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# Synthesis of 5,6-dihydroquinolines and succinates via the reaction of α,α-dicyanoolefins and acetylenic esters in a ratio of 2:1

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ABSTRACT

A one-pot, convergent method for the synthesis of 5,6-dihydroquinolines by simple mixing of two equivalents of acyclic α,α-dicyanoolefins and one equivalent of acetylenic ester in the presence of $Et_3N$ is described. Three new C–C and one C–N bonds are created in this operation. In the same reaction, cyclic α,α-dicyanoolefins led to the formation of succinates. Further hydrolysis and decarboxylation of 5,6-dihydroquinoline led to quinoline.



## 1. Introduction

The quinoline moiety is abundant in various natural and synthetic products[1] and has extensive applications, especially in medicinal chemistry.[2] They are considered as HIV-1 inhibitors,[3] and possess antimalarial,[4] antiasthmatic,[5] antibacterial,[6] antidiabetic,[7] tyrosine kinase inhibiting agents,[8] antileishmanial,[9] antitumor,[10] antihypertensive,[11] and antiobesity properties.[12] They are also used in the manufacture of dyes,[13] polymer chemistry,[14] rubber chemicals,[15] electronics and optoelectronics.[16] Among them, dihydroquinolines are specially attractive due to their potential utilities as brain delivery carriers,[17] calcium channel modulators,[18] and antiurease compounds.[19] Classical strategies for the synthesis of quinoline scaffolds involve Friedländer synthesis,[20] Doebner–Miller reaction,[21] and Skraup reaction.[22] However, many of these methods have some drawbacks such as high reaction temperatures, use of expensive catalysts, long reaction times and lack of easily accessible starting materials.[23] Due to the interesting properties of quinolines, the development of new techniques for facile access to these molecules has received much attention. Umasish Jana et al. reported the synthesis of dihydroquinoline derivatives via an iron(III) chloride-catalyzed intramolecular alkyne–carbonyl metathesis of *N*-propargyl-2-aminobenzaldehyde/acetophenone.[24] Zhang et al. reported the synthesis of 1,2-dihydroquinolines through the cascade reaction of arylamines and α-ketoesters using iodine as catalyst.[25]

α,α-Dicyanoolefins are highly versatile four-carbon synthons, which have been widely used in annulation reactions leading to the formation of aliphatic cyclic and aromatic compounds.[26] For example, Esmaeili et al. reported the synthesis of biaryl derivatives via the cyclocondensation of vinyl malononitriles and acetylenic esters.[27] Likewise, Yu et al. achieved dihydroquinoline derivatives through the reaction of aldehydes and arylethylidenemalononitriles in ethylene glycol using NaOH as a base promoter under microwave irradiation.[28] Considering the widespread applications of quinoline derivatives and in continuation of our efforts to develop facile access to interesting molecules by applying α,α-dicyanoolefins,[29] we considered the reaction of α,α-dicyanoolefins with acetylenic esters in a ratio of 2:1.

## 2. Results and discussion

For the preliminary investigation, the reaction of α,α-dicyanoolefin **1a** (2 mmol) and dimethyl acetylenedicarboxylate **2a** (1 mmol) was chosen as the model reaction. Various bases and

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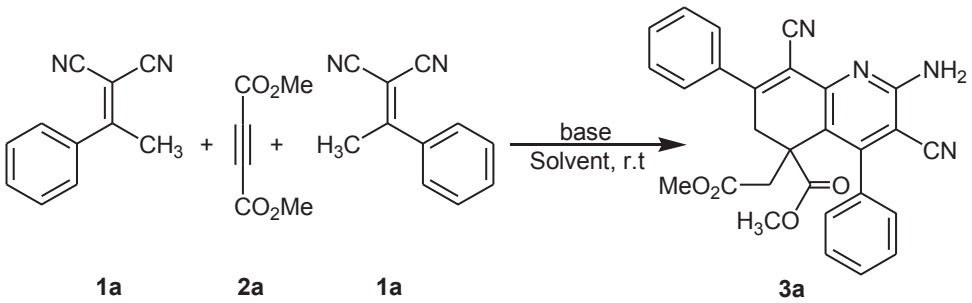
solvents were screened for their efficiency in this reaction. In the absence of any bases and with EtOH as the reaction medium, we did not observe the desired product, even after 24 h of stirring at room temperature. We obtained the best yield of 5,6-dihydroquinoline **3** when the reaction was performed in EtOH and catalyzed by triethylamine (Table 1).

The structures of the synthesized compounds **3a**–**f** and **5a**–**d** were established by IR, $^1$H NMR, and $^{13}$C NMR spectroscopy, mass spectrometry and the structures of **3b** and **5b** were successfully confirmed by X-ray crystallographic analysis.

**Table 1**
Synthetic results of **3a** under different reaction conditions



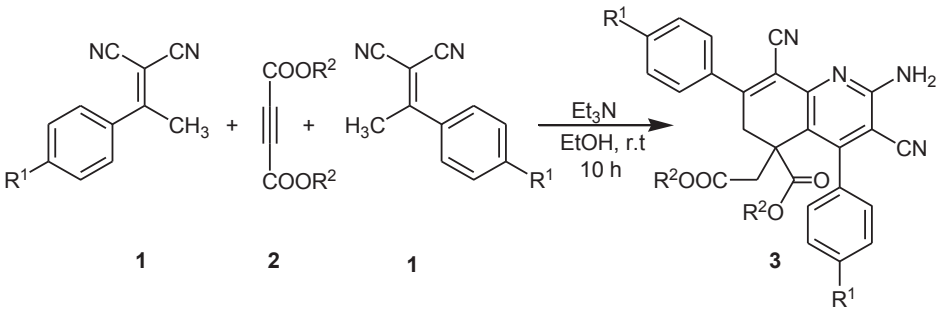

**1a** **2a** **1a** **3a**

| Entry | Solvent | Base | Yield (%) | Time/h |
|---|---|---|---|---|
| 1 | EtOH | — | 0 | 24 |
| 2 | **EtOH** | **$Et_3N$** | **88** | **8** |
| 3 | EtOH | $Na_2CO_3$ | 70 | 8 |
| 4 | EtOH | NaOH | 65 | 8 |
| 5 | MeOH | $Et_3N$ | 75 | 10 |
| 6 | MeOH | $Na_2CO_3$ | 72 | 10 |
| 7 | $CH_2Cl_2$ | $Et_3N$ | 40 | 10 |
| 8 | $CH_2Cl_2$ | $Na_2CO_3$ | 35 | 10 |
| 9 | $CH_3CN$ | $Et_3N$ | 80 | 10 |
| 10 | $CH_3CN$ | $Na_2CO_3$ | 55 | 10 |
| 11 | THF | $Et_3N$ | 40 | 12 |
| 12 | THF | $Na_2CO_3$ | 30 | 12 |

Using these optimized conditions, we then investigated the scope and general applicability of this methodology by using different α,α-dicyanoolefins **1** and acetylenic esters **2** (Table 2).

