Steric and Electronic Control in the Addition of Hydrazine and Phenylhydrazine to α-[(Dimethylamino)methylene]-β-oxoarylpropanenitriles

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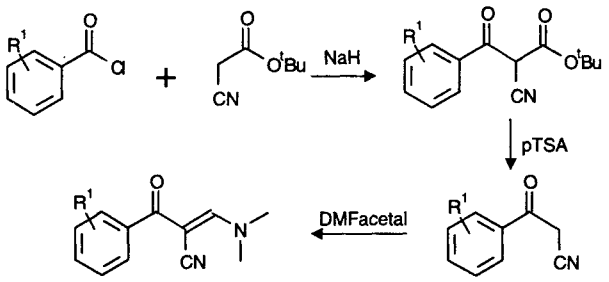
Received 15 May 1996; revised 2 July 1996

Reaction of hydrazine with α-[(dimethylamino)methylene]-β-oxoarylpropanenitriles **2** gives a mixture of the 4-aroyl-5-aminopyrazoles **3** and the 5-aryl-4-cyanopyrazoles **4**. Similarly reaction of **2** with phenylhydrazine gives rise to the 5-amino-4-aroyl-1-phenylpyrazoles **5** and 5-aryl-4-cyano-1-phenylpyrazoles **6**. The regioselectivity of addition has been investigated with respect to the electronic nature and steric requirements of the aromatic substitution. The ratio of products was found to be independent of the electronic nature of the substituent. The outcome of the reaction was however very sensitive to steric factors. Substituents in the *para*- and *meta*-positions favoured formation of the pyrazole-nitrile products **4** and **6**, whereas sterically demanding *ortho*-substituents favoured the pyrazole-amino ketones **3** and **5**.

Despite their ease of preparation, α-[(dimethylamino)-methylene]-β-oxoarylpropanenitriles have found little application in synthesis. A small number of patent references detail their use in the preparation of substituted acrylonitriles useful as herbicides,[1-4] and there is one report of a dimerisation reaction to yield 3,5-dicyano-4-(*N*,*N*-dimethylformamidino)-2,6-diphenyl-4*H*-pyran.[5] One patent reports that a range of α-[(dimethylamino-methylene]-β-oxo-arylpropanenitriles undergo condensation with aminoguanidine nitrate giving rise to a series of 5-amino-4-aroylpyrazoles[6] of general structure **3**. Grothaus and Dains,[7] and Nishiwaki et al.[8] report that reaction of α-[(anilino)methylene]-β-oxo-benzenepropanenitrile with hydrazine gives rise to 4-cyano-5-phenylpyrazole **(4a)** as the sole product. These two papers disagree however on the outcome of reaction of α-[(anilino)-methylene]-β-oxobenzenepropanenitrile with phenylhydrazine. Grothaus et al. report a product melting at 182°C which they claim to be 1,5-diphenylpyrazole-4-carbonitrile **(6a)**, on the grounds that hydrolysis yielded the known 1,5-diphenylpyrazole-4-carboxylic acid. Nishiwaki et al., however, obtained a product of identical melting point which they formulate as the 5-amino-4-benzoyl-1-phenylpyrazole **(5a)** on the basis of IR and mass spectroscopic data. In this paper we report the reaction of variously substituted β-oxobenzenepropanenitrile enamines **2a–j** with hydrazine to afford not only the amino ketones **3**, analogous to those reported,[6] but also the 3-phenylpyrazole-4-carbonitriles **4**.[7,8] Additionally, we report the results of reaction of **2a–e,2g** and **2h** with phenylhydrazine to give both 5-amino-4-aroyl-1-phenylpyrazoles **5**[8] and 1,5-diarylpyrazole-4-carbonitriles **6**.[7]

