was performed via the procedure described by Koyama-Yoshino.[8]

9,10-Benzo-1,4,7-tris(*p*-tolylsulfonyl)-1,4,7-triazacycloundecane (13). *N,N',N''*-Tris(*p*-tolylsulfonyl)diethylenetriamine (15 g, 26 mmol) was dissolved in DMF (430 mL) containing finely ground, anhydrous K_2CO_3 (8.6 g, 62 mmol) and stirred for 1 h at 30 °C. A solution of α,α'-dibromo-*o*-xylene (8.4 g, 32 mmol) in DMF (220 mL) was added dropwise over a period of 16–20 h. The reaction progress was monitored by TLC (small aliquots were removed, evaporated to dryness under vacuum, and redissolved in CH_2Cl_2 for spotting on plates; the chromatograms were developed in 95/5 v/v CH_2Cl_2/MeOH). After 16–20 h, the volume was reduced to 65 mL, and excess ice–water was added. The resulting white solid was collected by filtration and washed with water to neutral pH. The wet solid was suspended in ethanol (100 mL) and gradually heated to reflux. After 1 h, the solid was filtered off while hot and dried at 50 °C under vacuum for 12 h. A minor product (5%) likely corresponding to the 2:2 addition product was separated by silica gel column chromatography (99/1 CH_2Cl_2/MeOH), yielding 15 g of **13** (85% yield): mp 208–210 °C; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 2.46 (s, 6 H), 2.95 (t, 4 H), 3.38 (s, 4 H), 4.40 (br, 4 H), 7.24–7.75 (m, 16 H); ^{13}C NMR δ 21.56, 49.68, 52.09, 52.78, 127.48, 128.90, 129.56, 130.00, 132.12, 143.91. Anal. Calcd for $C_{33}H_{37}N_3S_3O_6$: C, 59.35; H, 5.58; N, 6.29; O, 14.38. Found: C, 58.93; H, 5.60; N, 6.25; O, 14.36.

11,12-Benzo-1,5,9-tris(*p*-tolylsulfonyl)-1,5,9-triazacyclotridecane (14) was prepared as described above from *N,N',N''*-tris(*p*-tolylsulfonyl)dipropylenetriamine and α,α'-dibromo-*o*-xylene in 87% yield. Analytical sample recrystallized from CH_2Cl_2/MeOH: mp 259–263 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (m, 4 H), 2.41 (s, 3 H), 2.44 (s, 6 H), 2.90 (t, 4 H), 3.18 (t, 4 H), 4.45 (s, 4 H), 7.23–7.76 (m, 16 H); ^{13}C NMR δ 21.52, 28.24, 46.00, 46.50, 49.43, 127.18, 128.68, 129.67, 129.81, 129.96, 134.31, 143.70. Anal. Calcd for $C_{35}H_{41}N_3S_3O_6$: C, 60.40; H, 5.94; N, 6.04; O, 13.80. Found: C, 60.69; H, 6.03; N, 6.10; O, 13.59.

9,10-Benzo-1,4,7-triazacycloundecane (15). To a suspension of compound **13** (4.0 g, 6 mmol) in 48 mL of dry methanol was added dibasic sodium phosphate (4.3 g) and 3% sodium amalgam (56 g). The mixture was gently refluxed overnight, and second equal portions of dibasic sodium phosphate (4.3 g) and sodium amalgam (56 g) were added. After the mixture was refluxed for an additional 12 h, water (300 mL) was added, and the solution was extracted with 4 × 100-mL portions of chloroform. The extracts were dried over anhydrous sodium sulfate, and the solvent was removed under vacuum to give **15** as a light yellow oil in 90% yield: ^{1}H NMR ($CDCl_3$) δ 2.76 (s, 8 H), 3.63 (s, 4 H), 7.18–7.20 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 43.36, 47.92, 51.89, 127.75, 130.55, 139.20. The trihydrochloride salt was prepared by dissolving **15** in 50 mL of absolute ethanol, and, after the solution was cooled in an ice–acetone bath, 15 mL of concentrated (37%) HCl was added to give a white solid. This was filtered, washed with absolute ethanol, and dried under vacuum to afford the trihydrochloride salt in 94% yield: mp 262–267 °C; ^{1}H NMR (D_2O) δ 3.32–3.35 (m, 8 H), 4.25 (s, 4 H), 7.53 (s, 4 H); ^{13}C NMR (D_2O) δ 44.05, 47.84, 130.83, 132.59, 133.34; MS *m/e* 315 (M^+, 5.2) 214 (100). Anal. Calcd for $C_{12}H_{22}N_3Cl_3$: C, 45.80; H, 7.05; N, 13.35. Found: C, 46.03; H, 7.39; N, 13.42.

11,12-Benzo-1,5,9-triazacyclotridecane (16) was prepared in 65% yield as described above except the detosylation reaction was carried out in a 1:1 mixture of methanol/acetonitrile to improve solubility: ^{1}H NMR ($CDCl_3$) δ 1.62 (p, 4 H), 2.60–2.68 (m, 8 H), 3.00 (s, 3 H), 3.68 (s, 4 H), 7.14 (s, 4 H); ^{13}C NMR δ 27.73, 47.86, 53.52, 127.40, 130.95, 139.09. The trihydrochloride salt was prepared in 91% yield as described above: mp 274–283 °C; ^{1}H NMR (D_2O) δ 2.25 (s, 4 H), 3.34 (s, 8 H), 4.41 (s, 4 H), 7.57 (s, 4 H); ^{13}C NMR δ 22.60, 44.88, 45.21, 48.13, 133.30; MS *m/e* 308 (M^+ - 36, 1.3), 234 (100). Anal. Calcd for $C_{14}H_{26}N_3Cl_3$: C, 49.06; H, 7.65; N, 12.26. Found: C, 49.28; H, 7.73; N, 11.66.

