Oxidation of 3-aminoquinazolinones with lead tetraacetate. A novel synthesis of naphtho-fused azirino-pyrazolo- and 1,4,5-oxadiazepino-quinazolinones

J. Chem. Research (S), 2002, 205–208
J. Chem. Research (M), 2002, 0541–0552

A.M. Sh. El-Sharief*, Y.A. Ammar, M.A. Zahran and A.H. Ali

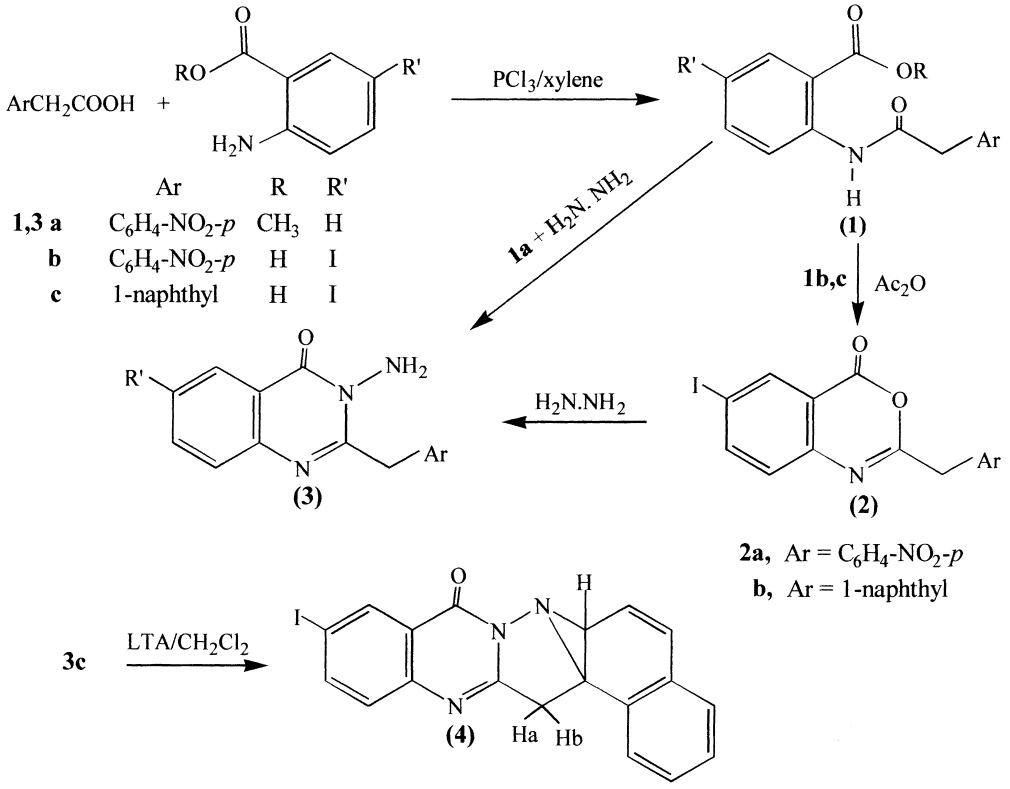
Chemistry Department, Faculty of Science, Al-Azhar University, Nasr City, Cairo, Egypt

Oxidation of 3-aminoquinazolin-4(3*H*)-one derivative **3c** using lead tetraacetate in methylene chloride at –20°C gave aziridine **4,** while reaction of **7b** and **7c** under similar conditions gave the oxadiazepine derivatives 7*H*-naphtho[2′,1′:6,7][1,4,5]oxadiazepino[3,4-*b*]quinazolin-9(15*H*)-one (**9**) and 16*H*-naphtho[1′,2′:6,7][1,4,5]oxadiazepino[3,4-*b*]quinazolin-14(8*H*)-one (**11**), respectively.