The starting benzoylacetonitrile derivatives required for this work can be obtained by a number of methods including reaction of benzoate esters with acetonitrile under basic conditions,[9,10] by reaction of benzoyl halides with the dianion of cyanoacetic acid,[11] or by reaction of benzoic acids with cyanoacetic acid esters[12] followed by ester hydrolysis and decarboxylation. In this case we chose to obtain the required materials using a modification of the method of Wemple[13] involving reaction of the appropriate acid chloride with the anion of *tert*-butyl cyanoacetate, formed using sodium hydride in toluene. The *tert*-butyl cyanoesters thus formed were de-esterified and decarboxylated by heating in toluene in the presence of *p*-toluenesulfonic acid to give the required benzoylacetonitrile derivatives **1a–j** in high yield. Reaction of **1a–j** with dimethylformamide dimethyl acetal in toluene gave the expected enamines **2a–j** in yields of between 70 and 95% (Scheme 1). Reaction of the enamines **2** with hydrazine in methanol usually proceeded at room temperature in 2–18 hours. Yields and molar ratios reported are for purified products following column chromatography. An attempt was made to establish a HPLC assay to assess product ratios during the reaction but the almost complete absence of a UV chromophore for the pyrazole-nitrile products precluded any accurate attempt at quantitation.

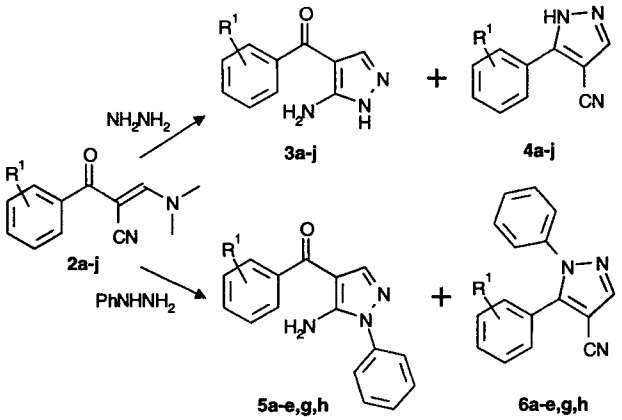


1-6	a	b	c	d	e
R^1	H	*p*-Cl	*p*-OMe	*p*-CF_3	*p*-NO_2
1-6	f	g	h	i	j
R^1	*m*-NO_2	*o*-Cl	*o*-OMe	*o*-NO_2	*o*-F

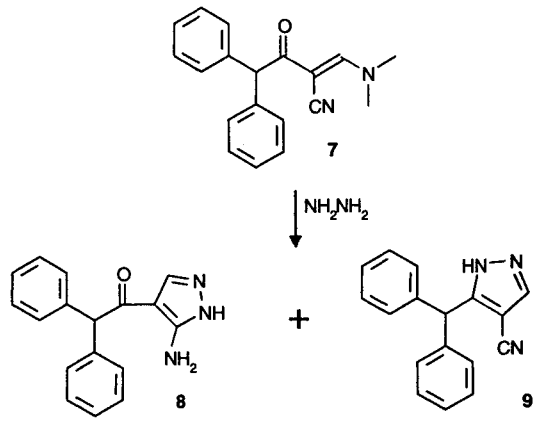
Scheme 1

Reaction of the unsubstituted derivative **2a** with hydrazine gave an 82% yield of the pyrazole-4-carbonitrile product **4a** with 18% of the amino ketone derivative **3a**, representing a quantitative recovery based on the enamine (Scheme 2). The range of substituents shown in Table 1 were chosen to test whether the outcome of the reaction was under electronic control based on the reactivity of the ketone, or steric control from the aromatic ring. As can be seen from Table 1 there is no significant effect based on the nature of a *para*-substituent in the aromatic ring of the starting enamines **2a–e**, the predominant products being the pyrazole-nitrile derivatives