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Registry No. **1**, 52667-89-7; **2**, 35980-65-5; **3**, 35980-66-6; **4**, 35980-67-7; **5**, 52667-88-6; **6**, 71089-73-1; **7**, 71089-74-2; **8**, 52601-79-3; **9**, 52601-74-8; **10**, 56187-04-3; **11**, 35980-64-4; **12**, 91-13-4; **13**, 120637-12-9; **14**, 120637-13-0; **15**, 120637-14-1; **15**·3HCl, 120637-16-3; **16**, 120637-15-2; **16**·3HCl, 120637-17-4; 1,4,8-triazaoctane tritosylate, 35980-63-3; 1,4,7,10-tetraazadecane tetratosylate, 55442-07-4; 1,4,8,11-tetraazaundecane tetratosylate, 111514-29-5; *N,N'*-bis[2-[(*p*-toluenesulfonyl)oxy]ethyl]-*p*-toluenesulfonamide, 16695-22-0; 1,2-dibromoethane, 106-93-4; 1,3-dibromopropane, 109-64-8.

Syntheses and Rearrangements of Spiro-Fused Dihydroisoquinolones[1]

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We have shown that the addition of lithiated *N,N*-diethyl-*o*-toluamides to benzaldimines and subsequent electrophilic trapping of 4-lithio-3-aryl-3,4-dihydro-1(2*H*)-isoquinolones is a viable route to *trans*-3-aryl-4-substituted-3,4-dihydro-1(2*H*)-isoquinolones and to a number of benzo[*c*]phenanthridines and other natural products.[3] We wished to ascertain if this lithiated toluamide strategy could be used to construct spiro annelated isoquinolones of structure **1** by addition of lithiated *N,N*-diethyl-*o*-toluamide **2** to ketimines of general structure **3**. We reasoned that these spiro compounds might undergo rearrangement to fused isoquinolones such as **4** (n = 1) whose ring system is found in a large number of amaryllidaceae alkaloids[4] (Scheme I).

We now report the results of a study on the generality of spiroisoquinolone synthesis by two routes: An annelation–trapping sequence and a carboxylate dianion addition/hydrolysis route. We also present our results from the study of the cationic rearrangement of these spiroisoquinolones.

Discussion

N,N-Diethyl-*o*-toluamide (**5**) was deprotonated with LDA in THF at −70 °C and treated with *n*-butyl-, cyclobutyl-, cyclopentyl-, cyclohexyl-, cycloheptyl-, cyclooctyl-, and 4-*tert*-butylcyclohexylketimines **3a–f**.[5] Only in the cases of the ketimines corresponding to cyclohexanone, cycloheptanone, or 4-*tert*-butylcyclohexanone, (**3c**, **3d**, **3f**) were the expected spiro-fused isoquinolones (**6a–c**) obtained (Scheme II). In each of the other cases, the starting toluamide (**5**) and the corresponding ketones were recovered after acidic hydrolysis. These results indicated that deprotonation of the ketimine by the strongly basic lithiated species **2** might be much faster than the desired nucleophilic addition/annelation.

Attempts to mediate the basicity of lithio species **2** through the use of anhydrous cerium chloride or zinc chloride failed to produce the desired cycloadducts. Instead, only starting toluamide **5** and the ketones resulting

(1) Contribution No. 776 from the Syntex Institute of Organic Chemistry.

(2) Syntex Postdoctoral Fellow, 1987–1988.

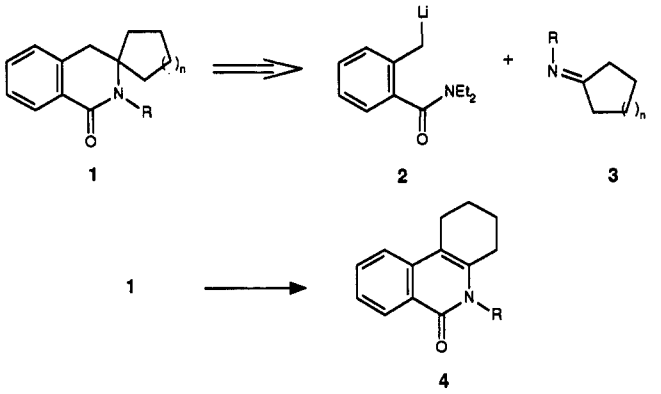
(3) (a) Clark, R. D.; Jahangir *J. Org. Chem.* **1987**, *52*, 5378. (b) Clark, R. D.; Jahangir *Heterocycles* **1988**, *27*, 871. (c) Clark, R. D.; Jahangir *J. Org. Chem.* **1988**, *53*, 2378.

(4) For examples, see: Fuganti, C. *The Alkaloids*; Manske, R. H. F., Ed.; Academic: New York, 1975; Vol. XV, p 83.

