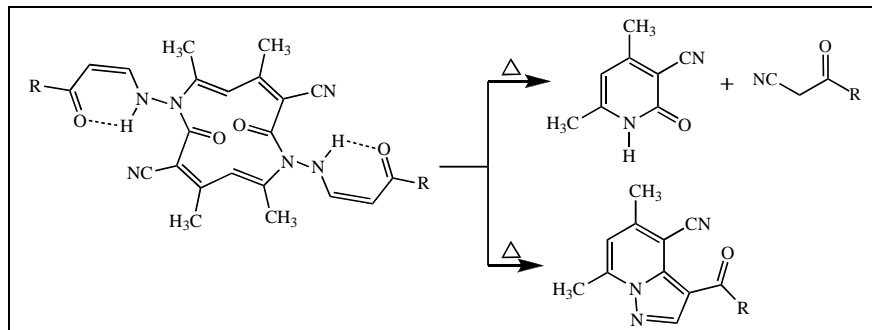


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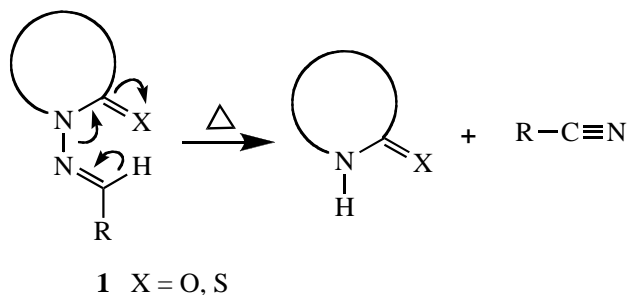
Flash vacuum pyrolysis (FVP) of 1,7-bis-(3-arylideneamino)-4,6,10,12-tetramethyl-2,8-dioxo-1,7-diazacyclododeca-3,5,9,11-tetraene-3,9-dicarbonitriles **11a-c** at 650°C and 0.02 Torr yielded 5,7-dimethyl-3-(4-methylbenzoyl)-pyrazolo[1,5-*a*]pyridine-4-carbonitrile **14**, 4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile **16** and 3-aryl-3-oxo-propionitriles **17a,b**. A plausible mechanism is suggested to account for the formation of the products.

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INTRODUCTION

Selective deprotection of the *N*-arylideneamino moiety from heterocyclic amides of general formula **1** were shown to be an efficient, clean and general synthetic procedure for regioselective synthesis of potential biologically active pyridine, pyrimidines, triazoles and triazines and their derivatives [1-4].

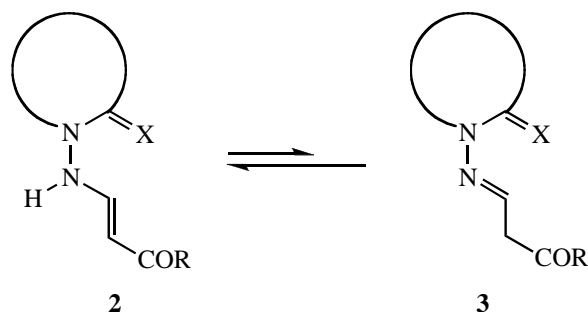
Scheme 1



In the present study we have extended the investigation to include the thermal behavior of system **2**, which in theory may exist as enamines **2** or imines **3**.

We have attempted to prepare system **2** from the reaction of *N*-aminopyridone **4** and enamines **5a-c**. According to literature procedure [5] *N*-aminopyridone **4** is reported to be readily obtained from refluxing cyanoacetyl hydrazide **6** with acetylacetone **7** in ethanolic diethylamine solution. Spectroscopic characterization of

