

Role of Cyanoacetanilides in heterocyclic synthesis: Toxicological aspects of azobenzene derivatives against the highly polyphagous insect, Egyptian cotton leafworm, *Spodoptera littoralis* (Boisd.)

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Abstract

A wide variety of interesting heterocyclic cyanoacetanilide derivatives were amalgamated via the interaction of the key precursor 2-Cyano-*N*-(4-(phenyl diazenyl) phenyl) acetamide (1) with salicylaldehyde, 2-Hydroxy-1-naphthaldehyde, phenacyl bromide, acetylacetone, benzoylacetone, malononitrile dimer, elemental sulfur under Gewald conditions, various diazonium salts and chalcone derivatives to yield innovative coumarins, pyrazolones, pyridinones, pyridines, thiazoles, thiophenes, hydrazone derivatives, pyrazolotriazine and triazolotriazine end products incorporating azobenzene nucleus. The skeletons of the innovatively created compounds were clarified by diverse spectroscopic methods such as FT-IR, mass spectroscopy and ¹H NMR. In conclusion, the insecticidal efficiency of the newly output compounds was assessed against the cotton leafworm, *Spodoptera littoralis* under laboratory conditions. According to the observed LC₅₀ and LC₉₀ values, azobenzene derivatives 18c, 21c, 18b, 21b and 18d exhibit excellent toxic effects with LC₅₀ values of 13.248, 15.554, 18.370, 21.777 and 25.845 ppm, respectively, and toxicity index being 82.82, 70.54, 59.73, 50.38 and 42.45%, respectively, comparing with the recommended, methomyl insecticide, lannate 90% SP which was the utmost active compound (the lowermost LC₅₀ value, 10.972 ppm, toxicity index, 100%).

Keywords: cyanoacetamide; cyanoacetanilide; azobenzene; insecticidal activity, cotton leafworm; *spodoptera littoralis*

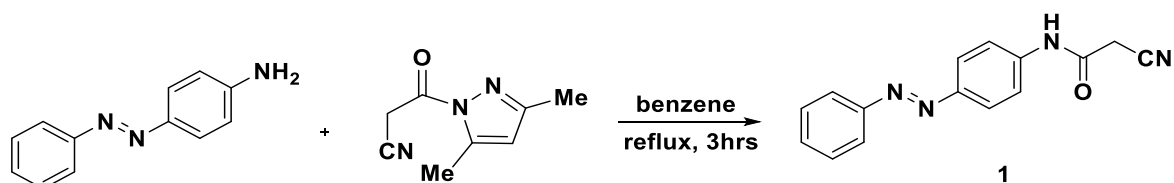
Introduction

Azobenzene is characterized by two phenyl rings connected to each other by an N=N double bond and known as diazene (diimide), aryl azo photoswitchable chemical compound, as they absorb light strongly ^[1]. Azobenzene derivatives have a remarkable biocidal activity towards the pathogenic Gram-negative bacteria, Gram-positive bacteria, fungi and yeast ^[2]. Thus, it has brilliant larvicidal activity towards mosquito larvae. Particularly, also it displayed insecticidal action alongside *Mythimna separate* ^[3]. The Egyptian cotton leafworm, *Spodoptera littoralis*, Boisduval (Lepidoptera: Noctuidae) is a highly polyphagous defoliator of numerous cultivated plants. It's severely attack field crops, vegetable, fruit and ornamental plants causing heavy damage in different parts of the host plants subsequently fatal loss to the economy. So, scientists produced several innovative synthesized organic compounds of anticipated biological response to the desired insect ^[4]. Our goal of this work was the assessment of the insecticidal efficacy of the innovatively synthesized cyanoacetanilide end product towards the cotton leafworm, *S. littoralis*.

Results and Discussion

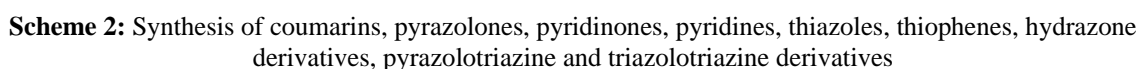
Chemistry

The synthetic approaches approved in schemes (1-3). Cyano acetylation of 4-amino azobenzene using 1-cyano acetyl-3,5-dimethyl pyrazole in dry solvent benzene furnished the preliminary 2-cyano-*N*-(4-(phenyl diazenyl) phenyl) acetamide (1) ^[5] (Scheme 1).



Scheme 1: Synthesis of starting cyanoacetanilide 1

Regarding to its spectral data, the structure 1 was clarified. IR spectrum revealed absorption bands at 3275 cm^{-1} for the NH function, a sharp band at 2250 cm^{-1} for the CN group and a strong band at 1670 cm^{-1} for the amidic CO function. Its ^1H NMR spectrum showed the presence of a singlet signal at $\delta_{\text{H}} 3.96\text{ ppm}$ owing to methylene protons, multiplet signal at $\delta_{\text{H}} 7.55\text{--}7.92\text{ ppm}$ due to aromatic protons and a singlet signal at $\delta_{\text{H}} 10.66\text{ ppm}$ for NH amidic. The MS displayed a (M^+) at m/z 264 consigned to $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}$. The current work refers to the preparation of Azobenzene containing a chromene moiety. Hence, Knoevenagel cyclocondensation in boiling EtOH of cyanoacetanilide derivative 1 with either salicylaldehyde or 2-hydroxy-1-naphthaldehyde enclosing catalytic piperidine as a base provided the coumarin derivatives 2 or 3, respectively (Scheme 2). IR spectrum of 2, exhibited two absorption bands at 3435 and 3440 cm^{-1} assigned to two NH groups besides one CO absorption band at 1758 cm^{-1} . The ^1H NMR spectrum revealed a singlet signal at $\delta_{\text{H}} 9.06\text{ ppm}$ assignable to H-4 proton of chromene moiety, additionally a multiplet signal equivalent to 13 protons at $\delta_{\text{H}} 7.42\text{--}8.02\text{ ppm}$, which ascribed to the aromatic protons and singlet signal for NH at $\delta_{\text{H}} 10.25$. The structure of the chromene derivative 2 has also MS indicated a (M^+) at m/z 368 which agree with its MF $\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}_2$, IR of 3 exhibited three absorption bands at 3435 , 3447 assigned to two NH groups besides one CO function at 1684 cm^{-1} . Its MS revealed a (M^+) at m/z 418, corresponding to its MF $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}_2$ [4] (Scheme 2). Heterocyclic aromatic nitrogen compounds containing pyrrole nucleus displaying a broad range of biological activity [6]. Only just, the reaction of cyanoacetanilide moiety with α -halocarbonyl compounds yielded pyrrole derivatives [7]. So, cyclocondensation of 1 with phenacyl bromide in hot ethanol containing a catalytic TEA developed the pyrrole derivative 4 (Scheme 2). IR spectrum showed the existence of CO stretching at 1668 cm^{-1} , 2259 for CN. The MS displayed a (M^+) at m/z 364 ascribed to $\text{C}_{23}\text{H}_{16}\text{N}_4\text{O}$. The synthetic potentiality of the cyanoacetanilide precursor 1 was explored through the cyclocondensation with β -diketones. Subsequently, the interaction of 1 with 1,3-dicarbonyl compounds established pyridine derivatives with active biological actions [8]. Consequently, it reacted with acetylacetone and benzoylacetone upon heating in ethanol under reflux conditions in the existence of piperidine to smoothly afford the 2-pyridinone derivative 5 and 6, respectively. It can be assumed that the reaction was initially proceeded *via* a nucleophilic aggression to form the Michael adduct which undergo intramolecular cyclization and elimination of two water molecules, furnishing the conclusive product 5, 6 (Scheme 2). IR 5 revealed two absorption bands at 2219 and 1658 cm^{-1} as a result of CN and CO functions, respectively. ^1H NMR spectrum showed three new singlets at $\delta_{\text{H}} 2.03$, 2.41 and 6.49 ppm ascribed to two methyl protons and the pyridinone H-5. Multiplet signal of aromatic protons appeared at $\delta_{\text{H}} 7.56\text{--}8.05$. The MS exhibited a (M^+) at m/z 328, which in agreement with the molecular formula $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}$. Furthermore, the reaction of compound 1 with two mole of malononitrile in catalytic piperidine yielded pyridine derivatives 7. IR spectrum demonstrated three absorption bands at 3445 , 3408 , 2199 and 1668 cm^{-1} acquired to NH_2 , NH, CN and CO functions, respectively The MS exhibited a (M^+) at m/z 396, which compatible with $\text{C}_{21}\text{H}_{16}\text{N}_8\text{O}$ (Scheme 2). Under Gewald reaction conditions of cyanoacetanilide 1 with both phenyl isothiocyanate and elemental sulfur in warming EtOH using catalytic TEA as a base generated the remarkable bioactive thiazole output 8 (Scheme 2) [4]. On the other hand, heterocyclization of 1 with cyclohexanone and elemental sulfur in refluxed ethanol and presence of catalytic morpholine furnished the corresponding thiophene derivatives 9 (Scheme 2).



