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Received July 27, 1977

The synthesis of a series of tetronic acids was accomplished by ring opening of new 4-ethoxycarbonyl-3(2H)furanones.

J. Heterocyclic Chem., 15, 327 (1978)

Derivatives of α -acyltetronic acids are frequently found as natural products and some synthetic routes of such compounds were reported (1-6). Through our investigations of the synthetic approach near these products recently we have demonstrated that the treatment of 4-ethoxycarbonyl-3-(2H)furanones with aqueous sodium hydroxyde gave α -acyltetronic acids (8-10). We now report the development of this procedure leading to the new α -acetyl- γ -substituted-tetronic acids 5 and 6.

The precursors, 4-carbethoxy-3(2H)furanones 3 or 4, were readily synthesized in nearly quantitative yields by catalytic hydrogenation over palladium charcoal of 1 or 2 previously described (10,11). Treatment of 3 or 4 with *N* aqueous potassium hydroxide for 24 hours undergoes opening of the furan ring followed by lactonization to tetronic acids 5 or 6.

Compounds 1, 2 were prepared as previously described (10,11).

Compounds 3 and 4

General Method.

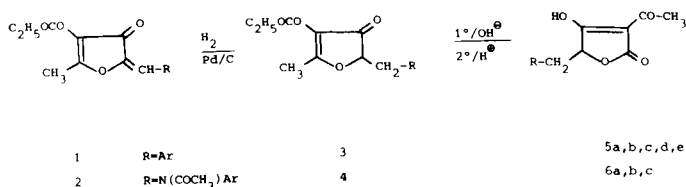
A suspension of 3 (0.01 mole) in ethyl acetate or 4 (0.01 mole) in dioxane (120 ml.) was hydrogenated with 5% palladium on carbon (1.5 g.) at room temperature using a low pressure (ca. 1 atmosphere) hydrogenation apparatus with magnetic stirring. After uptake of the calculated amount of hydrogen, the catalyst was filtered off and the solvent was evaporated under reduced pressure. The crude product was distilled or recrystallized from hexane-ethyl acetate for 3 or ethyl acetate for 4, yield, 75%.

Compounds 5 and 6

General Method.

Compounds 3 or 4 (0.01 mole) was added to a *N* aqueous potassium hydroxyde (100 ml.). The mixture was allowed to stand at room temperature with stirring for 24 hours. The reaction mixture was extracted with ether. The aqueous layer was acidified with ice-cold concentrated hydrochloric acid. After extraction with methylene chloride, the solvent was evaporated and the residue was recrystallized from hexane-ethyl acetate (80-20) or ethyl acetate, yield, 70% of 5 and 60% of 6.

Scheme 1



Ar = a: C₆H₅; b: 4-CH₃C₆H₄; c: 4-CH₃OC₆H₄; d: 4-ClC₆H₄; e: 3,4-(CH₃O)₂C₆H₃

The ir, nmr and uv spectra were all consistent with the required structure (Tables).

EXPERIMENTAL

All melting points were taken on a Kofler block. The ir and uv spectra were obtained with a Beckman Model Acculab 2 and DB spectrophotometers. The nmr spectra were measured using tetramethylsilane as the internal standard, with a Varian A-60 spectrometer. Microanalyses were performed by Microanalytical Laboratory, Centre National de la Recherche Scientifique, Villeurbanne, France.

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Physical Data for Compounds 4

Compound	M.p. °C	Molecular Formula	Analyses		Uv in Ethanol		Ir (cm ⁻¹) Potassium Bromide	¹ H Nmr/(Deuteriochloroform): δ ppm		
			Calcd.	Found	λ max (nm)	ε		CH ₃ (s)	CH ₂ (b)	H (c)
4a	139	C ₁₇ H ₁₉ O ₅ N (317.33)	C	64.34	6.04	4.41	1720	1.92	2.62	4.92
			H	64.29	6.11	4.48	1705 (sh) 1660 1600			
4b	112	C ₁₈ H ₂₁ O ₅ N (331.36)	C	65.24	6.39	4.23	1720	1.92	2.63	4.90
			H	65.32	6.49	4.05	1705 1665 1600			
4c	85	C ₁₈ H ₂₁ O ₆ N (347.36)	C	62.24	6.10	4.03	1720	1.90	2.63	4.87
			H	63.37	6.13	3.77	1710 1665 1600			

(a) Acetyl group. (b) Obscured by the methylene protons of the ethoxy carbonyl group. (c) Deformed triplet.

