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AZIRIDINATION BY OXIDATIVE ADDITION OF N-AMINOQUINAZOLONES TO ALKENES: EVIDENCE FOR NON-INVOLVEMENT OF N-NITRENES

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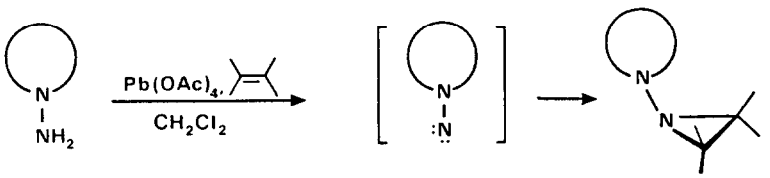
Abstract - Oxidation of 3-aminoquinazolones e.g. (22) with lead tetra-acetate at -20°C gives N-acetoxyaminoquinazolones e.g. (23) which are stable in solution at this temperature. These N-acetoxyaminoquinazolones function as inter- and intramolecular aziridinating agents for alkenes and appear to be playing the role previously ascribed to the corresponding N-nitrenes. An analogous N-acetoxy-aminophthalimide intermediate (31) is implicated in the lead tetra-acetate oxidation of N-aminophthalimide (4).

INTRODUCTION

There exists a family of heterocyclic compounds, aminated on nitrogen, oxidation of whose members in the presence of alkenes gives aziridines, often in excellent yields.[1] The reactive intermediates in these oxidations have been assumed to be N-nitrenes (2) although no direct spectroscopic evidence to support this assumption has been forthcoming.

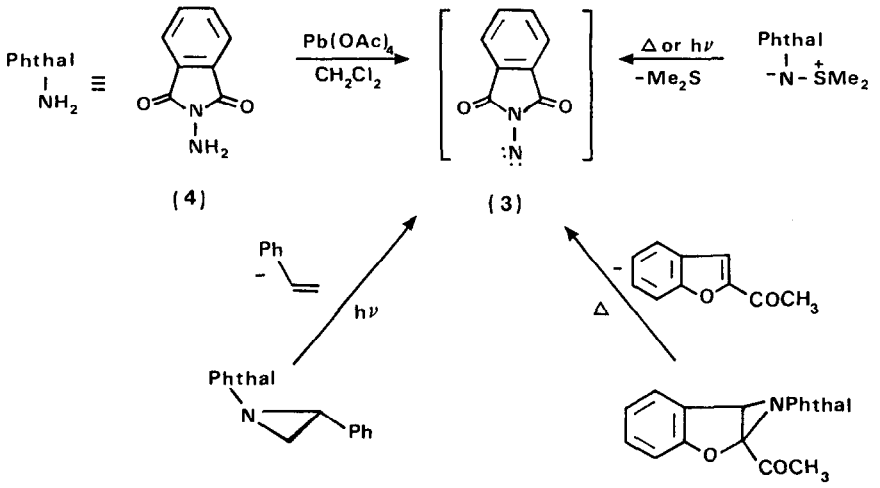


(1) (2)

The most compelling evidence for the intermediacy of N-nitrenes (2) in these oxidations has been the generation of apparently the same intermediate - phthalimidonitrene (3) - from several different sources (Scheme 1) including oxidation of N-aminophthalimide (4).[2,3,4,5]

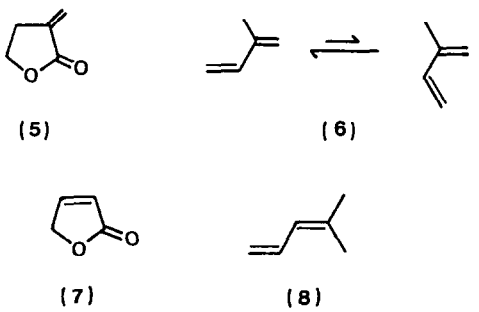
This presumed common intermediate N-nitrene (3) was shown in every case to add stereo-specifically to cis- and trans-substituted alkenes. In three cases also,[2,3,4] the intermediate was shown to exhibit ambiphilic character giving good yields of aziridines in addition to both electron-rich alkenes (e.g. styrene) and electron-deficient alkenes (e.g. methyl acrylate).

In spite of the evidence above, however, there has been some disquiet[6,7] with the assignment of nitrenes to these intermediates whose properties were at variance with those anticipated from the behaviour of other bona fide nitrenes[8] (alkoxycarbonyl-, cyano-, and sulphonylnitrenes) although the latter, unlike (2), all have the nitrene nitrogen substituted by a strongly electron-withdrawing group.



Scheme 1

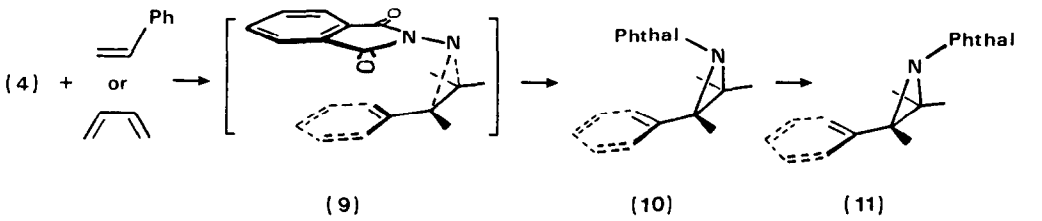
To us, one of the most puzzling features of the behaviour of these intermediates as N-nitrenes has been their selectivity in reacting only with the s-cis conformations of e.g. α,β-unsaturated esters and 1,3-dienes.[9] Thus whereas α-methylene-γ-butyrolactone (5)[10] and isoprene (6) are efficiently aziridinated by oxidative addition of N-aminophthalimide (4), their s-trans locked or biassed counterparts, butenolide (7) and 4-methylpenta-1,3-diene (8) give no aziridine products at all.[9,10]



(5) (6)

