Microwave-assisted organic synthesis: the Gabriel approach as a route to new pyrazolylhydrazonoazoles

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Abstract

The pyrazole **7** was diazotized in the presence of hydrochloric acid in acetic acid to give *in situ* the diazonium chloride **9**. The latter was coupled with malononitrile to afford 2-pyrazolylhydrazonomesoxalonitrile **10**, which could be converted into aminopyrazolone **11** by reaction with hydrazine hydrate. The phenylhydrazone **13** reacted with hydroxylamine hydrochloride to afford the oxime **18** that could be readily converted into the nitrile **19** either by refluxing in a solution of sodium acetate in acetic acid or by heating in a microwave oven (MW). Compound **19** reacted with hydroxylamine hydrochloride to give amidooxime **20** either by refluxing in dioxane or by heating in MW.

Keywords: Gabriel synthesis, pyrazoles, enaminones, microwave irradiation, methyl ketones

Introduction

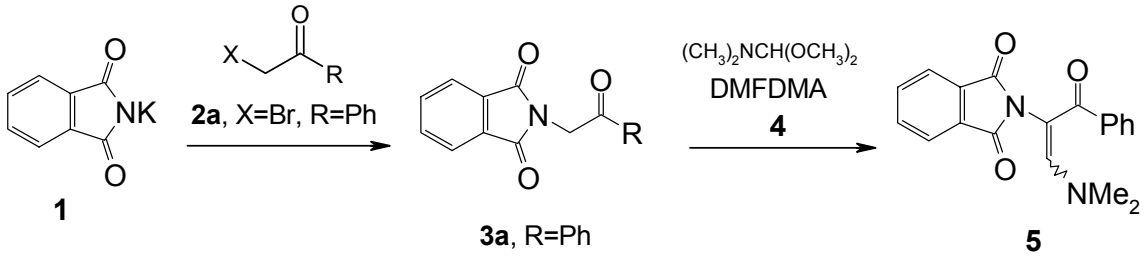
Pyrazole azo dyes occupy a central place in dye chemistry. Pyrazole dyes are prepared either by coupling of diazopyrazoles with a suitable coupler or by coupling aromatic and heteroaromatic diazonium salts with pyrazolones[1,2] or aminopyrazoles.[3-8] Cyclization of 1,3-bifunctionally substituted-2-arylhydrazones by hydrazines have been extensively employed. We have investigated the possible utility of the Gabriel approach for the synthesis of amino acids from alkyl halides and indolidenedione for the synthesis of both heteroaromatic amines and 2-arylhydrazono-1,3-bifunctional pyrazole precursors with methylamino substituents.

Results and Discussion

In previous work we have shown that methylene group in *N*-alkylazolyl ketones is activated toward electrophiles and that this activity is enhanced by microwave heating[9]. In continuation of

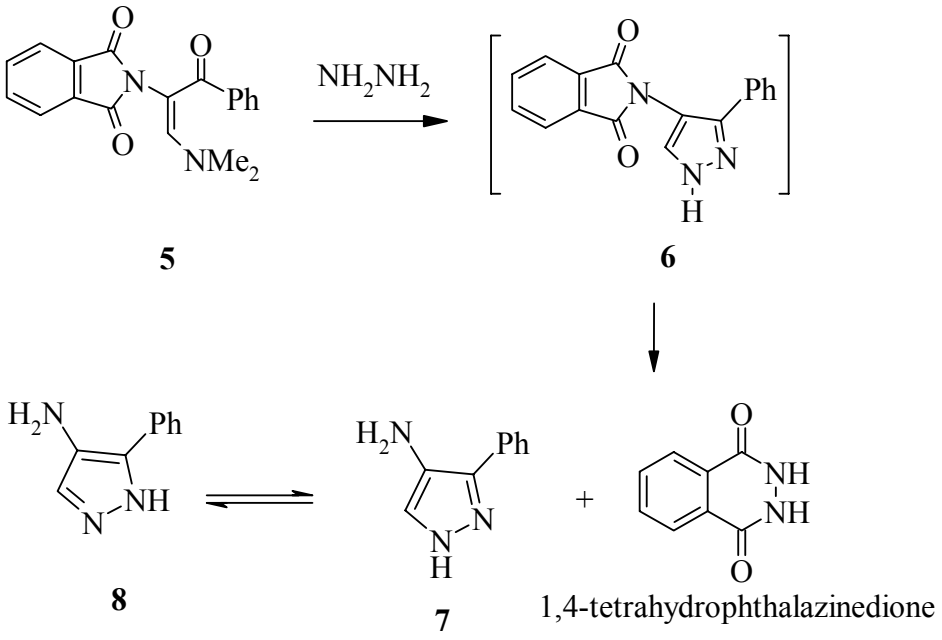
this work we report on the synthesis of 2-(4-dimethylamino-2-oxo-3-butenyl) isoindole-1,3-dione and 2-(1-benzoyl-2-dimethylaminovinyl) isoindole-1,3-dione as precursors to the title compounds. Thus, reaction of potassium phthalimide **1** with phenacyl bromide either by refluxing in DMF for 30 min or by heating in a microwave oven (MW) at 55 °C for 10 min afforded the phenacyl isoindolidinedione **3a** in 68% yield. Interaction of **3a** with dimethylformamide dimethylacetal (DMFDMA) **4** either by refluxing in excess of DMFDMA for 10 h or by heating in MW without solvent at 150 °C for 1 h has resulted in the formation of the corresponding enaminone **5** in 59% and 76% yields, correspondingly. The yields by MW approach were higher than those obtained by reflux. This parallel with literature reports.[10-14] Moreover, the reaction could be brought to completion in a shorter time and no solvent was wasted in such procedure (*cf*. Scheme 1).