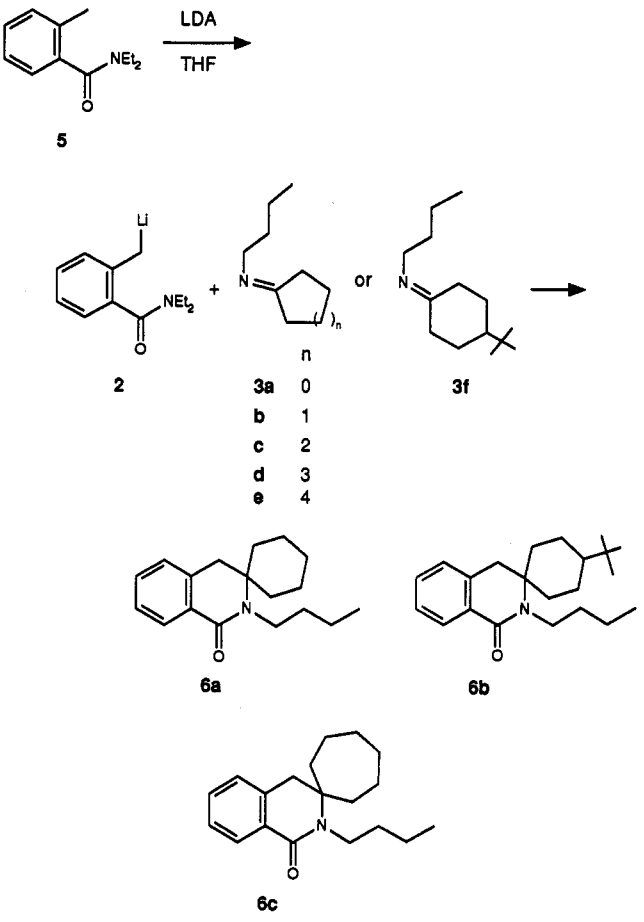
(5) Each *n*-butylcycloalkylimine was prepared from its corresponding ketone in benzene by azeotropic removal of water. *n*-Butyl was chosen for ease of preparation.

0022-3263/89/1954-2992$01.50/0

Scheme I



Scheme II



from imine hydrolysis were isolated.[6,7]

Therefore an alternative, general method was developed to synthesize the desired spiroisoquinolones. *o*-Toluic acid was esterified with i-PrOH/H_2SO_4 and brominated with NBS to give **11**. This bromo ester underwent smooth nucleophilic addition with the dianion of cycloalkyl carboxylic acids **12a–c** and indanecarboxylic acid (LDA, 2.2 equiv, 50 °C, THF). Carboxylic acids **13a–c** were converted to their isocyanates (**15a–c**) by the Curtius rearrangement using the Weinstock protocol[8] and treated with sodium benzyloxide in toluene heated under reflux to give the desired fused isoquinolones (**17a–c**) (Scheme III), presumably via amines **16a–c**. In an analogous manner, indanecarboxylic acid **14** was converted to the fused spiroisoquinolone **19**.

Bromination of spiroisoquinolones **17a–c** was achieved photochemically with *N*-bromosuccinimide. In the case of **20a**, rearrangement to fused isoquinolone **21a** occurred upon bromination. Bromoisoquinolones **20b** and **20c** and **22a–c** required treatment with $AgBF_4$ to induce their rearrangement. Spiroisoquinolone **19** gave a mixture of diastereomers (**24**) upon bromination which all rearranged to **25**, probably due to the greater migratory aptitude of the phenyl ring versus that of the benzylic methylene group (Scheme IV). The structure of **25** was determined by a long-range Homo Cosy experiment in which a coupling of approximately 0.5 Hz between the protons attached to C_6 and C_7 of the two phenyl rings in **25** was found.

Conclusion

We have shown that the annelation/trapping sequence described above is useful for the construction of C_6 and C_7 fused spiro isoquinolones. Further, a general method has been developed to produce C_4–C_8 and indane-fused spiroisoquinolones. These spiroisoquinolones can be induced to undergo smooth cationic rearrangement to ring-expanded isoquinolones. In the case of the indanecarboxylic acid derived isoquinolone, an unusual and apparently never before synthesized fused benzphenanthridine isoquinolone was obtained from this cationic rearrangement.

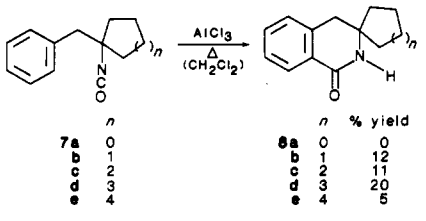
Experimental Section

Proton magnetic resonance spectra were recorded on Varian HA-100 and Bruker WM 300 and WM 500 spectrometers and are reported in ppm (δ) down field from an internal standard of tetramethylsilane. Mass spectra were obtained on a MAT-311A, 112S, or CH-7 instrument. High-resolution mass spectra were recorded on a MAT-311A spectrometer. Medium-pressure (flash) chromatography was performed with 230–400-mesh Merck kieselgel. Melting points are uncorrected. Elemental analyses were obtained from the Syntex analytical department. Imines were prepared from the ketones and *n*-butylamine in benzene solution by azeotropic removal of water and were purified by distillation.

Typical Procedure for the Condensation of *N,N*-Diethyl-*o*-toluamide (5) with Ketimines 3a–e. A solution of LDA was prepared at −70 °C by adding 3.75 mL (6 mmol) of *n*-butyllithium in hexane to 0.84 mL (6 mmol) of diisopropylamine in 10 mL of freshly distilled THF. A solution of *N,N*-diethyl-*o*-toluamide (955 mg, 5 mmol) in 4 mL of THF was added dropwise at such a rate to maintain the internal temperature below

(6) Several workers have reported basicity mediation by replacement of lithium with a different cation. Ce(III), and Ce(III)–Mg(II): Imamoto, T.; Kusumoto, T.; Yohoijaha, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1042. Imamoto, T.; Yasushi, S.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233. Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hataraka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904. Imamoto, T.; Takiyama, Nakamura, K. *Tetrahedron Lett.* **1985**, *26*, 4763. Fukuzawa, S. I.; Tsuruta, T.; Fujinami, T.; Sakui, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1473. Ce(III), Al(III), Ti(III), Zn(I): Denmark, S. E.; Weber, T.; Piotrowski, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 2224.

