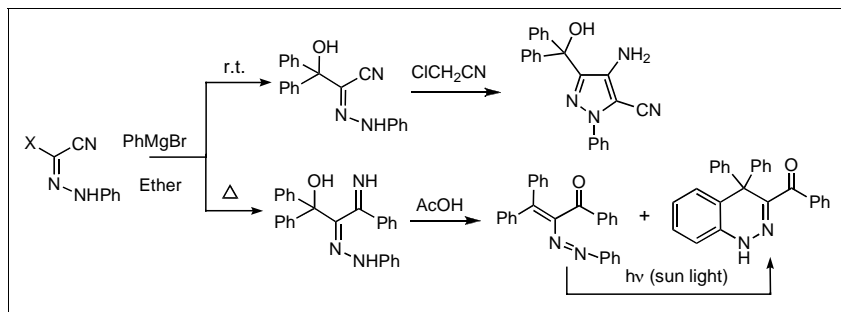


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3-Amino-3-phenyl-2-phenylazoacrylonitrile **6** is obtained in good yield *via* reaction of **5** with phenyl magnesium bromide. The compound **6** is readily converted into **4a**. The so formed alkanenitrile reacted with phenylmagnesium bromide to yield **8**. Compound **8** could be also obtained from reaction of **9** with phenylmagnesium bromide. The arylhydrazononitriles **8** and **4a** reacted with chloroacetonitrile to yield the 4-aminopyrazoles **12a,b**. Compound **12a** reacted with acetic anhydride to yield the **15a** and with benzoyl chloride to yield the pyrazole **16** which was converted into **15b**. Refluxing **10** in acetic acid gave a mixture of the azadiene **21** and the cinnoline **22** is obtained. The azadiene **21** is converted into **22** either thermally or photochemically.

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The chemistry of 3-substituted-3-oxo-2-arylhydrazononitriles **4** has received considerable attention [1-4] Elnagdi *et al.*, have obtained these derivatives either *via* coupling 3-substituted-3-oxoalkane nitriles **1** with aromatic diazonium salts [1] or *via* reacting 3-oxo-2-arylhydrazonals **2** with hydroxylamine in acetic acid and in presence of sodium acetate [2]. On the other hand Shawalli *et al.*, [3] has obtained these compounds *via* reacting the hydrazidic halides **3** with cyanide ion. The coupling reaction approach is not attractive as substituted **1** are not readily obtainable. On the other hand, the utility of the arylhydrazonal and hydrazonyl halides is neither economic nor eco-friendly. In the present work we report a new general route to **4** and its utility as precursor to 4-aminopyrazole-5-carbonitriles, azadienes and cinnolines.

Thus, reacting the readily obtainable 2-phenylhydrazonomalononitrile **5** with phenylmagnesium bromide in ether solution at room temperature, afforded product of addition of Grignard reagents at CN group. This can be formulated as **6** or tautomeric **7**. ¹H NMR indicated amino signals at δ 5.6 ppm, thus structure **6** was established. The eneazo compound **6** could be readily hydrolyzed into **4a** on reflux in aqueous acetic acid, in presence of hydrochloric acid. Compound **4a** reacted with phenylmagnesium bromide to yield the hydroxynitrile **8**. This same product was obtained from reaction of ethyl 2-phenyl-

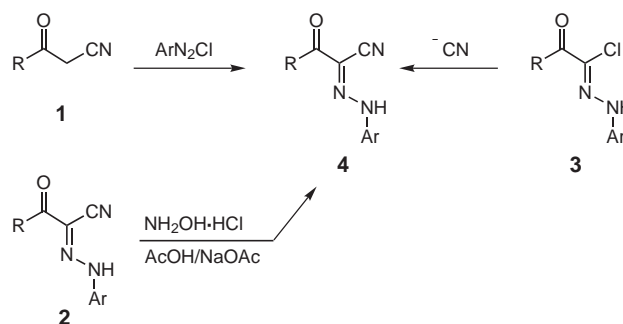


Figure 1

hydrazono-2-cyanoethanoate **9** with phenyl-magnesium bromide in ether at room temperature, while refluxing of **9** with excess of ethereal PhMgBr afforded **10**. ¹³C NMR indicated that **10** exist as an equilibrium mixture of more than one geometrical isomeric forms.