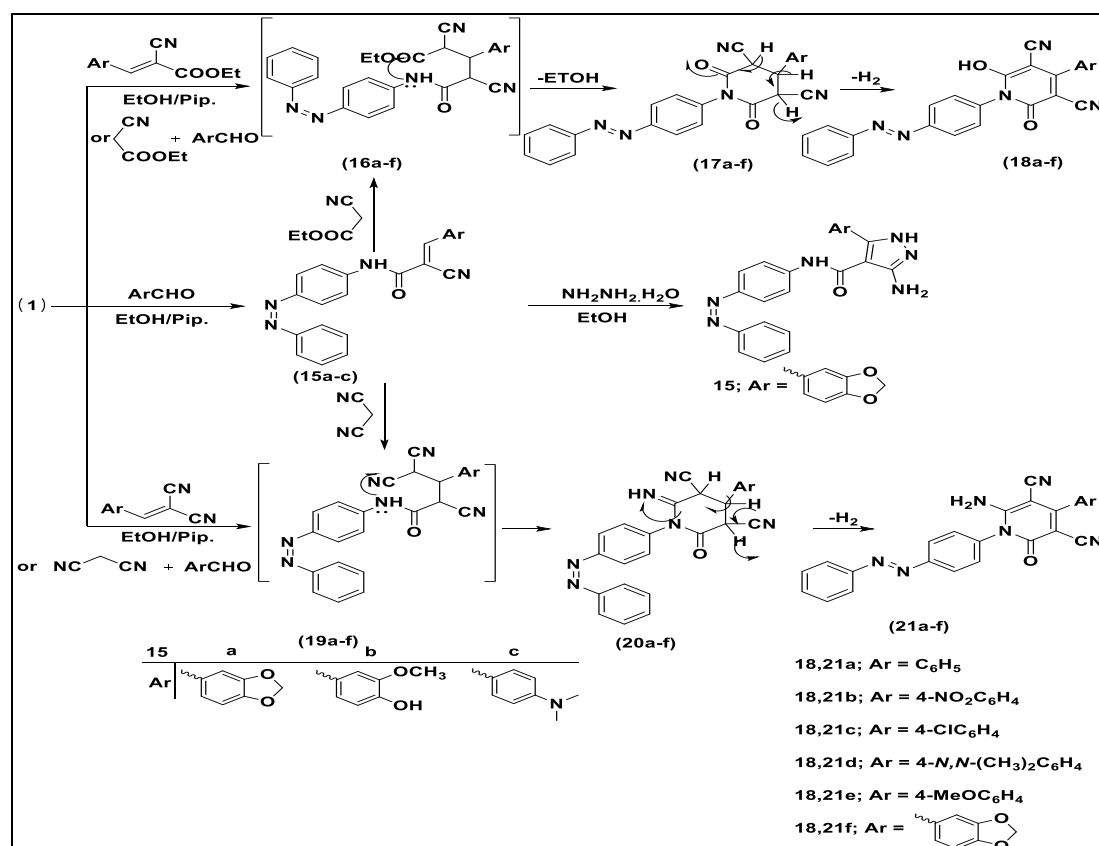
8

$C_{23}H_{16}N_4O_3$. 1H NMR of 15a: δ_H ppm 6.2 (s, 2H, $1CH_2$), 7.16-7.96 (m, 12H, aromatic protons), 8.22 (s, 1H, olefinic H), 10.61 (s, 1H, NH amidic). Furthermore, absence of CN function the IR spectrum of 15 and instead, the presence of a new absorption band at 3445 (NH_2), 3280, 3152 (2NH), 1638 (CO) group. Its MS revealed a (M^+) at m/z (426) which attributable for its molecular formula $C_{23}H_{18}N_4O_3$. Furthermore, the IR assignment of 15b exhibited absorption bands at 3445 (OH), 3501 (NH), 1638 amidic and 2206 (CN). Its 1H NMR: δ_H ppm 3.73 (s, 3H, OCH_3), 6.51-7.85 (m, 12H, aromatic protons), 7.95 (s, 1H, olefinic H), 9.71 (s, 1H, NH amidic). The MS of 15b displayed a (M^+) at m/z 398 ascribed to $C_{23}H_{18}N_4O_3$. Also, IR of 15c revealed absorption bands at 3356 (NH), 2200 (CN) and 1678 (amidic CO). 1H NMR exhibited a singlet signal at δ_H 3.3 ppm for (2 CH_3), multiplet signals for aromatic protons at δ_H ppm (6.85-7.11) and two singlet signals of olefinic H and amidic NH at δ_H 8.11 and 10.36 ppm respectively. Furthermore, the reaction of 15a with hydrazine hydrate in boiling ethanol furnished compound 15. Its IR revealed absence of cyano appearance of new absorption band (NH_2) at 3445, 3280, 3150 for (NH) and 1638 for amidic CO. Its MS displayed molecular ion peak at m/z 426 which corresponding to its molecular formula $C_{23}H_{18}N_4O_3$ (Scheme 3). 2-pyridones 18a-f were yielded upon one-pot reaction of cyanoacetanilide 1 with ethyl cyanoacetate and different aromatic aldehydes namely benzaldehyde, *p*-nitrobenzaldehyde, *p*-chlorobenzaldehyde, 4-*N,N*-dimethylbenzaldehyde, *p*-methoxybenzaldehyde and piperonal, respectively, (molar ratio 1:1:1) in boiling ethanol containing drops of piperidine as a basic catalyst (Scheme 3). On the other hand, the 2-pyridones 18a-f, were also acquired *via* reaction of cyanoacetanilide 1 with arylidene ethyl cyanoacetate, in refluxing ethanol containing piperidine. Structures, 18a-f were postulated to be formed *via* an initial Michael type-adduct, 16a-f followed by elimination of EtOH molecule and dehydrogenation (Scheme 3). Another route for the synthesis of 2-pyridone derivatives, was the reaction of the cyanoacetanilide derivative 1 *via* one-pot reaction, with malononitrile and the same previously mentioned aromatic aldehydes (1:1:1 molar ratio) and refluxed in ethanol containing few drops of piperidine to furnish pyridinones 21a-f (Scheme 3). Moreover, when arylidene malononitrile refluxed with the cyanoacetanilide derivative 1 in ethanol in the presence of piperidine afforded 2-pyridone derivatives 21a-f through the formation of an initial Michael type-adduct, 19a-f followed by intramolecular cyclization and subsequent oxidation to the final products [13] (Scheme 3).

