Diastereoselective multicomponent synthesis of (4*RS*,6*SR*)-4,6-diaryl-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylates*

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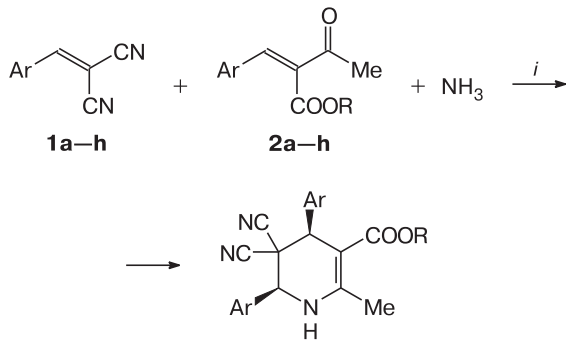
Multicomponent reaction of benzylidenemalononitrile, 2-acetyl-3-arylacrylates, and aqueous ammonia in alcohols at room temperature proceeds stereoselectively to give (4*RS*,6*SR*)-4,6-diaryl-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylates in 55—87% yields. In this reaction, ammonia acts as both the catalyst and the source of nitrogen for constructing tetrahydropyridine cycle.

Key words: tetrahydropyridines, multicomponent reactions, stereoselectivity, benzylidenemalononitriles, 2-acetyl-3-arylacrylates.

Tetrahydropyridine and its analogs, such as 1,4-dihydropyridine, piperidine, and pyridine, exhibit a wide range of biological and pharmacological activities.[1—4] Thus, tetrahydropyridines are efficiently used for the treatment of hypertension and stenocardia[5,6] and are well known for other types of pharmacological activities, *e.g.*, neuroprotection, noncompetitive inhibition of topoisomerase I, antitumor activity, and inhibition of HIV protease.[7—9] Tetrahydropyridine and its analogs are valuable building blocks for construction of different fused polycyclic systems[10,11] and nitrogen heterocycles.[12—14] Tetrahydropyridines are commonly synthesized from imines, the nitrogen atom of which serves as a source of nitrogen for the newly forming tetrahydropyridine cycle. Syntheses of tetrahydropyridines by aza-Diels—Alder[15,16] reactions (both aza-dienophiles and aza-dienes can be employed) and domino addition—cyclization reactions[17,18] involving imines were also described. The reactions of the last type are multicomponent ones. Over the years, the multicomponent synthesis is recognized as a versatile tool of the organic chemistry.[19] Several publications were devoted to multicomponent synthesis of 4-aminotetrahydropyridines from aromatic amines, CH acids, and aromatic aldehydes.[20,21] Recently, we have synthesized substituted piperidines using ammonium acetate as the source of nitrogen for the piperidine cycle.[22—24] In continuation of our research on the application of electron-deficient olefins as the building blocks in the synthesis of various cyclic (cyclopropanes[25,26] and cyclohexanes[27]) and heterocyclic (pyrrolidines,[28] spiro-pyrimidines,[29,30] chromenes,[31] pyranopyridines,[32] *etc.*), in the present work we describe multicomponent synthesis of substituted tetrahydropyridines from alkylidenemalononitriles, 2-acetyl-3-arylacrylates, and aqueous ammonia as a source of the nitrogen atom for tetrahydropyridine cycle (Scheme 1, Table 1; for clarity, in Scheme 1 only one enantiomer for each structure is shown).

Scheme 1



i. MeOH, ~20 °C.

Compound 1—3	Ar	R	Compound 1—3	Ar	R
a	Ph	Me	**e**	2-ClC_6H_4	Me
b	4-MeC_6H_4	Et	**f**	4-ClC_6H_4	Me
c	4-$MeOC_6H_4$	Me	**g**	4-BrC_6H_4	Me
d	4-FC_6H_4	Me	**h**	4- $O_2NC_6H_4$	Me

* Dedicated to Academician of the Russian Academy of Sciences B. A. Trofimov on the occasion of his 80th birthday.