Compounds **4a** or **8** reacted with chloroacetonitrile to yield the 4-aminopyrazole-5-carbonitrile **12**, most likely *via* intermediacy of **11**. This is a further extension to our recently reported pyrazole synthesis from reaction of **2** with functionally substituted alkyl halide [2,5]. It is of value here to report that when alkylation was first conducted in acetone in presence of potassium carbonate,

as described in earlier work, the alkyl halides only hydrolyzed and **4a** or **8** were recovered unreacted. Only when a recent alkylation procedure in excess triethylamine [6] or in toluene in presence of two equivalents of triethylamine was used, the reaction proceeded and **12** was obtained in 87 % and 58 % yields respectively.

Compounds **12** were successfully used as precursors to condensed pyrazoles. Thus, acetylation of **12a** afforded the pyrazolo[4,3-*d*]pyrimidine **15a**, which formed most likely *via* intermediacy of **13** and **14** (*cf.* Figure 3). On the other hand reacting **12a** with benzoyl chloride afforded **16** that could be cyclized on reflux in AcOH, AcONH₄ into **15b**, which formed most likely *via* a Dimroth rearrangement of a pyrazolopyrane. However, possible hydrolysis of nitrile into amide and subsequent cyclization cannot be overlooked.

Refluxing **8** in acetic acid afforded the eneazo derivative **17**. Attempted utility of **17** as precursor to arylazopyrazoles **18** failed. Refluxing **17** with hydrazine hydrate resulted only in reduction of the arylazo moiety to yield **19** or isomeric **20**. ¹H NMR indicated the presence of a proton linked to an sp³ carbon atom and only one NH signal at δ 8.60 and 8.75. ¹H NMR indicated that the compound is a mixture of both *E* and *Z* forms **20** and **20a** in a ratio of 3:1.

Thus structure **20** was established. On the other hand, a mixture of the red eneazo derivative **21** and colorless cinnoline **22** was obtained upon refluxing **10** in acetic

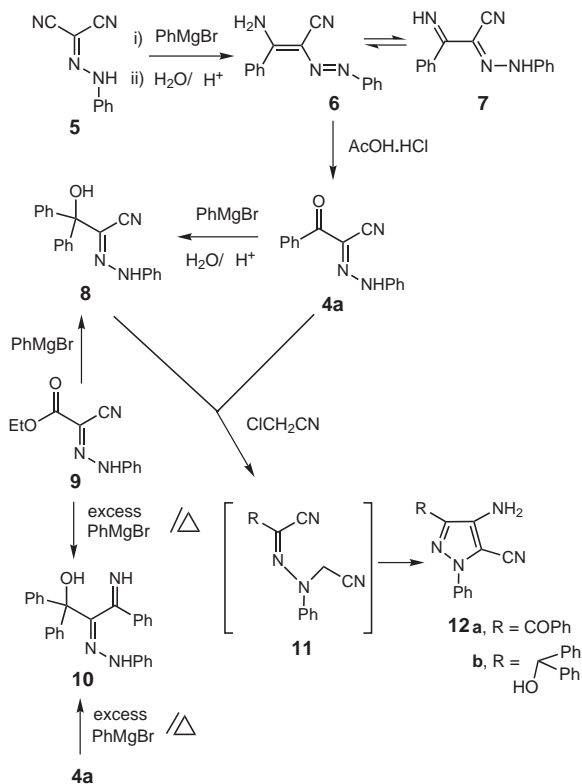


Figure 2

acid. Compound **21** was converted into **22** on long reflux in acetic acid or on exposure to sunlight for a long period in toluene solution. We believe that in acetic acid the protonated species **23** undergoes cyclization into **22**. On the other hand, the photo-chemical conversion is a 6π electrocyclization (*cf.* Figure 4).

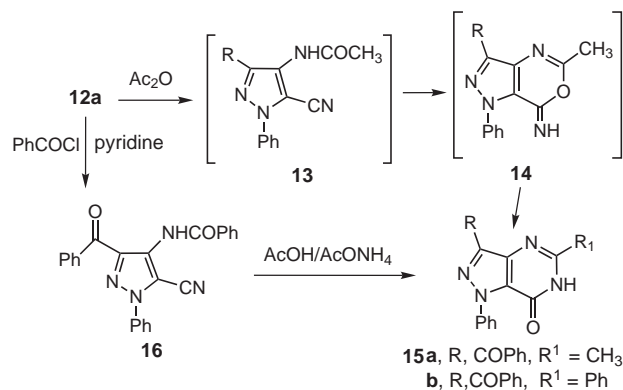


Figure 3

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr pellets with Satellite 2000 spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC-300 300 MHz spectrometer in DMSO-*d*₆ and CDCl₃ as solvents and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were

