SYNTHESIS OF 5-(4-METHYL PHENYL SULFONYL)–10-PHENYL-6,7-DIHYDRO-5H-BENZO [B] IMIDAZO [2',1':2,3][1,3] THIAZOLO [4,5-D]AZEPIN-5-YL[+]

Lingaiah Nagarapu* and Kalyani Sambaru
Division of Organic Chemistry – II, Indian Institute of Chemical Technology, Hyderabad 500007,India

Abstract: Synthesis, physical and analytical properties of 5-(4-methyl phenylsulfonyl) –10-phenyl-6,7- dihydro-5H-benzo[b] imidazo [2',1':2,3] [1,3] thiazolo [4,5-d] azepin –5-yl derivatives are described. These new compounds were prepared by the reaction of 2-(2-imino-6- (4-methyl phenyl sulfonyl)-1,4,5,6-tetrahydro-2H-benzo [b][1,3] thiazolo[4,5-d]azepin – 1-yl) –1-phenyl-1-propen-1-ol intermediates with phenacyl bromide, in good yields.

Introduction

A number of biologically interesting polynuclear compounds incorporating a fused thiophene ring via. Thiasteroids[1], analogues of indole alkaloids[2,3], carcinogenic compounds[4] etc. consist of six-membered rings annelated to thiophene. But examples of polycondensed systems incorporating a thiophene, imidazole or thiazole ring fused to a seven – membered ring (viz. Benzazepinones) are sparse. In continuation of our previous studies[5-7] in the synthesis of biologically active fused heterocycles we have synthesized the hitherto unreported phenylimidazo thiazolobenzazepine derivatives **4a-c** from 1,2,3,4-tetrahydro-1-benzazepin-5-one **1a-c**[8-10].

