SUPPORTING INFORMATION

A Radical Cyclization Approach to Spirocyclohexadienones

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1. GENERAL METHODS

All experiments were done under an atmosphere of argon unless otherwise stated. Chloroform, benzene and ethyl acetate were used as received from manufacturer. THF, diethyl ether and dichloromethane were dried by activated alumina according to: Pangborn, A. B.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics*, **1996**, *15*, 1518-1520. Melting Points were measured in a Mel-Temp II from Laboratory Devices and are uncorrected. All NMR spectra were recorded on a Bruker model AC-300 or DPX-300 (^1H : 300 MHz, ^{13}C : 75 MHz). Chemical shifts were reported in parts per million (ppm) from internal residual solvent signal of CDCl_3 or DMSO (^1H -NMR spectra, δ 7.27 ppm for CHCl_3 , δ 2.49 ppm for DMSO; ^{13}C -NMR spectra, δ 77.1 for CHCl_3 , δ 40.4 ppm for DMSO). In reporting spectral data, the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, bs = broad singlet, bd = broad doublet. Carbon multiplicities have been assigned by Distortionless Enhancement by Polarization Transfer (DEPT 135 and DEPT 90) experiments. Infrared spectra were taken on a Matteson Genesis Series FTIR. Peaks are reported in wavenumbers (cm^{-1}). High resolution mass spectra were taken on a VG 70/70 double focusing instrument under EI mode and are reported in units of m/e . Low resolution mass spectra were taken on a VG model 700 system and are reported in units m/e . Flash chromatography was performed using ICN silica gel 60 (230-400 mesh) or aluminum oxide 90 active basic (activity II) (70-230 Mesh ASTM). Thin layer chromatography (TLC) was done with Merck silica gel 60 F-254 aluminum-backed plates.

2. EXPERIMENTAL DETAILS

2.1 SYNTHESSES OF SPIROOXYINDOLES (TABLE 1)

4-(*tert*-Butyldimethylsilyloxy)-*N*-(2-iodophenyl)-*N*-methylbenzamide, **14a**:

To a stirred solution of the 2-iodoaniline **11**¹⁴ (388 mg, 1.66 mmol) in dichloromethane (15 mL) at r.t. was successively added triethylamine (1.99 mmol, 0.28 mL) and a solution of the acyl chloride **13**¹⁵ (494 mg, 1.83 mmol) in dichloromethane (5 mL). The resulting reaction mixture was stirred for 3 h and then diluted with dichloromethane (80 mL) and NaHCO₃ (40 mL, saturated aqueous solution). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:0, 1) gave amide **14a** (480 mg, 62%) as a white solid: mp 65-70 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.77 (d, 1H, *J* = 7.7 Hz), 7.27 (d, 2H, *J* = 7.2 Hz), 7.16 (dd, 1H, *J* = 6.8, 6.8 Hz), 7.07 (d, 1H, *J* = 6.6 Hz), 6.86 (dd, 1H, *J* = 6.4, 6.4 Hz), 6.60 (d, 2H, *J* = 7.2 Hz), 3.34 (s, 3H), 0.91 (s, 9H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 170.1 (C), 156.8 (C), 147.0 (C), 139.8 (CH), 130.1 (CH), 129.8 (CH), 129.1 (CH), 128.6 (CH), 128.3 (C), 118.9 (CH), 98.8 (C), 37.5 (CH₃), 25.4 (CH₃), 17.9 (C), - 4.7 (CH₃); IR 2953, 2859, 1630, 1605, 1473, 1265 cm⁻¹; HRMS calcd for C₂₀H₂₆NO₂¹²⁷ISi (M⁺) 467.0778, found 467.0780; LRMS (M⁺) 467 (20), 452 (15), 410 (35), 340 (65), 235 (100), 73 (50).

4-Hydroxy-*N*-(2-iodophenyl)-*N*-methylbenzamide, **16:**

To a stirred solution of the silyl-protected phenol **14a** (500 mg, 1.07 mmol) in dry THF was added dropwise via syringe a solution of TBAF (1.0 M solution in THF, 1.3 mL) at r.t. The reaction was stirred for 10 min and then diluted with diethyl ether (80 mL) and water (40 mL). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 0:1) gave alcohol **16** (350 mg, 93%) as a white solid: ¹H NMR (300 MHz, d6-DMSO) δ 9.75 (s, 1H), 7.82 (d, 1H, *J* = 7.4 Hz), 7.33 (bs, 2H), 7.10 (d, 2H, *J* = 5.5 Hz), 6.97 (bs, 1H), 6.51 (d, 2H, *J* = 5.5 Hz), 3.18 (s, 3H); ¹³C NMR (75 MHz, d6-DMSO) δ 169.8 (C), 159.2 (C), 147.5 (C), 140.1 (CH), 130.8 (2 x CH), 130.1 (CH), 129.7 (CH), 126.7 (C), 114.7 (CH), 100.5 (C), 37.8 (CH₃); HRMS calcd for C₁₄H₁₂NO₂¹²⁷I (M⁺) 352.9913, found 352.9906; LRMS (M⁺) 353 (15), 294 (25), 233 (90), 226 (95), 121 (100), 93 (35), 77 (20), 65 (35).

***N*-(2-Iodophenyl)-*N*-methyl-4-trityloxybenzamide, **14b**:**

To a stirred solution of alcohol **16** (350 mg, 0.99 mmol) in dry dichloromethane (20 mL) was successively added triethylamine (0.21 mL, 1.48 mmol), DMAP (24 mg, 0.20 mmol) and trityl chloride (320 mg, 278 mmol). The resulting reaction mixture was stirred for 3 h and then diluted with dichloromethane (80 mL) and NaHCO₃ (saturated aqueous solution, 40 mL). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:0, 1) gave **14b** (500 mg, 85%) as a white solid: mp 155-160 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.85 (d, 1H, *J* = 7.7 Hz), 7.51-7.40 (bs, 7H), 7.32-7.28 (m, 10H), 7.08-6.98 (m, 4H), 6.54 (d, 2H, *J* = 7.5 Hz), 3.39 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.4 (C), 157.7 (C), 147.3 (C), 143.7 (C), 140.0 (CH), 129.8 (CH), 129.2 (CH), 128.8 (3 x CH), 128.3 (C), 127.7 (CH), 127.2 (CH), 120.0 (CH), 98.9 (C), 90.9 (C), 37.7 (CH₃); IR 1635, 1602, 1371, 1232 cm⁻¹; HRMS calcd for C₃₃H₂₇NO₂I (M⁺ + H) 596.1087 found 596.1087; LRMS (M⁺ + H) 596 (25), 541 (30), 525 (50), 513 (20), 496 (20), 428 (30), 375 (35), 324 (100), 308 (45), 230 (55), 218 (60), 202 (75), 174 (55), 155 (30), 121 (45), 77 (50).

