Pergamon

Tetrahedron Letters, Vol. 35, No. 29, pp. 5293-5296, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00984-8

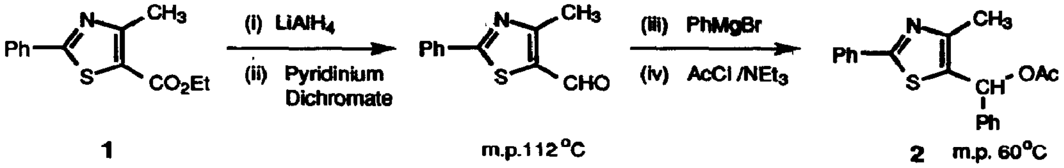
Thiazole *o*-Quinodimethanes: The Generation, Electrocyclisation and Diels-Alder Reactions of Phenyl Substituted Derivatives

Andrew J. Potter and Richard C. Storr*

School of Chemistry, The University of Liverpool, P.O. Box 147, Liverpool L69 3BX

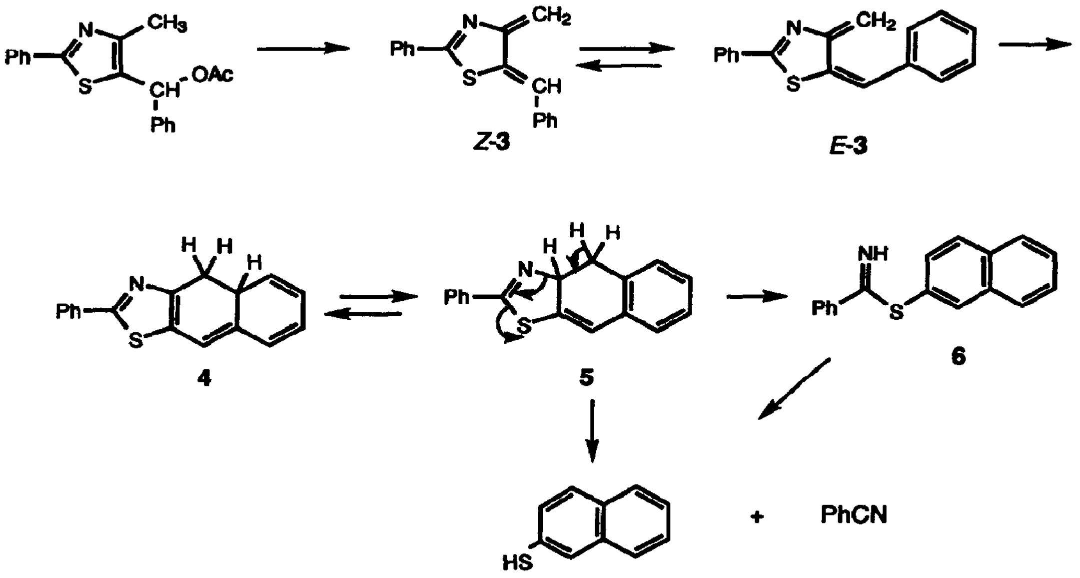
Abstract: *α-(2-Phenyl-4-methylthiazol-5-yl)-α-phenylmethyl acetate 2 undergoes thermal elimination of acetic acid to give the o-quinodimethane 3. In solution this can be intercepted in Diels-Alder reactions but under flash pyrolytic conditions naphthalene-2-thiol is formed by electrocyclisation and fragmentation.*

Flash pyrolytic generation of heterocyclic *o*-quinodimethanes bearing an aryl or heteroaryl substituent on the exocyclic methylene group appears to offer considerable potential for the formation of fused heterocycles. For example, aryl and heteroaryl substituted *o*-azaquinodimethanes give acridine analogues[1] and phenyl substituted thiophene *o*-quinodimethanes give naphthothiophenes by electrocyclisation and dehydrogenation.[2] As part of our studies of the scope of this process we have investigated the flash pyrolysis of the thiazole **2** in the expectation that it would lead to naphthothiazoles. In the event, an alternative pathway was observed which reveals a severe limitation for this approach to fused heterocycles.

