Novel Heterocycles Derived from 3-Acyloxy- and 3-Acetamidoquinuclidines

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New quinuclidine derivatives with 3-spiro annelated oxathioline, furanone, and pyrrolinone heterocycles have been synthesized from 3-mesyloxy-, 3-acetoxy-, and 3-acetamidoquinuclidine-3-carbonitrile, respectively, by treatment with base. Treatment of 3-acetamidoquinuclidine-3-carbonitrile (**3**) with potassium hydride resulted in decyanation whereas alkyllithium reagents attacked the cyano group in **3** to produce the corresponding imines. Oxidative cyclization of the *N*-benzylated derivative of **3** with palladium acetate gave the tetracyclic compound 5-acetyl-1,4-ethano-1,2,3,4,5,6-hexahydrobenzo[*c*]-1,5-naphthyridine.

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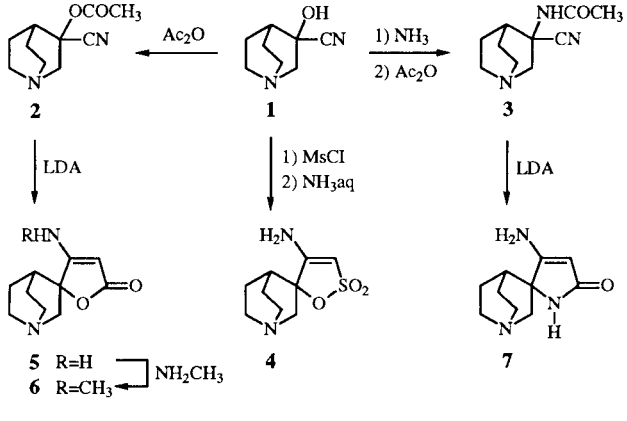
A number of spirocyclic derivatives of quinuclidine have pharmacological activities [1-5]; *e.g.* several quinuclidine-3-spiro-5'-hydantoins are anticonvulsant agents [3], whereas quinuclidine-3-spirooxolane and tetrahydrofuran derivatives exhibit antimuscarinic properties [4,5]. We now describe the synthesis of some novel derivatives of 3-spiroquinuclidine and 3-aminoquinuclidine which may be considered as potential muscarinic agents. In addition, these compounds are of potential interest as antagonists to substance P because of their structural similarity with CP 96,345, the first potent, selective and non-peptidergic NK_1-receptor antagonist [6].

The syntheses of the spirocyclic quinuclidine derivatives **4**-**7** (Scheme 1) were carried out utilizing efficient

Scheme 1

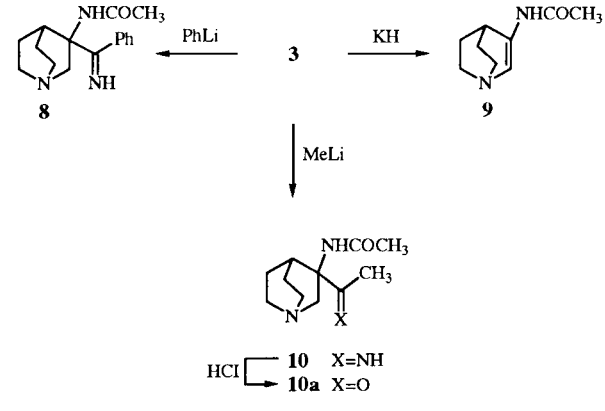


cyanohydrine transformations [7,8]. 3-Methanesulfonyloxyquinuclidine-3-carbonitrile, which was derived from cyanohydrine **1** [1], was cyclized to **4** by treatment with aqueous ammonia. Ammonia is a sufficiently strong base to deprotonize the methanesulfonyl group. Thus, it promotes an intramolecular attack of the resulting carbanion on the cyano group. Nitrile **2** was converted into the spirofuran **5** in acceptable yield (68%) on treatment with a stronger base (LDA). Compound **5** was transaminated to **6** by treatment with methylamine [9,10].

Treatment of **1** with ammonia led to amination at C-3 and subsequent reaction with acetic anhydride afforded the acetamido derivative **3**. LDA-promoted cyclization of **3** was slow and inefficient giving a low yield (8%) of the target compound **7**, the major product being quinuclidin-3-one. This result is probably a consequence of preferential deprotonation of N-3 in **3**.