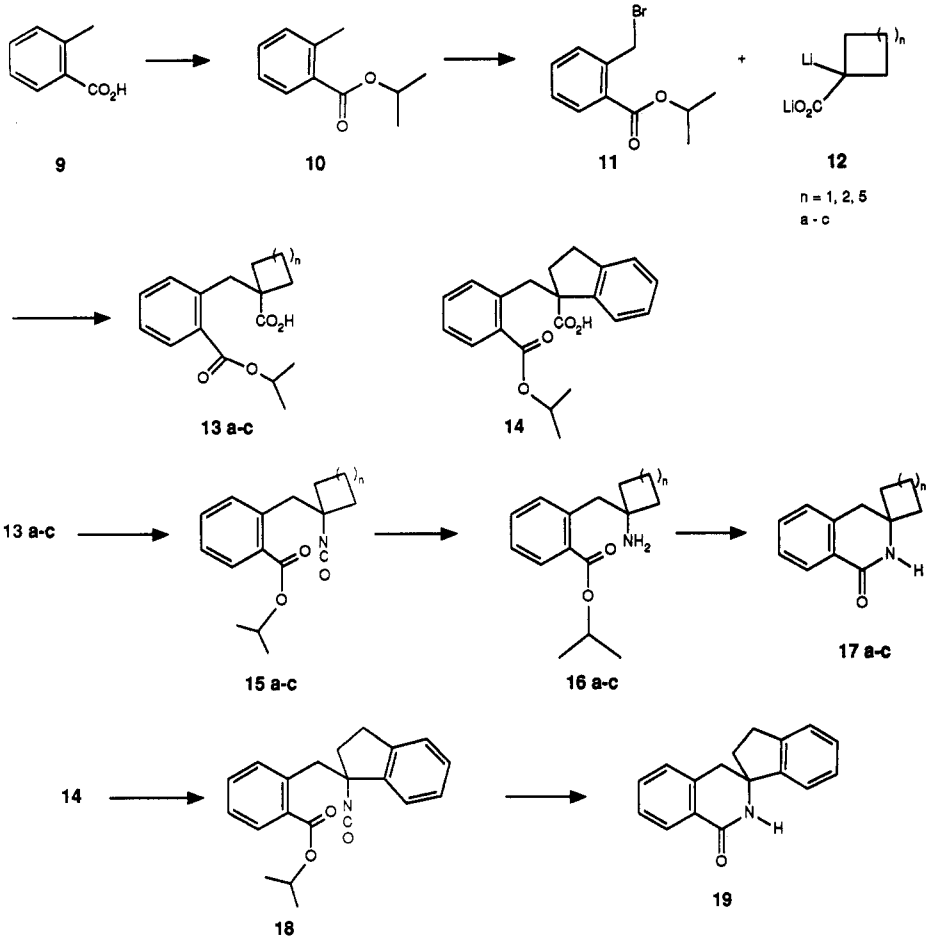
(7) A survey of the literature for methodology to construct isoquinolones of the type we desired showed only methods which relied on intramolecular cyclizations onto highly activated benzene rings. See: (a) Gomez-Parra, V.; Gracian, D.; Madronero, R. *Anales De Qumica* **1974**, *70*, 980. (b) Boyd, G. V.; Monteil, R. L.; Lindley, P. F.; Mahmoud, M. M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1352. (c) Harcourt, D. N.; Hussain, F.; Taylor, N.; Nasir, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1329. Further, it was reported that unactivated phenyl rings gave poor yields of isoquinolones. Indeed, we were unable to effect ring closure in satisfactory yields using unactivated benzene rings, as illustrated below.



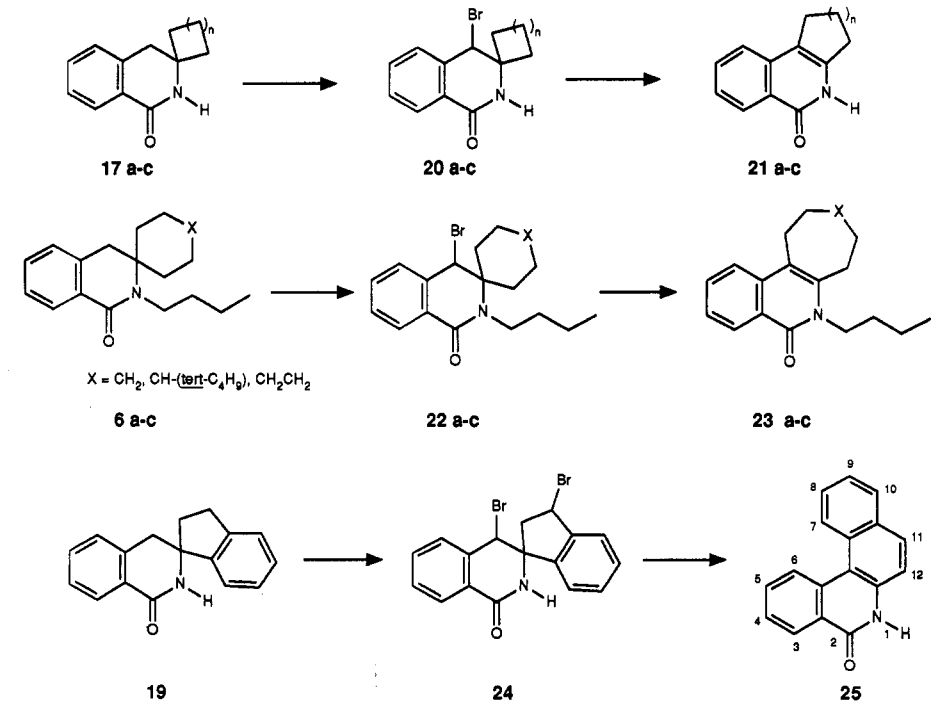
	n		*n*	% yield
7a	0	**8a**	0	0
b	1	**b**	1	12
c	2	**c**	2	11
d	3	**d**	3	20
e	4	**e**	4	5

(8) Weinstock, J. *J. Org. Chem.* **1961**, *26*, 3511.