Interaction of enaminone **5** with hydrazine hydrate either by refluxing in toluene for 5 h or by heating in MW with the same solvent at 140 °C for 15 min has resulted in the formation of the corresponding pyrazole **7** in 92% and 90% yields, correspondingly.



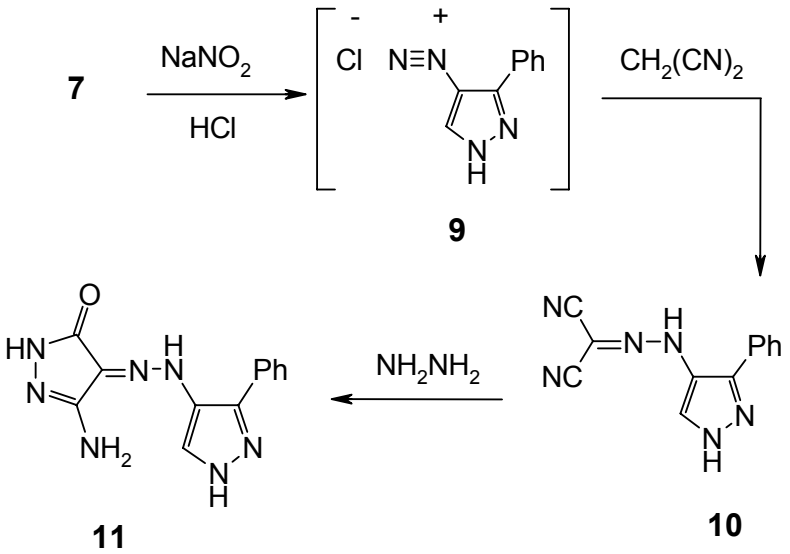
Scheme 1

It is assumed that pyrazole **7** was formed *via* non-isolable intermediate **6**. Cleavage of indolidene ring resulted in the formation of 1,4-tetrahydrophthalazinedione that could be isolated and characterized (*cf*. Scheme 2). Pyrazole **7** has been prepared earlier[15] in 70% yield by the reaction of enaminone **5** with 2.5 equivalent of hydrazine hydrate in EtOH at room temperature for 1 h followed by refluxing the mixture for 2 h. Pyrazole **7** may exist also in another tautomeric form **8**. The ^{1}H NMR revealed two low field signals at δ 12.47 and δ 12.21. In the ^{1}H NMR it simply means that the signal intensity ratio is 1:1) (cf. Scheme 2).