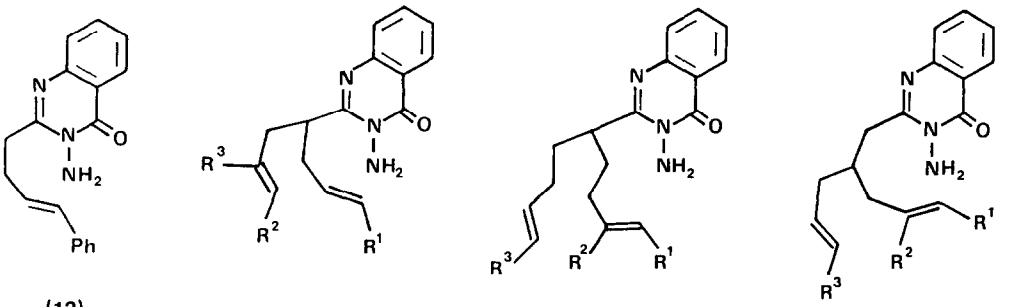
(7) (8)

Although we have reconciled this demand for the s-cis configuration in terms of a secondary interaction between the heterocycle and the alkene substituent in the aziridination transition state (e.g. (9) for the addition of phthalimidonitrene (3) to butadiene or styrene) and have shown that the kinetically-formed syn-aziridines from these additions invert at nitrogen to the thermodynamically preferred trans-aziridines on warming above 0°C ((9) → (10) → (11)),[9] nevertheless it was not obvious why a reactive intermediate should fail to react with an alkene without this (presumably small) supplementary assistance from the secondary interaction.



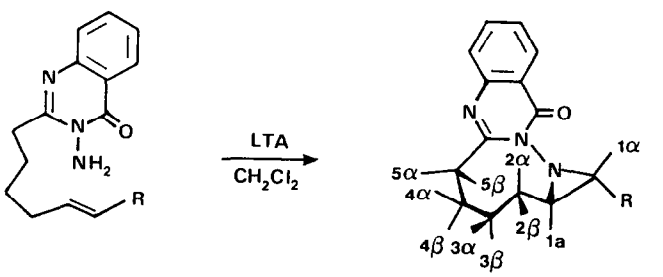
(9) (10) (11)

In intramolecular oxidative aziridinations, however, this secondary interaction between the alkene substituent and the heterocyclic group did not appear to be mandatory. Thus efficient aziridination of the styrenoid double bond in (12) occurred in a reaction in which a secondary interaction analogous to that shown in (9) is inconceivable.[11]



(12) (13) (14) (15)

From oxidation of a variety of N-aminoquinazolones bearing bifurcated chains at positions 2 e.g. (13), (14), and (15) and by examining the selectivity (between double bonds) and facial selectivity (in addition to each double bond) of the resulting aziridination, we concluded that the preferred transition state for concerted addition of the presumed intermediate N-nitrenes to alkenes was in agreement with that shown in (9) i.e. with the N-N bond orthogonal to the C=C bond.[12]

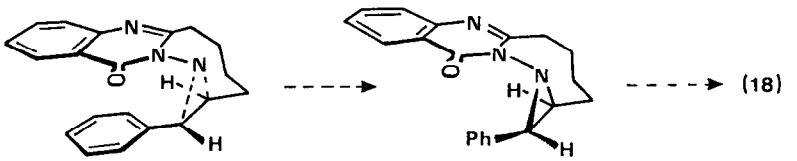


(16) R = Ph
(17) R = Me

(18) R = Ph
(21) R = Me

As part of this work we also re-examined the intramolecular aziridination of the double bonds in (16) and (17).[13] The presumed entropic advantage in intramolecular aziridination of (13), (14) and (15) in which only 3 or 4 carbon-carbon bonds link the quinazolone 2-position to two double bonds is diminished in (16) and (17) and addition of lead tetra-acetate (LTA) to a solution of (16) resulted in polymer formation. This was assumed to be the result of preferential and consecutive intermolecular aziridination of the styrenoid double bond in one molecule by the N-nitrene of another (in which a favourable secondary interaction is operative).

However, by contrast with the situation in intermolecular aziridinations using (13)-(15), an examination of models of (16) with 5 carbon-carbon bonds linking the alkene to the quinazolone ring suggested that a secondary interaction between the phenyl ring and the quinazolone ring analogous to that in (9) was conceivable in the derived nitrene i.e. (19) although under the conditions used above in the oxidation of (16), intermolecular aziridination was more favourable.



(19) (20)

This transition state (19) should lead to (20) as the kinetically-formed invertomer at nitrogen (cf (9) → (10)) and our previous experience[13] suggested to us that this kinetically-formed aziridine might be observable in solution before inversion to the thermodynamically preferred (18) occurred if oxidation of the N-aminoquinazolone (16) could be carried out at -20°C and the solution examined by n.m.r. at -20°C without any intermediate warming.

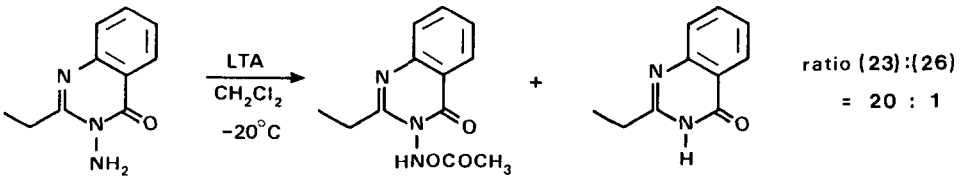
RESULTS

Intramolecular aziridination to give (18) was successfully accomplished by slow addition of both LTA and the N-aminoquinazolone (16) to a dichloromethane solution. The conformation assumed by the 8-membered ring in (18) was identical to that previously deduced[13] for (21). Instead of oxidising (16) to test for the intermediacy of (20), we chose first to examine the corresponding oxidation of (17) at low temperature since the presumed intermediate nitrene in this case showed a lesser predilection for intermolecular addition.