Physical Data for Compounds 5

Compound	M.p. °C	Molecular Formula	Analyses		Uv in Ethanol		Ir (cm ⁻¹)	¹ H Nmr/(Deuteriochloroform): δ ppm					
			Calcd.	Found	λ max (nm)	ε		CH ₃ (s)	B (ab)	CH ₂ (2q)	A (ac)	H (2q)	OH
5a	77	C ₁₃ H ₁₂ O ₄ (232.23)	C	67.23	5.21	266	6,800	1775	2.50	3.13	3.34	5.05	10.90
			H	67.47	5.23	234	9,450	1700					
5b	65	C ₁₄ H ₁₄ O ₄ (246.25)	C	68.28	5.73	267	6,950	1770	2.53	3.09	3.30	5.05	10.70
			H	68.13	5.89	230	9,200	1700					
5c	112	C ₁₄ H ₁₄ O ₅ (262.25)	C	64.11	5.38	266	6,550	1780	2.50	3.07	3.29	5.0	12.2
			H	64.37	5.51	230	6,200	1705 1675 1620					
5d	90	C ₁₃ H ₁₁ ClO ₄ (266.68)	C	58.55	4.15 (d)	265	7,175	1780	2.53	3.11	3.32	5.0	12.6
			H	58.63	4.16	227	6,775	1705 1675 1620					
5e	160	C ₁₅ H ₁₆ O ₆ (292.28)	C	61.64	5.52	266	5,300	1780	2.50	3.09	3.29	5.0	11.0
			H	61.62	5.63	231	4,950	1705 1675 1620					

(a) J_{AB} = 15 Hz. (b) J_{BX} = 4.6 Hz. (c) J_{AX} = 6.9 Hz. (d) Percent Cl Calcd. 13.29. Found: 13.29.

Physical Data for Compounds 6

Compound	M.p. °C	Molecular Formula	Analyses		Uv in Ethanol		Ir (cm ⁻¹) Potassium Bromide	CH ₃ (s) (a)	¹ H Nmr/(Deuteriochloroform): δ ppm			OH	
			Calcd. %	Found	λ max (nm)	ε			CH ₃ (s) (b)	CH ₂ (2q)	CH ₂ (2q)		H (2q)
6a	86	C ₁₅ H ₁₅ O ₅ N (289.28)	62.28	5.23	4.84	265	15,900	1.90	2.55	3.98	4.35	5.07	9.45
			62.02	5.27	4.68	230	15,800						
6b	96	C ₁₆ H ₁₇ O ₅ N (303.30)	63.36	5.65	4.62	265	16,500	1.89	2.53	3.95	4.28	5.02	11.70
			63.16	5.66	4.38	230	17,400						
6c	123	C ₁₆ H ₁₇ O ₆ N (319.30)	60.18	5.37	4.39	265	16,500	1.90	2.56	3.97	4.33	5.10	11.98
			60.01	5.45	4.25	230	21,100						

(a) Amide group. (b) Acetyl group. (c) J_{AB} = 14 Hz. (d) J_{BX} = 4.1 Hz. (e) J_{AX} = 8.9 Hz.

Physical Data for Compounds 3

Compound	M.p. °C or B.p. °C mm	Molecular Formula	Analyses		Uv in Ethanol λ max (nm) ε	Ir (cm ⁻¹) Chloroform	¹ H Nmr/(Deuteriochloroform): δ ppm			
			Calcd. %	Found			CH ₃ (d) (a)	CH ₂ (2q)	H (m) X (cda)	
3a	160/0.1	C ₁₆ H ₁₆ O ₄ (260.28)	69.21	6.20	264	7,900	2.57	3.00	3.33	4.83
			69.33	6.32	214	9,900				
3b	84	C ₁₆ H ₁₈ O ₄ (274.30)	70.05	6.61	264	8,400	2.55	3.02	3.30	4.78
			69.81	6.75	214	9,900				
3c	88	C ₁₆ H ₁₈ O ₅ (290.30)	66.19	6.25	263	11,350	2.58	3.00	3.33	4.80
			65.91	6.29	222	10,350				
3d	110	C ₁₅ H ₁₅ ClO ₄ (294.73)	61.13	5.13 (e)	262	9,100	2.60	3.33	3.33	4.83
			61.16	5.18	218	14,700				
3e	78	C ₁₇ H ₂₀ O ₆ (320.33)	63.74	6.29	264	9,900	2.56	3.05	3.39	4.81
			63.49	6.25	216	14,700				

(a) J CH₃-H = 1 Hz. (b) J_{AB} = 15 Hz. (c) J_{BX} = 3.8 Hz. (d) J_{AX} = 8.2 Hz. (e) Percent Cl; Calcd. 12.03. Found: 11.93.