Scheme 2

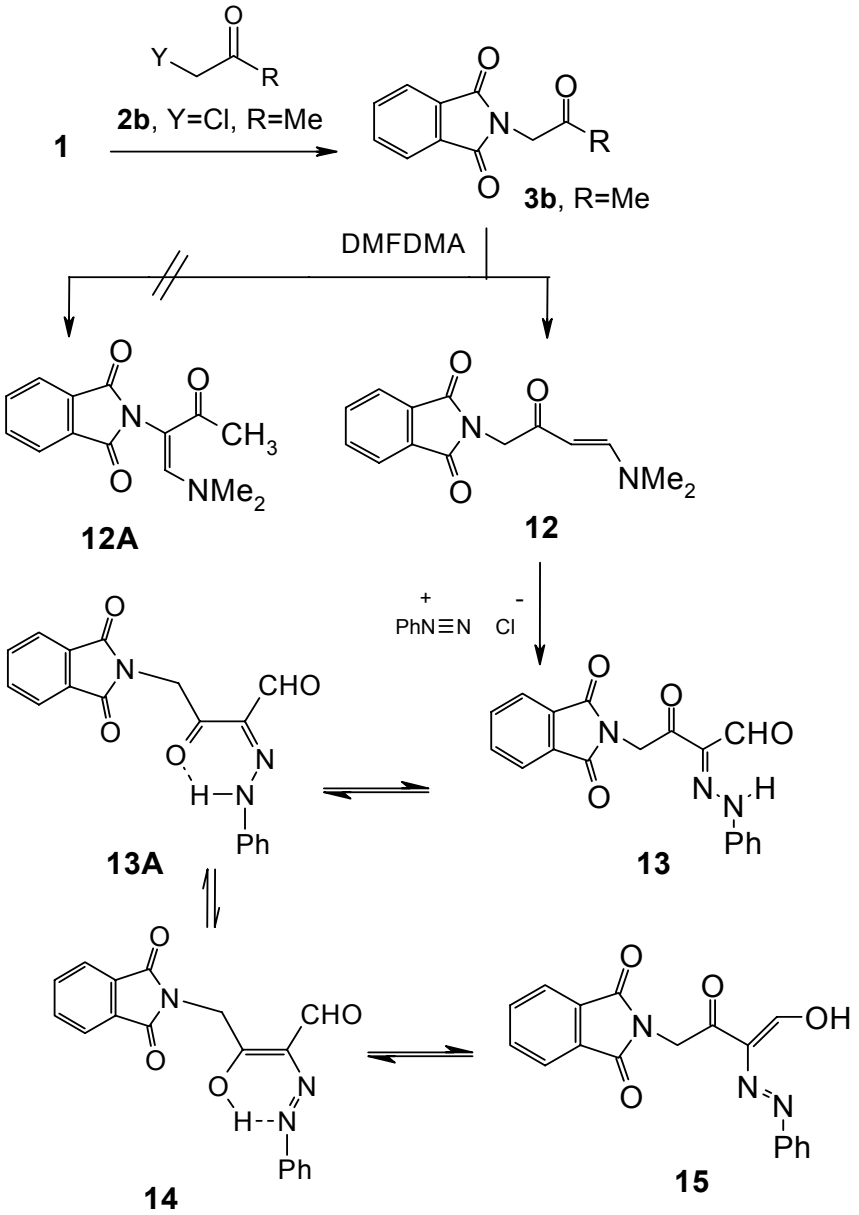
Compound **7** could be dissolved in acetic acid and diazotized in the presence of hydrochloric acid to yield, in situ, the diazonium chloride **9** which then coupled with malononitrile to yield 2-pyrazolylhydrazonomesoxalonitrile **10**. Compound **10** in turn could be converted into the new aminopyrazolone **11** by the reaction with hydrazine hydrate either by refluxing in EtOH for 6 h or by heating in MW with the same solvent at 140 ^{0}C for 30 min in 37% and 87% yields, correspondingly (Scheme 3).



Scheme 3

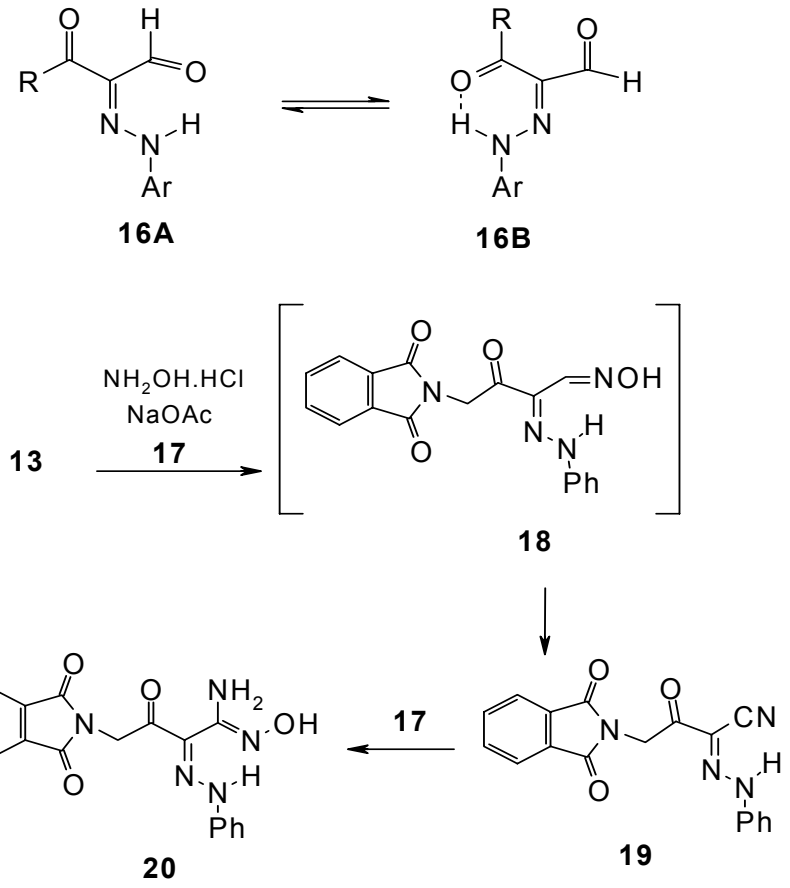
It is of value to report that phenylhydrazonoxalonitrile as well and phenylazoaminopyrazolone have been reported to possess diverse biological and medicinal activities.[16,17] Moreover, the product of reacting phenylhydrazonomesoxalonitrile with hydrazine has also been patented as a potential hair and keratin fiber dyes.[18]

