

SYNTHESIS OF DIMERIC BARBITURATES

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Abstract

The dimerisation reaction of 1,3-diphenyl barbituric acid 1 and 1,3-diphenyl 2-thiobarbituric acid 3 has been studied. Alkaline solution of these acids when treated with vinyl acetate, yielded 5,5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-2,4-dioxo pyrimidine 2 and 5,5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-4-oxo-2-thio pyrimidine 4 respectively. The structures of these compounds have been confirmed from their spectral and analytical data.

Introduction

A large number of barbiturate and thiobarbiturate derivatives have been reported to exhibit a broad spectrum of biological activities, such as anticonvulsant^{1,2}, sedative and hypnotic³⁻⁶, antibacterial⁷, insecticidal^{8,9} and antineoplastic activities¹⁰. In addition, synthetic studies of fused pyrimidines have been documented extensively because of their structural diversity and to carry out further for the study of above activities. We have recently reported^{11,12} the synthesis of novel pyranobis quinolines, pyranobis benzopyrans and benzopyrano-pyranoquinolines through the intermediate quinone methides. In continuation of our ongoing interest in the preparation of dimerized product, we now report the synthesis of 5,5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-2,4-dioxo pyrimidine 2.

Experimental

General Information

Thin layer chromatography was used to access reactions and purity of products. Melting points were determined on a Boetius Microheating Table and Mettler-FP5 Melting-Point apparatus and are uncorrected. IR spectra were recorded in Shimadzu -8201 FT instrument in KBr disc and only noteworthy absorption levels(reciprocal centimeter) are listed. ¹H-NMR spectra were recorded in a AMX-400 MHz spectrometer in DMSO-d₆ solution; chemical shifts are expressed in ppm(δ) relative TMS, coupling constants (J) in Hz and signal multiplicities are represented by s(singlet), d(doublet), q(quartet) and m(multiplet). Mass spectra were recorded on a Jeol - 300 mass spectrometer .

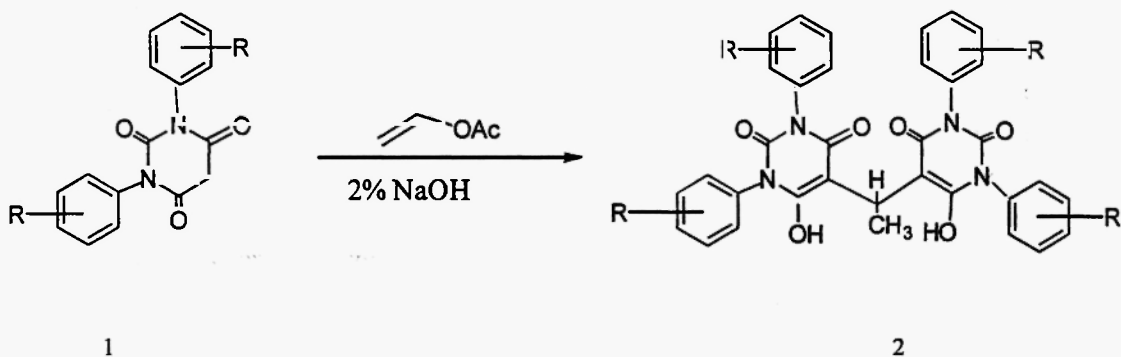
General Procedure

1,3-Diphenyl barbituric acid (0.002 mole) or 1,3-Diphenyl-2-thiobarbituric acid (0.002 mole) was stirred at room temperature in 100 ml of 2% sodium hydroxide solution taken in a 250 ml round bottom flask. To the alkaline solution vinyl acetate (0.02 mole) was added and the stirring was continued for 5-6 hours. The precipitated product was filtered carefully, washed with water and dried. The crude product was purified by recrystallising from CHCl_3 - CH_3OH solution.