The mass spectrum of **3a** displayed a molecular ion peak at *m*/*z*=458, which is in agreement with the proposed structure. In the IR spectrum of **3a**, two absorption bands at 3471 and 3348 cm$^{-1}$,

**Table 2**
Synthesis of substituted 5,6-dihydroquinoline derivatives **3a**–**f**




**1** **2** **1** **3**

| Entry | $R^1$ | $R^2$ | Product | Yield (%) |
|---|---|---|---|---|
| 1 | H | Me | **3a** | 88 |
| 2 | H | Et | **3b** | 85 |
| 3 | $CH_3$ | Me | **3c** | 86 |
| 4 | $CH_3$ | Et | **3d** | 80 |
| 5 | $OCH_3$ | Me | **3e** | 84 |
| 6 | $OCH_3$ | Et | **3f** | 76 |

Cyclic aliphatic α,α-dicyanoolefins displayed different reactivity to acyclic α,α-dicyanoolefins **1** in reaction with acetylenic esters **2**. This is probably due to the steric effects. Treatment of 2-(3,4-dihydronaphthalen-1(2*H*)-ylidene)malononitrile **4** with acetylenic esters **2** in the presence of $Et_3N$ in ethanol gave acyclic succinates **5** a sharp band at 2221 cm$^{-1}$, and absorption bands at 1726, 1629 and 1182 cm$^{-1}$ attributed to $NH_2$, CN, C=O, C=C and C–O stretching frequencies, respectively, indicated the most significant functional groups of the product. The $^1$H NMR spectrum of **3a** showed one AB system, and two doublets at $\delta$=2.71, 3.37 and 3.56 ppm,

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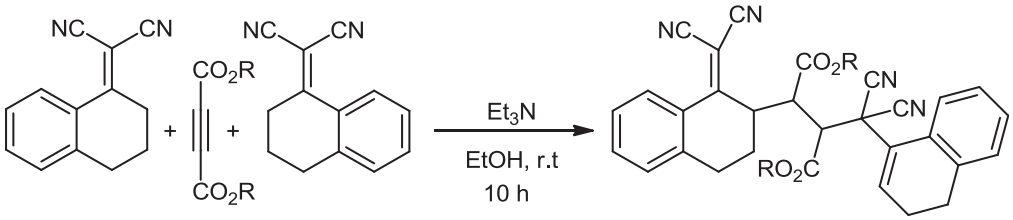
**Table 3**
Synthesis of succinates **5a**–**d** via the reaction of 2-(3,4-dihydronaphthalen-1(2*H*)-ylidene)malononitrile with acetylenic esters




| Entry | R | Product | Yield (%) |
|---|---|---|---|
| 1 | Me | **5a** | 85 |
| 2 | Et | **5b** | 83 |
| 3 | $(Me)_2CH$ | **5c** | 80 |
| 4 | $(Me)_3C$ | **5d** | 79 |

respectively, attributed to two $CH_2$ groups. Two methoxy groups were observed at $\delta$=3.30 and 3.45 ppm. The $NH_2$ group appeared as a singlet at $\delta$=7.19 ppm. 10 aromatic hydrogen atoms gave rise to characteristic resonances in the aromatic region of the spectrum. Observation of 28 distinct signals in the $^1$H-decoupled $^{13}$C NMR spectrum of **3a** is in agreement with the proposed structure. Finally, the structure of related compound **3b** was confirmed by X-ray crystallographic analysis (Fig. 1).

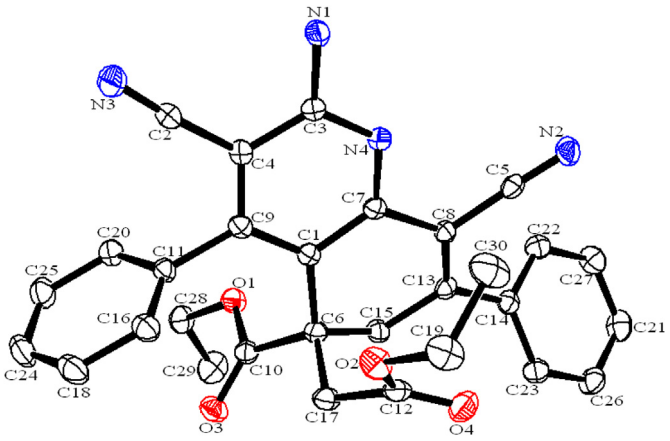



**Fig. 1.** ORTEP diagram for compound **3b**.

In the IR spectrum of **5a**, two bonds at 2229 and 1745 cm$^{-1}$ are related to stretching frequencies of CN and C=O, respectively. The $^1$H NMR spectrum of **5a** exhibited one multiplet signal at $\delta$=1.72–1.80 ppm related to one $CH_2$ group. A multiplet at $\delta$=1.98–2.28 ppm with an integral of seven was ascribed to one CH and three $CH_2$ groups. Two methoxy groups appeared at $\delta$=3.58 and 3.90 ppm. Protons of two CH groups neighboring the ester appeared as a triplet and doublet signal at $\delta$=4.02 and 4.41 ppm, respectively. A triplet at $\delta$=6.65 ppm was attributed to a methine proton (=CH). The eight aromatic hydrogen atoms gave rise to characteristic resonances in the aromatic region of the spectrum. Observation of 32 distinct signals in the $^1$H-decoupled $^{13}$C NMR spectrum of **5a** is in agreement with the proposed structure. Finally, the structure of related compound **5b** was confirmed by X-ray crystallographic analysis (Fig. 2).

On the basis of the above experimental results, together with the related reports of the vinyl malononitrile,[14] a plausible

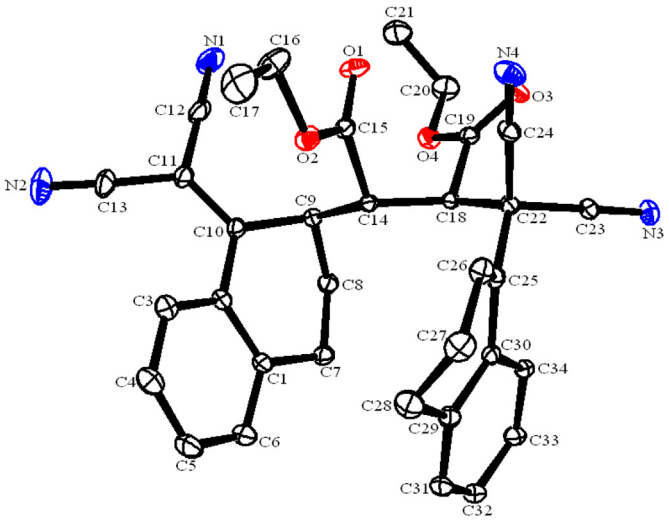



**Fig. 2.** ORTEP diagram for compound **5b**.

mechanism for the formation of the dihydroquinoline **3** is illustrated in Scheme 1.