4a–e. A nitro substituent in the *meta*-position also gives rise mainly to the pyrazole nitrile **4f**. Sterically demanding substituents such as chloro or nitro in the *ortho*-position entirely reverse the observed product ratio giving predominantly the amino ketone derivatives **3g** and **3i**. The *ortho*-methoxy derivative **2h**, however, gives almost exclusively the pyrazole nitrile **4h**, albeit only after a reaction time of 48 h. Thus the electron releasing *ortho*-methoxy substituent slows the reaction down but is not sufficiently sterically demanding to affect the course of the reaction. The sterically undemanding and electron withdrawing *ortho*-fluoro substituent in enamine **2j** gives mainly the pyrazole nitrile derivative **4j** (Scheme 2). This is in keeping with a mechanism in which the hydrazine reacts first with the enamine function and then closes preferentially to the ketone in the absence of a pronounced steric effect. Closure to the nitrile is, however, permitted in the presence of pronounced steric hindrance from an *ortho*-substituent. In order to further test this hypothesis the sterically crowded diphenylmethyl derivative **7** was made and its reaction with hydrazine studied both at room temperature and at reflux in methanol. At room temperature the major product of the reaction was the pyrazole amino ketone **8** but at reflux a 1:2 ratio of **8** and **9** was obtained (Scheme 3). This suggests that at the higher temperature the steric hindrance of the diphenylmethyl group was being overcome to allow reaction with the ketone.



Scheme 2



Scheme 3

Reaction of **2a–e,2g** and **2h** with phenylhydrazine in methanol usually took 18 hours at reflux to go to completion. Both phenylhydrazine free base and hydrochloride salt were used without appreciable difference in rate of reaction or product ratio. Table 1 shows the yields and product ratios for a range of enamines with phenylhydrazine. Yields in general remained high but did drop off somewhat with *ortho*-substituents. The unsubstituted enamine **2a** gave, in this case, a 56% yield of pyrazole nitrile **5a** and a 34% yield of the amino ketone **6a** (Scheme 2). This result is consistent with the more nucleophilic primary amino end of the hydrazine reacting first with the enamine function followed by closure of the phenyl substituted terminus. The extra steric crowding occasioned by the close proximity of the two aromatic rings in the final product accounts for the lower regioselectivity observed in these cases compared with the hydrazine reactions. The presence of an *ortho*-substituent in this case invariably reversed the observed product ratio in favour of the pyrazole amino ketones **6**.

Table 1. Yields and Molar Ratios of Products for Reactions of **2a–j**

Starting	Hydrazine		Phenylhydrazine	
Enamine	Yield (%) of **3** + **4**[a]	Ratio of **3**:**4**[d]	Yield (%) of **5** + **6**[a]	Ratio of **5**:**6**
2a	100	18:82	98	37:63
2b	96	11:89	87	15:85
2c	100	12:88	65	22:78
2d	94	11:89	82	22:78
2e	81	19:81	54	8:92
2f	99	15:85	–	–
2g	89	82:18	55	95:5
2h	87	5:95	55	72:28
2i	82	95:5	–	–
2j	85	6:94	–	–
7[b]	73	89:11	–	–
7[c]	97	37:63	–	–

[a] Based on isolated products after chromatography.
[b] Reaction carried out at room temperature.
[c] Reaction carried out at reflux.
[d] For entry **7** ratio is for **8**:**9**.

It seems likely from the identical melting points obtained by Grothaus et al.[7] and by Nishiwaki et al.,[8] and the similarity of this figure to our recorded melting point for **5a**, that both the earlier workers obtained a material which was predominantly **5a** but which contained some **6a**. The 1,5-diphenylpyrazole-4-carboxylic acid obtained by Grothaus following hydrolysis presumably arose from this contaminant.