Insecticidal activity

Toxicity test for Cotton leaf worm (*S. littoralis*, Order; *Lepidoptera*, Family; *Noctuidae*)

Table 1 showed the insecticidal bio responses of the 2nd instar larvae of the laboratory strain of the polyphagous pest, cotton leafworm, *S. littoralis* (Boisd.) towards the innovatively fifteen synthesized cyanoacetanilides incorporating azobenzene moiety tested compounds. All the examined compounds showed a potent toxic effect after 3 days of treatment by comparing the outputs with the already recommended, methomyl insecticide, Lannate 90% SP (based on LC_{50} value), which was the most operative compound (the lowermost LC_{50} value, 10.972 ppm, toxicity index, 100%).



Scheme 3: Synthesis of arylidene, aminopyrazole and 2-pyridone derivatives

Among all, compounds 18c, 21c, 18b and 21b exhibits excellent results with LC₅₀'s values 13.248, 15.554, 18.370 and 21.777 ppm, respectively, and the toxicity index being 82.82, 70.54, 59.73 and 50.38%, respectively.

Table 1: Bioresponse of the 2nd instar larvae of *S. littoralis* (Boisd.) to the the newly synthesized compounds comparing with Methomyl insecticide, Lannate 90% SP after 3 day of treatment.

Tested compounds	LC ₅₀ (ppm) and confidence limits at 95%	LC ₉₀ (ppm) and confidence limits at 95%	Slope	Toxicity index % at LC ₅₀ value
Lannate 90% SP	10.972 6.947 15.228	75.772 49.592 154.00	1.527+/-0.243	100
18c	13.248 8.615.320	98.129 62.069 214.722	1.474+/-0.234	82.82
21c	15.554 10.282.560	124.058 75.499 296.123	1.421+/-0.229	70.54
18b	18.370 12.393.546	153.632 90.220 347.364	1.390+/-0.226	59.73
21b	21.777 15.006 30.452	186.219 106.001 516.203	1.375+/-0.225	50.38
18d	25.845 18.163 36.453	220.516 122.407 645.540	1.377+/-0.226	42.45
21d	30.635 21.887 43.697	254.492 138.797 772.683	1.394+/-0.228	35.82
6	37.071 26.926 53.501	286.058 155.368 871.566	1.444+/-0.234	29.60
18f	42.417 31.041 61.886	309.213 167.578 945.370	1.486+/-0.239	25.87
10f	45.584 31.959 64.127	390.091 209.377 1354.187	1.375+/-0.252	24.07
8	53.610 38.410 76.590	445.470 234.197 1621.291	1.394+/-0.255	20.47
4	62.765 45.687 91.341	494.971 257.240 1843.568	1.429+/-0.260	17.48
9	72.952 53.719 108.054	532.092 276.533 1970.114	1.485+/-0.268	15.04
11	83.905 62.386 125.818	550.506 289.906 1964.657	1.569+/-0.279	13.08
14	95.086 71.506 142.798	542.478 294.213 1803.119	1.695+/-0.298	11.54
5	108.225 79.896 183.034	642.535 308.492 4247.389	1.657+/-0.385	10.14

Experimental

Synthesis of (E)-2-Cyano-N-(4-(Phenyldiazenyl) Phenyl) acetamide (1)

1-cyano-acetyl-3, 5-dimethylpyrazole (1.63 g, 0.01 mol) was added to a solution of *p*-amino azobenzene (1.97 g, 0.01 mol) in dry benzene (30 ml), and the reaction mixture heated for 3 hrs. cyanoacetanilide (1) was obtained after purification and recrystallization from dry EtOH. Golden yellow crystals; Yield (92%); mp 188-191 °C. IR (KBr) ν_{max} /cm⁻¹: 3275 (NH), 2250 (CN), 1670 (CO). ¹H NMR (DMSO-*d*₆): δ_{H} ppm 3.96 (*s*, 2H, CH₂), 7.55-7.92 (*m*, 9H, Ar-H), 10.67 (*s*, ¹H, NH). MS: *m/z* 264 (M⁺, 31.7), 160 (65), 77 (100), 66 (19.91), 51 (23). Anal. for C₁₅H₁₂N₄O, (264.31). Calcd: C 68.14; H 4.53; N 21.12 %. Found: C 68.18; H 4.55; N 21.00%.

Synthesis of chromene-3-carboxamide (2) and chromene-2-carboxamide (3)

Salicylaldehyde (0.3 ml, 0.001 mol), or 2-hydroxy-1-naphthaldehyde (0.3 g, 0.001 mol) was added to cyanoacetanilide (1) (0.3 g, 0.001 mol) in (25 ml) absolute ethanol /Pip. (0.5 ml), refluxed for 3 h. The precipitate that formed was filtered off, purified by washing with ethanol, air dried and recrystallization from ethanol to afford 2 and 3.

Synthesis of (E)-2-imino-N-(4-(phenyldiazenyl) phenyl)-2H-chromene-3-carboxamide (2)

Red crystals; mp 220-225 °C; yield 84%. IR (KBr) ν /cm⁻¹: 3437, 3440 (2NH), 1684, 1758 (CO). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} ppm 7.42-8.02 (*m*, 13H, aromatic protons), 10.25 (*s*, 1H, NH), 9.06 (*s*, 1H, chromene CH=), 12.8(*s*, 1H NH). MS *m/z* (%): 370 (M⁺+2, 0.5), 368 (M⁺, 0.3), 365 (0.08), 353 (0.08), 335 (0.11), 301 (100.00), 196 (87.2), 141 (11.89), 77 (50.3). Analysis for C₂₂H₁₆N₄O₂ (368.40). Calcd.: C, 71.70; H, 4.35; N, 15.22%. Found: C, 71.75; H, 4.40; N, 15.23%.

Synthesis of (E)-3-imino-N-(4-(phenyldiazenyl) phenyl)-3H-benzof[chromene-2-carboxamide (3)

Yellow crystals; mp 215-217 °C; yield 88%. IR (KBr) ν /cm⁻¹: 3435, 3447 (2NH), 1684 (CO). MS *m/z* (%): 419 (M⁺+1, 40), 418 (M⁺, 2.79), 405 (0.60), 375 (0.80), 281 (0.28), 231 (0.86), 189 (1.43), 117 (31.83), 113 (29.30), 87 (0.63), 59 (100). Analysis for C₂₆H₁₈N₄O₂ (418.46). Calcd.: C, 74.63; H, 4.32; N, 13.39%. Found: C, 74.65; H, 3.36; N, 13.37%.

Synthesis of (E)-2-oxo-5-phenyl-1-(4-(phenyldiazenyl) phenyl)-2, 5-dihydro-1H-pyrrole-3-carbonitrile (4)

phenacyl bromide (0.3 g, 0.001 mol) was added to (25 ml) ethanolic solution of (1) (0.3 g, 0.001 mol) in presence of drops of TEA. The reaction was heated for 3 h. pyrrole (4) was obtained after purification and recrystallization from dry EtOH.