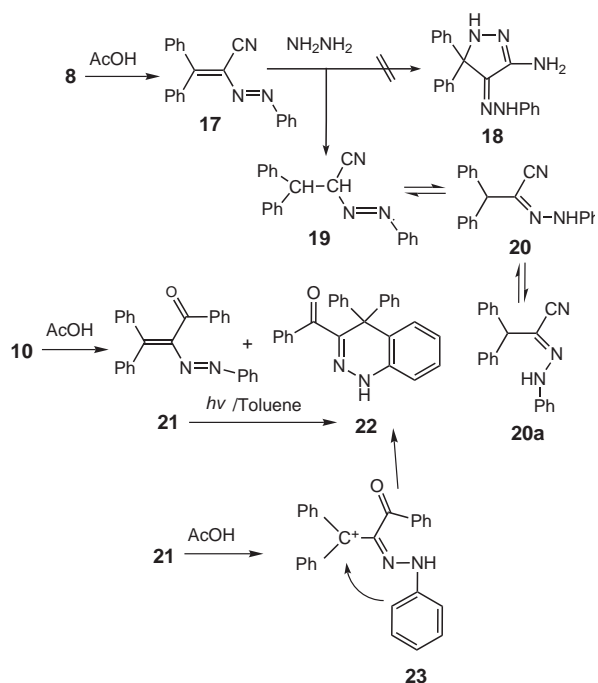


Figure 4

measured at 70 eV using Shimadzu GCMS-QP 1000 EX spectrometer. Microanalytical Data were obtained from the Microanalytical data Unit at Cairo University. Compounds **5**, **9** were prepared following published procedure [1].

2-Phenylhydrazono-3-phenyl-3-oxopropanenitrile (**4a**).

Method A: Benzoylacetone (1.45 g, 10 mmol) was coupled with benzene diazonium chloride utilizing procedure described earlier [7,8].

Method B: A solution of **6** (2.5 g, 10 mmol) in acetic acid (20 mL) containing few drops of hydrochloric acid was refluxed for 3 h and allowed to cool to r.t. The solid product so formed was collected by filtration washed with water and crystallized from ethanol as yellow crystals.

This compound was obtained in 1.8 g (72%) yield; mp 136°C, literature [2] mp. 141 °C. IR (KBr): 3223, (NH), 2213 (CN), 1653 cm⁻¹(H-bonded C=O). MS (EI): m/z (%) = 249 (M⁺, 14.3%), and 250 (M⁺+1, 3.0%).

Anal. Calcd. for C₁₅H₁₁ N₃O (249.27): C, 72.28; H, 4.45; N, 16.86. Found: C, 72.08; H, 4.15; N, 16.47.

3-Amino-2-phenylazocinnamonitrile (**6**).

To a solution of **5** (1.7 g, 10 mmol) in dry ether was added gradually a solution of phenylmagnesium bromide (prepared from 10 mmol of bromobenzene and the appropriate amounts of magnesium and dry ether). The reaction mixture was left at r.t. and stirred for 24 h, then poured onto saturated ammonium chloride solution and extracted with ether. The ether layer was separated and evaporated under reduced pressure. The residue, so formed, was washed with petroleum ether and crystallized from toluene.

This compound was obtained in (95%) yield; mp 133 °C. IR (KBr): 3450, 3308 (NH₂), 2201 (CN), 1618 cm⁻¹(C=C). MS (EI): m/z (%) = 248 (M⁺, 28.2) and 249 (M⁺ + 1 26.1%). ¹H NMR (CDCl₃): δ = 5.6 (br, 2 H, NH₂), and 7.3-7.85 (m, 10 H, arom-H). ¹³C NMR (CDCl₃): δ = 162.22 (C-3), 152.91 (C-2), 133.38, 132.42, 129.84, 129.50, 129.42, 128.75, 122.38, 106.35 (2 phenyl carbons), 116.67 (CN).

Anal. Calcd. for C₁₅H₁₂ N₄ (248.28): C, 72.55; H, 4.87; N, 22.57. Found: C, 72.35; H, 4.66; N, 22.40.

