Synthesis and Spectral Data of Unknown Lilolidine Spiro Derivatives

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A new series of halo and methyl substituted spiro annulated tetrahydropyrrolo[3,2,1-*ij*]quinolines, analogues of lilolidine alkaloids has been prepared in a two-step route from easily accessible dihydroquinoline precursors.

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Introduction.

The condensed tricyclic system of 1,2,5,6-tetrahydropyrrolo[3,2,1-*ij*]quinoline is the basic skeleton of lilolidine alkaloids [1,2]. Hydrolilolidine has been used as an intermediate substrate in the total syntheses of the pentacyclic Melodinus alkaloids, meloscine and epimeloscine, and the hexacyclic Aspidosperma alkaloid deoxoapodine [3,4]. A variety of biological properties has been reported for relatively simple synthetic pyrroloquinolines. These include serotonin antagonists [5,6] and protein kinase inhibitors [7]. Some of these heterocycles show antidepressant activity [8] and others are used in the treatment of autoimmune and metabolic bone diseases and as antirheumatic agents [9]. Fungicidal activity is also shown by some tetrahydropyrroloquinolinones [10,11]. It is also noteworthy that lilolidine and its derivatives have found recent interest as dye materials for the dyeing or printing of textiles [12] and as sensitizers for photopolymerization at longer wavelengths [13].

Despite the relatively large number of published synthetic routes to lilolidone and its derivatives [14] there are very few works that describe the construction of the tetrahydroquinoline ring spiro annulated at position C-2 with cycloalkanes or heterocycles, and simultaneously fused at positions 1,8 with a pyrrole ring. The chemistry and biological activity of these spiro compounds remain largely unexplored [15]. In a previous paper we described a practical synthesis of 4-methyl-1*H*-3,4-dihydroquinolines spiro annulated *via* the C-2 carbon atom with a cycloalkane ring [16]. The easy three-step synthesis of these heterocycles from readily available ketones and anilines, allowed us to study some of their chemical transformations [17,18]. Herein, we report a facile conversion of substituted 4-methyl-3,4-dihydrospiro[1*H*-quinoline-2,1'-cyclohexanes(cycloheptanes)] into new pyrrolidino[3,2,1-*ij*]-quinoline derivatives, spirocyclic analogues of lilolidine-type alkaloids.

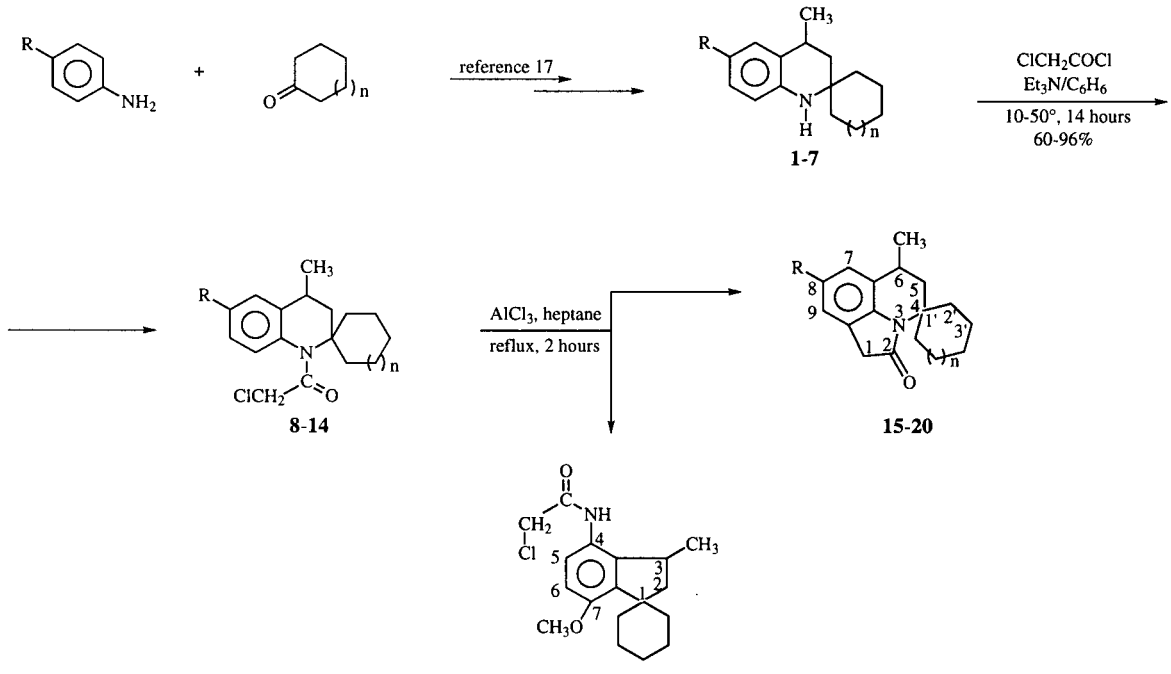
The basic lilolidine structure can be obtained both from indoline or tetrahydroquinoline derivatives by alkylation or acylation reactions followed by intramolecular cyclization [14]. We considered that functionalized 3,4-dihydrospiro[1*H*-quinoline-2,1'-cycloalkanes] **1-7** are suitable precursors in the synthesis of spirocyclic lilolidine alkaloids. The latter were obtained in a two-step manner from cited precursors using the classical reactions of *N*-acylation and the Friedel-Crafts intramolecular alkylation.

