Synthesis of 7- and 5,7-Substituted-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinolines: Convenient Precursors of Quinolone Antibacterial Agents

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An original procedure to obtain substitution at the 7 or 5, 7 positions on 6-halogenated tetrahydroquinaldines is described. The title products are a new class of precursors of quinolone antibacterial agents.

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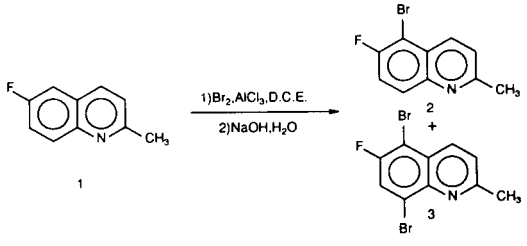
In recent years numerous antibacterial agents derived from 6,7-dihydro-9-fluoro-5-methyl-1-oxo-1*H*,5*H*-benzo-[*i*,*j*]quinolizine-2-carboxylic acid have been synthesized.

A convenient method for the synthesis of these products is the condensation of diethyl ethoxymethylenemalonate with 6-fluoro-2-methyl-1,2,3,4-tetrahydroquinolines followed by intramolecular cyclization [1].

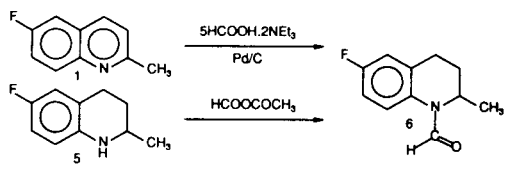
In such a synthesis it is first necessary to prepare fluorotetrahydroquinaldines correctly substituted on the aromatic ring. These compounds are generally obtained by hydrogenation, from corresponding substituted fluoroquinaldines. These last products are synthesized either by electrophilic substitution on 6-fluoroquinaldine or by a Skraup reaction from substituted 4-fluoroaniline. The use of this last method is very difficult to generalize because this reaction gives a mixture of products with polysubstituted anilines.

For the electrophilic substitution, it is well known that substitution on 6-halogenated quinolines gives only 5- or 5,8-substituted compounds [2]. By analogy with this result we have brominated 6-fluoro-2-methylquinoline (**1**) with aluminium chloride as the catalyst [3]. This reaction gives

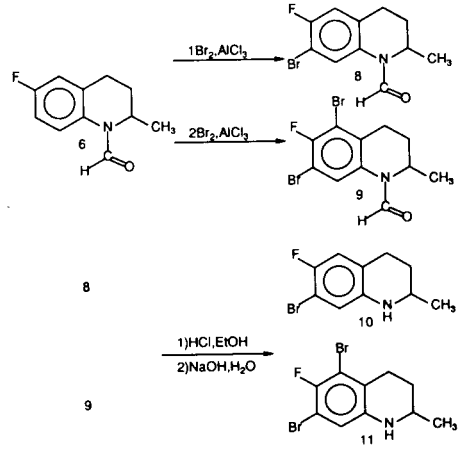
Scheme 1



Scheme 2



Scheme 3



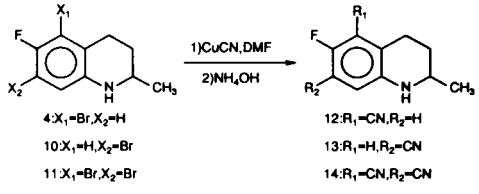
essentially 5-bromo-6-fluoro-2-methylquinoline (**2**) and a small amount (10%) of 5,8-dibromo-6-fluoro-2-methylquinoline (**3**) (Scheme 1).

This orientation results from deactivation of the pyridine ring by complexation with aluminium chloride [4], the complex obtained having a higher electron density at the 5 or 8 positions [5]. The fluorine atom has no influence on the position of substitution. In this case the corresponding tetrahydroquinaldine **4** is obtained by catalytic hydrogenation in acetic acid with platinum on activated carbon as the catalyst [3].

