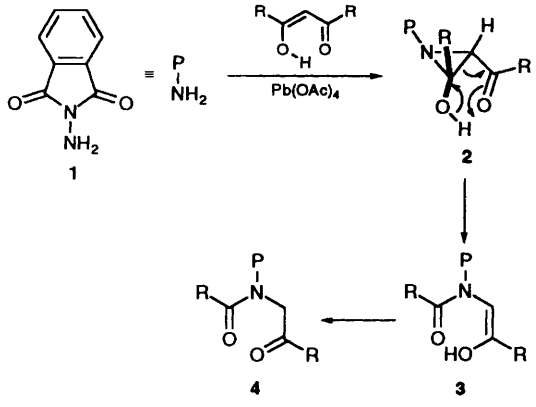
Reaction of 3-(Acetoxyamino)quinazolin-4(3*H*)-ones with Enolic β-Diketones: the N–N Bond as a Chiral Axis in *N*-(3,4-dihydro-4-oxoquinazolin-3-yl)-*N*-acyl-α-aminoketones; Reductive and Base-catalysed Cleavage of the N–N Bond in *N*-Acetyl-*N*-(3,4-dihydro-4-oxoquinazolin-3-yl)-α-amino Acid Esters

Robert S. Atkinson,[a] Paul J. Edwards[a] and Gordon A. Thomson[b]
[a] *Department of Chemistry, Leicester University, Leicester LE1 7RH, UK*
[b] *Zeneca Specialties, PO Box 42, Hexagon House, Blackley, Manchester M9 3DA, UK*

Following the method of Foucaud and coworkers, reaction of pentane-2,4-dione with 3-(acetoxyamino)quinazolin-4-one **8** gave the keto amide **9** (15%). 3-Methylpentane-2,4-dione reacts with compound **8** to give a relatively stable enol **11** (66%) which can be isolated in a crystalline form. Rotation around the N–N bonds in both compounds **9** and **11** is believed to be slow on the real time-scale and hence the N–N bonds can be considered as a chiral axes. As a result, protonation of the enol double bond in compound **11** and the creation of an additional chiral centre, gives rise to the separable keto amides **14** and **15**; this protonation can be accomplished completely diastereoselectively. Lead tetraacetate acetoxylation of compound **11** to give compound **19** is also completely diastereoselective. Brief heating of the enol effects the elimination of the quinazolinone and the formation of the *N*-acetylimine **16** *via* an 8-membered transition state. Base-catalysed elimination of the quinazolinone ring from compound **22** is surprisingly easy: reductive cleavage of this N–N bond in compound **22** is facile by comparison with the 3-(alkylamino)quinazolin-4-ones.

In 1977, Foucaud and coworkers reported[1] that the oxidation of *N*-aminophthalimide **1** with lead tetraacetate (LTA) in the presence of 1,3-diketones gave rise to *N*-acyl-*N*-phthalimido-α-amino ketones **4** (Scheme 1).

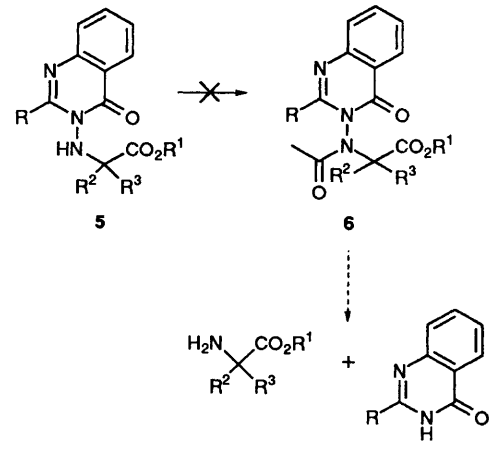


Scheme 1

As indicated in Scheme 1, the reaction was assumed to occur *via* the aziridination of the enolic form of the β-diketone followed by an unusual C–C bond cleavage of the intermediate aziridine **2** followed by the keto amide **4** formation *via* the enol **3**. Although the aziridinating species in Scheme 1 was presumed at the time to be a *N*-nitrene, it is most likely that it is *N*-(acetoxyamino)phthalimide in the light of subsequent work.[2]

Our interest in this work of Foucaud arose initially from the need to bring about N–N bond cleavage in compounds of type **5** (Scheme 2).[3]

Some work of Mellor and Smith[4] suggested that cleavage of the N–N bond in compounds similar to compound **5** would be facilitated by the acylation of the exocyclic nitrogen to give compound **6**. However, all our attempts to acylate this nitrogen by direct means were unsuccessful. It appeared that an alternative route to compounds resembling the amide ester **6**, whose susceptibility to reductive N–N bond cleavage could then be tested, was by the aziridination of the enolic form of a β-keto

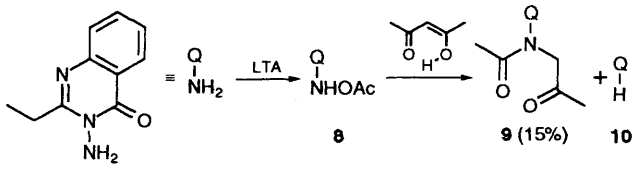


Scheme 2

ester using, for example, 3-(acetoxyamino)-2-ethylquinazolin-4-one **8**[2,5] (Scheme 3) in an analogous manner to the reaction described by Foucaud and coworkers in Scheme 1. The aziridination of β-diketones was initially studied since this class of compounds contain a greater proportion of the enol tautomer than do the β-keto esters.

Reaction of pentane-2,4-dione with *N*-(acetoxyamino)-2-ethylquinazolin-4-one **8**, prepared in solution in CH_2Cl_2 at −20 °C by oxidation of compound **7** with LTA, gave the keto amide **9** (15%) which was analogous to that isolated by Foucaud and coworkers (Scheme 3).[6] The major product was the 3*H*-quinazolin-4-one **10**, the product usually recovered from the aziridination of unreactive alkenes using compound **8**.[2]

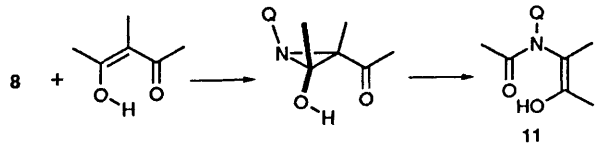
A striking feature of the NMR spectrum of the keto amide **9** was the degree of non-equivalence of the two protons in the methylene group adjacent to the ketone carbonyl (δ_H 3.76 and 4.98, 2 × d, *J* 17.3 Hz). The chiral element which gives rise to the non-equivalence of the protons in this methylene group (and in that of the quinazolin-4-one 2-ethyl group) is the N–N chiral axis. It is known that the barrier to rotation around the N–N bond is > 70 kJ mol^{-1} when both nitrogens are acylated.[7]



Scheme 3

The keto amide **9** also contains several minor peaks in its NMR spectrum, including two doublets at δ 4.34 and 5.04 (J 18.7 Hz) which, from their resemblance to those above, are assigned to a minor amide rotamer (ratio major : minor 7.6 : 1). It should be noted that the N–N bonds in the analogous keto amides **4** prepared by Foucaud and coworkers are not chiral axes because of the C_2-symmetry of the phthalimide group.

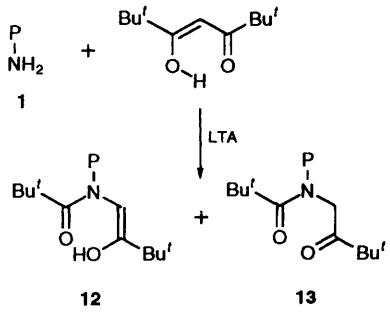
Although the yield of compound **9** was low, aziridination of 3-methylpentane-2,4-dione (in its enol form) with 3-(acetoxyamino)-2-ethylquinazolin-4-one **8** gave a crystalline product in 66% yield when the reaction mixture was worked up with a minimal base wash as soon as the reaction had reached ambient temperature. Spectroscopic data for this compound as well as its chemical properties (*vide infra*) show that it had the enol amide structure **11** (Scheme 4).