Discussion and Results.

The acylation of spiro compounds **1-7** was carried out with chloroacetyl chloride in dry benzene in the presence of triethylamine (Scheme 1). The corresponding *N*-α-chloroacetyl derivatives **8-14** were isolated by column chromatography on silica gel in 60-96% yield as colorless, or maroon or yellow crystalline substances. The structure of these amides was confirmed by ir, nmr and mass spectra. The ^{1}H nmr spectra of these compounds are very similar to those of the parent compounds [16-18] except for a singlet at 3.95-4.00 ppm, which we assign to a deshielded -CH_2Cl group. The mass spectra of these compounds exhibit molecular ion peaks of high intensity which agree with the expected molecular mass.

The final step in the synthetic route is the aluminum chloride-promoted intramolecular ring closure of the *N*-α-chloroacetyl derivatives **8-14**. This reaction, performed by heating the reagents in heptane, afforded the lilolidone spiro derivatives **15-20**. These were isolated by column chromatography on silica gel as crystalline substances. The structures of these new derivatives of lilolidone were confirmed by ir, ^{1}H nmr and mass spectrometry. The ir spectra of these compounds exhibit a C=O stretching band at higher energies (1697-1703 cm^{-1}) than in the parent *N*-acetyl derivatives, which is indicative of the formation of the pyrrolidone ring. Stronger evidence of this ring formation is the change in the relative areas of the aromatic region of the ^{1}H nmr spectra, which corresponded to four or three protons in the precursors **8-14** and to three or two protons in the final products. The methylene protons at C-1 are non-equivalent and their signals appear as a double doublet at 3.34-3.52 ppm. The 5-H_{eq} and 5-H_{ax} protons appear as double doublets at 2.17-2.54 and 1.26-1.40 ppm, respectively. The signals from the methyl protons at C-6 are doublets at 1.32-1.36 ppm. The protons from the cyclohexane and cycloheptane rings give rise to a complex multiplet between 1.35-1.90 ppm.

Scheme 1



n = 1: 1, 8, 15 R = H; 2, 9, 16 R = Br; 3, 10, 17 R = Cl; 5, 12, 19 R = F; 6, 13, 20 R = CH_3; 7, 14 R = OCH_3; n = 2 : 4, 11, 18 R = Cl.