Oxidation of (17) was carried out at -30°C in deuterochloroform and the solution obtained after separation of lead di-acetate was examined by n.m.r. at -30°C without any intermediate warming of the solution. This n.m.r. spectrum revealed that there had been no aziridination of the alkene since the two olefinic protons were still intact. Most surprisingly, however, warming of the solution to room temperature and re-examination by n.m.r. indicated that a small yield (~10%) of aziridine (21) had been produced from the presence of its characteristic signals at δ3.30 (ddd, J 13, 12, and 1 Hz) and 2.94 (ddd, J 13, 8, and 1 Hz) for 5β-H and 5α-H, respectively.[13] An experiment using a 2:1 ratio of N-aminoquinazolone (17):LTA showed clearly that oxidation of (17) proceeds to completion at -30°C and leads to the conclusion that an intermediate was present at -30°C which was converted, in part, to aziridine (21) only on warming to room temperature.

It was quickly established that analogous intermediates, stable at -20°C, were also obtained in oxidation of simple N-aminoquinazolones e.g. (22). Addition of an alkene to a solution of this intermediate at -20°C and then allowing the solution to warm to ambient brought about intermolecular aziridination of the alkene in good yield.

It was clear that the intermediates in these oxidations of N-aminoquinazolones (17) or (22) were not lead salts since the lead was recovered almost quantitatively as the di-acetate by filtration of solutions of the intermediate at -20°C which then show an undiminished aziridinating ability.



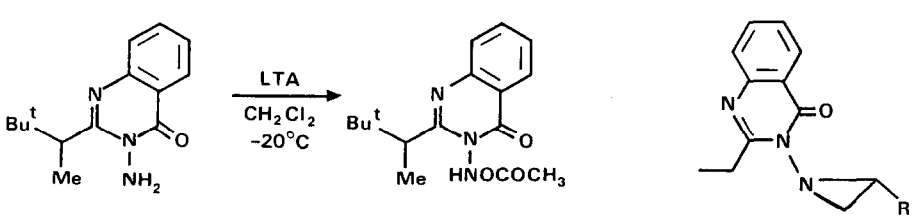
(22) (23) (26)

Structure of the Intermediate in LTA Oxidation of (22)

The unstable intermediate above in the LTA oxidation of (22) has been shown to be the N-acetoxyaminoquinazolone (23).[14] An important finding was that solutions of (23) could be freed from acetic acid (produced in the oxidation) by washing with a sodium hydrogen carbonate solution at -20°C; an n.m.r. spectrum then revealed the presence of an additional methyl singlet (δ2.15) which had been previously obscured by the acetic acid. The presence of an acetoxy group $OCOCH_3$ was confirmed by the carbon signals at δ18.98 and 169.46 in the ^{13}C spectrum of the acetic acid-free solution and by the additional carbonyl stretching frequency at 1768 cm^{-1} in an i.r. spectrum carried out at -20°C.

A striking feature of the n.m.r. spectrum of the N-acetoxyaminoquinazolone (23) is the non-equivalence of the methylene protons at position 2 which appear as a doublet of quartets (δ3.19 and 3.03). The chirality which is rendering those two protons diastereotopic is presumably either retarded inversion at the acetoxyamino nitrogen or restricted rotation around the N-N bond (a chiral axis) but a distinction between these two has been hampered by the fragility of (23).

This chiral element in (23) is also responsible for the observation of two diastereoisomers (ratio 4:1) in the n.m.r. spectrum of the N-acetoxyaminoquinazolone (24) prepared in solution from the corresponding N-aminoquinazolone (25) by oxidation at -20°C. Other N-acetoxyaminoquinazolones which we have prepared (see below) show similar non-equivalence of the methylene protons at C-2 (as in (23)) or the presence of stereoisomers (as in (24)).



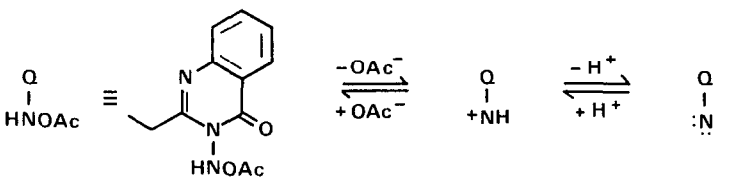
(25) (24)

(27) R = Ph
(28) R = CO_2Me

Mechanism of Aziridination of Alkenes by N-acetoxyaminoquinazolone (23)

Successive and alternate additions of very small quantities of solid LTA and N-aminoquinazolone (22) to a deuterochloroform solution at -20°C gave solutions of (23) containing only ~5% of the deaminated quinazolone (26) as an impurity. The rate of disappearance of (23) in the presence of styrene was 1st order in styrene and (23). Similarly the rate of disappearance of (23) was accelerated by the addition of methyl acrylate. Aziridines (27) and (28) were the sole products from the above aziridinations using 1.5 mole equivalents of the alkene and were isolated in yields of 76% and 80% using styrene and methyl acrylate, respectively.

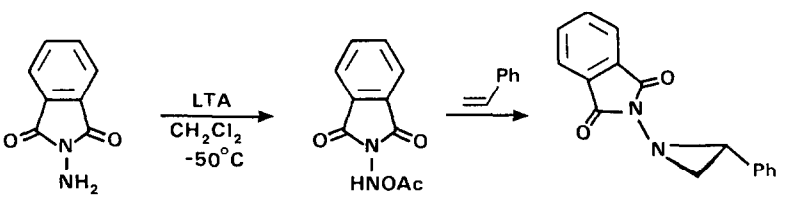
From the above results it appears that the N-acetoxyaminoquinazolone (23) is playing the role previously assigned to the N-nitrene (29). The possible involvement of the N-nitrene (29) or the N-nitrenium ion[7] (30) by the presence of a reversible equilibrium between these species and (23) could be eliminated since no exchange of either the NH or OAc took place in the n.m.r. spectrum of (23) when an acetic acid-free solution was treated with 4 mole equivalents of CD_3CO_2D at -20°C.



