1-Substituted 3-dimethylaminoprop-2-en-1-ones as building blocks in heterocyclic synthesis: new routes to 6-aroylpyridazin-3-ones, 4,6-diaroylpyridazin-3-imines and 3-aroylpyrazolo[5,1-c][1,2,4]triazines

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The Wittig reaction of 3-aryl/heteroaryl-2-arylhydrazono-3-oxopropanals **2c,d** with ethyl triphenylphosphonioacetate in the presence of methanesulfinylmethyl carbanion affords 2-substituted 6-aroylpyridazin-3(2*H*)-ones (**5a,b**) in moderate yields. Compounds **5a,b** were also obtained from the reaction of **2c,d** with acetic anhydride in presence of potassium acetate. 1-Substituted-3-dimethylaminoprop-2-ene-1-ones **1b,d** couple with 5-methylisoxazole-3-diazonium chloride to yield isoxazolylhydrazonopropanals **2g,h**. Compounds **1a,b** couple with 5-methylpyrazole-3-diazonium chloride to yield pyrazolylhydrazonopropanals that readily cyclise to the corresponding pyrazolo[5,1-*c*][1,2,4]triazines. The reactivity of 2-arylhydrazono-3-oxopropanals **2a–f** towards a variety of active methylene reagents was investigated.

Keywords: pyridazinones, Wittig reactions, enaminones, fused 1,2,4-triazines, fused pyrazoles

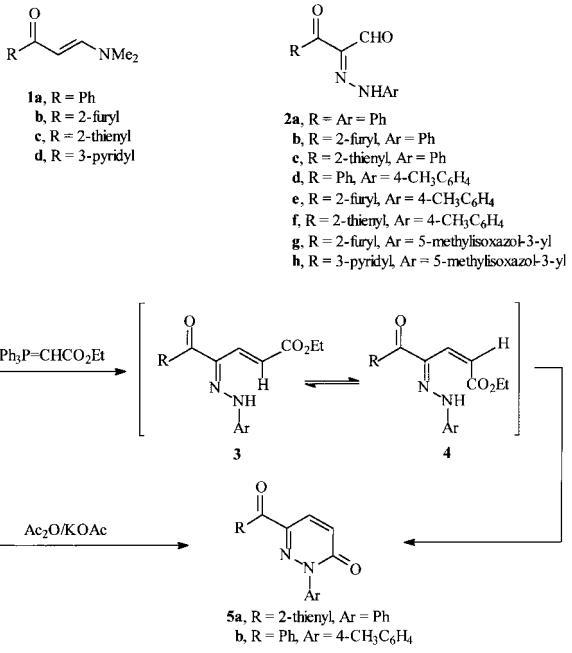
In the last decade, several novel syntheses of pyridazines have been developed.[13–16] Recently, it has been shown that 3-substituted-2-arylhydrazono-3-oxopropanals **2**, which are prepared in excellent yields *via* coupling of enaminones **1** with aryldiazonium salts, could be utilised for the synthesis of pyridazinones.[17] In an attempt to establish more detailed structure-activity relationships in this series, it seemed of value to explore further the utility of **2** as a precursor to the ring system.

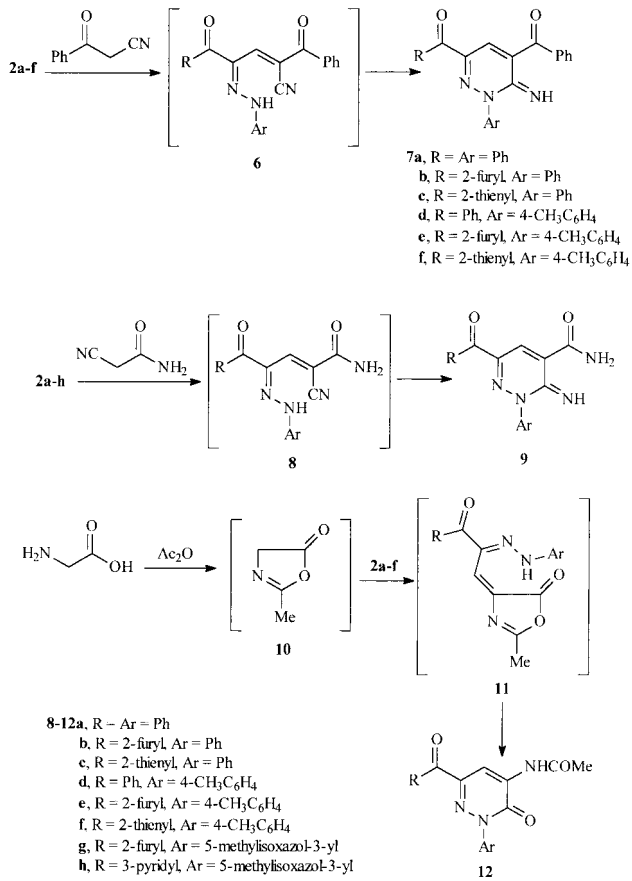
It is found that 2-arylhydrazono-3-oxopropanals **2c,d** react readily with ethyl triphenylphosphonioacetate in dimethyl sulfoxide in the presence of sodium hydride to yield products that are formulated as the pyridazin-3-ones **5a,b** (method A) in yields of 64 and 62 % respectively. The same compounds (**5a,b)** could also be obtained from a Perkin reaction of **2c,d** with acetic anhydride and dry, freshly fused potassium acetate in absence of solvent at 150 °C (method B) in yields of 59 and 63 % respectively.

