SYNTHESIS OF SOME NEW BENZOTHIAZOLOTRIAZINE DERIVATIVES

Prashant Kriplani, Pawan Swarnkar and K.G.Ojha*
Department of Pure and Applied Chemistry,M.D.S.University Ajmer-305 009(India)

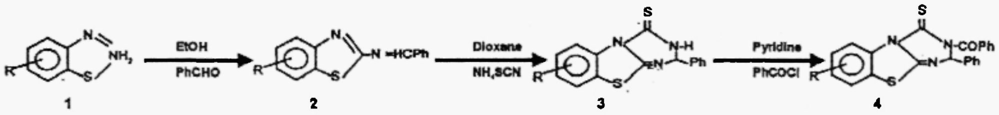
Abstract : Synthesis of some new benzothiazolotriazine derivatives is reported .2-Amino-6-substitutedbenzothiazoles 1 on treatment with benzaldehyde afforded 2-benzylidenoimino-6-substitutedbenzothiazoles 2 which underwent cyclisation with ammoniumthiocyanate in dioxane to give 2-phenylbenzothiazolo[3,2-α]-s-triazine-4-[3H] thione 3.Compound 3 with benzoyl chloride in anhydrous pyridine gave 2-phenyl –3-(benzoyl)benzothiazolo [3,2-α]-s-triazine-4- thione 4 in good yields.The structures of all these compounds have been supported by their elemental analysis and their spectral data.

Introduction

A number of compounds with benzothiazole moiety are known to possess biological and pharmacological activities[1-2] such as fungicidal, antibacterial, antituberculotic antirhumetic, anti-inflammatory, antiallergic, insecticidal, anthelmintics and herbicidal. Benzothiazoles also show significant effects against cancer[3-5].Triazine derivatives are also associated with broad spectrum antiviral activity[6-8] against numerous viruses viz.*Rauscher viruses Leukemia,Moloney viruses Leukemia,Rhinovirus type-2,influenza virus type-2,Vaccinia viruses,Vasicular stomatitis and Measules viruses*.In addition recently anti-HIV activity of some known nucleoside s-triazine derivatives against susceptible human host cell (CEM cell line) over a wide range of concentrations has been demonstrated[9].In view of the activities exhibit by benzothiazole derivatives and triazine derivatives,it was considered of interest to couple these rings together with the hope of achieving compounds with enhanced biological activities and therefore it has been planned to synthesise some new derivatives of benzothiazolotriazine ring system.

Results and Discussions

The required 2-amino-6-substitutedbenzothiazoles 1 were prepared by following the methods reported earlier[10 11]. Compounds 1 were condensed with benzaldehyde to get Schiff base 2 and were cyclised to s-triazines 3 in the presence of ammoniumthiocynate in dioxane.Compounds 3 on treatment with benzoyl chloride in the presence of anhydrous pyridine gave 2-phenyl–3-(benzoyl)benzothiazolo[3,2-α]-s-triazine-4- thione 4 . (Scheme-1)



Scheme-1

IR spectra of **2a-d** exhibited sharp peak in the region of 1640-1680 cm^{-1} due to C=N stretching vibrations.The absorption bands between 3050-3180 are due to =C-H stretching and between 2800-2930cm^{-1} are due to -C-H stretching.The absorption bands in the region 1535-1630 cm^{-1} are assigned for Ar C-C stretching. IR spectra of **3a-d** exhibited sharp peak in the region of 1150-1177 cm^{-1} is due to C=S stretching and in the region of 3400-3450cm^{-1} is due to –N-H stretching. The absorption bands between 3050-3100 are due to =C-H stretching.The absorption bands in the region 1480-1620 cm^{-1} are assigned for Ar C-C stretching.

IR spectra of **4a-d** exhibited sharp peak in the region of 1150-1177 cm^{-1} due to C=S stretching and in the region of 1690-1650 cm^{-1} due to C=O stretching. The absorption bands between 3050-3100 are due to =C-H stretching and bands in the region 1480-1620 cm^{-1} are due to Ar C-C stretching.The physical data of these compounds are reported in **Table-1.**

Table-1: Characterisation data of compounds:

Compound	**R**	**M.P.(°C)**	**Yield (%)**	**Mol. Formula**	**% Found/(Cald.)**		
					C	**N**	**H**
2a	-Cl	160	66	$C_{14}H_9N_2SCl$	60.09 (61.65)	11.11 (10.27)	0.028 (0.03)
2b	-Br	190	60	$C_{14}H_9N_2SBr$	51.96 (52.99)	7.98 (8.83)	0.018 (0.02)
2c	$-NO_2$	260	58	$C_{14}H_9N_3SO_2$	59.23 (59.36)	15.10 (14.84)	0.028 (0.03)
2d*	$-OC_2H_5$	120	75	$C_{16}H_{14}N_2SO$	68.01 (68.08)	9.98 (9.92)	0.041 (0.04)
3a	-Cl	110	70	$C_{15}H_{10}N_3S_2Cl$	55.54 (54.29)	13.48 (12.66)	0.027 (0.03)
3b	-Br	125	55	$C_{15}H_{10}N_2S_2Br$	47.79 (47.87)	11.14 (11.17)	0.018 (0.02)
3c	$-NO_2$	285	49	$C_{15}H_{10}N_4S_2O_2$	51.99 (52.63)	16.23 (16.37)	0.029 (0.03)
3d*	$-OC_2H_5$	165	68	$C_{17}H_{15}N_3S_2O$	56.88 (59.82)	12.34 (12.31)	0.039 (0.04)
4a	-Cl	136	63	$C_{22}H_{14}N_3S_2Cl$	61.74 (62.93)	9.97 (10.01)	0.04 (0.03)
4b	-Br	105	46	$C_{22}H_{14}N_3S_2Br$	55.67 (56.89)	9.10 (9.05)	0.026 (0.03)
4c	$-NO_2$	298	55	$C_{22}H_{14}N_4S_2O_2$	60.28 (61.39)	12.76 (13.02)	0.031 (0.03)
4d*	$-OC_2H_5$	130	70	$C_{24}H_{119}N_3S_2O$	66.78 (67.13)	9.65 (9.79)	0.034 (0.04)