(23) (30) (29)

It was of particular interest to examine whether an analogous N-acetoxyamino intermediate (31) was involved in oxidation with LTA of N-aminophthalimide (4) since it was the generation of apparently the same intermediate by four different routes which had constituted the best evidence for an N-nitrene intermediate (Scheme 1).

Low temperature (-50°C) oxidation of N-aminophthalimide (4) followed by separation of the insoluble lead di-acetate at -45°C and then addition of styrene (3 mole equivalents) gave aziridine (32) in 40% yield.†

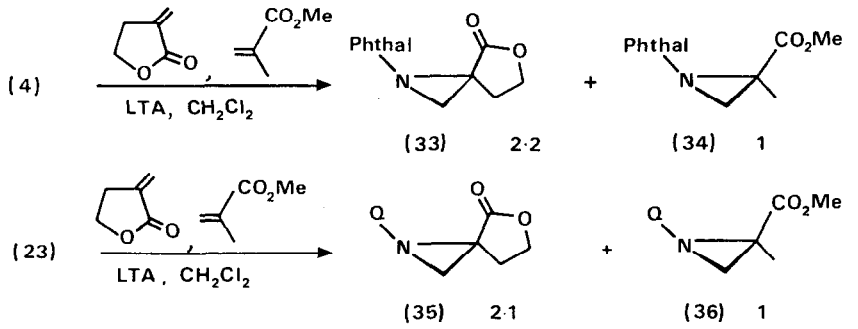


(4) (31) (32)

† Dr Lienhard Hoesch (University of Zürich) has drawn our attention to his previous finding that oxidation of (4) with LTA at -50°C produces an intermediate which is stable in solution at this low temperature and brings about aziridination of tetracyclone (L. Hoesch, Thesis, University of Zürich, 1974). We thank Dr Hoesch for his exchange of information and helpful comments.

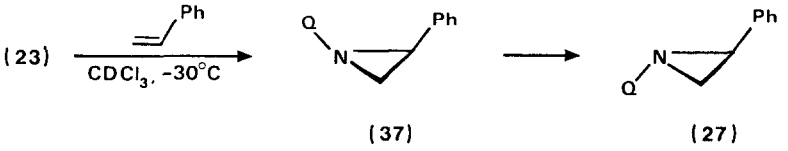
It appears, therefore, that in the oxidation of (4) also, an intermediate, presumably (31), is formed which is stable in solution at low temperature and brings about aziridination of styrene. Further support for this interpretation comes from a comparison of the selectivities of the intermediates in LTA oxidation of N-aminophthalimide (4) and N-aminoquinazolone (22) in reaction with two alkenes. Thus oxidation of (4) in the presence of a 1:1 mixture of α-methylene-γ-butyrolactone and methyl methacrylate gave aziridines (33) and (34) in a 2.2:1 ratio. This selectivity is very close to that of (23) in its reaction with the same two alkenes (2.1:1) (Scheme 2).

Similarly, aziridination of geraniol and geranyl chloride by oxidative addition of N-aminophthalimide (4) and by solutions of (23) gives similar ratios of attack on the two double bonds suggesting similar intermediates are involved.[15]



Scheme 2

An observation of particular significance was that the first-formed product from reaction of (23) with styrene at -30°C was the syn-aziridine (37) with aziridine ring protons at δ($CDCl_3$, -30°C) 3.81 (t, J 7 Hz), 3.7 (dd, J 7 and 4 Hz), and 3.45 (dd, J 7 and 4 Hz): conversion to the thermodynamically preferred (27) was rapid above -20°C (Scheme 3).*



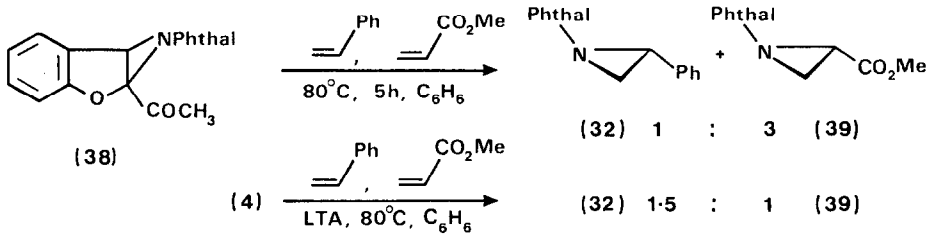
Scheme 3

It was pointed out earlier that formation of syn-aziridines as kinetically-formed products was a characteristic feature of the reactivity of nitrenes (2) (including 'phthalimidonitrene') with styrene, methyl acrylate or butadiene[9] but it now appears that this syn-stereospecificity is actually a feature of the reactivity of N-acetoxyaminoheterocyclic intermediates.

If the active aziridinating agent in oxidation of N-aminophthalimide (4), therefore. is the N-acetoxyaminophthalimide (31), how can this be reconciled with the apparent generation of the same intermediate by four different routes as in Scheme 1?

*Strictly speaking, we cannot exclude the possibility that some direct conversion of styrene to the aziridine (27) by (23) occurs since slow inversion of (37) to (27) occurs even at -30°C. However, the rate of formation of (37) is ~10 times that of (27) and we believe that all of (27) is produced via (37)

Closer examination of the aziridinating species produced in the thermolysis of aziridine (38)[3] shows that its selectivity for alkenes is different from that of (31). Thus heating aziridine (38) in a benzene solution containing a 1:1 mixture of styrene and methyl acrylate (3 mole equivalents each) for 5 hours gave a 1:3 ratio of aziridines (32) and (39) (Scheme 4). By contrast, oxidation of (4) with LTA in the presence of the same ratio of alkenes in boiling benzene over 20 minutes gave the same aziridines but in a ratio of 1.5:1. The ratio of (32):(39) was not affected by heating for 4 hours in benzene under reflux, with or without the addition of 2 mole equivalents of acetic acid (which is also produced in oxidation of (4) with LTA).