Scheme 2



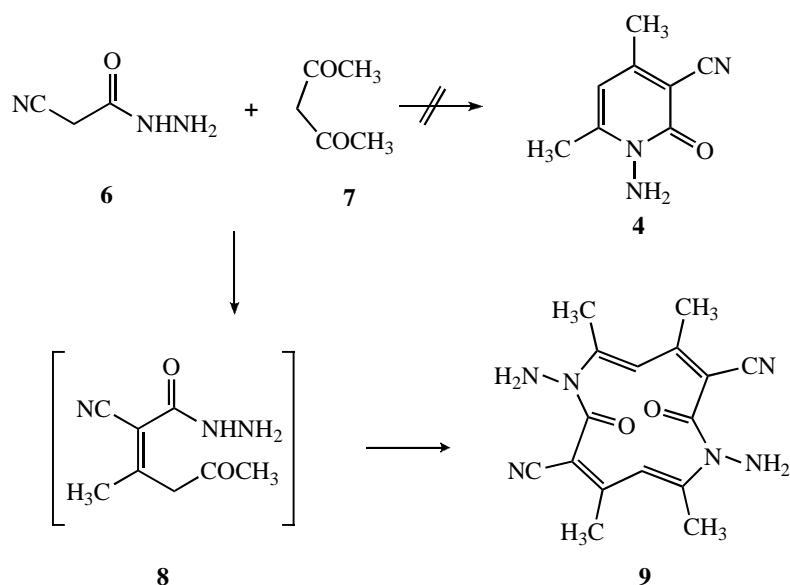
the product by IR and ¹H nmr agree well with its reported structure. However the mass spectra of the product by LCMS and GCMS revealed a molecular ion peak at 327 (M⁺) corresponding to a dimeric product **9**. Formation of the latter could be attributed to the initial formation of condensation product **8**, that would further self condensed to produce **9** (cf. Scheme 3).

Several attempts to prepare **4** were not successful, so we have decided to proceed with **9** by reacting it with enamines **5a-c**, prepared *via* condensing aryl methyl ketones with dimethylformamide dimethyl acetal under microwave irradiation reported recently [6]. This yielded a dienaminone, which may be represented as imine **10**, *Z* enaminone **11** or *E* enaminone **12** (Scheme 4). ¹H nmr data revealed that the product is *Z* enaminone **11a-c**. Two types of products were characterized from the flash

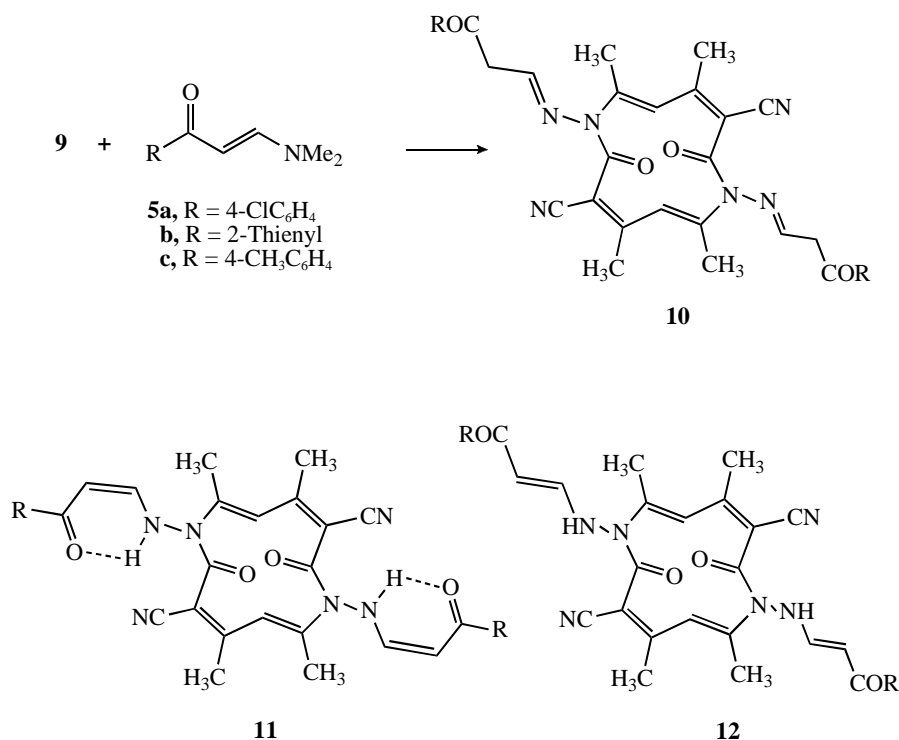
vacuum pyrolysis of **11a-c** depending on the nature of aryl substituents in which an intramolecular reaction takes place leading to intermediates **13** and **15**. Thus **11c** was completely converted into **14** by pyrolytic cyclization, which may arise from the generated enaminone **13** from initial 6π electrocyclicization [7] followed by water elimination.