The products were characterised on the basis of their IR, ^{1}H NMR, MS data and elemental analyses. Physical properties and spectral data are listed in Tables 2 and 3. The amino ketone products **3,5** and **8** exhibited a characteristic resonance in the ^{1}H NMR spectrum between $\delta = 7.19$ and 7.83 for the pyrazole 3-proton. For the pyrazole nitrile derivatives **4,6** and **9** this resonance was

Table 2. Physical Data for Amino Ketone Derivatives **3**, **8** and **5**

Product[a]	mp (°C) found (solvent)	mp (°C) reported	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	MS (200 eV) m/z ($M+H^+$)
3a	178–180 (EtOAc)	177–179[6]	3406, 3381, 1616	7.62 (s, 1 H, pyrazole H-3), 7.43–7.57 (m, 3 H_{arom}, H-4, 5), 7.76 (d, 2 H_{arom}, H-2, 6, J = 8.6)	188
3b	231–233 (EtOAc)	235–237[6]	3411, 3311, 1608	7.46 (d, 2 H_{arom}, H-3, 5, J = 8.6), 7.61 (s, 1 H, pyrazole H-3), 7.73 (d, 2 H_{arom}, H-2, 6, J = 8.6)[b]	222
3c	176–178 (EtOH)	172–174[6]	3421, 3308, 1607	3.88 (s, 3 H, OCH_3), 6.98 (d, 2 H_{arom}, H-3, 5, J = 8.6), 7.65 (s, 1 H, pyrazole H-3), 7.77 (d, 2 H_{arom}, H-2, 6, J = 8.6)	218
3d	170–172 (EtOAc)	172–174[6]	3453, 3328, 1636	~ 6.1 (br s, 2 H, NH_2), 7.57 (s, 1 H, pyrazole H-3), 7.73 (d, 2 H_{arom}, H-3, 5, J = 8.6), 7.88 (d, 2 H_{arom}, H-2, 6, J = 8.6)	256
3e	> 250 (EtOH)	–	3446, 3322, 1624	~ 6.1 (br s, 2 H, NH_2), 7.56 (s, 1 H, pyrazole H-3), 7.94 (d, 2 H_{arom}, H-2, 6, J = 8.6), 8.36 (d, 2 H_{arom}, H-3, 5, J = 8.6)	233
3f	52–56 (Et_2O)	–	3401, 3331, 1637	6.74 (s, 2 H, NH_2), 7.65 (s, 1 H, pyrazole H-3), 7.76 (t, 1 H_{arom}, H-5, J = 8.6), 8.12 (d, 1 H_{arom}, H-6, J = 8.6), 8.38 (m, 2 H_{arom}, H-2, 4)	233
3g	58–60 (Et_2O)	glass[6]	3403, 3328, 1645	~ 6.0 (br s, 2 H, NH_2), 7.25–7.48 (m, 5 H_{arom}, H-4, 4 H_{arom} + pyrazole H-3)	222
3h	60–62 (Et_2O)	glass[6]	3437, 3344, 1639	3.82 (s, 3 H, OCH_3), 6.98–7.45 (m, 4 H_{arom}), 7.40 (s, 1 H, pyrazole H-3)	218
3i	190–192 (EtOAc)	–	3468, 3316, 1616	6.80 (br s, 2 H, NH_2), 7.19 (br s, pyrazole H-3), 7.64 (d, 1 H_{arom}, H-6), 7.74 (t, 1 H_{arom}, H-5), 7.83 (t, 1 H, H-4), 8.09 (d, 1 H, H-3)[c]	233
3j	glass	–	3410, 3315, 1635	5.72 (br s, 2 H, NH_2), 7.05–7.55 (m, 5 H, 4 H_{arom} + pyrazole H-3)	206
8	137–139 (EtOAc)	–	3469, 3359, 1653	5.53 (br s, 2 H, NH_2), 7.54 (s, 1 H, pyrazole H-3), 7.17–7.36 (m, 10 H_{arom})	278
5a	188–190 (EtOH)	182[8]	3410, 3283, 1619	6.10 (s, 2 H, NH_2), 7.78 (s, 1 H, pyrazole H-3), 7.40–7.60 ((m, 8 H_{arom}, C_6H_5 + H-3, 4, 5), 7.83 (d, 2 H_{arom}, H-2, 6)	264
5b	228–230 (EtOAc)	215–217[8]	3445, 3321, 1605	6.10 (s, 2 H, NH_2), 7.52 (m, 1 H_{arom}, C_6H_5), 7.53 (d, 2 H H_{arom}, H-3, 5, J = 8.6), 7.59 (m, 4 H_{arom}, C_6H_5), 7.75 (s, 1 H, pyrazole H-3), 7.79 (d, 2 H_{arom}, H-2, 6, J = 8.6)	298
5c	172–174 (EtOAc)	166–168[8]	3450, 3375, 1609	3.88 (s, 3 H, OCH_3), 6.09 (s, 2 H, NH_2), 7.01 (d, 2 H_{arom}, H-3, 5, J = 8.6), 7.40–7.60 (m, 5 H, C_6H_5), 7.83 (s, 1 H, pyrazole H-3), 7.86 (d, 2 H_{arom}, H-2, 6, J = 8.6)	294
5d	210–212 (EtOAc)	–	3462, 3359, 1616	6.13 (s, 2 H, NH_2), 7.48–7.62 (m, 5 H, C_6H_5), 7.74 (s, 1 H, pyrazole H-3), 7.80 (d, 2 H_{arom}, H-3, 5, J = 8.6), 7.95 (d, 2 H_{arom}, H-2, 6, J = 8.6)	332
5e	245–247 (EtOAc)	–	3450, 3321, 1617	6.17 (s, 2 H, NH_2), 7.48–7.62 (m, 5 H, C_6H_5), 7.72 (s, 1 H, pyrazole H-3), 7.97 (d, 2 H_{arom}, H-2, 6, J = 8.6), 8.38 (d, 2 H_{arom}, H-3, 5, J = 8.6)	309
5g	192–194 (EtOAc)	–	3435, 3333, 1627	6.08 (s, 2 H, NH_2), 7.33–7.60 (m, 10 H, 9 H_{arom} + pyrazole H-3)	294
5h	198–200 (EtOH)	–	3427, 3266, 1625	3.86 (s, 3 H, OCH_3), 6.09 (s, 2 H, NH_2), 7.01 (dd, 1 H_{arom}, H-3 or 5), 7.06 (dd, 1 H_{arom}, H-3 or 5), 7.54 (s, 1 H, pyrazole H-3), 7.40–7.60 (m, 7 H, C_6H_5, 2 H_{arom}, H-4, 6)	294

