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Reaction of N^1,N^2-Diarylacetamidines with Ethyl 2-Oxoindolin-3-ylidenecyanoacetate and Benzylidenemalononitriles

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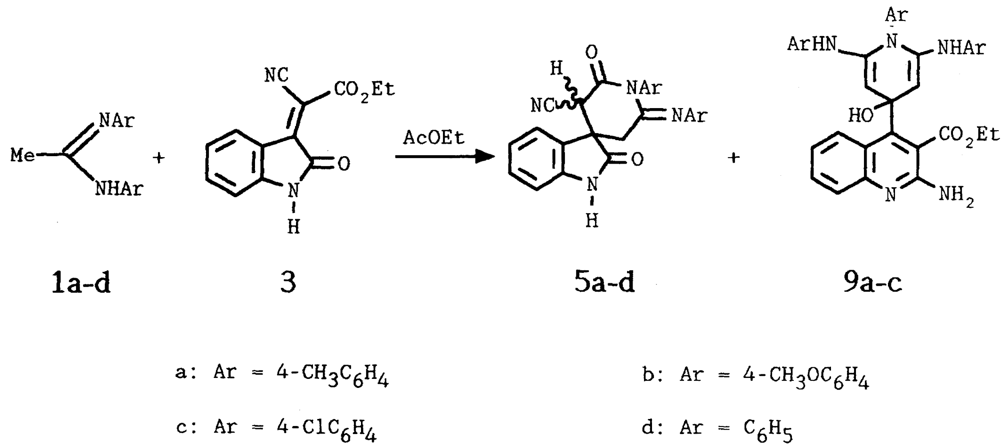
1′-Aryl-6′-arylimino-2,2′-dioxospiro[(2,3-dihydro-1*H*-indole)-3,4′-perhydropyridine]-3′-carbonitriles **5a**—**d** together with ethyl 2-amino-4-[1-aryl-2,6-bis(arylamino)-4-hydroxy-1,4-dihydro-4-pyridyl]quinoline-3-carboxylate **9a**—**c** were obtained from the reaction of N^1,N^2-diarylacetamidines **1a**—**d** with ethyl 2-oxoindoline-3-ylidenecyanoacetate **3**. Acetamidines **1a**—**c** also reacted with the benzylidenemalononitriles **10a**—**d** to afford the adducts 1,4,5,6-tetrahydropyridines **13a**—**f**.

Spiro[3*H*-indole-3,4′-pyridines] are of great biological importance and have shown anticonvulsant, antidepressant tranquilizing, central-nerve inhibiting, analgesic, antihypertensive, antirheumatic, local anesthetic, hypotensive, antiinflammatory, and ganglion blocking activities.(1) Much effort has been undertaken to synthesize many derivatives of these compounds.(1) Joshi et al. have reported that benzamidine hydrochloride reacts with ethyl 2-oxoindoline-3-ylidenecyanoacetate **3** to afford spiro[3*H*-indole-3,4′(3′*H*)-pyrimidine]-5′-carboxylic acid ethyl ester together with a fused system [1,3]-diazepino[4,5-*b*]indole.(2) Recently we succeeded to prepare spiro[indole-3,4′-pyridines] in good yield by reacting N^1,N^2-diarylacetamidines with 2-(2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)propanedinitrile.(3) This prompted us to extend our work and to synthesize new spiro[3*H*-indole-3,4′-pyridines].

N^1,N^2-Diarylacetamidines **1a**—**d** reacted with ethyl 2-oxoindoline-3-ylidenecyanoacetate **3** in ethyl acetate under reflux for 9 h to furnish 2,2′-dioxospiro[(2,3-dihydro-1*H*-indol)-3,4′-perhydropyridine]-3′-carbonitriles **5a**—**d** in 40—58% yield together with ethyl 2-amino-4-[1-aryl-2,6-bis(arylamino)-4-hydroxy-1,4-dihydro-4-pyridyl]quinoline-3-carboxylate derivatives **9a**—**c** in 36—40% yield (Scheme 1).