Keywords: fused quinazolinones, pyrazoles, intramolecular aziridination, lead(IV) acetate, nitrenes and nitrenoids

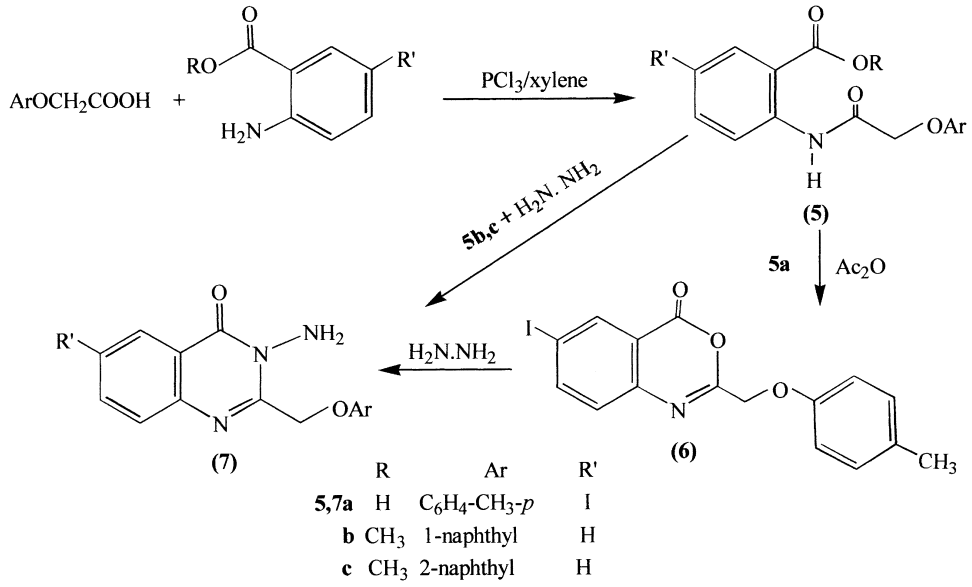
The use of 3-acetoxyaminoquinazolin-4(3*H*)-one derivatives as aziridinating agents is advantageous.[1,2] Previously, aziridination was carried out by lead tetraacetate (LTA) oxidation of the 3-amino heterocycle in the presence of an alkene. The ability to prepare stable solutions of 3-acetoxyaminoquinazolinones at <–10°C allows alkenes to be aziridinated which would otherwise be attacked by LTA.[3] Atkinson[4] has shown that evidence for an approach of QNHOAc and the alkene double bond in nearly parallel planes comes from a study of intramolecular aziridination using 3-acetoxyaminoquinazolinones. The changes in double bond reactivity in the bifurcated side chain with tether length suggested that reaction was better accommodated via a three-atom rather than a two-atom chain.[5] In continuation of our work on quinazoline chemistry,[6-9] we planned to prepare different types of 3-aminoquinazolinones and to study the effect of LTA on such compounds.

Thus, interaction of arylacetyl chlorides with either methyl anthranilate or anthranilic acid derivatives gave the amides **1a–c**. Refluxing of the amides **1b,c** in acetic anhydride effected cyclisation to give 6-iodo-2-(1-arylmethyl)-3,1-benzoxazin-4(3*H*)-ones **2a,b**. 3-Amino-2-(1-arylmethyl) quinazolin-4(3*H*)-one derivatives **3a–c** were obtained by reflux of **1a** and **2a,b** with hydrazine hydrate in *n*-butanol for 4–6 h. Reaction of 3-aminoquinazolin-4(3*H*)-one derivative **3c** with LTA at –20°C gave the aziridine derivative **4** (Scheme 1) whose structure was confirmed by IR, ^{1}H NMR, mass spectra and elemental analysis; the mass spectrum exhibited a molecular ion peak together with a base peak at *m*/*z* 425 and the IR spectrum showed the disappearance of the NH_2 group. Unfortunately, interaction of **3a** and **3b** with LTA under the same conditions resulted in deamination, which can be attributed to the presence of an electron-withdrawing group (NO_2).