This approach was then utilized for the synthesis of other pyrazole derivatives. Condensation of potassium phthalimide with chloroacetone afforded phthalimidoacetone **3b**. However, condensation of **3b** with DMFDMA has afforded enaminone **12** either by refluxing in xylene for 8 h or by heating in MW without solvent at 180 °C for 20 min in 76% and 77% yields, correspondingly (cf. Scheme 4).



Scheme 4

Enaminone **12** may exist unlike other enaminones in the *Z*-form as reported earlier[19] with *J* value 10 ppm Hz. This is not a proof for the existence of sterically crowded *Z*-form. In our ^{1}H NMR spectrum *J* was found to be 12 ppm Hz which is a value intermediate between the expected *E* or *Z*-forms. As Al-Omran *et.al.,*[19] have assigned *Z*-form of this product while Al-Mousawi *et al.,* have assigned *E*-form for the same product.



Scheme 5

We have run NOE difference experiment to establish stereo-orientation of either *E* or *Z*-forms for enaminone **12**. NOE showed that irradiating the alkene CH at δ 5.04 ppm has enhanced dimethylamino protons at δ 2.79 and 3.08 ppm confirming that they are proximal in space as required by the *E*-form. Moreover a colleague of ours[20] has recently obtained X-ray crystal structure for this compound that clearly revealed the double bond in *E*-form. Having concluded the stereochemistry of enaminone **12**, we have coupled the latter with benzenediazonium chloride whereby **13** was formed. Compound **13** can exist either in *E* or *Z*-form **13** or **13A** (or the enol forms **14** and **15**). Structures **14** and **15** could be readily eliminated based on ^{13}C NMR that revealed two carbonyl carbons at δ 189.74 and 185.84 ppm Hz. Despite the reported existence of

3-oxo-2-arylhydrazonals **16** as a mixture of both *E* and *Z*-forms **16A** and **16B**,[21] the ^{1}H NMR of the reaction product revealed only one form, most likely the *E*-form **13**.

Compound **13** reacted with hydroxylamine hydrochloride to afford the oxime **18** that could be converted readily into the nitrile **19** either by refluxing with acetic acid and sodium acetate for 8 h or by heating in MW in acetic acid and sodium acetate at 160 °C for 10 minutes in 98% and 65% yields, correspondingly. As expected ^{13}C NMR revealed cyano carbon at δ 117.8 ppm.. Compound **19** reacted with hydroxylamine hydrochloride to give amidooxime **20**,[22,23] either by refluxing in dioxane for 10 h or by heating in MW at 160 ^{0}C for 1 h in 54% and 82% yields, correspondingly (*cf*. Scheme 5).

Conclusions

In summary, we could show that the enaminones **5** and **12** are valuable precursors to the bifunctionally substituted arylhydrazones that may be used, as such, as dyes. Simple chemistry can convert this into arylazopyrazoles with a unique substitution pattern. It is worthwhile to mention here that thermal and microwave assisted reactions were conducted in different solvents with exception of **12** which was prepared by microwave heating without solvent. We have also revealed that the reactions described have proceeded to completion in a much shorter time when irradiated in a focused microwave oven. Moreover microwave assisted reactions produced somewhat higher yield than those obtained by conventional heating.

Experimental Section

General Procedures. All the reactions were conducted under microwave irradiation in heavy-walled Pyrex tubes (capacity 10 mL) fitted with PCS cap [closed vessel under pressure]. Microwave heating was carried out with a single mode cavity Explorer Microwave Synthesizer (CEM Corporation, NC, USA), producing continuous irradiation and equipped with simultaneous external air-cooling system. IR spectra were recorded in KBr disks using a Perkin-Elmer System 2000 FT-IR spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX 400, NMR spectrometer in $CDCl_3$ or DMSO as solvent and TMS as an internal standard. Mass spectra were measured on a VG Autospec-Q (high resolution, high performance, tri-sector GC/MS/MS). Microanalyses were performed on a LECO CHNS-932 Elemental Analyzer.