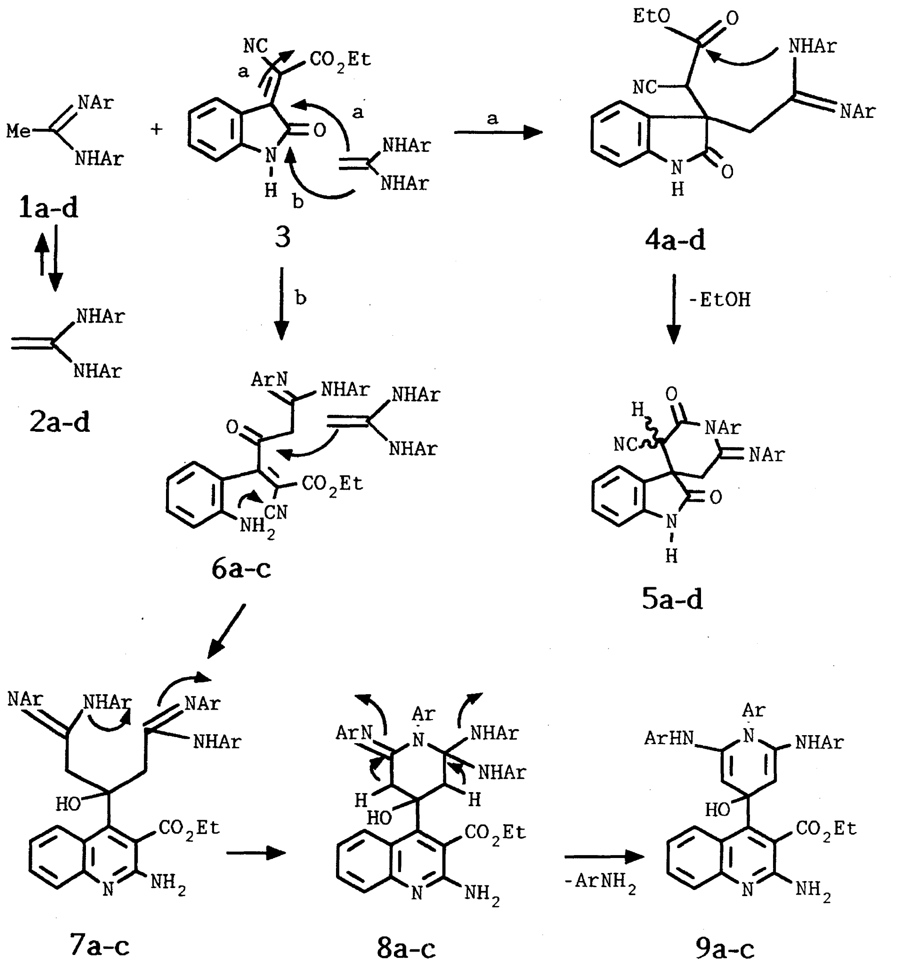
The IR spectra of the spiro compounds **5a**—**d** showed absorptions at 1740 and 1690 cm^{-1} for the two carbonyl groups, but no cyano group was influenced by electron-attracting substituents.(4) The ^{1}H NMR spectra showed **5a**—**d** to be a mixture of diastereoisomers. AB-Patterns with δ_A in the range 3.01—3.30 and δ_B between 3.37 and 3.55 ppm with $|^2J|$-values between 17.46 and 17.54 Hz were assigned to the C-5′ methylene group adjacent to the chiral spiro carbon atom in addition to signals between 5.11 and 5.35 for the proton of C-3′ and between 10.95 and 11.05 ppm for the NH. The ^{13}C DEPT spectra showed signals with a negative amplitude over the range between 34.42 and 34.90 ppm, thus confirming the presence of a CH_2 group, and ^{13}C signals between 41.21 and 41.99 were assigned to the spiro carbon atoms. The structure of compounds **9a**—**c** was elucidated on the basis of elemental analysis and spectral data.



Scheme 1.

The IR spectra of **9a**—**c** showed absorptions between 3450 and 3420 for (OH), 3382—3360 for (NH_2), 3213—3210 for (NH), and 1720 cm^{-1} for the carbonyl group. The ^1H NMR spectra showed that signals between 0.81—0.92 ppm can be assigned to the ester methyl group and between 3.65—3.73 ppm can be assigned to the ester methylene group and between 6.60—7.0 ppm for the olefinic protons (H-3′ and H-5′) of the pyridine nucleus. The difference in the chemical shift of these two olefinic protons is due to the atropisomerism. In these molecules, i.e. **9a**—**c**, the ester group is large enough to be impeded by the *ortho*-hydrogen atoms of the pyridine nucleus; this steric effect results in a restricted rotation around the pyridyl-quinoline C–C single bond. The ^{13}C DEPT spectra showed signals with negative amplitude over the range between 58.11 and 59.61 for the methylene carbon atom of the ester and ^{13}C-signals between 80.75 and 82.48 were assigned for the quaternary carbon atom (C-4′). A further confirmation of the products **9a**—**c** was obtained from a correct elemental analysis. The formation of spiro compounds **5a**—**d** may be rationalized as follows (Scheme 2). In route a an initial nucleophilic attack by the terminal methylene carbon atom of the tautomer **2a**—**d** (being in equilibrium with **1a**—**d**)[5,6] on the C-3 of the indoline moiety gives **4a**—**d**. The amino group of the latter attacks the ester carbonyl carbon atom, followed by liberation of an ethanol molecule to give **5a**—**d**. However the formation of the **9a**—**c** through route b can also be rationalized as being an initial attack by the terminal methylene carbon atom of **2a**—**c** on the indoline C=O of **3** to give **6a**—**c** which may be attacked by another molecule of **2a**—**c**, giving rise to **7a**—**c**. Thereby the latter undergoes the elimination of an amine molecule to afford **9a**—**c**. A ring enlargement of indolinylidenemalononitriles into quinolines was recently reported.[7]