3-Hydroxy-3,3-diphenyl-2-phenylhydrazonopropane-nitrile (**8**).

To a solution of **4a** or **9** (10 mmol) in dry ether was added gradually a solution of phenylmagnesium bromide (prepared from 10 mmol of bromobenzene and the appropriate amounts of magnesium and dry ether). The reaction mixture was left at r.t. and stirred for 24 h, then poured onto a saturated ammonium chloride solution and extracted with ether. The solvent was eliminated under reduced pressure and the residue so formed was washed with petroleum ether and crystallized from toluene.

This compound was obtained in (60%) yield; mp 126-28 °C. IR (KBr): 3331 (OH), 3279 (NH), 2218 (CN), 1602 cm⁻¹(C=N). MS (EI): m/z (%) = 327 (M⁺, 10.2%) and 328 (M⁺+1, 1.1%). ¹H NMR (CDCl₃): δ = 3.15 (s, 1 H, OH) and 7.0 -7.5 (m, 10 H, arom-H), 10.25 (br, 1 H, NH). ¹³C NMR (CDCl₃): δ = 142.54, 141.49, 135.56, 133.33, 129.70, 129.65, 129.40, 127.38 (3 phenyl carbons), 123.48 (C-2), 114.41 (CN), 83.35 (C-3).

Anal. Calcd. for C₂₁H₁₇ N₃O (327.38): C, 77.04, H, 5.23, N, 12.84. Found: C, 77.22; H, 5.00; N, 12.59.

3-Imino-2-phenylhydrazono-1,1,3-triphenyl-1-propanol (**10**).

To a solution of **4a** or **9** (10 mmol) in dry ether was added gradually a solution of phenylmagnesium bromide (prepared from 23 mmol of bromobenzene and the appropriate amounts of magnesium and dry ether). The reaction mixture was refluxed for 2 h then triturated with ammonium chloride solution and separated with ether. The solvent was eliminated under reduced pressure and the residue so formed was washed with petroleum ether and crystallized from toluene.

This compound was obtained in (71%) yield; mp 162-64°C. IR (KBr): 3559, (OH), 3268, 3190 cm⁻¹ (2 NH). MS (EI): m/z (%) = 405 (M⁺, 1.0 %) and 406 (M⁺+1, 0.5 %). ¹H NMR (CDCl₃): δ = 6.2 (s, 1 H, OH), and 6.9-7.6 (m, 20 H, arom-H), 7.9 (s, 1 H, NH) and 9.4 (br, 1H, imine NH). ¹³C NMR: (CDCl₃): δ = 144.26 (imine C), 143.50, 142.08, 141.85, 129.99, 129.54, 129.44, 128.87, 128.81, 128.73, 128.36, 128.16, 127.93, 127.67, 122.19, 114.53, 113.63 (4 phenyl carbons), 123.67 (C-2), 82.27 (C-3).

Anal. Calcd. for C₂₇H₂₃ N₃O (405.49): C, 79.97; H, 5.72; N, 10.36. Found: C, 79.67; H, 5.32; N, 10.21.

General Procedure for Preparation of 4-Amino-1-phenyl-1H-pyrazole-5-carbonitriles (**12a,b**).

Equimolar amounts of chloroacetone and **4** or **8** (10 mmol) were refluxed in triethylamine (10 mL) for 30 min. The reaction mixture was allowed to cool and poured into acidified ice-water. The solid product so formed was collected by filtration and crystallized from ethanol.

4-Amino-3-benzoyl-1-phenyl-1H-pyrazole-5-carbonitrile (**12a**).

This compound was obtained in (87%) yield; mp 170 °C. IR (KBr): 3460, 3352 (NH₂), 2216 (CN), 1637 cm⁻¹ (CO). MS (EI): m/z (%) = 288 (M⁺, 32.4) and 289 (M⁺+1, 6.4 %).

Anal. Calcd. for C₁₇H₁₂N₄O (288.30): C, 70.82; H, 4.20; N, 19.43. Found: C, 70.42; H, 4.00; N, 19.33.

4-Amino-3-[hydroxy(diphenyl)methyl]-1-phenyl-1H-pyrazole-5-carbonitrile (**12b**).

This compound was obtained in (58%) yield; mp 149°C. IR (KBr): 3440 (OH), 3244, 3135 (NH₂), 2219 cm⁻¹ (CN). MS (EI): m/z (%) = 366 (M⁺, 1.1 %).