We observed a significant shift to lower fields for two signals, a doublet-triplet (1.97-2.01 ppm, cyclohexane) or a doublet-doublet (1.99-2.01 ppm, cycloheptane) and a doublet-doublet (3.25-3.45 ppm, both rings), each one belonging to one proton of the cyclohexane or cycloheptane rings. We explained these shifts as a result of the deshielding effect of the π cloud of the carbonyl function. A molecular dynamics simulation of the motions experienced by compound **19** in an NVT ensemble at 298 K for 10 ps was used to sample the distances between the carbonylic oxygen and the four neighboring protons on the cyclohexane ring every 10 fs. Average distances of 0.274 ±0.002, 0.386 ±0.002, 0.440 ±0.002, and 0.467 ±0.001 nm were found for hydrogens 3'-H_{ax}, 2'-H_{eq}, 3'-H_{eq} and 2'-H_{ax}, respectively. Based on these distances, the double doublet was assigned to the axial proton on C-3' and the doublet-triplet (double doublet) to the equatorial proton on C-2'. The mass spectra of these compounds contain molecular ion $M^{+\bullet}$ peaks of high abundance (69-85%) which confirm their molecular formula (Table 1). The main fragmentation route for molecular ions (Scheme 2) involves the successive loss of fragments $CH_3^{\bullet}$ and CO, accompanied by the formation of ions Φ_1, $[M\text{-}CH_3]^+$ and Φ_2, $[M\text{-}CH_3\text{-}CO]^+$. While ions Φ_2 are the most abundant in the mass spectra of **15-17**, **19** and **20**, fragment Φ_1 is the base peak in the spectrum of **18**. Fragments Φ_3 (39-49%) and Φ_4 (7-12%) are products of the dissociation of the saturated hydrocarbon ring, which decays *via* elimination of molecules C_4H_8 (n = 1) or C_5H_{10} (n = 2) from ions Φ_3 and Φ_2, respectively. The presence of the tetrahydroquinoline fragment is confirmed by the retro-Diels-Alder rupture of the nitrogen-containing ring, with migration of hydrogen to the nitrogen atom and formation of ion Φ_5 of medium intensity (40-52%). The presence of the carbonylic group in **15-20** is manifested in their spectra by the appearance of a fragment $[M\text{-}CH_3\text{-}CO]^+$ and the formation of ion Φ_6 of low intensity (9-15%). Ions Φ_7 and Φ_8, corresponding to the elimination of Cl (**17**,**18**) or Br (**16**) from ion Φ_5 or the loss of hydrogen chloride (**17**,**18**) or hydrogen bromide (**16**) from fragment Φ_6, are observed only in the mass spectra of **16-18**.

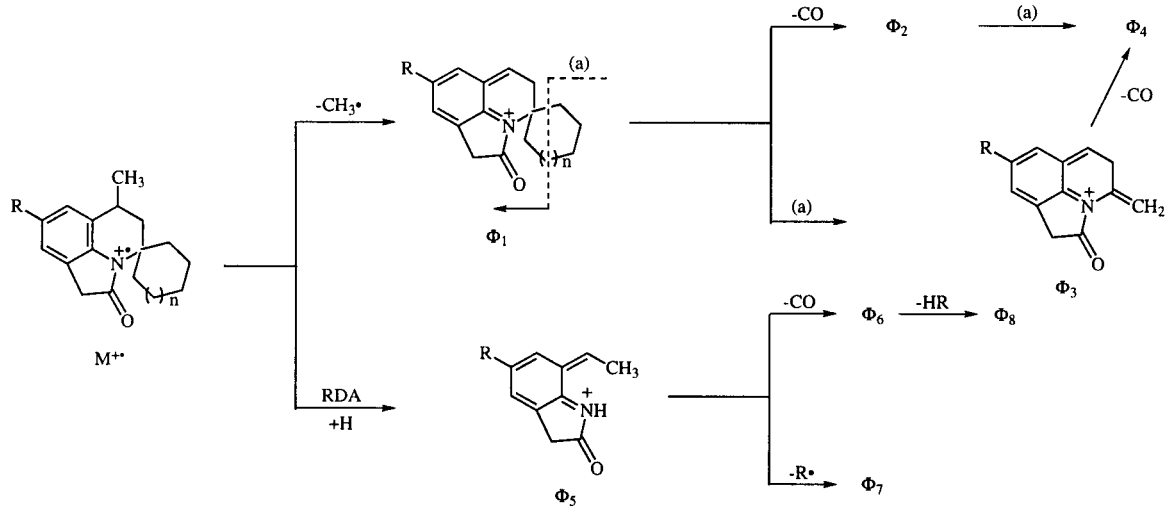
Table 1

Characteristic Ions (m/z) and their Relative Intensities (%) in the Mass Spectra of Compounds **15-20**