Scheme 4

Thus, compound **11** is the enol formed by the homo [1,5]-sigmatropic rearrangement and hence the double bond is assigned the Z-configuration. In the NMR spectrum, the OH is observed as a singlet at δ 9.80 (exchangeable in D_2O) and the methylene protons of the 2-ethyl substituent on the quinazolin-4-one are non-equivalent (δ 2.80, ABX_3 J_{AB} 16.8 and $J_{AX(BX)}$ 7.3 Hz), implying that the chiral N–N axis is still operative in this molecule.

Foucaud and coworkers[1] had previously reported that the oxidative addition of *N*-aminophthalimide to 2,2,6,6-tetramethylheptane-3,5-dione gave a mixture of the enol **12** and its tautomeric keto amide **13** (Scheme 5).



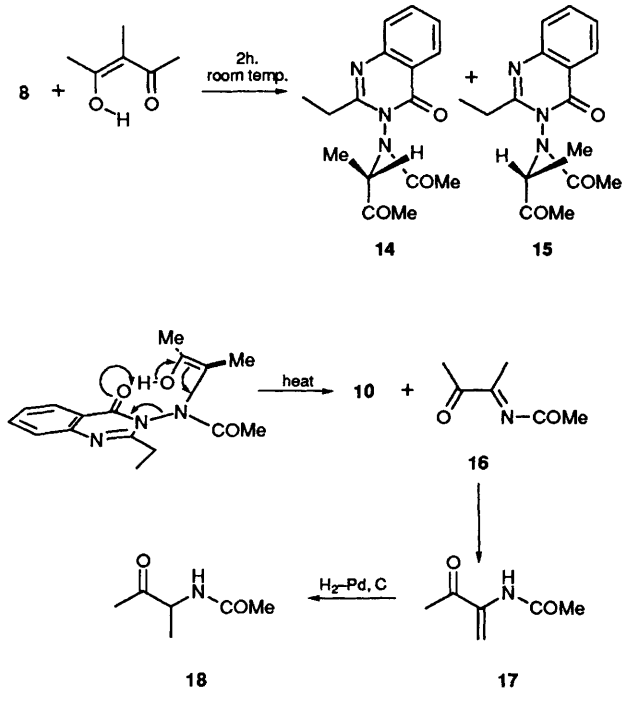
Scheme 5

We repeated the preparation of compounds **12** and **13** described by Foucaud and coworkers in order to obtain the (previously unreported) ^{13}C NMR spectrum of compound **12** and to compare it with that for compound **11**. The δ_C resonances of the enol double bond carbons (N–C=C–OH) in both compound **11** and compound **12** at δ 107.7 and 100.8 were in reasonable agreement. In neither compound was a δ_C resonance signal for a ketone carbonyl present, but both compounds gave the keto forms under mild conditions (see below) in which this signal was present at $\delta_C \sim 200$.

When the reaction mixture from compound **8** and 3-methylpentane-2,4-dione was set aside to stir for 2 h at room temperature before work up, a mixture of the keto amides **14** m.p. 162–163.5 °C and **15** m.p. 127–129 °C was obtained, which could be separated by fractional crystallisation. However, it was subsequently found that the enol amide **11** was converted quantitatively into only the keto amide **14** by boiling briefly in ethanol or by stirring in acetic acid overnight. Moreover, setting aside a solution of this keto amide **14** in acetonitrile for three days resulted in the epimerisation and the complete conversion to the keto amide **15**.

The relative configurations at the chiral centre and chiral axis in compound **14** and in compound **15** are as yet unknown, but it is clear that the barrier to rotation around their N–N bonds must be considerable: no interconversion between them occurred on briefly heating each to 200 °C, as judged from their NMR spectra compared to those obtained for the unheated products.

Thermolysis of the Enol Amide **11**.—Heating the enol amide **11** for 1 min in boiling ethyl acetate resulted in the quantitative conversion to the 2-ethylquinazolin-4-one **10** and the *N*-acetylimine **16**[8] (Scheme 6); compound **16** was purified by distillation and was isolated as an unstable oil.



Scheme 6

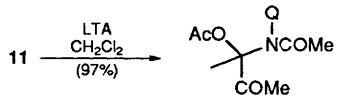
On treatment of compound **16** with reagents that were either acidic (allyltrimethylsilane, $BF_3 \cdot OEt_2$) or basic (ethyl acetoacetate, Et_3N), it was converted into the enamide **17**. This crystalline tautomer was also unstable and was therefore characterised by reduction with palladium–charcoal and hydrogen to give 3-acetamidobutan-2-one **18**, which was identical with an authentic sample.[9]

Interestingly, neither of the diastereoisomeric keto amides **14** or **15** were intermediates in the conversion of the enol amide **11** into the *N*-acetylimine **16** (and compound **10**), since both were recovered unchanged after heating in ethyl acetate. Accordingly, the reaction in Scheme 6 is assumed to proceed *via* the 8-membered transition state, as illustrated. Although this

transition state is *via* an unusual ring-size, the component atoms are contained in two planes and it is this conformational rigidity which lowers the entropy requirement for the elimination.

Asymmetric Induction Mediated by an N–N Chiral Axis.—The double bond of the enol amide **11** possesses diastereomeric faces by virtue of the chiral N–N axis. In the conversion of the enol amide to the keto amide **14** by briefly boiling in ethanol, the protonation occurs exclusively from only one diastereoisomeric face. It was of interest to examine the diastereoselectivity of the addition of other reagents to this enol double bond, *i.e.* to determine whether the N–N chiral axis could bring about asymmetric induction in other cases.

Oxidation of the enol amide **11** with LTA gave a crystalline product in over 90% yield, which was assigned structure **19**.

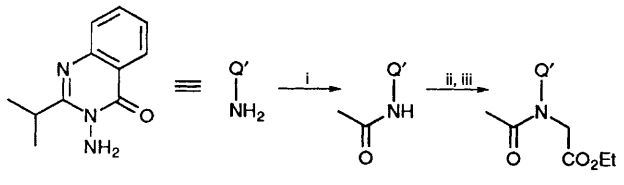


19

The presence of a chiral centre as well as a chiral N–N axis in compound **19** meant that it should be capable of existing as two diasteroisomers (*cf* compounds **14** and **15**). However, compound **19** appeared by NMR to be a single diastereoisomer with its four methyl resonances each appearing as singlets. Attempts at the thermal conversion of this single diastereoisomer, at least partially, into the other diastereoisomer were unsuccessful; at 200 °C, the compound partially decomposed, but none of the new resonances in the proton NMR spectrum of the crude mixture could be reasonably assigned to the other diastereoisomer.

N–N Bond Reduction in Ethyl N-*Acetyl*-N-(2-*isopropyl*-3,4-*dihydro*-4-*oxoquinazolin*-3-*yl*)-2-*aminoacetate* **22**.—As indicated earlier, our initial interest in the Foucaud reaction was as a means for preparing 3-[(*N*-acyl-*N*-alkyl)amino]quinazolin-4-one derivatives, to test whether the reductive cleavage was facilitated by the presence of the acyl group on the exocyclic nitrogen.

Attempts to apply the Foucaud reaction to acyclic β-ketoesters were unsuccessful, presumably because of the poor contribution of the enol tautomer. However, an alternative route to the synthesis of the ester **22** was pursued using the route shown in Scheme 7 [the 2-isopropyl-substituted quinazolin-4-one **20** ($Q'NH_2$) was used in these experiments].