Scheme III



Scheme IV



–65 °C, and the resulting purple solution was stirred for 10 min at this temperature under dry a nitrogen atmosphere. To this solution the appropriate ketimine (7 mmol) in 4 mL of THF was added dropwise, and the resulting mixture was stirred below –60 °C for 2 h and then quenched with saturated ammonium chloride solution. The mixture was concentrated in vacuo, diluted with water, and thoroughly extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were successively washed with 5% HCl solution, water, and brine and dried (Na_2SO_4). Removal of the solvent in vacuo gave the products, which were purified by medium-pressure chromatography on silica gel.

1′,4′-Dihydro-2′-*n*-butylspiro[cyclohexane-1,3′(2′*H*)-iso-

quinolin]-1′-one (6a): 44%; oil; IR ($CHCl_3$) 1644, 1605, 1586 cm^{-1}; NMR ($CDCl_3$) δ 8.05 (dd, J = 7.6, 1.1 Hz, 1 H), 7.39 (m, 1 H), 7.32 (m, 1 H), 7.14 (d, J = 7.3 Hz, 1 H), 3.55 (m, 2 H), 3.06 (s, 2 H), 1.80–1.60 (m, 10 H), 1.52–1.35 (m, 4 H), 0.97 (t, J = 7.3 Hz, 3 H); MS m/e (relative intensity) 271 (88, M^+), 254 (26), 228 (98), 214 (25), 200 (100), 172 (41), 159 (93), 118 (36). Anal. Calcd for $C_{18}H_{25}NO$: C, 79.70; H, 9.23; N, 5.17. Found: C, 79.50; H, 9.41; N, 4.94.

1′,4′-Dihydro-2′-*n*-butyl-4-*tert*-butylspiro[cyclohexane-1,3′(2′*H*)-isoquinolin]-1′-one (6b): 40% two isomers (3:1); oil; IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.05, 8.0 (2 dd, J = 7.5, 1.3 Hz, total 1 H), 7.42–7.27 (m, 2 H), 7.15, 7.09 (2 d, J = 7.4 Hz, 1 H), 3.67, 3.54 (2 m, total 2 H), 3.02, 2.86 (2 s, total 2 H), 2.10 (m, 2 H), 1.80–1.60 (m, 6 H), 1.46–1.30 (m, 4 H), 0.97, 0.96 (2 t, J = 7.3 Hz, total 3 H), 0.89, 0.88 (2 s, total 9 H); MS m/e (relative intensity) 327 (35, M^+), 312 (6), 284 (17), 270 (9), 228 (100), 214 (16), 200 (49), 172 (14), 159 (9) 118 (12); exact mass calcd for $C_{22}H_{33}NO$ 327.2562, found 327.2553.

1′,4′-Dihydro-2′-*n*-butylspiro[cycloheptane-1,3′(2′*H*)-isoquinolin]-1′-one (6c): 40%; oil; IR ($CHCl_3$) 1644, 1605, 1584 cm^{-1}; NMR ($CDCl_3$) δ 8.03 (dd, J = 7.6, 1.3 Hz, 1 H), 7.39 (d, t, J = 7.4, 1.5 Hz, 1 H), 7.32 (dt, J = 6.5, 1.5 Hz, 1 H), 7.12 (d, J = 6.5 Hz, 1 H), 3.51 (m, 2 H), 2.98 (s 2 H), 1.95 (m, 2 H), 1.80–1.34 (m, 14 H), 0.97 (t, J = 7.3 Hz, 3 H); MS m/e (relative intensity 285 (93, M^+), 268 (75), 242 (34), 228 (50), 214 (23), 200 (100), 186 (16), 172 (29), 159 (70), 118 (22); exact mass calcd for $C_{19}H_{27}NO$ 285.2092, found 285.2087.

Typical Procedure for the Preparation of Dihydroisoquinolones 17a–c and 19. A solution of carboxylic acid (**12a–c**) (10 mmol) in 10 mL of dry THF was added to a −20 °C solution of LDA (prepared from 3.08 mL (22 mmol) of diisopropylamine and 13.75 mL (22 mmol) of 1.6 M *n*-butyllithium in hexane) in 30 mL of THF under nitrogen with constant stirring. The resulting mixture was stirred first at 0 °C for 15 min and then at 30–35 °C for 1 h. The mixture was then cooled back to −20 °C and treated with a solution of isopropyl 2-(bromomethyl)benzoate (**11**) (3.34 g, 13 mmol) in 10 mL of THF. The resulting reaction mixture was first stirred at −10 °C for 1 h and then the temperature was gradually raised to 30–35 °C, and the mixture was stirred for a further 1 h and quenched with saturated ammonium chloride solution. The mixture was concentrated under reduced pressure, and the residue was taken up in 5% NaOH solution and washed three times with ether. The aqueous layer was acidified with concentrated HCl solution and thoroughly extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine and dried (Na_2SO_4), and solvent was removed in vacuo to give the adduct **13a–c** or **14** in 60–95% yields. The adducts were used in the next step without further purification.

