Tetrahedron Letters Vol. 21, pp 3795 - 3796 0040-4039/80/0922-3795$02.00/0

SYNTHESIS OF HETEROCYCLES : SYNTHESIS OF 4H-1,4-BENZOTHIAZINES

R.P.Soni* and M.L.Jain
Department of Chemistry, University of Jodhpur, Jodhpur, India

Summary:- A new synthesis of fluorinated 4H-1,4-benzothiazines is being reported for the first time, obtained by condensing O-aminobenzenethiol with fluorinated β-diketones. An oxidative cyclisation mechanism, involving an intramolecular nucleophilic attack in an intermediate enamine system is suggested.

This paper describes the synthesis of some new fluorinated 4H-1,4-benzothiazines. These compounds are of interest as potential pharmaceutical agents. The aminothiol normally reacts with β-diketones or β-oxoesters to give dihydrobenzothiazoles or bisdihydrobenzothiazoles[1].

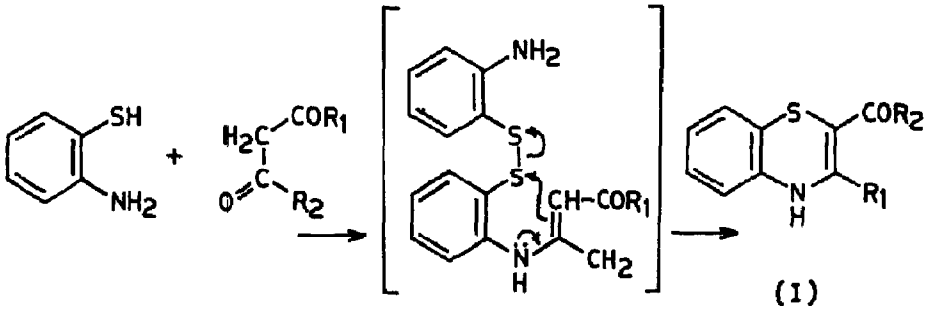
A persual of the literature reveals scanty information on fluorinated benzothiazines and it appears worthwhile to synthesise the title compounds in view of the interesting changes associated with the introduction of fluorinated group[2].

In this communication we wish to report for the first time a new method for the synthesis of fluorinated 4H-1,4-benzothiazines (I). O-aminobenzenethiol (0.01 mole), the fluorinated β-diketones[3] (0.01 mole) and dimethylsulphoxide (5 ml) were heated at 140°C for 30-50 min. The mixture was concentrated under reduced pressure to give I (yield 60-70%).

A known product Ethyl 3-methyl-4H-1,4-benzothiazine -2-carboxylate has also been synthesised by this method. m.p. 144-145°C (lit[4] 144-145°C). The identity of this synthesised product with an authentic sample was further shown by Cotlc, comparison of their IR and H-NMR spectra.

The physical data of I : IR(KBr)NH (3310), C=O (1725), C-F and C-F_3 (1115 cm^{-1}). UV λ_{max}^{EtOH} 245, 260, 320 nm. 100 MHz PMR Ia; (DMSO + $CDCl_3$) δ 8.3 (4H aromatic), δ 10.9 (1H-NH). ^{19}F NMR : δ 4.0 (-CF_3), δ -3.0 (-$COCF_3$).

Reaction Mechanism: The reaction is considered to proceed via the intermediate, which is cyclised to final product (I) by scission of the S-S bond[5-6] upon attack by the nucleophilic enamine system.



(I)

(INTERMEDIATE)

(a) $R_1 = R_2 = CF_3$; (b) $R_1 = C_6H_5$, $R_2 = CF_3$

(c) $R_1 = C_6H_4F(p)$; $R_2 = CF_3$; (d) $R_1 = C_6H_4F(p)$, $R_2 = C_2H_5$

Extension of this reaction to other active compounds and its detailed synthetic utility are in progress.

Acknowledgement: The authors are grateful to the Director, CDRI, Lucknow for analysis and spectral data.

References:

1. A.I.Kiprinov and U.A.Portnyagina, Zhur. Obshcheikhim. 25, 2257 (1955).
2. R.Filler, Chem. Tech., 4, 752 (1974).
3. E.I.Anderson, J.E.Casy (Jr), L.C.Greene, J.J.Lafferty and H.E.Reiff, J. Mednl. Chem., 7, 259 (1964).
4. Y.Maki, M.Suzuki and T.Yamada, Chem. and Pharm. Bull. (Japan), 14, 770 (1966).
5. F.M.Moracci, M.Cardellini, F.Liberatore, P.Marchini, G.Liso and U.Gulini, Internat. J. Sulphur Chem., 8, 341 (1973).
6. T.Fujiwara, K.Hata and T.Kojima, Chem. Letters, 207 (1973).
7. All new compounds had correct elemental analysis.

(Received in UK 7 July 1980)