Compound	$M^{+\bullet}$	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6	Φ_7	Φ_8
15	255	240	212	184	156	160	132	----	----
	(72)	(76)	(100)	(43)	(11)	(40)	(9)		
16	333*	318	290	262	234	238	210	159	130
	(85)	(72)	(100)	(41)	(10)	(51)	(15)	(61)	(50)
17	289**	274	246	218	190	194	166	159	130
	(71)	(64)	(100)	(44)	(8)	(52)	(12)	(15)	(17)
18	303**	288	260	218	190	194	166	159	130
	(69)	(100)	(13)	(39)	(7)	(51)	(9)	(20)	(19)
19	273	258	230	202	174	178	150	----	----
	(73)	(70)	(100)	(41)	(12)	(49)	(13)		
20	269	254	226	198	170	174	146	----	----
	(81)	(69)	(100)	(49)	(13)	(48)	(11)		

* Relative to isotope ^{79}Br; ** Relative to isotope ^{35}Cl.

Scheme 2



We were surprised that the cyclization of methoxy-derivative **14** did not take place under the reaction conditions chosen. This is probably due to the inability of the oxygen belonging to the methoxy group to donate electronic density to the benzene ring, as a result of its coordination with the Lewis acid. The partial positive charge on this oxygen deactivates the ring, disabling the electrophilic substitution. Simultaneously, the interaction of the Lewis acid with the carbonyl oxygen induces the rupture of the N-C-2 bond, with generation of a stable tertiary carbocation that attacks the *meta* position relative to amide group leading to spiroindane **21**. An analogous situation is observed with *N*-acetyltetrahydroquinolines in polyphosphoric acid and concentrated sulfuric acid [19].

This new spiro compound was isolated by column chromatography, recrystallized from heptane and identified by ir, ^{1}H nmr and mass spectrometry. The ir spectrum contained bands at 1666 and 3247 cm^{-1} corresponding to the C=O and NH groups. A broad singlet at 8.15 ppm in the ^{1}H nmr spectrum was assigned to the amide proton. Protons 5-H and 6-H were assigned to the doublets at 7.68 and 6.74 ppm. The CH_2Cl protons appear as a singlet at 4.22 ppm. The base peak in the mass spectrum of this compound corresponds to its molecular ion.

Thus the present synthetic route provides a facile access to unknown lilolidine spiro derivatives and allows the study of their biological properties.

EXPERIMENTAL

The purity of the compounds synthesized and the composition of the reaction mixtures were controlled by thin-layer chromatography (tlc) on chromatoplates of Silufol uv_{254}. The separation was carried out by column chromatography on silica gel using as eluents mixtures of ethyl acetate-heptane with gradual increase of polarity (1:20; 1:10; 1:5). The ir spectra were obtained on a Perkin-Elmer 599B-FT spectrophotometer. The ^{1}H and ^{13}C nmr spectra were measured in deuteriochloroform with tetramethylsilane as the internal standard on a Bruker WM-400 (400 MHz) or a Bruker AMX-600 (600 MHz) spectrometer and are reported in ppm on the δ scale. Data are reported as follows: chemical shift (multiplicity, number of protons, coupling constants and group). Molecular dynamics calculations were performed on a Silicon Graphics Indigo2 with the program Discover (Molecular Simulations, Inc., San Diego, CA U.S.A.). A Hewlett-Packard (HP) 5890A Series II Gas Chromatograph interfaced to an HP 5972 Mass Selective Detector with an HP MS ChemStation Data system was used for ms identification. The column employed was an HP-5MS (Hewlett-Packard) cross-linked fused silica capillary column (30 m, 0.25 mm I.D.) coated with 5%-phenyl-polymethylsiloxane (0.25 μm phase thickness). The oven was programmed from 100° (10 minute hold) to 250° at 10°/minute. The helium inlet pressure was 78 kPa, with linear velocity 38 cm/seg (split 10 ml/minute). The injector temperature was kept at 250° and the volume injected was 0.5 μl (20% in dichloromethane). The temperatures of the ionization chamber and of the transfer line were 180 and 285°, respectively. The electron beam energy was 70 eV. Mass spectra and reconstructed chromatograms were obtained by automatic scanning in the mass range m/z 50-400 a.m.u.'s at 2.2 scan/second. Elemental analyses were performed on a Leco CHN-600 analyzer. The melting points (uncorrected) were determined on a Fisher-Johns melting point apparatus. Solvents and common reagents, obtained from Merck and Aldrich, were reagent grade.

