Tetrahedron Letters, Vol.32, No.20, pp 2225-2228, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

A Selective Electrochemical Way to Functionalized 6H-1,3-Thiazines and /or Pyrroles.

Abdesselam ABOUELFIDA[a], Michel JUBAULT[b]*, Jean-Paul PRADERE[a], Jean-Claude ROZE[a] and André TALLEC[c]

[a] Laboratoire de Synthèse Organique , URA-C.N.R.S. N° 475, 2 rue de la Houssinière, 44072 Nantes Cédex 03, France

[b] Laboratoire de Synthèse Organique et d'Electrochimie, URA-C.N.R.S. N° 439, 2 Boulevard Lavoisier, 49045 Angers cédex, France

[c] Laboratoire d'Electrochimie, URA-C.N.R.S. N° 439, Campus de Beaulieu , 35042 Rennes Cédex, France.

Key-words : *1-Thia-3-Aza-Butadienes ; Hetero Diels-Alder ; Electrochemical Reductions ; 4H- and 6H-Thiazines ; functionalized Pyrroles.*

Abstract : *4H-1,3-thiazines, easily prepared from 1-thia-3-azabutadienes, appear electroactive in protic medium. Controlled potential electroreductions of 4H-1,3-thiazines lead either to substituted 6H-1,3-thiazines or to pyrroles according to the nature of the C-4 substituent and the acidity of the supporting electrolyte.*

Hetero Diels-Alder reactions have been extensively applied in heterocyclic chemistry during the last few years[1,2]. For instance regioselective synthesis of 6H-1,3-thiazines by cycloaddition of electrophilic dienophiles on 1-thia-3-azabutadienes were reported[3]. However, reaction of methyl acrylate or dimethyl maleate with 4-dimethylamino-4-ethoxycarbonyl-1-thia-3-azabutadiene does not take place easily and require modifications for multistep syntheses[4] ; moreover the access to 6H-1,3-thiazines bearing an alkoxy substituent at C-2 and/or an ester group at C-4 requires high pressure[5] or acid catalysis .[3]

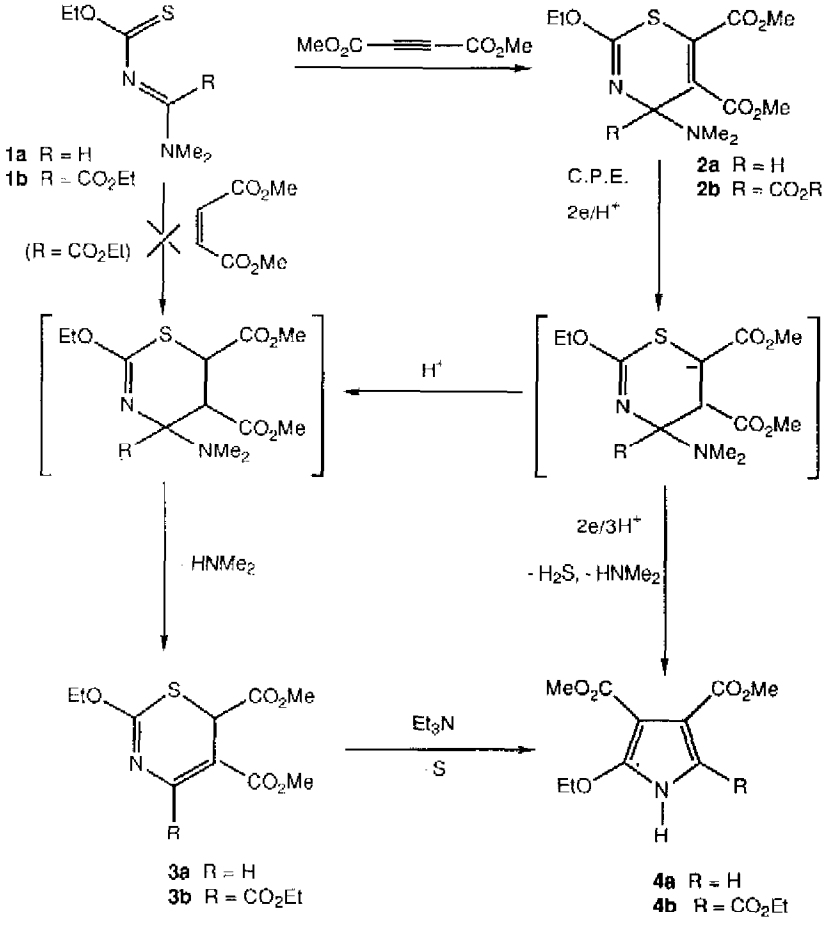
We now report a mild and efficient two-steps procedure (cycloaddition-reduction), starting from heterodienes **1a** or **1b**, which leads selectively either to functionalized 6H-1,3-thiazines or to pyrroles depending on electrochemical conditions.