Benzoic acid 4-[(2-iodophenyl)methylcarbamoyl]phenyl ester, 14c:

To a stirred solution of alcohol **16** (1.0 g, 2.83 mmol) in dry dichloromethane (15 mL) at r.t. was successively added triethylamine (0.78 mL, 5.66 mmol), and benzoyl chloride (0.66 mL, 5.66 mmol). The resulting reaction mixture was stirred for 3 h and then diluted

with dichloromethane (300 mL) and NaHCO₃ (100 mL, saturated aqueous solution). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:0, 1) gave amide **14c** (890 mg, 68%) as a white solid: mp 115-120 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.13-8.09 (m, 2H, *J* = 7.7 Hz), 7.80 (d, 1H, *J* = 7.8 Hz), 7.60 (dd, 1H, *J* = 7.4, 7.4 Hz), 7.49-7.41 (m, 4H), 7.24 (dd, 1H, *J* = 8.4, 7.4 Hz), 7.13 (d, 1H, *J* = 7.4 Hz), 7.03 (d, 2H, *J* = 8.4 Hz), 6.91 (dd, 1H, *J* = 7.3, 7.3 Hz), 3.39 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.8 (C), 164.5 (C), 151.9 (C), 146.7 (C), 140.2 (CH), 133.7 (CH), 133.0 (C), 130.1 (CH), 130.0 (CH), 129.5 (CH), 129.2 (CH), 129.1 (C), 128.5 (CH), 128.3 (CH), 120.9 (CH), 98.9 (C), 37.7 (CH₃); IR 1737, 1639, 1473, 1367 cm⁻¹; HRMS calcd for C₂₁H₁₇NO₃¹²⁷I (M⁺ + H) 458.0253, found 458.0251; LRMS (M⁺ + Na) 480 (100), 458 (90), 331 (5), 225 (5).

***N*-(2-Iodophenyl)-4-methoxy-*N*-methylbenzamide, 14d:**

To a stirred solution of alcohol **16** (250 mg, 0.71 mmol) in dichloromethane (8 mL) was successively added DBU (0.12 mL, 0.78 mmol) and methyl iodide (48 μL, 0.78 mmol). The resulting solution was stirred for 16 h at r.t. and then diluted with dichloromethane (60 mL) and NaHCO₃ (saturated aqueous solution, 40 mL). The separated aqueous layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave **14d** (170 mg, 65%) as

a white solid: mp 75-80 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.81 (d, 1H, $J = 8.0$ Hz), 7.32 (d, 2H, $J = 7.9$ Hz), 7.22 (bd, 1H, $J = 7.2$ Hz), 7.10 (d, 1H, $J = 7.0$ Hz), 6.91 (dd, 1H, $J = 7.4$ Hz, 7.4 Hz), 6.66 (d, 2H, $J = 7.9$ Hz), 3.73 (s, 3H), 3.35 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.4 (C), 160.8 (C), 147.5 (C), 140.2 (CH), 130.6 (CH), 130.1 (CH), 129.5 (CH), 128.9 (CH), 127.9 (C), 113.0 (CH), 99.1 (C), 55.2 (CH_3), 37.9 (CH_3); IR 1641, 1608, 1473, 1365 1268 cm^{-1} ; HRMS calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_2^{127}\text{I}$ (M^+) 367.0069, found 367.0074; LRMS (M^+) 367 (5), 240 (65), 135 (100), 92 (25), 77 (40), 64 (15).

(2-Iodo-4-methylphenyl)methylamine, 12:

To a stirred solution of 2-iodo-4-methyl-phenylamine (1.85 g, 7.94 mmol) at -78 °C in dry THF (60 mL) was added a commercial solution of LDA (2 M in THF/heptane, 4.3 mL) and the resulting solution was stirred for 20 min at this temperature. Methyl iodide (0.49 mL, 7.94 mmol) was added and the resulting solution allowed to warm to r.t. for 1 hour. The reaction was then diluted with diethyl ether (300 mL) and water (100 mL) and the separated organic layer was dry (MgSO_4), filtered and concentrated in vacuo. Column chromatography of the residue residue (gradient of elution: hexanes: Et_2O ; 1:0, 2:1, 1:0, 1) gave **12** (1.41 g, 72%) as a brown oil: ^1H NMR (300 MHz, CDCl_3) δ 7.57 (bs, 1H), 7.12 (bd, 1H, $J = 8.2$ Hz), 6.54 (d, 1H, $J = 8.2$ Hz), 4.1 (bs, 1H), 2.93 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 146.1 (C), 139.2 (CH), 130.1 (CH), 127.9 (C), 110.0 (CH), 85.2 (C), 31.2 (CH_3), 19.8 (CH_3); HRMS calcd for $\text{C}_8\text{H}_{10}\text{N}^{127}\text{I}$ (M^+) 246.9858, found 246.9856.

4-(*tert*-Butyldimethylsilanyloxy)-*N*-(2-iodo-4-methylphenyl)-*N*-methylbenzamide,

15a:

The compound was prepared following the same procedure employed for the synthesis of **14a** but using aniline **12** and acyl chloride **13**. The product **15a** was isolated in 67% yield as a white solid: mp 75-80 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.62 (s, 1H), 7.28 (d, 2H, J = 8.1 Hz), 7.01 (d, 1H, J = 7.7 Hz), 6.96 (d, 1H, J = 7.7 Hz), 6.62 (d, 2H, J = 8.1 Hz), 3.34 (s, 3H), 2.24 (s, 3H), 0.93 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.8 (C), 157.0 (C), 144.7 (C), 140.4 (CH), 139.2 (C), 130.3 (CH), 130.2 (CH), 129.5 (CH), 128.8 (C), 119.3 (CH), 98.8 (C), 37.8 (CH_3), 25.6 (CH_3), 20.4 (CH_3), 18.2 (C), - 4.4 (CH_3); IR 2953, 2859, 1632, 1604, 1509, 1488, 1259 cm^{-1} ; HRMS calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_2$ $\text{Si}^{127}\text{I}(\text{M}^+ + \text{H})$ 482.1012, found 482.1028; LRMS ($\text{M}^+ + \text{Na}$) 504 (45), 482 (100).

4-Hydroxy-*N*-(2-iodo-4-methylphenyl)-*N*-methylbenzamide, 17:

The compound was prepared following the same procedure employed for the synthesis of **16** but using silyl-protected phenol **15a**. The product **17** was isolated in 91% yield as a white solid: ^1H NMR (300 MHz, $\text{d}_6\text{-DMSO}$) δ 9.76 (s, 1H), 7.64 (bs, 1H), 7.20-7.11 (m,

4H), 6.52 (d, 2H, $J = 7.4$ Hz), 3.15 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $\text{d}_6\text{-DMSO}$) δ 169.9 (C), 159.1 (C), 145.0 (C), 140.2 (CH), 139.4 (C), 130.7 (2 x CH), 130.2 (CH), 126.9 (C), 114.7 (CH), 100.2 (C), 37.8 (CH_3), 20.3 (CH_3); IR; 2958, 2859, 1633, 1510, 1363 cm^{-1} ; HRMS calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_2^{127}\text{I}$ ($\text{M}^+ + \text{H}$) 368.0148, found 368.0163; LRMS ($2\text{M}^+ + \text{Na}$) 757 (90), 390 (100), 368 (50), 241 (10).