To further investigate the reactivity of **3** it was treated with potassium hydride in THF, methyllithium or phenyllithium (Scheme 2). Addition of potassium hydride smoothly converted **3** to the decyanated derivative **9**, whereas the strongly nucleophilic organometallics attacked the cyano group to provide the corresponding imines **8** and **10**, respectively, in high yields (Scheme 2).

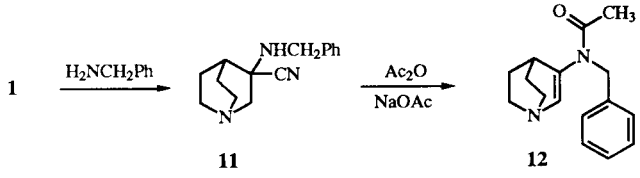
Scheme 2



In order to prevent deprotonation of the amido group of **3** and thereby improve the conversion to **7**, we decided to

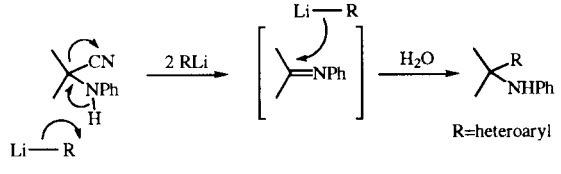
convert **3** into its *N*-benzylated derivative. Since a direct benzylation of **3** was expected to result in alkylation also on the quinuclidine nitrogen, we attempted to acetylate the benzylamino derivative **11** (Scheme 3). Common acetylation reagents (acetic anhydride in combination with either

Scheme 3



pyridine or triethylamine) smoothly acetylated **11** according to tlc but the target compound was found to be unstable and the acetyl group was lost when water was added during the work-up. Further, the use of sodium acetate in acetic anhydride at elevated temperature resulted in acetylation of **11** with a simultaneous decyanation yielding **12**. This latter observation may be related to a recently published modification of the Bruylants reaction in which a cyano group in secondary α-phenylaminonitriles is substituted for heteroaryl groups by treatment with lithiated heterocycles (Scheme 4) [11]. The Bruylants reaction proceeds *via* a Schiff base which is formed by elimination of the cyano group after addition of 1 eq of organolithium reagent. The cyano group in **11** was eliminated also under weakly basic conditions, affording **12** (Scheme 3). However, treatment of **3** with alkyllithium resulted in nucleophilic attack on the cyano group (Scheme 2).

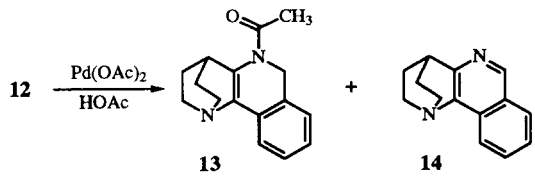
Scheme 4



The elimination product **12** underwent oxidative heterocyclization in the presence of palladium acetate [15] to produce the tetracyclic **13** in a yield of 37% (Scheme 5). The moderate yield of **13** is due to competing processes leading to further oxidation including aromatization of the fused 1,2-dihydropyridine fragment in **13** (see Experimental) and polymerization.

The present study devises convenient synthetic routes to new quinuclidine derivatives with 3-spiroannelated dihydrofuranone, pyrrolinone or oxathioline heterocycles. These compounds may be useful for further modification *e.g.* by substitution [12,13] or reduction [14] into a variety of derivatives of potential pharmacological interest.

Scheme 5



EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The ^1H nmr and ^{13}C nmr spectra were run on a JEOL JNM-EX 270 NMR spectrometer and the chemical shifts were determined relative to internal tetramethylsilane. The ^{13}C-^1H correlation experiments were carried out to assign the signals in the ^{13}C nmr spectra. Mass spectral data together with gc data were obtained using a combined Hewlett-Packard GC(5890)-MS(5791) unit. The reactions were monitored by tlc on aluminum sheets precoated with silica gel $60F_{254}$ (E. Merck) in 5, 10 or 20% methanol in dichloromethane. The elemental analyses were performed by MikroKemi AB, Uppsala, Sweden.