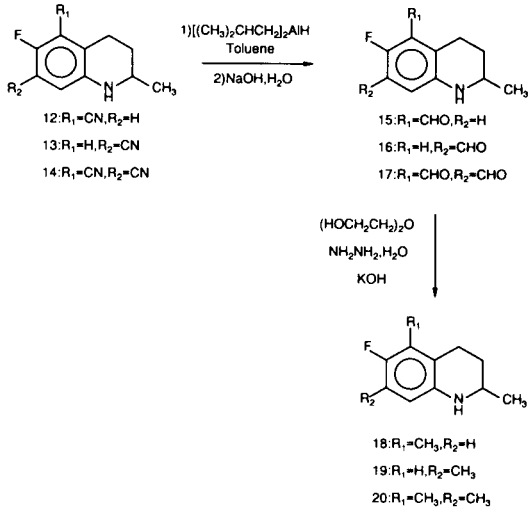
To obtain substitution at position 7 it is necessary to avoid the complexation with aluminium chloride. It is for this reason that we have chosen to synthesize the 7- and 5,7-substituted-6-fluorotetrahydroquinaldines from the 6-fluoro-1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**6**), which is obtained in two ways, either from 6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**5**) which has been *N*-formylated by acetic-formic anhydride, or from 6-fluoro-2-methylquinoline (**1**) by triethylammonium formate with palladium on activated carbon as the catalyst [6] (Scheme 2).

In the same way, the first method is applicable to the *N*-formylation of **4** to obtain 5-bromo-6-fluoro-1-formyl-2-

Scheme 4



Scheme 5



methyl-1,2,3,4-tetrahydroquinoline (**7**) in good yield.

The bromination of **6** under mild conditions (one equivalent of bromine at 45°) gives 7-bromo-6-fluoro-1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**8**). With two equivalents of bromine at 70° we obtained 5,7-dibromo-6-fluoro-1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**9**). Compounds **8** and **9** are not isolated but directly deformylated to give the corresponding tetrahydroquinaldines **10** and **11** (Scheme 3).

By the direct dibromation reaction we obtained an important part (approximately 45%) of a mixture of 5,8- and 7,8-dibromo derivatives. To decrease the proportion of these two products, we have brominated compound **7** under monobromation conditions. This reaction gives easily purified **11** in better yield.

The position of the bromine atom in **4** and **10** is confirmed by ^{1}H nmr. For compound **4**, the protons at 7 and 8 are in the *ortho* position and give, respectively, three and four peaks. This figure is the consequence of a spin-spin coupling between the two protons and the coupling between each proton and the fluorine atom. For compound **10** the protons in **5** and **8** are in the *para* position and the coupling constant H_5-H_8 is not observable; each proton gives only two peaks.

After obtaining these new substituted tetrahydroquinolines, we used the specific mobility of the bromine atom to obtain nucleophilic substitution. For this, we have utilized a Rosenmund-von Braun reaction with copper(I) cyanide in *N,N*-dimethylformamide. This reaction gives the corresponding cyano compounds, in all cases in good yields (Scheme 4).

This process of functionalization is a good alternative, in comparison with a direct alkylation reaction, to create a C-C bond on quinaldine or its derivatives.

We have also studied the reactivity of the cyano group in the presence of several reducing agents. In all cases this group has poor reactivity except for the diisobutylaluminium hydride which gives the corresponding aldehydes in very good yields [7]. This formyl group is also reduced by a Wolff-Kischner procedure to obtain the methylated tetrahydroquinaldines in excellent yields (Scheme 5).

Recently we have applied this general procedure to obtain 7-bromo-6-fluoro-2,5-dimethyl-1,2,3,4-tetrahydroquinoline from **18**.

According to those described above, the *N*-formyltetrahydroquinaldines permit us to obtain an improved functionalization at the 10 or the 8,10 positions in the synthesis of 6,7-dihydro-9-fluoro-5-methyl-1-oxo-1*H*,5*H*-benzo[i,j]-quinolizine-2-carboxylic acid. The application of this methodology for other electrophilic substitutions is currently under study.

EXPERIMENTAL

Melting points were determined on a Leitz 350 microscope hot stage and are uncorrected. The ir spectra of solids were recorded in potassium bromide pellets and liquids as thin film between sodium chloride plates on a Perkin-Elmer 297 spectrophotometer. The ^{1}H nmr spectra were recorded on a Brucker AM 300 W.B. (300.134 MHz) with TMS as the internal standard. The oils or the low melting point products were purified by column chromatography on silica gel with chloroform or chloroform/-methanol as the eluents.