At first, carbanion **6**, generated by deprotonation of α,α-dicyanoolefin **1** with $Et_3N$, attacks the acetylenic ester **2** to give an intermediate **7**. Again deprotonated α,α-dicyanoolefin **6** adds to intermediate **7** through Michael addition to form intermediate **8**, which in the presence of $Et_3N$ converts to carbanion intermediate **9**. Then the intramolecular addition of **9** to one cyano group followed by the second intramolecular addition of the resulted imino group to the second cyano group produces the cyclized intermediate **10**. At last, the dihydroquinoline **3** is formed by a [1,5]*H* shift in **10**.

Mechanistically, the formation of **5** can be interpreted as follows: the carbanion **11** generated by deprotonation of **4** by $Et_3N$ adds to acetylenic ester **2**, to furnish the intermediate **12**. Then, the carbanion **11′** a resonance form of **11**, attacks the double bond in intermediate **12** to form succinate **5** (Scheme 2).

As an application of this method, conversion of the compound **3a** to the new molecule using hydrolysis and decarboxylation reaction was next attempted (Scheme 3). The reaction of **3a** with NaOH in the mixture of MeOH and $H_2O$ at 70 °C for 6 h produced quinoline **13a**. The disappearance of one $CO_2Me$ and one aliphatic CH group and presence of one CH group in the aromatic region in $^1$H and $^{13}$C NMR confirm the formation of quinoline **13a**.

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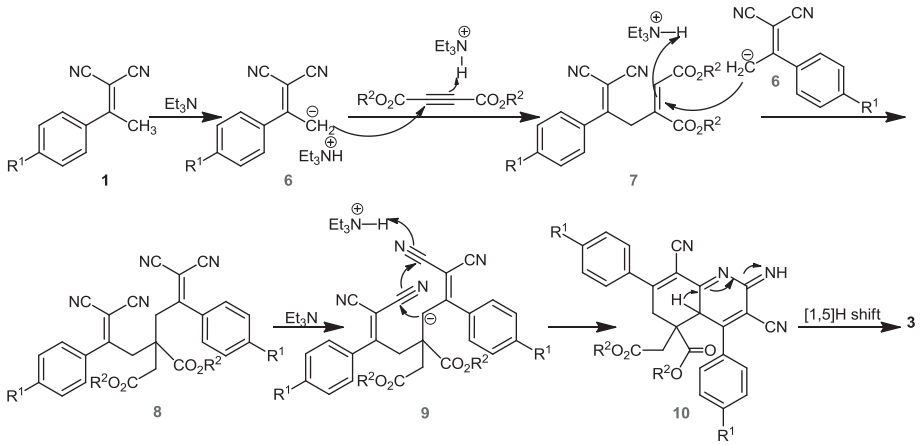
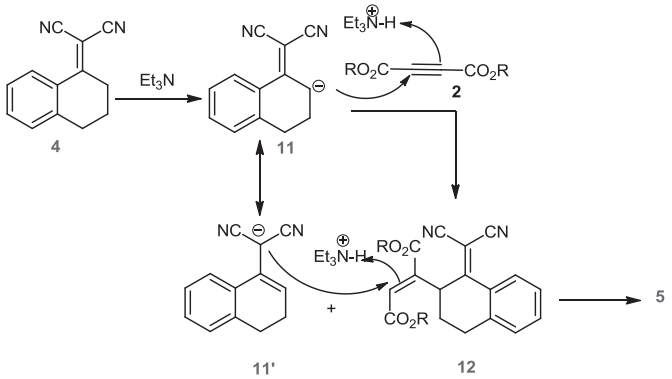
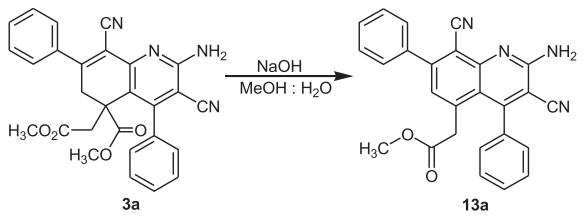


**Scheme 1.** Mechanistic rationalization for the synthesis of **3**.



**Scheme 2.** Mechanistic rationalization for the synthesis of **5**.



**Scheme 3.** Conversion of 5,6-dihydroquinoline **3a** to quinoline **13a**.

## 3. Conclusion

In conclusion, we report a one-pot reaction of two equivalents of α,α-dicyanoolefins with one equivalent of acetylenic esters. Acyclic α,α-dicyanoolefins led to the formation of 5,6-dihydroquinoline derivatives in good yields. The reaction proceeds from simple building blocks and generates two new rings, one C–N and three C–C bonds in this double annulation reaction. The reaction of cyclic α,α-dicyanoolefins with acetylenic esters generates succinates. Other values of this protocol include simple filtration, metal-catalyst free, and high atom economy.

## 4. Experimental

### 4.1. General

Elemental analyses for C, H and N were performed using a Heraeus CHN–O–Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. $^1$H NMR (300 and 400 MHz) and $^{13}$C NMR (75 and 100 MHz) spectra were obtained using Bruker DRX-300 and DRX-400 AVANCE spectrometers. IR spectra were recorded as KBr pellets on a NICOLET FTIR 100 spectrometer; absorbencies are reported in cm$^{-1}$.

### 4.2. General procedure for the preparation of compounds 3a–f

To a mixture of α,α-dicyanoolefin **1** (2 mmol) and dialkyl acetylenedicarboxylate **2** (1 mmol) in EtOH (5 mL) was added triethylamine (6 drops). The mixture was stirred at room temperature. After completion, monitored by TLC, the mixture was filtered and the precipitate washed with ethanol (2×4 mL) to afford the pure product **3a–f**.