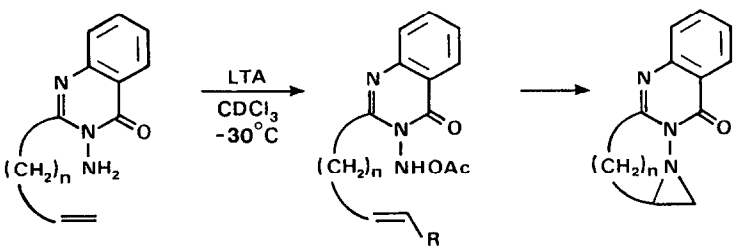
Scheme 4

It appears, therefore, that the intermediate in the thermal decomposition of aziridine (38) is not identical with that generated by oxidation of N-aminophthalimide (4) under similar conditions whether the intermediate in the thermal decomposition of (38) is the N-nitrene (3) is still under investigation.

Nature of the Intermediates in Intramolecular Aziridinations of 2-Substituted N-Aminoquinazolones

Prior to our recognition of the N-acetoxyaminoquinazolone (23) as an aziridinating agent, we had attempted to describe the preferred transition state geometry for concerted N-nitrene addition (as we thought) to double bonds from a study of intramolecular aziridination using substrates as (13), (14) and (15).[12]

We have re-examined the oxidations of some of these N-aminoquinazolones at low temperatures by n.m.r. spectroscopy and it is clear that N-acetoxyaminoquinazolones and not N-nitrenes are the intermediates in these aziridinations also. Thus the intermediates in oxidation of (17) (see earlier) (40) and (41) are the corresponding N-acetoxyaminoquinazolones (42), (43), and (44), respectively. Conversion of (43) into the aziridine (45) was monitored by n.m.r. at -20°C: after 30 minutes at this temperature, the mixture comprised aziridine (45) (35%) and N-acetoxyaminoquinazolone (43) (65%).



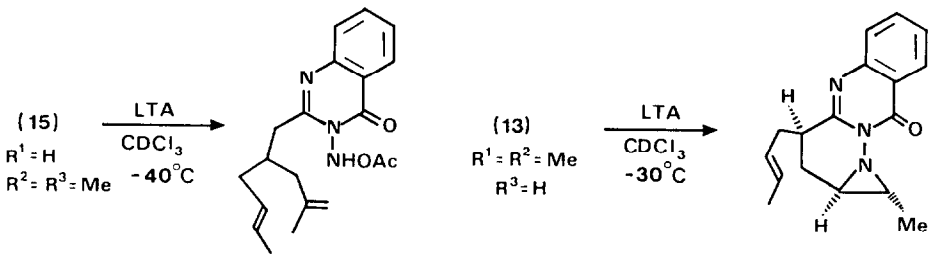
(40) n = 3
(41) n = 2

(42) n = 4, R = Me
(43) n = 3, R = H
(44) n = 2, R = H

(45) n = 3
(46) n = 2

For the case of the 2-butenyl-3-aminoquinazolone (41) in which only 3 bonds separate the quinazolone ring from the alkene double bond, the corresponding N-acetoxyaminoquinazolone (44) could not be generated in solution free from the corresponding aziridine (46) into which it was completely transformed on raising the temperature.

For the bifurcated chain bearing N-aminoquinazolones, a similar pattern emerges: the N-acetoxyaminoquinazolone (47), like the case of (24), shows diastereoisomers to be present (at least on the n.m.r. time-scale) at -40°C. However, oxidation of ((13), R^1=R^2=Me, R^3=H) could not be accomplished at a temperature low enough to allow observation of any product other than the derived aziridine (48).



(47) (48)

Can our conclusions previously drawn for the preferred transition state geometry for concerted N-nitrene addition to alkenes be simply transferred to describe the preferred transition state for the aziridination using N-acetoxyamino compounds? The answer to this question is tentatively yes but further work is in progress to confirm this.

EXPERIMENTAL

IR spectra were determined as nujol mulls using a Perkin Elmer 298 spectrometer or in deuterochloroform solution using a Perkin Elmer 580. The high resolution mass spectrum for (18) was obtained using a VG ZAB-E mass spectrometer (University of Swansea). The ^{1}H n.m.r. spectrum for (18) was obtained using a Bruker WH-400 spectrometer (University of Warwick): all other ^{1}H and ^{13}C spectra were obtained using a Bruker AM-300 spectrometer and deuterochloroform solutions with tetramethylsilane as internal standard. Filtration of solutions at low temperatures (-45°C) under gravity or vacuum was accomplished by carrying out these operations at the bottom of a lagged tank containing shelves lined with solid carbon dioxide with access through a removable top. For other experimental details see Ref. 12.

Preparation and Oxidation of 3-Amino-2-(6-Phenylhex-5-enyl)quinazolin-4(3H)-one (16). - 7-Phenylhept-6-enoic acid[16] was converted to its acid chloride and reacted with methyl anthranilate to give methyl N-(7-phenylhept-6-enoyl)anthranilate using the method previously described.[11] Heating this amide with hydrazine in ethanol under reflux and work up as described previously gave the N-aminoquinazolone (16) as colourless crystals, m.p. 85-89°C (from ethanol) (Found: C, 75.0; H, 6.7; N, 13.2. $C_{20}H_{21}N_3O$ required C, 75.2; H, 6.6; N, 13.2%); δ8.18(d, J 8 Hz, 5-H), 7.7-7.2 (m, 8 x ArH), 6.32(m, CH=CH), 4.85br(s, NH_2), 3.02(t, CH_2-quinaz.), 2.32(m, CH_2CH-CH), and 1.78 (m, CH_2CH_2).

