 7.02−6.96 (m, 2H), 6.69 (tdd, J = 7.6, 5.2, 1.3 Hz, 2H), 6.44 (dd, J = 8.1, 1.2 Hz, 2H), 4.47 (s, 1H), 4.22 (s, 1H), 3.24 (dd, J = 17.3, 5.9 Hz, 1H), 2.80 (dd, J = 17.2, 5.8 Hz, 1H), 2.70−2.50 (m, 2H), 2.13−1.32 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3 (2C), 141.1 (2C), 129.9 (2C), 129.1 (2C), 127.1 (2C), 126.9 (2C), 120.2 (2C), 118.4 (2C), 117.9 (2C), 117.6 (2C), 115.7 (2C), 115.4 (2C), 64.4, 39.7 (2C), 38.5 (2C), 29.4 (2C), 29.2 (2C), 29.0 (2C), 28.7 (2C), 25.3 (2C); HRMS (ESI), calcd for $C_{20}H_{23}N_2$ (M + H^+): 291.1861; found: 291.1875; microanalysis, calcd for $C_{12}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65; found: C, 82.70; H, 7.73; N, 9.66.

*3,3′,4,4′-Tetrahydro-1H,1′H-spiro[benzo[h]quinoline-2,2′-quinoline] (**24a**).* *o*-Azidobenzaldehyde (**15a**) (147 mg, 1.0 mmol, 1.0 equiv) was dissolved in absolute EtOH (20 mL) and cooled in an ice bath. Me_2CO (73 μL, 1.0 mmol, 1.0 equiv) was added, followed by the dropwise addition of 2 M NaOH (2.5 mL, 5.0 mmol, 5.0 equiv), with stirring. After 2 h, the aldehyde was consumed (TLC), and at this time, 1-azido-2-naphthaldehyde (**15b**) (197 mg, 1.00 mmol, 1.0 equiv) was added in one portion. After a further 2 h, the resultant precipitate was collected by filtration and washed with ice-cold absolute EtOH. The slurry was resuspended in EtOH (20 mL) with 10% Pd/C (10 wt %) and stirred under a hydrogen atmosphere (balloon) for 16 h. The catalyst was removed by filtration, and the solvent, rotary-evaporated. The residue was chromatographed (gradient; pentane/CH_2Cl_2 1:0 to 1:1) to give unsymmetrical spirobiquinoline **24a** (219 mg, 73%) as an orange oil: IR ν = 3389, 2922, 2851, 1473, 1398, 797, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79−7.74 (m, 1H), 7.69−7.66 (m, 1H), 7.43−7.38 (m, 2H), 7.22 (q, J = 8.4 Hz, 2H), 7.10−6.98 (m, 2H), 6.71 (td, J = 7.4, 1.2 Hz, 1H), 6.50 (dd, J = 8.1, 1.1 Hz,

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1H), 4.80 (s, 1H), 4.37 (s, 1H), 3.05 (t, J = 6.8 Hz, 2H), 2.96 (d, J = 12.1 Hz, 2H), 2.13−2.03 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 137.0, 133.3, 129.2, 128.7, 128.0, 127.3, 125.3, 125.1, 123.1, 120.4, 119.4, 117.8, 117.7, 114.6, 114.3, 64.0, 33.3, 32.9, 24.2, 23.5; HRMS (ESI), calcd for $C_{21}H_{19}N_2$ ($M - H^+$): 299.1548; found: 299.1542; microanalysis, calcd for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33; found: C, 83.84; H, 6.67; N, 9.48.