3-Acetamido-3-cyanoquinuclidine (**3**).

3-Cyanoquinuclidine-3-ol (**1**) [1] (1.52 g, 10 mmoles) was stirred with 25% aqueous ammonia (10 ml) at room temperature for 10 hours. The solvent was removed *in vacuo* and the residue coevaporated with acetonitrile. Acetic anhydride (4.7 ml, 50 mmoles), pyridine (25 ml) and DMAP (10 mg) were added and stirring continued for an additional 3 hours. The cooled mixture was quenched with water (10 ml), concentrated and repeatedly coevaporated with toluene *in vacuo*. The viscous residue was passed through alumina oxide using 2% methanol in chloroform as eluent to afford **3** (1.41 g, 73%), mp 143-145°; ^1H nmr (deuteriochloroform): δ 1.35-2.00 (m, 4H, 5-H's, 7-H's), 1.96 (s, 3H, Me), 2.33-2.38 (m, 1H, 4-H), 2.67-2.75 (m, 4H, 6-H's, 8-H's), 3.01 (d, 1H, J = -14.3 Hz, 2a-H), 3.41 (d, 1H, 2b-H), 7.98 (bs, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 19.0 (C-5, C-7), 22.6 (Me), 28.0 (C-4), 45.4, 45.8 (C-6, C-8), 60.5 (C-2), 76.5 (C-3), 120.9 (CN), 171.1 (C=O); ms: m/z 193 (M^+).

Anal. Calcd. for $C_{10}H_{15}N_3O$: C, 62.2; H, 7.8; N, 21.8. Found: C, 62.1; H, 7.6; N, 21.7.

Quinuclidine-3-spiro-5'-[4'-amino-Δ^3-1', 2'-oxathioline 2',2'-dioxide] (**4**).

A solution of methanesulfonyl chloride (2.34 ml, 30 mmoles) in pyridine (10 ml) was added to a solution of **1** (1. 52 g, 10 mmoles) in pyridine (10 ml) at 0°. The mixture was stirred at 0° for 5 hours and thereafter cautiously quenched with water (50 ml). The solution was concentrated *in vacuo*, made alkaline (*p*H 9) with aqueous sodium carbonate and extracted with chloroform (2 x 30 ml). The organic extract was dried (magnesium sulfate), concentrated and coevaporated with toluene. The residue was filtered through a short silica gel column using a gradient of 5-10% methanol in chloroform as eluent to yield 3-methanesulfonyloxyquinuclidine-3-carbonitrile (1.95 g, 85%) as a yellow oil; R_f 0.5 (5% methanol/chloroform); ms: m/z 230 (M^+, 4%),

151 (M^+-SO_2Me, 100%), 135 (M^+-OSO_2Me, 22%). Part of this material (0.5 g, 2.17 mmoles) was stirred with 25% aqueous ammonia (5 ml) for 12 hours at room temperature. The solvent was removed at reduced pressure to leave a solid residue which was crystallized from water to give **4** (0.41 g, 82%), mp 210° dec; ^1H nmr (deuterioacetone): δ 1.35-2.15 (m, 4H, 5-H's, 7-H's), 2.18-2.22 (m, 1H, 4-H), 2.65-2.90 (m, 4H, 6-H's, 8-H's), 2.95 (d, 1H, J = -15.0 Hz, 2a-H), 3.30 (d, 1H, 2b-H), 5.40 (s, 1H, 3'-H), 6.05 (bs, 2H, NH_2); ^{13}C nmr (deuterioacetone): δ 23.5, 24.1 (C-5, C-7), 33.7 (C-4), 46.7, 47.5 (C-6, C-8), 58.7 (C-2), 89.9 (C-3'), 90.2 (C-3), 160.8 (C-4'); ms: m/z 272 (M^+).

Anal. Calcd. for $C_9H_{14}N_2O_3S$: C, 46.9; H, 6.1; N, 12.2. Found: C, 46.6; H, 6.2; N, 12.0.

Quinuclidine-3-spiro-5'-[4'-amino-2' (5'*H*)-furanone] (**5**).