Synthesis of *N*-α-Chloroacetyl-3,4-dihydro-4-methylspiro-[quinoline-2,1'-cyclohexanes(cycloheptanes)] **8-14**.

General Procedure.

To a stirred and cooled (5-10°) solution of spiranes **1-7** [17] (0.10 mole) and triethylamine (0.11 mole) in dry benzene (100 ml),

a solution (10 ml) of chloroacetyl chloride (0.10 mole) was added dropwise during fifteen minutes. After the addition was complete, the solution was stirred at 50° overnight. The reaction mixture was then neutralized with saturated sodium carbonate solution and extracted with ether (2 x 50 ml). The ether layer was separated, dried (sodium sulfate) and the solvent was evaporated. The residue was purified by column chromatography to give **8-14**.

N-α-Chloroacetyl-3,4-dihydro-4-methylspiro[quinoline-2,1'-cyclohexane] (**8**).

This compound was obtained in 70% yield as colorless crystals, mp 70-71° (heptane); ir: ν C=O 1670 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (dd, 1H, J = 14.0, 13.5 Hz, 3-H_{ax}), 1.4 (d, 3H, J = 6.8 Hz, 4-CH_3), 2.4 (dd, 1H, J = 14.0, 3.5 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 4.0 (s, 2H, CH_2Cl), 6.6 (t, 1H, J = 7.8, 8.0, 1.8 Hz, 6-H), 7.0 (d, 1H, J = 8.0, 1.8 Hz, 8-H), 7.2 (d, 1H, J = 7.8, 2.0 Hz, 5-H), 7.4 (t, 1H, J = 8.0, 2.0 Hz, 7-H); ms: m/z 291 (42, M^+, ^{35}Cl), 276 (14), 256 (82), 249 (11), 242 (22), 234 (12), 214 (24), 196 (100).

Anal. Calcd. for $C_{17}H_{22}ClNO$: C, 69.98; H, 7.55; N, 4.80. Found: C, 69.70; H, 7.22; N, 4.48.

6-Bromo-*N*-α-chloroacetyl-3,4-dihydro-4-methylspiro[quinoline-2,1'-cyclohexane] (**9**).

This compound was obtained in 65% yield as colorless crystals, mp 123-125° (heptane); ir: ν C=O 1662 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 13.9, 13.2 Hz, 3-H_{ax}), 1.4 (d, 3H, J = 6.8 Hz, 4-CH_3), 2.3 (dd, 1H, J = 13.2, 3.4 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 4.0 (s, 2H, CH_2Cl), 6.9 (d, 1H, J = 7.2 Hz, 8-H), 7.3 (s, 1H, 5-H), 7.3 (d, 1H, J = 7.2 Hz, 7-H); ms: m/z 371 (35, M^+, ^{79}Br, ^{35}Cl), 356 (9), 336 (36), 328 (7), 322 (16), 314 (8), 294 (18), 276 (100).

Anal. Calcd. for $C_{17}H_{21}BrClNO$: C, 55.06; H, 5.67; N, 3.78. Found: C, 54.79; H, 5.29; N, 3.38.

6-Chloro-*N*-α-chloroacetyl-3,4-dihydro-4-methylspiro[quinoline-2,1'-cyclohexane] (**10**).

This compound was obtained in 63% yield as maroon crystals, mp 88-90° (heptane); ir: ν C=O 1665 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 14.3, 13.2 Hz, 3-H_{ax}), 1.3 (d, 3H, J = 6.8 Hz, 4-CH_3), 2.4 (dd, 1H, J = 13.2, 3.4 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 4.0 (s, 2H, CH_2Cl), 6.9 (d, 1H, J = 7.9 Hz, 8-H), 7.2 (s, 1H, 5-H), 7.2 (d, 1H, J = 7.9 Hz, 7-H); ms: m/z 325 (45, M^+, ^{35}Cl), 310 (9), 290 (63), 282 (8), 276 (27), 268 (9), 248 (30), 230 (100).