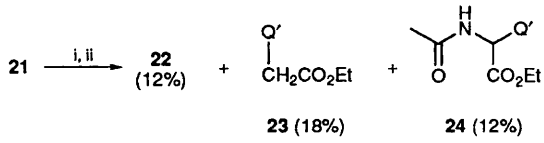


20 **21** **22**

Scheme 7 *Reagents:* i, Ac_2O; ii, NaH, DMF; iii, $BrCH_2CO_2Et$

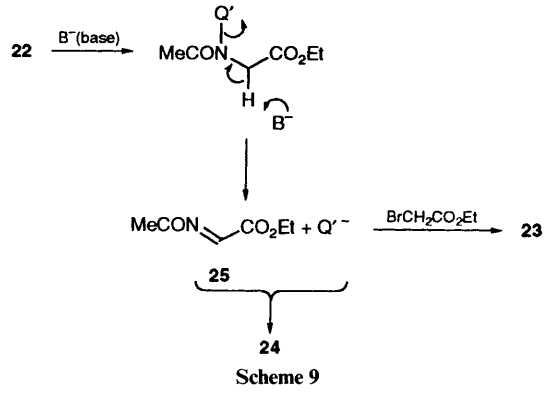
Our initial attempts to prepare the ester **22** by reaction of the sodium salt of compound **21** with ethyl bromoacetate, led to the mixture of compounds in the isolated yields shown in Scheme 8.

This mixture of products, we believe, arose from the initial product, the amide ester **22**, which lost the quinazolin-4-one anion following deprotonation adjacent to the ester (Scheme 9).



23 (18%) **24** (12%)

Scheme 8 *Reagents:* i, NaH, DMF; ii, $BrCH_2CO_2Et$



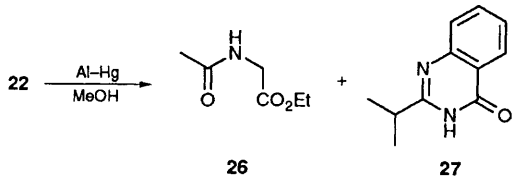
Scheme 9

The *N*-acetyl imine intermediate **25** (*cf* compound **16**) was re-attacked by the quinazolinone anion Q'^- to form the rearranged amide ester **24**. Alternatively, the quinazolinone anion could have been alkylated with the ethyl α-bromoacetate to give the ester, **23**.

When alkylation of the monoanion of the amide **21** was performed by adding this anion slowly to a solution of ethyl bromoacetate at −20 °C, the required amide ester **22** was isolated in 83% yield after chromatography. Under these conditions, there is little excess base present which would cause the elimination of the quinazolin-4-one anion, according to Scheme 9.

An aluminium amalgam reduction of the amide ester **22** furnished the ethyl *N*-acetylglycinate **26** in 74% yield, identical with an authentic sample.

Since N–N bonds in compounds similar to compound **5**, are not reduced under these conditions, acetylation of the exocyclic nitrogen does indeed facilitate the reductive cleavage of the N–N bond. However, we subsequently found that, using samarium diiodide, reduction of these type of compounds can be accomplished without the need for an acyl group on the exocyclic nitrogen.[10]

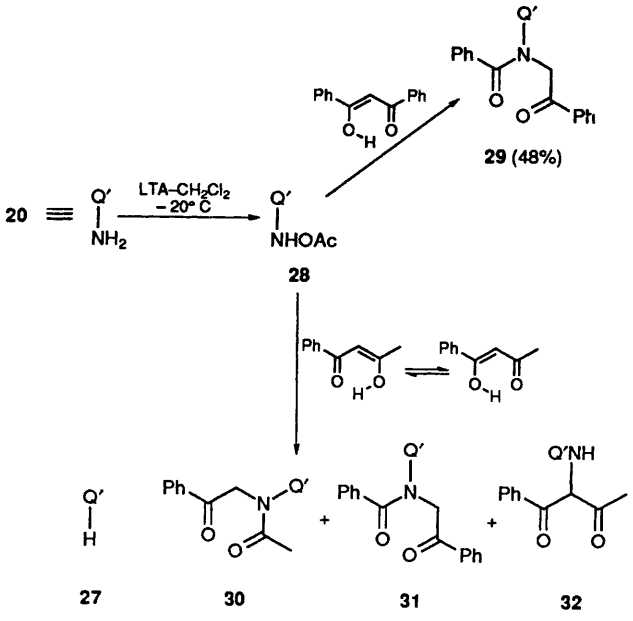


26 **27**

Aziridination of other Acyclic β-*Diketones.*—Two additional β-diketones, 1,3-diphenylpropane-1,3-dione and 1-phenylbutane-1,3-dione were also reacted with 3-(acetoxyamino)quinazolin-4-one **28** (Scheme 10). In neither case were the intermediate enol amides, which are analogous to compound **11**, ever isolated.

The keto amide **29** exists as a 1.2 : 1 ratio of amide rotamers on the NMR timescale: the diastereotopic methylene protons are separated by 1.82 ppm in the major rotamer, but by only 0.2 ppm in the minor rotamer (*vide infra*).

For 1-phenylbutane-1,3-dione (which exists as 91% in the enol form at 40 °C in $CDCl_3$,[11]), the interconversion between both tautomeric enol forms, can be assumed to be fast by comparison with the rate of aziridination. However, the phenyl-substituted enol would be expected to be the more nucleophilic



Scheme 10

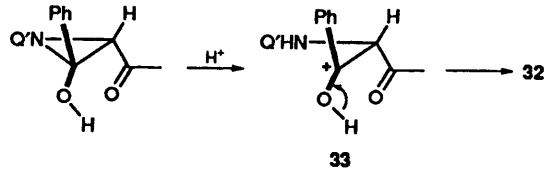
Table 1

Keto amide	δ CH_2, J (Hz) major rotamer	δ CH_2, J (Hz) minor rotamer	Ratio major : minor rotamer
9	3.76 and 4.98, J 17.3	4.34 and 5.04, J 18.7	7.6 : 1
29	4.29 and 6.11, J 17.5	5.22 and 5.42, J 19.3	1.2 : 1
31	3.83 and 5.15, J 17.2	4.54 and 4.82, J 19.6	1.6 : 1
30	4.15 and 5.88, J 17.4	4.90 and 5.67, J 19.4	5.8 : 1
22 (Ester amide)	3.59 and 4.98, J 16.9	4.14 and 4.87, J 18.7	3.55 : 1

and thus the more reactive towards aziridination. After chromatography of the crude reaction mixture, the keto amides **31** and **30** were obtained (75%) in a 3.3 : 1 ratio, as determined from integration of appropriate resonances in the NMR spectrum of the mixture. Pure samples of these keto amides **31** (m.p. 112–114 °C) and **30** (m.p. 115–117 °C) were obtained by fractional crystallisation. Structural assignments to these two isomers were supported by IR spectroscopy: compound **31** ν_{max}/cm^{-1} at 1732 and 1700 for the ketone and amide carbonyl groups whereas compound **30** has a single peak at ν_{max}/cm^{-1} 1685, presumably as a result of overlap of the benzoyl and amide carbonyl stretching frequencies. These assignments are supported by the chemical shifts of the ^{13}C carbonyl carbons, with the lowest field peak at δ 200.06 for the acetyl carbonyl in compound **31** compared with δ 191.51 for the benzoyl carbonyl in compound **30** for their respective major rotamers. Finally, the ratio of the amide rotamers is significantly more disparate in the *N*-acetyl isomer **30** than in the *N*-benzoyl isomer **31**, which is consistent with the corresponding ratios between compounds **9** and **29** (*vide infra*).

Two other products isolated from the reaction of 3-(acetoxyamino)quinazolin-4-one **28** with 1-phenylbutane-1,3-dione were 2-isopropylquinazolin-4-one **27** (9%) and the diketo amine **32** (13%) (Scheme 10). It is assumed that this latter product arises by C–N bond cleavage of the intermediate aziridine, mediated by the acetic acid present (Scheme 11).

Although compound **32** could also arise by an analogous



Scheme 11

ring-opening of the isomeric aziridine formed from the alternative enol tautomer, the greater stability of the incipient benzyl carbocation **33** leading to compound **32** makes it likely that this is the origin of the latter. If this is the case, then the ratio of the attack on the two enolic forms of 1-phenylbutane-1,3-dione could be as high as 4.2 : 1 in favour of the phenyl substituted one.