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Table 1. Multicomponent synthesis of (4*RS*,6*SR*)-4,6-diaryl-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylates **3a**—**h** from benzylidenemalononitriles **1a**—**h**, 2-acetyl-3-arylacrylates **2a**—**h**, and aqueous ammonia[a]

Entry	Reactants	*t*/h	Product	Yield (%)[b]
1	**1a** + **2a**	4	**3a**	79
2	**1b** + **2b**	8	**3b**	70
3	**1c** + **2c**	12	**3c**	66
4	**1d** + **2d**	4	**3d**	78
5	**1e** + **2e**	4	**3e**	73
6	**1f** + **2f**	4	**3f**	72
7	**1g** + **2g**	4	**3g**	87
8	**1h** + **2h**	2	**3h**	55

[a] Reaction conditions: compound **1** (3 mmol), compound **2** (3 mmol), ammonia (6 mmol, 25% aqueous solution), MeOH (5 mL), stirring, room temperature. TLC-monitoring of the reaction progress (TLC plates were developed with hexane—ethyl acetate, 5 : 1).
[b] Isolated yields.

The reaction of benzylidenemalononitrile **1a**, methyl 2-acetyl-3-phenylacrylate **2a**, and ammonium acetate in refluxing MeOH for 2 h (optimal reaction conditions for the synthesis of 2,6-diphenyl-3,3,5,5-tetracyanopiperidine from benzylidenemalononitrile, paraformaldehyde, and NH_4OAc[22]) proceeds with very low conversion of the starting olefins and gives only trace amounts of the target tetrahydropyridine **3a**.

Recently,[33] we published multicomponent synthesis of piperidines that employed ammonia. The replacement of ammonium acetate with 25% aqueous ammonia dramatically changed the reaction outcome. Thus, significant conversion of the starting olefins and formation of product **3a** were observed after stirring compounds **1a**, **2a**, and ammonia in MeOH at room temperature for 2 h. After 4 h stirring, complete conversion of compounds **1a** and **2a** was achieved and the yield of tetrahydropyridine **3a** reached 79%. Tetrahydropyridines **3b**—**h** were synthesized under similar conditions (see Table 1). It is of note that the reactions with the substrates bearing electron-withdrawing groups at the aromatic ring proceed faster (2—4 h, entries *1*, *4*—*8*) than the reactions involving substrates with electron-donating substituents (8 and 12 h, entries *2* and *3*, respectively).

All the recorded ^1H and ^{13}C NMR spectra of compounds **3** show one set of the signals evidencing the formation of only one diastereomer. The NOESY NMR experiment revealed the dipolar coupling between the 4- and 6-protons thus unambiguously indicating the 4*RS*,6*SR* configuration (Fig. 1).

A plausible mechanism of the reaction is given in Scheme 2. Ammonia acting as both the nitrogen source and the base adds to benzylidenemalononitrile **1** *via* the aza-Michael addition mechanism. Further nucleophilic

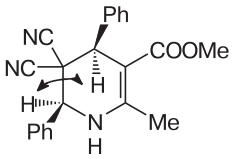
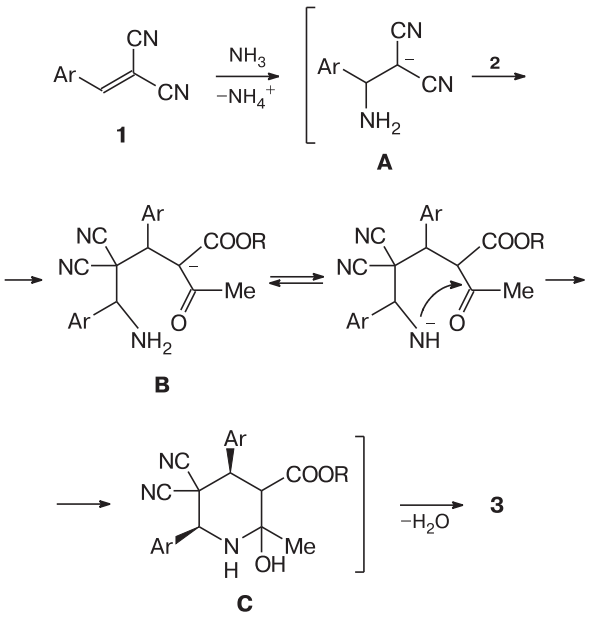


Fig. 1. Proton correlation in NOESY NMR spectrum of compound **3a**.

addition of anion **A** to 2-acetyl-3-arylacrylate **2** gives anion **B**. Subsequent intramolecular cyclization dictated by steric reasons gives the unstable intermediate (4*RS*,6*SR*)-2-hydroxypiperidine **C**. Decomposition of intermediate **C** results in the final product **3**.