Oxidation of the above N-aminoquinazolone (37 mg) dissolved in dry dichloromethane (40 ml) with LTA (60 mg) dissolved in dry dichloromethane (40 ml) was carried out as previously described[12] by adding both solutions dropwise from different dropping funnels to dry dichloromethane solution (40 ml) over 20 min. Crystallisation of the crude product (with separation of a small quantity of insoluble impurity) from ethanol gave aziridine (18) (10 mg), m.p. 181-183°C (Found: M^+ 317.1528 $C_{20}H_{21}N_3O$ requires M^+ 317.1518); δ(400 MHz) (for numbering see text) 8.14 (dd, J 8 and 1.6 Hz, 5-H), 7.62(ddd, J 8.3, 7, and 1.6 Hz, 7-H), 7.55(dd, J 8.3 and 1.2 Hz, 8-H), 7.44(m, 2 x ArH), 7.33(m, 6-H and 2 x ArH), 7.25(m, ArH), 3.44(d, J 5.9 Hz, 1α-H), 3.31(ddd, J 13.5, 11.8, and 1 Hz, 5β-H), 2.92(ddd, J 13.5, 7.7, and 1 Hz, 1a-H), 2.00 (ddddd, J 13.8, 6, 5.8, 1.2, and 1.2 Hz, 3α-H), 1.94(ddddd, J 13, 12.7, 11.8, 5.8, and 1 Hz, 4α-H), 1.68(ddddd, J 13.8, 12.7, 12.3, 5.3, and 1.4 Hz, 3β-H), and 1.09(dddd, J 15.9, 12.3, 10.4, and 1.2 Hz, 2α-H).

Oxidation of 3-Amino-2-(E-hept-5-enyl)quinazolin-4(3H)-one (17) at -30°C. - Over a period of 30 min. very small portions of dry LTA (total 160 mg) and N-aminoquinazolone (17) (total 80 mg) were added alternately and continuously to magnetically-stirred deuterochloroform (2.5 ml) cooled at -30°C with a dry ice - acetone bath. The mixture was stirred for a further 20 min. and then lead di-acetate separated and a portion of the solution transferred to an n.m.r. tube, all operations being carried out at <-25°C. The n.m.r. spectrum of this solution at -30°C showed only the N-acetoxy-aminoquinazolone (42) to be present (besides acetic acid) with δ8.26(dd, J 8 and 1.4 Hz, 5-H), 7.83 (ddd, J 8.3, 7, and 1.4 Hz, 7-H), 7.74(dd, J 8.3 and 1.5 Hz, 8-H), 7.52(ddd, J 8, 7, and 1.5 Hz, 6-H), 5.45(m, CH=CH), 3.16(ddd, J 13.5, 9, and 6.4 Hz, CHH-quinaz.), 2.97(ddd, J 13.5, 9, and 6.4 Hz, CHH-quinaz.), 2.07 (q, J 6 Hz, $CH_2CH=CH_2$), 1.85(m, CH_2CH_2-quinaz.), 1.65(dd, J 4.5 and 1.5 Hz, CH=CHMe), and 1.52(quint. J 7 Hz, $CH_2CH_2CH=CH_2$). Allowing the solution to warm to ambient gave a small yield (~10%) of aziridine (21) identified by its characteristic signals at δ3.30(ddd, J 13, 12, and 1 Hz, 5β-H) and 2.94(ddd, 13, 8, and 1 Hz, 5α-H) (for numbering see (18)).[13]

Oxidation of N-Aminoquinazolones (22) and (25) was carried out in a similar way to that described above by adding the N-aminoquinazolone (1.0 mol equiv.) and dry LTA (1.05 mol equiv.) to deuterochloroform (1 ml/100 mg N-aminoquinazolone) at -20°C. After stirring for a further 20-30 min. the lead di-acetate was separated and the solution washed with a cold (-25°C) saturated solution of sodium hydrogen carbonate, dried by passing through a small pre-cooled column of magnesium sulphate before recording its n.m.r. spectrum at the temperature indicated and without allowing the temperature to rise above -25°C throughout. Oxidation of (22) (100 mg) at -20°C as above gave (23), $\nu_{max.}$ ($CDCl_3$, -20°C) 1768s, 1710s, and 1626s cm^{-1}; δ^1H (-40°C) 10.98 (s, NH), 8.25(ddd, J 8, 1.4, and 0.6 Hz, 5-H), 7.84(ddd, J 8, 7.4, and 1.4 Hz, 7-H), 7.71(ddd, J 8, 1.4, and 0.6 Hz, 8-H), 7.52(ddd, J 8, 7.4, and 1.4 Hz, 6-H), 3.19(dq, J 17 and 7 Hz, $CHHCH_3$), 3.03(dq, J 17 and 7 Hz, $CHHCH_3$), 2.15(s, $OCOCH_3$), and 1.43(t, J 7 Hz, CH_2CH_3); ^{13}C (-40°C) 169.46(s, $OCOCH_3$), 159.9 (s, 4-C), 158.52(s, 2-C), 146.56 (s), 135.48 (d), 127.29 (d), 126.97 (d), 124.44 (d), 119.56 (s), 27.02(t, CH_2), 18.98 (q, $OCOCH_3$), and 11.29(q, CH_2CH_3); a minor (~5%) product in this oxidation was 2-ethylquinazolin-4(3H)-one (26) identified by its (observable) signals at δ11.6(s, NH), 8.23(d, J 8 Hz, 5-H), and 2.8(q, J 7.2 Hz, CH_2CH_3).

Oxidation of (25) (100 mg) at -20°C as above gave (24) major stereoisomer: δ(-40°C) 11.1 (s, NH), 8.26(ddd, J 8, 1.4, and 0.6 Hz, 5-H), 7.84(ddd, J 8, 7.5 and 1.4 Hz, 7-H), 7.72(ddd, J 8, 1.4, and 0.6 Hz, 8-H), 7.51(ddd, J 8, 7.5, and 1.4 Hz, 6-H), 3.78(q, J, 7.1 Hz, CHMe), 2.13(s, $OCOCH_3$), 1.38 (d, J 7.1 Hz, CHMe), and 0.99(s, Bu^t); minor stereoisomer: δ10.89(s, NH), 3.67(q, J 7Hz, CHMe), 1.31(d, J 7.1 Hz, $CHCH_3$), and 1.11(s, Bu^t) (other signals coincident with major stereoisomer): ratio major:minor stereoisomers 4:1.