Stereostructures of the Keto Amides **9**, **29**, **30** *and* **31**.—The chemical shifts and coupling constants for the methylene (NCH_2) protons and amide rotamer ratios in the keto amides **9** and **29**–**31** are summarised in Table 1.

The following generalisations emerge from Table 1: (*a*) the difference in the chemical shifts for the diastereotopic protons of the methylene groups in the major rotamers are consistently larger than those in the minor rotamers, with a remarkable 1.82 ppm difference in the major diastereoisomer of compound **29**; (*b*) the coupling constants are always larger for the minor rotamer; and (*c*) the ratio of major : minor rotamers is significantly higher (~ 6–7 : 1) for the *N*-acetyl isomers **9** and **30** than for the *N*-benzoyl isomers **29** and **31**.

We interpret the gross difference in chemical shift between the protons of the methylene group in the major rotamers in Table 1 as evidence for a highly preferred conformation in each case, in which one proton is deshielded. At the present time, the identity of this preferred conformation is unknown, but is under investigation.

Experimental

For general experimental details see ref. 10. Unless otherwise indicated, ^1H NMR spectra were run in $CDCl_3$ at 300 MHz and ^{13}C NMR spectra in $CDCl_3$ at 75 MHz, with tetramethylsilane as the internal standard and *J* values given in Hz. Magnesium sulfate was used as the drying agent and 2,2,6,6-tetramethylheptane-3,5-dione and ethyl *N*-acetylglycinate were purchased from Aldrich and used without further purification. 3-Methylpentane-2,4-dione (Aldrich), was distilled under reduced pressure before use.

Reaction of 3-(*Acetoxyamino*)-2-*ethylquinazolin*-4(3H)-*one* **8** *with pentane*-2,4-*dione*.—A solution of compound **8** was obtained by the alternate addition of 3-amino-2-ethylquinazolin-4(3*H*)-one (1.3 g) and powdered lead tetraacetate (LTA) (2.54 g), in very small portions over 15 min, to a vigorously stirred solution of dry dichloromethane (10 cm^3) cooled to −20 to −25 °C. After stirring for an additional 5 min at this temperature, pentane-2,4-dione (1.64 g) was added and the solution allowed to warm to room temperature. The insoluble lead diacetate was separated by filtration, washed with dichloromethane and the combined organic solution washed with sodium hydrogen caerbonate solution followed by water and then dried, after which the solvent was removed under reduced pressure. Trituration of the solid–oil mixture obtained with cold diethyl ether gave 2-ethylquinazolin-4(3*H*)-one **10** (0.77 g, 75%) which was identical with an authentic sample. Chromatography of the diethyl ether-soluble fraction over silica with ethyl acetate as the eluent (R_f 0.55) gave the *keto amide* **9** (0.23 g; 15%) as colourless crystals; m.p. 116–118 °C

(from ethanol) (Found: C, 62.7; H, 6.0; N, 14.65. $C_{15}H_{17}N_3O_3$ requires C, 62.7; H, 5.95; N, 14.65%). This compound exists in $CDCl_3$ solution as a 7.6:1 ratio of amide rotamers: δ_H major rotamer 1.40 (t, *J* 7.3, CH_2*Me*), 1.90 (s, CH_2CO*Me*), 2.24 (s, NHCO*Me*), 3.05 (2 × dq, *J* 17.5 and 7.3, C*H*$_2$Me), 3.76 and 4.98 (2 × d, *J* 17.3, CH_2N), 7.48 (ddd, *J* 7.9, 7.0 and 1.3, Q 6-H), 7.67–7.83 (m, Q 7- and 8-H) and 8.20 (ddd, *J* 7.9, 1.5 and 0.4, Q 5-H); δ_C 10.43 (CH_2*Me*), 19.44 (CH_2CO*Me*), 26.27 (*C*H$_2$Me), 27.53 (NCO*Me*), 59.21 (N*C*H$_2$CO), 120.39, (Q *C*CO), 126.74, 126.82, 127.46 and 135.10 (4 × Q CH), 146.58 (Q *C*N=C), 158.21, 159.98 (Q C=N and Q C=O), 172.66 (N*C*OMe) and 200.35 (*C*OMe); δ_H minor rotamer (observable peaks) 1.31 (t, *J* 7.3, CH_2*Me*), 2.20 (s, CH_2CO*Me*), 2.22 (s, NCO*Me*), 2.95 (2 × dq, *J* 17.2 and 7.3, C*H*$_2$Me) and 4.34 and 5.04 (2 × d, *J* 18.7, CH_2N); δ_C 10.34 (CH_2*Me*) 20.41 (CH_2CO*Me*), 25.48 (*C*H$_2$Me), 27.03 (NCO*Me*), 61.44 (N*C*H$_2$CO), 126.13, 126.47, 127.22 and 134.52 (4 × Q CH) and 159.00 (Q C); ν_{max}/cm^{-1} 1738m, 1700s and 1603s.

Reaction of the N*-Amino Compound* **8** *with* 3*-methylpentane*-2,4*-dione*.—The procedure described above was followed using compound **8** (1.0 g), LTA (2.46 g) in dichloromethane (10 cm^3) followed by the addition of 3-methylpentane-2,4-dione (1.81 g). In the work up, the washing with sodium hydrogen carbonate solution (2 mol dm^{-3}) was limited (two or three brief shakings of the separating funnel). Trituration of the solid–oil mixture obtained with ice-cold diethyl ether gave a solid which crystallised from chloroform–light petroleum (minimum heating necessary) to give the *enol amide* **11** as a colourless solid (1.05 g, 66%); m.p. 114 °C (decomp.) (Found: C, 63.8; H, 6.35; N, 14.05. $C_{16}H_{19}N_3O_3$ requires C, 63.75; H, 6.35; N, 13.95%); δ_H 1.38 (t, *J* 7.3 CH_2*Me*), 1.83 (s, C=C*Me*), 1.91 (s, C=C*Me*), 2.30 (s, NCOMe), 2.80 (2 × dq, *J* 16.8 and 7.3, C*H*$_2$Me), 7.45 (ddd, *J* 8.1, 7.2 and 1.3, Q 6-H), 7.70 (dd, *J* 8.2 and 1.3, Q 8-H), 7.78 (ddd, *J* 8.2, 7.2 and 1.5, Q H-7), 8.23 (ddd, *J* 8.1, 1.5 and 0.5, Q 5-H) and 9.80 (s, OH, exch. D_2O); δ_C 10.76 (CH_2*Me*), 15.28 (C=C*Me*), 17.43 (C=C*Me*), 19.85 (NCO*Me*), 25.55 (*C*H$_2$Me), 107.65 (N*C*=C), 120.29 (Q *C*CO), 126.28, 127.00, 127.18 and 135.14 (4 × Q *C*H), 146.78 (Q *C*N=C), 152.27 (C=*C*–OH), 157.98, 162.35 (Q C=N and Q C=O) and 169.81 (NCO); ν_{max}/cm^{-1} 3181m, 1686m and 1661s.