Scheme 2



In summary, we succeeded in synthesizing (4*RS*,6*SR*)-4,6-diaryl-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylates in 55—87% yields by the multicomponent reaction between benzylidenemalononitrile, 2-acetyl-3-arylacrylates bearing both electron-withdrawing and electron-donating substituents at the aromatic ring, and aqueous ammonia. The reaction is simple, easy to perform, and clean; the products can be isolated pure by filtration.

Experimental

^1H and ^{13}C NMR spectra were run on a Bruker AM-300 instrument with working frequencies of 300.13 and 75.47 MHz, respectively. Mass spectrometry was performed with a Finningan MAT INCOS 50 instrument. IR spectra were recorded with a Specord M82 FTIR spectrometer in KBr pellets using Soft

Spectra software. Melting points were measured with a Gallenkamp apparatus.

Compounds **1** and **2** were synthesized by Knoevenagel condensation of aromatic aldehydes with malononitrile and ethyl acetoacetate, respectively, using AcONa as a catalyst.[34] Thin layer chromatography was carried out with Merck precoated plates DC-Alufolien Kieselgel 60 F_{254}.

Multicomponent synthesis of (4*RS*,6*SR*)-4,6-diaryl-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylates 3 (general procedure). A mixture of benzylidenemalononitrile **1** (mmol), 2-acetyl-3-arylacrylate **2** (3 mmol), 25% aqueous ammonia (0.45 mL, 6 mmol), and MeOH (5 mL) was stirred for the time specified in Table 1. The reaction progress was monitored by TLC (development with hexane—ethyl acetate, 5 : 1). After the reaction completion, the mixture was maintained at −10 °C for 30 min for the complete precipitation of the product, the precipitate was collected by filtration and dried to give pure tetrahydropyridine **3**.

Methyl (4*RS*,6*SR*)-5,5-dicyano-2-methyl-4,6-diphenyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3a). Yield 0.84 g (79%), white powder, m.p. 218—219 °C. ^{1}H NMR (DMSO-d_6), δ: 2.32 (s, 3 H, CH_3); 3.11 (s, 3 H, OCH_3); 4.83 (s, 1 H, CH); 5.27 (s, 1 H, CH); 7.28—7.34 (m, 5 H, Ar + NH); 7.52 (dd, 4 H, Ar, ^1J = 5.9 Hz, ^2J = 1.6 Hz); 7.63 (m, 2 H, Ar). ^{13}C NMR (DMSO-d_6), δ: 19.0 (s, CH_3); 47.8 (s, $C(CN)_2$); 49.1 (s, CH); 49.7 (s, OCH_3); 59.5 (s, CH—N); 94.4 (s, $C(CO_2Me)$); 112.8 (s, CN); 114.0 (s, CN); 127.5 (s, 1 C, Ar); 127.9 (s, 2 C, Ar); 128.2 (s, 2 C, Ar); 128.4 (s, 2 C, Ar); 128.6 (s, 2 C, Ar); 129.9 (s, 1 C, Ar); 134.3 (s, 1 C, Ar); 139.1 (s, 1 C, Ar); 153.9 (s, $C(CH_3)$); 166.3 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3387 (N—H), 3063 (C—H, Ar), 2839 (C—H, Ar), 2253 (C≡N), 1645 (C—H), 1431 (C=C), 1142 (C—N). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 357 $[M]^+$ (78), 298 $[M - CO_2Me]^+$ (40), 202 $[M - 2\,Ph - H]^+$ (100), 154 $[M - C_{12}H_{13}NO_2]^+$ (15), 127 $[M - C_{12}H_{13}NO_2 - CN - H]^+$ (43), 103 $[M - C_{12}H_{13}NO_2 - 2\,CN]^+$ (41). Found (%): C, 73.91; H, 5.37; N, 11.73. $C_{22}H_{19}N_3O_2$. Calculated (%): C, 73.93; H, 5.36; N, 11.76.