[a] Satisfactory microanalyses obtained for all new compounds: C ± 0.41, H ± 0.33, N ± 0.32.
[b] Recorded in CD_3OD.
[c] Recorded in DMSO-d_6.

between δ = 7.88 and 8.80. The IR spectra were particularly useful, demonstrating appropriate NH stretching frequencies for the unsubstituted pyrazole derivatives **3,4,8** and **9**, and NH_2 stretching frequencies for the amino ketones **3,5** and **8** (see Tables 2 and 3). Compounds of structures **3,5** and **8** also exhibited carbonyl stretching frequencies in the range ν = 1605–1653 cm^{-1}. The pyrazole nitrile derivatives **4,6** and **9** had strong nitrile bands in the range ν = 2229–2250 cm^{-1}.

In order to increase further the scope of this reaction we attempted the condensation of **2a** with hydroxylamine hydrochloride in the hopes of preparing the analogous isoxazole amino ketone or nitrile. Grothaus and Dains[7] obtained a product melting at 154 °C from the reaction of α-[(anilino)methylene]-β-oxobenzenepropanenitrile with hydroxylamine hydrochloride in pyridine, which they claim was probably 4-benzoyl-5-iminoisoxazole on the grounds that it was unreactive under a number of reaction conditions. Instead of any of the expected products, we obtained a single polar material in high yield which, from its spectroscopic data, was characterised as the enol form of the previously unreported 2-cyano-3-oxo-3-phenylpropanamide (**10**). Formation of **10** can be