Based on our pervious work,[3] the addition of the amino nitrogen atom of the acetamidine moiety on the cyano group of **3** should be expected, rather than an attack on the ester carbonyl group of **3**, resulting in another alternative spiro structure related to **5a**—**d**. However, the absence of the



a: Ar = $4\text{-}CH_3C_6H_4$

b: Ar = $4\text{-}CH_3OC_6H_4$

c: Ar = $4\text{-}ClC_6H_4$

d: Ar = C_6H_5

Scheme 2.

protons of the ester group in ^{1}H NMR and the difference in the number of signals in ^{13}C NMR excluded this alternative spiro structure. From the above findings it may be appropriate to use acetamidines **1a—c** to synthesize the tetrahydropyridine derivatives by reacting the former **1a—c** with the open-chain benzylidenemalononitriles **10a—d**. Thus, equimolar amounts of **1a—c** and benzylidenemalononitriles **10a—d** were kept in an ethyl acetate solution at reflux for 3—12 h to afford solid products of tetrahydro-2-aminopyridines **13a—f** in 16—57% yield (Scheme 3).

The structure of **13a—f** was assigned on the basis of the spectral data. ^{1}H NMR spectra showed the AB part of ABX with δ_A = 2.72—2.80 and δ_B = 2.81—2.90 ppm with $|^2J|$ = 14 Hz, which indicates that a methylene carbon atom is adjacent to a chiral carbon atom and the X part is between δ_X = 3.74—3.82 ppm with $|^3J|$ = 7 Hz for H-4. In the case of the alternative structure **14**, it would be difficult to assign these signals. The IR spectra of **13a—d** exhibited characteristic absorptions for the amino groups between 3490 and 3200 and between 2200 and 2180 cm^{-1} for the cyano group.

The formation of 2-aminotetrahydropyridines **13a—d** can be rationalized as an initial nucleophilic attack by the terminal methylene carbon atom (of the tautomer **2a—c**) on the β-carbon atom of **10a—d** to give **11a—f** (Scheme 4). The amino group of the latter attacks one of the two cyano groups of the benzylidenemalononitrile moiety forming **12a—f**, which is ultimately isolated as **13a—f**.

Conclusion

The results show that the acetamidines used in this study behave like keten aminals or enamines[6)] in a Michael-type addition towards the ylidene malononitrile derivatives. Therefore, acetamidines as **1a—d** allow for the synthesis of new spiropyridne derivatives, 4-pyridylquinoline derivatives and tetrahydropyridine derivatives.

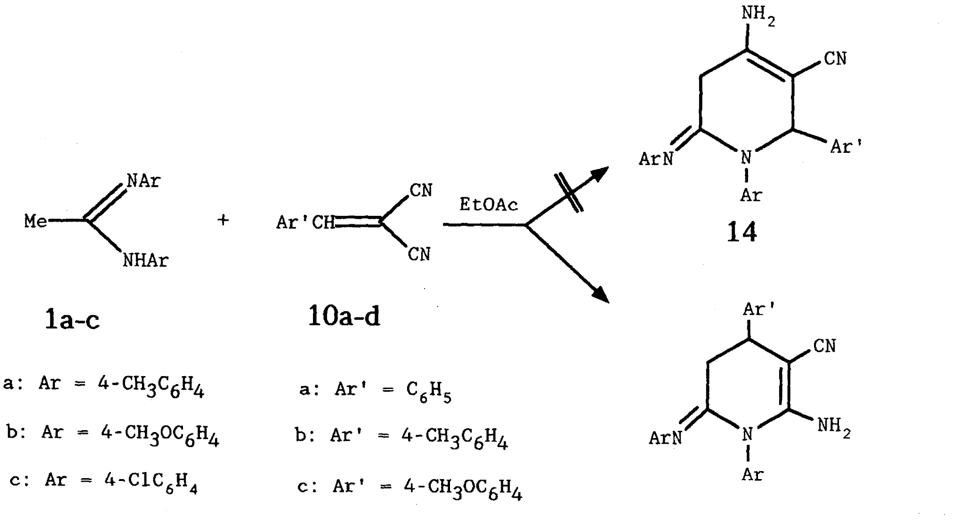
Experimental

The melting points were determined on a Griffin & Georg melting-point apparatus and are uncorrected. IR spectra were obtained on a Shimadzu 470 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a Bruker WM 300 spectrometer (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) with TMS as an internal standard. The mass spectra were obtained on an AMD 604 spectrometer operating at 70 eV. Elemental analyses were performed using a Carlo Erba 1106 CHN analyzer.

Preparative-layer chromatography (PLC): 48 cm wide and 20 cm tall glass plates covered with 1-mm thick layer of slurry, air dried silica gel Merck PF_{254}.

Starting materials: ethyl 2-oxoindoline-3-ylidenecyanoacetate **3**,[8)] benzylidenemalononitriles **10a—d**,[9)] and N^1,N^2-diarylacetamidines **1a—d**[10)] were prepared according to quoted literature procedures.