5-Bromo-6-fluoro-2-methylquinoline (**2**).

To a solution of 4.83 g (0.03 mole) of 6-fluoro-2-methylquinoline in 18 ml of dry 1,2-dichloroethane is added first at 5°, 8 g (0.06 mole) of aluminium chloride then 5.28 g (0.033 mole) of bromine. During the addition the temperature rises spontaneously to 60°. This temperature is maintained during 3 hours, then cooled to 0° and a mixture of 40 ml of 30% aqueous sodium hydroxide and 10 ml of 1,2-dichloroethane is added slowly. The aqueous layer is removed and the 1,2-dichloroethane is flash distilled. The crude oil **2** is dissolved in 50 ml of 10% hydrochloric acid, then extracted with 10 ml of 1,2-dichloroethane to eliminate the 5,7-dibromo-6-fluoro-2-methylquinoline hydrochloride. The 5-bromo-6-fluoro-2-methylquinoline is obtained after alkalinization, filtration and washing with water, yield 5.67 g (80%), mp 95°; ^{1}H nmr (deuteriochloroform): δ 2.7 (s, 3H, -CH_3), 7.3-8.5 (m, 4H, Ar-H).

Anal. Calcd. for $C_{10}H_7BrFN$: C, 50.00; H, 2.92; N, 5.83. Found: C, 49.85; H, 2.93; N, 5.84.

5-Bromo-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**4**).

Compound **2** (5 g, 0.021 mole) is hydrogenated in a Parr apparatus in glacial acetic acid (20 ml) with 150 mg of platinum on activated carbon (5%) as the catalyst. The catalyst is filtered from the mixture and the filtrate evaporated *in vacuo*. The residue is mixed with 30% aqueous sodium hydroxide and the tetrahydroquinaldine **4** is extracted with diethyl ether. The organic layer is washed with water and dried over anhydrous magnesium sulfate. The drying agent is removed by filtration and the diethyl ether removed by flash distillation. The product **4** is obtained as an oil, yield 4.83 g (95%); ir: 3400 (N-H); cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.4-2 (m, 2H, H3), 2.5-2.9 (m, 2H, H4), 2.9-3.4 (m, 1H, H2); 3.4-3.9 (m, 1H, N-H), 6-6.8 (m, 2H, Ar-H).

Anal. Calcd. for $C_{10}H_{11}BrFN$: C, 49.18; H, 4.51; N, 5.74. Found: C, 49.16; H, 4.52; N, 5.72.

6-Fluoro-1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**6**).

Method A.

To cooled acetic anhydride (13.2 ml, 0.14 mole 0°) is slowly added 2.6 ml (0.07 mole) of formic acid followed by heating at 50° for 15 minutes, then cooled immediately to 0°. Then add 10 g (0.06 mole) of **5** followed to reflux during 2 hours, followed distillation to dryness. The residue is dissolved in 1,2-dichloromethane (100 ml), washed twice with with 20 ml of 10% hydrochloric acid and twice with water. The organic layer is dried with magnesium sulfate and after evaporation of the solvent compound **6** is crystallized from diisopropyl ether.

Method B.

A mixture of 16.1 g (0.1 mole) of **1**, 50 ml of triethylammonium formate and 0.3 g of palladium on charcoal (5%) is heated. The triethylamine formed is distilled during the reaction. The residue is dissolved in 1,2-dichloromethane, the catalyst filtered and the organic layer washed twice with 20 ml of 10% hydrochloric acid and twice with water, then dried magnesium sulfate. After evaporation of the solvent compound **6** is crystallized from diisopropyl ether, yield method A, 8.22 g (71%), method B, 16.4 (85%), mp 65°; ir: 1670 (C=O) cm^{-1}; ^1H (deuteriochloroform): δ 1.1 (d, J = 6 Hz, 3H, CH_3), 1.3-2.3 (m, 2H, H3), 2.5-2.8 (m, 2H, H4), 4.5-4.9 (m, 1H, H2), 6.7-7.1 (m, 3H, Ar-H), 8.6 (s, 1H, HCO).

Anal. Calcd. for $C_{11}H_{12}FNO$: C, 68.39; H, 6.21; N, 7.25. Found: C, 68.43; H, 6.19; N, 7.22.