Brown powder; mp 215-220 °C; yield 80%. IR (KBr) ν /cm⁻¹: 1668 (CO) 2259 (CN). MS *m/z* (%): 364 (M⁺, 2.61), 310 (100), 283 (23.80), 266 (50.02), 247 (25.22), 227 (11.85), 217 (54.64), 185 (25.11), 179 (34.31), 169 (62.84), 140 (40.04), 107 (26.92), 73 (44.33), 60 (42.22). Anal. for C₂₃H₁₆N₄O (364.41). Calcd: C, 75.81; H, 4.43; N, 15.38%. Found: C, 75.83; H, 4.45; N, 15.40%.

Synthesis of (E)-4, 6-dimethyl-2-oxo-1-(4-(phenyldiazenyl) phenyl)-1, 2-dihydropyridine-3-carbonitrile (5)
Acetylacetone (0.11 ml, 0.001 mol) was added to (25 ml) ethanolic solution of (1) (0.3 g, 0.001 mol) in presence of drops of Pip. The reaction was heated for 3 hrs. Compound (5) was obtained after purification and recrystallization from dry EtOH.

Pal yellow crystals; mp 200-210 °C; yield 65%. IR (KBr) ν/cm^{-1} : 2219 (CN), 1658 (CO). ^1H NMR (400 MHz, DMSO- d_6): δ_{H} ppm 2.03 (s, 3H, 1CH₃), 2.41 (s, 3H, CH₃), 6.49 (s, 1H, olefenic H), 7.56-8.05 (m, 9 aromatic H). MS m/z (%): 328 (M⁺, 43.98), 317(2.85), 305 (5.61), 223 (80.48), 145 (2.03), 117 (31.98), 77 (47.29), 59.05 (100). Anal. for C₂₀H₁₆N₄O (328.38). Calcd.: C, 73.12; H, 4.88; N, 17.01%. Found: C, 73.16; H, 4.93; N, 17.07.

Synthesis of (E)-6-methyl-2-oxo-4-phenyl-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3-carbonitrile (6): Benzoyl acetone (0.3 g, 0.001 mol) was added to (25 ml) ethanolic solution of (1) (0.3 g, 0.001 mol) in presence of drops of TEA. The reaction was heated for 3 hrs. Compound (6) was obtained after purification and recrystallization from dry EtOH.

Pale yellow powder; mp 200-205 °C; yield 82%. IR (KBr) ν/cm^{-1} : 2259 (CN), 1678 (CO amidic). MS m/z (%): 390 (M⁺, 31.92), 351 (15.33), 310 (96.23), 283 (25.33), 266 (48.24), 217 (55.22), 196 (68.11), 140 (40.66), 129 (42.11), 107 (26.23), 73 (48.45), 60 (42.12). Anal. for C₂₅H₁₈N₄O (390). Calcd.: C, 76.93; H, 4.66; N, 14.33%. Found: C, 76.95; H, 4.68; N, 14.38%.

Synthesis of (E)-2-(4, 6-diamino-3, 5-dicyanopyridin-2-yl)-N-(4-(phenyldiazenyl)phenyl)acetamide (7)

In 3 h refluxing ethanolic solution (25 ml) including 3 drops of TEA, Equimolar quantities of precursor (1) (0.3 g, 0.001 mol) and malononitrile dimer (0.3 g, 0.001 mol), were added. The formed output was filtered, purified and recrystallized from dry EtOH to give pyridine derivative (7).

Black powder; mp 295 °C; yield 87%. IR (KBr) ν/cm^{-1} : 3415 (NH), 3445(NH₂), 1668 (CO), 2199 (CN). MS m/z (%): 397 (M⁺+1, 0.37), 396 (M⁺, 0.33), 379 (0.36), 363 (1.24), 306 (1.62), 305 (5.06), 289 (0.95), 245 (1.37), 189 (10.87), 113 (31.95), 101 (20.38), 87 (23.37), 59 (100). Anal. for C₂₁H₁₆N₈O (396.14). Calcd.: C, 63.63; H, 4.07; N, 28.27%. Found: C, 63.65; H, 4.08; N, 28.29%.

Synthesis of (E)-4-amino-3-phenyl-N-(4-(phenyldiazenyl) phenyl)-2-thioxo-2, 3-dihydrothiazole-5-carboxamide (8)

To a 3 h 60°C continuously stirring solution of cyanoacetanilide (1) (0.3 g, 0.001 mol), in (25 ml) ethanol enclosing 3 drops of TEA, elemental sulfur (0.032 g, 0.001 mol) followed by phenyl isothiocyanate (0.12 ml, 0.001 mol) were added. The reaction was finished in acidified ice/water mixture. The solid end product filtered, recrystallized from a blend of DMF/Ethanol (3:1) to provide (8).

Black powder; yield 75%; mp 248-250 °C. IR (KBr) ν/cm^{-1} : 3373 (NH), 3464 (NH₂), 1646 (CO), 1232 (CS). MS m/z (%): 431 (M⁺+16.27), 427 (19.04), 363 (1.72), 342 (2.17), 306 (2.08), 291 (1.29), 278 (2.12), 197 (20.69), 120 (19.86), 118 (17.79), 77 (100). Anal. for C₂₂H₁₇N₅OS₂ (431.51). Calcd.: C, 61.22; H, 3.95; N, 16.22%. Found: C, 61.25; H, 3.98; N, 16.26%.

Synthesis of thiophene derivative (9)

A mixture of 1 (0.3 g, 0.001 mol), morpholine (0.5 ml), elemental sulfur (0.032g, 2 0.002 mol) and cyclohexanone (0.001 mol) in ethanolic solution (20 ml) were 3 h continuously stirring at 60 °C, and then the reaction was finished in acidified ice/water mixture. The solid end product filtered, recrystallized from a blend of DMF/Ethanol (3:1) to provide (9).

Synthesis of (E)-2-amino-N-(4-(phenyldiazenyl) phenyl)-4, 5, 6, 7-tetrahydrobenzo[b]thiophene-3-carboxamide (9)

Brown powder; mp 235-240 °C; yield 75%. IR (KBr) ν/cm^{-1} : 3427 (NH), 3444 (NH₂), 1658 (CO). ^1H NMR (400 MHz, DMSO- d_6): δ_{H} ppm 1.17 (br s, 4H, 2CH₂), 3.08 (br s, 2H, CH₂), 7.57-7.88 (m, 9 aromatic H), 9.48 (s, 1H, NH). MS m/z (%): 376 (M⁺+1, 0.67), 366 (0.57), 347 (0.70), 331 (0.52), 306 (1.00), 260 (1.00), 245(1.14), 217 (1.00), 203 (1.8), 189 (11.22), 113 (40.27), 87 (31.11), 59 (100). Anal. for C₂₁H₂₀N₄OS (376.48). Calcd.: C, 66.64; H, 5.86; N, 14.80%. Found: C, 66.66; H, 5.89; N, 14.82%.

Azo coupling of (1) with different primary aromatic amine diazonium salts

Solution of a cold (0-5 °C) cyanoacetanilide (1) (0.3 g, 0.001 mol) in pyridine (20 ml), was added the applicable diazonium chloride [prepared by dissolving sodium nitrite (0.07 g, 0.001 mol) in cold water (3 ml) and adding to a cold solution of the applicable aromatic amine (0.001 mol) such as aniline derivatives (10a-g), 3-amino pyrazolopyridine and 3-amino triazole as heterocyclic aromatic amines in the presence of suitable quantity of hydrochloric acid (1.5 ml) under continuously stirring] portion wise. The reaction mixture was kept overnight in the refrigerator and then diluted with water. Filtration, purification and recrystallization from EtOH/DMF (2:1) were carried out to furnish arylazo derivatives (10a-g), 11 and 12.