Keto Amides **14** *and* **15**.—Repetition of the above experiment using compound **8** (0.46 g), LTA (1.21 g) and dichloromethane (5 cm^3) with the addition of 3-methylpentane-2,4-dione (1.19 g) gave, after allowing to stir for 2 h before work up, a solid–oil mixture which was triturated with ice-cold diethyl ether to give 2-ethylquinazolin-4-one **10** (211 mg, 46%). Removal of the diethyl ether and crystallisation of the residue twice from ethanol gave the *keto amide* **14** (84 mg, 12%); m.p. 162–163.5 °C (Found: C, 63.7; H, 6.35; N, 13.95. $C_{16}H_{19}N_3O_3$ requires C, 63.75; H, 6.35; N, 13.95%); δ_H 1.33 (d, *J* 7.2, NCH*Me*), 1.43 (t, *J* 7.3 CH_2*Me*), 1.94 (s, COMe), 2.39 (s, NCOMe), 2.80 (ABX$_3$, C*H*$_2$Me), 4.45 (q, *J* 7.2, NC*H*Me), 7.52 (ddd, *J* 8.4, 8.0 and 1.5, Q 6-H), 7.74 (d, *J* 7.4, Q 8-H), 7.83 (ddd, *J* 8.4, 7.4 and 1.3, Q 7-H) and 8.26 (dd, *J* 8.0 and 1.3, Q 5-H); δ_C 10.42 (CH_2*Me*), 13.60 (*Me*), 20.43 (*Me*), 26.24 (*C*H$_2$Me) 63.97 (NCH), 120.54 (Q *C*CO), 127.15, 127.17, 127.56 and 135.24 (4 × Q CH), 146.33 (Q *C*CN), 157.84, 160.72 (Q C=N and Q C=O), 171.57 (N*C*OMe) and 203.90 (CH*C*OMe); ν_{max}/cm^{-1} 1690s and 1606s; *m*/*z*(%) 258 (14, M$^+$ − 43), 216 (90), 174 (97) and 173 (100).

Further crystallisation from ethanol after removal of compound **14** gave *keto amide* **15** (76 mg, 10%); m.p. 127–129 °C (Found: C, 63.7; H, 6.45; N, 13.85. $C_{16}H_{19}N_3O_3$ requires C, 63.75; H, 6.35; N, 13.95%); δ_H 0.97 (d, *J* 7.4, NCH*Me*), 1.42 (t, *J* 7.3, CH_2*Me*), 1.89 (s, COMe), 2.38 (s, NCOMe), 3.20 (2 × dq, *J* 17.8 and 7.3, C*H*$_2$Me), 4.88 (q, *J* 7.4, NC*H*Me), 7.51 (ddd, *J* 8.0, 7.1 and 1.3, Q 6-H), 7.75 (dd, *J* 7.0 and 1.3, Q 8-H), 7.82 (ddd, *J* 8.0, 7.0 and 1.5, Q 7-H) and 8.25 (ddd, *J* 8.0, 1.5 and 0.4, Q 5-H); δ_C 10.55 (CH_2*Me*), 13.01 (Me), 20.25 (Me), 26.56 (*C*H$_2$Me), 27.52 (Me), 61.52 (CH), 120.11 (Q *C*CO), 127.11, 127.14, 127.73 and 135.44 (4 × Q CH) 146.99 (Q *C*N=C), 159.54 and 160.95 (Q C=N and Q C=O), 173.14 (N*C*OMe) and 204.74 (*C*OMe); ν_{max}/cm^{-1} 1699s and 1606m; *m*/*z*(%) 301 (M$^+$ 11), 258 (18), 216 (100), 174 (24) and 173 (18).

Conversion of the Enol **11** *into the Keto Amide* **14**.—The enol amide **11** (0.19 g) was dissolved in the minimum quantity of acetic acid (5 cm^3) without warming and stirred overnight at room temp. Removal of the acetic acid under reduced pressure and examination of the residue by NMR spectroscopy showed only the keto amide **14** present. The same quantitative conversion was effected when the enol amide (0.25 g) was dissolved in boiling ethanol (3 cm^3) and heated under reflux for approx. 1 min.

Conversion of the Keto Amide **14** *into the Diastereoisomer* **15**.—The keto amide **14** (0.05 g) was dissolved in acetonitrile (1 cm^3) and the solution set aside at ambient temperature for 3 days. Removal of the solvent and examination of the residue by NMR showed only the keto amide **15** was present.

Reaction of N*-Aminophthalimide with LTA in the presence of* 2,2,6,6*-Tetramethylheptane*-3,5*-dione*.—This reaction was carried out according to the procedure of Foucaud and coworkers[1] and the enol amide **12** was isolated (17%); m.p. 107–110 °C (from ethanol) (lit.,[1] m.p. 120 °C); δ_H 1.16 (s, CMe), 1.35 (s, NCOCMe_3), 5.80 (s, CH=), 7.78 and 7.87 (2 × dd, *J* 5.5 and 3.2, 4 × phthal H) and 8.06 (s, OH) lit.,[1] 1.15 (s, 9 H), 1.34 (s, 9 H) and 5.72 (s, 1 H); δ_C 27.05 (C*Me*$_3$), 27.28 (C*Me*$_3$), 34.65 (*C*Me$_3$), 39.09 (*C*Me$_3$), 100.82 (CHN), 124.11 (2 × phthal C), 129.94 (2 × phthal *C*C=O), 134.79 (2 × phthal C), 165.45 and 166.69 (C=O and C–OH) and 177.52 (C=O).

Thermolysis of the Enol Amide **11**.—The enol amide **11** (0.1 g) was heated under reflux for ~1 min in ethyl acetate (2 cm^3). Cooling the solution in ice–water and separation of the solid formed gave 2-ethylquinazolin-4-one **10** (0.05 g, 86%). The residue was evaporated under reduced pressure and then distilled b.p. 50 °C/0.1 mmHg (Kugelrohr, bath temp.) to give the *N*-acetylimine **16** (0.04 g, 95%) as an unstable oil; δ_H 1.95 (s, MeC=N), 2.12 (MeCO) and 2.27 (MeCO); δ_C 15.66 (*Me*C=N), 24.29 (Me), 24.44 (Me) 161.1 (C=N), 185.18 (Me*C*ON) and 198.55 (Me*C*O); ν_{max}/cm^{-1} 1706s, 1673s and 1650s.

Attempted Allylation of the N*-Acetylimine* **16**.—To a solution of the *N*-acetylimine **16** (0.147 g), prepared above, in dry THF (10 cm^3), was added allyltrimethylsilane (0.132 g) and boron trifluoride–diethyl ether (0.16 g). After stirring for 2 h, followed by standing overnight, the volatile solvents were removed under reduced pressure, the residue dissolved in ethyl acetate and this solution washed with sodium hydrogen carbonate solution and then water, dried and finally evaporated under reduced pressure. The residue was crystallised from ethyl acetate–light petroleum to give the unstable α,β*-unsaturated ketone* **17** as a colourless solid; m.p. 47–48 °C; δ_H(90 MHz) 2.13 (s, C=CCOMe), 2.41 (NCOMe), 5.75 (s, CH= *trans* to NH), 6.87 (s, CH= *cis* to NH), 7.70–8.52 (s, br NH). This compound was characterised in its reduced form, obtained when compound **17** (0.11 g), dissolved in dry ethanol (10 cm^3) containing palladium on charcoal (0.11 g), was hydrogenated for ~7 h. Removal of the catalyst followed by evaporation of the solvent and distillation of the residue [b.p. 150 °C/0.15 mmHg (Kugelrohr, bath temp.)] gave the 3-(acetamido)-butan-3-one **18** as a colourless oil (0.1 g, 89%), which was identical with an authentic sample prepared by the method of Wiley and Borum.[9]

Reaction of the Enol Amide **11** *with LTA*.—To a stirred solution of the enol amide **11** in dichloromethane (3 cm^3) was added LTA (0.75 g) continually, and in very small portions, over a period of 15 min. After addition, stirring was continued for a further 10 min before the lead diacetate was separated, washed with dichloromethane and the organic layer washed with sodium hydrogen carbonate solution, dried and evaporated under reduced pressure. Chromatography of the residual solid over silica with ethyl acetate–light petroleum as the eluent (R_f 0.71) gave the *α-acetoxy keto amide* **19** as a colourless solid (0.269 g, 97%); m.p. 149–149.5 °C (from ethanol) (Found: C, 60.1; H, 5.95; N, 11.65. $C_{18}H_{21}N_3O_5$ requires C, 60.15; H, 5.9; N, 11.7%); δ_H 1.41 (t, *J* 7.4, CH_2Me), 1.92 (s, Me), 1.94 (s, Me), 1.99 (s, MeCON), 2.58 ($MeCO_2$), 3.21 (2 × dq, *J* 17.5 and 7.4, CH_2Me), 7.52 (ddd, *J* 8.0, 7.2 and 1.2, Q 6-H), 7.76 (dd, *J* 8.1 and 0.6, Q 8-H), 7.84 (ddd, *J* 8.1, 7.2 and 1.1, Q 7-H) and 8.27 (dd, *J* 8.0 and 1.1, Q 5-H); δ_C 10.93 (CH_2Me), 20.35 (Me), 20.67 (Me), 20.78 (Me), 26.42 (CH_2Me), 26.99 ($MeCO_2$), 94.70 (AcO*C*N), 120.68 (Q *C*CO), 127.04, 127.29, 127.62 and 135.45 (4 × Q CH), 146.55 (Q *C*N=C), 160.31 and 161.11 (Q C=N and Q C=O), 167.48 (N*C*OMe), 171.41 (Me*C*OO) and 199.63 (*C*COMe); ν_{max}/cm^{-1} 1760s, 1725s, 1693s and 1609s.