***N*-(2-Iodo-4-methylphenyl)-*N*-methyl-4-trityloxybenzamide, 15b:**

The compound was prepared following the same procedure employed for the synthesis of **14b** but using alcohol **17**. The product **15b** was isolated in 81% yield as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 7.60 (s, 1H), 7.40-7.38 (bs, 7H), 7.26-7.18 (m, 8H), 7.03 (d, 2H, $J = 8.0$ Hz), 6.97 (d, 1H, $J = 7.7$ Hz), 6.84 (d, 1H, $J = 7.7$ Hz), 6.48 (d, 2H, $J = 8.0$ Hz), 3.29 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ ^{13}C NMR (75 MHz, CDCl_3) δ 170.4 (C), 157.6 (C), 144.7 (C), 143.7 (C), 140.3 (CH), 138.8 (C), 130.0 (CH), 129.2 (2xCH), 128.8 (CH), 128.5 (C), 127.6 (CH), 127.2 (CH), 120.0 (CH), 98.7 (C), 90.9 (C), 37.7 (CH_3), 20.4 (CH_3); IR 1633, 1602, 1448, 1363, 1232 cm^{-1} ; HRMS calcd for $\text{C}_{34}\text{H}_{28}\text{NO}_2^{127}\text{INa}$ ($\text{M}^+ + \text{Na}$) 632.1063, found 632.1078; LRMS ($\text{M}^+ + \text{Na}$) 632 (90), 610 (20), 243 (100), 186 (20).

General Procedure for the Cyclization reaction with Precursors **14a-d**, **15b**:

To a stirred solution of precursor **14a** (100 mg, 0.21 mmol) in benzene (3.2 mL) was successively added Et₃B (1.0 M solution in hexanes, 0.26 mL) and (Me₃Si)₃SiH (79 μ L, 0.26 mmol). The resulting reaction mixture was stirred open to air for 2 h and the resulting yellow solution concentrated in vacuo. Analysis of the crude ¹H NMR showed both the biaryl and spirocyclic products in ratios show in Table 1. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave in order of elution the biaryl compound **20a** and the spirocyclic product **18** in yields shown in Table 1.

9-(*tert*-Butyldimethylsilanyloxy)-5-methyl-5*H*-phenanthridin-6-one, **20a**:

The product was isolated as a brown solid: mp 65-70 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.53 (d, 1H, *J* = 8.7 Hz), 8.25 (dd, 1H, *J* = 8.0, 1.4 Hz), 7.72 (d, 1H, *J* = 2.3 Hz), 7.66-7.60 (m, 1H), 7.48 (dd, 1H, *J* = 8.0, 1.4 Hz), 7.42-7.35 (m, 1H), 7.15 (dd, 1H, *J* = 8.7, 2.3 Hz), 3.88 (s, 3H), 1.13 (s, 9H), 0.16 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 161.5 (C), 159.7 (C), 138.4 (C), 135.6 (C), 131.1 (CH), 129.7 (CH), 123.3 (CH), 122.3 (CH), 121.2 (CH), 119.8 (C), 119.1 (C), 115.1 (CH), 111.5 (CH), 29.9 (CH₃), 25.7 (CH₃), 18.4 (C), -4.2 (CH₃); IR 2927, 2854, 1644, 1610, 1446, 1340, 1267 cm⁻¹; HRMS calcd for C₂₀H₂₆NO₂Si (M⁺ + H) 340.1733, found 340.1747.

1'-Methyl-1'*H*,4*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-2',4(3'*H*)-dione, 18:

The product was isolated as a pale solid: mp 275-280 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.41 (dd, 1H, $J = 8.0, 7.7$ Hz), 7.11 (dd, 1H, $J = 7.5, 7.5$ Hz), 7.03 (d, 1H, $J = 7.4$ Hz), 6.97 (d, 1H, $J = 7.9$ Hz), 6.59 (d, 2H, $J = 9.9$ Hz), 6.54 (d, 2H, $J = 9.9$ Hz), 3.32 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 185.3 (C), 171.4 (C), 143.9 (C), 143.6 (CH), 131.6 (CH), 130.0 (CH), 126.0 (C), 124.8 (CH), 123.8 (CH), 109.2 (CH), 55.9 (C), 27.4 (CH_3); IR 2971, 1720, 1666, 1610, 1490, 1344 cm^{-1} ; HRMS calcd for $\text{C}_{14}\text{H}_{11}\text{NO}_2$ (M^+) 225.0790, found 225.0790; LRMS (M^+) 225 (100), 197 (50), 182 (25), 168 (20), 154 (15), 139 (15), 127 (10), 115 (10), 77 (10), 63 (10).

9-Methoxy-5-methyl-5*H*-phenanthridin-6-one, 20b:

The product was isolated as a pale oil: ^1H NMR (300 MHz, CDCl_3) δ 8.49 (d, 1H, $J = 8.8$ Hz), 8.22 (d, 1H, $J = 8.1$ Hz), 7.65 (d, 1H, $J = 2.3$ Hz), 7.59-7.53 (m, 1H), 7.41 (d, 1H, $J = 8.4$ Hz), 7.35-7.28 (m, 1H), 7.15 (dd, 1H, $J = 8.8, 2.0$ Hz), 4.00 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 163.0 (C), 161.6 (C), 138.6 (C), 135.6 (C), 131.2 (CH), 129.8 (CH), 123.3 (CH), 122.3 (CH), 119.5 (C), 119.2 (C), 116.0 (CH), 115.2 (CH),

104.5 (CH), 55.6 (CH₃), 29.9 (CH₃); IR 2925, 1644, 1612, 1267 cm⁻¹; HRMS calcd for C₁₅H₁₃NO₂ (M⁺) 239.0946, found 239.0956; LRMS (M⁺) 239 (35), 169 (15), 135 (95), 119 (25), 91 (25), 77 (25), 73 (30), 69 (100).

1',5'-Dimethyl-4*H*-spiro[cyclohexa-2,5-diene-1,3'-indole]-2',4(1'*H*)-dione, 19:

The product was isolated as a pale solid: mp 185-190 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.19 (d, 1H, *J* = 8.1 Hz), 6.86-6.83 (m, 2H), 6.59 (d, 2H, *J* = 10.2 Hz), 6.54 (d, 2H, *J* = 10.2 Hz), 3.30 (s, 3H), 2.32 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 185.4 (C), 171.4 (C), 143.9 (CH), 141.5 (C), 133.6 (C), 131.4 (CH), 130.2 (CH), 125.9 (C), 125.5 (CH), 109.0 (CH), 56.1 (C), 27.4 (CH₃), 21.0 (CH₃); IR 1716, 1666, 1625, 1604, 1498, 1346 cm⁻¹; HRMS calcd for C₁₅H₁₃NO₂ (M⁺) 239.0944, found 225.0946; LRMS (M⁺) 239 (100), 211 (80), 196 (25), 182 (15), 168 (20), 115 (15).