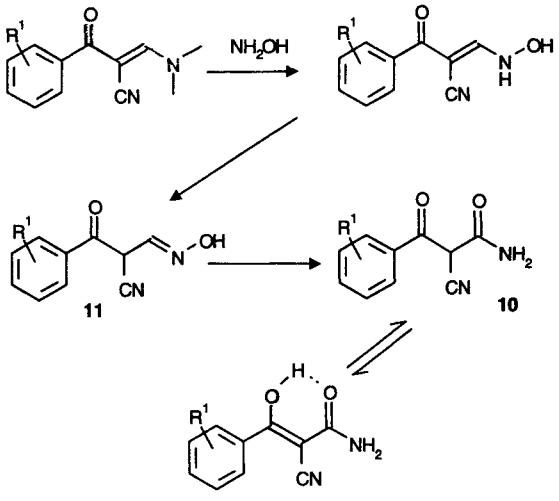
Table 3. Physical Data for Pyrazole Nitrile Derivatives **4**, **9** and **6**

Product[a]	mp (°C) (solvent)	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	MS (200 eV) m/z $(M+H)^+$
4a	136–138 (EtOAc)	3113, 2234	7.53–7.86 (m, 5H, C_6H_5), 8.03 (s, 1H, pyrazole H-3)	169 (M^+)
4b	208–210 (hexane)	3156, 2238	7.43 (d, 2H_{arom}, H-3, 5, J = 8.6), 7.84 (d, 2H_{arom}, H-2, 6, J = 8.6), 8.01 (s, 1H, pyrazole H-3)	203 (M^+)
4c	150–152 (hexane)	3131, 2232	3.88 (s, 3H, OCH_3), 7.03 (d, 2H_{arom}, H-3, 5, J = 8.6), 7.80 (d, 2H_{arom}, H-2, 6, J = 8.6), 7.97 (s, 1H, pyrazole H-3)	200
4d	146–148 (Et_2O)	3172, 2237	7.74 (d, 2H_{arom}, H-2, 6, J = 8.6), 8.01 (s, 1H, pyrazole H-3), 8.12 (d, 2H, H-3, 5, J = 8.6), ~13.5 (brs, 1H, pyrazole NH)	237 (M^+)
4e	240–242 (EtOAc)	3135, 2232	8.10 (s, 1H, pyrazole H-3), 8.17 (d, 2H_{arom}, H-2, 6, J = 8.6), 8.36 (d, 2H_{arom}, H-3, 5, J = 8.6)	214 (M^+)
4f	180–182 (EtOAc)	3347, 2243	6.87 (t, 1H_{arom}, H-5, J = 8.6), 8.34 (d, 2H_{arom}, H-4, 6, J = 8.6), 8.69 (t, 1H_{arom}, H-2, J = 8.6), 8.80, (s, 1H, pyrazole H-3), 14.16 (s, 1H, pyrazole NH)	214 (M^+)
4g	138–140 (Et_2O)	3229, 2250	7.47–7.66 (m, 4H_{arom}), 8.02 (s, 1H, pyrazole H-3)	204
4h	158–160 (Et_2O)	3359, 2232	4.04 (s, 3H, OCH_3), 7.09 (dd, 1H_{arom}, H-3, J = 8.6), 7.17 (dt, 1H_{arom}, H-5), 7.48 (dt, 1H_{arom}, H-4), 7.93 (s, 1H, pyrazole H-3), 8.04 (dd, 1H_{arom}, H-6, J = 8.6)	200
4i	150–152 (EtOAc)	3279, 2232	7.87–7.88 (m, 3H_{arom}, H-4, 5, 6), 8.08 (d, 1H_{arom}, H-3, J = 8.6), 8.77 (1H, pyrazole H-3), 14.04 (s, 1H, pyrazole NH)[b]	215
4j	128–130 (EtOAc)	3166, 2237	7.28 (d, 1H, H-3), 7.33 (t, 1H_{arom}, H-4 or H-5), 7.48 (t, 1H_{arom}, H-4 or H-5, J = 8.6), (s, 1H, pyrazole H-3), 8.06 (d, 1H_{arom}, H-6, J = 8.6)	187 (M^+)
9	220–222 (EtOAc)	3230, 2238	7.16–7.38 (m, 10H_{arom}), 7.88 (s, 1H, pyrazole H-3)	259 (M^+)
6a	102–104 (EtOH)	2229	7.23–7.48 (m, 10H_{arom}), 8.05 (s, 1H, pyrazole H-3)	246
6b	oil	2232	7.24 (m, 4H_{arom}, H-2, 3, 5, 6), 7.39 (m, 5H_{arom}), 8.02 (s, 1H, pyrazole H-3)	280
6c	110–112 (EtOAc)	2236	3.84 (s, 3H, OCH_3), 6.91 (d, 2H_{arom}, H-3, 5), 7.26 (d, 2H_{arom}, H-2, 6, J = 8.6), 7.28–7.39 (m, 5H, C_6H_5), 8.00 (s, 1H, pyrazole H-3)	276
6d	106–108 (EtOAc)	2233	7.27–7.42 (m, 5H, C_6H_5), 7.48 (d, 2H_{arom}, H-3, 5, J = 8.6), 7.68 (d, 2H_{arom}, H-2, 6, J = 8.6), 8.07 (s, 1H, pyrazole H-3)	314
6e	146–148 (EtOH)	2233	7.25–7.48 (m, 5H, C_6H_5), 7.55 (d, 2H_{arom}m H-2, 6, J = 8.6), 8.10 (s, 1H, pyrazole H-3), 8.28 (d, 2H_{arom}, H-3, 5, J = 8.6)	291
6g	98–100 (EtOH)	2234	7.25–7.44 (m, 9H_{arom}, 8.06 (s, 1H, pyrazole H-3)	280
6h	108–110 (Et_2O)	2234	3.49 (s, 3H, OCH_3), 6.88 (d, 1H_{arom}, H-3, J = 8.6), 7.02 (t, 1H_{arom}, H-5, J = 8.6), 7.22–7.36 (m, 6H, C_6H_5, 1H_{arom}, H-6), 7.43 (dt, 1H_{arom}, H-4, J = 8.6), 8.03 (s, 1H, pyrazole H-3)	276