3-*Amino-2-isopropylquinazolin-4-one* **20**.—To methyl anthranilate (255 g) was added isobutyric anhydride (267 g) and the stirred mixture heated at 100 °C for 2.5 h with the exclusion of moisture. After cooling, the mixture was dissolved in diethyl ether (600 cm^3), washed with sodium hydrogen carbonate solution (4 × 500 cm^3) and then with water. The organic layer was dried, evaporated under reduced pressure and the residue crystallised from light petroleum to give *methyl* N-(*isopropanoyl*)*anthranilate* (231 g, 78%) as a white solid; m.p. 51–52 °C (Found: C, 65.2; H, 6.85; N, 6.35. $C_{12}H_{15}NO_3$ requires C, 65.15; H, 6.85; N, 6.35%); δ_H 1.30 (d, *J* 6.9, Me_2CH), 2.62 (hept, *J* 6.9, Me_2CH), 3.91 (s, OMe), 7.04 (ddd, *J* 8.5, 7.4 and 1.2, ArH *p*- to CO_2Me), 7.51 (ddd, *J* 8.0, 7.4 and 1.4, ArH *p*- to N), 8.00 (dd, *J* 8.0 and 1.2, ArH *o*- to CO_2Me), 8.75 (dd, *J* 8.5 and 1.4, ArH *o*- to N) and 11.13 (s, br, NH); ν_{max}/cm^{-1} 3262w, 1682s and 1606m.

The amide above (231 g) and hydrazine hydrate (325 g) were heated under reflux in ethanol (650 cm^3) for 16 h under nitrogen. After standing overnight, the title 3-aminoquinazolinone **20** was separated. The ethanol filtrate was evaporated under reduced pressure, the residue dissolved in dichloromethane (500 cm^3), and the organic layer washed twice with water, dried and evaporated to yield more product **20**. Crystallisation of the combined solids from ethanol gave the *product* **20** (272 g, 92%); m.p. 101–102 °C (Found: C, 65.05; H, 6.5; N, 20.65. $C_{11}H_{13}N_3O$ requires C, 65.0; H, 6.45; N, 20.70%); δ_H 1.35 (d, *J* 6.8, Me_2CH), 3.72 (hept, *J* 6.8, Me_2CH), 4.93 (s, NH_2), 7.36 (dd, *J* 8.0 and 2.2 Q′ 6-H), 7.64 (m, Q′ 7-H and 8-H) and 8.14 (ddd, *J* 8.0, 1.5 and 0.7 Q′ 5-H); δ_C 20.35 (Me_2CH), 30.88 (Me_2CH), 119.73 (Q′ *C*CO), 125.85, 126.08, 127.17 and 133.77 (4 × Q′ CH), 146.90 (Q′ *C*NC) and 161.80 and 161.93 (Q′ C=N and Q′ C=O); ν_{max}/cm^{-1} 3304w, 3192m, 1666m and 1640s.

Acetylation of 3-*Amino-2-isopropylquinazolin-4-one* **20**.—3-Amino-2-isopropylquinazolinone **20** (20.82 g) was dissolved in acetic anhydride (100 cm^3) and stirred at room temp. for 48 h. The solution was poured into water (1 dm^3) and the solid obtained separated, dried and crystallised from chloroform–light petroleum to give 3-(*acetylamino*)-2-*isopropylquinazolin*-4-*one* as a hydrate **21** (16.6 g, 66%), m.p. 74–76 °C (Found: C, 59.05; H, 6.5; N, 15.9. $C_{13}H_{15}N_3O_2 \cdot H_2O$ requires C, 59.30; H, 6.5; N, 15.95%); δ_H([$^2H_6$]DMSO) 1.22 (2 × d, *J* 6.7, Me_2CH), 2.12 (s, NCOMe), 3.13 (hept, *J* 6.7, Me_2CH), 3.32 (s, br, H_2O of crystallisation), 7.53 (dd, *J* 8.0 and 1.0, Q′ 6-H), 7.67 (d, *J* 8.1, Q′ 8-H), 7.85 (ddd, *J* 8.1, 7.3 and 1.6, Q′ 7-H), 8.10 (dd, *J* 8.0 and 1.6, Q′ 5-H) and 10.95 (s, br, NH; D_2O exch.); ν_{max}/cm^{-1} 3420s, 3420br s, 3180m, 1700s and 1677s.

Alkylation of N-*Acetylamino-2-isopropylquinazolinone* **21** *with Ethyl α-Bromoacetate*.—To dry dimethylformamide (15 cm^3) was added sodium hydride (0.21 g) followed by the *N*-(acetylamino)-2-isopropylquinazolin-4-one **21** (1.14 g). The mixture was stirred at room temp. until effervescence ceased and then cooled to −20 °C. Ethyl α-bromoacetate (2.34 g) was added in one portion and the solution stirred at this temperature for 3 h, then allowed to warm to room temp. and then stirred overnight. Addition of dry diethyl ether and ethyl acetate (1 : 1) precipitated the bulk of the sodium bromide which was separated, washed with diethyl ether, and the combined filtrates evaporated under reduced pressure. Chromatography of the residue over silica, with ethyl acetate–light petroleum (1 : 1) as the eluent (R_f 0.68), gave the amide ester **22** as colourless crystals (0.2 g, 12%); m.p. 102–103 °C (from ethanol) (Found: C, 61.6; H, 6.4; N, 12.7. $C_{17}H_{21}N_3O_4$ requires C, 61.6; H, 6.4; N, 12.7%). This compound exists in $CDCl_3$ solution as a 3.55 : 1 ratio of amide rotamers: δ_H major rotamer: 1.31 (t, *J* 7.1, CH_2Me), 1.31 and 1.41 (2 × d, *J* 6.6, Me_2CH), 1.91 (s, NCOMe), 3.89 (hept, *J* 6.6, Me_2CH), 3.59 and 4.98 (2 × d, *J* 16.9, CH_2N), 4.26 (ABX_3, CH_2Me), 7.48 (ddd, *J* 8.0, 7.0 and 1.3, Q′ 6-H), 7.71 (dd, *J* 7.6 and 0.7, Q′ 8-H), 7.80 (ddd, *J* 7.6, 7.0 and 1.5, Q′ 7-H) and 8.23 (ddd, *J* 8.0, 1.5 and 0.7, Q′ 5-H); δ_C 14.09 and 19.83 (Me_2CH), 21.34 (CH_2Me), 22.22 (NCO*Me*), 29.94 (Me_2CH), 52.99 (NCH_2), 61.45 (OCH_2Me), 120.55 (Q′ *C*CO), 126.97, 127.03, 127.70 and 135.27 (4 × Q′ CH), 146.95 (Q′ *C*N=C), 160.31 and 162.45 (Q′ C=N and Q′ C=O), 167.35 (N*C*OMe) and 173.16 (CO_2Et); minor rotamer (observable peaks): 2.35 (s, NCOMe), 4.14 and 4.87 (2 × d, *J* 18.7, CH_2N), 7.41 (ddd, *J* 8.0, 7.0 and 1.3, Q′ 6-H), 7.65 (dd, *J* 7.6 and 0.7, Q′ 8-H), 8.18 (dd, *J* 8.0 and 0.7, Q′ 5-H); δ_C (observable peaks) 20.90 (*Me*CHMe); 21.50 (CH_2Me), 22.05 (NCO*Me*), 30.07 (Me_2CH), 54.23 (OCH_2Me) 62.03 (CH_2N), 126.27, 126.82, 127.42 and 134.70 (4 × Q′ CH) and 147.30 (Q′ *C*N=C); ν_{max}/cm $^{-1}$ 1739s, 1698s and 1600s.