Anal. Calcd. for $C_{17}H_{21}Cl_2NO$: C, 62.58; H, 6.44; N, 4.29. Found: C, 62.13; H, 6.12; N, 3.98.

6-Chloro-*N*-α-chloroacetyl-3,4-dihydro-4-methylspiro[quinoline-2,1'-cycloheptane] (**11**).

This compound was obtained in 60% yield as maroon crystals, mp 102-104° (heptane); ir: ν C=O 1675 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 14.2, 13.0 Hz, 3-H_{ax}), 1.3 (d, 3H, J = 7.0 Hz, 4-CH_3), 2.2 (dd, 1H, J = 13.0, 2.5 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 1.0-2.7 (m, 12H, $(CH_2)_6$), 4.0 (s, 2H, CH_2Cl), 6.9 (d, 1H, J = 8.5 Hz, 8-H), 7.1 (d, 1H, J = 8.5 Hz, 7-H), 7.2 (s, 1H, 5-H); ms: m/z 339 (32, M^+, ^{35}Cl), 324 (16), 304 (49), 290 (27), 282 (8), 262 (23), 248 (17), 230 (100).

Anal. Calcd. for $C_{18}H_{23}Cl_2NO$: C, 63.53; H, 6.76; N, 4.12. Found: C, 63.10; H, 6.22; N, 3.88.

N-α-Chloroacetyl-3,4-dihydro-6-fluoro-4-methylspiro-[quinoline-2,1'-cyclohexane] (**12**).

This compound was obtained in 70% yield as colorless crystals, mp 55-56° (heptane); ir: ν C=O 1662 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (dd, 1H, J = 13.0, 12.5 Hz, 3-H_{ax}), 1.3 (d, 3H, J = 7.0 Hz, 4-CH_3), 2.4 (dd, 1H, J = 13.0, 3.5 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 4.0 (s, 2H, CH_2Cl), 6.8 (t, 1H, J = 8.5, 8.0, 3.0 Hz, 7-H), 6.9 (d, 1H, J = 8.5, 3.0 Hz, 5-H), 7.0 (d, 1H, J = 8.5 Hz, 8-H); ^{13}C nmr (100 MHz): δ = 167.9, 125.9, 116.2, 112.8, 112.7, 110.4, 109.6, 63.9, 44.6, 36.5, 29.3, 24.9, 23.8, 22.9; ms: m/z 309 (35, M^+, ^{35}Cl), 294 (8), 274 (64), 266 (9), 260 (32), 252 (10), 232 (38), 234 (100).

Anal. Calcd. for $C_{17}H_{21}FClNO$: C, 65.91; H, 6.79; N, 4.52. Found: C, 65.54; H, 6.22; N, 4.08.

N-α-Chloroacetyl-3,4-dihydro-4,6-dimethylspiro[quinoline-2,1'-cyclohexane] (**13**).

This compound was obtained in 96% yield as colorless crystals, mp 59° (heptane); ir: ν C=O 1661 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 14.0, 14.0 Hz, 3-H_{ax}), 1.3 (d, 3H, J = 7.5 Hz, 4-CH_3), 2.3 (dd, 1H, J = 14.0, 3.4 Hz, 3-H_{eq}), 2.4 (s, 3H, 6-CH_3), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 4.0 (s, 2H, CH_2Cl), 6.9 (d, 1H, J = 7.5 Hz, 8-H), 7.0 (d, 1H, J = 7.5 Hz, 7-H), 7.0 (s, 1H, 5-H); ms: m/z 305 (28, M^+, ^{35}Cl), 290 (7), 270 (40), 262 (6), 256 (13), 248 (7), 228 (22), 210 (100).

Anal. Calcd. for $C_{18}H_{24}ClNO$: C, 70.70; H, 7.86; N, 4.58. Found: C, 70.03; H, 7.32; N, 4.08.

N-α-Chloroacetyl-3,4-dihydro-6-methoxy-4-methylspiro[quinoline-2,1'-cyclohexane] (**14**).