Ethyl (4*RS*,6*SR*)-5,5-dicyano-2-methyl-4,6-bis(4-methylphenyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3b). Yield 0.83 g (70%), white powder, m.p. 224—225 °C. ^{1}H NMR (DMSO-d_6), δ: 0.59 (t, 3 H, CH_3, J = 7.3 Hz); 2.31 (s, 6 H, 2 CH_3); 2.37 (s, 3 H, CH_3); 3.64 (qd, 2 H, OCH_2, ^1J = 12.2 Hz, ^2J = 6.6 Hz); 4.76 (s, 1 H, CH); 5.21 (s, 1 H, CH); 7.20 (dd, 4 H, Ar, ^1J = 8.8 Hz, ^2J = 2.2 Hz); 7.33 (d, 2 H, Ar, J = 8.1 Hz); 7.42 (s, 1 H, NH); 7.52 (d, 2 H, Ar, J = 8.1 Hz). ^{13}C NMR (DMSO-d_6), δ: 13.4 (s, CH_3); 18.9 (s, CH_3); 20.6 (s, CH_3); 20.8 (s, CH_3); 48.0 (s, $C(CN)_2$); 48.9 (s, CH); 58.1 (s, CH—N); 59.3 (s, OCH_2); 94.5 (s, $C(CO_2Me)$); 113.0 (s, CN); 114.1 (s, CN); 128.2 (s, 2 C, Ar); 128.6 (s, 2 C, Ar); 129.1 (s, 2 C, Ar); 129.6 (s, 2 C, Ar); 131.4 (s, 1 C, Ar); 136.2 (s, 1 C, Ar); 137.0 (s, 1 C, Ar); 139.5 (s, 1 C, Ar); 153.6 (s, $C(CH_3)$); 165.8 (s, C=O (CO_2Et)). IR (KBr), ν/cm^{-1}: 3366 (N—H), 3097 (C—H, Ar), 2902 (C—H, Ar), 2263 (C≡N), 1458 (C—H), 1372 (C=C), 1120 (C—N). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 399 $[M]^+$ (28), 298 $[M - CO_2Et]^+$ (28), 230 $[M - C_{11}H_8N_2 - H]^+$ (100), 202 $[M - 2\,(4\text{-Me})C_6H_4 - CH_3]^+$ (32), 158 $[M - C_{14}H_{17}NO_2]^+$ (18). Found (%): C, 75.14; H, 6.32; N, 10.50. $C_{25}H_{15}N_3O_2$. Calculated (%): C, 75.16; H, 6.31; N, 10.52.

Methyl (4*RS*,6*SR*)-5,5-dicyano-4,6-bis(4-methoxyphenyl)-7-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3c). Yield 0.82 g (66%), white powder, m.p. 155—156 °C. ^{1}H NMR (DMSO-d_6), δ: 2.29 (s, 3 H, CH_3); 3.14 (s, 3 H, OCH_3); 3.75 (s, 3 H, OCH_3); 3.79 (s, 3 H, OCH_3); 4.73 (s, 1 H, CH); 5.17 (s, 1 H, CH); 6.92 (d, 2 H, Ar, J = 8.8 Hz); 7.07 (d, 2 H, Ar, J = 8.8 Hz); 7.21 (d, 2 H, Ar, J = 8.8 Hz); 7.40 (s, 1 H, NH); 7.54 (d, 2 H, Ar, J = 8.8 Hz). ^{13}C NMR (DMSO-d_6), δ: 19.0 (s, CH_3); 40.4 (s, $C(CN)_2$); 45.9 (s, CH); 48.4 (s, OCH_3); 55.0 (s, OCH_3); 55.2 (s, OCH_3); 55.3 (s, OCH_3); 59.0 (s, CH—N); 94.6 (s, $C(CO_2Me)$); 113.1 (s, CN); 113.5 (s, 2 C, Ar); 113.6 (s, 2 C, Ar); 114.0 (s, CN); 128.6 (s, 1 C, Ar); 128.6 (s, 1 C, Ar); 129.8 (s, 2 C, Ar); 130.8 (s, 2 C, Ar); 153.5 (s, $C(CH_3)$); 158.8 (s, C=O); 160.4 (s, 1 C, Ar); 166.5 (s, 1 C, Ar). IR (KBr), ν/cm^{-1}: 3387 (N—H), 3063 (C—H, Ar), 2937 (C—H, Ar), 2253 (C≡N), 1445 (C—H), 1432 (C=C), 1130 (C—N). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 417 $[M]^+$ (39), 232 $[M - C_{11}H_8N_2O - H]^+$ (100), 184 $[M - C_{13}H_{15}NO_3]^+$ (18), 134 $[M - C_{13}H_{15}NO_3 - 2\,CN]^+$ (43). Found (%): C, 69.03; H, 5.56; N, 10.06. $C_{24}H_{23}N_3O_4$. Calculated (%): C, 69.05; H, 5.55; N, 10.07.