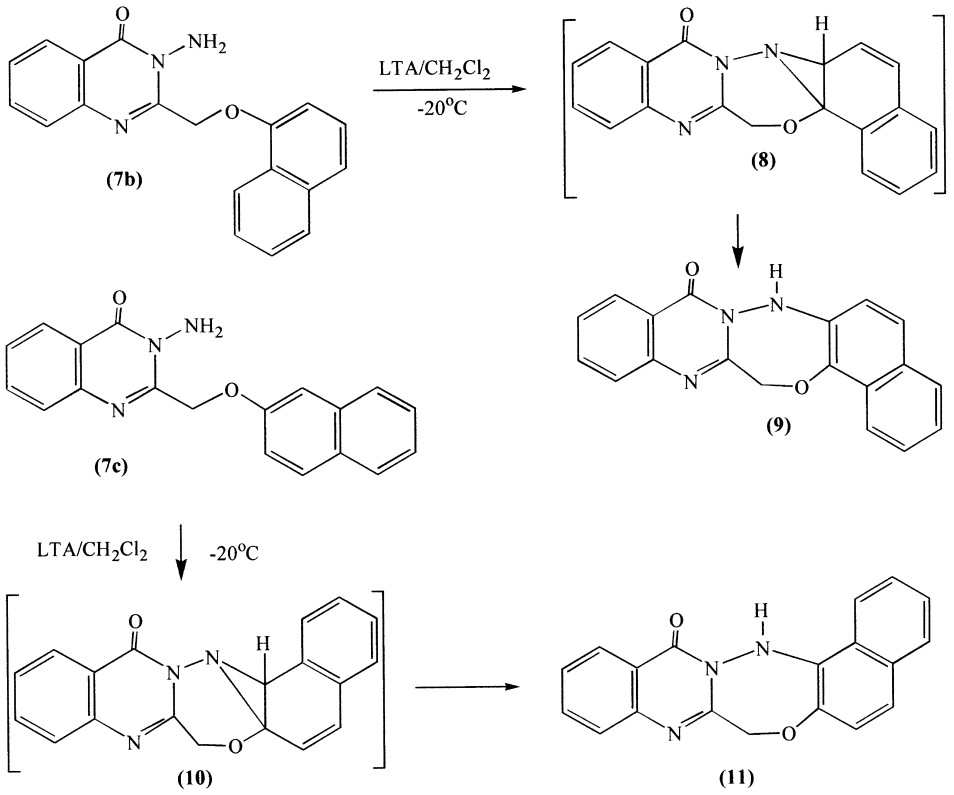


Scheme 1

* To receive any correspondence E-mail: m-elgaby@hotmail.com



Scheme 2



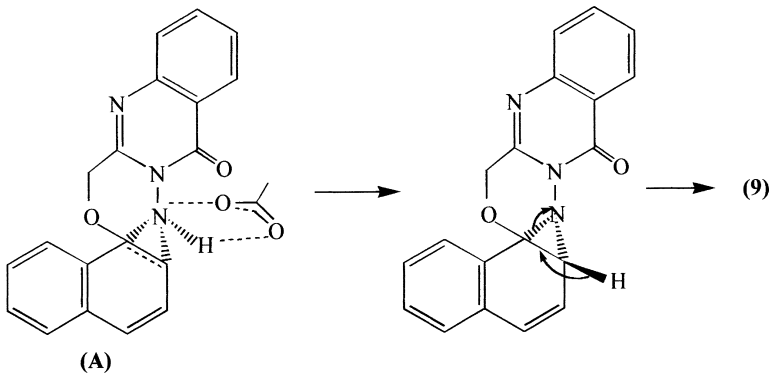
Scheme 3

Likewise, the reaction of the iodoanthranilic acid or methyl anthranilate with the aryloxyacetyl chloride took place successfully to give the amides **5a–c**, the benzoxazine **6** and finally the 3-aminoquinazoline derivatives **7a–c** containing an oxygen atom in the tether (Scheme 2).