*4.2.1. Methyl 2-(2-amino-3,8-dicyano-5-methyloxycarbonyl-4,7-diphenyl-5,6-dihydro-5-quinolinyl)acetate (**3a**).* Yellow powder, mp=250–252 °C, 0.42 g, yield: 88%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3471 and 3348 ($NH_2$), 2221 (CN), 1734 (C=O), 1629, 1552 and 1496 (Ar), 1182 (C–O). Anal. Calcd for $C_{28}H_{22}N_4O_4$ (478.50): C, 70.28; H, 4.63; N, 11.71%. Found: C, 70.20; H, 4.56; N, 11.66%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 2.71 (2H, $AB_{system}$, $^2J_{HH}$=15.6 Hz, $CH_2$), 3.30 (3H, s, $OCH_3$), 3.37 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.45 (3H, s, $OCH_3$), 3.56 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 7.16–7.17 (1H, m, CH of Ph), 7.18 (2H, s, $NH_2$), 7.30–7.32 (1H, m, CH of Ph), 7.47–7.56 (6H, m, 6CH of Ph), 7.70–7.71 (2H, m, 2CH of Ar). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 38.87 ($CH_2$), 40.14 ($CH_2$), 47.64 ($C^5$), 51.38 ($OCH_3$), 52.51 ($OCH_3$), 91.91 ($C^3$), 109.90 ($C^8$), 115.46 (CN), 115.98 (CN), 116.59 ($C^{4a}$), 128.00 ($2CH_{meta}$ of Ar), 128.16 ($CH_{para}$ of Ar), 128.18 ($CH_{para}$ of Ar), 128.37 ($CH_{ortho}$ of Ar), 128.57 ($2CH_{meta}$ of Ar), 129.07 ($CH_{ortho}$ of Ar), 129.14 ($CH_{ortho}$ of Ar), 130.55 ($CH_{ortho}$ of Ar), 135.11 ($C_{ipso}$), 136.96 ($C_{ipso}$), 151.23 ($C^7$), 153.92 ($C^4$), 158.47 ($C^{8a}$), 159.19 ($C^2$–$NH_2$), 170.84 (C=O), 172.81 (C=O). MS (EI, 70 eV): 478 ($M^+$, 1), 461 (3), 443 (2), 419 (16), 405 (100), 387 (1), 373 (28), 359 (81), 345 (16), 332 (10), 319 (8), 302 (4), 279 (3), 255 (3), 236 (8), 206 (4), 192 (8), 166 (8), 146 (24), 105 (15), 91 (28), 69 (5), 55 (8).

*4.2.2. Ethyl 2-(2-amino-3,8-dicyano-5-ethyloxycarbonyl-4,7-diphenyl-5,6-dihydro-5-quinolinyl)acetate (**3b**).* Yellow powder, mp=245–247 °C, 0.43 g, yield: 85%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3486 and 3346 ($NH_2$), 2223 (CN), 1732 (C=O), 1628, 1553 and 1451 (Ar), 1184 (C–O). Anal. Calcd for $C_{30}H_{26}N_4O_4$ (506.56): C, 71.13; H, 5.17; N, 11.06%. Found: C, 71.07; H, 5.10; N, 11.00%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 1.02 (3H, t, $^3J_{HH}$=7.2 Hz, $CH_3$), 1.03 (3H, t, $^3J_{HH}$=7.2 Hz,

$CH_3$), 2.67 (2H, $AB_{system}$, $^2J_{HH}$=15.6 Hz, $CH_2$), 3.35 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.53 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.66 (2H, dq, $^2J_{HH}$=10.4, $^3J_{HH}$=7.2 Hz, $OCH_2$), 3.90 (2H, dq, $^2J_{HH}$=19.6, $^3J_{HH}$=7.2 Hz, $OCH_2$), 7.16 (2H, s, $NH_2$), 7.18–7.19 (1H, m, CH of Ph), 7.30–7.32 (1H, m, CH of Ph), 7.48–7.56 (6H, m, CH of Ph), 7.69–7.71 (2H, m, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 13.33 ($CH_3$), 13.71 ($CH_3$), 39.38 ($CH_2$), 39.98 ($CH_2$), 47.55 ($C^5$), 60.11 ($OCH_2$), 61.44 ($OCH_2$), 91.88 ($C^3$), 109.96 ($C^8$), 115.47 (CN), 115.96 (CN), 116.79 ($C^{4a}$), 128.05 ($2CH_{meta}$ of Ar), 128.11 ($CH_{para}$ of Ar), 128.12 ($CH_{para}$ of Ar), 128.43 ($CH_{ortho}$ of Ar), 128.54 ($2CH_{meta}$ of Ar), 129.09 ($CH_{ortho}$ of Ar), 129.10 ($CH_{ortho}$ of Ar), 130.54 ($CH_{ortho}$ of Ar), 135.21 ($C_{ipso}$), 136.96 ($C_{ipso}$), 151.31 ($C^7$), 153,92 ($C^4$), 158.45 ($C^{8a}$), 159.23 ($C^2$–$NH_2$), 170.30 (C=O), 172.45 (C=O). MS (EI, 70 eV): 506 ($M^+$, 2), 433 (11), 419 (91), 405 (16), 391 (11), 373 (82), 359 (100), 345 (28), 330 (14), 315 (8), 301 (8), 282 (13), 264 (4), 239 (3), 215 (3), 179 (3), 164 (2), 139 (2), 91 (6), 77 (13), 60 (4), 51 (3). Crystal data for **3b** $C_{30}H_{25}N_4O4$ (CCDC 1033426): $M_W$=505.6, orthorhombic, Pbca, $a$=23.5560(4) Å, $b$=17.6196(2) Å, $c$=11.9742(5) Å, α=90.0, β=90.0, γ=90.0, V=4969.9(2) Å$^3$, $Z$=8, Dc=1.3513 mg/m$^3$, $F$ (000)=2120, Cu K\a ($\lambda$=1.54184 Å), 3.75≤2θ≤67, intensity data were collected at 120 K with a Xcalibur, Atlas, Gemini ultra area-detector diffractometer, and employing ω/2θ scanning technique, and employing ω/2θ scanning technique, in the range of −27≤h≤27, −20≤k≤20, −13≤l≤10; the structure was solved by a direct method, all non-hydrogen atoms were positioned and anisotropic thermal parameters refined from 2406 observed reflections with $R$ (int)=0.0346 by a full-matrix least-squares technique converged to $R$=0.0359 and w$R_2$=0.1166 [I>2sigma(I)].