Methyl (4*RS*,6*SR*)-5,5-dicyano-4,6-bis(4-fluorophenyl)-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3d). Yield 0.92 g (78%), white powder, m.p. 210—211 °C. ^{1}H NMR (DMSO-d_6), δ: 2.34 (s, 3 H, CH_3); 3.18 (s, 3 H, OCH_3); 4.87 (s, 1 H, CH); 5.33 (s, 1 H, CH); 7.25 (t, 2 H, Ar, J = 8.8 Hz); 7.33—7.45 (m, 4 H, Ar); 7.62 (s, 1 H, NH); 7.69 (dd, 2 H, Ar, ^1J = 8.9 Hz, ^2J = 5.7 Hz). ^{13}C NMR (DMSO-d_6), δ: 19.2 (s, CH_3); 47.9 (s, $C(CN)_2$); 48.2 (s, CH); 49.9 (s, OCH_3); 58.7 (s, CH—N); 94.3 (s, $C(CO_2Me)$); 112.8 (s, CN); 113.9 (s, CN); 115.2 (d, 2 C, Ar, $^2J_{C-F}$ = 22.1 Hz); 115.7 (d, 2 C, Ar, $^2J_{C-F}$ = 22.1 Hz); 130.5 (d, 4 C, Ar, $^3J_{C-F}$ = 8.8 Hz); 135.2 (d, 2 C, Ar, $^4J_{C-F}$ = 3.3 Hz); 154.1 (s, $C(CH_3)$); 161.7 (d, 1 C, Ar, $^1J_{C-F}$ = 245.5 Hz); 163.0 (d, 1 C, Ar, $^1J_{C-F}$ = 245.5 Hz); 166.2 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3351 (N—H), 3004 (C—H, Ar), 2844 (C—H, Ar), 2251 (C≡N), 1507 (C—H), 1435 (C=C), 1249 (C—F), 1118 (C—N). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 393 $[M]^+$ (66), 334 $[M - CO_2Me]^+$ (19), 220 $[M - C_{10}H_5FN_2 - H]^+$ (100), 172 $[M - C_{12}H_{12}FNO_2]^+$ (20), 145 $[M - C_{12}H_{12}FNO_2 - CN - H]^+$ (17). Found (%): 67.15; H, 4.37; F, 9.66; N, 10.68. $C_{22}H_{17}F_2N_3O_2$. Calculated (%): C, 67.17; H, 4.36; F, 9.66; N, 10.68.