Oxidation of N-Aminoquinazolones (40) and (41) was carried out as described above for (20) and (21) with addition of solids over 30 min. and subsequent stirring for 30 min. but without washing with sodium hydrogen carbonate solution. Oxidation of (40) (150 mg) at -40°C in this way gave (43) δ(-30°C) 0.96(s, NH), 8.26(dd, J 8 and 1.5 Hz, 5-H), 7.84(ddd, J 8, 7.4, and 1.5 Hz, 7-H), 7.71 (dd, J 8 and 1.5 Hz, 8-H), 7.52(ddd, J 8, 7.4, and 1.5 Hz, 6-H), 5.82(m, $CH=CH_2$), 5.1(dd, J 16.5, and 2 Hz, $CH_2C=CHH$(cis)), 5.03(dd, J 10 and 2 Hz, $CH_2C=CHH$(trans)), 3.16(ddd, J 17, 8, and 7 Hz, CHH-quinaz.), 2.99(ddd, J 17, 8, and 7 Hz, CHH-quinaz.), and 2.31-1.82(m, $CH_2CH_2CH=CH_2$). Oxidation of (41) (150 mg) at -40°C by the same method gave (44) and aziridine (46) in a 65:35 ratio. For (44) δ(-30°C) 10.98(s, NH), 8.24(dd, J 8 and 1.4 Hz, 5-H), 7.84(ddd, J 8, 7.4, and 1.4 Hz, 7-H), 7.72(d, J 8 Hz, 8-H), 7.53(ddd, J 8, 7.4, and 1.5 Hz, 6-H), 5.98(m, $CH=CH_2$), 5.17(dd, J 17 and 2 Hz, $CH_2C=CHH$ (cis)), 5.07(dd, J 10 and 2 Hz, $CH_2C=CHH$ (trans)), 3.27(ddd, J 16, 8, and 6 Hz, CHH-quinaz.), 3.16-3.03(m, CHH-quinaz. and $CHHCH\ CH_2$), and 2.64 br(q, J 7 Hz, $CHHCH=CH_2$); aziridine (46) was identified by its characteristic aziridine ring proton signals at δ3.00(dd, J 5.5 and 2 Hz) and 1.96(dd, J 6.5 and 2 Hz).[11]

Oxidation of (15; R^1 = H, R^2 = R^3 = CH_3) was carried out by dissolving the N-aminoquinazolone (100 mg) in deuterochloroform (5 ml), dissolving LTA (156 mg 1.05 mol equiv.) in deuterochloroform (5 ml) and adding both solutions at the same rate over 30 min. from separate dropping funnels to a stirred deuterochloroform solution (2 ml) maintained at -30°C.[17] After stirring for a further 20 min. the lead di-acetate was separated and the solution examined by n.m.r. at -30°C without any intermediate warming of the solution to give (47) as a 1:1 mixture of stereoisomers: δ(-30°C) 10.97 and 10.94 (2 x s, NH), 8.25(dd, J 8 and 1.5 Hz, 5-H), 7.85(ddd, J 8, 7.4, and 1.5 Hz, 7-H), 7.72 (d, J 8 Hz, 8-H), 7.53(ddd, J 8, 7.4, and 1.5 Hz, 6-H), 5.4(m, CH=CH), 4.73(m, $C=CH_2$), 3.12(ddd, J 15, 9, and 6 Hz, CHH-quinaz.), 2.79(ddd, J, 16, 16, and 7.5 Hz, CHH-quinaz.), 1.82 and 1.70(2 x s, $CH_3C=CH_2$), and 1.6 and 1.5(2 x d, J 5.5 Hz, $C=CHCH_3$) (other peaks obscured by acetic acid methyl).

Oxidation of (13; R^1 = R^2 = Me, R^3 = H) (100 mg) was carried out as described for (15; R^1 = H, R^2 = R^3 = CH_3) with the deuterochloroform maintained at -40°C. An n.m.r. spectrum showed that the solution contained only aziridine (48) identical with that previously reported.[12]

Aziridination Reactions using Solutions of (23). - To the solution of (23) prepared at -20°C as described above but using dichloromethane instead of deuterochloroform was added the alkene in one portion and the solution allowed to warm to ambient with stirring. The solution was washed with aqueous sodium hydrogen carbonate solution, dried and evaporated. Reaction with styrene (1.5 mol equiv.) gave aziridine (27) as colourless crystals (79%) m.p. 102-105°C (from ethanol) (Found: C, 74.1; H, 6.0; N, 14.4. $C_{18}H_{17}N_3O$ requires C, 74.2; H, 5.9; N, 14.4%) νmax 1665s and 1597s cm^{-1}; δ8.2(ddd, J 8, 1.5, and 0.6 Hz, 5-H), 7.67(ddd, J 8, 7.5, and 1.5 Hz, 7-H), 7.62(ddd, J 8, 1.3, and 0.6 Hz, 8-H), 7.42-7.34(m, 6 x ArH), 3.69(dd, J 8 and 5.5 Hz, CHPh), 3.12(dd, J 8 and 2.3 Hz, azir. H trans to Ph), 2.99(q, J 7.3 Hz, CH_2CH_3), 2.87(dd, J 5.5 and 2.3 Hz, azir. H cis to Ph), and 1.35 (t, J 7.3 Hz, CH_2CH_3).