*4.2.3. Methyl 2-[2-amino-3,8-dicyano-5-methyloxycarbonyl-4,7-di(4-methylphenyl)-5,6-dihydro-5-quinolinyl]acetate (**3c**).* Yellow powder, mp=247–249 °C, 0.44 g, yield: 86%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3465 and 3357 ($NH_2$), 2220 (CN), 1736 (C=O), 1622, 1552 and 1439 (Ar), 1188 (C–O). Anal. Calcd for $C_{30}H_{26}N_4O_4$ (506.56): C, 71.13; H, 5.17; N, 11.06%. Found: C, 71.06; H, 5.09; N, 11.12%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 2.39 (6H, s, $2CH_3$), 2.69 (2H, $AB_{system}$, $^2J_{HH}$=15.6 Hz, CH of $CH_2$), 3.30 (3H, s, $OCH_3$), 3.31 (1H, d, $^2J_{HH}$=17.6 Hz, CH of $CH_2$), 3.43 (3H, s, $OCH_3$), 3.52 (1H, d, $^2J_{HH}$=17.6 Hz, CH of $CH_2$), 7.04 (1H, dd, $^3J_{HH}$=7.8 Hz, $^4J_{HH}$=1.6 Hz, CH of Ph), 7.12 (2H, s, $NH_2$), 7.16 (1H, dd, $^3J_{HH}$=7.8 Hz, $^4J_{HH}$=1.6 Hz, CH of Ph), 7.28 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.32 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.35 (2H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.61 (2H, d, $^3J_{HH}$=8.0 Hz, 2CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 20.90 ($CH_3$), 20.98 ($CH_3$), 39.75 ($CH_2$), 39.95 ($CH_2$), 47.58 ($C^5$), 51.36 ($OCH_3$), 52.51 ($OCH_3$), 91.97 ($C^3$), 109.19 ($C^8$), 115.54 (CN), 116.15 (CN), 116.77 ($C^{4a}$), 128.00 (2CH of Ar), 128.24 (CH of Ar), 128.64 (CH of Ar), 128.77 (CH of Ar), 128.95 (CH of Ar), 129.18 (2CH of Ar), 132.25 ($C_{ipso}$), 134.03 ($C_{ipso}$), 138.47 ($C_{ipso}$-Me), 140.69 ($C_{ipso}$-Me), 151.34 ($C^7$), 154.34 ($C^4$), 158.41 ($C^{8a}$), 158.96 ($C^2$–$NH_2$), 170.80 (C=O), 172.89 (C=O). MS (EI, 70 eV): 506 ($M^+$, 4), 448 (16), 433 (91), 402 (72), 387 (88), 372 (26), 348 (5), 324 (5), 293 (4), 271 (5), 234 (8), 205 (8), 182 (17), 155 (17), 140 (17), 117 (16), 99 (25), 84 (100), 57 (33).

*4.2.4. Ethyl 2-[2-amino-3,8-dicyano-5-ethyloxycarbonyl-4-(3-methylphenyl)-7-(4-methylphenyl)-5,6-dihydro-5-quinolinyl]acetate (**3d**).* Yellow powder, mp=248–250 °C, 0.43 g, yield: 80%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3458 and 3351 ($NH_2$), 2224 (CN), 1721 (C=O), 1633, 1553 and 1450 (Ar), 1196 (C–O). Anal. Calcd for $C_{32}H_{30}N_4O_4$ (534.61): C, 71.89; H, 5.66; N, 10.48%. Found: C, 71.81; H, 5.59; N, 10.43%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 1.02 (3H, t, $^3J_{HH}$=7.2 Hz, $CH_3$), 1.03 (3H, t, $^3J_{HH}$=7.2 Hz, $CH_3$), 2.38 (6H, s, $2CH_3$), 2.66 (2H, $AB_{system}$, $^2J_{HH}$=16.0 Hz, CH of $CH_2$), 3.30 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.51 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.62–3.70 (2H, m, $CH_2$), 3.83–3.96 (2H, m, $CH_2$), 7.04 (1H, dd, $^3J_{HH}$=8 Hz, $^4J_{HH}$=1.6 Hz, CH of Ph), 7.12 (2H, s, $NH_2$), 7.17 (1H, dd, $^3J_{HH}$=8.0 Hz, $^4J_{HH}$=1.6 Hz, CH of Ph), 7.30 (2H, t, $^3J_{HH}$=6.8 Hz, 2CH of Ph), 7.35 (2H, t, $^3J_{HH}$=8.0 Hz, 2CH of Ph), 7.61 (2H, d, $^3J_{HH}$=8.4 Hz, 2CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 13.29 ($CH_3$), 13.71 ($CH_3$), 20.88 ($CH_3$), 20.97 ($CH_3$), 39.75 ($CH_2$), 39.99 ($CH_2$), 47.50 ($C^5$), 60.09 ($OCH_3$), 61.48 ($OCH_3$), 91.91 ($C^3$), 109.25 ($C^8$), 115.57 (CN), 116.16 (CN), 116.97 ($C^{4a}$), 128.06 (2CH of Ar), 128.31 (CH of Ar), 128.63 (CH of Ar), 128.68 (CH of Ar), 128.96 (CH of Ar), 129.08 (2CH of Ar), 132.34 ($C_{ipso}$), 134.03 ($C_{ipso}$), 138.44 ($C_{ipso}$-Me), 140.69 ($C_{ipso}$-Me), 151.42 ($C^7$), 154.01 ($C^4$), 158.45 ($C^{8a}$), 159.03 ($C^2$–$NH_2$), 170.27 (C=O), 172.56 (C=O). MS (EI, 70 eV): 534 ($M^+$, 3), 462 (10), 447 (100), 419 (12), 402 (95), 387 (99), 372 (54), 357 (15), 330 (8), 311 (5), 295 (4), 282 (4), 264 (4), 239 (3), 209 (4), 186 (6), 165 (1), 151 (2), 121 (1), 91 (6), 65 (3), 50 (1).