Acetic anhydride (4.7 ml, 50 mmoles) and **1** (1.52 g, 10 mmoles) were mixed in pyridine (30 ml) and DMAP (10 mg) was added. The mixture was stirred at room temperature for 10 hours, quenched with water (50 ml), and concentrated *in vacuo*. The residue was partitioned between an aqueous solution of sodium carbonate and chloroform (2 x 30 ml). The organic phase was dried (magnesium sulfate), concentrated and coevaporated with toluene to yield **2** (1.88 g, 97%) as a colourless oil, R_f 0.45 (5% methanol/chloroform). Part of this material (0.5 g, 2.58 mmoles) was dissolved in dry tetrahydrofuran (5 ml) and added dropwise to a solution of lithium diisopropylamide (2*M* in *n*-heptane/tetrahydrofuran) (1.35 ml, 2.7 mmoles) in tetrahydrofuran (5 ml) at -70°. The mixture was stirred at 0° for 30 minutes, quenched with water (50 ml) and concentrated *in vacuo*. The residue was passed through a short silica gel column using a gradient of 30-50% methanol in chloroform as eluent. The crude product was recrystallized from water to give **5** (0.34 g, 68%), mp 254-256°; ^1H nmr (10% deuteriomethanol in deuteriochloroform): δ 1.48-2.25 (m, 4H, 5-H's, 7-H's), 2.02-2.06 (m, 1H, 4-H), 2.77-3.00 (m, 4H, 6-H's, 8-H's), 3.06 (d, 1H, J = -15.0 Hz, 2a-H), 3.18 (d, 1H, 2b-H), 4.67 (s, 1H, 3'-H); ^{13}C nmr (10% deuteriomethanol in deuteriochloroform): δ 22.5, 24.4 (C-5, C-7), 32.8 (C-4), 46.9, 47.7 (C-6, C-8), 58.7 (C-2), 83.7 (C-3'), 85.1 (C-3), 176.9, 177.5 (C-2', C-4'); ms: m/z 194 (M^+).

Anal. Calcd. for $C_{10}H_{14}N_2O_2 \cdot 0.5\ H_2O$: C, 59.1; H, 7.4; N, 13.8. Found: C, 59.3; H, 7.3; N, 13.5.

Quinuclidine-3-spiro-5'-[4'-methylamino-2'(5'*H*)-furanone] (**6**).

A mixture of **5** (150 mg, 0.77 mmole) and a 40% methanolic solution of methylamine (5 ml) was heated in a closed vessel at 100-110° for 48 hours. The mixture, which still contained some residual starting material (lower R_f), was concentrated *in vacuo* and coevaporated with acetonitrile. The residue was purified on alumina oxide using 2% methanol in chloroform as eluent to give **6** (100 mg, 62%), mp 236-237°; ^1H nmr (deuteriochloroform): δ 1.37-2.24 (m, 4H, 5-H's, 7-H's), 1.98-2.01 (m, 1H, 4-H), 2.84-3.0 (m, 4H, 6-H's, 8-H's), 2.88 (d, 3H, J = 4.8 Hz, Me), 3.08 (d, 1H, J = -15.4 Hz, 2a-H), 3.17 (d, 1H, 2b-H), 4.58 (s, 1H, 3'-H), 5.57 (app bd, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 22.1, 23.2 (C-5, C-7), 31.3, 32.0 (C-4, Me), 46.2, 46.3 (C-6, C-8), 58.7 (C-2), 81.3 (C-3'), 82.9 (C-3), 173.6, 173.9 (C-2', C-4'); ms: m/z 208 (M^+).

Anal . Calcd. for $C_{11}H_{16}N_2O_2$: C, 63.5; H, 7.7; N, 13.5. Found: C, 63.6; H, 7.8; N, 13.5.

Quinuclidine-3-spiro-5'-[4'-amino-3'-pyrrolin-2'-one] (**7**).