[a] Satisfactory microanalyses obtained for all new compounds: C ± 0.40, H ± 0.39, N ± 0.31.
[b] Recorded in CD_3OD.
[c] HRMS: m/z calc. for $C_{16}H_{11}ClN_3$ 280.06415, observed 280.06443.

explained by initial reaction of hydroxylamine at the enamine centre as expected followed by tautomerisation to the aldehyde oxime intermediate **11**. Rearrangement of this intermediate under the acidic reaction conditions leads to the observed product **10** (Scheme 4). When the reaction was run in pyridine at room temperature to remove any effect of supplying the hydroxylamine as its hydrochloride salt the only isolable product remained compound **10**, albeit in a much lower yield (30%). The closeness of our melting point to that reported by Grothaus and Dains suggests that their material may also have been **10**.

Melting points were determined using a Kofler hot-stage and are uncorrected. The ^1H NMR spectra were recorded on a Bruker AM300 spectrometer in $CDCl_3$ using TMS as reference. IR spectra were recorded on a Bruker IFS 48 spectrometer. Mass spectra were recorded on a VG 7070E double focusing spectrometer using chemical ionisation with NH_3 at 200eV. Column chromatography was carried out using Sorbsil C60 40/60H flash silica. Reactions were



Scheme 4

followed by TLC (silica gel 60F-254, Merck) using 50% EtOAc/hexane).

Benzoylacetonitrile Derivatives 1; General Procedure:
A solution of *tert*-butyl cyanoacetate (28.2 g, 0.2 mol) in anhyd toluene (20 mL) was added to a suspension of NaH (50% dispersion in oil, 4.8 g, 0.1 mol) in anhyd toluene (250 mL) under a N_2 atmosphere, keeping the temperature below 20°C by means of an ice-water bath. The mixture was stirred until gas evolution ceased. The appropriate benzoyl chloride (0.1 mol) in anhyd toluene (10 mL) was added and the reaction stirred overnight. Water (250 mL) was added and the solvent layer separated, washed with water and the combined aqueous layers washed with Et_2O. After acidification with 2 M HCl the product was extracted into Et_2O, washed with water, dried and evaporated to dryness under reduced pressure to give the intermediate *tert*-butyl cyanoester in essentially quantitative yield. This material was dissolved in anhyd toluene (200 mL) containing a small amount of TsOH and heated at reflux for 18 h. The solvent was evaporated under reduced pressure to give the benzoylacetonitrile. Yields ranged from 70–100%.