Anal. Calcd. for C₂₃H₁₈ N₄O (366.42): C, 75.39; H, 4.95; N, 15.29. Found: C, 75.16; H, 4.88; N, 15.16.

3-Benzoyl-5-methyl-1-phenyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (**15a**).

A solution of **12a** (0.75 g, 2.5 mmol) in acetic anhydride (5 mL) was refluxed for 4 h. The reaction was left to cool and acidified with hydrochloric acid. The solid product obtained on standing was collected by filtration and crystallized from ethanol.

This compound was obtained in (87%) yield; mp^o154. IR (KBr): 3278 (NH), 1733 (CO), 1650 cm⁻¹(amide CO). MS (EI): m/z (%) = 330 (M⁺, 32.3) and 331 (M⁺+1, 6.5). ¹H NMR (CDCl₃): δ = 1.56 (s, 3 H, CH₃), 7.49-8.27 (m, 10 H, arom-H), 9.96 (br. 1 H, NH).

Anal. Calcd. for C₁₉H₁₄N₄O₂ (330.34): C, 69.08; H, 4.27; N, 16.96. Found: C, 69.20; H, 4.22; N, 16.75.

3-Benzoyl-1,5-diphenyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (**15b**).

A mixture of **16** (0.4 g, 1.0 mmol), ammonium acetate (1 g) and acetic acid (5 mL) was refluxed for 4 h. The reaction mixture was left to cool to r.t. and the solid so formed was collected by filtration and crystallized from acetic acid.

This compound was obtained in (62%) yield; mp 211 °C. IR (KBr): 3445 (NH), 1686, 1630 (two conjugate CO). MS (EI): m/z (%) = 392 (M⁺, 17.4), 393 (M⁺+1, 5.2). ¹H NMR (CDCl₃): δ = 7.58-8.96 (m, 15 H, arom-H), 10.89 (br, 1 H, NH).

Anal. Calcd. for C₂₄H₁₆N₄O₂ (392.41): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.43; H, 4.00; N, 14.21

N-(3-Benzoyl-5-cyano-1-phenyl-1*H*-pyrazol-4-yl)benzamide (**16**).

A mixture of **12a** (0.75 g, 2.5 mmol) and benzoyl chloride (0.35 g, 2.5 mmol) in pyridine was refluxed for 3 h. The solvent was evaporated to one third of its volume under vacuum and the solid product obtained upon neutralization with hydrochloric acid was collected by filtration and crystallized from acetic acid.

This compound was obtained in (75%) yield; mp 230-32 °C. IR (KBr): 3287 (NH), 2229 (CN), 1688, 1629 (two conjugate CO). MS (EI): m/z (%) = 392 (M⁺, 22.7), 393 (M⁺+1, 7.8). ¹H NMR (DMSO-d₆): δ = 7.57-7.69 (m, 9 H, arom-H), 7.84 (d, 2 H, arom-H) 7.98 (d, 2 H, arom-H), 8.15 (d, 2 H, arom-H) and 10.85 (brs, 1H, NH). ¹³C NMR: (DMSO-d₆): δ = 187.30, 164.61, (2CO), 137.86, 136.15, 135.26, 133.72, 132.69, 132.55, 130.24, 130.10, 129.83, 128.88, 128.61, 127.73, 124.25, 122.01, 121.07, (3ph, carbons and pyrazole ring carbons), 110.1 (CN).

Anal. Calcd. for C₂₄H₁₆N₄O₂ (392.41): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.39; H, 4.01; N, 14.11

3,3-Diphenyl-2-phenylazoacrylonitrile (**17**).

Compound **8** (1.0 g, 0.03 mmol) in acetic acid (15 mL) was refluxed for 3 h then allowed to cool to room temperature. The solid product, so formed, was collected by filtration and crystallized from ethanol.

This compound was obtained in (75%) yield; mp 154 °C. IR (KBr): 2216 (CN), 1592, 1580 cm⁻¹ (N=N, C=C). MS (EI): m/z (%) = 309 (M⁺, 14.1), 310 (M⁺+1, 10.8); ¹H NMR: (DMSO-d₆): δ = 7.3-7.8 (m, 15 H, arom-H). ¹³C NMR (DMSO-d₆): δ = 162.28 (C-3), 152.71 (C-2), 138.42, 137.83, 133.16, 132.26, 131.49, 131.11, 131.02, 129.61, 129.04, 128.68, 128.11, 124.04 (3 phenyl carbons), 114.68 (CN).