5-Bromo-6-fluoro-1-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**7**).

The general procedure is the same as the one described for the synthesis of **6**, method A, yield 89%, colourless oil; ir: 1670 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.4-2.3 (m, 2H, H3) 2.5-3 (m, 2H, H4), 4.6-5 (m, 1H, H2), 6.8-7.2 (m, 2H, Ar-H), 8.6 (s, 1H, H-CO).

Anal. Calcd. for $C_{11}H_{11}BrFNO$: C, 48.53; H, 4.04; N, 5.15. Found: C, 48.50; H, 4.00; N, 5.13.

7-Bromo-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**10**).

Compound **6** (5.5 g, 0.028 mole) is dissolved in 25 ml of 1,2-dichloroethane, cooled to 0° and 6.8 g (0.05 mole) of aluminium chloride is added followed by 5 g (1.6 ml, 0.03 mole) of bromine. The temperature is maintained between 0 and 5° during the addition. It is then warmed 2 hours at 45°, cooled to 0° and 10 g of crushed ice is added cautiously then 35 ml of 10% hydrochloric acid. It is extracted twice with 50 ml of dichloromethane then flash distilled to dryness. The residue is refluxed during 2 hours with 30 ml of 10% hydrochloric acid and 10 ml of ethyl alcohol, cooled to 0° and filtered to provide 7-bromo-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline hydrochloride. The corresponding free base is obtained by stirring with 30% aqueous sodium hydroxide and extraction with dichloromethane, yield 4.78 g (77%) of colourless oil; ir: 3400 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.3-2 (m, 2H, H3), 2.5-2.8 (m, 2H, H4), 3-3.4 (m, 1H, H2), 3.4-3.6 (m, 1H, N-H), 6.5-6.8 (m, 2H, Ar-H).

Anal. Calcd. for $C_{10}H_{11}BrFN$: C, 49.18; H, 4.51; N, 5.74. Found: C, 49.21; H, 4.53; N, 5.73.

5,7-Dibromo-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**11**).

From **6**.

The general procedure is the same as the one described for the synthesis of **10**. The reaction is carried out at 70° with 2 equivalents of bromine. Compound **11** is recrystallized from cyclohexane, yield 53%.

From **7**.

The general procedure is the same as the one described for the synthesis of **10**, yield 83%, mp 84°; ir: 3420 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.3-2.3 (m, 2H, H3), 2.5-2.9 (m, 2H, H4), 3.1-3.5 (m, 1H, H2), 3.6 (m, 1H, N-H), 6.5 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{10}H_{10}Br_2FN$: C, 37.15; H, 3.09; N, 4.33. Found: C, 37.12; H, 3.07; N, 4.35.

General Procedure for the Rosenmund-von Braun Reaction.

A mixture of 0.09 mole of brominated derivative, 0.9 g (0.1 mole) of copper(I) cyanide and 70 ml of dry *N,N*-dimethylformamide is refluxed for 3 hours, then 500 ml of water in added and filtered. The precipitate is triturated with 300 ml of concentrated ammonium hydroxide and extracted twice with 150 ml of dichloromethane, then the organic layer is washed with 100 ml of concentrated ammonium hydroxide and then washed twice with water. The organic solution is dried over magnesium sulfate then flash distilled to dryness. The cyano compounds are recrystallized from cyclohexane.

5-Cyano-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**12**).

The yield is 86%, mp 74-76°; ir: 3400 (N-H), 2230 (CN) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.3-2 (m, 2H, H3), 2.5-3 (m, 2H, H4), 3-3.5 (m, 1H, H2), 3.8 (m, 1H, N-H), 6.3-7.6 (m, 2H, Ar-H).

Anal. Calcd. for $C_{11}H_{11}FN_2$: C, 69.47; H, 5.79; N, 14.74. Found: C, 69.51; H, 5.80; N, 14.75.

7-Cyano-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**13**).

The yield is 66%, mp 118°; ir: 3390 (N-H), 2230 (CN) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.3-2.2 (m, 2H, H3), 2.6-3 (m, 2H, H4), 3.1-3.8 (m, 2H, H2, N-H), 6.5-6.8 (m, 2H, Ar-H).