2.2 FORMAL SYNTHESIS OF SR121463A

(4-Ethoxy-2-iodophenyl)carbamic acid *tert*-butyl ester, **23**:

To a stirred of the protected aniline **22**¹⁶ (1.0 g, 4.22 mmol) at -20°C in diethyl ether (40 mL) was added *t*-BuLi (1.7 M solution in pentane, 6.2 mL) dropwise over 5 min. After stirring at -20°C for 3 h the solution was cooled to -78°C and a solution of 1,2-diiodoethane (1.78 g, 6.33 mmol) in diethyl ether (10 mL) was added dropwise over 5 min. The resulting mixture was allowed to warm to r.t. over 16 h and then diluted with diethyl ether (80 mL) and water (60 mL). The separated organic layer was dried (MgSO_4), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes: Et_2O ; 1:0, 3:1, 2:1, 1:1, 0:1) gave **23** (0.95 g, 62%) as a brown oil followed by a small amount of **22** (98mg, 10%): ^1H NMR (300 MHz, CDCl_3) 7.73 (d, 1H, $J = 8.9$ Hz), 7.24 (d, 1H, $J = 2.7$ Hz), 6.81 (dd, 1H, $J = 9.0, 2.8$ Hz), 6.56 (bs, 1H), 3.91 (q, 2H, $J = 7.0$ Hz), 1.50 (s, 9H), 1.34 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 155.3 (C), 152.9 (C), 132.0 (C), 124.2 (CH), 123.1 (CH), 115.2 (CH), 90.5 (C), 80.4 (C), 63.8 (CH_2), 28.2 (CH_3), 14.7 (CH_3); IR 3404, 2983, 2933, 1724, 1512, 1251, 1157; HRMS calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_3^{127}\text{I}$ (M^+) 363.0331 found 363.0344; LRMS (M^+) 363 (15), 307 (80), 289 (50), 263 (95), 261 (55), 235 (65), 234 (90), 180 (15), 108 (30), 57(100).

[4-(*tert*-Butyldimethylsilanyloxy)-benzoyl]-(4-ethoxy-2-iodophenyl)carbamic acid *tert*-butyl ester, **24:**

To a stirred solution of **23** (1.50 g, 4.1 mmol) in chloroform (15 mL) was successively added triethylamine (1.7 mL, 12.4 mmol), DMAP (377 mg, 3.1 mmol) and the acyl chloride **13**¹⁵ (1.67 g, 6.2 mmol) in chloroform (5 mL), and the resulting solution was stirred for 10 min at r.t. The reaction was heated to reflux for 30 min, then cooled to r.t. and more triethylamine (1.7 mL, 12.4 mmol), DMAP (377 mg, 3.1 mmol) and the acyl chloride **13** (1.67 g, 6.2 mmol) were added. After refluxing the mixture for another 30 min, the reaction was cooled to r.t. and diluted with dichloromethane (80 mL) and NaHCO₃ (saturated aqueous solution, 40 mL). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave **24** (1.52 g, 62%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) 7.73 (d, 2H, *J* = 8.6 Hz), 7.41 (d, 1H, *J* = 2.7 Hz), 7.16 (d, 1H, *J* = 8.7 Hz), 6.92 (dd, 1H, *J* = 8.7, 2.7 Hz), 6.86 (d, 2H, *J* = 9.7 Hz), 4.01 (q, 2H, *J* = 6.9 Hz), 1.41 (t, 3H, *J* = 6.9 Hz), 1.30 (s, 9H), 1.00 (s, 9H), 0.23 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 171.3 (C), 159.1 (C), 158.7 (C), 152.7 (C), 134.7 (C), 130.8 (CH), 130.0 (CH), 129.5 (C), 125.2 (CH), 119.6 (CH), 115.5 (CH), 99.8 (C), 83.4 (C), 64.1 (CH₂), 27.7 (CH₃), 25.7 (CH₃), 18.3 (C), 14.8 (CH₃), - 4.3 (CH₃); IR 2981, 2956, 2931, 2859, 1733, 1679, 1600, 1508, 1473, 1253, 1151; HRMS calcd for C₂₆H₃₆NO₅¹²⁷ISi (M⁺)

597.1407 found 597.1400; LRMS (M^+) 597 (80), 526 (15), 497 (25), 370 (25), 312 (20), 289 (65), 235 (100), 73 (35).

(4-Ethoxy-2-iodophenyl)-(4-hydroxybenzoyl)carbamic acid *tert*-butyl ester, 25:

The compound was prepared following the same procedure employed for the synthesis of **16** but using silyl-protected phenol **24**. The product **25** was isolated in 93% yield as a white solid: mp 75-80 °C; ^1H NMR (300 MHz, CDCl_3) 7.73 (d, 2H, $J = 8.6$ Hz), 7.41 (d, 1H, $J = 2.7$ Hz), 7.15 (d, 1H, $J = 8.6$ Hz), 6.91 (dd, 1H, $J = 8.7, 2.7$ Hz), 6.81 (d, 2H, $J = 8.6$ Hz), 4.00 (q, 2H, $J = 6.8$ Hz), 1.41 (t, 3H, $J = 6.8$ Hz), 1.31 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.7 (C), 160.2 (C), 158.8 (C), 153.0 (C), 134.6 (C), 131.3 (CH), 129.9 (CH), 127.7 (C), 125.1 (CH), 115.5 (CH), 115.2 (CH), 99.7 (C), 83.7 (C), 64.1 (CH_2), 27.7 (CH_3), 14.8 (CH_3); IR 3585, 2981, 1733, 1680, 1608, 1592, 1473, 1247, 1151; HRMS calcd for $\text{C}_{20}\text{H}_{22}\text{NO}_5^{127}\text{I}$ (M^+) 483.0543 found 483.0520; LRMS (M^+) 483 (10), 383 (20), 363 (20), 307 (20), 289 (55), 263 (40), 142 (50), 121 (100), 69 (30).

(4-Ethoxy-2-iodophenyl)-(4-trityloxybenzoyl)carbamic acid *tert*-butyl ester, 26:

The compound was prepared following the same procedure employed for the synthesis of **14b** but using alcohol **25**. The product **26** was isolated in 60% yield as a white solid: mp 128-132 °C; ¹H NMR (300 MHz, CDCl₃) 7.51 (d, 2H, *J* = 8.8 Hz), 7.48-7.45 (m, 6H), 7.38 (d, 1H, *J* = 2.7 Hz), 7.32-7.21 (m, 9H), 7.08 (d, 1H, *J* = 8.7 Hz), 6.88 (dd, 1H, *J* = 8.7, 2.7 Hz), 6.77 (d, 2H, *J* = 8.6 Hz), 4.01 (q, 2H, *J* = 6.9 Hz), 1.41 (t, 3H, *J* = 6.9 Hz), 1.15 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 171.8 (C), 159.5 (C), 158.8 (C), 152.7 (C), 146.9 (C), 143.6 (C), 134.5 (C), 130.0 (CH), 129.9 (CH), 128.7 (CH), 128.0 (CH), 127.4 (CH), 125.1 (CH), 119.2 (CH), 115.6 (CH), 99.8 (C), 90.6 (C), 83.5 (C), 64.0 (CH₂), 27.6 (CH₃), 14.8 (CH₃); IR 3585, 2981, 1733, 1680, 1608, 1592, 1473, 1247, 1151; HRMS calcd for C₃₉H₃₆NO₅¹²⁷I²³Na (M⁺ + Na) 748.1536 found 748.1583; LRMS (M⁺ + Na) 748 (5), 483 (10), 383 (20), 363 (20), 307 (20), 289 (55), 263 (40), 142 (50), 121 (100), 69 (30).

