Tetrahedron Letters,Vol.24,No.46,pp 5147-5150,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF NOVEL 8H-THIENO[2,3-d]AZEPINES BY PHOTOLYSIS OF 6-AZIDO-2,3-DIHYDROBENZO[b]THIOPHEN

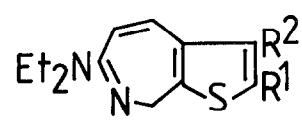
Christopher M. Daly, Brian Iddon*, and Hans Suschitzky
The Ramage Laboratories, Department of Chemistry and Applied Chemistry,
University of Salford, Salford M5 4WT

Ulrich Jordis and Fritz Sauter*
Institut für Organische Chemie, Technische Universität Wien,
Getreidemarkt 9, A-1060 Wien, Austria

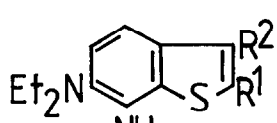
Summary: Reduction of 6-amino-2,3-dihydrobenzo[b]thiophen-1,1-dioxide with DIBAL-H gave 6-amino-2,3-dihydrobenzo[b]thiophen from which the title azide was prepared; its photolysis in diethylamine-THF gave 7-diethylamino-2,3-dihydro-8H-thieno[2,3-d]azepine which was converted into 7-diethylamino-8H-thieno[2,3-d]azepine.

Photolysis of several 6-azidobenzo[b]thiophens in an excess of diethylamine gives either the corresponding 6-diethylamino-8H-thieno[2,3-c]azepine (1) or o-diamine (2), or a mixture of both, depending on the substituents, R^1 and R^2.[1] Other bicyclic heterocycles (e.g. 6-azidobenzothiazoles) behave similarly.[2-4] Products such as (1) and (2) are formed probably via the intermediacy of nitrenes, azirines, and aziridines, e.g. (3) and (4), although the intermediacy of didehydrothienoazepines, such as (5), cannot be ruled out.[4,5] Localisation of π-electrons (bond fixation) in the 6,7-bonds of the azides leading to (3) appears to be an important controlling factor in our reactions, since products arising from isomeric azirines (6) have not been detected, which may be due to a loss of aromaticity in the thiophen ring of these intermediates (6) [this is true also of (5)]. In order to test the importance of bond fixation it was of interest to study the photolysis of 6-azido-2,3-dihydrobenzo[b]thiophen in diethylamine.

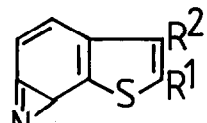
Nitrogen functionality is introduced into the 6-position of benzo[b]thiophen readily and selectively by oxidation to the 1,1-dioxide followed by nitration, which gives a high yield



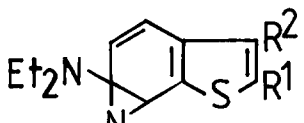
(1)



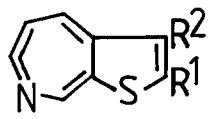
(2)



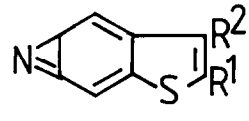
(3)



(4)



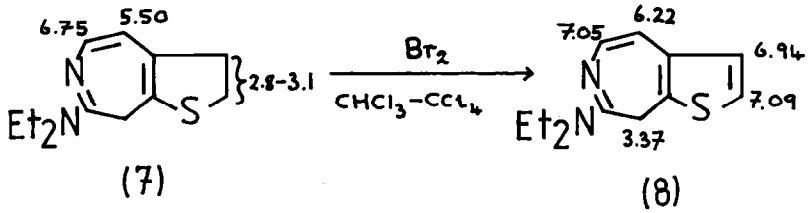
(5)



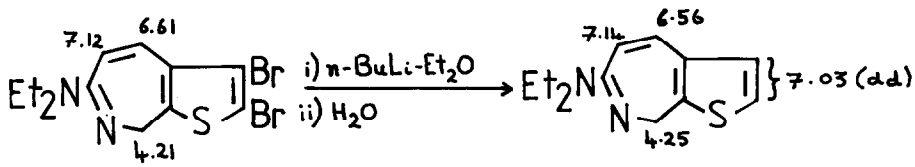
(6)

of 6-nitrobenzo[b]thiophen-1,1-dioxide.[1,6] This compound can be converted into 6-aminobenzo-[b]thiophen-1,1-dioxide or its 2,3-dihydro-derivative but our previous attempts to reduce the sulphone moiety in these products have proved unsuccessful.[1,6] Reduction of 6-nitrobenzo[b]-thiophen-1,1-dioxide to 6-amino-2,3-dihydrobenzo[b]thiophen with lithium aluminium hydride has been reported[7] but in our hands this reaction gave a complex micture (t.l.c.). However, DIBAL-H (purchased from Aldrich as a 25% w/w solution in toluene) reduces a suspension of 6-amino-2,3-dihydrobenzo[b]thiophen-1,1-dioxide[6] in toluene cleanly and in high yield, to give 6-amino-2,3-dihydrobenzo[b]thiophen (73%), b.p. (Kugelrohr apparatus) 125-130°C at 0.004-0.10 mmHg, m.p. 69-71°C. From this amine we prepared 6-azido-2,3-dihydrobenzo[b]-thiophen (96%) in the usual way[8] as a yellow oil which can be purified by distillation, b.p. 79-82°C (Kugelrohr apparatus) at 0.02 mmHg, or by chromatography on alumina (elution with ether), $\nu_{max.}$ (film) 2125 cm^{-1} (N_3).[9] We have kept this azide at -20°C for up to 12 months.