Reaction with methyl acrylate (1.5 mol equiv.) gave aziridine (28) as colourless crystals (80%) m.p. 116-118°C (from ethanol) (Found: C, 61.6; H, 5.6; N, 15.25. $C_{14}H_{15}N_3O_3$ requires C, 61.5; H, 5.55; N. 15.35%) νmax 1755s, 1670s, and 1592s cm^{-1}; δ8.17(ddd, J, 8, 1.4 and 0.6 Hz, 5-H), 7.72(ddd, J 8.1, 7.4, and 1.4 Hz, 7-H), 7.62(ddd, J 8.1, 1.3, and 0.6 Hz, 8-H), 7.42(ddd, J 8, 7.4 and 1.3 Hz, 6-H), 3.86 (s, OCH_3), 3.65(dd, J 7.5 and 5.4 Hz, $CHCO_2Me$), 3.18(dd, J 7.5 and 1.5 Hz, azir. H trans to CO_2Me), 3.08 (2 x dq; J 17 and 6.6 Hz, CH_2CH_3), 2.92(dd, J 5.4 and 1.5 Hz, azir. H cis to CO_2Me), and 1.42(t, J 6.6 Hz, CH_2CH_3).

Oxidation of N-Aminoquinazolone (22) in the Presence of Methyl Methacrylate and α-Methylene-γ-butyrolactone (5). - Powdered (22) (250 mg) and LTA (617 mg) were added separately and alternately to a stirred solution of (5) (260 mg) in dry dichloromethane (2.5 ml). After stirring for an additional 30 min., the lead di-acetate was separated, washed with dichloromethane and the dichloromethane solution washed successively with sodium hydrogen carbonate solution and water then dried and evaporated under reduced pressure. Chromatography of the crude product on alumina eluting with ethyl acetate - light petroleum (2:1) gave aziridine (35) (65%) as colourless crystals, m.p. 168 - 171°C (from ethanol) (Found: C, 63.1; H, 5.35; N, 14.6. $C_{15}H_{15}N_3O_3$ requires C, 63.15; H, 5.3; N, 14.7%) νmax 1765s, 1680s and 1598s cm^{-1}; δ8.16(ddd, J 8, 1.5 and 0.6 Hz, 5-H), 7.69(ddd, J 8.2, 6.7, and 1.5 Hz, 7-H), 7.63(ddd, J 8.2, 1.5, and 0.6 Hz, 8-H), 7.40(ddd, J 8, 6.7, and 1.5 Hz, 6-H), 4.98br(ddd, J 8, 8, and 8 Hz, CHHOCO), 4.55(ddd, J 9.3, 8, and 3.8 Hz, CHHOCO), 3.05br (s, azir. H cis to quinaz.), 3.00(q, J 7.4 Hz, CH_2CH_3), 2.97br (s, azir. H trans to quinaz.), 2.87(ddd, J 14, 8, and 3.8 Hz, $CHHCH_2OCO$), 2.62(ddd, J 14, 9.3, and 8 Hz, $CHHCH_2OCO$), and 1.45 (t, J 7.4 Hz, CH_2CH_3).

A similar oxidation using (22) (460 mg), LTA (1.12 g) and methyl methacrylate (1.21 g) in dry dichloromethane (5 ml) and chromatography of the crude reaction product on silica eluting with ethyl acetate - light petroleum (1:1) gave aziridine (36) (67%) as colourless crystals, m.p. 90-93°C (from ethanol) (Found: C, 62.7; H, 6.0; N, 14.6. $C_{15}H_{17}N_3O_3$ requires C, 62.7; H, 5.95; N, 14.6%) νmax 1730s, 1665s, and 1595s cm^{-1}; major invertomer δ8.15(ddd, J 8, 1.5, and 0.6 Hz, 5-H), 7.7(dd, J 8 and 7.3 Hz, 7-H), 7.64 (8-H), 7.39(ddd, J 8, 7.3, and 1.3 Hz, 6-H), 3.56 (s, CO_2CH_3), 3.26br (s, azir. H cis to CO_2CH_3), 2.98 (2 x dq, J 17 and 7.3 Hz, CH_2CH_3), 2.85(d, J 1.5 Hz, azir. H trans to CO_2CH_3), 1.77 (s, C-CH_3) and 1.42 (t, J 7.3 Hz, CH_2CH_3); minor invertomer 8.19(dd, J 8 and 1.5 Hz, 5-H), 7.7(dd, J 8.1 and 7.3 Hz, 7-H), 7.64 (8-H), 7.42(dd, J 8 and 7.3 Hz, 6-H), 3.84 (s, CO_2CH_3), 3.4br (s, azir. H trans to CO_2CH_3), 2.77 (2 x dq, J 17 and 7.3 Hz, CH_2CH_3), 1.73 (s, C-CH_3), and 1.39 (t, J 7.3 Hz, CH_2CH_3)(the signal for azir. H cis to CO_2Me was obscured.

Oxidation of (22) (105 mg) using LTA (260 mg) in dichloromethane (1 ml) containing α-methylene -γ-butyrolactone (5) (98 µl; 2 mol equiv.) and methyl methacrylate (119 µl; 2 mol equiv.) using the method given above and examination of the crude product by n.m.r. showed the aziridines (35) and (36) to be present in a 2.2:1 ratio respectively from comparison of the signals at 4.98 (for (35)) and 3.56, 3.84 (for (36)).

An analogous oxidation using N-aminophthalimide (4) in the presence of the same two alkenes gave the corresponding aziridines (33)[10] and (34)[2] in a 2.1:1 ratio.

Oxidation of N-Aminophthalimide (4) with LTA at Low Temperature. - To a suspension of N-aminophthalimide (300 mg) in dry dichloromethane (5 ml) at -50°C was added a solution of LTA (863 mg) in dry dichloromethane (35 ml) dropwise over 3½ h. After stirring for a further 30 min; the insoluble lead di-acetate was separated and styrene (3 mol equiv.) added to the filtrate, maintaining the temperature at < -45°C. The solution was allowed to warm to ambient with stirring then washed successively with aqueous sodium hydrogen carbonate solution and water, dried and evaporated. Rapid chromatography over silica and elution with light petroleum - ethyl acetate gave the aziridine (32)[2] (41%).

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