A more polar fraction containing alcohol **25** (59 mg, 10%) was also isolated.

***tert*-Butyl-6'-ethoxy-2',4-dioxo-2',3'-dihydro-1'*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-1'-carboxylate, **1**:**

To a stirred solution of precursor **26** (100 mg, 0.14 mmol) in benzene (2.1 mL) was successively added Et₃B (1.0 M solution in hexanes, 0.16 mL) and (Me₃Si)₃SiH (51 μL, 0.16 mmol). The reaction mixture was stirred open to air for 2 h and the resulting yellow solution concentrated in vacuo. Purification by column chromatography over basic

alumina (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave **1** (17 mg, 34%) as a white solid: mp 275-280 °C; ¹H NMR (300 MHz, CDCl₃) 7.87 (d, 1H, *J* = 8.7 Hz), 6.92 (dd, 1H, *J* = 8.7, 2.7 Hz), 6.66 (d, 2H, *J* = 9.4 Hz), 6.56 (d, 1H, *J* = 2.7 Hz), 6.53 (d, 2H, *J* = 9.4 Hz), 4.01 (q, 2H, *J* = 7.0 Hz), 1.64 (s, 9H), 1.39 (t, 3H, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) 184.9 (C), 169.4 (C), 156.9 (C), 148.8 (C), 143.2 (CH), 132.9 (C), 131.4 (CH), 126.2 (C), 117.1 (CH), 115.8 (CH), 110.9 (CH), 85.3 (C), 64.1 (CH₂), 56.5 (C), 28.1 (CH₃), 14.8 (CH₃); IR 2983, 2358, 2339, 2256, 1789, 1668, 1492, 1251; HRMS calcd for C₂₀H₂₁NO₅ (M⁺) 355.1420 found 355.1432; LRMS (M⁺) 355 (20), 255 (100), 227 (75), 198 (20), 170 (20).

***tert*-Butyl-6'-ethoxy-2',4'-dioxo-2',3'-dihydro-1'*H*-spiro[cyclohexa-1,4'-quinoline]-1'-carboxylate, **27**:**

To a stirred solution of **1** (40 mg, 0.11 mmol) in ethyl acetate (2 mL) was added Pd/C (10 mol%, 12 mg) and the system was evacuated and placed under a H₂ atmosphere. The reaction was stirred at r.t. for 3 h after which more Pd/C (10 mol%, 12 mg) was added. After stirring for 12 h, the crude reaction mixture was filtered over celite diluting with diethyl ether (80 mL). The solvent was concentrated in vacuo and the resulting residue purified by column chromatography (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) to give **27** (23 mg, 58%) as a white solid: mp 295-300 °C; ¹H NMR (300 MHz, CDCl₃) 7.76 (d, 1H, *J* = 8.9 Hz), 6.83 (dd, 1H, *J* = 8.8, 2.5 Hz), 6.76 (d, 1H, *J* = 2.5 Hz), 4.01 (q,

2H, $J = 7.0$ Hz), 3.24-3.12 (m, 2H), 2.44 (dt, 2H, $J = 15.3, 4.2$ Hz), 2.21-2.14 (m, 4H), 1.66 (s, 9H), 1.42 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (75 MHz, CDCl_3) 210.4 (C), 177.7 (C), 156.4 (C), 149.3 (C), 133.4 (C), 131.8 (C), 116.1 (CH), 113.4 (CH), 109.7 (CH), 84.6 (C), 64.0 (CH_2), 45.7 (C), 36.8 (CH_2), 34.3 (CH_2), 28.2 (CH_3), 14.9 (CH_3); IR 3153, 2983, 1783, 1714, 1473; HRMS calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_5$ (M^+) 359.1733 found 359.1735; LRMS (M^+) 359 (25), 259 (100), 230 (20), 189 (95), 161 (60), 57 (50).

6'-Ethoxy-1'*H*,4*H*-spiro[cyclohexane-1,4'-quinoline]-2',4(3'*H*)-dione, **2:**

To a stirred solution of **27** (20 mg, 0.055 mmol) in CDCl_3 (1 mL) was added dropwise via syringe neat TFA (0.05 mL, 0.55 mmol) at r.t. After 2 h, the reaction was diluted with dichloromethane (30 mL) and NaHCO_3 (saturated aqueous solution, 15 mL). Column chromatography of the residue (gradient of elution: hexanes: Et_2O ; 1:0, 2:1, 1:1, 0:1) gave **2** (10 mg, 71%) as a white solid: mp 175-180 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) 8.7 (bs, 1H), 6.88-6.75 (m, 3H), 4.00 (q, 2H, $J = 6.9$ Hz), 3.17-3.10 (m, 2H), 2.50 (dt, 2H, $J = 15.1, 4.7$ Hz), 2.24-2.14 (m, 4H), 1.41 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (75 MHz, CDCl_3) 210.8 (C), 182.1 (C), 155.4 (C), 135.1 (C), 133.0 (C), 113.1 (CH), 111.2 (CH), 110.6 (CH), 64.2 (CH_2), 46.6 (C), 36.8 (CH_2), 33.5 (CH_2), 14.9 (CH_3); IR 3438, 1712, 1494; HRMS calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_3$ (M^+) 259.1208 found 259.1216; LRMS (M^+) 259 (100), 230 (20), 189 (75), 161 (65).

2.3 SYNTHESIS OF SPIRODIHYDROQUINOLONES (TABLE 2)

General Procedure for the Preparation of Amide 30:

To a stirred solution of the protected aniline **11**¹⁴ (600 mg, 2.58 mmol) in dry dichloromethane (30 mL) at r.t. was successively added pyridine (0.41 mL, 5.16 mmol), DMAP (31 mg, 0.26 mmol) and a solution of the acyl chloride **29**¹⁷ (805 mg, 2.84 mmol) in dichloromethane (5 mL). The resulting reaction mixture was stirred for 10 h at r.t. and then diluted with dichloromethane (80 mL) and NaHCO₃ (saturated aqueous solution, 30 mL). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:0, 1) gave the desired amide **30a** (740 mg, 60%).