Further elution gave the *ester* **23** (R_f 0.6) as colourless crystals (0.225 g, 18%), m.p. 81–82 °C (from ethyl acetate–light petroleum) (Found: C, 65.7; H, 6.7; N, 9.95. $C_{15}H_{18}N_2O_3$ requires C, 65.65; H, 6.6; N, 10.2%); δ_H 1.29 (t, *J* 7.2, CH_2Me), 1.37 (d, *J* 6.6, Me_2CH), 2.91 (hept, *J* 6.6, Me_2CH), 4.25 (q, *J* 7.2, CH_2Me), 4.92 (s, CH_2N), 7.42 (ddd, *J* 7.9, 6.9 and 1.5, Q′ 6-H), 7.66 (ddd, *J* 7.6, 1.5 and 0.4, Q′ 8-H), 7.72 (ddd, *J* 7.6, 6.9 and 1.5, Q′ 7-H) and 8.23 (ddd, *J* 7.9, 1.5 and 0.4, Q′ 5-H).

Further elution gave the *ester amide* **24** (R_f 0.39) as colourless crystals (0.193 g, 12%), m.p. 160–162 °C (from ethanol) (Found: C, 61.5; H, 6.4; N, 12.55. $C_{17}H_{21}N_3O_4$ requires C, 61.6; H, 6.4; N, 12.7%); δ_H 1.21 (t, *J* 7.1, CH_2Me), 1.43 (2 × d, *J* 6.6, Me_2CH), 2.08 (s, NCOMe), 3.75 (hept, *J* 6.6, Me_2CH), 4.25 (ABX_3, CH_2Me), 6.85 (d, *J* 9.1, NHC*H*), 7.43 (ddd, *J* 8.0, 6.8 and 1.6, Q′ 6-H), 7.63 (d, *J* 9.1, N*H*CH), 7.67–7.77 (m, Q′ 7- and 8-H) and 8.15 (ddd, *J* 8.0, 1.3 and 0.5, Q′ 5-H); proton decoupling at δ 6.85 (d, NHC*H*) collapses 7.63 (d, N*H*CH) to a singlet; δ_C (75 MHz) 13.95, 20.71 (Me_2CH), 21.70 (OCH_2Me), 22.89 (NCO*Me*), 31.49 (Me_2CH), 60.72 (NHCH), 62.78 (OCH_2Me), 120.09 (Q′ *C*C=O), 126.22, 126.53, 127.50 and 134.76 (4 × Q′ CH), 147.58 (Q′ *C*N=C), 160.07 and 163.22 (Q′ C=N and Q′ C=O), 166.66 (N*C*OMe) and 170.29 (CO_2Et); ν_{max}/cm^{-1} 3311m, 1755s, 1690s and 1658s.

Alkylation of N-(*Acetylamino*)-2-*isopropylquinazolin*-4-*one* **21** *with Ethyl α-Bromoacetate to give Compound* **22**.—The sodium salt of compound **21** was prepared as described above using sodium hydride (0.126 g), dimethylformamide (15 cm^3) and compound **21** (1.16 g). This solution was then added

dropwise over 30 min to a vigorously stirred solution of ethyl α-bromoacetate (2.38 g) in dry dimethylformamide held at −20 °C. The resulting mixture was stirred for 2.5 h at this temperature and then allowed to stand overnight at room temp. The reaction mixture was worked up as described above and the ester **22** isolated by chromatography (1.49 g, 83%), identical to the material described above.

Aluminium Amalgam Reduction of the Ester **22**.—The ester amide **22** (0.296 g) was dissolved in dry methanol (30 cm^3), aluminium amalgam [prepared from aluminium turnings (2 g)] was added and the solution stirred under a nitrogen atmosphere in a flask immersed in water at ambient temperature for 48 h. The solution was centrifuged, the methanol decanted, the solid re-suspended in methanol (~ 20 cm^3), again centrifuged and the methanol separated. Evaporation of the combined methanol extracts under reduced pressure and chromatography of the residue over silica, eluting with ethyl acetate, gave impure 2-isopropylquinazolin-4-one **27**. Further elution with methanol–ethyl acetate (1:1) (R_f 0.16) gave ethyl *N*-acetylglycinate **26** (0.096 g, 74%) (R_f 0.16) after distillation (Kugelrohr). The NMR spectrum of this material was identical with that of an authentic sample (Aldrich): δ_H (90 MHz) 1.25 (t, *J* 7.5, CH_2Me), 2.00 (s, NCOMe), 3.97 (d, *J* 5.4, $NHCH_2$), 4.21 (q, *J* 7.5, CH_2Me) and 6.29 (s, br, NH).

Reaction of 3-(*Acetoxyamino*)-2-*isopropylquinazolin*-4-*one* **28** *with* 1,3-*Diphenylpropane*-1,3-*dione*.—The procedure given earlier for the reaction of compound **7** with pentane-2,4-dione was followed, this time using compound **20** (3.45 g, 17 mmol), LTA (7.92 g, 18 mmol) and 1,3-diphenylpropane-1,3-dione (11.44 g, 50 mmol) in dry dichloromethane (35 cm^3). After the same work up as before, an oil was obtained from which the bulk of the excess 1,3-diphenylpropane-1,3-dione crystallised on standing. After separation, the residual oil was chromatographed on silica with ethyl acetate–light petroleum (1:4) (R_f 0.21) as the eluent and the *keto amide* **29** was obtained as colourless crystals (2.97 g, 48%); m.p. 154–155 °C (from ethanol) (Found: C, 73.35; H, 5.5; N, 9.85. $C_{26}H_{23}N_3O_3$ requires C, 73.4; H, 5.45; N, 9.9%). In $CDCl_3$ solution, this compound was present as a 1.2:1 ratio of amide rotamers; major rotamer δ_H 1.34 (2 × d, *J* 6.8, Me_2CH), 4.23–4.35 (m, Me_2CH), 4.29 and 6.11 (2 × d, *J* 17.5, CH_2), 7.16–7.78 (11 H, m, Q′ 6-, 7-, 8-H and 8 × PhH), 8.03 (m, 2 × PhH) and 8.10 (ddd, *J* 8.3, 1.5 and 0.3, Q′ 5-H); minor rotamer δ_H (observable peaks) 1.18, 1.52 (2 × d, *J* 6.5, Me_2CH), 5.22 and 5.42 (2 × d, *J* 19.3, CH_2) and 8.24 (d, *J* 8.1, Q′ 5-H); ν_{max}/cm^{-1} 1700s, 1673s and 1598s; *m*/*z* (%) 188 (100), 187 (94), 173 (100), 166 (72), 119 (63), 106 (93) and 105 (100). Further elution gave 2-isopropylquinazolin-4-one **27** (4%).