*7′-(Trifluoromethyl)-3,3′,4,4′-tetrahydro-1H,1′H-spiro-[benzo[h]quinoline-2,2′-quinoline] (**24b**).* Using the procedure described for the preparation of spirobiquinoline **20**; 2-azido-4-(trifluoromethyl)benzaldehyde (215 mg, 1.0 mmol, 1.0 equiv) (**15e**) and 1-azido-2-naphthaldehyde (**15b**) (197 mg, 1.0 mmol, 1.0 equiv) were converted into spirobiquinoline **24b** (206 mg, 56%), obtained as an orange oil: IR ν = 3397, 2925, 1473, 1332, 1114, 799 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.75 (m, 1H), 7.69−7.64 (m, 1H), 7.43−7.39 (m, 2H), 7.26 (m, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 7.8 Hz, 1H), 6.94−6.89 (m, 1H), 6.72 (d, J = 1.6 Hz, 1H), 4.73 (s, 1H), 4.55 (s, 1H), 3.06 (t, J = 6.8 Hz, 2H), 3.01−2.89 (m, 2H), 2.18−1.95 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8 (2C), 136.6, 133.3, 129.9, 129.5, 128.8, 128.0, 125.4, 125.2, 124.0, 123.1, 119.3, 118.1, 114.3, 114.1, 110.9, 64.1, 33.3, 32.6, 24.1, 23.6; HRMS (ESI), calcd for $C_{22}H_{18}N_2F_3$ ($M - H^+$): 367.1422; found: 367.1428; microanalysis, calcd for $C_{22}H_{19}N_2F_3$: C, 71.73; H, 5.20; N, 7.60; found: C, 71.53; H, 4.97; N, 7.86.

Procedure for the Bromination of Spirobiquinoline 14a with NBS. Freshly recrystallized NBS (700 mg, 4.0 mmol, 2.0 equiv or 1400 mg, 8.0 mmol, 4.0 equiv) was added in one portion to spirobiquinoline **14a** (500 mg, 2.0 mmol, 1.0 equiv) in MeCN (200 mL), with stirring, at 0 °C, and the resultant solution was allowed to warm to room temperature. After 16 h, the solvent was removed by rotary evaporation, and the resultant slurry, dissolved in CH_2Cl_2 and H_2O (1:1, 250 mL). The layers were separated, and the aqueous layer was further extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$), the solvent was removed by rotary evaporation, and the residue was chromatographed (gradient; pentane/CH_2Cl_2 1:0 to 4:1 to 1:1) to yield spirobiquinolines **25** and **26** as white solids.

*6,6′-Dibromo-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**25**).* Using 2.0 equiv of NBS gave dibromide **25** (509 mg, 56%) as a white crystalline solid: mp 178−181 °C (CH_2Cl_2); IR ν = 3403, 2928, 1467, 1290, 856, 801 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, J = 2.3 Hz, 2H), 7.11 (dd, J = 8.5, 2.3 Hz, 2H), 6.38 (d, J = 8.5 Hz, 2H), 4.25 (s, 2H), 2.87 (t, J = 6.8 Hz, 4H), 1.95 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.5 (2C), 131.7 (2C), 130.0 (2C), 122.2 (2C), 116.2 (2C), 109.5 (2C), 63.6, 32.8 (2C), 23.2 (2C); HRMS (ESI), calcd for $C_{17}H_{17}N_2{}^{79}Br^{81}Br$ ($M + H^+$): 408.9660; found: 408.9748; microanalysis, calcd for $C_{17}H_{16}N_2Br_2$: C, 50.03; H, 3.95; N, 6.86; found: C, 50.17; H, 3.92; N, 6.63.

*6,6′,8,8′-Tetrabromo-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi[quinoline] (**26**).* Using 4.0 equiv of NBS afforded tetrabromide **26** (830 mg, 74%) as a white crystalline solid: mp 172−173 °C ($CHCl_3$); IR ν = 3397, 2831, 1691, 1480, 1449, 1173, 859 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 2.2 Hz, 2H), 7.14 (d, J = 2.2 Hz, 2H), 4.80 (s, 2H), 2.88 (td, J = 6.5, 1.5 Hz, 4H), 2.06−1.96 (m, 2H), 1.93−1.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7 (2C), 132.5 (2C), 130.9 (2C), 123.2 (2C), 109.3 (2C), 108.7 (2C), 64.8, 32.9 (2C), 23.9 (2C); HRMS (ESI), calcd for $C_{17}H_{15}N_2{}^{79}Br_2{}^{81}Br_2$ ($M + H^+$): 566.7928; found: 566.7924; microanalysis, calcd for $C_{17}H_{14}N_2Br_4$: C, 36.08; H, 2.49; N, 4.95; found: C, 35.93; H, 2.52; N, 5.08.