Photolysis of 6-azido-2,3-dihydrobenzo[b]thiophen (1.0 g) in a mixture of diethylamine (20 ml) and THF (130 ml) (this solvent behaves as a singlet nitrene stabilizer[4]) for approximately 7 h under nitrogen (reaction followed by disappearance of azide stretching frequency in the i.r.) and removal of the volatiles by distillation under reduced pressure gave an oil which was chromatographed on alumina. Light petroleum (b.p. 40-60°C) gave starting material (0.1 g, 10% recovery) whilst light petroleum-diethyl ether (9:1) gave 7-diethylamino-2,3-dihydro-8H-thieno[2,3-d]azepine (7) (0.55 g, 55% based on a starting material consumed) as an oil, $\nu_{max.}$ (film) 1590 cm^{-1} (C=N). We assigned earlier the structures of the isomeric 8H-thieno[2,3-c]azepines, e.g. (9), on the basis that the protons of a methylene group adjacent to an amidine C-atom resonate at a higher field than those in one next to an amidine N-atom.[10] Further evidence for structure (9) was provided by addition



(7) (8)



(9) (10)

to the ^{1}H n.m.r. sample of Eu(fod)$_3$, which resulted in a considerable downfield shift of the signal at δ 4.21 p.p.m. for the methylene group at position 8 owing to complexation of the shift reagent mainly with the ring N-atom, whilst the signal for the olefinic proton (H-5) at δ 7.12 was shifted no more than the signal for the side-chain methylene group. For compound (7) the reverse is true, namely that the signal for the methylene group at position 8 is at higher field (a multiplet appears at δ 3.40 p.p.m. which consists of this signal overlapping with the quartet for the side-chain methylene protons) and addition of Eu(fod)$_3$ to the ^{1}H n.m.r. sample produces a small downfield shift of the signal for this methylene group while the olefinic protons (H-5) signal at δ 6.75 p.p.m. suffers a considerable downfield shift.

To confirm structures (7) and (9) we prepared compounds (8) and (10). Their ^{1}H n.m.r. data (see formulae) are consistent with the structures assigned. A significant difference between the pairs of compounds (7) and (8) and (9) and (10) lies in the coupling constants for their olefinic protons, namely J = 8.0 and 12.0 Hz, respectively.

Treatment of compound (7) with bromine in trichloromethane-tetrachloromethane at low temperatures gave a low yield (10%) of 7-diethylamino-8H-thieno[2,3-d]azepine (8), m.p. 56.5-57.5°C, whilst debromination of compound (9)[1] using n-butyl-lithium gave the isomeric compound, 6-diethylamino-8H-thieno[2,3-c]azepine (10) (37% based on starting material consumed), as a pale yellow oil, together with starting material (9) (32% recovery).

The ring-expansion of 6-azido-2,3-dihydrobenzo[b]thiophen to the 8H-thienoazepine (7)

is the first example in our series of a reaction proceeding via an azirine intermediate of type (6) rather than type (3).

We thank the S.E.R.C. for a studentship (to CMD) and The British Council for travel grants which have enabled this collaboration to take place.

References

1. B. Iddon, M.W. Pickering, H. Suschitzky, and D.S. Taylor, J. Chem. Soc., Perkin Trans. I, 1975, 1686.

2. P.T. Gallagher, B. Iddon, and H. Suschitzky, J. Chem. Soc., Perkin Trans. I, 1980, 2362.

3. B. Iddon, O. Meth-Cohn, E.F.V. Scriven, H. Suschitzky, and P.T. Gallagher, Angew. Chem., Int. Ed. Engl., 1979, 18, 900.

4. E.F.V. Scriven, in "Reactive Intermediates", ed. R.A. Abramovitch, Plenum, New York, 1982, Vol. 2, ch. 1, p.1.

5. I.R. Dunkin and P.C.P. Thomson, J. Chem. Soc., Chem. Commun., 1980, 499.

6. F. Sauter, Monatsh.Chem., 1968, 99, 1591.

7. A. Kh. Kadyrov, Dokl. Akad. Nauk Tadzh SSR, 1979, 22, 667 (Chem. Abs., 1980, 93, 7930).

8. e.g., see B. Iddon, H. Suschitzky, D.S. Taylor, and M.W. Pickering, J. Chem. Soc., Perkin Trans. I, 1974, 575.

9. All new compounds have been characterised by ^{1}H n.m.r. spectroscopy and elemental analysis.

10. W. von E. Doering and R.A. Odum, Tetrahedron, 1966, 22, 81.

(Received in UK 7 September 1983)