Reaction of compound **28** *with* 1-*Phenylbutane*-1,3-*dione*.—The reaction was performed as described above using compound **20** (3.2 g), LTA (7.38 g) and 1-phenylbutane-1,3-dione (6.3 g) in dry dichloromethane (32 cm^3). The solid–oil mixture obtained was triturated with ice-cold diethyl ether to give 2-isopropylquinazolin-4-one **27** (9%). Chromatography of the residue over silica with ethyl acetate–light petroleum (1:4) (R_f 0.30) gave the *diketo amine* **32** as colourless crystals (from ethanol) (0.74 g, 13%), m.p. 125–127 °C (decomp.) (Found: C, 69.3; H, 5.95; N, 11.7. $C_{21}H_{21}N_3O_3$ requires C, 69.4; H, 5.85; N, 11.55%); δ_H 1.22 (2 × d, *J* 6.7, Me_2CH), 2.28 (s, MeCO), 3.38 (hept, *J* 6.7, Me_2CH), 5.02 (d, *J* 2.9, CHNH), 6.71 (d, *J* 2.9, NH), 7.37 (ddd, *J* 8.1, 6.7 and 1.6, Q′ 6-H), 7.46 (dd, *J* 7.4 and 1.6, 2 × PhH), 7.65 (2 H, m, Q′ 7- and 8-H), 8.00 (m, 3 × ArH) and 8.11 (dd, *J* 8.1 and 1.1, Q′ 5-H); δ_C 20.68 and 20.92 (Me_2CH), 26.19 (MeCO), 30.81 (Me_2CH), 77.80 (CHNH), 120.56 (Q′ *C*CO), 126.29, 126.39, 127.42, 128.89 and 129.34 (5 × ArCH), 134.06 (*C*CO), 134.39 and 134.45 (2 × ArCH), 147.0 (Q′ *C*N=C), 162.06 and 162.95 (Q′ C=N and Q′ C=O), 193.11 (Ph*C*O) and 201.42 (Me*C*O); ν_{max}/cm^{-1} 3174m, br, 1700s, 1620s and 1600s.

Further elution gave a mixture of keto amides **30** and **31** (R_f 0.21) (4.31 g, 75%) in a 1:3.3 ratio. Crystallisation from ethanol (3 ×) gave the *keto amide* **31** (0.245 g, 4%) as colourless crystals, m.p. 112–114 °C (Found: M 363.1583. $C_{21}H_{21}N_3O_3$ requires *M* 363.1583). In $CDCl_3$ solution, this compound is present as a 1.6:1 ratio of rotamers; major rotamer δ_H 1.21 and 1.28 (2 × d, *J* 6.5, Me_2CH), 2.34 (s, MeCO), 3.99 (hept, *J* 6.5, Me_2CH), 3.83 and 5.15 (2 × d, *J* 17.2, CH_2), 7.20–7.77 (8 H, m, Q′ 6-, 7-, 8-H and 5 × PhH) and 8.09 (d, Q′ 5-H); δ_C 20.50 and 22.91 (Me_2CH), 27.62 (*Me*CO), 29.97 (Me_2CH), 60.82 (CH_2), 120.20 (Q′ *C*CO), 126.29, 126.68, 126.77, 126.84, 127.36, 127.44, 128.13 and 130.92 (8 × ArCH), 132.44 (Ph*C*CO), 135.02 (Q′ CH), 146.60 (Q′ *C*N=C), 160.66 and 162.24 (Q′ C=N and Q′ C=O), 172.52 (N*C*OPh), and 200.06 (*C*OMe); minor rotamer (observable peaks) 1.47 (d, *J* 6.5, Me_2CH), 1.96 (s, COMe), 4.14 (hept, *J* 6.5, Me_2CH), 4.54 and 4.82 (2 × d, *J* 19.6, CH_2) and 8.22 (d, *J* 7.7, Q′ 5-H); δ_C (observable peaks) 21.72 and 22.15 (Me_2CH), 27.11 (COMe), 30.36 (Me_2CH), 61.80 (CH_2), 121.05 (Q′ *C*CO), 126.29, 126.77, 126.84, 127.36, 127.44, 130.92 and 131.66 (7 × ArCH), 132.94 (Ph*C*CO), 134.75 (Q′ CH), 147.24 (Q′ *C*N=C), 159.63 and 163.75 (Q′ C=N and Q′ C=O), 171.41 (N*C*OPh) and 201.62 (*C*OMe); ν_{max}/cm^{-1} 1732s, 1700s and 1601; *m*/*z*(%) 188 (38), 173 (72) and 105 (100).

Further crystallisation of the mixture of compounds **30** and **31** from chloroform–light petroleum gave the *keto amide* **30** as a colourless solid (0.148 g, 2%) m.p. 115–117 °C (Found: M 363.1583. $C_{21}H_{21}N_3O_3$ requires *M* 363.1583). In $CDCl_3$ solution this compound exists as a 5.8:1 ratio of rotamers; major rotamer δ_H 1.25 and 1.44 (2 × d, *J* 6.6, Me_2CH), 1.95 (COMe), 4.03 (hept, *J* 6.6, Me_2CH), 4.15 and 5.88 (2 × d, *J* 17.4, CH_2), 7.38–7.83 (6 H, m, Q′ 6-, 7-, 8-H and 3 × PhH), 7.95–8.00 (m, 2 × PhH) and 8.25 (dd, *J* 8.0 and 1.2, Q′ 5-H); δ_C 19.90 and 21.34 (Me_2CH), 22.25 (CO*Me*), 29.82 (Me_2CH), 57.12 (CH_2), 120.52 (Q′ *C*CO=O), 126.94, 127.69, 128.08, 128.74 (2 peaks) and 133.71 (6 × ArCH), 134.82 (Ph*C*CO), 135.28 (Q′ CH), 147.01 (Q′ *C*N=C), 160.63 and 162.76 (Q′ C=N and Q′ C=O), 173.07 (N*C*OMe) and 191.51 (COPh); minor rotamer (observable peaks) δ_H 1.19 and 1.37 (2 × d, *J* 6.7, Me_2CH), 2.27 (s, COMe), 3.76 (hept, *J* 6.7, Me_2CH), 4.90 and 5.67 (2 × d, *J* 19.4, CH_2) and 8.19 (dd, *J* 8.1 and 1.1, Q′ 5-H); δ_C (observable peaks) 20.82 (*Me*CHMe), 29.94 (Me_2CH) 59.11 (CH_2), 126.24, 126.72, 127.44, 127.91, 129.07, 134.45 and 134.72 (7 × ArCH) and 192.30 (*C*OPh); ν_{max}/cm^{-1}, 1685s and 1596s; *m*/*z*(%) 188 (50), 173 (100) and 105 (63).

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References

1 H. Person, K. Luanglath and A. Foucaud, *Tetrahedron Lett.*, 1977, 221.
2 R. S. Atkinson, M. J. Grimshire and B. J. Kelly, *Tetrahedron*, 1989, **45**, 2875; R. S. Atkinson, D. W. Jones and B. J. Kelly, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1344.
3 R. S. Atkinson, B. J. Kelly and J. Williams, *J. Chem. Soc., Chem. Commun.*, 1992, 373.
4 J. M. Mellor and N. M. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2927; L. Horner and M. Jordan, *Justus Leibigs Ann. Chem.*, 1978, 1505.
5 R. S. Atkinson and B. J. Kelly, *J. Chem. Soc., Chem. Commun.*, 1987, 1362.

6 Preliminary communication: R. S. Atkinson, P. J. Edwards and G. A. Thomson, *J. Chem. Soc., Chem. Commun.*, 1992, 1256.
7 Y. Shvo, in *The Chemistry of Hydrazo, Azo and Azoxy Groups*, ed. S. Patai, Interscience, New York, 1974, part 2.
8 For a review of *N*-acylimines, see S. M. Weinreb and P. M. Scola, *Chem. Rev.*, 1989, **89**, 1525; see also T. Bretschneider, W. Miltz, P. Münster and W. Steglich, *Tetrahedron*, 1988, **44**, 5403.
9 R. H. Wiley and O. H. Borum, *Org. Synthesis*, 1953, **33**, 5.
10 R. S. Atkinson, B. J. Kelly and J. Williams, *Tetrahedron*, 1992, **48**, 7713.
11 M. Bassetti, G. Cerichelli and B. Floris, *Tetrahedron*, 1988, **44**, 2997.

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