*6,6′,8,8′-Tetraphenyl-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi[quinoline] (**27**).* 6,6′,8,8′-Tetrabromo-3,3′,4,4′-tetrahydro-1*H*,1′*H*-2,2′-spirobi[quinoline] (**26**) (28 mg, 0.05 mmol, 1.0 equiv), phenylboronic acid (30 mg, 0.25 mmol, 5.0 equiv), K_2CO_3 (28 mg, 0.20 mmol, 4.0 equiv), and XPhos (5 mg, 0.01 mmol, 0.2 equiv) were loaded into a vial. DMF and H_2O (4:1, 500 μL) were added, and the mixture was sparged for 20 min with argon. $PdCl_2(PPh_3)_2$ (4 mg, 57 μmol, 11 mol %) was added, and the mixture was heated at 90 °C for 16 h. The mixture was cooled to room temperature, the solvent was removed in vacuo, and the residue was chromatographed (gradient; pentane/CH_2Cl_2 1:4 to 1:1) to afford spirobiquinoline **23** (19 mg, 67%) as a white solid: mp 167−171 °C ($CHCl_3$); IR ν = 3391, 2925, 1599, 1462, 1207, 943, 761, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.2 Hz, 2H), 7.41−7.35 (m, 8H), 7.32−7.24 (m, 14H), 4.67 (s, 2H), 2.99 (dt, J = 16.4, 6.5 Hz, 2H), 2.83 (ddd, J = 16.4, 8.6, 6.5 Hz, 2H), 2.00 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2 (2C), 139.2 (2C), 139.0 (2C), 130.4 (2C), 129.2 (4C), 129.2 (4C), 129.8 (4C), 127.8 (2C), 127.5 (2C), 127.3 (2C), 127.0 (2C), 126.5 (4C), 126.4 (2C), 121.3 (2C), 64.6, 33.8 (2C), 24.1 (2C); HRMS (ESI), calcd for $C_{41}H_{35}N_2$ ($M + H^+$): 555.2800; found: 555.2813; microanalysis, calcd for $C_{41}H_{24}N_2$: C, 88.77; H, 6.18; N, 5.05; found: C, 89.05; H, 6.05; N, 4.87.

General Procedure for the Reaction of Spirobiquinoline 14a with Electrophiles. 3,3′,4,4′-Tetrahydro-1*H*,1′*H*-2,2′-spirobi[quinoline] (**14a**) (50 mg, 0.2 mmol, 1.0 equiv) was dissolved in a mixture of anhydrous THF (2 mL) and HMPA (170 μL, 1.0 mmol, 5.0 equiv) and cooled to −78 °C under argon. *n*-BuLi (2.5 M in hexanes; 160 μL, 0.4 mmol, 0.2 equiv) was added dropwise with stirring over 30 s. After 5 min, the electrophile (0.44 mmol, 2.2 equiv) in THF (1 mL) was added dropwise with stirring over 5 min. After a further 5 min at −78 °C, the cooling bath was removed and the solution was allowed to warm to room temperature. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the resultant mixture, extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and rotary-evaporated, and the residue was chromatographed on silica (pentane/CH_2Cl_2 1:4 + 1% NEt_3).