Anal. Calcd. for $C_{11}H_{11}FN_2$: C, 69.47; H, 5.79; N, 14.74. Found: C, 69.49; H, 5.77; N, 14.78.

5,7-Dicyano-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**14**).

The yield is 62%, mp 134°; ir: 3380 (N-H), 2240 (CN) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.5-2.1 (m, 2H, H3), 2.8-3.1 (m, 2H, H4), 3.3-3.5 (m, 1H, H2), 4-4.2 (m, 1H, N-H), 6.8 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{12}H_{10}FN_3$: C, 66.98; H, 4.65; N, 19.53. Found: C, 67.03; H, 4.60; N, 19.58.

General Procedure for the Reduction of Cyano Groups.

The cyano derivative (0.022 mole) is dissolved under nitrogen in 40 ml of dry toluene, cooled to 0°, and 20 ml of solution of diisobutylaluminium hydride (1 *M* in toluene) is added dropwise. The temperature is maintained under 10° during the addition, then warmed 2 hours at 45° then cooled to 0°. A solution of 1.2 ml of methyl alcohol in 8 ml of toluene is added followed by a solution of 0.4 ml of water in 8 ml of methyl alcohol. The precipitate is filtered and washed with dichloromethane. The solvents are flash distilled and the residue dissolved in 30 ml of 10% hydrochloric acid, then extracted with 10 ml of diethyl ether and the solution poured into 15 ml of 30% aqueous sodium hydroxide and then cooled at 0°. It is filtered and washed with water. The crude aldehydes are dried by azeotropic distillation in cyclohexane and recrystallized from the same solvent.

6-Fluoro-5-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**15**).

The yield is 92%, mp 71°; ir: 3380 (N-H), 1670 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.4-2.1 (m, 2H, H3), 2.5-3.8 (m, 4H, H4, H2, N-H), 6.5-7 (m, 2H, Ar-H), 10.4 (s, 1H, CHO).

Anal. Calcd. for $C_{11}H_{12}FNO$: C, 68.39; H, 6.21; N, 7.25. Found: C, 68.35; H, 6.18; N, 7.20.

6-Fluoro-7-formyl-2-methyl-1,2,3,4-tetrahydroquinoline (**16**).

The yield is 83%, mp 80°; ir: 3340 (N-H), 1670 (C=O) ^1H nmr (deuteriochloroform); δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.3-2 (m, 2H, H3), 2.6-2.9 (m, 2H, H4), 3.1-3.8 (m, 2H, H2, N-H), 6.5-6.9 (m, 2H, Ar-H), 10.1 (s, 1H, -CHO).

Anal. Calcd. for $C_{11}H_{12}FNO$: C, 68.39; H, 6.21; N, 7.25. Found: C, 68.35; H, 6.25; N, 7.20.

5,7-Diformyl-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**17**).

The yield is 77%, mp 136°; ir: 3390 (N-H), 1670 cm^{-1}; (C=O) ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3), 1.4-2.1 (m, 2H, H3), 2.9-3.5 (m, 4H, H4, H2, N-H), 7.1 (d, J = 6 Hz, 1H, Ar-H), 10.3 (s, 1H, CHO at 7), 10.5 (s, 1H, CHO at 5).

Anal. Calcd. for $C_{12}H_{12}FNO_2$: C, 65.16; H, 5.43; N, 6.33. Found: C, 65.05; H, 5.48; N, 6.35.

General Procedure for the Wolff-Kishner Reduction.

A mixture of 0.01 mole of formyl derivative, 12 ml of diethylene glycol, 1.2 ml of hydrazine monohydrate and 1.6 g of potassium hydroxide is heated at 80° during 1 hour then refluxed 2 hours. The mixture is poured into 60 ml of water and the methylated compound extracted with diethyl ether. The organic layer is washed with water, dried over magnesium sulfate, filtered and flash distilled.

2,5-Dimethyl-6-fluoro-1,2,3,4-tetrahydroquinoline (**18**).

The yield is 97%, colorless oil, ir: 3400 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.4-2 (m, 2H, H3), 2.1 (d, J = 2.1 Hz, 3H, CH_3 at 5), 2.5-2.9 (m, 2H, H4), 3-3.7 (m, 2H, H2, N-H), 6-7 (m, 2H, Ar-H).