On the other hand, pyrolysis of **11a-b** resulted in the formation of pyridone **16** and oxoalkanonitriles **17a-b**. This could be attributed to the electron withdrawing effect of the *p*-Cl and 2-thienyl substituent which will help facilitate N-N bond breaking *via* enamine formation; although derivatives of **17** can be obtained by reacting haloketones with cyanide ion [8] or reacting ester with

Scheme 3



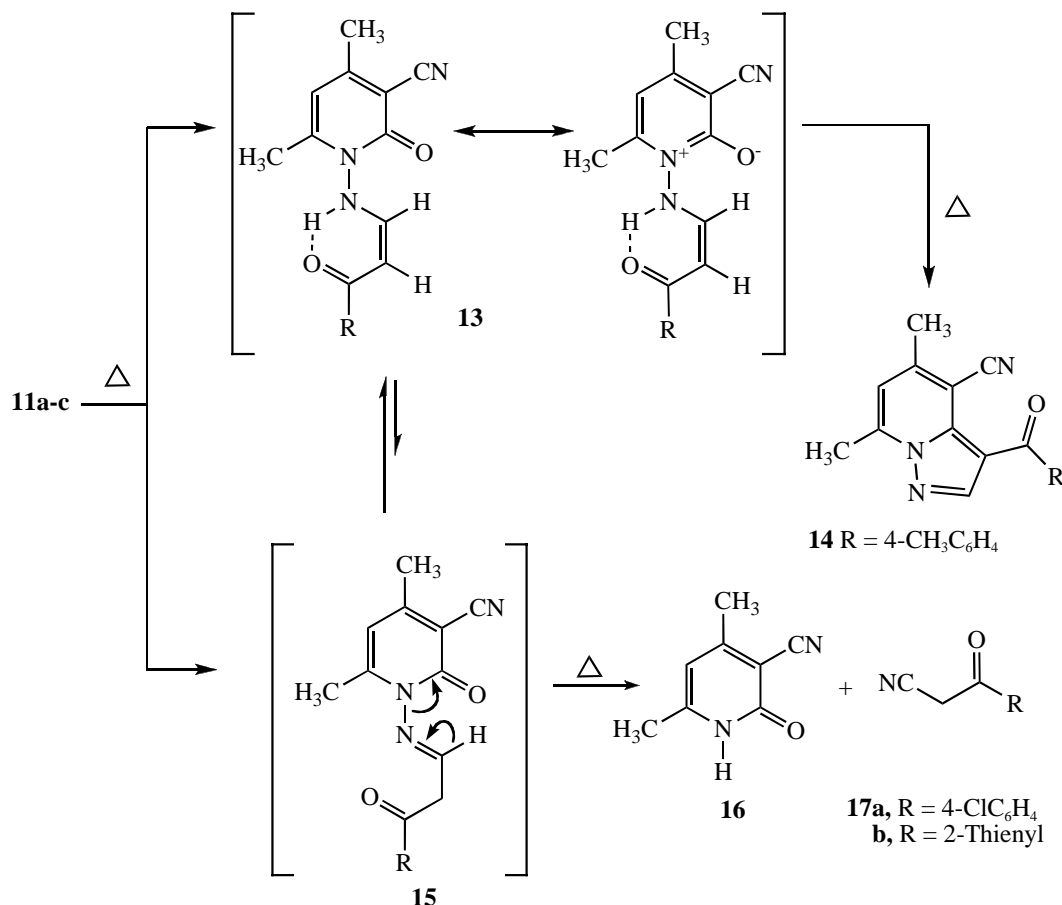
Scheme 4



acetonitrile [9]. These approaches either employ hazardous chemicals (haloketones and cyanide ion) or not readily obtainable substituted acid esters. Formation of **16** and **17** indicates clearly that the reactive species in this case is the intermediate imine form **15** (*cf.* Scheme 5).

yield (94 %, 3.0 g); mp 171-172 °C; ir: 3420, 3332 (NH₂) and 2216 (CN); MS: $m/z = 327$ (M⁺). ¹H NMR (DMSO): $\delta = 2.31$ (s, 6H, 2CH₃), 2.42 (s, 6H, 2CH₃), 6.15 (br s, 4H, 2NH₂, D₂O exchangeable), 6.33 (s, 2H). *Anal.* Calcd. for C₁₆H₁₈N₆O₂ (326.36): C 58.89, H 5.56, N 25.75. Found C 59.00, H 5.49, N 25.89.