α-[(Dimethylamino)methylene]-β-oxobenzenepropanenitriles 2; General Procedure:
A solution of benzoylacetonitrile (0.1 mol) and DMF dimethyl acetal (13.2 g, 0.11mol) in anhyd toluene (100 mL) was stirred for 18 h at r.t. The solvent was evaporated under reduced pressure and the product chromatographed using CH_2Cl_2. Fractions containing product were collected and evaporated to low volume, addition of hexane causing crystallisation of the product, which was collected by filtration. Yields ranged from 70–95%.

Reaction of 2a–j with Hydrazine; General Procedure:
The appropriate nitrile **2** (1 mmol) in MeOH (10 mL) was treated with $H_2NNH_2 \cdot H_2O$ (0.1 g, 2 mmol) and the mixture stirred for 18 h. The solvent was evaporated under reduced pressure and the resulting product chromatographed using 50% EtOAc/hexane to give first 3-phenylpyrazole-4-carbonitrile **4** and secondly 5-amino-4-aroylpyrazoles **3**. (Tables 2 and 3).

Reaction of 2a–e, 2g and 2h with Phenylhydrazine; General Procedure:
The appropriate nitrile **2** (1 mmol) in MeOH (10 mL) was treated with $PhNHNH_2$ (0.12 g, 1.1 mmol) and the mixture refluxed for 18 h. The solvent was evaporated under reduced pressure and the resulting product chromatographed using 50% EtOAc/hexane to give first 1,5-diarylpyrazole-4-carbonitrile **6** and secondly 5-amino-4-aroyl-1-phenylpyrazole **5** (Tables 2 and 3).

Reaction of 2a with Hydroxylamine Hydrochloride; 2-Cyano-3-oxo-3-phenylpropanamide (10):
Method A: The enamine **2a** (0.2 g, 1 mmol) and $NH_2OH \cdot HCl$ (0.07 g, 1 mmol) in MeOH (10 mL) was refluxed for 24 h. The solvent was evaporated under reduced pressure and the product chromatographed by elution with 5% EtOAc/CH_2Cl_2, crystallisation from EtOAc gave 166 mg (88%) of **10**, mp 152–154°C.

$C_{10}H_8N_2O_2$	calc.	C 63.82	H 4.28	N 14.89
(188.2)	found	63.59	4.52	14.61

IR (KBr): ν = 3435, 3505, 2219, 1653, 1606, 1593 cm^{-1}.

MS: m/z = 206 ($[M + NH_4]^+$), 189 ($[M + H]^+$), 163, 105.

^1H NMR ($CDCl_3$): δ = 5.64, 6.23 (2 s 2H, NH_2), 7.52 (t, 2H, J = 8.6 Hz, Ph H), 7.60 (m, 1H, Ph H), 7.99 (d, 2H, J = 8.6 Hz, Ph H), 16.52 (s, 1H, enol OH).

Method B: The enamine **2a** (0.2 g, 1 mmol) and $NH_2OH \cdot HCl$ (0.07 g, 1 mmol) in pyridine (10 mL) was stirred at r.t. for 24 h. The mixture was diluted with water, extracted with EtOAc, washed with water, dried and evaporated under reduced pressure. Chromatography using 5% EtOAc/CH_2Cl_2 and crystallisation from EtOAc gave 63 mg (30%) of **10** identical to that obtained from Method A.

The authors would like to thank Dr. A. Geeson for the mass-spectroscopic data and Dr. W. Prowse for the NMR Data.

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