A solution of **3** (0.3 g, 1.55 mmoles) in dry tetrahydrofuran (5 ml) was added dropwise at -20° to a solution of LDA (2*M* in *n*-heptane/tetrahydrofuran) (1.94 ml, 3.88 mmoles) in tetrahydrofuran (3 ml). The mixture was kept at room temperature under nitrogen for 4 hours before quenching with water (20 ml). The organic phase was discarded and the water phase was concentrated *in vacuo*. The residue was purified first on silica gel using a gradient of 30-100% methanol in chloroform as eluent (fractions with small R_f values were collected), and on alumina oxide using 5% methanol in chloroform as eluent to yield **7** (24 mg, 8%), mp 263° dec; ^1H nmr (10% deuteriomethanol in deuteriochloroform): δ 1.55-2.25 (m, 4H, 5-H's, 7-H's), 1.85-1.89 (m, 1H, 4-H), 2.84-3.00 (m, 4H, 6-H's, 8-H's), 2.98 (d, 1H, J = -15.8 Hz, 2a-H), 3.16 (d, 1H, 2b-H), 4.7 (s, 1H, 3'-H); ^{13}C nmr (10% deuteriomethanol in deuteriochloroform): δ 22.4, 25.0 (C-5, C-7), 32.0 (C-4), 46.6, 46.7 (C-6, C-8), 58.8 (C-2), 62.6 (C-3), 89.5 (C-3'), 172.0, 177.5 (C-2', C-4'); ms: m/z 193 (M^+).

Anal. Calcd. for $C_{10}H_{15}N_3O$: C, 62.2; H, 7.8; N, 21.8. Found: C, 62.2; H, 7.7; N, 21.7.

3-Acetamido-3-[α-iminobenzyl]quinuclidine (**8**).

A solution of **3** (0.3 g, 1.55 mmoles) in dry tetrahydrofuran (3 ml) was added dropwise to a solution of phenyllithium (2*M* in cyclohexane/ether; 0.85 ml, 1.7 mmoles) in tetrahydrofuran (3 ml) at -78° under nitrogen. The mixture was warmed to room temperature during 1 hour. The reaction was quenched with water (5 ml), concentrated under reduced pressure, and coevaporated with acetonitrile. The residue was passed through alumina oxide using 2% methanol in chloroform as eluent to give **8** (0.37 g, 87%) as a white powder. An analytical sample was prepared by recrystallization from acetone/ether (1:1), mp 161-162°; ^1H nmr (10% deuteriomethanol in deuteriochloroform): δ 1.50-2.06 (m, 4H, 5-H's, 7-H's), 1.78 (s, 3H, Me), 2.20-2.25 (m, 1H, 4-H), 2.67-3.08 (m, 4H, 6-H's, 8-H's), 2.95 (d, 1H, J = -13.6 Hz, 2a-H), 4.38 (d, 1H, 2b-H), 7.17-7.40 (m, 5H, Ph); ^{13}C nmr (10% deuteriomethanol in deuteriochloroform): δ 20.3, 21.9 (C-5, C-7), 27.6 (C-4), 44.8, 47.7 (C-6, C-8), 56.3 (C-2), 60.1 (C-3), 125.2, 127.7, 127.9, 128.3 (Ph), 170.9 (C=O), 183.1 (C=N); ms: m/z 271 (M^+).

Anal. Calcd. for $C_{16}H_{21}N_3O$: C, 70.8; H, 7.7; N, 15.5. Found: C, 70.6; H, 7.3; N, 15.2.

3-Acetamidoquinuclidin-2-ene (**9**).

A suspension of potassium hydride in mineral oil was added in portions to a stirred solution of **3** (0.3 g, 1.55 mmoles) in dry tetrahydrofuran (10 ml). Potassium hydride was added until the evolution of hydrogen ceased. The heterogeneous mixture was refluxed with stirring under nitrogen for 1 hour, cooled, cautiously quenched with water (30 ml) and extracted with chloroform (2 x 20 ml). The extract was dried (magnesium sulfate), concentrated and treated with ether to afford crystalline **9** (155 mg). The mother liquor was concentrated and the residue was passed through a short alumina oxide column using a gradient of 0-10% methanol in chloroform as eluent to remove the mineral oil. The product was treated with ether to give a total amount of 224 mg of **9** (87%), mp 136-138°; ^1H nmr (deuteriochloroform): δ 1.60-1.73 (m, 4H, 5-H's, 7-H's), 2.08 (s, 3H, Me), 2.54-2.58 (m, 1H, 4-H), 2.58-2.98 (m, 4H, 6-H's, 8-H's), 6.8 (s, 1H, 2-H), 7.85 (bs, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 23.8 (C-4), 28.4 (C-5, C-7), 30.7 (Me), 49.4 (C-6, C-8), 124.3 (C-2), 142.0 (C-3), 168.8 (C=O); ms: m/z 166 (M^+).