Scheme 5



EXPERIMENTAL

Melting points were determined on a Shimadzu-Gallenkamp apparatus and are uncorrected. Elemental analysis was obtained by means of a LECO CHNS-932 Elemental Analyzer. NMR spectra were measured using a Bruker DPX 400 MHz superconducting spectrometer, and FT-IR measurements were from a Perkin Elmer 2000 FT-IR system. Mass spectrometric analysis was carried out on a VG-Autospec-Q high performance tri-sector GC/MS/MS, and the instrument for HPLC was an Agilent 1100 series LC/MSD with an API-ES/APCI ionization mode.

1,7-Diamino-4,6,10,12-tetramethyl-2,8-dioxo-1,7-diazacyclododeca-3,5,9,11-tetraene-3,9-dicarbonitrile (9). Compound **9** was prepared following published procedure [Lit. mp. 174°C]. This compound was obtained as white crystals from ethanol in

General procedure for the preparation of 11a-c. Compound **9** (3.26 g, 10 mmol) was treated with each of enamines **5a-c** (10 mmol) in ethanol/hydrochloric acid mixture 8:2 (10 ml). The reaction mixture was heated under reflux for 20 min. and left to cool at room temperature to deposit a solid that was collected by filtration and crystallized from ethanol.

1,7-Bis-[3-(4-chlorophenyl)-3-oxo-propylideneamino]-4,6,10,12-tetramethyl-2,8-dioxo-1,7-diazacyclododeca-3,5,9,11-tetraene-3,9-dicarbonitrile (11a). This compound was obtained as yellow crystals from DMF in yield (84 %, 5.5 g); mp 226-227 °C; ir: 3069 (NH) and 2216 (CN), 1668 (CO); MS: $m/z = 666$ (M⁺), ¹H NMR (DMSO): $\delta = 2.09$ (s, 6H, 2CH₃), 2.31 (s, 6H, 2CH₃), 5.83 (d, 2H, 2-H, J = 7.8Hz), 6.45 (s, 2H, 5-H and 11-H), 7.52 (d, 4H, J = 8.4 Hz, arom. H), 7.84 (d, 4H, arom. H, J = 8.4 Hz), 7.98 (d, 2H, 3-H J = 7.8Hz), 10.61 (br s, 2H, 2NH). *Anal.*

Calcd. for $C_{34}H_{28}Cl_2N_6O_4$ (655.54): C 62.30, H 4.31, N 12.82. Found C 61.93, H 4.66, N 13.06.

4,6,10,12-Tetramethyl-2,8-dioxo-1,7-bis-(3-oxo-3-thiophen-2-yl-propylideneamino)-1,7-diazacyclododeca-3,5,9,11-tetraene-3,9-dicarbonitrile (11b). This compound was obtained as yellow crystals from DMF in yield (87 %, 5.2 g); mp 188-189 °C; ir: 3258 (NH) and 2216 (CN), 1669 (CO); MS: $m/z = 599$ (M^+). 1H NMR (DMSO): $\delta = 2.32$ (s, 6H, 2CH₃), 2.40 (s, 6H, 2CH₃), 5.79 (d, 2H, 2-H, $J = 8$ Hz), 6.46 (s, 2H, 5-H and 11-H), 7.15 (t, 2H, thienyl 3-H, $J = 5.0$ Hz), 7.74-7.91 (m, 6H, vinyl 3-H, thienyl 2-H and 4-H), 10.08 (br s, 2H, 2NH). *Anal.* Calcd. for $C_{30}H_{26}N_6O_4S$ (598.69): C 60.18, H 4.38, N 14.04, S 10.71. Found C 59.92, H 4.28, N 14.20, S 10.59.