*^{1}**HNMR** ($CDCl_3$)(δ in ppm)
2d: 1.4(t,3H,CH_3),4.0(q,2H,OCH_2),5.5(s,1H,=CHPh),7.25-7.50(m,8H,ArH)
3d:1.3(t,3H,CH_3),4.2(q,2H,OCH_2),6.9(s,1H,=CHPh),7.28-8.09(m,8H,ArH),3.9(s,1H,NH)
4d:1.4(t,3H,CH_3),4.0(q,2H,OCH_2),5.7(s,1H,=CHPh),7.25-8.0(m,13H,ArH).

Experimental

All the melting points are uncorrected.The purity of synthesised compounds has been checked by thin layer chromatography.IR spectra are recorded on FT-IR Perkin-Elmer (model 157) spectrophotometer(ν_{max} in cm^{-1}) using KBr disc.^1H NMR spectra are recorded in $CDCl_3$ on a varian A_{60} D instrument (300MHZ) using TMS as internal standard.The chemical shifts are reported as parts per million (ppm).

Synthesis of 2-benzylidenoimino-6-substituted benzothiazoles 2

A mixture of 2-amino-6-substituted benzothiazoles 1 (0.01mol) and benzaldehyde (0.01 mol) in anhydrous ethanol (25ml) was refluxed for 4 hours Ethanol was distilled off and the residual solid was washed with water,dried in vacuo and recrystallized from ethanol.

Synthesis of 2-phenyl benzothiazolo [3,2-α]-s-triazine-4-[3H] thione 3

2-Benzylidenoimino-6-substituted benzothiazoles 2 (0.01mol) and ammoniumthiocyanate (0.02 mol) were dissolved in 1,4-dioxane(20ml)by gentle warming and shaking.The reaction mixture was stirred for half an hour at room temprature and subsequently refluxed for 6 hours.Solvent was removed by distillation and the solid thus obtained was washed repeatedly with water,dried in vacuo and recrystallised from ethanol.

Synthesis of 2-phenyl –3-(benzoyl)benzothiazolo [3,2-α]-s-triazine-4- thione 4

2-Phenyl benzothiazolo [3,2-α]-s-triazine-4-[3H] thione 3 (0.005 mol)was dissolved in minimum quantity of anhydrous pyridine (10ml).To this solution was added benzoyl chloride (0.01mol) dropwise with constant shakingin cold conditions.The reaction mixture was further stirred for 1 hour and poured into ice cold acidified water.The solid separated out was filtered and washed repeatedly with water,dried in vacuo and recrystallised from ethanol.

Acknowledgements

The authors are thankful to the Head of Department of Pure and applied Chemistry M.D.S.University, Ajmer,Rajasthan(India) for providing necessary laboratory facilities and to the Director CDRI, Lucknow (India) for providing spectral data. Authors also express thanks to CSIR New Delhi (India) for providing JRF to one of them (P.Kriplani).

References

1. K. Bujdakova and E. Sidoova, *Pharmazie.* **49**, 375 (1994).
2. T. Toda and T. Tokunaga. *Chemotherapy* **7,** 332 (1959); S. Akerteldt. *J. Med. Chem. Soc.* **13** 1012 (1970).

3. R.C. Schnur, R.J. Gallaschnum, D.H. Singleton, M. Grissom, D.E. Sloan, P. Goodwin, P.A. Mcniff, A.F. Fliri, F.M. Mangano, T.H. Olson and V.A. Pollack. *J. Med. Chem.* **34** 1975 (1991)
4. W. Goeffrey, B. Tracey D., D. Patrizia, S. Angela, S. Dong-fang,W. Andrew D. and S. Malcolm and F.G. Biorg. *Med.Chem.Lett.*, **10(5)**, 513 (2000).
5. B. Valerie, B. Thierry, G. Jerome, L. Stephane and P. Bruno, *Eur. J. Med. Chem.*, **34(12)** 1053 (1999).
6. M.S. Poonian, E.F. Nowoswiat, J.F. Blount and M.J. Karmer, *J. Med. Chem.* **19** 1017 (1976).
7. V.S. Misra, S. Dhar and B.L. Chowdhary, *Pharmazie*, **33** 790 (1976).
8. M.A.Chirigos, J.B. Moloney, S.R. Humphreys, N. Mantle and A.Goldin, *Cancer Res.*, **21**, 803 (1961).
9. N.C. Desai, J.J. Bhatt, D.R. Shah, P.B. Trivedi and N.K. Undavia, *Ind. J. Exp. Biol.* **34** 584 (1996)
10. R.R.Gupta, S.K. Jain and K.G. Ojha. *Synth.Commun.* **9(6)** 457 (1979).
11. R.R. Gupta, K.G. Ojha and M. Kumar. *J.Heterocycl. Chem.* **17**,1325 (1980).