Reaction of N^1,N^2-Diarylacetamidines 1a—d with 3. (General procedure). A solution of **3** (242 mg, 1.0 mmol) in ethyl acetate (20 cm^3) was added to solutions of **1a—d** (1.0 mmol) in ethyl acetate (10 cm^3). The mixtures were heated to reflux temperature



1a-c

a: Ar = 4-$CH_3C_6H_4$
b: Ar = 4-$CH_3OC_6H_4$
c: Ar = 4-ClC_6H_4

10a-d

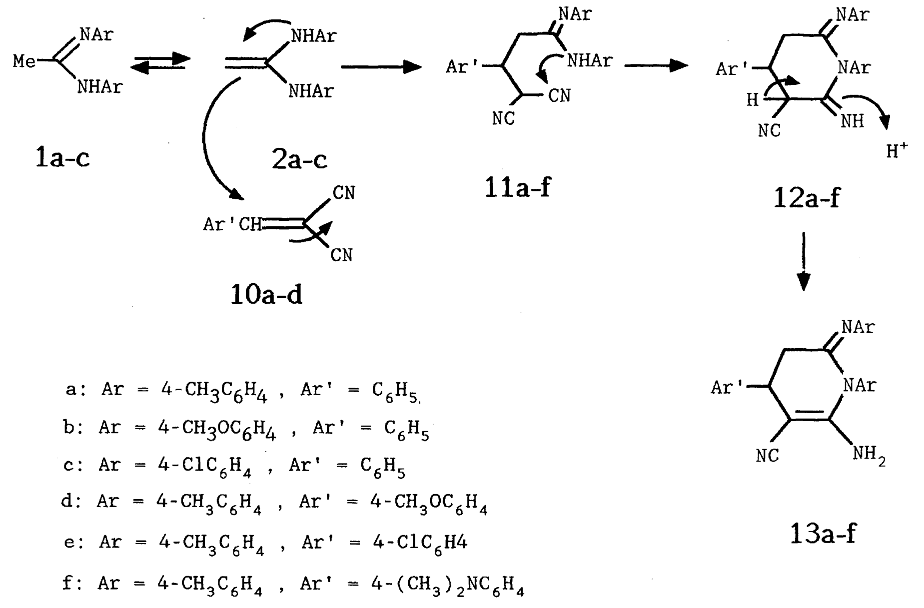
a: Ar' = C_6H_5
b: Ar' = 4-$CH_3C_6H_4$
c: Ar' = 4-$CH_3OC_6H_4$
d: Ar' = 4-$(CH_3)_2NC_6H_4$

14

13a-f

a: Ar = 4-$CH_3C_6H_4$, Ar' = C_6H_5
b: Ar = 4-$CH_3OC_6H_4$, Ar' = C_6H_5
c: Ar = 4-ClC_6H_4 , Ar' = C_6H_5
d: Ar = 4-$CH_3C_6H_4$, Ar' = 4-$CH_3OC_6H_4$
e: Ar = 4-$CH_3C_6H_4$, Ar' = 4-ClC_6H_4
f: Ar = 4-$CH_3OC_6H_4$, Ar' = 4-$(CH_3)_2NC_6H_4$

Scheme 3.



a: Ar = 4-$CH_3C_6H_4$, Ar' = C_6H_5

b: Ar = 4-$CH_3OC_6H_4$, Ar' = C_6H_5

c: Ar = 4-ClC_6H_4 , Ar' = C_6H_5

d: Ar = 4-$CH_3C_6H_4$, Ar' = 4-$CH_3OC_6H_4$

e: Ar = 4-$CH_3C_6H_4$, Ar' = 4-ClC_6H4

f: Ar = 4-$CH_3C_6H_4$, Ar' = 4-$(CH_3)_2NC_6H_4$

Scheme 4.

for 9 h. After this period, colorless crystals of **5a**—**d** precipitated, which were filtered and crystallized from ethyl acetate. The filtrates were concentrated and the residues were subjected to PLC using toluene/ethyl acetate (2 : 1) as the developing solvent, to give one or two main zones. The faster moving one contained **9a**, **9b**, or **9c**, respectively, while the more slowly moving zone contained **5a**, **5b**, **5c**, or **5d**, respectively, as mixtures of two diastereoisomers. In documentations of their ^{1}H and ^{13}C NMR spectra, the chemical shifts of the major isomers are given first, where applicable. Additional minor zones were discarded. The zones were extracted, crystallized, and identified as follows:

1′-(4-Methylphenyl)-6′-(4-methylphenylimino)-2,2′-dioxospiro[(2,3-dihydro-1*H*-indol)-3,4′-perhydropyridine]-3′-carbonitrile (5a). Colorless crystals (240 mg, 55%), mp 270—272 °C (from ethyl acetate). Found: C, 74.59; H, 5.15; N, 12.65%. Calcd for $C_{27}H_{22}N_4O_2$: C, 74.63; H, 5.10; N, 12.89%. IR ν_{max} (KBr) 1740 and 1690 cm^{-1} (CO); ^{1}H NMR (300 MHz, $[^2H_6]$-DMSO) δ_H = 2.15, 2.20 (3H, s, CH_3), 2.40, 2.45 (3H,s, CH_3), 3.01, 3.26 (1H, d), 3.37, 3.54 (1H, d, J = 17.54 Hz, 1-CH_2), 5.15, 5.25 (1H, s, 3′-H), 6.75, 6.95, 7.05, 7.11, 7.13, 7.20, 7.23, 7.28, 7.30, 7.36, 7.38, 7.42, and 7.50 (12H, all m, aryl-H), 10.95, 11.05 (1H, s, NH); ^{13}C NMR (75 MHz, $[^2H_6]$-DMSO) δ_C = 20.40, 20.49 (CH_3) 20.71, 20.84 (CH_3), 34.95, 35.02 (C-5′), 42.07, 43.01 (C-3 = C-4′); 49.01, 49.56 (C-3′), 116.50, 117.01 (CN), 120.29, 120.31, 120.39, 120.43, 123.50, 123.66, 127.49, 127.59, 129.40, 129.57, 129.72, 129.82, 131.01 and 131.62 (aryl-CH), 132.12, 132.88 (C-3a), 136.51, 136.75 (aryl-C–N), 138.20, 138.31 (aryl-C–CH_3), 145.02, 146.03 (C-7a), 157.60, 158.05 (C-6′), 160.20, 160.31 (C-2′), 175.13, 175.23 (C-2); MS m/z 434 (M^+; 37%), 408 (2), 300 (14), 286 (5), 184 (8), 140 (44), 107 (12), 91 (44).

1′-(4-Methoxylphenyl)-6′-(4-methoxylphenylimino)-2,2′-dioxospiro[(2,3-dihydro-1*H*-indol)-3,4′-perhydropyridine]-3′-carbonitrile (5b). Colorless crystals (270 mg, 58%), mp 254—255 °C (from ethyl acetate). Found: C, 69.40; H, 4.79; N, 12.07%. Calcd for $C_{27}H_{22}N_4O_4$: C, 69.52; H, 4.75; N, 12.01%. IR ν_{max} (KBr) 1735 and 1685 cm^{-1} (CO); ^{1}H NMR (300 MHz, $[^2H_6]$-DMSO) δ_H = 3.05, 3.12 (1H,d), 3.32, 3.42 (1H, d, J = 17.54 Hz, CH_2), 3.70, 3.73 (3H, s, OCH_3), 3.78, 3.81 (3H, s, OCH_3), 5.10, 5.17 (1H, s, 3′-H), 6.83, 6.96, 7.04, 7.08, 7.15, 7.19, 7.28, 7.30, 7.35, and 7.46 (12H, all m, aryl-H), 10.85, 10.96 (1H, s, NH); ^{13}C NMR (75 MHz, $[^2H_6]$-DMSO) δ_C = 35.01, 35.11 (C-5′), 42.50, 43.13 (C-3 = C-4′); 48.97, 49.71 (C-3′), 55.55, 55.62 (OCH_3), 55.70, 55.82 (OCH_3), 114.72, 114.92 (CN), 115.32, 115.65, 117.21, 121.28, 122.01, 123.28, 124.22, 125.72, 126.27, 126.53, 129.34, 130.07 and 130.41 (aryl-CH), 136.52, 136.93 (aryl-C–N), 137.44, 137.85 (C-3a), 141.18, 141.50 (C-7a), 156.24, 156.31, 156.84, and 157.62 (aryl-C–OCH_3), 159.45, 159.59 (C-6′), 160.65, 160.73 (C-2′), 174.52, 174.95 (C-2); MS m/z 466 (M^+; 100%), 451 (5), 316 (29), 184 (34), 149 (25), 123 (41), 108 (38), 77 (12).

1′-(4-Chlorophenyl)-6′-(4-chlorophenylimino)-2,2′-dioxospiro[(2,3-dihydro-1*H*-indol)-3,4′-perhydropyridine]-3′-carbonitrile (5c). Colorless crystals (272 mg, 57%), mp 283—285 °C (from ethyl acetate). Found: C, 63.17; H, 3.56; N, 11.66%. Calcd for $C_{25}H_{16}Cl_2NO_2$: C, 63.16; H, 3.59; N, 11.79%. IR ν_{max} (KBr) 1742 and 1683 cm^{-1} (CO); ^{1}H NMR (300 MHz, $[^2H_6]$-DMSO) δ_H = 3.06, 3.16 (1H, d), 3.46, 3.58 (1H, d, J = 17.46 Hz, 1-CH_2), 5.14, 5.18 (1H, s, 3′-H), 6.88, 6.90, 7.06, 7.13, 7.15, 7.27, 7.34, 7.41, 7.42, 7.54, 7.60, 7.65 and 7.67 (12H, all m, aryl-H), 10.92, 11.03 (1H, s, NH); ^{13}C NMR (75 MHz, $[^2H_6]$-DMSO) δ_C = 34.48, 34.90 (C-5′), 41.21, 42.61 (C-3 = C-4′); 48.73, 49.49 (C-3′), 114.94, 116.7 (CN), 116.94, 120.35, 122.35, 123.88, 125.68, 126.16, 128.14, 128.97, 129.26, 129.33, 129.49, 129.66, and 131.87 (aryl-CH), 132.15, 133.25 (C-3a), 136.60, 137.50 (aryl-C–N), 146.53, 146.84 (C-7a), 156.95, 157.60 (C-6′), 160.07, 160.23 (C-2′), 173, 174.52 (C-2); MS m/z 475 ($M^+ + 1$; 37%), 474 (M^+; 100), 322 (14), 320 (11), 262 (16), 184 (96), 155 (33), 144 (51), 130 (11), 90 (5), 75 (4).