The adduct (**13a–c** or **14**) (13 mmol) was suspended in 3 mL of water and dissolved by adding 40 mL of acetone. The solution was cooled to 0 °C and treated dropwise first with a solution of Et_3N (16.9 mmol) in 10 mL of acetone, and then with a solution of ethyl chloroformate (16.9 mmol) in 20 mL of acetone. The resulting mixture was stirred at 0 °C for 30 min and then treated dropwise with a solution of sodium azide (19.5 mmol) in 6 mL of water, and the resulting mixture was stirred at 0 °C for a further 1 h. The reaction mixture was poured onto crushed ice and thoroughly extracted with ether, the combined ether extracts were washed with water, dried ($MgSO_4$), and filtered, and solvent was removed in vacuo at room temperature. The residue (acyl azide) was dissolved in 150 mL of dry toluene 2–3 g $MgSO_4$ was added, and the resulting mixture was heated on a steam bath under dry conditions until the evolution of nitrogen ceased. The mixture was filtered, the residue was washed with dry toluene, and the combined filtrates were concentrated in vacuo to give the isocyanate (**15a–c** or **18**) (IR ($CHCl_3$) 2250, 1700 cm^{-1}) in 70–85% yield. The isocyanates were used as such in the next reaction.

A mixture containing the isocyanate (**15a–c** or **18**) (3 mmol), sodium hydride (12 mmol, 60% oil dispersion, prewashed with pentane), and 3 mL of benzyl alcohol in 25 mL of dry toluene was heated under reflux for 2 h in a dry nitrogen atmosphere. The reaction mixture was cooled, excess sodium hydride was carefully decomposed with water, and the mixture was acidified with concentrated HCl solution and diluted with EtOAc. The organic layer was separated, and the aqueous layer was thoroughly extracted with EtOAc. The combined EtOAc extracts were washed with water and brine and dried (Na_2SO_4), and solvent was removed in vacuo. The residual benzyl alcohol was removed by Kugelrohr distillation, and the residue was purified by medium-pressure chromatography on silica gel to give spirodihydroisoquinolone **17a–c** or **19**.

1′,4′-Dihydrospiro[cyclobutane-1,3′(2′*H*)-isoquinolin]-1′-one (17a): 76%; mp 164–166 °C dec (EtOAc–hexane); IR (KBr) 1665, 1607, 1576 cm^{-1}; NMR ($CDCl_3$) δ 8.04 (dd, J = 6.7, 1 Hz, 1 H), 7.46 (dt, J = 7.4, 1.1 Hz, 1 H), 7.35 (dt, J = 6.7, 1.4 Hz, 1 H), 7.25 (d, J = 7.4 Hz, 1 H), 6.25 (br s, 1 H, exchanges with D_2O), 3.13 (s, 2 H), 2.20–2.08 (m, 4 H), 1.90–1.78 (m, 2 H); MS m/e (relative intensity) 187 (38, M^+), 159 (100), 130 (24), 118 (24), 90 (34). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 6.89; N, 7.48. Found: C, 76.65; H, 6.78; N, 7.38.

1′,4′-Dihydrospiro[cyclopentane-1,3′(2′*H*)-isoquinolin]-1′-one (17b): 69%; mp 172–173 °C (EtOAc–hexane); IR ($CHCl_3$) 1651, 1609, 1578 cm^{-1}; NMR ($CDCl_3$) δ 8.04 (dd, J = 7.6, 1.1 Hz, 1 H), 7.43 (dt, J = 7.4, 1.5 Hz, 1 H), 7.34 (m, 1 H), 6.77 (br s, 1 H, exchanges with D_2O), 2.99 (m, 2 H) 1.97–1.70 (m, 8 H); MS m/e (relative intensity) 201 (44, M^+), 172 (24), 159 (100), 118 (10). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.53; H, 7.59; N, 6.88.

1′,4′-Dihydrospiro[cyclooctane-1,3′(2′*H*)-isoquinolin]-1′-one (17c): 60%; mp 182–183 °C (EtOAc); IR ($CHCl_3$) 1650, 1607, 1580 cm^{-1}; NMR ($CDCl_3$) δ 8.03 (d, J = 7.7 Hz, 1 H), 7.42 (m, 1 H), 7.31 (m, 1 H), 7.15 (d, J = 7.4 Hz, 1 H), 6.32 (br s, 1 H exchanges with D_2O), 2.91 (s, 2 H), 1.90–1.45 (m, 4 H); MS, m/e (relative intensity) 243 (27, M^+), 172 (39), 159 (100), 118 (10). Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.82; H, 8.65; N, 5.65.

1′,4′,2,3-Tetrahydrospiro[1*H*-indene-1,3′(2′*H*)-isoquinolin]-1′-one (19): 80%; mp 192–193 °C (EtOAc); IR ($CHCl_3$) 1661, 1580 cm^{-1}; NMR ($CDCl_3$) δ 8.12 (dd, J = 7.7, 1.2 Hz, 1 H), 7.47 (m, 1 H), 7.39 (m, 1 H), 7.30–7.16 (m, 5 H), 6.13 (br s, 1 H, exchanges with D_2O), 3.30 (d, J = 15.6 Hz, 1 H), 3.04 (d, J = 15.6 Hz, 1 H), 2.95 (m, 2 H), 2.40 (m, 1 H), 2.13 (m, 1 H); MS m/e (relative intensity) 249 (100, M^+), 248 (70), 220 (50), 118 (93), 90 (86), 89 (40). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.89; H, 6.07; N, 5.62. Found: C, 81.79; H, 6.17; N, 5.54.

