Reactions of Enol Ethers and Silyl Ketene Acetals with 3-Acetoxyamino-2-ethylquinazolin-4(3*H*)-one: Cleavage of N–N Bonds in 3-Alkylaminoquinazolin-4(3*H*)-ones

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Treatment of enol ethers and silyl ketene acetals with the *N*-acetoxyaminoquinazolone **1** gives α-aminoaldehyde, α-aminoketone or α-aminoacid derivatives in good yields: cleavage of the N–N bond in 3-alkylaminoquinazolinone derivatives can be accomplished by samarium diiodide in tetrahydrofuran.

We have recently shown that a solution of the *N*-acetoxyaminoquinazolone **1** is obtained by oxidation of the *N*-aminoquinazolone **2** with lead tetraacetate (LTA) at −20 °C and that **1** is the intermediate in oxidative addition of **2** to alkenes.[1]

Whereas previously, oxidation of **2** in the presence of alkenes required the latter to be stable to LTA, the use of solutions of **1** is not subject to this constraint.

We describe here the reaction of **1** with enol ethers and silyl ketene acetals: both these classes of nucleophilic alkenes are rapidly attacked by LTA in preference to, or in competition with, oxidation of **2**.

Reaction of **1** with ethyl vinyl ether (1.5 mol equiv.) gave the acetal **3** (69%) m.p. 53–55 °C having ν_{max}/cm^{-1} (Nujol) 1740s, and 1675s and δ ($CDCl_3$ 300 MHz) 8.23, 7.74, 7.67 and 7.45 (4 × ArH), 6.02 (t, *J* 5 Hz, CH_2CH), 5.74 (t, *J* 7.1 Hz, exch. D_2O, NH), 3.82 (dq, *J* 9 and 7 Hz, CH_3HCHO), 3.65 (dq, *J* 9 and 7 Hz, CH_3HCHO), 3.21 (m, br, HCHNH), 3.17 (m, br, HCHNH), 3.03 (q, br, *J* 7 Hz, CH_2CH_3), 2.11 (s, $OCOCH_3$), 1.38 (t, *J* 7 Hz, CH_2CH_3), and 1.23 (t, *J* 7 Hz, CH_3CH_2).

We presume that the aziridine **4** is an intermediate in this reaction but is ring-opened by the acid, which is present in the solution both as a by-product in the formation of **1** and in the formation of **4** from **1**.

Reaction of the enol silyl ether **5**[2] with **1** gave the chloroketone **6** (58%) identical with a sample isolated from attempted aziridination of the diethoxyphosphoryl analogue of **5** in the presence of trifluoroacetic acid.[3] Attempted chromatography of **6** over silica gel brought about its conversion to the iminoketone **7** m.p. 76–78 °C presumably *via* a Favorskii-type elimination of HCl.

The products from reaction of **1** with various silyl ketene acetals are shown in Scheme 1.

In the reactions to give **8**–**10**, an excess of silyl ketene acetal was used to allow for the reaction of the latter with any acetic acid that is present (see above). If 2,6-di-*tert*-butyl-4-methylpyridine (2 equiv.) was added instead and only 1.5 mol equiv. of the ketene acetal used, the product **8** was isolated in 63% yield based on the *N*-aminoquinazolone **2** used.

The structures of these aminoesters were confirmed by their spectral data:† in the NMR spectrum of **9** at −90 °C in CD_2Cl_2 sharp signals from two N–N bond rotamers (ratio 3 : 1) are present.

We have found that the N–N bond in compounds resembling **8**–**10** can be reductively cleaved using samarium diiodide in tetrahydrofuran in the presence of *tert*-butyl alcohol (Scheme 1).[4]

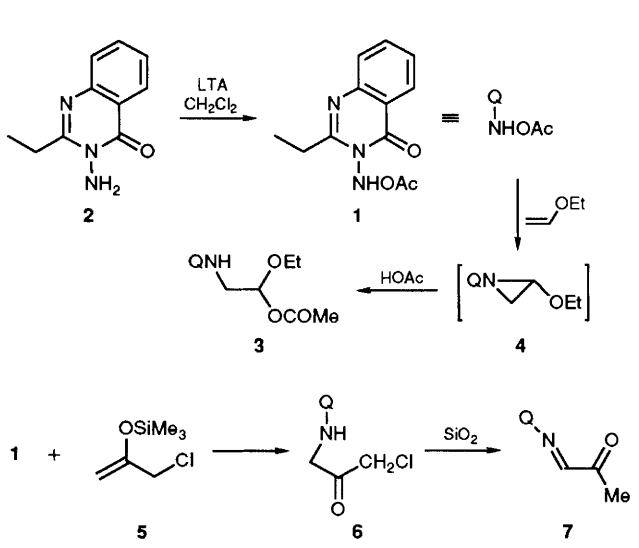
In the first example, reduction takes place even at −78 °C and is complete within 30 min. For ease of isolation, the product was benzoylated *in situ* and methyl *N*-benzoylglycinate, identical with an authentic sample, was obtained in 82% yield by chromatography.

The second example in Scheme 1 shows that the success of this reduction is not dependent on the presence of the ester function although a higher temperature is required in this case.