This compound was obtained in 85% yield as yellow crystals, mp 126-128° (heptane); ir: ν C=O 1657 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (dd, 1H, J = 13.6, 11.3 Hz, 3-H_{ax}), 1.3 (d, 3H, J = 6.8 Hz, 4-CH_3), 2.3 (dd, 1H, J = 13.6, 3.4 Hz, 3-H_{eq}), 2.7 (m, 1H, 4-H), 0.9-2.9 (m, 10H, $(CH_2)_5$), 3.8 (s, 3H, 6-OCH_3), 4.0 (s, 2H, CH_2Cl), 6.7 (d, 1H, J = 8.7, 2.3 Hz, 7-H), 6.8 (s, 1H, 5-H), 6.9 (d, 1H, J = 8.7 Hz, 8-H); ms: m/z 321 (40, M^+, ^{35}Cl), 306 (3), 286 (19), 278 (2), 272 (13), 264 (2), 244 (22), 226 (100).

Anal. Calcd. for $C_{18}H_{24}ClNO_2$: C, 67.19; H, 7.47; N, 4.35. Found: C, 66.77; H, 7.02; N, 3.98.

6-Methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo(3,2,1-*ij*)quinoline-4,1'-cyclohexanes(cycloheptanes)] **15-20**.

These compounds were obtained by the general procedure described in reference [11].

6-Methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo(3,2,1-*ij*)-quinoline-4,1'-cyclohexane] (**15**).

This compound was obtained in 75% yield as colorless crystals, mp 151-153° (heptane); ir: ν C=O 1708 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 13.5, 13.0 Hz, 5-H_{ax}), 1.4 (d, 3H, J = 7.0 Hz, 6-CH_3), 1.4-3.4 (m, 10H, $(CH_2)_5$), 2.5 (dd, 1H, J = 13.5, 4.5 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.4, 3.5 (2d, each, 1H, J = 21.5 Hz, 1-CH_2), 6.9 (t, 1H, J = 7.5 Hz, 8-H), 7.0 (d, 1H, J = 7.0 Hz, 9-H), 7.1 (d, 1H, J = 7.5 Hz, 7-H).

Anal. Calcd. for $C_{17}H_{21}NO$: C, 80.00; H, 8.24; N, 5.49. Found: C, 79.40; H, 7.92; N, 5.05.

8-Bromo-6-methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo-[3,2,1-*ij*]quinoline-4,1'-cyclohexane] (**16**).

This compound was obtained in 65% yield as colorless crystals, mp 188-190° (heptane); ir: ν C=O 1699 cm^{-1}; ^1H nmr (deu-

teriochloroform): δ 1.3 (dd, 1H, J = 13.9, 12.4 Hz, 5-H_{ax}), 1.4 (d, 3H, J = 6.8 Hz, 6-CH_3), 1.4-3.4 (m, 10H, $(CH_2)_5$), 2.5 (dd, 1H, J = 13.9, 4.5 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.4, 3.5 (2d, each, 1H, J = 22.2 Hz, 1-CH_2), 7.2 (s, 1H, 9-H), 7.3 (s, 1H, 7-H).

Anal. Calcd. for $C_{17}H_{20}BrNO$: C, 61.08; H, 5.99; N, 4.19. Found: C, 60.75; H, 5.42; N, 3.98.

8-Chloro-6-methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo-[3,2,1-*ij*]quinoline-4,1'-cyclohexane] (**17**).

This compound was obtained in 80% yield as maroon crystals, mp 173-174° (heptane); ir: ν C=O 1702 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 13.9, 12.4 Hz, 5-H_{ax}), 1.4 (d, 3H, J = 6.8 Hz, 6-CH_3), 1.4-3.5 (m, 10H, $(CH_2)_5$), 2.5 (dd, 1H, J = 13.9, 4.2 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.4, 3.5 (2d, each, 1H, J = 21.9 Hz, 1-CH_2), 7.0 (s, 1H, 9-H), 7.1 (s, 1H, 7-H).

Anal. Calcd. for $C_{17}H_{20}ClNO$: C, 70.47; H, 6.91; N, 4.84. Found: C, 70.07; H, 6.52; N, 4.58.

8-Chloro-6-methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo-[3,2,1-*ij*]quinoline-4,1'-cycloheptane] (**18**).