Synthesis of (E)-2-oxo-N-phenyl-2-((4-(E)-phenyldiazenyl) phenyl)amino) acetohydrazonoyl cyanide (10a)

Orang crystals; yield 81%; mp 225-230 °C. IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$: 3371, 3333 (2NH), 2220 (CN), 1679 (CO). MS m/z (%): 368 (M⁺, 18.42), 341 (11.45), 313 (13.95), 296 (57.84), 279 (58.92), 264 (10.67), 236 (44.70), 221

(61.45), 207 (34.00), 205 (100.00), 194 (43.58), 179 (54.71), 171 (13.04), 164 (17.17), 152 (29.18), 137 (16.02), 123 (22.12), 111 (22.91), 95 (46.71), 77 (83.60), 57 (77.70), 43 (66.34). Anal. for $C_{21}H_{16}N_6O$ (368.40). Calcd: C, 68.48; H, 4.37; N, 22.80%. Found: C, 68.49; H, 4.39; N, 22.83%.

Synthesis of (*E*)-*N*-(4-bromophenyl)-2-oxo-2-((4-((*Z*)-phenyldiazenyl) phenyl) amino) acetohydrazonoyl cyanide (10b)

Deep orang crystals; mp 235-240 °C; yield 80%. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3478, 3444 (NH), 2211(CN), 1665(CO). MS m/z (%): 447 (M^+ , 1.84), 446 (6.66), 398 (9.57), 368 (18.42), 341 (11.45), 313 (13.95), 296 (57.84), 279 (58.92), 264 (10.67), 236 (44.70), 221 (61.45), 207 (34.00), 205 (100.00), 194 (43.58), 179 (54.71), 152 (29.18), 123 (22.10), 95 (46.71), 77 (83.60), 57 (77.70), 43 (66.34). Anal. for $C_{21}H_{15}BrN_6O$ (447.30). Calcd: C, 56.39; H, 3.38; N, 18.79 %. Found: C, 56.40; H, 3.40; N, 18.80%.

Synthesis of (*E*)-*N*-(4-nitrophenyl)-2-oxo-2-((4-((*Z*)-phenyldiazenyl)phenyl)amino) acetohydrazonoyl cyanide (10c)

Pale yellow crystals; yield 82%; mp 225-230 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3338, 3320 (NH), 1689 (CO), 2224 (CN). MS m/z (%): 413 (M^+ , 42.19), 309 (6.54), 308 (35.97), 250 (2.74), 217 (1.38), 196 (2.55), 171 (5.50), 122 (17.06), 105 (21.90), 92 (22.17), 77 (100.00), 64 (11.01), 51 (8.83). Anal. for $C_{21}H_{15}N_7O_3$ (413). Calcd: C, 61.08; H, 3.69; N, 23.72 %. Found: C, 61.11; H, 3.72; N, 23.74%.

Synthesis of (*E*)-*N*-(4-methoxyphenyl)-2-oxo-2-((4-((*Z*)-phenyldiazenyl)phenyl)amino) acetohydrazonoyl cyanide (10d)

Red crystals; yield 85%; mp 235-237 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3348, 3388 (2NH), 2216 (CN), 1678 (CO). MS m/z (%) (M^+ , 6.65), 382 (4.07), 372 (6.00), 334 (6.52), 314 (13.49), 249 (6.53), 168 (17.45), 110 (24.82), 97 (100.00), 69 (69.79), 57 (30.48), 41 (48.71). Anal. for $C_{22}H_{18}N_6O_2$ (398.43). Calcd.: C, 66.33; H, 4.54; N, 21.07 %. Found: C, 66.35; H, 4.57; N, 21.10%.

Synthesis of 4-(2-((*E*)-1-cyano-2-oxo-2-((4-((*Z*)-phenyldiazenyl) phenyl) amino) ethylidene) hydrazinyl) benzoic acid (10e)

Yellow crystals; yield 85%; mp 220-225 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3487, 3445 (NH), 2213 (CN), 1668 (CO). MS m/z 412 (%) (M^+ , 2.23), 307 (4.48), 289 (0.9), 223 (2.43), 205 (2.71), 182 (2.25), 167 (3.14), 152 (3.10), 136 (4.69), 118 (8.22), 105 (16.45), 90 (16.65), 77 (100.00), 65 (21.40), 51 (26.68), 44 (24.08). Anal. for $C_{22}H_{16}N_6O_3$ (412.41). Calcd.: C, 64.07; H, 3.91; N, 20.38 %. Found: C, 64.09; H, 3.92; N, 20.39%.

Synthesis of (*E*)-2-oxo-*N*-(4-((*E*) - phenyldiazenyl) phenyl) -2- ((4-((*E*)-phenyldiazenyl) phenyl) amino) acetohydrazonoyl cyanide (10f)

Redish brown powder; yield 87% mp; 248-251 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3455, 3333 (2NH), 2209 (CN), 1678 (CO). MS m/z (%): 472 (M^+ , 42.58), 473 (13.86), 367 (23.29), 287 (11.05), 263 (9.61), 223 (2.73), 197 (9.10), 182 (21.04), 167 (4.70), 120 (10.29), 92 (22.04), 77.06 (100.00), 65 (8.28). Anal. for $C_{27}H_{20}N_8O$ (472.51). Calcd.: C, 68.63; H, 4.27; N, 23.71%. Found: C, 68.68; H, 4.28; N, 23.75%.

Synthesis of (*E*)-*N*-(4-acetylphenyl)-2-oxo-2-((4-((*E*)-phenyldiazenyl)phenyl)amino)acetohydrazonoyl cyanide (10g)

Red powder; yield 85%; mp 280-282 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3380, 3330, 2(NH), 2222 (CN), 1710, 1670 (2 CO). ^1H NMR (400 MHz, DMSO- d_6): δ_{H} ppm 2.49 (s, 3H, 1CH₃), 7.55-8.02 (m, 13H, aromatic H), 10.34 (s, 1H, NH amidic), 12.18 (s, 1H, NH hydrazo). MS m/z (%): 410 (M^+ , 84.16), 397 (0.57), 377 (0.82), 333 (6.11), 306 (15.64), 305 (70.27), 247 (5.23), 200 (0.63), 189 (6.50), 175 (5.83), 159 (6.71), 119 (23.35), 117 (32.15), 77 (77.09), 59 (100.00). Anal. for $C_{23}H_{18}N_6O_2$ (410.44). Calcd.: C, 67.31; H, 4.44; N, 20.48%. Found: C, 67.35; H, 4.46; N, 20.49%.

Synthesis of (*E*)-*N*-(4,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)-2-oxo-2-((4-((*E*)-phenyldiazenyl) phenyl) amino) acetohydrazonoyl cyanide (11)

Red crystals; yield 87%; mp 245-250 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3448, 3331, 3128 (3NH), 2221 (CN), 1676 (CO). MS m/z (%): 437 (M^+ , 0.82), 393 (4.48), 347 (4.12), 345 (7.85), 249 (14.31), 223 (15.81), 198 (7.77), 162 (30.79), 144 (21.91), 120 (91.93), 92 (100.00), 84 (27.84), 40 (37.91). Anal. for $C_{23}H_{21}N_9O$ (437.47). Calcd.: C, 62.86; H, 4.82; N, 28.68%. Found: C, 62.88; H, 4.84; N, 28%.

Synthesis of (*E*)-2-oxo-2-((4-((*E*)-phenyldiazenyl)phenyl)amino)-*N*-(1*H*-1,2,4-triazol-3-yl)acetohydrazonoyl cyanide (12)

Brown powder; yield 89%; mp 255-260 °C. IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3443, 3330, 3322 (3NH), 2218 (CN), 1665 (CO). MS m/z (%): 359 (M^+ , 41.75), 254 (100.00), 172 (10.09), 163 (5.83), 144 (4.97), 105 (11.06), 96 (36.21), 77 (74.02), 68 (22.80). Anal. for $C_{17}H_{13}N_9O$ (359.35). Calcd.: C, 56.82; H, 3.65; N, 35.08%. Found: C, 56.85; H, 3.68; N, 35.09%.