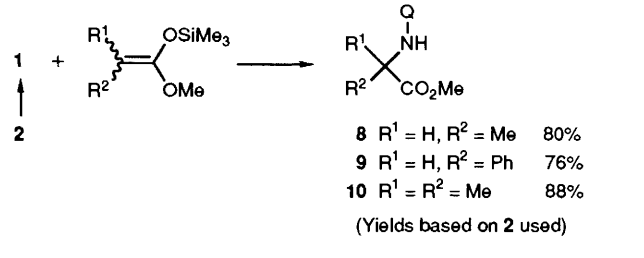
Amination of silyl ketene acetals has been accomplished with other electrophilic nitrogen species including nitroso compounds,[5] diazonium salts[6] and nitrenes.[7] Reaction of chiral enolates and chiral silyl ketene acetals with azodiesters has been successfully used to synthesise aminoacids with high levels of enantiomeric excess.[8]

We have prepared the *N*-aminoquinazolone **11** (Scheme 2) in enantiopure form from (+)-lactic acid. Oxidation with LTA at −20 °C gives the corresponding *N*-acetoxyamino derivative (*cf.* **1**), which reacts with the silyl ketene acetal **12** to give a 4 : 1 ratio of diastereoisomers of **13**, which were separated by crystallisation followed by chromatography.

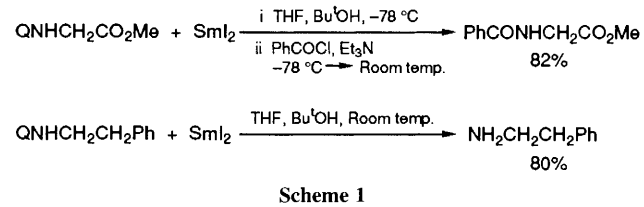
Reduction of the major diastereoisomer of **13** with samarium diiodide gives the methyl ester of α-phenylalanine **14**, which was shown to be enantiopure by comparison of the



2 **1** **3** **4** **5** **6** **7**

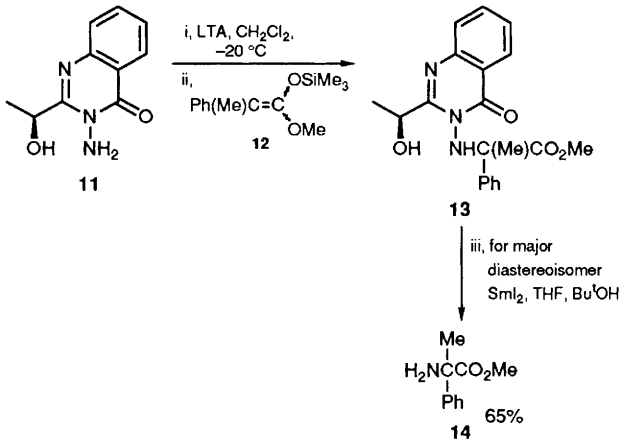


8 R^1 = H, R^2 = Me 80%
9 R^1 = H, R^2 = Ph 76%
10 R^1 = R^2 = Me 88%
(Yields based on **2** used)



Scheme 1

† Satisfactory analytical and spectroscopic data were obtained for all new compounds.



Scheme 2

NMR spectrum of its derived Mosher amide with that of the corresponding amides prepared from racemic material.[9] From its positive sign of rotation, **14** has the *S* configuration.[10]

This route to enantiopure aminoester **14** differs from those in ref. 8 in that the inducing chiral centre is contained in the electrophilic nitrogen species. Removal of this inducing chiral centre is an accompaniment to the necessary deprotection of the amino group.

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References

1 R. S. Atkinson and B. J. Kelly, *J. Chem. Soc., Chem. Commun.*, 1987, 1362.
2 H. Sakurai, A. Shirahata, Y. Araki and A. Hosomi, *Tetrahedron Lett.*, 1980, 2325.
3 R. S. Atkinson and B. J. Kelly, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1627.
4 J. A. Soderquist, *Aldrich Chim. Acta*, 1991, **24**, 15.
5 T. Sasaki, K. Mori and M. Ohno, *Synthesis*, 1985, 280.
6 T. Kakahura and M. Tanaka, *J. Chem. Soc., Chem. Commun.*, 1985, 1309.
7 M. A. Loreto, L. Pellacani and R. A. Tardella, *J. Chem. Res (S)*, 1988, 304; M. Mitani, O. Tachizawa, H. Takeuchi and K. Koyama, *Chem. Lett.*, 1987, 1029; S. Fioravanti, M. A. Loreto, L. Pellacani and P. A. Tardella, *Tetrahedron Asymm.*, 1990, 931.
8 C. Gennari, L. Colombo and G. Bertolini, *J. Am. Chem. Soc.*, 1986, **108**, 6394; D. A. Evans, T. C. Britton, R. L. Dorow and J. F. Dellaria, *J. Am. Chem. Soc.*, 1986, **108**, 6395; L. A. Trimble and J. C. Vederas, *J. Am. Chem. Soc.*, 1986, **108**, 6397; W. Oppolzer and R. Moretti, *Helv. Chim. Acta*, 1986, **69**, 1923.
9 J. A. Dale, D. L. Dull and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.
10 S. Yamada, S. Terashima and K. Achiwa, *Chem. Pharm. Bull. Jpn.*, 1966, **14**, 800.