Anal. Calcd. for $C_9H_{14}N_2O$: C, 65.1; H, 8.4; N, 16.9. Found: C, 64.8; H, 8.2; N, 16.5.

3-Acetamido-3-(1-iminoethyl)quinuclidine (**10**) and 3-Acetamido-3-acetylquinuclidine (**10a**).

A solution of **3** (0.3 q, 1.55 mmoles) in dry tetrahydrofuran (3 ml) was treated with a solution of methyllithium (2*M* in ether, 0.85 ml, 1.7 mmoles) in tetrahydrofuran (3 ml) at -70°. The reaction mixture was worked up in a similar way to that of **8**. Purification by column chromatography using 5% methanol in chloroform as eluent gave **10** (0.29 g, 90%) mixed with 5-8% of **10a**.

Compound **10** had ^{1}H nmr (deuteriochloroform): δ 1.30-1.95 (m, 4H, 5-H's, 7-H's), 1.93 (s, 3H, Me), 1.96-1.99 (m, 1H, 4-H), 2.55-2.90 (m, 4H, 6-H's, 8-H's), 2.85 (d, 1H, J = -14.0 Hz, 2a–H), 4.12 (d, 1H, 2b-H), 7.00 (bs, 1H, NH).

The mixture was hydrolyzed with hydrochloric acid (5*N*) at room temperature during 1 hour. Evaporation of the acid and purification of the residue on alumina oxide using a gradient of 2-4% methanol in chloroform as eluent afforded **10a** (0.254 g, 78%), mp 173-175°; ^{1}H nmr (deuteriochloroform): δ 1.35-1.93 (m, 4H, 5-H's, 7-H's), 1.94-1.98 (m, 1H, 4-H), 2.0, 2.09 (2 s, 6H, Me), 2.60-2.90 (m, 4H, 6-H's, 8-H's), 2.55 (d, 1H, J = -14.0 Hz, 2a-H), 4.02 (d, 1H, 2b-H), 7.22 (bs, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 21.0, 22.7, 23.0, 24.1, 27.2 (C-5, C-7, C-4, 2 Me), 45.2, 46.5 (C-6, C-8), 56.4 (C-2), 63.2 (C-3), 170.3 (C=O, amide), 207.3 (C=O, acetyl).

Anal . Calcd. for $C_{11}H_{18}N_2O_2$: C, 62.9; H, 8.6; N, 13.3. Found: C, 62.6; H, 8.5; N, 13.1.

3-Benzylamino-3-cyanoquinuclidine (**11**).

Compound **1** (1.52 g, 10 mmoles) was stirred with a solution of benzylamine (3 ml) in 50% aqueous methanol (10 ml) at room temperature for 15 hours. The volatile components were removed *in vacuo* and the residue was coevaporated several times with pyridine and toluene to remove the benzylamine. Purification by column chromatography on silica gel using 2% methanol in chloroform as eluent gave **11** (2.02 g, 84%) as an oil; ^{1}H nmr (deuteriochloroform): δ 1.36-2.13 (m, 4H, 5-H's, 7–H's), 2.13-2.18 (m, 1H, 4-H), 2.76-2.95 (m, 4H, 6-H's, 8-H's), 2.90 (d, 1H, J = -14.0 Hz, 2a-H), 3.31 (dd, 1H, J = 1.9, -14.0 Hz, 2b-H), 3.80-3.87 (m, 2H, CH_2Ph), 7.20-7.40 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 19.1, 23.7 (C-5, C-7), 28.8 (C-4), 46.9, 47.2 (C-6, C-8), 49.2 (CH_2Ph), 56.0 (C-3), 61.6 (C-2), 122.3 (CN), 127.8, 128.6, 128.7, 139.2 (Ph); ms: m/z 241 (M^+).

Anal . Calcd. for $C_{15}H_{19}N_3$: C, 74.7; H, 7.9; N, 17.4. Found: C, 75.1; H, 8.1; N, 17.0.