Methyl (4*RS*,6*SR*)-4,6-bis(2-chlorophenyl)-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3e). Yield 0.93 g (73%), white powder, m.p. 230—231 °C. ^{1}H NMR ($CDCl_3$), δ: 2.48 (s, 3 H, CH_3); 3.47 (s, 3 H, OCH_3); 5.34 (s, 1 H, CH); 5.38 (s, 1 H, CH); 7.36—7.52 (m, 3 H, Ar); 7.53—7.73 (m, 5 H, Ar + NH); 7.84 (d, 1 H, Ar, ^1J = 7.3 Hz); 8.06 (s, 1 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 20.1 (s, CH_3); 44.8 (s, $C(CN)_2$); 45.7 (s, CH); 50.6 (s, CH—N); 57.3 (s, OCH_3); 98.3 (s, $C(CO_2Me)$); 112.0 (s, CN); 112.4 (s, CN); 127.1 (s, 1 C, Ar); 128.0 (s, 2 C, Ar); 128.1 (s, 1 C, Ar); 129.5 (s, 1 C, Ar); 129.9 (s, 1 C, Ar); 130.6 (s, 1 C, Ar); 131.0 (s, 1 C, Ar); 131.7 (s, 1 C, Ar); 134.9 (s, 1 C, Ar); 135.0 (s, 1 C, Ar); 135.3 (s, 1 C, Ar); 152.8 (s, $C(CH_3)$); 166.3 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3410 (N—H), 3065 (C—H, Ar), 2833 (C—H, Ar), 2250 (C≡N), 1476 (C—H), 1436 (C=C), 1155 (C—N), 745 (C—Cl). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 425 $[M]^+$ (71), 390 $[M - Cl]^+$ (76), 366 $[M - CO_2Me]^+$ (100), 236 $[M - C_{10}H_5ClN_2 - H]^+$ (73), 202 $[M - 2\,(2\text{-Cl})C_6H_4 - H]^+$ (53),188 $[M - C_{12}H_{12}ClNO_2]^+$ (14). Found (%): C, 61.97; H, 4.03; Cl, 16.63; N, 9.86. $C_{22}H_{17}Cl_2N_3O_2$. Calculated (%): C, 61.99; H, 4.02; Cl, 16.63; N, 9.86.

Methyl (4*RS*,6*SR*)-4,6-bis(4-chlorophenyl)-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3f). Yield 0.92 g (72%), white powder, m.p. 181—182 °C. ^{1}H NMR ($CDCl_3$), δ: 2.34 (s, 3 H, CH_3); 3.19 (s, 3 H, OCH_3); 4.87 (s, 1 H, CH); 5.32 (s, 1 H, CH); 7.34 (d, 2 H, Ar, J = 7.7 Hz); 7.49 (d, 2 H, Ar,

J = 7.7 Hz); 7.65 (s, 4 H, Ar + NH). ^{13}C NMR ($CDCl_3$), δ: 19.2 (s, CH_3); 47.5 (s, $C(CN)_2$); 48.2 (s, CH); 50.0 (s, CH—N); 58.7 (s, OCH_3); 94.0 (s, $C(CO_2Me)$); 112.6 (s, CN); 113.7 (s, CN); 128.4 (s, 2 C, Ar); 128.8 (s, 4 C, Ar); 130.2 (s, 2 C, Ar); 132.5 (s, 1 C, Ar); 133.1 (s, 1 C, Ar); 134.8 (s, 1 C, Ar); 138.1 (s, 1 C, Ar); 154.4 (s, $C(CH_3)$); 166.1 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3403 (N—H), 3068 (C—H, Ar), 2991 (C—H, Ar), 2253 (C≡N), 1623 (C—H), 1433 (C=C), 1126 (C—N), 836 (C—Cl). MS (EI, 70 eV), m/z (I_{rel} (%)): 425 $[M]^+$ (62), 366 $[M - CO_2Me]^+$ (18), 236 $[M - C_{10}H_5ClN_2 - H]^+$ (44), 188 $[M - C_{12}H_{12}ClNO_2]^+$ (12), 138 $[M - C_{12}H_{12}ClNO_2 - 2\ CN]^+$ (95). Found (%): C, 61.96; H, 4.03; Cl, 16.62; N, 9.86. $C_{22}H_{17}Cl_2N_3O_2$. Calculated (%): C, 61.99; H, 4.02; Cl, 16.63; N, 9.86.