Anal. Calcd. for C₂₁H₁₅N₃ (309.36): C, 81.53, H, 4.89, N, 13.58. Found: C, 81.36; H, 4.42; N, 13.44.

3,3-Diphenyl-2-phenylhydrazonopropanenitrile (**20**).

A mixture of **17** (0.6 g, 2.0 mmol) and hydrazine hydrate (0.1 mL, 2.0 mmol) in dimethylformamide (10 mL) was refluxed for 4 h. The solid product, formed upon dilution with water was collected by filtration and crystallized from ethanol.

This compound was obtained in (55%) yield; mp 108 °C. MS (EI): m/z (%) = 311 (M⁺, 46.9 %) and 312 (M⁺+1, 8.8 %). IR (KBr): 3258 (NH), 2214 (CN), 1602, cm⁻¹ (C=N). ¹H NMR: (CDCl₃): δ = 5.18 (s, 0.25 H, CH), 5.30 (s, 0.75 H, CH), 6.9-7.4 (m, 15 H, arom-H), 8.6 (br, 0.75 H, NH), 8.75 (br., 0.25 H, NH).

Anal. Calcd. for C₂₁H₁₇N₃ (311.38): C, 81.00; H, 5.50; N, 13.49. Found: C, 80.90; H, 5.34; N, 13.26.

The Azoalkene (**21**) and the Cinnoline (**22**).

A solution of **10** (2 g, 0.05 mmol) in glacial acetic acid (20 mL) was refluxed for 3 h and left to cool. The solid product, so

formed was collected by filtration and identified as **22**. Then the mother liquor was concentrated and left to cool. The solid product formed was collected by filtration and identified as **21**.

1-Benzoyl-2,2-diphenyl-1-phenylhydrazonoethylene (**21**).

This compound was obtained in (31%) yield; mp 146 °C. MS (EI): m/z (%) = 388 (M⁺, 59.9 %) and 389 (M⁺+1, 20.5%). IR (KBr): 1670 (CO), 1592 cm⁻¹ (C=C). ¹H NMR (DMSO-d₆): δ = 6.4-7.9 (m, 20 H, arom-H). ¹³C NMR (DMSO-d₆): δ = 189.44 (CO), 149.6, 137.77, 137.69, 134.22, 134.01, 133.68, 130.39, 130.34, 129.88, 129.27, 129.11, 127.71, 126.14, 124.20, 122.75, 121.51, 120.79, 120.33 (4 phenyl carbons, C-1, C-2).

Anal. Calcd. for C₂₇H₂₀N₂O (388.46): C, 83.48; H, 5.19; N, 7.21. Found: C, 83.19; H, 5.34; N, 7.15.

3-Benzoyl-4,4-diphenyl-1,4-dihydrocinnoline (**22**).

This compound was obtained in (52%) yield; mp 176-78 °C. IR (KBr): 3334 (NH), 1626 cm⁻¹ (C=O). MS (EI): m/z (%) = 388 (M⁺, 49.7 %) and 389 (M⁺+1, 13 %). ¹H NMR: (DMSO-d₆): δ = 7.2-7.8 (m, 19 H, arom-H), 9.4 (brs, 1H, NH). ¹³C NMR (DMSO-d₆): δ = 197.91 (C=O), 153.09 (C-3), 150.48, 150.18, 139.37, 139.14, 137.18, 134.41, 132.99, 132.44, 130.63, 130.33, 130.23, 130.11, 129.85, 129.53, 129.21, 128.53, 123.19 (3 phenyl carbons and benzeno carbons), 31.19 (C-4).

Anal. Calcd. for C₂₇H₂₀N₂O (388.46): C, 83.48; H, 5.19; N, 7.21. Found: C, 83.30; H, 5.34; N, 7.11.

Conversion of **21** into **22**.

Method 1: A solution of **21** (10 mmol) in acetic acid (10 mL) (10 mmol) was refluxed for 24 hrs then left to cool. The solid product was collected by filtratoin and identified as **22** in 60 % yield.

Method 2: A solution of **21** (10 mmol) in toluene (10 mL) was left for several days in sunlight. The product precipitated was collected by filtratoin and identified as **22**.

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