The first step involves a 4+2 cycloaddition of dimethyl acetylenedicarboxylate with an equimolecular amount of 1-thia-3-azabutadienes[6] **1a** or **1b** in methylene chloride, and affords 2-ethoxy-4H-1,3-thiazines **2a** or **2b** (respectively 73% and 35 % isolated yield).[7]

The second step involves an electrochemical reduction which is strongly pH-dependent :

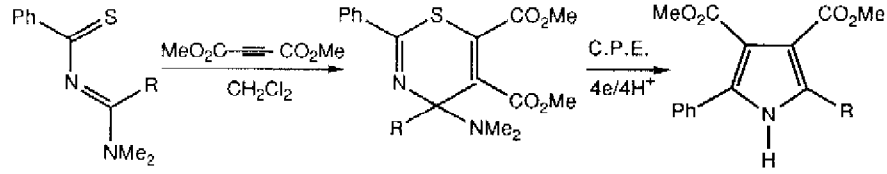
i) Controlled potential electrolysis [C.P.E. in Scheme][8] of **2a** in ammoniacal buffer (0.5 mol.l^{-1} NH_4Cl and NH_3 + ethanol)at a mercury cathode (E = -1.1 V/SCE) leads to the corresponding 6H-1,3-thiazine **3a** (90 % yield)[7].

ii) In acidic medium (0.5 mol.l^{-1} H_2SO_4 + ethanol) electroreduction of **2a** (E = -0.75 V/SCE) gives rise to the substituted pyrrole **4a** (40 % yield) and, similary, electrolysis of **2b** (E = -0.8 V/SCE) affords the tetrasubstituted pyrrole **4b** (46% yield). Moreover, a mixture of pyrrole **4b** (15% yield) and 6H-1,3-thiazine **3b** (45 % yield)[7] is obtained when C.P.E. is performed in acetic buffer (pH = 5 ; E = -0.75 V/SCE). At last, we have controlled that cathodic reduction of **3b**, never leads to the pyrrole **4b** whatever the electrolytic medium. Otherwise **4b** can also be obtained (87 % yield) from the reaction of the 6H-1,3-thiazine **3b** with triethylamine in THF (cf. scheme). The mechanism of this reaction is reminiscent of the one involved in the ring contraction of substituted 6H-1,3-thiazines under basic conditions[9] with sulfur elimination[10,11]. The two steps procedure (electrochemical reduction followed by Et_3N treatment) appears to be a preparative way to pyrrolic compound **4b** from 2b (54 % yield).



As suggested in the scheme, in all cases, the first step of the reduction takes place at the activated $C^5=C^6$ double bond. The intermediate carbanion can either lose dimethylamine after protonation with formation of 6H-1,3-thiazines **3a, 3b** or give rise to a ring contraction-reduction (elimination of hydrogen sulfide and dimethylamine) with formation of pyrroles **4a, 4b** in very acidic medium.

The described procedure seems to provide a general way to functionalized pyrroles : thus, 4+2 cycloaddition of 1-thia-3-azabutadienes[6] **5a** or **5b** with dimethyl acetylenedicarboxylate, in methylene chloride, gives 2-phenyl-4H-1,3-thiazines **6a** or **6b** ; electroreduction of **6a** (E = -0.7 V/SCE) or **6b** (E = -0.55 V/SCE) in 0.5 mol.l^{-1} H_2SO_4 + ethanol, leads to the corresponding pyrrole **7a** (88% yield) or **7b** (76 % yield)[7]. Moreover, access to the pyrrole tricarboxylate **7b** by electoreductive ring contraction of 4H-1,3-thiazine **6b** appears to be easier than the previously reported procedure.[12]



5a R = H
5b R = CO_2Et

6a R = H
6b R = CO_2Et

7a R = H
7b R = CO_2Et

Further investigations are necessary in order to explain the mechanism of this reductive ring contraction. It can probably be compared with the mechanism of formation of dimethyl pyrrole-2,5-dicarboxylates which occurs when dimethyl-1,2-diazine-3,6-dicarboxylates are reduced with zinc in acetic medium.[13]

References and Notes

1 Boger D.L. and Weinreb S.M. in "*Hetero Diels-Alder Methodology in Organic Synthesis*" Ed. H.H. Wasserman Vol. 47 of Organic Chemistry ; Academic Press Inc.: New-York. 1987; pp. 214-224.