2-[4-(*tert*-Butyldimethylsilanyloxy)phenyl]-*N*-(2-iodophenyl)-*N*-methylethanamide, **30a**:

The compound was isolated as a white solid: mp 105-110 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.04 (dd, 1H, *J* = 7.9, 1.3 Hz), 7.46 (ddd, 1H, *J* = 7.8, 7.8, 1.4 Hz), 7.22 (dd, 1H, *J* = 8.0, 1.4 Hz), 7.16 (dd, 1H, *J* = 7.4, 1.6 Hz), 7.02 (d, 2H, *J* = 8.5 Hz), 6.80 (d, 2H, *J* = 8.5 Hz), 3.47 (d, 1H, *J* = 14.8 Hz), 3.33 (d, 1H, *J* = 14.8 Hz), 3.29 (s, 3H), 1.09 (s, 9H), 0.30 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 170.7 (C), 154.2 (C), 145.8 (C), 140.0 (CH), 130.1 (CH), 129.7 (CH), 129.6 (CH), 129.5 (CH), 127.5 (C), 119.7 (CH), 99.9 (C),

40.6 (CH₂), 36.0 (CH₃), 25.6 (CH₃), 18.0 (C), - 4.5 (CH₃); IR 2950, 2931, 2859, 1655, 1510, 1471, 1380, 1257 cm⁻¹; HRMS calcd for C₂₁H₂₈NO₂¹²⁷I ²³NaSi (M⁺ + Na) 504.0832, found 504.0832.

2-(4-Hydroxyphenyl)-N-(2-iodophenyl)-N-methylacetamide, 33:

The compound was prepared following the same procedure employed for the synthesis of **16** but using silyl-protected phenol **30a**. The product **33** was isolated in 88% yield as a white solid: mp 100-105 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.96 (dd, 1H, *J* = 7.9, 1.3 Hz), 7.40 (ddd, 1H, *J* = 7.8, 7.8, 1.4 Hz), 7.18 (dd, 1H, *J* = 8.0, 1.4 Hz), 7.10 (ddd, 1H, *J* = 7.8, 7.8, 1.6 Hz), 6.86 (d, 2H, *J* = 8.5 Hz) 6.63 (d, 2H, *J* = 8.5 Hz), 3.32 (d, 1H, *J* = 15.2 Hz), 3.22 (d, 1H, *J* = 15.2 Hz), 3.21 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 172.0 (C), 155.3 (C), 145.8 (C), 140.3 (CH), 130.5 (CH), 130.1 (CH), 130.0 (CH), 129.5 (CH), 126.0 (C), 115.6 (CH), 99.8 (C), 40.6 (CH₂), 36.5 (CH₃); IR 3594, 1653, 1513, 1471, 1380, 1255 cm⁻¹; HRMS calcd for C₁₅H₁₄NO₂¹²⁷I²³Na (M⁺ + Na) 389.9967, found 389.9980; LRMS (2M⁺ + Na) 757 (40), 390 (100), 186 (30).

***N*-(2-Iodophenyl)-*N*-methyl-2-(4-trityloxyphenyl)acetamide, 30b:**

The compound was prepared following the same procedure employed for the synthesis of **14b** but using alcohol **33**. The product **30d** was isolated in 76% yield as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 7.96 (dd, 1H, $J = 7.9, 1.3$ Hz), 7.58 (d, 6H, $J = 7.9$ Hz), 7.40-7.29 (m, 10H), 7.11 (ddd, 1H, $J = 7.8, 7.8, 1.3$ Hz), 7.03 (dd, 1H, $J = 7.8, 1.4$ Hz), 6.76 (d, 2H, $J = 8.6$ Hz), 6.68 (d, 2H, $J = 8.6$ Hz), 3.32 (d, 1H, $J = 14.8$ Hz), 3.26 (s, 3H), 3.20 (d, 1H, $J = 14.8$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 170.7 (C), 155.0 (C), 145.7 (C), 144.1 (C), 139.9 (CH), 129.7 (CH), 129.6 (CH), 129.2 (2 x CH), 128.9 (CH), 127.6 (CH), 127.3 (C), 127.0 (CH), 120.5 (CH), 99.9 (C), 90.1 (C), 40.7 (CH_2), 36.1 (CH_3); IR 3062, 1655, 1506, 1472, 1448, 1378, 1255 cm^{-1} ; HRMS calcd for $\text{C}_{34}\text{H}_{28}\text{NO}_2^{127}\text{I}^{23}\text{Na}$ ($\text{M}^+ + \text{Na}$) 632.1063, found 632.1068; LRMS ($\text{M}^+ + \text{Na}$) 632 (100), 389 (5), 243 (5).

2-[4-(*tert*-Butyldimethylsilanyloxy)phenyl]-*N*-(2-iodo-4-methylphenyl)-*N*-methylacetamide, 31:

The compound was prepared following the same procedure employed for the synthesis of **30a** but using **12** and acyl chloride **29**¹⁷ as starting materials. The product **31** was isolated

in 62% yield as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.76 (bs, 1H), 7.16 (d, 1H, $J = 7.9$ Hz), 7.00 (d, 1H, $J = 7.9$ Hz), 6.92 (d, 2H, $J = 8.6$ Hz), 6.71 (d, 2H, $J = 8.6$ Hz), 3.34 (d, 1H, $J = 15.0$ Hz), 3.23 (d, 1H, $J = 15.0$ Hz), 3.17 (s, 3H), 2.36 (s, 3H), 0.99 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.0 (C), 154.2 (C), 143.3 (CH), 140.3 (C), 140.1 (C), 130.4 (CH), 130.2 (CH), 128.9 (CH), 127.6 (C), 119.7 (CH), 99.6 (C), 40.4 (CH_2), 36.2 (CH_3), 25.6 (CH_3), 20.5 (CH_3), 18.0 (C), - 4.5 (CH_3); IR 2950, 2931, 2859, 1655, 1510, 1471, 1380, 1257 cm^{-1} ; HRMS calcd for $\text{C}_{22}\text{H}_{31}\text{NO}_2^{127}\text{ISi}$ ($\text{M}^+ + \text{H}$) 496.1169, found 496.1176.

(4-Bromo-2-iodophenyl)methylamine, 28:

The compound was prepared following the same procedure employed for the synthesis of **12** but using 4-bromo-2-iodophenylamine as starting material. The product **28** was isolated in 82% yield as a brown oil: ^1H NMR (300 MHz, CDCl_3) δ 7.75 (d, 1H, $J = 2.2$ Hz), 7.30 (dd, 1H, $J = 8.7, 2.2$ Hz), 6.39 (d, 1H, $J = 8.7$ Hz), 4.23 (bs, 1H), 2.86 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.3 (C), 140.2 (CH), 132.1 (CH), 110.8 (CH), 108.4 (C), 85.0 (C), 31.0 (CH_3); IR 1583, 1506, 1267, 1311; HRMS calcd for $\text{C}_7\text{H}_7\text{Br}^{127}\text{IN}$ (M^+) 310.8807, found 310.8803; LRMS (M^+) 311 (100), 184 (20), 169 (15), 157 (10), 127 (15), 105 (35), 90 (10), 77 (20), 63 (30).

