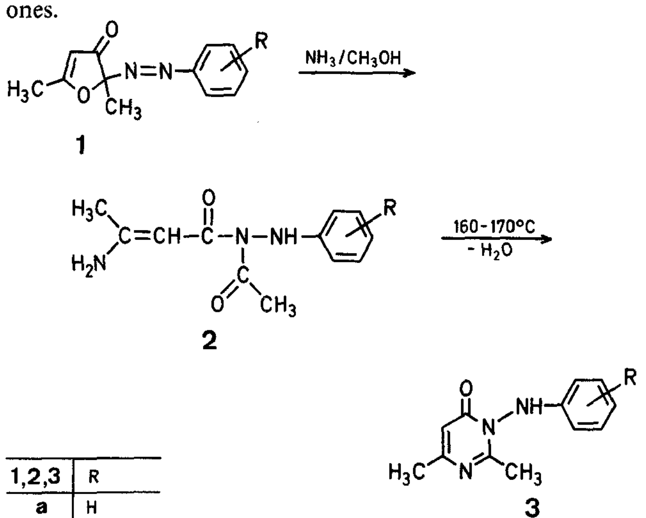
A Facile Synthesis of 2,6-Dimethyl-3-arylamino-4-oxo-3,4-dihydropyrimidines

Carlo VENTURELLO*, Rino D'ALOISIO

Istituto Guido Donegani S.p.A., I-28 100 Novara, Italy

2-Arylazo-2,5-dimethyl-3-oxo-2,3-dihydrofurans **1**[1,2] as well as the analogous phenylene-bis-azo compounds[3], easily obtainable by reaction of 2,5-dimethyl-3(2*H*)-furanone[4] with diazotized arylamines and bis-diazotized phenylenediamines, respectively, are interesting and valuable substrates in heterocyclic chemistry. Convenient syntheses of 3-pyrazolones[2], bis-3-pyrazolones[3], and 4-pyridazones[5] starting from these materials have been reported.

Recently[6], we have shown that ring opening of the furanones **1** with ammonia leads to the previously unknown β-acetyl-β-(3-amino-2-butenoyl)-arylhydrazines **2**. As a further example of the versatility of compounds **1** in the synthesis of heterocyclic compounds, we now report that their ring opening products **2** can easily be converted to 2,6-dimethyl-3-arylamino-4-oxo-3,4-dihydropyrimidines **3**, a new class of 4-pyrimidones.



1

2

3

1,2,3	R
a	H
b	4-H₃C
c	2-H₃CO
d	4-Cl

Experimentally, the reaction is very simple. It only requires heating of **2** at 160–170 °C, whereby cyclization to **3** occurs with loss of water. Chromatography on silica gel of the reaction mixture affords compounds **3** in an analytically pure state and in good yields (Table 1). The structure assigned to compounds **3** follows from spectral data and microanalyses (Tables 1 and 2).

The synthesis of 4(3*H*)-pyrimidones is of considerable practical interest because of the herbicidal[7] and biological[8] activity exhibited by many of these compounds. The current literature contains a considerable number of methods leading to these heterocyclic compounds[8–13]. However, they are generally cumbersome and/or involve rather expensive starting materials.

Table 1. 2,6-Dimethyl-3-arylamino-4-oxo-3,4-dihydropyrimidines (**3**)

Product	Reaction Conditions Time/Bath Temperature	R_f[a]	Yield[b] [%]	m.p. [°C][c] (solvent)	Molecular formula[d]
3a	40 min/ 160 °C	0.67	85	121–123° (ether, −25 °C)	$C_{12}H_{13}N_3O$ (215.2)
3b	10 min/ 170 °C	0.72	72	141–143° (ether, −25 °C)	$C_{13}H_{15}N_3O$ (229.3)
3c	7–8 min/ 170 °C	0.67	78	151–153° (ethyl acetate)	$C_{13}H_{15}N_3O_2$ (245.3)
3d	10 min/ 170 °C	0.66	80	175–176° (ethyl acetate)	$C_{12}H_{12}ClN_3O$ (249.7)

[a] T.L.C. performed on Merck pre-coated silica gel 60F-254 plates using acetone/diethyl ether (1 : 4) as eluent; spot detected by observation under a 254 nm source or by spraying with a $KMnO_4$ solution.

[b] Yields refer to isolated, uncrystallized product.

[c] Melting points were determined by the Kofler method and are uncorrected.

[d] Satisfactory microanalysis obtained: C ±0.20, H ±0.09, N ±0.11, Cl +0.15.

Table 2. Spectral Data of Compounds **3**

Compound	¹H-N.M.R. ($CDCl_3$/TMS)[a] δ [ppm]	I.R. (Nujol)[b] ν [cm⁻¹]	M.S. (70 eV)[c] m/e (M^+)
3a	2.31 (d, 3H, 6-CH_3, J=0.8 Hz); 2.54 (s, 3H, 2-CH_3); 6.32 (m, 1H, 5-H); 6.60–6.76 (m, 2H_{arom}); 6.88–7.38 (m, 3H_{arom}); 7.32 (s, 1H, NH)[d]	3238, 1682, 1546, 1496	215
3b	2.27 (s, 3H, ArCH_3); 2.31 (d, 3H, 6-CH_3, J=0.8 Hz); 2.53 (s, 3H, 2-CH_3); 6.31 (m, 1H, 5-H); 6.60, 7.07 (approx. AB d, 2H_{arom}, J_{AB}=8.6 Hz); 7.23 (s, 1H, NH)[d]	3265, 1683, 1535, 1510	229
3c	2.31 (d, 3H, 6-CH_3, J=0.8 Hz); 2.59 (s, 3H, 2-CH_3); 3.95 (s, 3H, OCH_3); 6.20–6.36 (m, 2H, 5-H and H_{arom}); 6.70–7.08 (m, 3H_{arom}); 7.46 (s, 1H, NH)[d]	3327, 1690, 1542, 1504	245
3d	2.31 (d, 3H, 6-CH_3, J=0.8 Hz); 2.52 (s, 3H, 2-CH_3); 6.32 (m, 1H, 5-H); 6.61, 7.21 (approx. AB d, 2H_{arom}, J_{AB}=8.9 Hz); 7.31 (s, 1H, NH)[d]	3222, 1673, 1543, 1491	249 (³⁵Cl)

[a] N.M.R. spectra were recorded with a Bruker WH-90 instrument.

[b] I. R. Spectra were recorded with a Perkin-Elmer 125 spectrophotometer.

[c] Mass spectra were recorded with a Varian MAT CH 5 instrument.

[d] Exchangeable with D_2O.

2,6-Dimethyl-3-arylamino-4-oxo-3,4-dihydropyrimidines 3; General Procedure:

Finely powdered β-acetyl-β-(3-amino-2-butenoyl)-arylhydrazine (**2**; 5 mmol), prepared from 2-arylazo-2,5-dimethyl-3-oxo-2,3-dihydrofuran (**1**) and ammonia as previously described[6], is stirred well in an inclined, rotating, round-bottomed flask at 160–170 °C for the prescribed time (see Table 1). The solid (oil for **3a**) material obtained is chromatographed on silica gel (70–230 mesh; 70 g) using acetone/diethyl ether (1 : 9) [1 : 4 for **3d**] as eluent, and the fraction having the prescribed R_f (see Table 1) is collected. Removal of the solvent affords the desired product in 72–85% yields as solids (**3b–d**). Product **3a** gives a syrup which slowly solidifies (Table 1).

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