2-(2-Oxo-2-phenylethyl)isoindole-1,3-dione: (3a)

Thermal method. A mixture of phthalimide potassium salt (1.85 g, 0.01 mol), phenacylbromide (1.99 g, 0.01 mol) and DMF (20 mL) was mixed gently until exothermic reaction ceased. The mixture was heated for 30 min, filtered and washed with water. The solid product was collected

and crystallized from EtOH to give 2.51 g, 95% (yield), mp 160-164 °C [Literature 80% [24], 90% [25] and 45% [26]. All data were agreed with the published one].

Microwave method. A mixture of phthalimide potassium salt (1.85 g, 0.01 mol) and phenacylbromide (1.99 g, 0.01 mol) in dry DMF (2 mL) was irradiated by focused microwave at 55 °C for 10 min. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The crude product was poured onto water, the solid product, so formed, was collected by filtration and crystallized from EtOH to give 1.80 g, 68% yield.

2-(1-Benzoyl-2-dimethylaminovinyl)isoindole-1,3-dione: (5).

Thermal method. A mixture of *N*-phenacylphthalimide (2.65 g, 0.01 mol) and DMFDMA (6.7g, 0.06 mol) was heated under reflux for 10 h. The solvent was removed under vacuum and the solid product was collected and crystallized from toluene. Compound **5** was formed as white crystals; yield 2.15g (59%), mp 179-182 °C. IR (KBr) ν 1783(CO), 1717 (CO) (cm^{-1}). ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.98(s, 6H, NMe_2), 7.38-7.60 (m,6H, phenyl-H and CH), 7.75-7.78 (m, 2H, phthalimidyl-H), 7.90-7.93 (m, 2H, phthalimidyl-H). ^{13}C NMR (DMSO-d_6): δ 189.0, 169.0 (CO), 140.0, 135.3, 134.7, 132.3, 130.5, 129.4, 128.6, 124.1, 123.3, 44.9 (CH_3). MS (EI) *m*/z (%): 320[M^+ ,100%], 303(90), 277(8), 243(35), 215(35), 172(20), 130(20), 105(68), 91(5), 77(60%). Anal. Calcd. For $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.21; H, 5.01; N, 8.80.

Microwave method. A mixture of *N*-phenacylphthalimide (2.65 g, 0.01 mol) and DMFDMA (1.19 g, 0.01 mol) was irradiated by focused microwave at 150 °C for 1 h. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The solid product, so formed, was collected by filtration and crystallized from toluene to give 2.43 g, 76% yield.

3-Phenyl-1*H*-pyrazol-4-ylamine: (7)

Thermal method. A mixture of compound **5** (3.2 g, 0.01 mol) and hydrazine hydrate (5 g, 0.07 mol) in toluene (15 mL) was refluxed for 5 h. The solvent was removed under vacuum and left to cool. The crude product was collected by filtration and washed with 10% sodium hydroxide solution to dissolve the side product (1,4-tetrahydrophthalazinedione). The precipitate was collected and crystallized from toluene to furnish compound **7** as white crystals, yield 0.92 g (92%), mp 149-150 °C, IR (KBr) ν 3429 and 3335 (NH_2) (cm^{-1}). ^{1}H NMR (DMSO-d_6): δ (ppm) 4.01(s, 2H, NH_2), 7.16 (s, 1H, pyrazol-H), 7.23 (t, 1H, *J = 7.3* Hz, phenyl-H), 7.39 (t, 2H, *J = 7.6* Hz, phenyl-H), 7.74 (s, 2H, phenyl-H), 12.47 (s, 1H, NH), 12.21(s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 138.9, 134.6, 132.0, 130.5, 128.8, 125.8, 124.7. MS (EI) m/z: (%) 159[M^+, 100%]. Anal. Calcd. For $C_9H_9N_3$: C, 67.91; H, 5.70; N, 26.40. Found C, 67.67; H, 5.82; N, 26.52.

Microwave method. A mixture of compound **5** (3.2 g, 0.01 mol) and hydrazine hydrate (0.03 mol) in toluene (2 mL) was irradiated in focused microwave at 140 °C for 15 min. The build-up

of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The solid product, so formed, was collected by filtration and crystallized from toluene to give 1.43 g, 90% yield.