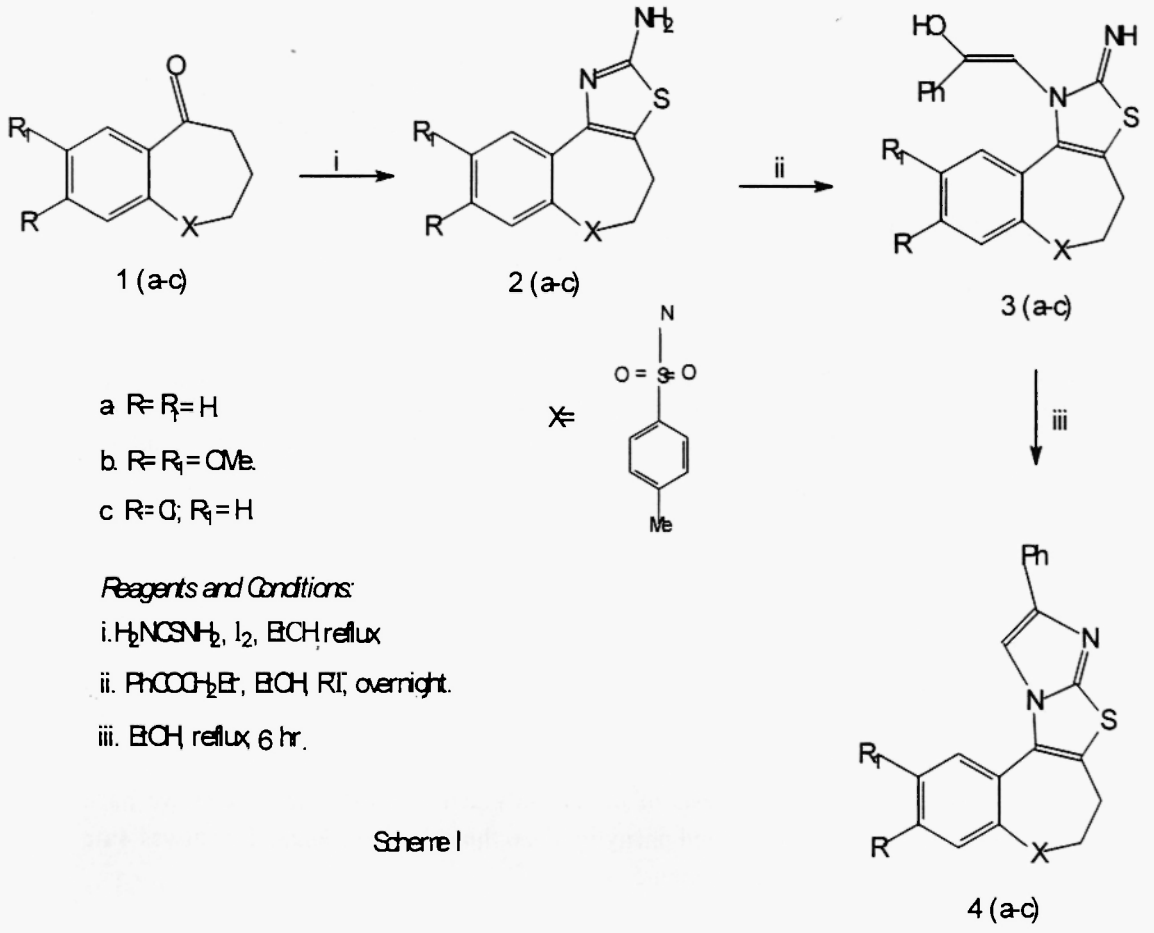
Chemistry

Reaction of the tetrahydro-1-benzazepin-5-ones **(1a-c)** with thiourea and iodine were heated under reflux to give expected 6-(4-methyl phenyl sulfonyl)-5,6-dihydro-4H-benzo[3,4]cyclohepta [d] thiazol-2-amines **2a-c** as colorless crystals (65-68%)[6,7] Cylcization of **(2a-c)** with phenacyl bromide at room temperature resulted in 2-(2-imino-6-(4-methylphenyl sulfonyl)- 1,4,5,6-tetrahydro-2H-benzo[b][1,3]thiazolo [4,5-d] azepin-1yl)-1-propen-1-ols **3a-c** as intermediate products. Subsequently compounds **(3a-c)** were assigned the enol form and gave 5-(4-methyl phenyl sulfonyl) –10- phenyl-6,7-dihydro-5H-benzo [3,4] cyclohepta [d] imidazo [2',1': 2,3] thiazolo [4,5-d] azepin-5-yls **4a-c** by heating in ethanol **(Scheme-I)**. Their structures were confirmed by IR, ^{1}H NMR and elemental analysis.

Experimental Section

Melting points were determined in open glass capillaries on a Metler FPS melting point apparatus and are uncorrected. ^{1}H NMR Spectra were recorded on a Gemini (200 MHz) Spectrometers (chemical shifts in δ ppm using TMS as internal standard) and IR spectra were recorded in KBr on a Perkin-Elmer bio-spectrometer. Elemental analyses were carried out with a Cario Erba Model 1106 Elemental Analyzer.

[+]IICT Communication No. 4647



Scheme I

Preparation of 2a-c: General Procedure.

A mixture of **1a** (15 mmole), thiourea (5 mmole and iodine (15 mmole) were refluxed for 48 hr. in abs. Ethanol (50mL). At this point TLC showed only a slight change in the substrate. After prolonged refluxing (4 to 5 days until TLC showed the absence of the ketone) the resulting hydride was dissolved in hot water. The solution was filtered while hot and the clear filtrate was neutralized with a strong solution of ammonia. The resulting precipitate was washed with water and (crystallized from ethanol).

6-(4-methylphenyl sulfonyl) –5,6- dihydro- 4H – benzo [3,4] cyclohepta [d] [1,3] thiazol-2-amine 2a.

Yield 65%, colorless crystals, m.p.>290° C (lit[7].m.p.>290°C). IR (KBr): ν 3385 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.31 (2H, t, 4-H), 4.00 (2H, t, 5-H), 2.25 (3H, s, -Me), 5.35 (2H, br, s, $-NH_2$, D_2O exchangeable) and 7.25-7.70 (8H, m, Ar-H). Found : C, 58.20; H, 4.66; N,11.21. Calcd for $C_{18}H_{17}N_3O_2S_2$: C,58.22; H,4.28; N,11.32%.

8,9-Dimethoxy-6-(4-methyl phenyl sulfonyl)-5,6-dihydro-4H-benzo[3,4] cyclohepta [d] [1,3] thiazol-2-amine 2b.