4,6,10,12-Tetramethyl-2,8-dioxo-1,7-bis-(3-oxo-3-p-tolylrolylideneamino)-1,7-diazacyclododeca-3,5,9,11-tetraene-3,9-dicarbonitrile (11c). This compound was obtained as yellow crystals from DMF in yield (88 %, 5.4 g); mp 211-212 °C; ir: 3069 (NH) and 2216 (CN), 1671 (CO); MS: $m/z = 615$ (M^+), 1H NMR (DMSO): $\delta = 2.31$ (s, 6H, 2CH₃), 2.37 (s, 6H, 2CH₃), 2.51 (s, 6H, 2CH₃), 5.80 (d, 2H, 2-H, $J = 8.0$ Hz), 6.46 (s, 2H, 5-H and 11-H), 7.25 (d, 4H, arom. H, $J = 8.4$ Hz), 7.72 (d, 4H, arom. H, $J = 8.4$ Hz), 7.87 (d, 2H, 3-H, $J = 8.0$ Hz), 10.05 (br s, 2H, 2NH). *Anal.* Calcd. for $C_{36}H_{34}N_6O_4$ (614.70): C 70.34, H 5.58, N 13.67. Found C 69.80, H 5.36, N 13.89.

General procedure for Flash Vacuum Pyrolysis (FVP) of 11a-c.

The apparatus used is similar to that described in our recent publications [10-11]. The sample was volatilized from a tube in a Büchi Kugelrohr oven through a 30 x 2.5 cm horizontal fused quartz tube. This was heated externally by a Carbolite Eurotherm tube furnace MTF-12/38A to a temperature of 650 °C, the temperature being monitored by a Pt/Pt-13%Rh thermocouple situated at the center of the furnace. The products were collected in a U-shaped trap cooled in liquid nitrogen. The whole system was maintained at a pressure of 10^{-2} Torr by an Edwards Model E2M5 high capacity rotary oil pump, the pressure being measured by a Pirani gauge situated between the cold trap and the pump. Under these conditions the contact time in the hot zone was estimated to be ≈ 10 ms. The different zones of the products collected in the U-shaped trap were analyzed by 1H nmr, LCMS and GC-MS. Relative and percent yields were determined from 1H NMR. Identities of compounds obtained were confirmed by comparison of their 1H -NMR spectra with data of products separated from preparative HPLC.

MS and NMR Characterization for Compounds 14, 16 and 17a,b.

5,7-Dimethyl-3-(4-methylbenzoyl)-pyrazolo[1,5-a]pyridine-4-carbonitrile (14). MS: $m/z = 289$ (M^+), $C_{18}H_{15}N_3O$ (289.34). 1H NMR (CDCl₃): $\delta = 2.42$ (s, 3H, CH₃), 2.46 (s,

3H, CH₃), 2.51 (s, 3H, CH₃), 6.09 (s, 1H, 6-H), 7.82 (d, 2H, arom. H, $J = 8.4$ Hz), 8.02 (d, 2H, arom. H, $J = 8.4$ Hz), 9.05 (s, 1H, 2-H).

4,6-Dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (16). MS: $m/z = 149$ (M^+), $C_8H_8N_2O$ (148.16). 1H NMR (CDCl₃): $\delta = 2.42$ (s, 3H, CH₃), 2.51 (s, 3H, CH₃), 6.47 (s, 1H), 12.05 (br s, 1H, NH D₂O exchangeable).

3-(4-Chlorophenyl)-3-oxo-propionitrile (17a). MS: $m/z = 180$ (M^+), C_9H_6ClNO (179.61). 1H NMR (CDCl₃): $\delta = 4.02$ (s, 2H, CH₂), 7.54 (d, 2H, arom. H, $J = 8.0$ Hz), 7.88 (d, 2H, arom. H, $J = 8.0$ Hz).

3-Oxo-3-thiophen-2-yl-propionitrile (17b). MS: $m/z = 152$ (M^+), C_7H_5NOS (151.18). 1H NMR (CDCl₃): $\delta = 4.02$ (s, 2H, CH₂), 7.15 (t, 1H, thienyl 3-H, $J = 5.0$ Hz), 7.74-7.82 (m, 2H, thienyl 2-H and 4-H).

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