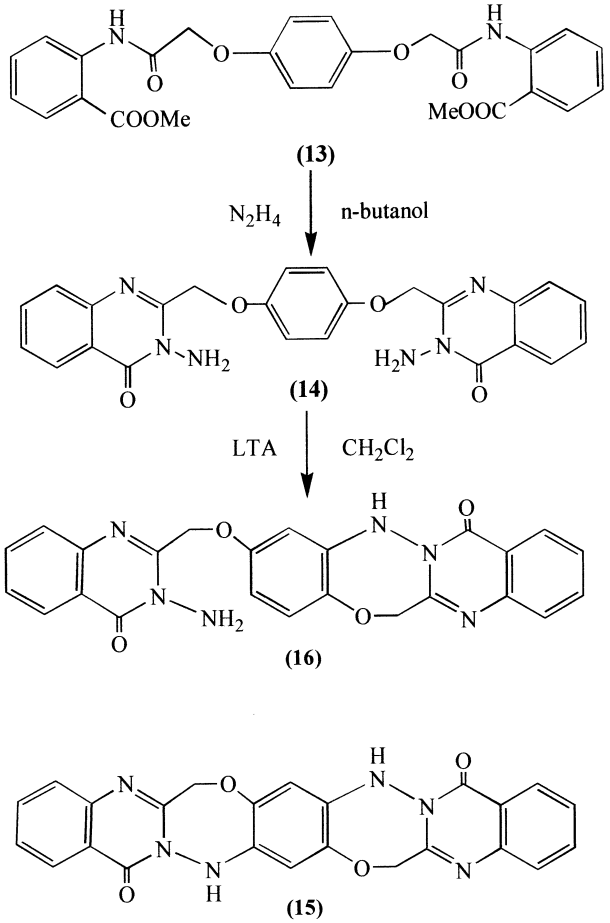
Oxidation of the 3-amino-2-(naphthyloxymethyl) quinazolin-4(3*H*)-ones **7b** and **7c** with LTA in methylene chloride under the same conditions caused cyclisation to give the oxadiazepino derivatives **9** and **11** (Scheme 3).

The formation of the oxadiazepines **9** and **11** instead of the expected aziridines **8** and **10** was explained by the formation of the transition state **A**. The oxygen is unable to stabilise the developing charge on the conjugate carbon and hence serves only to deactivate the charge on the naphthalene ring (Scheme 4).

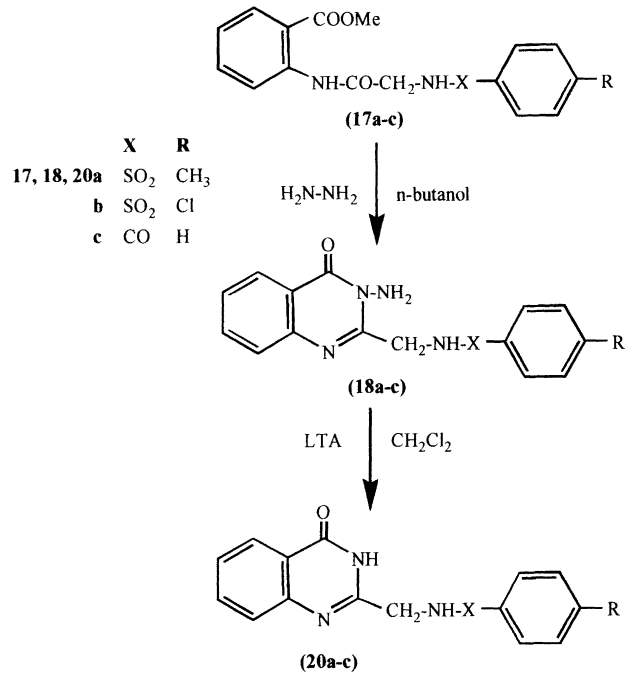
As an extension to this work we planned to synthesise a compound containing two 3-aminoquinazoline moieties linked through one aromatic ring and to study the effect of intramolecular aziridination on such a compound. The bis(aminoquinazolinone) **14** was synthesised by standard methods. Reaction of **14** with two equivalents of LTA in methylene chloride as solvent in the presence of trifluoroacetic acidled to the incorporation of only one NH_2 group into the fused ring system, to yield the 3-(3-amino-4-oxoquinazolin-2-