Results and Discussions

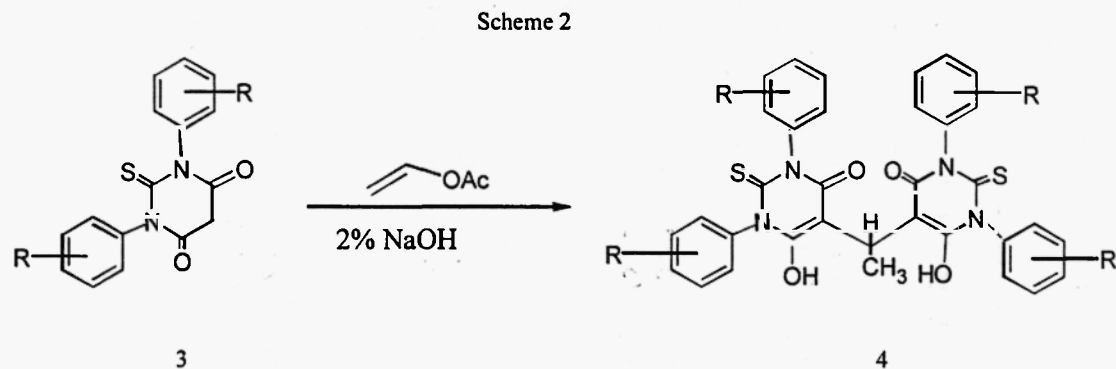
When a solution of 1,3-diphenyl barbituric acid in 2% sodium hydroxide was treated with vinyl acetate at room temperature, a yellow coloured solid separated out. It was filtered and recrystallised from CHCl_3 - CH_3OH solution (Yield: 85%; M.P.: 182.5°C). Its IR spectrum registered $>\text{C}=\text{O}$ absorption peaks at 1685 cm^{-1} and 1649 cm^{-1} , $-\text{OH}$ absorption in the region 3290 - 3650 cm^{-1} and $\text{C}-\text{N}$ peak at 1595 and 1544 cm^{-1} . The $^1\text{H-NMR}$ spectrum of the compound exhibited a doublet at $\delta 2.5$ which might be ascribed to methyl protons, a quartet at $\delta 7.1$ was accountable to methine proton. The low field shift of the methine proton may be due to the presence of $>\text{C}=\text{O}$ and $>\text{C}-\text{OH}$ groups adjacent to the proton. All the twenty aromatic protons gave multiplet between $\delta 6.95$ and 7.6 . A singlet at $\delta 8.6$ was assigned to $-\text{OH}$ group. The mass spectrum illustrated the molecular ion peak at m/z 586. The elemental analysis (CHN) agreed well with the molecular formula $\text{C}_{34}\text{H}_{26}\text{N}_4\text{O}_6$. All the above spectral data accredited the compound **2a** as 5,5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-2,4-dioxo pyrimidine (scheme 1)

Scheme 1



- 1,2 a: $\text{R} = \text{H}$
 b: $\text{R} = 2\text{-CH}_3$
 c: $\text{R} = 4\text{-CH}_3$
 d: $\text{R} = 2\text{-OCH}_3$

Having achieved in the dimerisation reaction of 1,3-diphenyl barbituric acids, we extended our reaction technique for 1,3-diphenyl 2-thiobarbituric acid also (Scheme 2). The products obtained were substantiated through IR, $^1\text{H-NMR}$, mass and elemental analysis and were given in the table 2.