*1,1′-Dimethyl-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**28a**).* Using the above general procedure, MeI (28 μL, 0.44 mmol) gave the dimethyl derivative **28a** (50 mg, 91%) as a white solid: mp 107−108 °C (CH_2Cl_2); IR ν = 2917, 1599, 1490, 1009, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.14 (m, 2H), 7.08−7.01 (m, 2H), 6.70 (dd, J = 7.5, 6.4 Hz, 4H), 2.99−2.87 (m, 2H), 2.80 (s, 6H), 2.73 (t, J = 4.4 Hz, 1H), 2.69 (t, J = 4.4 Hz, 1H), 2.12 (tdd, J = 12.5, 5.0, 1.2 Hz, 2H), 2.02 (ddd, J = 13.4, 5.1, 3.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1 (2C), 128.3 (2C), 127.5 (2C), 122.4 (2C), 116.4 (2C), 111.7 (2C), 74.2, 30.9 (2C), 28.9 (2C), 24.7 (2C); HRMS (ESI), calcd for $C_{19}H_{23}N_2$ ($M + H^+$): 279.1861; found: 279.1857; microanalysis, calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06; found: C, 81.92; H, 8.12; N, 9.95.

*1,1′-Diallyl-3,3′,4,4′-tetrahydro-1H,1′H-2,2′-spirobi-[quinoline] (**28b**).* Using the above general procedure, allyl bromide (38 μL, 0.44 mmol) gave the diallyl derivative **28b** (53 mg, 80%) as a colorless oil: IR ν = 2942, 2845, 1601, 1490, 1458, 910, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (td, J = 7.8, 1.7 Hz, 1H), 7.01 (dd, J = 7.3, 1.5 Hz, 1H), 6.71−6.61

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(m, 2H), 5.77 (ddt, J = 17.4, 9.5, 4.6 Hz, 1H), 5.16−5.05 (m, 2H), 3.86 (dt, J = 4.3, 2.0 Hz, 2H), 2.86 (ddd, J = 16.5, 9.9, 6.9 Hz, 1H), 2.72−2.61 (m, 1H), 2.14−2.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (2C), 136.2 (2C), 128.3 (2C), 127.1 (2C), 123.4 (2C), 116.8 (2C), 115.9 (2C), 113.2 (2C), 76.2, 46.3 (2C), 31.5 (2C), 24.9 (2C); HRMS (ESI), calcd for $C_{23}H_{27}N_2$ ($M - H^+$): 331.2169; found: 331.2164; microanalysis, calcd for $C_{23}H_{26}N_2$: C, 83.59; H, 7.93; N, 8.48; found: C, 83.54; H, 8.09; N, 8.33.

*1,4,10,11,12,13-Hexahydro-[1,3]diazepino[1,2-a:3,2-a′]diquinoline (**29**).* 1,1′-Diallyl-3,3′,4,4′-tetrahydro-1*H*,1′*H*-2,2′-spirobi[quinoline] (**28b**) (50 mg, 0.15 mmol, 1.0 equiv) was dissolved in anhydrous CH_2Cl_2 (1 mL) and sparged for 10 min with argon. The Hoveyda−Grubbs second-generation catalyst (4.6 mg, 7 μmol, 5 mol %) was added, and the mixture was heated at 40 °C for 6 h. The mixture was cooled to room temperature and chromatographed (gradient; pentane/CH_2Cl_2 17:3 to 4:1 + 1% NEt_3) to give pentacyclic spirobiquinoline **29** (39 mg, 86%) as a white solid: mp 230−231 °C (CH_2Cl_2); IR ν = 2952, 1597, 1488, 1451, 1360, 735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13−7.00 (m, 4H), 6.66 (td, J = 7.3, 1.0 Hz, 2H), 6.49 (dd, J = 8.1, 0.9 Hz, 2H), 5.86−5.77 (m, 2H), 4.06−3.91 (m, 2H), 3.63 (ddd, J = 16.4, 3.5, 1.9 Hz, 2H), 2.99−2.82 (m, 2H), 2.61 (dt, J = 15.4, 3.4 Hz, 2H), 2.30 (dt, J = 13.3, 3.4 Hz, 2H), 2.17−2.03 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2 (2C), 127.7 (2C), 127.3 (2C), 127.2 (2C), 124.6 (2C), 116.6 (2C), 111.0 (2C), 77.2, 42.6 (2C), 31.6 (2C), 24.8 (2C); HRMS (ESI), calcd for $C_{21}H_{23}N_2$ ($M - H^+$): 303.1861; found: 303.1869; microanalysis, calcd for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26; found: C, 83.45; H, 7.56; N, 9.19.