2,2′-Dioxo-1′-phenyl-6′-phenylimino)-spiro[(2,3-dihydro-1*H*-indole)-3,4′-perhydropyridine]-3′-carbonitrile (5d). Colorless crystals (162 mg, 40%), mp 265—267 °C (from ethyl acetate). Found: C, 73.99; H, 4.64; N, 13.45%. Calcd for $C_{25}H_{18}N_4O_2$: C, 73.87; H, 4.46; N, 13.79%. IR ν_{max} (KBr) 1740 and 1680 cm^{-1} (CO); ^{1}H NMR (300 MHz, $[^2H_6]$-DMSO) 3.01, 3.26 (1H, d), 3.37, 3.54 (1H, d, J = 17.52 Hz, CH_2), 5.14, 5.21 (1H, s, 3′-H), 6.84, 6.87, 6.98, 7.01, 7.05, 7.10, 7.15, 7.18, 7.20, 7.28, 7.33, 7.38, 7.45, 7.50, and 7.58 (12H, aryl-H); ^{13}C NMR (75 MHz, $[^2H_6]$-DMSO) δ_C = 34.42, 34.70 (C-5′), 41.42, 41.99 (C-3 = C-4′), 114.81, 115.11 (CN), 116.63, 116.75, 120.17, 120.30, 123.48, 123.72, 125.28, 125.72, 127.51, 127.67, 128.44, 128.59, 128.94, 129.01, 129.14, 129.19, 129.65, and 129.98 (aryl-CH), 133.99, 133.37 (C-3a), 136.42, 137.35 (aryl-C–N), 147.70, 148.01 (C-7a), 156.22, 156.94 (C-6′), 160.05, 160.16 (C-2′), 173.90, 174.37 (C-2); MS *m/z* 406 (M^+; 100), 377 (8), 286 (28), 184 (78), 141 (42), 117 (11), 91 (7), 77 (23).

Ethyl 2-Amino-4-[4-hydroxy-1-(4-methylphenyl)-2,6-bis-(4-methylphenylamino)-1,4-dihydro-4-pyridyl]quinoline-3-carboxylate (9a). Colorless crystals (107 mg, 36%), mp 245 °C (from ethanol). Found: C, 74.31; H, 5.88; N, 11.82%. Calcd for $C_{38}H_{37}N_5O_3$: C, 74.60; H, 6.07; N, 11.45%. IR ν_{max} (KBr) 3420 (OH), 3360, 3300 (NH_2), 3200 (NH), 1720 cm^{-1} (CO); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 0.81$ (3H, t, $J = 7$ Hz, ester-CH_3), 2.18 (3H, s, CH_3), 2.25 (3H, s, CH_3), 2.48 (3H, s, CH_3), 3.73 (2H, q, $J = 7$ Hz, ester-CH_2) 6.97 (1H, s, H-3′ or H-5′), 7.00 (1H, s, H-3′ or H-5′), 7.09, 7.16, 7.18, 7.26, 7.42, 7.45, 7.51, 7.63, 7.66, and 8.20 (16H, all m, aryl-H), 7.03 (2H, s, NH_2), 7.44 (2H, s, NH), and 8.72 (1H, s, OH); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta_C = 14.09$ (ester-CH_3), 20.17, 20.79, and 21.33 (3 CH_3-aryl), 58.11 (ester-CH_2), 80.75 (C-4′), 118.03, 119.58, 121.47, 123.45, 127.27, 127.36, 128.14, 128.50, 128.90, and 128.98 (all aryl and olefinic-CH), 125.86 (C-3), 129.13 (C-4a), 129.17 (C-4), 130.51, 132.51, and 136.97 (aryl-CCH_3), 137.92, 138.48, and 140.76 (aryl-CN), 148.65 (C-8a), 152.51 (C-2), 157.38 (C-2′ and C-6′), and 165.41 (C=O); MS *m/z* 583 (M^+-CO; 22), 565 (2) 476 (19), 431 (21), 406 (34), 133 (42), 107 (23), 91 (13).