***N*-(4-Bromo-2-iodophenyl)-2-[4-(*tert*-butyldimethylsilanyloxy)phenyl]-*N*-methylacetamide, **32**:**

The compound was prepared following the same procedure employed for the synthesis of **30a** but using **28** and acyl chloride **29**¹⁷ as starting materials. The product **32** was isolated in 67% yield as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 8.07 (d, 1H, *J* = 2.1 Hz), 7.47 (dd, 1H, *J* = 8.3, 2.1 Hz), 6.94 (d, 1H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 6.70 (d, 2H, *J* = 8.4 Hz), 3.35 (d, 1H, *J* = 14.9 Hz), 3.20 (d, 1H, *J* = 14.9 Hz), 3.15 (s, 3H), 0.97 (s, 9H), 0.18 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 170.8 (C), 154.5 (C), 145.2 (C), 142.2 (CH), 132.9 (CH), 130.6 (CH), 130.2 (CH), 127.3 (C), 122.6 (C), 120.0 (CH), 100.1 (C), 40.8 (CH₂), 36.2 (CH₃), 25.7 (CH₃), 18.2 (C), - 4.4 (CH₃); IR 2950, 2931, 2859, 1655, 1510, 1471, 1380, 1257 cm⁻¹; HRMS calcd for C₂₁H₂₈NO₂¹²⁷I⁷⁹BrSi (M⁺ + H) 560.0117, found 560.0106.

General Procedure for the Cyclization reaction with Precursors **30a,b, **31** and **32**:**

To a stirred solution of precursor **30a** (120 mg, 0.25 mmol) in benzene (3.7 mL) was successively added Et₃B (1.0 M solution in hexanes, 0.30 mL) and (Me₃Si)₃SiH (92 μL, 0.30 mmol). The reaction mixture was stirred open to air for 2 h and the resulting yellow solution evaporated in vacuo. Purification by column chromatography (gradient of

elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave the desired spirocyclic product **34** in yields shown in Table 2.

1'-Methyl-1'*H*, 4*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-2',4(3'*H*)-dione, 34:

The compound was isolated as a white solid: mp 100-105 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.41-7.35 (m, 1H), 7.13-7.07 (m, 3H), 6.96 (d, 2H, *J* = 10.0 Hz), 6.38 (d, 2H, *J* = 10.0 Hz), 3.47 (s, 3H), 2.80 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 185.1 (C), 166.8 (C), 149.5 (CH), 139.8 (C), 129.6 (2 x CH), 126.6 (CH), 124.4 (C), 124.1 (CH), 115.9 (CH), 43.1 (C), 40.8 (CH₂), 29.8 (CH₃); IR 3053, 2985, 1670, 1421, 1267 cm⁻¹; HRMS calcd for C₁₅H₁₃NO₂ (M⁺) 239.0946 found 239.0958; LRMS (M⁺) 239 (100), 210 (40), 196 (25), 182 (20), 168 (25), 154 (10), 127 (10), 115 (15), 77 (10), 63 (10).

1',6'-Dimethyl-1'*H*,4*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-2',4(3'*H*)-dione, 35:

The compound was isolated as a yellow oil; ¹H NMR (300 MHz, CDCl₃) δ 7.20 (d, 1H, *J* = 8.3 Hz), 7.03 (d, 1H, *J* = 8.3 Hz), 6.97 (d, 2H, *J* = 10.0 Hz), 6.91 (s, 1H), 6.42 (d, 2H, *J* = 10.0 Hz), 3.47 (s, 3H), 2.80 (s, 2H), 2.32 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 185.2

(C), 166.6 (C), 149.6 (CH), 137.5 (C), 133.8 (C), 129.9 (CH), 129.6 (CH), 127.1 (CH), 124.2 (C), 115.8 (CH), 43.1 (C), 40.9 (CH₂), 29.8 (CH₃), 20.6 (CH₃); IR 2927, 1668, 1508, 1369, 1251 cm⁻¹; HRMS calcd for C₁₆H₁₅NO₂ (M⁺) 253.1103 found 253.1115; LRMS (M⁺) 253 (10), 86 (65), 84 (100), 75 (10), 57 (5).

6'-Bromo-1'-methyl-1'*H*,4*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-2',4(3'*H*)-dione, 36:

The compound was isolated as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.48 (d, 1H, *J* = 8.7, 2.3 Hz), 7.19 (d, 1H, *J* = 2.3 Hz), 6.98 (d, 1H, *J* = 8.7 Hz), 6.92 (d, 2H, *J* = 10.2 Hz), 6.42 (d, 2H, *J* = 10.2 Hz), 3.44 (s, 3H), 2.79 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 184.7 (C), 166.3 (C), 148.4 (CH), 139.0 (C), 132.4 (CH), 130.1 (CH), 129.5 (CH), 126.5 (C), 117.5 (CH), 116.8 (C), 42.9 (C), 40.6 (CH₂), 29.9 (CH₃); IR 2925, 1672, 1489, 1359, 1139; HRMS calcd for C₁₅H₁₂BrNO₂ (M⁺) 317.0051 found 317.0057; LRMS (M⁺) 317 (100), 290 (20), 288 (20), 274 (15), 248 (15), 239 (35), 210 (50), 196 (15), 182 (20), 210 (50), 196 (15), 182 (20), 167 (40), 153 (20), 140 (15), 127 (20), 115 (25), 91 (25), 77 (35), 63 (35).

2.4 FORMAL SYNTHESIS OF AZA-GALANTHAMINE

(2-Iodo-6-methoxyphenyl)methylcarbamic acid *tert*-butyl ester, **38**:

The compound was prepared following the same procedure employed for the synthesis of **12** but using **37**¹⁸ (200 mg, 0.57 mmol) to give **38** (170 mg, 82%) as a brown oil: ¹H NMR (300 MHz, CDCl₃) δ 7.40 (dd, 1H, *J* = 8.2, 1.4 Hz), 6.95 (dd, 1H, *J* = 8.2, 8.2 Hz), 6.86 (dd, 1H, *J* = 8.2, 1.4 Hz), 3.80 (s, 3H), 3.03 (s, 3H), 1.33 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 156.2 (C), 154.7 (C), 134.9 (C), 130.5 (CH), 129.5 (CH), 111.6 (CH), 101.2 (C), 79.6 (C), 55.9 (CH₃), 34.7 (CH₃), 28.2 (CH₃); IR 2977, 1695, 1568, 1473, 1367, 1263 cm⁻¹; HRMS calcd for C₁₃H₁₈¹²⁷INO₃ (M⁺) 363.0331 found 363.0336; LRMS (M⁺) 363 (5), 304 (10), 290 (15), 263 (95), 248 (55), 220 (10), 195 (10), 149 (25), 128 (15), 91 (15), 57 (10).

(2-Iodo-6-methoxyphenyl)methylamine, **39**:

To a stirred solution of **38** (210 mg, 0.58 mmol) in CDCl₃ (6 mL) was added dropwise via syringe neat TFA (0.44 mL) at r.t. After 2 h with stirring the reaction was diluted with dichloromethane (80 mL) and NaHCO₃ (saturated aqueous solution, 30 mL). The separated organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Column

chromatography of the residue (gradient of elution: hexanes:Et₂O; 1:0, 2:1, 1:1, 0:1) gave **39** (150 mg, 98%) as a white solid: mp 80-85 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.40 (bs, 2H), 7.40 (dd, 1H, *J* = 7.2, 1.8 Hz), 7.08-7.02 (m, 2H), 3.97 (s, 3H), 3.09 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 152.7 (C), 131.8 (CH), 131.6 (C), 129.5 (CH), 112.3 (CH), 91.3 (C), 56.4 (CH₃), 35.7 (CH₃); IR 1735, 1660, 1573, 1471, 1265, 1199 cm⁻¹; HRMS calcd for C₈H₁₀NO¹²⁷I (M⁺) 262.9807 found 262.9813; LRMS (M⁺) 263 (100), 248 (60), 220 (30), 120 (35), 106 (15), 93 (15), 77 (20), 69 (50).