3-[(*N*-Benzyl)acetamido]quinuclidin-2-ene (**12**).

A mixture of **11** (1 g, 4.15 mmoles) and anhydrous sodium acetate (0.51 g, 6.22 mmoles) in acetic anhydride (15 ml) was heated to 70-80°. The mixture became coloured; first green and thereafter brown. When the reaction was complete according to tlc (1 hour), it was carefully quenched with water (50 ml), neutralized with sodium carbonate to *p*H 9-10 and extracted with chloroform (2 x 50 ml). The organic phase was washed with water (30 ml), dried (magnesium sulfate) and concentrated *in vacuo* to give crude **12** (1.04 g, 98%) as a brown oil. The compound appeared almost homogeneous both by tlc and gc (attempted purification by column chromatography did not result in a pure compound but the yield decreased). ^{1}H nmr (deuteriochloroform): δ 1.36-1.67 (m, 4H, 5-H's, 7-H's), 2.16 (s, 3H, Me), 2.40-2.91 (m, 4H, 6-H's, 8-H's), 2.47-2.51 (m, 1H, 4-H), 4.73 (s, 2H, CH_2Ph), 6.20 (s, 1H, 2-H), 7.20-7.35 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 22.4 (Me), 29.3 (C-5, C-7) 31.9 (C-4), 49.0 (C-6, C-8), 50.0 (CH_2Ph), 127.3, 128.0, 128.4, 137.5 (Ph), 138.6 (C-2), 147.5 (C-3), 169.7 (C=O); ms: m/z 256 (M^+).

5-Acetyl-1,4-ethano-1,2,3,4,5,6-hexahydrobenzo[*c*]-1,5-naphthyridine (**13**) and 1,4-Ethano-1,2,3,4-tetrahydrobenzo[*c*]-1,5-naphthyridine (**14**).

Compound **12** (0.5 g, 1.95 mmoles) was dissolved in a 25% solution of acetic acid in acetonitrile (15 ml) and palladium acetate (0.438 g, 1.95 mmoles) was added. The mixture was refluxed with stirring for 80 hours. Monitoring of the mixture (after the work-up) by gc-ms gave **13** as the major product (around 70%) together with **14** (20%), remaining **12** (5%) and quinuclidin-3-one (5%). Also a substantial amount of a polymeric product with a low R_f value was formed. The solvents were removed under reduced pressure and the black residue was triturated with a saturated aqueous solution of sodium bicarbonate (50 ml) and chloroform (50 ml) and filtered through *Celite*. The organic phase was separated, dried (magnesium sulfate) and concentrated *in vacuo*. The residue was dissolved in ethyl acetate and the insoluble polymer was filtered off. Purification on silica gel using ethyl acetate as eluent yielded **13** (0.184 g, 37%) as an oil which slowly crystallized from hexane, mp 37-40°; ^{1}H nmr (deuteriochloroform, 50° [16]): δ 1.80-1.96 (m, 4H, 3-H's, 11-H's), 2.24 (s, 3H, Me), 2.65-3.23 (m, 4H, 2-H's, 12–H's), 3.20-3.30 (m, 1H, 4-H), 4.80 (s, 2H, 6-H), 7.10-7.56 (m, 4H; Ar); ms: m/z 254 (M^+).

Anal . Calcd. for $C_{16}H_{18}N_2O$: C, 75.6; H, 7.1; N, 11.0. Found: C, 75.9; H, 7.4; N, 11.4.

Compound **14** had ^{1}H nmr (deuteriochloroform): δ 1.80-2.20 (m, 4H, 3-H's, 11-H's), 2.60-2.73, 3.25-3.37 (m, 4H, 2-H's, 12–H's), 3.48-3.54 (m, 1H, 4-H), 7.51-7.75 (m, 2H, 8-H, 9-H), 7.98 (d, 1H, J = 8.3 Hz, 10-H), 8.10 (d, 1H, J = 8.4 Hz, 7-H), 9.08 (s, 1H, 6-H); ms: m/z 210 (M^+).

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[16] At room temperature the signal due to the methyl group in the ^{1}H nmr spectrum of **13** was broadened whereas the signals of H-4 and H-6 were split into two, presumably a result of constrained rotation in the *N*-acetyl group.