*4.2.5. Methyl 2-[2-amino-3,8-dicyano-4-(3-methoxyphenyl)-7-(4-methoxyphenyl)-5-methyloxycarbonyl-5,6-dihydro-5-quinolinyl]acetate (**3e**).* Yellow powder, mp=222–225 °C, 0.45 g, yield: 84%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3460 and 3349 ($NH_2$), 2217 (CN), 1727 (C=O), 1613, 1551 and 1438 (Ar), 1196 (C–O). Anal. Calcd for $C_{30}H_{26}N_4O_6$ (538.56): C, 66.91; H, 4.87; N, 10.40%. Found: C, 66.83; H, 4.80; N, 10.34%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 2.71 (2H, $AB_{system}$, $^2J_{HH}$=15.6 Hz, CH of $CH_2$), 3.20 (1H, d, $^2J_{HH}$=17.6 Hz, CH of $CH_2$), 3.33 (3H, s, $OCH_3$), 3.44 (3H, s, $OCH_3$), 3.55 (1H, d, $^2J_{HH}$=17.6 Hz, CH of $CH_2$), 3.83 (3H, s, $OCH_3$), 3.84 (3H, s, $OCH_3$), 7.01–7.10 (5H, m, CH of Ph), 7.11 (2H, s, $NH_2$), 7.20 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.71 (2H, d, $^3J_{HH}$=8.8 Hz, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 39.70 ($CH_2$), 39.94 ($CH_2$), 47.62 ($C^5$), 51.34 ($OCH_3$), 52.55 ($OCH_3$), 55.15 ($OCH_3$), 55.42 ($OCH_3$), 92.04 ($C^3$), 108.09 ($C^8$), 113.37 (CH of Ar), 113.72 (CH of Ar), 113.99 (2CH of Ar), 115.66 (CN), 115.49 (CN), 117.08 ($C^{4a}$), 127.18 ($C_{ipso}$), 128.84 ($C_{ipso}$), 129.79 (CH of Ar), 130.04 (2CH of Ar), 130.51 (CH of Ar), 151.56 ($C^7$), 153.77 ($C^4$), 158.40 ($C^{8a}$), 158.46 ($C^2$–$NH_2$), 159.50 ($C_{ipso}$-OMe), 161.18 ($C_{ipso}$-OMe), 170.85 (C=O), 172.94 (C=O). MS (EI, 70 eV): 538 ($M^+$, 1), 479 (5), 464 (29), 433 (34), 419 (100), 405 (10), 390 (12), 375 (29), 361 (18), 345 (22), 332 (21), 319 (58), 304 (30), 290 (41), 276 (36), 263 (42), 239 (52), 227 (35), 213 (39), 202 (37), 189 (40), 178 (36).

*4.2.6. Ethyl 2-[2-amino-3,8-dicyano-5-ethyloxycarbonyl-4-(3-methoxyphenyl)-7-(4-methoxyphenyl)-5,6-dihydro-5-quinolinyl]acetate (**3f**).* Yellow powder, mp=227–229 °C, 0.43 g, yield: 76%. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3452 and 3346 ($NH_2$), 2219 (CN), 1714 (C=O), 1615, 1552 and 1454 (Ar), 1187 (C–O). Anal. Calcd for $C_{32}H_{30}N_4O_6$ (566.61): C, 67.83; H, 5.34; N, 9.89%. Found: C, 67.76; H, 5.27; N, 9.82%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 1.03 (6H, t, $^3J_{HH}$=6.4 Hz, CH of $CH_3$), 2.66 (2H, $AB_{system}$, $^2J_{HH}$=16.4 Hz, CH of $CH_2$), 3.28 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.53 (1H, d, $^2J_{HH}$=18.0 Hz, CH of $CH_2$), 3.69 (2H, q, $^3J_{HH}$=7.2 Hz, CH of $CH_2$), 3.82 (3H, s, $OCH_3$), 3.84 (3H, s, $OCH_3$), 3.87–3.98 (2H, m, CH of $CH_2$), 7.02 (2H, t, $^3J_{HH}$=7.2 Hz, 2CH of Ph), 7.07 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.09 (2H, s, $NH_2$), 7.10 (2H, t, $^3J_{HH}$=8.4 Hz, 2CH of Ph), 7.22 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.71 (2H, d, $^3J_{HH}$=8.8 Hz, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 13.33 ($CH_3$), 13.72 ($CH_3$), 39.68 ($CH_2$), 39.81 ($CH_2$), 47.53 ($C^5$), 55.16 ($OCH_3$), 55.43 ($OCH_3$), 60.09 ($OCH_2$), 61.47 ($OCH_2$), 92.03 ($C^3$), 108.16 ($C^8$), 113.32 (CH of Ar), 113.68 (CH of Ar), 113.96 (2CH of Ar), 115.70 (CN), 116.49 (CN), 117.27 ($C^{4a}$), 127.26 ($C_{ipso}$), 128.85 ($C_{ipso}$), 129.84 (CH of Ar), 130.09 (2CH of Ar), 130.52 (CH of Ar), 151.64 ($C^4$), 153.78 ($C^7$), 158.46 ($C^{8a}$), 158.53 ($C^2$–$NH_2$), 159.51 ($C_{ipso}$-OMe), 161.19 ($C_{ipso}$-OMe), 170.33 (C=O), 172.61 (C=O). MS (EI, 70 eV): 566 ($M^+$, 1), 493 (1), 478 (42), 433 (47), 419 (54), 404 (7), 390 (16), 375 (9), 361 (14), 348 (11), 332 (14), 319 (16), 305 (7), 291 (14), 276 (26), 256 (33), 239 (16), 215 (16), 198 (100), 174 (66), 159 (28), 145 (71), 121 (92), 108 (97).

### 4.3. General procedure for the preparation of compounds 5a–d

To a mixture of 2-(3,4-dihydronaphthalen-1(2*H*)-ylidene)malononitrile **4** (2 mmol) and dialkyl acetylenedicarboxylate **2** (1 mmol)

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in EtOH (5 mL) was added triethylamine (6 drops). The mixture was stirred at room temperature. After completion, monitored by TLC, the mixture was filtered and the precipitate washed with ethanol (2×4 mL) to afford the pure product **5a**–**d**.

*4.3.1. Dimethyl 2-dicyano(1,2-dihydro-4-naphthalenyl)methyl-3-(1-dicyanomethylene-1,2,3,4-tetrahydro-2-naphthalenyl)succinate (**5a**).* White powder, mp=218–220 °C, 0.45 g, yield: 85%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2229 (CN), 1745 (C=O), 1564 and 1442 (Ar), 1209 (C–O). Anal. Calcd for $C_{32}H_{26}N_4O_4$ (530.58): C, 72.44; H, 4.94; N, 10.56%. Found: C, 72.35; H, 4.88; N, 10.46%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 1.72–1.80 (2H, m, $CH_2$), 1.98–2.28 (7H, m, CH and $3CH_2$), 3.58 (3H, s, $OCH_3$), 3.90 (3H, s, $OCH_3$), 4.02 (1H, t, $^3J_{HH}$=3.2 Hz, CH), 4.41 (1H, d, $^3J_{HH}$=2.0 Hz, CH), 6.65 (1H, t, $^3J_{HH}$=4.8 Hz, CH), 6.88 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.34–7.39 (3H, m, CH of Ph), 7.43 (1H, d, $^3J_{HH}$=7.2 Hz, CH of Ph), 7.55 (1H, t, $^3J_{HH}$=7.2 Hz, CH), 7.72 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph), 7.89 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 21.37 ($CH_2$), 22.56 ($CH_2$), 22.68 ($CH_2$), 26.41 ($CH_2$), 40.11 ($C(CN)_2$), 41.29 (CH), 43.41 (CH), 44.88 (CH), 52.25 ($OCH_3$), 52.93 ($OCH_3$), 80.69 ($C(CN)_2$), 112.44 (CN), 112.84 (CN), 113.56 (CN), 114.31 (CN), 124.00 ($CH^{2'}$), 124.90 ($C^{8a'}$), 126.51 (CH of Ar), 127.04 (CH of Ar), 127.64 ($C^{4a}$), 127.76 ($C^{1'}$), 128.11 (CH of Ar), 129.10 (2CH of Ar), 129.53 (CH of Ar), 133.59 (CH of Ar), 136.15 (CH of Ar), 137.32 ($C^{4a'}$), 138.53 ($C^{8a}$), 168.19 (C=O), 169.39 (C=O), 173.82 ($C^1$). MS (EI, 70 eV): 531 ($M^+$, 2), 499 (3), 438 (3), 338 (3), 306 (3), 279 (2), 246 (4), 218 (4), 192 (24), 145 (100), 113 (70), 85 (6), 59 (12).