Scheme 4



Scheme 5



Scheme 7

ylmethylenoxy)-5*H*-quinazolino[2,3-*b*][5,1,2] benzoxadiazepin-7(13*H*)-one **16** (Scheme 5). None of the expected heptacyclic product **15** was found. The low yield of **16** prevented us from attempting the reaction of this product with LTA.

Some oxidation trials with 3-aminoquinazolinones: In continuation of our interest in oxidation we report here some aziridination trials with various *N*-aminoquinazolinones using LTA.

The starting materials **18a–c** were prepared via reaction of either a substituted phenylsulfonylglycine or hippuric acid with methyl anthranilate in presence of PCl_3 to give the respective amides **17a–c** which were refluxed with hydrazine hydrate in *n*-butanol to yield the *N*-amino compounds **18**.

Intramolecular aziridination by oxidation of **18a–c** with LTA was unsuccessful; instead deamination took place to give 2-(4′-substituted phenylsulfonamidomethyl)quinazolin-4(3*H*)-ones (**20a–c**) respectively, owing to the presence of the electron-withdrawing groups (SO_2NH, CONH) which served to deactivate the ring towards aziridination (Scheme 7).

Many thanks are due to Dr. R.S. Atkinson, Department of Organic Chemistry, The University, Leicester LE1 7RH (UK) for his great help in running the ^{1}H NMR data of most compounds and for his advice during the progress of this work.

Techniques used: IR, ^{1}H NMR, MS
Schemes: 7
References: 11
Table 1: Elemental analytical data for the compounds described in this paper

Received 5 May 2001; accepted 29 January 2002
Paper 01/898

References

1 R.S. Atkinson and C.W. Rees, *J. Chem. Soc*., 1969, 772; D.J. Anderson, D.C. Horwell, T.L.Gilchrist and C.W. Rees*, J. Chem. Soc.,* 1970, 576.

2 R.S. Atkinson and B.J. Kelly, *J. Chem. Soc. Perkin Trans. 1*, 1989, 1627.

3 R.S. Atkinson and B.J. Kelly, *J. Chem. Soc. Perkin Trans. 1*, 1989, 1515.

4 R.S. Atkinson, *Tetrahedron* 1999, **55**, 1519-1559.

5 R.S. Atkinson and J.M. Grimshire, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1135.

6 Y.A. Mohamed, A.M. Sh. El-Sharief, Y.A. Ammar, N.A.Amin, and M.M. Ghorab, *J. Serb. Chem. Soc*., 1989, **54,** 179.

7 Y.A. Ammar, A.M. Sh. El-Sharief, Y.A. Mohamed, and H.A. Ahmad, *J. Serb. Chem. Soc.,* 1987, **52**, 633.

8 A.A. Hassanein, O.M. Nassar, M.A. Zahran, and A.H. Ali, *Al-Azhar Bull. Sci*., 1997, **8**, 2 (Dec.), 417.

9 A.M. Sh. El-Sharief, Y.A.Ammar M.A. Zahran, A.H. Ali, and M.S.A. El-Gaby, *Molecules,* 2000, **6**, 267-278.

10 J.T. Gupton and A. Shah, *Synth. Commun*., 1989, **19**, 1875.

11 R.S. Atkinson and N. A. Gawad, *J. Chem.Soc., Perkin Trans. 1,* 1985, 335.

12 V. Ettel, J. Weichet and J. Specil, *Coll. Czech. Chem. Comm.* 1951, **15**, 1050-68; 1952, *C.A.* **47**, 7077.