Ethyl 2-Amino-4-[4-hydroxy-1-(4-methoxylphenyl)-2,6-bis(4-methoxyphenylamino)-1,4-dihydro-4-pyridyl]quinoline-3-carboxylate (9b). Colorless crystals (103 mg, 32%), mp 230—232 °C (from ethanol). Found: C, 68.96; H, 5.86; N, 10.70%. Calcd for $C_{38}H_{37}N_5O_6$: C, 69.18; H, 5.67; N, 10.61%. IR ν_{max} (KBr) 3420 (OH), 3382 and 3240 (NH_2), 3213 (NH), 1720 cm^{-1} (CO); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 0.92$ (3H, t, $J = 7.04$ Hz, ester-CH_3), 3.84 (2H, q, $J = 7.04$ Hz, ester-CH_2), 3.68 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.79 (3H, s, OCH_3) 6.25 (2H, br, NH_2), 6.56 (1H, s, H-3′ or H-5′), 6.60 (1H, s, H-3′ or H-5′), 6.63 (1H, s, OH), 6.69, 6.97, 7.07, 7.11, 7.38, 7.45, and 8.62 (16H, all m, aryl-H), 8.82 (2H, br, 2NH); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta_C = 14.42$ (ester-CH_3), 55.29, 55.43, 55.60 (3 CH_3O-aryl), 59.61 (ester-CH_2), 82.48 (C-4′), 113.78, 115.43, 119.28, 121.85, 128.75, and 129.72 (all aryl and olefinic-CH), 124.40 (C-3), 126.78 (C-4), 129.97 (C-4a), 132.38, 137.48, and 137.98 (aryl-C–N), 148.09 (C-8a), 152.78 (C-2), 155.16, 156.01, and 156.89 (aryl-OCH_3), 160.66 (C-2′ and C-6′) and 166.40 (C=O); MS *m/z* 631 (M^+ −CO; 6%), 508 (24), 462 (35), 437 (23), 149 (11), 123 (3), 108 (4).

Ethyl 2-Amino-4-[1-(4-chlorophenyl)-2,6-bis(4-chlorophenylamino)-4-hydroxy-1,4-dihydro-4-pyridyl]quinoline-3-carboxylate (9c). Colorless crystals (130 mg, 40%), mp 237—239 °C (from ethyl acetate/cyclohexane). Found: C, 62.12; H, 4.15; N, 10.50%. Calcd for $C_{35}H_{28}Cl_3N_5O_3$: C, 62.25; H, 4.19; N, 10.40%. IR ν_{max} (KBr) 3400 (OH), 3380 and 3310 (NH_2 and NH), 1710 cm^{-1} (CO); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 0.91$ (3H, t, $J = 7.03$ Hz, ester-CH_3), 3.65 (2H, q, $J = 7.03$ Hz, ester-CH_2), 6.95 (1H, s, H-3′ or H-5′), 7.01 (1H, s, H-3′ or H-5′), 7.06, 7.22, 7.30, 7.40, 7.45, 7.65, 7.74, and 8.25 (16H, all m, aryl-H), 7.15 (2H, s, NH_2), 7.85 (1H, s, OH), and 8.92 (1H, s, NH); MS *m/z* 645 (M^+-CO; 2%), 625 (5), 562 (10), 516 (9), 490 (11), 444 (28), 153 (100), 127 (77), 91 (6).

Reaction of N^1,N^2-Diarylacetamidines 1a—c with Benzylidenemalononitriles 10a—d. (General procedure). Solutions of acetamidines **1a**—**c** (1 mmol each), in ethyl acetate (10 cm^3) were added to solutions of **10a**—**d** (1 mmol each) in ethyl acetate (20 cm^3). The mixtures were heated to reflux temperature for 3—12 h (in the case of **13c** only after heating the mixture to reflux for 48 h), concentrated, and subjected to PLC using toluene/ethyl acetate (2 : 1) as the developing solvent. The main zones in each case contained compounds **13a**—**f**. All other zones contained too small amounts of material for the successful characterization, and were therefore discarded.

2-Amino-3-cyano-1-(4-methylphenyl)-6-(4-methylphenylimino)-4-phenyl-1,4,5,6-tetrahydropyridine (13a). Buff crystals (218 mg, 56%), mp 164 °C (from aqueous ethanol). Found: C, 79.55; H, 6.05; N, 14.09%. Calcd for $C_{26}H_{24}N_4$: C, 79.59; H, 6.12; N, 14.29%. IR ν_{max} (KBr) 3300 and 3200 (NH_2), 2200 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 2.15$ (3H, s, CH_3), 2.35 (3H, s, CH_3), 2.72 (1H, dd), 2.81 (1H, dd, $J = 14$ Hz, CH_2), 3.73 (1H, t, $J = 7$ Hz, 4-H), 4.31 (2H, s, NH_2), 6.04, 6.82, 7.12, 7.21, 7.28, 7.30, and 7.32 (13H, all m, aryl-H); MS *m/z* 392 (M^+; 100), 304 (6).