*4.3.2. Diethyl 2-dicyano(1,2-dihydro-4-naphthalenyl)methyl-3-(1-dicyanomethylene-1,2,3,4-tetrahydro-2-naphthalenyl)succinate (**5b**).* White powder, mp=217–220 °C, 0.46 g, yield: 83%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2229 (CN), 1741 (C=O), 1631, 1565 and 1457 (Ar), 1200 (C–O). Anal. Calcd for $C_{34}H_{30}N_4O_4$ (558.63): C, 73.10; H, 5.41; N, 10.03%. Found: C, 73.18; H, 5.35; N, 9.93%. $\delta_H$ 1.18 (3H, t, $^3J_{HH}$=7.2 Hz, $CH_3$), 1.40 (3H, d, $^3J_{HH}$=7.2 Hz, $CH_3$), 1.99–2.29 (9H, m, CH and $4CH_2$), 4.00–4.11 (3H, m, CH and $OCH_2$), 4.28–4.42 (3H, m, CH and $OCH_2$), 6.63 (1H, t, $^3J_{HH}$=4.4 Hz, CH), 6.81 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph), 7.34–7.40 (3H, m, CH of Ph), 7.45 (1H, t, $^3J_{HH}$=7.2 Hz, CH of Ph), 7.54 (1H, t, $^3J_{HH}$=7.2 Hz, CH), 7.68 (1H, d, $^3J_{HH}$=9.0 Hz, CH of Ph), 7.89 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 13.29 ($CH_3$), 13.56 ($CH_3$), 21.38 ($CH_2$), 22.61 ($2CH_2$), 22.33 ($CH_2$), 40.10 ($C(CN)_2$), 41.65 (CH), 43.58 (CH), 44.69 (CH), 61.48 ($OCH_2$), 62.35 ($OCH_2$), 80.54 ($C(CN)_2$), 112.55 (CN), 112.88 (CN), 113.53 (CN), 114.46 (CN), 123.90 ($CH^{2'}$), 124.71 ($C^{8a'}$), 126.39 (CH of Ar), 127.01 (CH of Ar), 127.71 ($C^{4a}$), 127.74 ($C^{1'}$), 128.09 (CH of Ar), 129.03 (CH of Ar), 129.22 (CH of Ar), 129.74 (CH of Ar), 133.44 (CH of Ar), 136.00 (CH of Ar), 137.33 ($C^{4a'}$), 138.64 ($C^{8a}$), 167.51 (C=O), 168.81 (C=O), 174.46 ($C^1$). MS (EI, 70 eV): 559 ($M^+$, 8), 513 (8), 467 (4), 411 (3), 386 (3), 366 (16), 320 (19), 292 (8), 273 (8), 247 (19), 218 (19), 193 (83), 166 (91), 145 (28), 127 (100), 99 (86), 83 (28), 55 (16). Crystal data for **5b** $C_{60}H_{60}N_{20}O40$ (CCDC 1001616): $M_W$=1701.28, monoclinic, P21/c, $a$=17.8276(16) Å, $b$=8.9183(7) Å, $c$=20.3456(19) Å, α=90.0, β=109.450(10), γ=90.0, V=3050.2(5) $Å^3$, $Z$=4, Dc=1.217 mg/$m^3$, $F$ (000)=880, Mo Kα (λ=0.71073 Å), 3.26≤2θ≤25.10, intensity data were collected at 295(2) K with a Bruker APEX area-detector diffractometer, and employing ω/2θ scanning technique, and employing ω/2θ scanning technique, in the range of −21≤h≤21, −10≤k≤9, −17≤l≤24; the structure was solved by a direct method, all non-hydrogen atoms were positioned and anisotropic thermal parameters refined from 3278 observed reflections with $R$ (int)= 0.0954 by a full-matrix least-squares technique converged to $R$=0.0505 and w$R_2$=0.1320 [I>2sigma(I)].

*4.3.3. Diisopropyl 2-dicyano(1,2-dihydro-4-naphthalenyl)methyl-3-(1-dicyanomethylene-1,2,3,4-tetrahydro-2-naphthalenyl)succinate (**5c**).* White powder, mp=218–220 °C, 0.22 g, yield: 80%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2225 (CN), 1733 (C=O), 1571 and 1458 (Ar), 1206 (C–O). Anal. Calcd for $C_{36}H_{34}N_4O_4$ (586.69): C, 73.70; H, 5.84; N, 9.55%. Found: C, 73.62; H, 5.76; N, 9.59%. $^1$H NMR (400 MHz, DMSO-$d_6$)): $\delta_H$ 1.19 (3H, t, $^3J_{HH}$=6.0 Hz, $CH_3$), 1.29 (3H, t, $^3J_{HH}$=6.0 Hz, $CH_3$), 1.37 (3H, t, $^3J_{HH}$=6.0 Hz, $CH_3$), 1.42 (3H, t, $^3J_{HH}$=6.0 Hz, $CH_3$), 2.08–2.44 (9H, m, CH and $4CH_2$), 4.00 (1H, t, $^3J_{HH}$=3.2 Hz, CH), 4.26 (1H, d, $^3J_{HH}$=2.8 Hz, CH), 4.85 (1H, h, $^3J_{HH}$=6.4 Hz, OCH), 5.15 (1H, h, $^3J_{HH}$=6.4 Hz, OCH), 6.64 (1H, dd, $^3J_{HH}$=6.0 Hz, $^3J_{HH}$=3.6 Hz, CH), 6.76 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph), 7.31–7.45 (5H, m, CH of Ph), 7.54 (1H, t, $^3J_{HH}$=6.8 Hz, CH), 7.66 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.89 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph). $^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 20.92 ($CH_3$), 21.03 ($CH_3$), 21.06 ($CH_3$), 21.31 ($CH_3$), 21.49 ($CH_2$), 22.61 ($CH_2$), 22.83 ($CH_2$), 26.28 ($CH_2$), 41.68 ($C(CN)_2$), 42.12 (CH), 43.07 (CH), 44.77 (CH), 69.72 (OCH), 70.62 (OCH), 80.69 ($C(CN)_2$), 112.44 (CN), 112.84 (CN), 113.56 (CN), 114.31 (CN), 123.80 ($CH^{2'}$), 124.65 ($C^{8a'}$), 126.33 (CH of Ar), 126.95 (CH of Ar), 127.67 ($C^{4a}$), 127.77 ($C^{1'}$), 127.87 (CH of Ar), 128.97 (CH of Ar), 129.35 (CH of Ar), 129.97 (CH of Ar), 133.30 (CH of Ar), 135.87 (CH of Ar), 137.30 ($C^{4a'}$), 138.81 ($C^{8a}$), 166.75 (C=O), 168.81 (C=O), 173.84 ($C^1$). MS (EI, 70 eV): 586 ($M^+$, 2), 527 (8), 485 (4), 467 (4), 394 (4), 352 (4), 310 (4), 292 (8), 253 (29), 236 (16), 211 (69), 193 (100), 166 (54), 117 (24), 99 (1).