Structures **5a,b** were established for the reaction products on the basis of their spectral data. The IR spectra revealed two carbonyl bands at ν_{max} = 1685, 1631 and 1672, 1638 cm^{-1} respectively. It is assumed that the reaction of **2c,d** with the ylide affords initially an equilibrium mixture of olefins **3** and **4**. Cyclisation of **4** disturbs the equilibrium, resulting in isomerisation of **3** to **4**. Thus only cyclised compounds **5** are isolated.

Compounds **2a–f** condensed with benzoylacetonitrile to yield products assigned the pyridazinimine structures **7a–f** rather than the arylhydrazones **6**. Structures **7a–f** were based on their IR spectra and ^{13}C NMR that revealed the absence of a CN signal.

The reaction of **2a–h** with cyanoacetamide afforded yellow products of condensation via elimination of one molecule of





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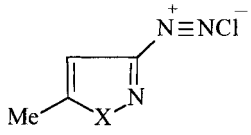
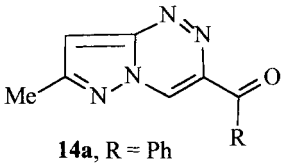


13a, X = NH
b, X = O



14a, R = Ph
b, R = 2-furyl

water. These can thus be assigned the hydrazone structure **8a–h** or the isomeric pyridazin-3-imine **9a–h**. Structure **9** is established for the reaction products based on the IR spectrum, which revealed the absence of any CN absorption. The arylhydrazones **2a–f** reacted with glycine in acetic anhydride to yield colourless products for which several isomeric structures are possible. Structure **12** is proposed for these products based on their spectral data.

It is assumed that, in presence of acetic anhydride, glycine is first acylated yielding acetylglycine which then cyclises to form 2-methyloxazol-5-one **10**. This then condenses with **2a–f** to yield the intermediate arylhydrazones **11a–f**, which then rearrange *via* attack of the hydrazone moiety at the ring carbonyl group, yielding the pyridazinones **12a–f**.

Compounds **1a,b** couple readily with 5-methylpyrazole-3-diazonium chloride **13a** to yield pyrazolo[5,1-*c*][1,2,4]triazines **14a,b** *via* the assumed intermediacy of acyclic hydrazones. However, 5-methylisoxazole-3-diazonium chloride **13b** couples with **1b,d** to yield **2g,h** that could not be further cyclised to isoxazolo-triazines under a variety of conditions.

Techniques used: IR, ^{1}H and ^{13}C NMR, Mass spectra, elemental analysis

References: 17

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References cited in this synopsis

13 H. Al-Awadi, F. Al-Omran, M. H. Elnagdi, L. Infantes, C. Foces-Foces, N. Jagerovic and J. Elguero, *Tetrahedron*, 1995, **51**, 12745.
14 M.H. Elnagdi, A.M. Negm, K.U. Sadek, *Synlett*, 1994, 27-37.
15 M.H. Elnagdi. A.H. Elghandour, A.F.A. Harb, A.H.M. Hussein and S.A.M. Metwally, *Heterocycles*, 1994, **38**, 739
16 M.H. Elnagdi. N.S. Ibrahim, F.M. Abdelrazek and A.W. Erian, *Liebigs Ann. Chem*. 1988, 909.
17 F. Al-Omran, M.M. Abdel-Khalik, A. Abou El-Khair and M.H. Elnagdi, *Synthesis* 1997, 91.