Synthesis of ((E)-4-imino-8, 10-dimethyl-N-(4-(phenyldiazenyl)phenyl)-4,6-dihydropyrido[2',3':3,4]pyrazolo [5,1-c] [1,2,4] triazine-3-carboxamide (13)

In hot glacial acetic acid (25 mL), compound 11 (0.2 g, 0.0006 mol) was added for 3 h, cooling followed by filtration, purification and recrystallization from a mixture of EtOH–DMF (1 : 1) to afford 13.

Red crystals; yield 87%; mp 245-250 °C. IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$: 3448, 3331, 3128 (3NH), 1676 (CO). MS m/z (%): 437 (M^+ , 0.82), 393 (4.48), 347 (4.12), 345 (7.85), 249 (14.31), 223 (15.81), 198 (7.77), 162 (30.79), 144 (21.91), 120 (91.93), 92 (100.00), 84 (27.84), 40 (37.91). Anal. for $C_{23}H_{21}N_9O$ (437.47). Calcd.: C, 62.86; H, 4.82; N, 28.68%; Found: C, 62.88; H, 4.84; N, 28%.

Synthesis of ((E)-4-imino-N-(4-(phenyldiazenyl)phenyl)-4,6-dihydro-[1,2,4]triazolo[5,1-c][1,2,4]triazine-3-carboxamide (14)

In hot glacial acetic acid (25 mL), compound 12 (0.2 g, 0.0006 mol) was added for 3 h, cooling followed by filtration, purification and recrystallization from a mixture of EtOH–DMF (1 : 1) to afford 14.

Brown powder; yield 88%; mp 255-260 °C. IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$: 3443, 3330, 3322 (3NH), 1670 (CO). MS m/z (%): 359 (M^+ , 41.75), 254 (100.00), 172 (10.09), 163 (5.83), 144 (4.97), 105 (11.06), 96 (36.21), 77 (74.02), 68 (22.80). Anal. for $C_{17}H_{13}N_9O$ (359.35). Calcd.: C, 56.82; H, 3.65; N, 35.08%; Found: C, 56.85; H, 3.68; N, 35.09%.

General method for the synthesis of arylidenes 15a–c

In 3 h refluxing ethanol (25 ml), a mixture of (1) (0.3g, 0.001 mol), and the applicable aldehyde (explicitly piperonal, vanilline, and 4-*N,N*-dimethylbenzaldehyde) (0.001 mol) were added in basic catalyst, piperidine (0.5 ml), after cooling, the formed precipitate was isolated and recrystallized from EtOH to give (15a–c).

Synthesis of (E)-3-(benzo[*d*][1,3]dioxol-5-yl)-2-cyano-N-(4-((Z)-phenyldiazenyl)phenyl)acrylamide (15a)

Yellow crystals; mp 215-220 °C; yield 65%. IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$: 3333, 3342 (NH, NH₂), 2206 (CN) and 1678 amidic. ¹H NMR (400 MHz, DMSO-*d*₆): δ_H ppm 6.2 (*s*, 2H, 1CH₂), 7.16-7.96 (*m*, 12H, aromatic protons), 8.22 (*s*, 1H, olefinic H), 10.61 (*s*, 1H, NH amidic). MS m/z (%): 396 (M^+ , 16.62), 317 (1.22), 303 (0.37), 305 (1.75), 203 (1.89), 291 (20.22), 253 (1.78), 117 (27.55), 111 (3.87), 101 (18.40), 59 (100). Anal. for $C_{23}H_{16}N_4O_3$ (396.41). Calcd.: C, 69.66; H, 4.05; N, 14.11%. Found: C, 69.71; H, 4.08; N, 14.15%.

Synthesis of (E)-2-cyano-3-(4-hydroxy-3-methoxyphenyl)-N-(4-((Z)-phenyldiazenyl) phenyl)acrylamide (15b)

Orange crystals; mp 225-230 °C; yield 69%. IR (KBr) ν/cm^{-1} : 3445 (OH), 3501 (NH), 1638 amidic and 2206 (CN). ¹H NMR (400 MHz, DMSO-*d*₆): δ_H ppm 3.73 (*s*, 3H, OCH₃), 6.51-7.88 (*m*, 12H, aromatic protons), 7.95 (*s*, 1H, olefinic H), 9.71 (*s*, 1H, NH amidic). MS m/z (%): 398 (M^+ , 23.59), 295 (1.63), 252 (0.28), 228 (1.00), 117 (30.21), 101 (0.49), 87 (3.44), 77 (2.66), 59 (100). Anal. for $C_{23}H_{18}N_4O_3$ (398.42). Calcd.: C, 69.34.73; H, 4.55; N, 14.06%. Found: C, 69.36; H, 4.57; N, 14.08%.

Synthesis of (E)-2-cyano-3-(4-(dimethylamino) phenyl)-N-(4-((Z)-phenyldiazenyl) phenyl) acrylamide (15c):

Orange crystals; mp 225-230 °C; yield 72%. IR (KBr) ν/cm^{-1} : 3356 (NH), 2200 (CN) and 1678 amidic. ¹H NMR (400 MHz, DMSO-*d*₆): δ_H ppm 3.3 (*s*, 6H, 2CH₃), 6.85-7.95 (*m*, 13H, aromatic protons), 8.11 (*s*, 1H, olefinic H), 10.36 (*s*, 1H, NH amidic). MS m/z (%): 395 (M^+ , 44.56), 380 (0.1), 318 (0.24), 290 (12.56), 199 (100), 171 (29.20), 96 (0.12), 77 (13.02). Anal. for $C_{24}H_{21}N_5O$ (395.47). Calcd.: C, 72.89; H, 5.35; N, 17.69%. Found: C, 72.92; H, 5.38; N, 17.73%.

Synthesis of (E)-3-amino-5-(benzo[*d*] [1, 3] dioxol-5-yl)-N-(4-(phenyldiazenyl)phenyl)-1*H*-pyrazole-4-carboxamide (15)

In 3 h refluxing 20 mL of ethanol enclosing drops of piperidine, equimolar mixture of arylidene derivative (15a) (0.3 g, 0.001 mol), and hydrazine hydrate (80%, 0.1mL, 0.001 mol), were added. After cooling, the formed end product was isolated and recrystallized from EtOH to provide (15).

Pale yellow powder; mp 296-298 °C; yield 56%; IR (KBr) ν/cm^{-1} : 3445 (NH₂), 3285, 3150(NH), 1640 (CO). MS m/z (%): 426 (M^+ , 6.94), 340 (6.45), 309 (15.0), 308 (38.12), 295 (100), 276 (20.35), 265 (81.12), 252 (12.65), 212 (10.21), 198 (8.95), 172 (9.65), 157 (19.12), 155 (22.69), 145 (24.35), 128 (26.89), 116 (28.55), 102 (28.32), 94 (33.54), 77 (40.75), 69 (43.92), 54 (41.85). Anal. for $C_{23}H_{18}N_6O_3$ (426.44). Calcd.: C, 64.78; H, 4.25; N, 19.71%. Found: C, 64.75; H, 4.27; N, 19.73%.