Anal. Calcd. for $C_{11}H_{14}FN$: C, 73.74; H, 7.82; N, 7.82. Found: C, 73.70; H, 7.81; N, 7.75.

6-Fluoro-2,7-dimethyl-1,2,3,4-tetrahydroquinoline (**19**).

The yield is 93%, mp <50°; ir: 3370 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.5-2 (m, 2H, H3), 2.1 (d, J = 1.6 Hz, 3H, CH_3 at 7), 2.4-2.9 (m, 3H, H4, N-H), 3.2-3.4 (m, 1H, H2), 6.2-6.7 (m, 2H, Ar-H).

Anal. Calcd. for $C_{11}H_{14}FN$: C, 73.74; H, 7.82; N, 7.82. Found: C, 73.81; H, 7.85; N, 7.78.

6-Fluoro-1,2,3,4-tetrahydro-2,5,7-trimethylquinoline (**20**).

The yield is 51%, colorless oil; ir: 3390 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.5-2 (m, 2H, H3), 2-2.2 (m, 6H, CH_3 at 5 and 7), 2.3-2.8 (m, 3H, H4, N-H), 3.2-3.4 (m, 1H, H2), 6.2 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{12}H_{16}FN$: C, 74.61; H, 8.29; N, 7.25. Found: C, 74.55; H, 8.30; N, 7.21.

2,5-Dimethyl-6-fluoro-1-formyl-1,2,3,4-tetrahydroquinoline (**21**).

The general procedure is the same as the one described for the synthesis of **6**, method A, yield 88%, mp <50°; ir: 1680 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.3-2 (m, 2H, H3), 2.2 (d, J = 2 Hz, CH_3 at 5), 2.5-3 (m, 2H, H4), 4.6-5.1 (m, 1H, H2), 7 (m, 2H, Ar-H), 8.7 (s, 1H, CHO).

Anal. Calcd. for $C_{12}H_{14}FNO$: C, 69.56; H, 6.76; N, 6.76. Found: C, 69.60; H, 6.71; N, 6.82.

7-Bromo-2,5-dimethyl-6-fluoro-1,2,3,4-tetrahydroquinoline (**22**).

The general procedure is the same as the one described for the synthesis of **10**, yield 55% colourless, oil; ir: 3400 (N-H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.4-2 (m, 2H, H3), 2.1 (d, J = 2 Hz, CH_3 in 5), 2.4-2.8 (m, 2H, H4), 3-3.8 (m, 2H, H2, N-H), 6.5 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{11}H_{13}BrFN$: C, 51.16; H, 5.04; N, 5.43. Found: C, 51.06; H, 4.98; N, 5.51.

7-Cyano-2,5-dimethyl-6-fluoro-1,2,3,4-tetrahydroquinoline (**23**).

See the general procedure for the Rosenmund-von Braun reaction; the yield is 55%, mp 103°; ir: 3400 (N-H), 2230 (CN), cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.4-2 (m, 2H, H3), 2.1 (d, J = 2 Hz, CH_3 at 5), 2.4-2.8 (m, 2H, H4), 3-3.8 (m, 2H, H2, N-H), 6.4 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{12}H_{13}FN_2$: C, 70.59; H, 6.37; N, 13.72. Found: C, 70.71; H, 6.41; N, 13.78.

7-Formyl-2,5-dimethyl-6-fluoro-1,2,3,4-tetrahydroquinoline (**24**).

See the general procedure for the reduction of cyano group; the yield is 75%, mp 62°; ir: 3400 (N-H) 1680 cm^{-1}; (C=O) ^1H nmr (deuteriochloroform): δ 1.2 (d, J = 6 Hz, 3H, CH_3 at 2), 1.4-2 (m, 2H, H3), 2.1 (d, J = 2 Hz, CH_3 at 5), 2.4-2.8 (m, 2H, H4), 3-3.8 (m, 2H, H2, N-H), 6.7 (d, J = 6 Hz, 1H, Ar-H).

Anal. Calcd. for $C_{12}H_{14}FNO$: C, 69.56; H, 6.76; N, 6.76. Found: C, 69.62; H, 6.59; N, 6.91.

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