2-(2-(3-phenyl-1*H*-pyrazol-4-yl)hydrazono)malononitrile (10). A cold solution of diazonium salt [prepared by addition of solution of sodium nitrite (0.4 g) (0.005 mol) in small amount of water to a solution of amine 7 (0.8 g, 0.005 mol)] was added to a solution of malononitrile (0.33 g, 0.01 mol) in EtOH (8 mL) containing sodium acetate (0.68 g). The mixture was then stirred in ice for 1 h, poured into water; the solid product was collected by filtration and crystallized from toluene. The reaction gave orange powder compound, yield 0.28 g, (64%), mp 113-114 °C, IR (KBr) ν 3221, 3130 (2 NH), 2226, 2204 (2 CN) (cm^{-1}). ^{1}H NMR (DMSO-d_6): δ (ppm) 7.37-7.65 (m, 6H, phenyl-H, pyrazolyl-H), 7.87 (s, 1H, NH), 12.45 (br s, 1H, NH). MS (EI) *m*/z (%)= 236[M^+, 68%]. Anal. Calcd. for $C_{12}H_8N_6$: C, 61.01; H, 3.41; N, 35.57; Found: C, 61.01; H, 3.46; N, 35.10.

5-Amino-4-[(3-phenyl-1*H*-pyrazol-4-yl)-hydrazono]-2,4-dihydropyrazol-3-one (11)

Thermal method. A mixture of compound **10** (2.36 g, 0.01 mol) and hydrazine hydrate (0.02 mol) in EtOH was heated under reflux for 6 h. The solid product was collected by filtration and crystallized from EtOH. The reaction gave green powder, yield 0.99 g, (37%), mp 262 °C, IR (KBr) ν 3446, 3391 (NH_2), 3294, 3198 and 3117 (3NH) (cm^{-1}). ^{1}H NMR (DMSO-d_6): δ(ppm) 4.37(s, 2H, NH_2), 7.40-7.93 (m, 6H, phenyl-H, pyrazolyl-H), 10.72 (s, 1H, NH), 13.01 (br s, 1H, NH), 13.23 (s, 1H, NH). MS (EI) *m*/z (%) = 269 [M^+, 18%].

Microwave method. A mixture of compound **10** (2.36 g, 0.01 mol) and hydrazine hydrate (0.02 mol) in (2 mL) EtOH was irradiated by focused microwave at 140 °C for 15 min. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled with high-pressure air through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The solid product, so formed, was collected by filtration and crystallized from ethanol to give 2.34 g, 90% yield.

2-(4-Dimethylamino-2-oxobut-3-enyl)isoindole-1,3-dione (12)

Thermal method. A mixture of phthalimidoacetone (2.03 g, 0.01 mol) and DMFDMA (1.19 g, 0.01 mol) in xylene (5 mL) was heated under reflux for 8 h. The solid product was collected by filtration and crystallized from EtOH. The reaction gave yellow crystal, yield 1.96 g (76%), mp 159-162 °C [Literature mp.155 °C[18]]. IR (KBr) ν 1769 (CO), 1714 (CO), 1660 (CO) (cm^{-1}). ^{1}H NMR (DMSO-d_6): δ(ppm) 2.72 (s, 3H, CH_3), 3.05 (s, 3H, CH_3), 4.40 (s, 2H, CH_2), 5.04 (d,1H, *J = 12* Hz, CH), 7.61 (d,1H, *J = 12* Hz, CH), 7.85-7.91 (m, 4H, phthalimidyl-H). MS (EI) *m*/z (%): 258.1[M^+, 20%], 160(20), 76(10). Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85; Found: C, 65.18; H, 5.44; N, 10.76

Microwave method. A mixture of phthalimidoacetone (2.03 g, 0.01 mol) and DMFDMA (1.19 g, 0.01 mol) was irradiated by focused microwave at 180 °C for 20 min. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled with high-pressure air through an inbuilt system in the instrument until the temperature

had fallen below 50 °C. The solid product, so formed, was collected by filtration and crystallized from EtOH to give 2.0 g, 77% yield.

