

Synthesis of Steroidal Oxospirothiazolotetrazines

SHAFIULLAH*, SHAMSUZZAMAN, ISHRAT HUSAIN SIDDIQUI and RAJESH KUMAR PATHAK

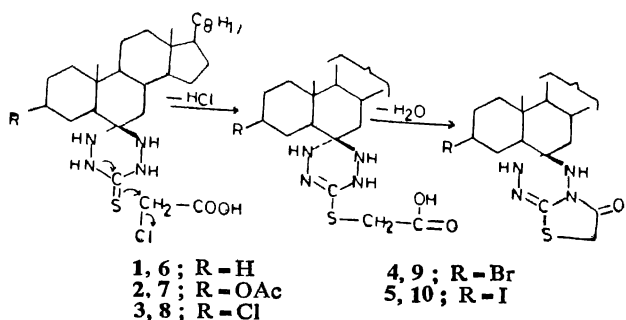
Steroid Research Laboratory, Department of Chemistry, Aligarh Muslim University, Aligarh-202 002

Manuscript received 15 January 1990, accepted 30 March 1990

Syntheses of 6' (7'H)-oxospiro[5 α -cholestane-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (6) and its 3 β -substituted analogues (7-10) are described.

THE synthesis of steroidal compounds having hetrocyclic ring systems containing spiro linkage have been reported by us¹. We report the synthesis and spectral studies of steroidal oxospirothiazolotetrazines (6-10). The steroidal spiro-tetrazine thiones (1-5)² when treated with chloroacetic acid-fused sodium acetate in anhydrous ethanol under reflux condition provided 6' (7'H)-oxospiro[5 α -cholestane-6,3-(4'H)-[2H]thiazolo[3,2-b]-s-tetrazine (6) and its 3 β -substituted analogues (7-10). Structures of the compounds have been established on the basis of their analytical and ir, pmr and mass spectral data (Table 1). The mechanism for their formation is given in Scheme 1.

The oxospirothiazolotetrazines (6-10) exhibited the characteristic ir bands at 3 500-3 200 (NH),



Scheme 1

TABLE 1 - PHYSICAL AND SPECTRAL DATA OF COMPOUNDS*

| Compd. no. | M.p. °C | Yield % | Mol. Formula | ν_{\max} cm ⁻¹ | PMR δ_H (60 MHz) ^a | m/z $M^+ - (C_8H_8OS + RH)^b$ |
|------------|---------|---------|---|---|---|---------------------------------|
| 6 | 139 | 50 | C ₃₀ H ₅₀ N ₄ OS | 3 490-3 200 (NH), 1 705 (C=O), 1 630 (C-N), 1 480 (C-N) | 5.5 (brs, 2 x NH), 2.2 (2H, s, CH ₂ CO) | 440 |
| 7 | 154 | 49 | C ₃₂ H ₅₈ N ₄ O ₂ S | 3 500-3 420 (NH), 1 740 (CH ₂ CO), 1 710 (C=O), 1 630 (C-N), 1 490 (C-N), 1 040 (C-O) | 4.8 (brs, 2 x NH), 4.0 (mc, $W_{1/2}$ 18 Hz, C β - α H, axial), 2.2 (2H, s, CH ₂ CO), 1.9 (3H, s, CH ₃ CO) | 438 |
| 8 | 161 | 50 | C ₃₀ H ₄₈ N ₄ ClOS | 3 480-3 240 (NH), 1 710 (C=O), 1 630 (C-N), 1 470 (C-N) | 5.6 (brs, 2 x NH), 3.9 (mc, $W_{1/2}$ 16 Hz, C β - α H, axial), 2.0 (2H, s, CH ₂ CO) | 438 |
| 9 | 197 | 48 | C ₃₀ H ₄₈ N ₄ BrOS | 3 420-3 340 (NH), 1 725 (C=O), 1 620 (C-N), 1 480 (C-N) | 5.5 (brs, 2 x NH), 3.8 (mc, $W_{1/2}$ 14 Hz, C β - α H, axial), 2.1 (2H, s, CH ₂ CO) | 438 |
| 10 | 181 | 48 | C ₃₀ H ₄₈ N ₄ IOS | 3 400-3 240 (NH), 1 740 (C=O), 1 640 (C-N), 1 500 (C-N) | 5.6 (brs, 2 x NH), 3.7 (mc, $W_{1/2}$ 14 Hz, C β - α H, axial), 2.0 (2H, s, CH ₂ CO) | 438 |

*All compounds gave satisfactory C, H and N analyses.

^aAngular and side-chain methyl protons appeared at δ 1.2-0.65.

^bLoss of RH from (7-10).

1 740–1705 (C=O), 1 640–1 620 (C=N) and 1 500–1 470 cm^{-1} (C–N)³, and the pmr spectra showed protons attached to the nitrogen at δ 5.6–4.8 (exchangeable with deuterium)⁴ and signals at δ 2.2–1.9 for methylene protons of –S–CH₂–CO–N grouping.

Experimental

All melting points are uncorrected. Ir spectra (KBr) were determined on a Pye-Unicam SP3-100 spectrophotometer, pmr spectra (CDCl_3) on a Varian A 60D spectrometer with Me_4Si as the internal standard and mass spectra on a JM5D-300 spectrometer at 70 eV.

Reaction of steroidal tetrazine thiones (1–5) with chloroacetic acid fused sodium acetate-anhydrous ethanol. General procedure: A mixture of 5 α -cholestan-6-spiro-1',2',4',5'-tetrazine-3'-thione³ (1) (2 g, 4.20 mmol), chloroacetic acid (g) and fused sodium acetate (0.9 g) in anhydrous ethanol (50 ml) was refluxed for 5 h. The progress of the reaction was monitored by tlc. The reaction mixture was then concentrated, cooled and kept overnight. The resulting solid was washed with water and recrystallised from ethanol to give 6'(7'H)-oxospiro[5 α -

cholestane-6,3'(4'H)-[2H]thiazolo[3,2-b]-s-tetra-zine (6). Under identical reaction conditions 2–5 furnished 7–10 (Table 1).

Acknowledgement

The authors are thankful to Prof. S. A. A. Zaidi, Chairman, Department of Chemistry, for facilities and to Prof. Asifuzzaman Siddiqui, for useful discussion. Financial support from U.G.C., New Delhi, to one of the authors (R K.P.) is gratefully acknowledged.

References

1. SHAFIULLAH and H. ALI, *Steroid Biochem.*, 1980, 13, 467; SHAFIULLAH, H. ALI, H. OGURA and H. TAKAYANAGI, *Bull. Chem. Soc. Jpn.*, 1981, 54, 3006; SHAFIULLAH, M. A. GHAFARI and S. HUSAIN, *J. Prakt. Chem.*, 1982, 324, 155; SHAFIULLAH, H. ALI and M. R. ANSARI, *J. Indian Chem. Soc.*, 1981, 58, 1211.
2. SHAFIULLAH, P. R. DUA, SHAMSUZZAMAN and R. K. PATHAK, *Indian J. Chem.*, communicated.
3. R. M. SILVERSTEIN, G. C. BASSLER and T. C. MORRILL, "Spectrometric Identification of Organic Compounds" Wiley, New York, 1981.
4. N. S. BHACCA and D. H. WILLIAMS, "Applications of NMR Spectroscopy in Organic Chemistry", Holden Day, San Fransisca, 1964, p. 79.