1,3,10,12-Tetrabromo-5,5a,6,7,7a,8,13,14-octahydrocyclopenta[1,2-b:1,5-b′]diquinoline. Using the procedure for **26**, 5,5a,6,7,7a,8,13,14-octahydrocyclopenta[1,2-*b*:1,5-*b*′]diquinoline (**18**) (5 mg, 18 μmol) and freshly recrystallized NBS (13 mg, 72 μmol, 4.0 equiv) gave 1,3,10,12-tetrabromo-5,5a,6,7,7a,8,13,14-octahydrocyclopenta-[1,2-*b*:1,5-*b*′]diquinoline (6 mg, 58%) as a white solid. A sample was purified by chromatography (pentane/CH_2Cl_2 4:1). Slow evaporation of the major fraction gave crystals suitable for X-ray crystallographic determination: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 2.2 Hz, 2H), 7.13 (d, J = 2.1 Hz, 2H), 4.68 (s, 2H), 2.88 (dd, J = 16.0, 5.4 Hz, 2H), 2.63 (dd, J = 16.0, 7.1 Hz, 2H), 2.21 (t, J = 6.4 Hz, 2H), 1.93−1.83 (m, 2H), 1.34 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.81 (2C), 132.23 (2C), 130.62 (2C), 123.91(2C), 108.60 (2C), 108.47 (2C), 76.19, 43.19 (2C), 30.05 (2C), 26.76 (2C); HRMS (ESI), calcd for $C_{19}H_{17}N_2{}^{79}Br_2{}^{81}Br_2$ ($M + H^+$): 592.8079; found: 592.8085.

1,3,11,13-Tetrabromo-5a,6,7,8,8a,9,14,15-octahydro-5H-quinolino[3,2-d]acridine. Using the general procedure for **26**, 5a,6,7,8,8a,9,14,15-octahydro-5*H*-quinolino[3,2-*d*]acridine (**19**) (5 mg, 17 μmol) and freshly recrystallized NBS (13 mg, 72 μmol, 4.0 equiv) were used to afford 1,3,11,13-tetrabromo-5a,6,7,8,8a,9,14,15-octahydro-5*H*-quinolino[3,2-*d*]acridine (7 mg, 68%) as a white solid. A sample was purified by chromatography (pentane/CH_2Cl_2 4:1). Slow evaporation of the major fraction gave crystals suitable for X-ray crystallographic determination: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 2H), 7.18−7.10 (m, 2H), 4.95 (s, 1H), 4.76 (s, 1H), 3.23 (dd, J = 17.4, 5.6 Hz, 1H), 2.89−2.63 (m, 2H), 2.58 (d, J = 17.4 Hz, 1H), 2.09−1.88 (m, 3H), 1.80−1.65 (m, 2H), 1.52−1.36 (m, 3H), 1.22 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.39, 137.09, 132.61, 132.43, 131.69, 131.03, 122.98, 121.46, 110.32, 110.13, 109.01, 108.69, 64.74, 39.60, 37.81, 29.46, 29.17, 28.62, 28.13, 25.00; HRMS (ESI), calcd for $C_{20}H_{19}N_2{}^{79}Br_2{}^{81}Br_2$ ($M + H^+$): 606.8236; found: 606.8163.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b00482.

Selected research data is available from the data repository cited as ref 28

X-ray crystallographic data for selected compounds. Additional experimental procedures, crystallographic data, and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

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