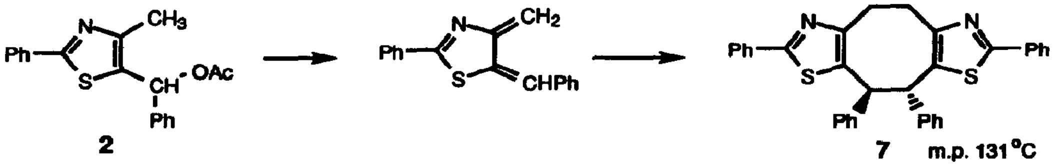


The thiazole **2** was readily obtained as shown from the known ester **1** [3] in 31% overall yield.[4] Flash pyrolysis was carried out by sublimation through a hot tube (750°C/10^{-3}mm Hg) with gentle heating of the thiazole to volatilise it at a rate of ca. 100 mg/hour. Some decomposition occurred before sublimation leaving an involatile residue so the total yield of pyrolysate was variable (50-80%) but the mass balance of residue and pyrolysate was good. In addition to acetic acid, the pyrolysate contained two major products shown by comparison with authentic samples to be naphthalene-2-thiol and benzonitrile; these were formed in equimolar amounts.[5] A small amount of 2-naphthyl disulfide was also detected; this presumably arises from oxidation of the thiol during handling of the pyrolysate. Significantly, no naphthothiazoles were detected.

A possible mechanism for the formation of the thiol is as follows. Thermal elimination of acetic acid leads to the *o*-quinodimethane **3** which under the high temperature gas phase conditions exists as an equilibrating mixture of *E* and *Z* isomers. The dihydro-naphthothiazole **4** formed by electrocyclisation of the *E* quinodimethane can equilibrate with **5** by an allowed 1,5 H shift and this is set up to undergo aromatisation by an elimination leading to the thiol with formation of benzonitrile either directly or via an intermediate thioimide **6**. In principle, such eliminative aromatisation can occur with other heterocyclic *o*-quinodimethanes having a potential nitrile fragment, for example oxazoles and imidazoles, and so the flash pyrolytic approach to their fused derivatives may be precluded.[6]

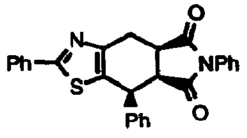
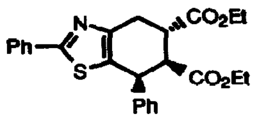
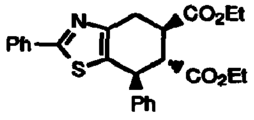
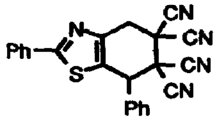
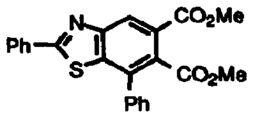


The involatile residue from the sublimation was investigated and shown to be virtually pure head to head 4 + 4 dimer of thiazole *o*-quinodimethane **7**. This was also formed in high yield on heating the thiazole acetate **2** alone or in dichlorobenzene at 180°C for 7h.[7] The head to head structure follows clearly from the NMR spectrum which shows a singlet for the methine protons at 5.25ppm and an AA'BB' system for the methylene groups at 3.85 and 3.62ppm. Only one diastereoisomer, presumably the *trans*, is observed.



Heating **2** in dichlorobenzene (180°C, ca 1h.) in the presence of a range of dienophiles gave the Diels-Alder adducts shown in the Table. With N-phenylmaleimide a single adduct **8** was formed for which the stereochemistry shown in the Table was confirmed by X-ray crystallography. This stereochemistry results from *endo* addition of the imide to the less sterically hindered Z *o*-quinodimethane which is produced preferentially in the elimination of acetic acid. With diethyl fumarate, the nmr spectrum of the adduct fraction showed two pairs of ethyl groups in a ratio $\sim$1:2, consistent with the presence of two adducts, **9** and **10** respectively,[8] which are diastereoisomeric about carbons 6 and 7. The absence of more ethyl groups suggests that the two ester groups are *trans* either as a result of stereospecific addition or thermodynamic control. In the case of dimethyl acetylenedicarboxylate only the dehydrogenated adduct was observed. The yield was only moderate because of extensive decomposition of the acetylene at the high temperatures required.