General method for the synthesis of pyridin-2-ones (18a-f)**Technique A**

In (25 ml) ethanol enclosing piperidine (0.5 ml), cyanoacetanilide(1) (0.3g, 0.001 mol) and the applicable 2-(arylidene)-ethyl cyanoacetate [explicitly 2-(benzylidene)-ethyl cyanoacetate, 2-(4-nitrobenzylidene)-ethyl cyanoacetate, 2-(4-chlorobenzylidene)-ethyl cyanoacetate, 2-(4-*N,N*-dimethylbenzylidene)-ethyl cyanoacetate, 2-(4-methoxybenzylidene)-ethyl cyanoacetate and ethyl (E)-3-(benzo[*d*][1,3]dioxol-5-yl)-2-cyanoacrylate] (0.001

mol), were added in equimolar quantities, after 3 h refluxing. Isolation and recrystallization from EtOH was carried out to the formed end product.

Technique B

In 3 h refluxing ethanol (25 ml), a mixture of (1) (0.3g, 0.001 mol), and the applicable aldehyde (explicitly benzaldehyde, *p*-nitrobenzaldehyde, *p*-chlorobenzaldehyde, 4-*N,N*-dimethylbenzaldehyde, *p*-methoxybenzaldehyde and piperonal) (0.001 mol), and ethyl cyanoacetate (0.001 mol) in basic catalyst piperidine (0.5 ml) were added, after cooling, the formed precipitate was isolated and recrystallized from EtOH.

Method C

To a (25 ml) ethanol including (0.5 ml) piperidine, a mixture of (15a) or (15c) (0.001 mol) and ethyl cyanoacetate (0.11 ml, 0.001 mol) was refluxed for 3 hrs. The acquired end product was filtered and recrystallized from ethanol to give (18f) or (18d), respectively.

Synthesis of (*E*)-6-hydroxy-2-oxo-4-phenyl-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (18a)

Pale yellow crystals; mp 288-290 °C; yield 63%. IR (KBr) ν/cm^{-1} : 3470 (OH), 2219 (2CN), 1695 (CO). MS m/z (%): 417 (M^+ , 21.24), (2.92), 165 (5.7), 139 (3.44), 127 (3.16), 85 (3.88), 56 (4.57). Anal. for $C_{25}H_{15}N_5O_2$ (417.43). Calcd.: C, 71.93; H, 3.62; N, 16.78%. Found: C, 71.90; H, 3.63; N, 16.74%.

Synthesis of (*Z*)-6-hydroxy-4-(4-nitrophenyl)-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (18b)

Deep yellow crystals; mp 220-225 °C; yield 92%. IR (KBr) ν/cm^{-1} : 3454 (OH), 2215 (CN), 1682 (CO). MS m/z (%): 462 (M^+ , 5.75), 450 (2.44), 412 (15.34), 403 (46.49), 367 (90.00), 357 (16.69), 307 (27.24), 290 (14.87), 287 (100.00), 276 (19.28), 213 (26.32), 182 (93.36), 120 (63.62), 92 (79.07). Anal. for $C_{25}H_{14}N_6O_4$ (462.43). Calcd.: C, 64.64; H, 3.05; N, 18.17%. Found: C, 64.67; H, 3.07; N, 18.19%.

Synthesis of (*E*)-4-(4-chlorophenyl)-6-hydroxy-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (18c)

Deep yellow crystals; mp 220-225 °C; yield 92%. IR (KBr) ν/cm^{-1} : 3450 (OH), 2215 (CN), 1679 (CO). MS m/z (%): 452 ($M^+ + 1$, 3.48), 451 (M^+ , 2.36), 407 (15.65), 388 (11.06), 327 (6.49), 320 (12.58), 286 (11.48), 264 (18.16), 248 (20.65), 197 (100.00), 164 (15.52), 139 (15.98), 120 (34.28), 90 (30.79), 65 (96.70). Anal. for $C_{25}H_{14}ClN_5O_2$ (451.87). Calcd.: C, 66.48; H, 3.13; N, 15.56 %. Found: C, 66.49; H, 3.15; N, 15.57%.

Synthesis of (*E*)-4-(4-(dimethylamino)phenyl)-6-hydroxy-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (18d)

Orange crystals; mp 260-265 °C; yield 90%. IR (KBr) ν/cm^{-1} : 3453 (OH), 2221 (CN), 1651 (CO). ^1H NMR (400 MHz, DMSO- d_6): δ_H ppm 3.08 (s, 6H, 2CH₃), 6.85-8.11 (m, 13H, Ar-H), 10.36 (s, 1H, OH). MS m/z (%): 460 (M^+ , 0.26), 431 (0.31), 411 (0.41), 395 (40.07), 290 (11.79), 199 (100.00), 171 (29.03), 117 (22.71), 77 (13.91), 59 (75.08). Anal. for $C_{27}H_{20}N_6O_2$ (460.50). Calcd.: C, 70.42; H, 4.38; N, 18.25 %. Found: C, 70.44; H, 4.39; N, 18.27%.

Synthesis of (*E*)-6-hydroxy-4-(4-methoxyphenyl)-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (18e)

Pale yellow crystals; mp 255-260 °C; yield 90%. IR (KBr) ν/cm^{-1} : 3452 (OH), 2221 (CN), 1651 (CO). MS m/z (%): 447 (M^+ , 5.43), 413 (42.46), 382 (14.50), 320 (63.70), 277 (61.37), 261 (48.50), 217 (63.35), 203 (22.57), 197 (32.44), 185 (24.00), 137 (31.27), 120 (73.04), 55 (100.00), 43 (90.99). Anal. for $C_{26}H_{17}N_5O_3$ (447.45). Calcd.: C, 69.79; H, 3.82; N, 15.64%. Found: C, 69.78; H, 3.85; N, 15.67%.

Synthesis of 4-(Benzo[d][1,3]dioxol-5-yl)-2,6-dioxo-1-(4-(phenyldiazenyl)phenyl)-1,2,3,6-tetrahydropyridine-3,5-dicarbonitrile (18f)

Red crystals; mp 250-255 °C; yield 91%. IR (KBr) ν/cm^{-1} : 3455 (OH), 2206 (CN), 1678 (CO). MS m/z (%): 461 (M^+ , 0.84), 460 (1.01), 442 (1.18), 417 (1.60), 392 (1.26), 331 (1.06), 259 (1.40), 227 (85.00), 187 (90.00), 169 (5.60), 117 (26.63), 59 (100.00). Anal. for $C_{26}H_{15}N_5O_4$ (461.44). Calcd.: C, 67.68; H, 3.28; N, 15.18 %. Found: C, 67.69; H, 3.29; N, 15.19%.

General method for the synthesis of pyridin-2-ones (21a-f)

Technique A

In (25 ml) ethanol enclosing piperidine (0.5 ml), cyanoacetanilide(1) (0.3g, 0.001 mol) and the applicable 2-(arylidene)-malononitrile [namely 2-(benzylidene)-malononitrile, 2-(4-nitrobenzylidene)-malononitrile, 2-(4-chlorobenzylidene)-malononitrile, 2-(4-*N,N*-dimethylbenzylidene)-malononitrile, 2-(4-methoxybenzylidene)-malononitrile and 2-(benzo[d][1,3]dioxol-5-ylmethylene)-malononitrile] (0.001 mol), were added in equimolar quantities, after 3 h refluxing. Isolation and recrystallization from EtOH was carried out to the formed end product.

Technique B

In 3 h refluxing ethanol (25 ml), a mixture of (1) (0.3g, 0.001 mol), and the applicable aldehyde (explicitly benzaldehyde, *p*-nitrobenzaldehyde, *p*-chlorobenzaldehyde, 4-*N,N*-dimethylbenzaldehyde, *p*-methoxybenzaldehyde and piperonal) (0.001 mol), and malononitrile (0.001 mol) in basic catalyst piperidine (0.5 ml) were added, after cooling, isolation and recrystallization from EtOH was carried out to the formed precipitate.