2-Amino-3-cyano-1-(4-methoxyphenyl)-6-(4-methoxyphenylimino)-4-phenyl-1,4,5,6-tetrahydropyridine (13b). Buff crystals (190 mg, 45%), mp 140—142 °C (from ethyl acetate). Found: C, 73.42; H, 5.72; N, 12.95%. Calcd for $C_{26}H_{24}N_4O_2$: C, 73.56; H, 5.70; N, 13.20%. IR ν_{max} (KBr) 3400 and 3300 (NH_2), 2190 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) 2.80 (1H, dd) 2.95 (1H, dd, $J = 14$ Hz, CH_2), 3.75 (3H, s, CH_3O), 3.72 (1H, t, $J = 7$ Hz, 4-H), 3.80 (3H, s, CH_3O), 4.40 (2H, s, NH_2), 6.15, 6.65, 7.05, 7.20, 7.30, and 7.40 (13H, all m, aryl-H); MS *m/z* 424 (M^+; 5%), 356 (20), 330 (17), 243 (23), 191 (10), 140 (12), 123 (100).

2-Amino-1-(4-chlorophenyl)-6-(4-chlorophenylimino)-3-cyano-4-phenyl-1,4,5,6-tetrahydropyridine (13c). Buff crystals (70 mg, 16%), mp 206—207 °C (from ethyl actate/cyclohexane). Found: C, 66.60; H, 4.20; N, 12.80%. Calcd for $C_{24}H_{18}Cl_2N_4$: C, 66.50; H, 4.19; N, 12.93%. IR ν_{max} (KBr) 3420 and 3305 (NH_2), 2180 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 2.79$ (1H, dd), 2.81 (1H, dd, $J = 14$ Hz, CH_2), 3.81 (1H, t, $J = 7$ Hz, 4-H), 4.35 (2H, s, NH_2), 7.03, 7.23, 7.26, 7.39, and 7.48 (13H, all m, aryl-H); MS *m/z* 432 (M^+; 100), 391 (8), 367 (9), 251 (9), 158 (8), 154 (16), 128 (33).

2-Amino-3-cyano-4-(4-methoxyphenyl)-1-(4-methylphenyl)-6-(4-methylphenylimino)-1,4,5,6-tetrahydropyridine (13d). Pale yellow crystals (193 mg, 46%), mp 204 °C (aqueous ethanol). Found: C, 76.65; H, 6.01; N, 13.02%. Calcd for $C_{37}H_{26}N_4O$: C, 76.75; H, 6.20; N, 13.26%. IR ν_{max} (KBr) 3410 and 3300 (NH_2), 2190 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 2.28$ (3H, s, CH_3), 2.48 (3H, s, CH_3), 2.85 (1H, dd), 2.90 (1H, dd, $J = 14$ Hz, CH_2), 3.82 (1H, t, $J = 7$ Hz, 4-H), 3.90 (3H, s, CH_3O), 4.45 (2H, s, NH_2), 6.23, 6.96, 7.25, and 7.36 (12H, all m, aryl-H); MS *m/z* 422 (M^+; 100%), 315 (8), 239 (6), 192 (6), 185 (16), 154 (18).

2-Amino-4-(4-chlorophenyl)-3-cyano-1-(4-methylphenyl)-6-(4-methylphenylimino)-1,4,5,6-tetrahydropyridine (13e). Faint brown crystals (244 mg, 57%), mp 166—167 °C (from aqueous ethanol.) Found: C, 72.80; H, 5.52; N, 12.82%. Calcd for $C_{26}H_{24}ClN_4$: C, 72.96; H, 5.65; N, 13.09%. IR ν_{max} (KBr) 3390 and 3300 (NH_2), 2180 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) $\delta_H = 2.20$ (3H, s, CH_3), 2.35 (3H, s, CH_3), 2.75 (1H, dd), 2.85 (1H, dd, $J = 14$ Hz, CH_2), 3.75 (1H, t, $J = 7$ Hz, 4-H), 4.35 (2H, s, NH_2), 6.11, 6.16, 6.90, 7.14, 7.18, 7.24, 7.26, 7.30, and 7.34 (12H, all m, aryl-H); MS *m/z* 426 (M^+; 100%), 393 (8), 315 (8), 239 (22), 207 (10).

2-Amino-3-cyano-4-(4-dimethylaminophenyl)-1-(4-methoxyphenyl)-6-(4-methoxyphenylimino)-1,4,5,6-tetrahydropyridine (13f). Brown crystals (217 mg, 49%) mp 80 °C (from ethanol.)

Found: C, 71.78; H, 6.10; N, 14.75%. Calcd for $C_{28}H_{29}N_5O_2$: C, 71.92; H, 6.25; N, 14.98%. IR $\nu_{\max}$ (KBr) 3400 and 3300 (NH_2), 2200 (CN), 1620 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) δ_H = 2.74 (1H, dd), 2.82 (1H, dd, J = 14 Hz, CH_2), 2.93 (6H, s, NMe_2), 3.68 (3H, s, CH_3O), 3.70 (1H, t, J = 7 Hz, 4-H), 3.81 (3H, s, CH_3O), 4.28 (2H, s, NH_2), 6.22, 6.64, 6.72, 6.88, 7.10, 7.18, and 7.25 (12H, all m, aryl-H); MS m/z 467 (M^+; 100%), 467 (23), 402 (9), 347 (10), 271 (8), 200 (36), 134 (38).

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