4-(1,3-Dioxo-1,3-dihydroisoindol-2-yl)-3-oxo-2-(phenylhydrazono)-butyraldehyde (13). A cold solution of diazonium salt [prepared by adding a cold solution of sodium nitrite (0.69 g, 0.01 mol) in small amount of water to a solution of aniline (0.93 g, 0.01 mol)] was added to a solution of enaminone **12** (2.58 g, 0.01 mol) in EtOH (30 mL) containing sodium acetate (4 g). The mixture was then stirred for 1 h. The solid precipitated was collected and crystallized from EtOH. The reaction gave an orange powder, yield 0.84 g (25%), mp 209-210 °C. IR (KBr) ν 3442 (NH), 1172(CO), 1720(CO), 1683 (CO) (cm^{-1}). ^{1}H NMR (DMSO-d_6): δ(ppm) 5.06 (s, 2H, CH_2), 7.29-7.75 (m, 5H, phenyl-H), 7.90-7.98 (m, 4H, phthalimidyl-H), 9.67 (s, 1H, NH), 14.24 (s,1H, CHO). ^{13}C NMR (DMSO-d_6): δ 189.7 (CHO), 185.7 (CH_2CO), 167.5 (CO), 141.3, 134.7, 130.7, 129.5, 126.6, 123.2, 119.8, 117.3, 42.4 (CH_2). MS (EI): *m/*z (%) 335 [M^+, 69%]. Anal. Calcd. for $C_{18}H_{13}N_3O_4$: C, 64.48; H, 3.91; N, 12.53. Found: C, 64.44; H, 3.91; N, 12.68.

4-(1,3-Dioxo-1,3-dihydroisoindol-2-yl)-3-oxo-2-(phenylhydrazono)butyronitrile (19)

Thermal method. A mixture of compound **13** (3.35 g, 0.01 mol) and hydroxylamine hydrochloride (0.69g, 0.01 mol) and sodium acetate (6 g) in AcOH (10 mL) was refluxed for 8 h, and then poured into water. The solid product was collected by filtration and crystallized from dioxane. The reaction gave yellow crystals, yield 3.25 g (98.5%), mp 248-250 °C. IR (KBr) ν 3441(NH), 2217 (CN), 1769, 1725 (CO) (cm^{-1}). ^{1}H NMR (DMSO-d_6), δ(ppm) 5.06 (s, 2H, CH_2), 7.23 (t, 1H, *J* = *8* Hz, phenyl-H), 7.45 (t, 2H, *J* = *8* Hz, phenyl-H), 7.64 (d, 2H, *J* = *8* Hz, phenyl-H), 7.90-7.92 (m, 2H, phthalimidyl-H), 7.95-7.97 (m, 2H, phthalimidyl-H), 12.68 (s, 1H, NH). ^{13}C NMR: δ 188.13, 168.4 (CO), 135.8 (oxime carbon), 132.5, 130.6, 126.6, 124.4, 124.0, 117.8 (CN), 112, 111.4, 43.6 (CH_2). MS (EI): *m*/z (%) = 332[M^+, 85%]. Anal. Calcd. for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.64; N, 16.86. Found: C, 64.67; H, 3.73; N, 16.47.

Microwave method. A mixture of compound **13** (3.35 g, 0.01 mol) and hydroxylamine hydrochloride (0.69g, 0.01 mol) and sodium acetate (6 g) in AcOH (2 mL) was irradiated by focused microwave at 160 °C for 10 min. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled with high-pressure air through an inbuilt system in the instrument until the temperature had fallen below 50 °C, and then poured into water. The solid product was collected by filtration and crystallized from dioxane to give 2.15 g, 65% yield.

4-(1,3-Dioxo-1,3-dihydroisoindol-2-yl)-*N*-hydroxy-3-oxo-2-(phenyl-hydrazono) butyramidine (20)

Thermal method. A mixture of compound **19** (3.32 g, 0.01 mol) and hydroxylamine hydrochloride (0.69 g, 0.01 mol) and sodium acetate (6 g) in (20 mL) of EtOH was refluxed for 10 h. The solvent was removed under vacuum. The remaining product was poured into water. The solid product was collected by filtration and crystallized from EtOH. The reaction gave yield 1.97 g (54%), mp 209-211°C. IR (KBr) ν 3427(NH_2), 1711(CO) (cm^{-1}). ^{1}H NMR (DMSO-d_6):

δ(ppm) 5.09 (s, 2H, CH_2), 7.16 (s, 2H, NH_2), 7.16-7.59 (m, 5H, phenyl-H), 7.89-7.92 (m, 2H, phthalimidyl-H), 7.94-7.97 (m, 2H, phthalimidyl-H); 10.32 (s, 1H, NH), 14.69 (s, 1H, OH). ^{13}C NMR (DMSO-d_6): δ (ppm) 192.0, 168.7 (CO), 151.8 (oxime carbon), 143.0 (hydrazone carbon), 135.8, 132.6, 130.8, 125.5, 125.1, 124.3, 116.5, 44.4 (CH_2). MS (EI) *m/z* (%)= 365 [M^+, 63%]. Anal. Calcd. for $C_{18}H_{15}N_5O_4$: C, 59.18; H, 4.14; N, 19.17. Found: C, 59.34; H, 4.35; N, 18.76

Microwave method. A mixture of compound **19** (3.32 g, 0.01 mol), hydroxylamine hydrochloride (0.69 g, 0.01 mol) and sodium acetate (6 g) in EtOH (2 mL) was irradiated in focused microwave at 160 °C for 1 h. The build-up of pressure in the closed reaction vessel was carefully monitored. After the irradiation, the reaction tube was cooled with high-pressure air through an inbuilt system in the instrument until the temperature had fallen below 50 °C. The solvent was removed under vacuum. The remaining product was poured into water. The solid product was collected by filtration and crystallized from EtOH to give 2.99 g, 82% yield.