Typical Procedure for the Benzylic Bromination of Spirodihydroisoquinolones 17a–c, 19, and 6a–c. To solution of the spiroisoquinolone (1 mmol) in 20 mL of CCl_4 was added *N*-bromosuccinimide (1.15 mmol) and a catalytic amount of AIBN. The reaction mixture was heated under reflux for ca. 2 h while exposed to a 200-W white lamp. After being cooled to room temperature, the reaction mixture was filtered, and the residue was washed several times with CCl_4. The combined filtrate and washings were concentrated in vacuo, and the residue was purified by medium-pressure chromatography on silica gel. All spirodihydroisoquinolones, except **20a** which yielded the rearranged product **21a**, gave the corresponding bromo derivatives in 80–90% yield. Some bromo compounds were used directly in the next step without any purification.

4′-Bromo-1′,4′-dihydrospiro[cyclopentane-1,3′(2′*H*)-isoquinolin]-1′-one (20b): mp 138–139 °C (EtOAc–hexane); IR ($CHCl_3$) 1672, 1607, 1581 cm^{-1}; NMR ($CDCl_3$) δ 8.10 (dd, J = 7.5, 1.6 Hz, 1 H), 7.52 (dt, J = 7.4, 1.6 Hz, 1 H), 7.45 (dt, J = 7.5, 1.6 Hz, 1 H), 7.36 (dd, J = 7.4, 1.4 Hz, 1 H), 6.75 (br s, 1 H exchanges with D_2O), 5.13 (d, J = 1.4 Hz, 1 H), 2.20–1.70 (m, 8 H). Anal. Calcd for $C_{13}H_{14}BrNO$: C, 55.73; H, 5.04; N, 5.00. Found: C, 55.61; H, 5.07; N, 4.91.

4′-Bromo-1′,4′-dihydro-2′-*n*-butylspiro[cyclohexane-1,3′-(2′*H*)-isoquinolin]-1′-one (22a): mp 94–95 °C (EtOAc–hexane); IR ($CHCl_3$) 1634, 1607, 1584 cm^{-1}; NMR ($CDCl_3$) δ 8.09 (dd, J = 7.3, 1.7 Hz, 1 H), 7.51–7.40 (m, 2 H), 7.31 (dd, J = 6.9, 1.7 Hz, 1 H), 5.66 (s, 1 H), 3.76 (m, 1 H), 3.51 (m, 1 H), 2.55 (m, 1 H), 2.0–1.20 (m, 13 H), 0.98 (t, J = 7.3 Hz, 3 H); MS m/e (relative intensity) 351, 349 (18, M^+), 308 (10), 306 (18), 270 (100), 228 (16), 214 (33), 200 (10), 198 (10). Anal. Calcd for $C_{18}H_{24}BrNO$: C, 61.71; H, 6.91; N, 3.99. Found: C, 61.53; H, 6.97; N, 3.97.

4′-Bromo-1′,4′-dihydro-2′-*n*-butyl-4-*tert*-butyl[cyclohexane-1,3′(2′*H*)-isoquinolin]-1′-one (22b): oil; IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) isomeric mixture (3:1) δ 8.10, 8.04 (2 dd, J = 7.3, 1.7 Hz, total 1 H), 7.44 (m, 2 H), 7.33, 7.25 (2 m, total 1 H), 5.54, 4.94 (2 s, total 1 H), 3.80 (m, 1 H), 3.50 (m, 1 H), 2.65 (m, 2 H), 2.0–1.10 (m, 12 H), 0.98, 0.97 (2 t, J = 7.3 Hz, total 3

H), 0.90, 0.88 (2s, total 9 H); MS *m/e* 407, 405 (14, M^+), 364 (12), 362 (12), 350 (5), 348 (5), 326 (100), 284 (12), 270 (18), 228 (27), 214 (33); exact mass calcd for $C_{22}H_{32}BrNO$ 405.1667, found 405.1669.

4′-Bromo-1′,4′-dihydro-2′-*n*-butylspiro[cycloheptane-1,3′(2′*H*)-isoquinolin]-1′-one (22c): oil; IR ($CHCl_3$) 1638, 1609, 1586 cm^{-1}; NMR ($CDCl_3$) δ 8.07 (dd, J = 7.3, 1.7 Hz, 1 H), 7.44 (m, 2 H), 7.28 (dd, J = 6.6, 1.5 Hz, 1 H), 5.34 (s, 1 H), 3.79 (m, 1 H), 3.37 (m, 1 H), 2.40–1.13 (m, 16 H), 0.98 (t, J = 7.3 Hz, 3 H); MS *m/e* (relative intensity) 365, 363 (10, M^+), 348 (10), 346 (10), 322 (7), 320 (7), 284 (100), 242 (10), 228 (21), 214 (16), 200 (28); exact mass calcd for $C_{19}H_{26}BrNO$ 363.1198, found 363.1197.

8,9-Dihydro-7*H*-cyclopenta[*c*]isoquinolin-5(6*H*)-one (21a). Under the above reaction conditions, the spirodihydroisoquinolone **20a** yielded the rearranged isoquinolone **21a** in 63% yield: mp 227–230 °C (MeOH); IR (KBr) 1644, 1607 cm^{-1}; NMR ($CDCl_3$ δ 10.90 (br s, 1 H, exchanges with D_2O), 8.37 (dd, J = 8.6, 1.5 Hz, 1 H), 7.64 (dt, J = 7.9, 1.3 Hz, 1 H), 7.40 (m, 2 H), 2.91 (m, 4 H), 2.20 (quintet, J = 7.3 Hz, 2 H); MS *m/e* (relative intensity) 185 (94, M^+), 184 (100). Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.51; H, 6.13; N, 7.46.