2 Weinreb S.M. and Scola P.M. *Chem. Rev.* **1989**, *89*, 1525-1534.

3 Pradère J.P., Rozé J.C., Quiniou H., Danion-Bougot R., Danion D. and Toupet L. *Can. J. Chem.* **1986**, *64*, 597-602.

4 Bakasse M., Reliquet A., Reliquet F., Duguay G. and Quiniou H. *J. Org. Chem.*, **1989**, *54*, 2889-2893.

5 Cellerin C., Tea C.G., Pradère J.P., Guingant A. and Guenot P. *Sulfur Letters.* **1988**, *8*, 205-209.

6 For preparation of compounds **1a**, **1b**, **5a** and **5b** see Tea C.G., Chehna M., Pradère J.P., Duguay G. and Toupet L. *Phosphorus and Sulfur* . **1986**, *27*, 327-339.

7 All new compounds gave satisfactory combustion analysis : **2a**- m.p. : 48-50°C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 5.5 (s, H^4); ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 78.7 (C^4, J_{C-H} = 84.5 Hz), 128.6 and 128.8 (C^5 and C^6), 152.8 (C^2), 162.9 and 167.2(CO_2^-); - **2b** ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 86.5 (C^4), 128.7 and 131.9 (C^5 and C^6), 154.2 (C^2), 161.9, 166.2 and 167.5 (CO_2^-). Compounds **3a** - m.p. : 36 °C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 4.75 (s, H^6), 7.82 (s, H^4); ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 39.4 (C^6, J_{C-H} = 143.6 Hz), 104.6 (C^5), 146.9 (C^4, J_{C-H} = 183.2 Hz), 164.2, 166.0 and 169.8(C^2 and CO_2^-). **3b** - m.p. : 81 °C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 4.85 (s, H^6) ; ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 40.3 (C^6, J_{C-H} = 145.1 Hz), 101.9 (C^5), 149.7 (C^4), 164.5, 165.4 165.9 and 169.1 (C^2 and CO_2^-). Compounds **4a** - m.p. : 96 °C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 6.92 (d, H^5, J_{H-NH} = 3Hz), 9.76 (NH); ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 97.9, 114.1,117.9 149.7 and 164.9(C^2 to C^5 and CO_2^-) ; IR (KBr) ν_{NH} = 3255 cm^{-1}. **4b** - m.p. : 128 °C; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 9.6 (NH); ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 98.9, 111.5, 123.8 and 150.8 (C^2 to C^5), 159.9, 162.6 and 165.9 (CO_2^-) ; IR (KBr) ν_{NH} = 3276 cm^{-1}. **7a** - m.p. : 96°C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 10.39 (se, NH) ; ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 112.9, 115.3, 124.6, 127.0, 127.8, 128.2, 130.6 and 134.1 (C^2 to C^4 and Ph), 164.3 and 167.3(CO_2^-) ; IR (KBr) ν_{NH} = 3306 cm^{-1}. **7b** - m.p. : 106 °C ; ^{1}H-N.M.R. : δ ppm ($CDCl_3$) 9.9 (NH) ; ^{13}C-N.M.R. : δ ppm ($CDCl_3$) 112.2, 119.9, 124.9 128.2, 129.6, 130.3, 131.6 and 140.3(C^2 to C^5 and Ph), 160.1, 163.4 and 166.1 (CO_2^-) ; IR (KBr) ν_{NH} = 3310 cm^{-1}. For compound **6a** and **6b** see Tea C.G., Pradère J.P. and Quiniou H. *J. Org. Chem.* **1985**, *50*, 1545-1547.

8 For a typical experimental procedure in electrolysis, see Bujoli B., Jubault M., Rozé J.C. and Tallec A. *Tetrahedron* . **1987**, *43* , 2709-2719.

9 Tea C.G., Pradère J.P., Quiniou H. and Toupet L. *J. Chem. Soc. Perkin Trans I* **1985**, pp. 1875-1878.

10 Schmidt R.R. and Dimmler M. *Chem. Ber.* **1975**, *108*., 6-16.

11 Spitzner R. and Schroth W. *Tetrahedron Lett.* **1985**, *26*, 3971-3974.

12 Grigg R., Gunaratne H.Q.N. and Kemp J. *Tetrahedron* . **1990**, *46*, 6467-6482.

13 Boger D.L. *Bull. Soc. Chim. Belg.*. **1990**, *99*, 599-615.

(Received in France 7 January 1991)