2-[4-(*tert*-Butyldimethylsilanyloxy)phenyl]-N-(2-iodo-6-methoxyphenyl)-N-methylacetamide, 40:

The compound was prepared following the same procedure employed for the synthesis of **30** using aniline **39** and acyl chloride **29**.¹⁸ The desired compound **40** was isolated as a colorless oil (64%): ¹H NMR (300 MHz, CDCl₃) δ 7.48 (d, 1H, *J* = 8.0 Hz), 7.04 (dd, 1H, *J* = 8.2, 8.2 Hz), 6.86 (d, 3H, *J* = 8.4 Hz), 6.67 (d, 2H, *J* = 8.4 Hz), 3.63 (s, 3H), 3.29 (d, 1H, *J* = 14.8 Hz), 3.17 (d, 1H, *J* = 14.9 Hz), 3.08 (s, 3H), 0.96 (s, 9H), 0.15 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 171.7 (C), 156.4 (C), 154.2 (C), 134.6 (C), 130.9 (CH), 130.7 (CH), 130.3 (CH), 127.7 (C), 119.7 (CH), 111.7 (CH), 101.7 (C), 55.6 (CH₃), 40.2 (CH₂), 34.5 (CH₃), 25.7 (CH₃), 18.2 (C), - 4.4 (CH₃); IR 2931, 2858, 1655, 1510, 1471, 1377,

1261 cm^{-1} ; HRMS calcd for $\text{C}_{22}\text{H}_{31}\text{NO}_3\text{Si}^{127}\text{I}$ ($\text{M}^+ + \text{H}$) 512.1118 found 512.1124; LRMS ($\text{M}^+ + \text{Na}$) 534 (100), 512 (100), 264 (5).

8'-methoxy-1'-methyl-1'*H*,4*H*-spiro[cyclohexa-2,5-diene-1,4'-quinoline]-2',4(3'*H*)-dione, 4:

The compound was prepared following the same procedure employed for the synthesis of spirocyclic compound **34**. The product was isolated as a yellow oil in 40% yield: ^1H NMR (300 MHz, CDCl_3) δ 7.07 (dd, 1H, $J = 8.3, 8.3$ Hz), 6.96 (dd, 1H, $J = 8.3, 1.2$ Hz), 6.88 (d, 2H, $J = 10.2$ Hz), 6.69 (dd, 1H, $J = 7.6, 1.2$ Hz), 6.40 (d, 2H, $J = 10.2$ Hz), 3.90 (s, 3H), 3.49 (s, 3H), 2.72 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 185.1 (C), 168.3 (C), 150.5 (C), 149.1 (CH), 130.4 (C), 129.9 (CH), 129.4 (C), 125.6 (CH), 118.3 (CH), 113.3 (CH), 56.1 (CH_3), 43.6 (C), 41.9 (CH_2), 34.8 (CH_3); IR 2929, 1668, 1483, 1367, 1265 cm^{-1} ; HRMS calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_3$ (M^+) 269.1052 found 269.1046; LRMS (M^+) 269 (100), 240 (20), 226 (25), 212 (15), 198 (15), 184 (15), 149 (25), 115 (15), 91 (15), 84 (20), 57 (35).

3. REFERENCES

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- ¹⁷ The acyl chloride **23** was prepared according to the procedure described in reference 2, starting from [4-(tert-Butyl-dimethyl-silanyloxy)-phenyl]-acetic acid. This compound was prepared following the 3 step sequence described in: Brümmer, O; Clapham, B.; Janda, K. D. *Tetrahedron Lett.* **2001**, *42*, 2257-2259.
- ¹⁸ For a synthesis of **28** see: Dumez, E; Snaith, J. S.; Jackson, F. W.; McElroy A. B.; Overington, J.; Wythes, M. J.; Withka, J. M.; McLellan, T. J. *J. Org. Chem.* **2002**, *67*, 4882-4892.

7.86933
7.84386
7.46535
7.44740
7.32051
7.30091
7.08079
6.98811
6.56478
6.53951

F65325.After column.

3.38715

3.38662

1.26070
1.20382
0.87654

FG6436 After column.

3.29326

2.30302

1.31364
1.30518
0.94709
0.92571
0.90228

18

8.5109
8.4814
8.2392
8.2162
8.2122
7.6610
7.6530
7.4311
7.3228
7.2697
7.1502

5.3071

4.0029
3.8452
3.8374
3.8068
3.7467
3.4942
3.2718
3.2101

2.1799
1.6903
1.6530
1.6511
1.6439
1.2896
1.2618
0.8858
0.8650
0.1798

FG6442

7.27039
7.20933
7.18231
6.86411
6.85439
6.83827
6.61689
6.60948
6.58274
6.55703
6.52293
FG6439a.

3.31613
3.29371

2.34243
2.32028

Integral

ppm

10

9

8

7

6

5

4

3

2

1

0

Integral

ppm

10

9

8

7

6

5

4

3

2

1

0

2.0000

0.8691

0.9428

1.1890

1.8966

2.0451

3.2651

9.6531

9.1340

5.9208

ppm

7.76314

7.73437

7.42578

7.41666

7.17794

7.14900

6.94109

6.93194

6.90258

6.89176

6.86322

F65329d.

4.03919

4.01612

1.51650

1.44067

1.41763

1.39418

1.29712

24

FG-S348.

7.52519
7.49577
7.48500
7.47955
7.45603
7.39432
7.38521
7.32297
7.31625
7.30981
7.29443
7.26910
7.25924
7.24625
7.23646
7.10729
7.07820
6.78485
6.75555

4.02169
3.99827

1.56538
1.42899
1.40606
1.38280
1.31741
1.28103
1.27159
1.14892
0.98918

F65354.

F65386.

33

7.99424
7.96783
7.59839
7.57525
7.57211
7.37851
7.35222
6.74768
6.70215
6.67327

3.35045
3.25578
3.24221
3.19257

1.41517
1.34294
1.02732

FG5387

7.76577
7.76399
7.75841
7.75650
7.34659
7.34085
7.33920
7.31768
7.31195
7.31032
6.41706
6.38810

F66445.

4.22943

2.85851

28

28

F35415.

ppm

147.298
140.177
132.088
110.807
108.414
84.979
77.525
77.101
76.678
31.040

32

F65388.

F86429D.

7.50081
7.49317
7.47174
7.46438
7.27077
7.19316
7.18582
6.99707
6.96815
6.94437
6.93438
6.90052
6.43143
6.39758

F36447.

3.73242
3.70902
3.46498
3.43678
3.11417
2.78905

1.26640
1.25775
1.24312
1.22046
1.20012
0.97530

FG6435. After column. Formal Synthesis of aza-Galanthamine.