This compound was obtained in 68% yield as maroon crystals, mp 136-138° (heptane); ir: ν C=O 1702 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.4 (dd, 1H, J = 13.2, 13.2 Hz, 5-H_{ax}), 1.3 (d, 3H, J = 6.7 Hz, 6-CH_3), 1.4-3.3 (m, 12H, $(CH_2)_6$), 2.2 (dd, 1H, J = 13.2, 4.8 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.4, 3.5 (2d, each, 1H, J = 22.0 Hz, 1-CH_2), 7.0 (s, 1H, 9-H), 7.1 (s, 1H, 7-H).

Anal. Calcd. for $C_{18}H_{22}ClNO$: C, 71.17; H, 7.25; N, 4.61. Found: C, 70.89; H, 6.97; N, 4.38.

8-Fluoro-6-methyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo-[3,2,1-*ij*]quinoline-4,1'-cyclohexane] (**19**).

This compound was obtained in 55% yield as colorless crystals, mp 118-119° (heptane); ir: ν C=O 1697 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 14.0, 12.5 Hz, 5-H_{ax}), 1.3 (d, 3H, J = 7.0 Hz, 6-CH_3), 1.4-3.4 (m, 10H, $(CH_2)_5$), 2.5 (dd, 1H, J = 14.0, 4.5 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.4, 3.5 (2d, each, 1H, J = 22.0 Hz, 1-CH_2), 6.7 (d, 1H, J = 8.5, 1.0 Hz, 9-H), 6.8 (d, 1H, J = 10.5 Hz, 7-H); ^{13}C nmr (100 MHz): δ ≠ 172.5, 126.2, 124.3, 110.7, 110.5, 109.7, 109.5, 58.2, 38.4, 37.7, 33.4, 31.3, 25.6, 25.2, 22.5, 21.9.

Anal. Calcd. for $C_{17}H_{20}FNO$: C, 74.73; H, 7.33; N, 5.13. Found: C, 74.40; H, 7.02; N, 4.87.

6,8-Dimethyl-2-oxo-1,2,5,6-tetrahydro-4*H*-spiro[pyrrolo[3,2,1-*ij*]-quinoline-4,1'-cyclohexane] (**20**).

This compound was obtained in 75% yield as yellow crystals, mp 145-147° (heptane); ir: ν C=O 1697 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.3 (dd, 1H, J = 14.0, 11.0 Hz, 5-H_{ax}), 1.4 (d, 3H, J = 6.7 Hz, 6-CH_3), 1.4-3.4 (m, 10H, $(CH_2)_5$), 2.5 (dd, 1H, J = 14.0, 4.3 Hz, 5-H_{eq}), 2.8 (m, 1H, 6-H), 3.3, 3.5 (2d, each, 1H, J = 22.0 Hz, 1-CH_2), 6.8 (s, 1H, 9-H), 6.9 (s, 1H, 7-H).

Anal. Calcd. for $C_{18}H_{23}NO$: C, 80.30; H, 8.55; N, 5.20. Found: C, 79.97; H, 8.10; N, 4.96.

4-*N*-(α-Chloroacetyl)amino-7-methoxy-3-methylspiro[indane-1,1'-cyclohexane] (**21**).

This compound was obtained in 60% yield as colorless crystals, mp 116-117° (heptane); ir: ν NH 3247, C=O 1666, cm^{-1}; ^1H nmr (400 MHz): δ = 1.20 (dd, 1H, 2-H_{ax}), 1.27 (d, 3H, 3-CH_3), 1.34-2.31 (m, 10H, $(CH_2)_5$), 1.80 (dd, 1H, 2-H_{eq}), 3.27 (m, 1H, 3-H), 3.82 (s, 3H, OCH_3), 4.22 (s, 2H, -CH_2Cl), 6.74 (d, 1H, 6-H), 7.68 (d, 1H, 5-H), 8.15 (s, 1H, NH); ms: m/z 321 (100, $M^{+\cdot}$, ^{35}Cl), 306 (1), 290 (2), 278 (74), 265 (24), 250 (15), 238 (2), 228 (19), 214 (13), 201 (16), 185 (24), 172 (41).

Anal. Calcd. for $C_{18}H_{24}ClNO_2$: C, 67.19; H, 7.47; N, 4.35. Found: C, 67.01; H, 7.13; N, 4.03.

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