*4.3.4. Di(tert-butyl) 2-dicyano(1,2-dihydro-4-naphthalenyl)methyl-3-(1-dicyanomethylene-1,2,3,4-tetrahydro-2-naphthalenyl)succinate (**5d**).* White powder, mp=222–224 °C, 0.49 g, yield: 79%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2226 (CN), 1734 (C=O), 1570 and 1460 (Ar), 1249 (C–O). Anal. Calcd for $C_{38}H_{38}N_4O_4$ (614.74): C, 74.25; H, 6.23; N, 9.11%. Found: C, 74.18; H, 6.16; N, 9.16%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta_H$ 1.41 (9H, s, $3CH_3$), 1.16 (9H, s, $3CH_3$), 1.92–2.42 (9H, m, CH and $4CH_2$), 3.96–3.98 (1H, m, CH), 4.08 (1H, s, CH), 6.71 (1H, t, $^3J_{HH}$=4.4 Hz, CH), 6.74 (1H, d, $^3J_{HH}$=7.6 Hz, CH of Ph), 7.30 (1H, d, $^3J_{HH}$=7.2 Hz, CH of Ph), 7.36–7.46 (3H, m, CH of Ph), 7.53 (1H, t, $^3J_{HH}$=7.2 Hz, CH), 7.71 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph), 7.88 (1H, d, $^3J_{HH}$=8.0 Hz, CH of Ph).$^{13}$C NMR (100.0 MHz, DMSO-$d_6$): $\delta_C$ 21.61 ($CH_2$), 22.65 ($CH_2$), 23.02 ($CH_2$), 26.21 ($CH_2$), 27.44 ($2^t$Bu), 40.09 ($C(CN)_2$), 42.55 (CH), 43.56 (CH), 45.52 (CH), 80.51 ($C(CN)_2$), 83.03 ($OCCH_3$), 83.80 ($OCCH_3$), 112.74 (CN), 113.34 (CN), 113.56 (CN), 114.91 (CN), 123.65 ($CH^{2'}$), 124.67 ($C^{8a'}$), 126.23 (CH of Ar), 126.94 (CH of Ar), 127.64 ($C^{4a}$), 127.76 (CH of Ar′), 128.07 ($C^{1'}$), 128.94 (CH of Ar), 129.45 (CH of Ar), 130.16 (CH of Ar), 133.29 (CH of Ar), 135.74 (CH of Ar), 137.23 ($C^{4a'}$), 138.98 ($C^{8a}$), 165.97 (C=O), 168.54 (C=O), 175.04 ($C^1$). MS (EI, 70 eV): 614 ($M^+$, 5), 599 (10), 584 (4), 570 (7), 557 (6), 541 (13), 527 (8), 485 (4), 467 (4), 394 (4), 352 (4), 310 (4), 292 (8), 253 (29), 236 (16), 211 (69), 193 (100), 166 (54), 117 (24), 99 (1).

### 4.4. Synthesis of quinoline 13a

To a solution of 5,6-dihydroquinoline **3a** (1 mmol) in EtOH: $H_2O$ (6 mL) was added NaOH (1.2 mmol) and the reaction mixture was stirred at 70 °C for 6 h. After completion of the reaction as indicated by TLC, the mixture was filtered and washed by MeOH (3 mL) to produce the pure product **13a**.

*4.4.1. Methyl 2-(2-amino-3,8-dicyano-4,7-diphenylquinolin-5-yl)acetate (**13a**).* Yellow powder, mp=265–267 °C, 0.42 g, yield: 90%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3441 and 3338 ($NH_2$), 2220 (CN), 1731 (C=O), 1634, 1554 and 1480 (Ar), 1212 (C–O). Anal. Calcd for $C_{26}H_{18}N_4O_2$ (418.45): C, 74.63; H, 4.34; N, 13.39%. Found: C, 74.56; H, 4.25; N, 13.32%. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta_H$ 2.07 (2H, s, $CH_2$), 3.08 (3H, s, $OCH_3$), 7.39–7.42 (1H, m, CH of Ph), 7.43 (2H, s, $NH_2$), 7.52–7.57 (6H, m, 6CH of Ph), 7.69–7.72 (4H, m, 2CH of Ar). $^{13}$C NMR (75.0 MHz, DMSO-$d_6$): 30.71 ($CH_2$), 52.10 ($OCH_3$), 98.24 ($C^3$), 108.64 ($C^8$), 115.20 (CN), 116.23 (CN), 116.60 ($C^{4a}$), 124.49 (CH of Ar), 128.33 (2CH of Ar), 128.83 (2CH of Ar), 128.97 (2CH of Ar), 129.36 (2CH of Ar), 129.70 (2CH of Ar), 135.55 ($C^5$), 136.32 ($C_{ipso}$), 136.77 ($C_{ipso}$),

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149.56 ($C^7$), 150.94 ($C^4$), 155.60 ($C^{8a}$), 156.96 ($C^2$–$NH_2$), 166.67 (C=O). MS (EI, 70 eV): 418 ($M^+$, 8), 404 (100), 373 (99), 345 (58), 327 (14), 315 (9), 302 (16), 389 (12), 276 (8), 264 (8), 240 (2), 227 (2), 214 (3), 202 (6), 172 (4), 158 (8), 145 (8), 131 (6), 118 (4), 105 (2), 89 (2), 77 (21), 51 (12).

## Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.08.033.

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