3,4 a: R = H

b: R = 2-CH₃

c: R = 4-CH₃

d: R = 2-OCH₃

Table 1. Physical and spectral data of 5, 5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-2,4-dioxo pyrimidine 2

Compound	Yield (%)	M.P. (°C)	IR (cm ⁻¹)	MS(70eV) m/e (m ⁻¹)	Molecular Formula	Analysis Found(Calc.d.)			¹ H-NMR (DMSO-d ₆)δ/ppm
						C	H	N	
2a	85	182.5	3200-3600(O-H), 1695,1649(C=O)	586	C ₃₁ H ₂₁ N ₄ O ₄	69.62 (69.58)	4.44 (4.43)	9.56 (9.57)	2.50(d,3H,CH ₃), 7.1(q,1H,-CH-), 6.9-7.9(m,20H,Ar-H), 8.6(s,2H,2XOH)
2b	56%	214.8	3200-3450(OH), 1647,1614(C=O)	642	C ₃₈ H ₃₄ N ₄ O ₅	71.03 (71.13)	5.30 (5.32)	8.72 (8.73)	2.2(d,3H,CH ₃), 2.5(s,12H,4xCH ₃), 6.8(q,1H,-CH-), 7-8.0(m,16H,Ar-H), 8.4(s,2H,2xOH)
2c	60	134.1	3250-3500(O-H), 1695,1647(C=O)	642	C ₃₈ H ₃₄ N ₄ O ₆	71.03 (71.09)	5.30 (5.29)	8.72 (8.75)	2.3(d,3H,CH ₃), 2.5(s,12H,4xCH ₃), 6.6(q,1H,-CH-), 7.1-8.2(m,16H,Ar-H), 8.3(s,2H,2xOH)
2d	62	210.3	3250-3600(O-H), 1697,1645(C=O)	706	C ₃₈ H ₃₄ N ₄ O ₁₀	64.59 (64.62)	4.82 (4.85)	7.93 (7.91)	2.5(d,3H,CH ₃), 3.7(s,12H,4xOCH ₃), 6.8(q,1H,-CH-), 7.0-8.1(m,16H,Ar-H), 8.8(s,2H,2xOH)

Table 2. Physical and spectral data of 5, 5'-(methyl)-methylene-bis-(6-hydroxy-1,2,3,4-tetrahydro-1,3-diphenyl)-4-oxo-2-thio pyrimidine 4

Compound	Yield (%)	M.P. (°C)	IR (cm ⁻¹)	MS (70eV) m/e(m ⁺)	Molecular Formula	Analysis			¹ H-NMR (DMSO-d ₆) δ/ppm
						Found	Calcd.		
						C	H	N	
4a	50	300	3200-3600(OH), 1600(C=O), 1323(C=S)	618	C ₃₄ H ₂₁ N ₄ O ₄ S ₂	66.02 (66.08)	4.21 (4.23)	9.06 (9.08)	2.4(d, 3H, CH ₃), 6.8(q, 1H, -CH-), 7.0-8.1(m, 16 H, Ar-H), 9.2(s, 2H, 2xOH)
4b	64	239	3250-3600(OH), 1612(C=O), 1323(C=S)	674	C ₃₈ H ₃₁ N ₄ O ₄ S ₂	67.66 (57.69)	5.05 (5.01)	8.31 (8.29)	2.3(d, 3H, CH ₃), 2.4(s, 12H, 4xCH ₃), 6.7(q, 1H, -CH-), 6.9-7.8(m, 16H, Ar-H), 9.5(s, 2H, 2xOH)
4c	48	172	3150-3500(OH), 1615(C=O), 1323(C=S)	674	C ₃₈ H ₃₁ N ₄ O ₄ S ₂	67.66 (67.63)	5.05 (5.03)	8.31 (8.32)	2.2(d, 3H, CH ₃), 2.5(s, 12H, 4xCH ₃), 6.9(q, 1H, -CH-), 7.0-7.9(m, 16H, Ar-H), 9.6(s, 2H, 2xOH)
4d	62	113	3150-3600(OH), 1620(C=O), 1325(C=S)	738	C ₃₈ H ₃₄ N ₄ O ₈ S ₂	61.79 (61.32)	4.61 (4.63)	7.59 (7.60)	2.3(d, 3H, CH ₃), 3.9(s, 12H, 4xOCH ₃), 6.7(q, 1H, -CH-), 7.0-8.2(m, 16H, Ar-H), 9.5(s, 2H, 2xOH)

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