Methyl (4*RS*,6*SR*)-4,6-bis(4-bromophenyl)-5,5-dicyano-2-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3g). Yield 1.34 g (87%), white powder, m.p. 197—198 °C. ^{1}H NMR (DMSO-d_6), δ: 2.34 (s, 3 H, CH_3); 3.19 (s, 3 H, OCH_3); 4.85 (s, 1 H, CH); 5.31 (s, 1 H, CH); 7.27 (d, 2 H, Ar, J = 8.5 Hz); 7.60 (dd, 4 H, Ar, ^1J = 8.5 Hz, ^2J = 2.9 Hz); 7.66 (s, 1 H, NH); 7.79 (d, 2 H, Ar, J = 8.5 Hz). ^{13}C NMR (DMSO-d_6), δ: 20.4 (s, CH_3); 47.7 (s, $C(CN)_2$); 50.4 (s, CH); 50.8 (s, CH—N); 61.2 (s, OCH_3); 97.4 (s, $C(CO_2Me)$); 111.6 (s, CN); 113.4 (s, CN); 122.6 (s, 1 C, Ar); 125.3 (s, 1 C, Ar); 129.5 (s, 4 C, Ar); 131.9 (s, 2 C, Ar); 132.1 (s, 1 C, Ar); 132.7 (s, 2 C, Ar); 136.8 (s, 1 C, Ar); 152.4 (s, $C(CH_3)$); 166.5 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3408 (N—H), 3063 (C—H, Ar), 2842 (C—H, Ar), 2250 (C≡N), 1461 (C—H), 1316 (C=C), 1130 (C—N), 679 (C—Br). MS (EI, 70 eV), m/z (I_{rel} (%)): 515 $[M]^+$ (6), 456 $[M - CO_2Me]^+$ (4), 280 $[M - C_{10}H_5BrN_2 - H]^+$ (35), 153 $[M - C_{12}H_{12}BrNO_2 - Br]^+$ (31). Found (%): C, 51.27; H, 3.34; Br, 31.02; N, 8.15. $C_{22}H_{17}Br_2N_3O_2$. Calculated (%): C, 51.29; H, 3.33; Br, 31.02; N, 8.16.

Methyl (4*RS*,6*SR*)-5,5-dicyano-2-methyl-4,6-bis(4-nitrophenyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3h). Yield 0.73 g (55%), white powder, m.p. 250—251 °C. ^{13}C NMR (DMSO-d_6), δ: 2.40 (s, 3 H, CH_3); 3.19 (s, 3 H, OCH_3); 5.10 (s, 1 H, CH); 5.55 (s, 1 H, CH); 7.61 (d, 2 H, Ar, J = 8.8 Hz); 7.02 (d, 3 H, Ar + NH, J = 8.8 Hz); 8.31 (s, 2 H, Ar, J = 8.8 Hz); 8.46 (d, 2 H, Ar, J = 8.8 Hz). ^{13}C NMR (DMSO-d_6), δ: 19.4 (s, CH_3); 46.5 (s, $C(CN)_2$); 48.2 (s, CH); 50.0 (s, CH—N); 58.6 (s, OCH_3); 93.6 (s, $C(CO_2Me)$); 112.2 (s, CN); 113.2 (s, CN); 123.6 (s, 2 C, Ar); 123.8 (s, 4 C, Ar); 130.0 (s, 2 C, Ar); 140.7 (s, 1 C, Ar); 146.7 (s, 1 C, Ar); 147.3 (s, 1 C, Ar); 148.7 (s, 1 C, Ar); 155.1 (s, $C(CH_3)$); 165.8 (s, CO_2Me). IR (KBr), ν/cm^{-1}: 3362 (N—H), 3087 (C—H, Ar), 2852 (C—H, Ar), 2253 (C≡N), 1553 (C—H), 1438 (C=C), 1348 (N—O), 1125 (C—N). MS (EI, 70 eV), m/z (I_{rel} (%)): 447 $[M]^+$ (100), 416 $[M - OMe]^+$ (60), 388 $[M - CO_2Me]^+$ (100), 247 $[M - C_{10}H_5N_3O_2 - H]^+$ (44). Found (%): C, 59.04; H, 3.84; N, 15.65. $C_{22}H_{17}N_5O_6$. Calculated (%): C, 59.06; H, 3.83; N, 15.65.

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