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SELECTIVE REDUCTION OF 4H-1,3-THIAZINE-4-ONES : EASY ACCESS TO SUBSTITUTED 6H-1,3-THIAZINES

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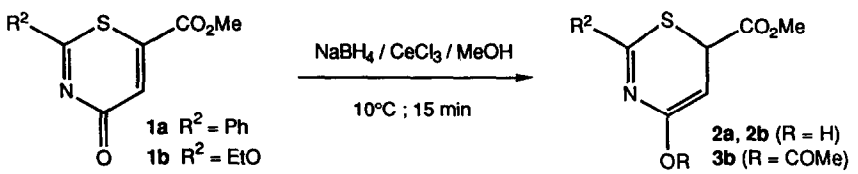
Abstract : Selective reduction of 4H-1,3-thiazine-4-ones leads to new substituted 6H-1,3-thiazines. The isomerisation from 6- to 5-methoxycarbonyl-6H-1,3-thiazines via substituted 4-acetoxy-1-thia-3-aza-butadienes by a cycloreversion-cycloaddition process can be performed in one step.

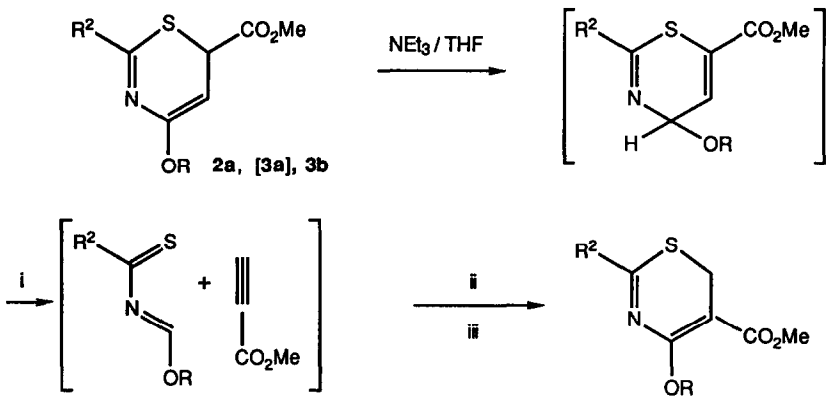
Access to 2,3-dihydro- and tetrahydro-4H-1,3-thiazine-4-ones from substituted 4H-1,3-thiazine-4-ones[1] precursors **1** by reduction of the unsaturated systems has been described recently[2]. We now report the possibility of isolating substituted 6H-1,3-thiazines with a carboxylate at position 6 or 5 by selective reduction of 4H-1,3-thiazine-4-ones. The course of the reaction depends on the nature of the reducing agent. Isomerisation of the carboxylate group occurs from the 6 to the 5-position on these thiazinic derivatives in basic medium. This can be explained by involving a 4-acetoxy-1-thia-3-aza-butadiene intermediate generated by cycloreversion which is then trapped by a regiospecific (4+2)-cycloaddition.

Selective reduction of the substituted 4H-1,3-thiazine-4-ones (**1a**, R^2=Ph ; **1b**, R^2=EtO ; 1 mmol), carried out using sodium borohydride (2 mmol) and $CeCl_3$ (2 mmol) in methanolic solution[3], gives the new substituted 6-methoxycarbonyl-4-hydroxy-6H-1,3-thiazines **2a** (50 %) and **2b** (57 %). The 4-acetoxy-6-methoxycarbonyl-6H-1,3-thiazine **3b** (78 %)[4] is easily obtained by the action of acetyl chloride (1.5 mmol) and triethylamine (3 mmol) on **2b** (1 mmol).



Treatment of compound **2a** under the same conditions leads to rearrangement to 5-acetoxy-6-methoxycarbonyl-6H-1,3-thiazine **4a** (43 %) without isolation of intermediates. The mechanism of these reactions can be corroborated by rearrangement of the 2,4,6-substituted 6H-1,3-thiazine **3b** to the 2,4,5-substituted 6H-1,3-thiazine **4b** in excellent yield (87 %)[4] using triethylamine in tetrahydrofuran.

Access to the thiazinic derivatives **4** from compounds **3** can be explained by the following process : rearrangement in basic medium to yield substituted 4-acetoxy-4H-1,3-thiazine followed by cycloreversion to a 4-acetoxy-1-thia-3-aza-butadiene which is trapped immediatly by the electrophilic dienophile released (cycloaddition 4+2). The last step leads to **4a** or **4b** with the expected regiospecificity.



i) cycloreversion ; ii) cycloaddition ; iii) transposition

4a, 4b (R = COMe)

The substituted 6H-1,3-thiazine **4a** (52 %) from **1a** can be obtained using Zn (4 eq.) in acetic acid (5 ml) and acetic anhydride (1.5 ml). Use of acetic anhydride allows trapping of the hydroxyl group of the 4H-1,3-thiazinic intermediate from the cycloreversion-cycloaddition process[5].

References and Notes

1.G.A. Mironova, V.N. Kuklin, E.N. Kirillova and B.A. Ivin, *Khim. Geterotsikl. Soedin.* **1**, 3 (1986) and references cited therein.

2.A. Abouelfida, J.C. Rozé, J.P. Pradère and M. Jubault, *Phosphorus, Sulfur and Silicon*, in press.

3.A.L. Gemal and J.L. Luche, *J. Am. Chem. Soc.*, **103**, 5454 (1981).

4.Satisfactory spectroscopic data and elementary analysis were obtained for all new compounds - **2a** (m.p. : 154°C) : ^{1}H-NMR ($CDCl_3$) d 6.6 and 6.45 (H^5 and H^6, d, J = 2.2 Hz); ^{13}C-NMR ($CDCl_3$) d 111.5 and 102.6 (C^5 and C^6) ; IR (CCl_4) 3380 cm^{-1} (OH). **2b** (m.p. : 95°C) : ^{1}H-NMR ($CDCl_3$) d 6.35 and 6.2 (H^5 and H^6, d, J = 1.76 Hz); ^{13}C-NMR ($CDCl_3$) d 111.9 (C^5, J_{C-H} = 168.5 Hz), 95.9 (C^6, J_{C-H} = 162.7 Hz), IR (CCl_4) 3220 cm^{-1} (OH). **3b** (m.p. : 43°C) : ^{1}H-NMR ($CDCl_3$) d 7.2 and 6.3 (H^5 and H^6, d, J = 1.75 Hz), ^{13}C-NMR ($CDCl_3$) d 112.8 (C^5, J_{C-H} = 169.3 Hz), 94.5 (C^6, J_{C-H} = 168.5 Hz), IR (CCl_4) 1749 and 1735 cm^{-1} (CO). **4a** (oil) : ^{1}H-NMR ($CDCl_3$) d 3.67 (2H, s) ^{13}C-NMR ($CDCl_3$) d 151.7 (C^4), 114.2 (C^5), 30.5 (C^6, J_{C-H} = 131.9 Hz), IR (CCl_4) 1782 and 1735 cm^{-1} (CO). **4b** (m.p. : 40°C) : ^{1}H-NMR ($CDCl_3$) d 3.51 (2H, s), ^{13}C-NMR ($CDCl_3$) d 145.0 and 104.8 (C^4 and C^5), 30.2 (C^6,J_{C-H} = 131.5 Hz), IR (CCl_4) 1782 and 1746 cm^{-1}.

5.For cycloreversion-cycloaddition process of analogous substituted 4-dimethylamino-1-thia-3-aza-butadienes see : C.G. Tea, J.P. Pradère and H. Quiniou, *J. Org. Chem.*, **50**, 1545 (1985).

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