Yield 62%, colorless crystals, m.p.>290°C (lit.[7] m.p. >290°C). IR (KBr): ν 3380 cm^{-1} ; ^1H NMR (DMSO-d_6): δ 2.95 (2H, t, 4-H), 4.15 (2H, t, 5-H), 2.25 (3H, s, -Me), 5.30 (2H, br, s, $-NH_2$, D_2O exchangeable) 3.95 (3H, s, -OMe), 4.00 (3H, s, -OMe) 6.41 (1H, s, 7-H), 7.28 (1H, s, 10-H) and 6.91-7.63 (4H, dd, Ar-H). Found: C, 55.66 ; H,4.84; N, 9.90. Calcd for $C_{20}H_{21}N_3O_4S_2$: C, 55.68; H, 4.87; N,.74%.

8-Chloro-6-(4-methyl phenyl sulfonyl) –5,6- dihydro-4H- benzo [3,4] cyclohepta [d] [1,3] thiazol –2-amine 2c.

Yield 62%, colorless crystals, m.p.729°C (lit.[7] m.p. > 290° C). IR (KBr): ν 3380 cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.00 (2H, t, 4-H), 4.31 (2H, t, 5-H), 2.25 (3H, s, -Me), 5.35 (2H, br, s.-NH_2, D_2O exchangeable) and 7.15-7.70 (7H, m, Ar-H). Found : 53.30; H 3.95;N,10.33. Calcd for $C_{18}H_{16}ClN_3O_2S_2$: C 53.33; H 3.95; N,10.37%.

Preparation of 3a-c:General Procedure.

A mixture of **2a** (12 mmole) and phenacyl bromide (12 mmole) in 50 ml ethanol was allowed to stand at room temperature overnight. The crystals, which separated, were collected by filtration and washed with a small amount of ethanol.

2-(2-Imino-6-(4-methyl phenyl sulfonyl) –1,4,5,6-tetrahydro-2H-benzo[b][1,3] thiazolo [4,5-d] azepin-1-phenyl-1-ethen-1-ol 3a.

Yield 65%,m.p. 271° C. IR (KBr): ν 3360, 2900, 2850 cm^{-1} ; ^1H NMR (DMSO-d_6) : δ 2.31 (2H, t, $-CH_2-$), 4.00 (2H, t, $-NCH_2-$), 7.14(1H, s, =CH), 8.67 (1H, br, s, =NH), 8.64 (1H, s, -OH), 2.25 (3H, s, -Me) and 7.25-7.80 (13H, m, Ar-H) . Found : C,63.75: H,4.70: N,8.55. Calcd for $C_{26}H_{23}N_3O_3S_2$: C,63.78; H,4.73; N,8.58 %.

2-(2-Imino-8,9-dimethoxy-6-(4-methyl phenyl sulfonyl)-1,4,5,6- tetrahydro –2H-benzo [b] [1,3] thiazolo [4,5-d] azepin –1-yl) –1-phenyl- 1-ethen –1-ol 3b.

Yield 66%, m.p. 263°C (dec). IR (KBr): ν 3382, 3360, 2910, 2840 cm^{-1}; ^1H NMR (DMSO-d_6) : δ 2.33 (2H, t, $-CH_2-$), 4.31 (2H, t, $-NCH_2-$), 7.20 (1H, s, =CH), 8.66 (1H, br, s, =NH), 8.65 (1H, s, -OH), 3.95 (3H, s, -OMe), 4.01 (3H, s, -OMe) 6.41(1H, s, 7-H), 7.26 (1H, s, 10-H) and 7.25-7.65 (9H, m, Ar-H). Found: C,61.31; H,4.77; N,7.66. Calcd for $C_{28}H_{26}N_3O_5S_2$: C,61.29; H,4.77; N,7.65 %.

2-(8-Chloro-2-imino –6- (4- methyl phenyl sulfonyl) –1,4,5,6- tetrahydro-2H-benzo [b] [1,3] thiazolo [4,5-d] azepin-1-yl) –1-phenyl-1-ethen-1-ol 3c.

Yield 68%, m.p. 248° C. IR(KBr) : ν 3380,3360,2910,2850 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.30 (2H, t, $-CH_2-$), 4.09 (2H, t, $-NCH_2-$), 7.14(1H, s, =CH), 8.66 (1H, br, s, =NH), 8.64 (1H, s, -OH), 2.26 (3H, s, -Me) and 7.25-7.62 (12H, m, Ar-H). Found:C,61.48; H,4.33; N,8.25. Calcd for $C_{26}H_{22}ClN_3O_2S_2$: C,61.46; H,4.36; N,8.27 % .