Typical Procedure for the Rearrangement of Bromospirodihydroisoquinolones 20b,c, 22a–c, and 24 to Isoquinolones 21b,c, 23a–c, and 25. A solution of 100 mg of bromospirodihydroisoquinolone and 100 mg of silver tetrafluoroborate in 10 mL of dry CH_2Cl_2 were stirred at room temperature under dry conditions for ca. 4 h. The reaction mixture was filtered, and the residue was washed with CH_2Cl_2. The filtrate and washings were concentrated in vacuo, and the residue was purified by medium-pressure chromatography (silica gel) and crystallization to afford the corresponding rearranged isoquinolone.

1,2,3,4-Tetrahydrophenanthridin-6(5*H*)-one (21b): 90%, mp 226–228 °C (MeOH); IR ($CHCl_3$) 1653, 1609 cm^{-1}; NMR ($CDCl_3$) δ 10.93 (br s, 1 H, exchanges with D_2O), 8.44 (d, J = 6.6 Hz, 1 H), 7.68–7.60 (m, 2 H), 7.45 (m, 1 H), 2.70 (m, 4 H), 1.89 (m, 4 H); MS *m/e* (relative intensity) 199 (100, M^+), 198 (44), 171 (93), 144 (17), 145 (14), 115 (27). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.09; H, 6.66; N, 6.97.

6-*n*-Butyl-8,9,10,11-tetrahydro-7*H*-cyclohepta[*c*]isoquinolin-5(6*H*)-one (23a): 92%; oil; IR ($CHCl_3$) 1638, 1612, 1588 cm^{-1}; NMR ($CDCl_3$) δ 8.49 (d, J = 6.3 Hz, 1 H), 7.70 (m, 1 H), 7.64 (m, 1 H), 7.41 (m, 1 H), 4.20 (m, 2 H), 3.02–2.92 (m, 4 H), 1.88 (m, 2 H), 1.66 (m, 6 H), 1.47 (m, 2 H), 0.9 (t, J = 7.3 Hz, 3 H); MS *m/e* (relative intensity) 269 (96, M^+), 252 (77), 240 (10), 226 (25), 213 (100), 198 (16), 184 (25), 159 (24); exact mass calcd for $C_{18}H_{23}NO$ 269.1780, found 269.1782.

6-*n*-Butyl-9-*tert*-butyl-8,9,10,11-tetrahydro-7*H*-cyclohepta[*c*]isoquinolin-5(6*H*)-one (23b): 98%; oil; IR ($CHCl_3$) 1640, 1588 cm^{-1}; NMR ($CDCl_3$) δ 8.48 (m, 1 H), 7.72 (m, 1 H), 7.64 (m, 1 H), 4.32 (m, 1 H), 4.11 (m, 1 H), 3.28 (m, 1 H), 3.09 (m, 1 H), 2.86 (m, 1 H), 2.58 (m, 1 H), 2.11 (m, 2 H), 1.80–1.40 (m, 6 H), 1.00 (t, J = 7.4 Hz, 3 H), 0.86 (s, 9 H); exact mass calcd for $C_{22}H_{31}NO$ 325.2406, found 325.2391.

6-*n*-Butyl-7,8,9,10,11,12-hexahydrocycloocta[*c*]isoquinolin-5(6*H*)-one (23c): 95%; mp 75–78 °C; IR ($CHCl_3$) 1638, 1612, 1588 cm^{-1}; NMR ($CDCl_3$) δ 8.47 (dd, J = 8.1, 1.2 Hz, 1 H), 7.63 (m, 1 H), 7.42 (m, 1 H), 4.14 (m, 2 H), 2.95 (m, 4 H), 1.74–1.42 (m, 12 H), 0.98 (t, J = 7.4 Hz, 3 H); MS *m/e* (relative intensity) 283 (100, M^+), 266 (84), 254 (11), 240 (20), 227 (52), 213 (26), 198 (23), 184 (29); exact mass calcd for $C_{19}H_{25}NO$ 283.1936, found 283.1936.

8,9,10,11,12,13-Hexahydro-7*H*-cyclonona[*c*]isoquinolin-5-(6*H*)-one (21c): 87%; mp 253–255 °C (EtOAc–hexane); IR ($CHCl_3$) 1653, 1609 cm^{-1}; NMR ($CDCl_3$) δ 9.90 (br s, 1 H, exchanges with D_2O), 8.45 (dd, J = 7, 0.9 Hz, 1 H), 7.68 (m, 2 H), 7.45 (m, 1 H), 2.89 (m, 2 H), 2.79 (m, 2 H), 1.83 (m, 2 H), 1.76 (m, 2 H), 1.61 (s, 2 H), 1.50–1.38 (m, 4 H); MS *m/e* (relative intensity) 241 (100, M^+), 212 (33), 199 (50), 198 (80), 184 (95), 172 (62), 159 (39); exact mass calcd for $C_{16}H_{19}NO$ 241.1467, found 241.1469.

Benzo[*a*]phenanthridin-8(7*H*)-one (25): 80% (from **19**); mp 240–244 °C dec; IR (KBr) 1640, 1586 cm^{-1}; NMR ($CDCl_3$ + DMSO-d_6) δ 8.83 (d, J = 8.6 Hz, 1 H), 8.80 (d, J = 8.3 Hz, 1 H), 8.57 (dd, J = 7.9, 1.5 Hz, 1 H), 7.92 (dd, J = 8.1, 1.1, Hz, 1 H), 7.86 (d, J = 9 Hz, 1 H), 7.85 (m, 1 H), 7.63 (m, 2 H), 7.56 (d, J = 8.7 Hz, 1 H), 7.50 (dt, J = 7.9, 1 Hz, 1 H); MS *m/e* (relative intensity) 245 (100, M^+), 217 (15), 216 (16), 189 (15); exact mass calcd for $C_{17}H_{11}NO$ 245.0841, found 245.0843.

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