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References

1. Ghoneim, M. M.; El-Desoky, H. S.; Amer, S. A.; Rizk, H. F.; Habazy, A. D. *Dyes and Pigments* **2008**, *77*, 493.
2. Karci, F.; Karci, F. *Dyes and Pigments* **2008**, *77*, 451.
3. Hill, G. B.; Mortlock, A. A. *Synthesis* **2007**, *11*, 1697.
4. Abdallah, T. A.; Salaheldin, A. M.; Radwan, N. F. *Z. Naturforsch*. **2007**, *62*, 261.
5. Infantes, L.; Foces-Foces, C.; Cabildo, P.; Claramunt, R.; Mo, O.; Yanez, M.; Elguero, J. *Heterocycles* **1998**, *49*, 157.
6. Hassaniein, H. M. E. *Synth. Commun*. **2007**, *37*, 3579.
7. Emelina, E. E.; Petrov, A. A.; Firsov, A. V. *Russian J. Org. Chem.* **2007**, *43*, 471.
8. Chien, T. C.; Smaldone, R. A.; Townsend, L. B. *Tetrahedron Letters* **2004**, *45*, 4105.
9. Al-Saleh, B.; El-Apasery, M. A.; Al-Kandery, N.; Elnagdi, M. H. *J. Het. Chem.* **2008**, *45*, 359.
10. Bisoyi, H. K.; Kumar, S. *Tetrahedron Letters* **2007***, 48*, 4399.
11. Sharma, A.; Mehta, V. P.; Eycken, E.V. *Tetrahedron* **2008,** *64*, 2605.
12. Mallakpour, S.; Taghavi, M. *Eur. Polymer J.* **2008**, *44*, 87.

13. Chebanov, V. A.; Sakhno, Y. I.; Desenko, S. M.; Chernenko, V. N.; Musatov, V. I..; Shishkina, S. V.; Shishkin, O. V.; Kappe**,** C. O. *Tetrahedron* **2007,** *63*, 1229.
14. Glasnov, T. N.; Tye, H.; Kappe, C. O. *Tetrahedron* **2008,** *64,* 2035.
15. Wilcoxen, K.; Huang, C. Q.; McCarthy, J. R.; Grigoriadis, D. E.; Chen, C. *Bioorg. Med. Chem. Letters* **2003**, *13,* 3367.
16. Fadel, S.; Hajbi, Y.; Rakib, E. M.; Khouili, M.; Pujol, M. D.; Guillaumet, G. *Synthetic Comm.* **2004**, *34*, 2195.
17. Quiroga, J.; Cruz, S.; Insuasty, B.; Abonia, R. *Het. Commun.* **2000**, *6*, 275.
18. Vidal, L. *L'Oreal*. U.S. Patent # 6916432. **2005**, Hair bleach composition and hair dye composition.
19. Al-Omran, F.; El-Khair, A. *J. Het. Chem.* **2005**, *42,* 307.
20. Al-Zaidi, K.; Elnagdi, M. H. unpublished results, personal communications.
21. El-Dusouqui, O. M. E.; Abdelkhalik, M. M.; Al-Awadi, N. A.; Dib, H. H.; George, B. J.; Elnagdi, M. H. *J. Chem. Res.* **2006**, *5*, 295.
22. Ibrahim, H. M.; Makhseed, S.; Abdel-Motaleb, R. M.; Elnagdi, M. H. *Heterocycles* **2007**, *71,*1951.
23. Aziz, S. I.; Anwar, H. F.; Fleita, D. H.; Elnagdi, M. H. *J. Het. Chem.* **2007**, *44,*725.
24. De Paulis, T.. Hemstapat, K.; Yelin, Z. C.; Saleh, S. Y.; David, B. A.; Tamagnan, R. M.; Gilles, D.; Jeffrey, C. P. *J. Med. Chem.* **2006**, *49,* 3332.
25. Hu, A.; Lin, W. *Org. Lett.* **2005**, *7*, 455.
26. Goossen, L. J.; Ghosh, K. *European J. Org. Chem.* **2002**, *19*, 3254.