Preparation of 4a-c: General procedure.

A suspension of **3a** (20 mmole) in 60 mL ethanol was heated under refluxed for 6hr. after cooling , the crystals which separated were collected by filtration.

5-(4-Methyl phenyl sulfonyl)-10- phenyl –6,7- dihydro-5H- benzo [b] imidazo [2,1:2,3] [1,3] thiazolo [4,5-d] azepin-5-yl 4a.

Yield 90%, m.p. 208° C . ^{1}H NMR (DMSO-d_6) : δ 2.32 (2H, t, -CH_2-), 4.28 (2H, t,-NCH_2), 7.56 (1H, s, 11-H), 2.26 (3H, s, -Me) and 6.58-7.41 (3H, m, Ar-H) . Found : C,66.20; H,4.50; N,8.91. Calcd for $C_{26}H_{21}N_3O_2S_2$: C,66.21; H,4.49; N,8.91%.

2,3-Dimethoxy-5- (4-methyl phenyl sulfonyl)-10-phenyl-6,7-dihydro-5H-benzo [b] imidazo [2,1:2,3][1,3] thiazolo [4,5-d] azepin-5-yl 4b.

Yield 92%, m.p.266° C (dec). ^{1}H NMR (DMSO-d_6): δ 2.30 (2H, t, -CH_2-) 4.18 (2H, t, -NCH_2-), 7.55 (1H, s, 11-H) 2.26 (3H, s, -Me), 6.48(3H, s, -OMe), 7.23 (3H, s, -OMe) 6.48 (1H, s, 7-H), 7.23 (1H, s, 10-H) and 6.58-7.28 (9H, m, Ar-H). Found: C,63.25; H,4.75; N,7.91 . Calcd for $C_{28}H_{25}N_3O_4S_3$: C,63.25; H,4.74; N,7.90 %.

3-Chloro-5- (4-methyl phenyl sulfonyl) –10- phenyl –6,7 – dihydro- 5H- benzo [b] imidazo [2,1:2,3] [1,3] thiaolo [4,5-d] azepin-5-yl 4c.

Yield 89%, m.p. 198° C. ^{1}H NMR (DMSO-d_6): δ 2.33 (2H, t, -CH_2-), 4.25 (2H, t,-NCH_2-), 7.56 (1H, s, 11-H), 2.24 (3H, S, -Me) and 6.45- 7.33 (12H, m, Ar,H). Found C,61.70; H,4.00; N,8.33. Calcd for $C_{26}H_{20}ClN_3O_2S_2$: C, ; H, ; N, %.

Acknowledgments

The authors are thankful to the Director, and the Head, Division of Organic Chemistry-II, IICT for providing facilities.

References

1. S .R. Ramdas, P. C Chennaiah, N.S Chandrakumar, M.V Krishna, P.S. Srinivasan, V. Sastry & J.Apparao, *Heterocycles* **19**, 861 (1982).
2. T.R Bosion & E. Campaign, *Adv. Drug Res.* **12**, 191 (1977).
3. E. E.Campaign, D.R Knapp, E.S Neiss & T.R Bosion , *Adv. Drug Res.* **5**, 1 (1970).
4. B.D. Tilak , *Tetrahedron* **9**, 76 (1960).
5. J. Mclean, V. Peesapati & G.R. Proctor, *J. Chem . Soc. Perkin 1*, 98 (1979).
6. L. Nagarapu & V.Peesapati, *Org.Prep. Proced. Int.* **24**, 27(1992).
7. L. Nagarapu & V.Peesapati *Org.Prep. Proced . Int.* **25**, 5 (1993).
8. I. Mc Call, G.R. Proctor & L.Purdie, *J.Chem Soc (C)* 1126 (1970).
9. A. Cromarty, G R. Proctor & M.Shabbir, *J. Chem. Soc. Perkin 1,* 2012 (1972)
10. P.D Carpenter, V.Peesapati & G.R. Proctor, *J. Chem. Soc. Perkin 1*, 103 (1979)
11. R.M Dodson & L.C King. *J. Am. Chem. Soc.* **67**, 2242 (1945).

Received on October 10, 2000