TABLE

Dienophile	Adduct	Yield %
N-Phenylmaleimide	 **8**	87[a]
Diethyl fumarate	 **9** (minor)  **10** (major)	80[b]
Tetracyanoethylene		33[c]
Dimethyl acetylenedicarboxylate		30[d]

[a] m.p. 228 °C

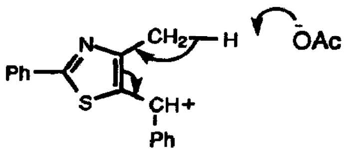
[b] inseparable mixture 9 :10 = 1 : 2

[c] m.p. 178 °C

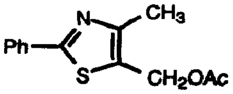
[d] m.p. 40 °C

These results [9] strongly implicate the formation of the thiazole *o*-quinodimethane **3** in solution by thermal elimination of acetic acid. This relatively mild 1,4-elimination of acetic acid from **2** is not catalysed by base (DBU) and is probably the result of ionisation of the diarylmethyl acetate and deprotonation of the resulting carbenium ion **11** by the acetate counterion. The primary acetate **12** was recovered unchanged from heating in *o*-dichlorobenzene at 180°C for 48h indicating that a carbenium ion stabilising group is necessary.

In this simple scheme the formation of the free *o*-quinodimethane is rate determining and the subsequent dimerisation or Diels-Alder additions should be relatively very fast. However, the rate of disappearance of **2** is significantly greater in the presence of dienophiles than in their absence (rate of formation of Diels-Alder adducts is greater than rate of formation of dimer). This dependence of the rate of elimination on dienophile could be accommodated if the elimination of acetic acid were reversible. However, recovered acetate from the incomplete decomposition of **2** in the presence of CD_3CO_2D showed that exchange of the acetoxy group occurred but failed to reveal any exchange of the 4-methyl hydrogens. The full implications of these intriguing observations are currently under investigation.



11



12

Acknowledgements

We thank SERC for a studentship (A.J.P.)

References and Notes

1. Bowen, R.D.; Davies, D.E.; Fishwick, C.W.G.; Glasbey, T.O.; Noyce, S. J .; Storr, R. C. *Tetrahedron Lett.*, 1982, 4501; Fishwick, C.W.G.; Storr, R. C.; Manley, P. W.; *J. C. S. Chem. Comm.*, 1984 ,1304
2. Chauhan, P.M.S.; Jenkins, G.; Walker, S.M.; Storr, R.C. *Tetrahedron Lett.*, **1988**, *29*, 117.
3. Csávassy, G.; Gyorfi, Z.A. *Liebigs Ann. Chem.*, **1974**, 1195.
4. All new compounds gave satisfactory analytical, mass spectral and spectral data
5. Naphthalene-2-thiol (90%) was isolated by column chromatography and the yield of benzonitrile (80%) was obtained by quantitative G.C. analysis. Both yields are corrected and apply to the material actually passing through the pyrolysis tube.
6. Preliminary experiments indicate that this is indeed the case for the corresponding oxazole which gives 2-naphthol on FVP.
7. No trace of naphthalene-2-thiol or naphthothiazole was detected.
8. Assigned on the basis of the magnitude of the vicinal coupling of the protons α to the phenyl group: 6 Hz for **9** and 10 Hz for **10**.
9. The corresponding α-phenyl oxazole and thiophene acetates give analogous adducts under the same conditions.

(*Received in UK* 26 *April* 1994; *revised* 17 *May* 1994; *accepted* 20 *May* 1994)