Technique C

To a (25 ml) ethanol including (0.5 ml) piperidine, a mixture of (15a) or (15c) (0.001 mol) and malononitrile (0.07 g, 0.001 mol) was refluxed for 3 hrs. The acquired end product was filtered and recrystallized from ethanol to give (21f) or (21d), respectively.

Synthesis of (*E*)-6-amino-2-oxo-4-phenyl-1-(4-(phenyldiazenyl)cyclohexa-2,4-dien-1-yl)-1,2-dihydropyridine-3,5-dicarbonitrile (21a)

Pale yellow powder; mp 241-243 °C; yield 77%. IR (KBr) ν/cm^{-1} : 3343 (NH₂), 2214, 2162 (2CN), 1639 (CO). MS m/z (%): 418 (M⁺, 0.8), 405 (40.3), 387 (26.2), 327 (54.05), 265 (100.00), 174 (78.02), 159 (36.11), 132 (44.12), 102 (36.22), 89 (36.05). Anal. for C₂₅H₁₈N₆O (418.46). Calcd.: C, 71.76; H, 4.34; N, 20.08%. Found: C, 71.74; H, 4.36; N, 20.05%.

Synthesis of (*E*)-6-amino-4-(4-nitrophenyl)-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile(21b)

Orange powder; mp 242-244 °C; yield 90%. IR (KBr) ν/cm^{-1} : 3342 (NH₂), 2215, 2212 (2CN), 1635 (CO), 1520 (NO₂). MS m/z (%): 461(M⁺, 35.4), 356 (55.22), 344 (18.21), 310 (10.11), 222 (20.10), 170 (10.14), 134 (38.10), 119 (100.00), 110 (55.08), 93 (96.12), 66 (35.10). Anal. for C₂₅H₁₅N₇O₃ (461.44). Calcd.: C, 65.07; H, 3.28; N, 21.25%. Found: C, 65.09; H, 3.29; N, 21.27%.

Synthesis of (*E*)-6-amino-4-(4-chlorophenyl)-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (21c)

Yellow crystals; mp 244-246 °C; yield 87%. IR (KBr) ν/cm^{-1} : 3338 (NH₂), 2211, 2212 (2CN), 1656 (CO). MS m/z (%): 450 (M⁺, 10.55), 424 (8.33), 345 (100.00), 281 (28.06), 201 (48.33), 146 (8.66), 85 (84.33), 45 (66.34). Anal. for C₂₅H₁₅ClN₆O (450.89). Calcd.: C, 66.60; H, 3.35; N, 18.66%. Found: C, 66.62; H, 3.37; N, 18.68 %.

Synthesis of (*E*)-6-amino-4-(4-(dimethylamino)phenyl)-2-oxo-1-(4-(phenyldiazenyl) phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (21d)

Deep yellow powder; mp 250-255 °C; yield 81%. IR (KBr) ν/cm^{-1} : 3343, (NH₂), 2210, 2163 (2CN), 1674 (CO). MS m/z (%): 459 (M⁺, 8.03), 452 (5.61), 434 (10.21), 393 (32.69), 351 (15.92), 342 (46.15), 320 (46.92), 311 (86.12), 282 (25.48), 248 (21.33), 198 (17.52), 131 (50.95), 108 (26.45), 102 (100.00), 74 (52.47). Anal. for C₂₇H₂₁N₇O (459.51). Calcd.: C, 70.57; H, 4.61; N, 21.34 %. Found: C, 70.59; H, 4.63; N, 21.35%.

Synthesis of (*E*)-6-amino-4-(4-methoxyphenyl)-2-oxo-1-(4-(phenyldiazenyl)phenyl)-1,2-dihydropyridine-3,5-dicarbonitrile (21e)

Deep orange crystals; mp 245-250 °C; yield 80%. IR (KBr) ν/cm^{-1} : 3481, 3197 (NH₂), 2212 2215 (2CN), 1656 (CO). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} ppm 3.85 (*s*, 3H, OCH₃), 7.12-8.26 (*m*, 13H, Ar-H), 10.17(*s*, 2H, NH₂ amidic). MS m/z (%): 447 (M⁺+1, 5.43), 446 (M⁺, 0.99), 413 (42.46), 382 (14.50), 320 (63.70), 277 (61.37), 261 (48.50), 217 (63.35), 197 (32.44), 142 (27.37), 137 (31.27), 131 (48.84), 120 (73.04), 95 (39.79), 55 (100.00), 43 (90.99). Anal. for C₂₆H₁₈N₆O₂ (446.47). Calcd.: C, 69.92; H, 4.04; N, 18.80 %. Found: C, 69.97; H, 4.08; N, 18.84 %.

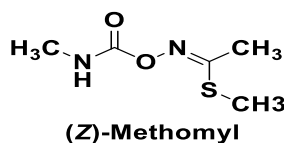
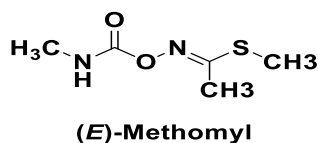
Synthesis of (*E*)-2-amino-4-(benzo[*d*][1,3]dioxol-5-yl)-1-(4-(phenyldiazenyl)phenyl)-1,6-dihydropyridine-3-carbonitrile (21f)

Red crystals; mp 235-240 °C; yield 80%. IR (KBr) ν/cm^{-1} : 3344, 3197 (NH₂), 2208 2218 (2CN), 1678 (CO). ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} ppm 6.20 (*s*, 2H, 1CH₂), 7.04-8.22 (*m*, 12H, Ar-H), 10.62 (*s*, 2H, NH₂). MS m/z (%): 421 (M⁺, 20.05), 396 (5.0), 247 (8.0), 131 (25.22), 113 (30.48), 87 (28.33), 59 (100.00). Anal. for C₂₅H₁₉N₅O₂ (421.46). Calcd.: C, 71.25; H, 4.54; N, 16.62 %. Found: C, 71.27; H, 4.56; N, 16.64 %.

Laboratory Bioassay**Toxicity test for Cotton leaf worm (*S. littoralis*, Order; *Lepidoptera*, Family; *Noctuidae*)**

A research laboratory cotton leafworm *S. littoralis* (Boisd.) susceptible strain was preserved in an incubator under well-ordered conditions of 25 ± 1°C and 70 ± 5% RH, and deprived of any contact to chemicals till the time of treatment as described by El-Defrawi *et al.* (1964) [14].

Pesticides: Methomyl, Lannate 90% SP (Figure 1).



(E, Z)-methyl-N-[[[(methylamino)carbonyl]oxy]ethanimidothioate

Toxicological studies

The investigations were assessed *via* the leaf dip technique as designated by Sadek (2003) ^[15]. Mortality was corrected as stated by Abbott's formula ^[16], and statistically analyzed according to Finney's method ^[17]. Furthermore, the efficiency of the tested insecticides was assessed by:

Toxicity index = LC_{50} of the utmost effective compound/ LC_{50} of the tested compound $\times 100$, according to Sun ^[18].

Conclusions

In the entire work, an innovative series of diverse heterocyclic derivatives bearing azobenzene nucleus has been well synthesized and designated. These compounds were estimated as insecticidal agents under laboratory conditions towards the 2nd instar larvae of cotton leafworm, *S. littoralis*. Compounds 18c, 21c, 18b, 21b and 18d demonstrated to be hopeful insecticides since they obviously displayed developed bioresponses than the other examined compounds.

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