

SYNTHESIS OF HETERO-BICYCLIC-COMPOUNDS

Part-VII. Formation of 2,2-Diphenyl-4, 5-Dioxopyridino-(4,3-d)-(1,3)-Dioxins

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Aminopyranodioxins derived from benzophenone isomerise to yield 6 substituted 1,2-dihydropyridino-dioxins (III). The I.R., U.V. data and chemical conversions supported the structure (II) and (III).

Key words : Pyrano-dioxin, Pyridino-dioxin

Introduction

The rearrangement of aminopyrano dioxins (II, R=aryl, R'=R''=CH₃) under the influence of bases such as sodium phenoxide in phenol or sodium creoxide in cresol to yield aryl substituted 7-hydroxy, 2,2 dimethyl pyridino dioxins has already been reported [1]. The present study deals with the formation of 2,2 diphenyl 4,5, dioxopyridino dioxins from the corresponding 2,2, diphenyl 4,5- dioxo 7-amino pyrano dioxins under the influence of the same bases and the characterization of these compounds by spectroscopic studies supported by elemental analysis, degradation to known products and formation of derivatives.

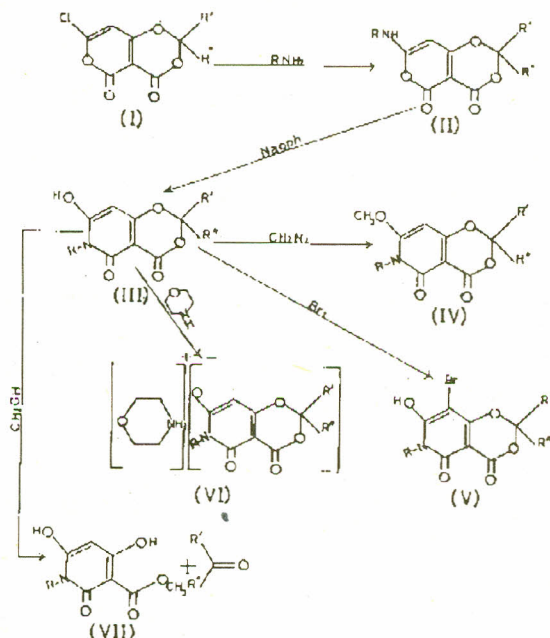


CHART 1

Experimental

7-Chloro-2,2-diphenyl-4,5-dioxopyrano(4,3-d)-(1,3)-dioxin (I, R'=R''=Ph). The title compound (I) was prepared according to the method of Davis and Elvidge [1] by heating benzophenone ((0.1 mole) and malonyl chloride (0.2 moles) on a water bath until the mass solidified. Trituration of the

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product with ether gave 7-chloro-2,2-diphenyl-4,5-dioxopyrano(4,3-d)-(1,3)-dioxin (I), which crystallized from benzene (m.p.179°) Found: C,63.9;H, 3.3; Cl,9.8% Calc: for C₁₉H₁₁O₅ Cl, C, 64.3; H,3.1; Cl, 10.0%.

7-Anilino-2,2-diphenyl-4,5-dioxopyrano (4,3-d)-(1,3)-dioxin (II, R=R'=R''=Ph). To a solution of 7-chloro-2,2-diphenyl-4,5-dioxopyrano (4,3-d)-(1,3) dioxin (5.0g, 14.1 mmol) in CHCl₃ (10ml), aniline (2.5ml, 28.2 mmol) in CHCl₃ (10ml) was added with constant stirring. The solid product obtained was washed with water and dried. 7-Anilino-2,2-diphenyl-4,5-dioxopyrano(4,3-d)-(1,3)-dioxin (5.1g, 88%) was crystallized from CHCl₃, m.p. 158° (Found : C, 72.80; H,4.0; N,3.40; C₂₅H₁₇NO₅ requires: C,73.00; H,4.10; N,3.40%).

Other 7-amino-2,2-diphenyl-4,5-dioxo-pyrano(4,3-d)-(1,3)-dioxins (II) prepared as above are listed in Table 1.

Reaction of 7-anilino-2,2-diphenyl-4,5-dioxopyrano (4,3-d)-(1,3)-dioxin with sodium phenoxide in phenol. 7-Anilino-2,2-diphenyl-4,5-dioxopyrano(4,3-d)-(1,3) dioxin (4 g: 9.7 mmole) was added to a solution of Na (0.9g, 39.0 mmol) in phenol (25 ml) and the mixture was heated at 120° for 2 min. The solution was cooled, diluted with water and extracted with ether to recover excess of phenol. The ethereal layer was again extracted with water and the combined aqueous extracts (150 ml) were acidified with HCl (2N). The solid product obtained 7-hydroxy-2,2-diphenyl-4,5-dioxo-6-phenylpyridino(4,3-d)-(1,3)-dioxin (III, R=R'=R''=Ph, 2.3g, 57%) was crystallized from MeOH, m.p. 182° decomp. It produced reddish brown colour with aq. FeCl₃ and gave effervescence with aq. NaHCO₃. Found: C, 72.60; H, 4.0; N,3.40. C₂₅H₁₇NO₅ requires: C,73.00; H,4.10; N,3.40%)

Other aryl amino pyrano dioxins (II) were reacted similarly with sodium phenoxide in phenol and the products obtained (represented by formula III) are listed in Table 2.

7-Methoxy-2,2-diphenyl-4,5-dioxo-6-phenyl-pyridino (4,3-d)-(1,3)-dioxin (IV). To 7-hydroxy-2,2-diphenyl-4,5-dioxo-6-phenyl-pyridino-(4,3-d)-(1,3)-dioxin (III, R=p-anisyl, R'=R''=Ph) (0.5g) in ether (10 ml) a solution of diazomethane in ether was added in portions until yellow colour persisted. The solution was kept overnight in a

TABLE 1. FORMATION OF 7-AMINO-2, 2-DIPHENYL-4, 5-DIOXOPYRANO (4,3-D) - (1,3) - DIOXINS.

S. NO.	Primary amine	Quantity (g)	7-chloro-2,2-diphenyl-4,5-dioxopyrano-(4,3-d)(1,3)-dioxin (I) (g)	Product (R)	yield (%)	m.p. °C	Solvent for crystallization	Molecular formula	Analysis						UV light absorption in methanol max log	
									Found			Requires				
									C	H	N	C	H	N		
1.	Aniline	2.6	5	Phenyl	86.0	158°	MeOH+CHCl ₃	C ₂₅ H ₁₇ NO ₅	72.80	4.00	3.40	73.0	4.10	3.40	345	4.36
2.	<i>o</i> -Toluidine	3.0	5	<i>o</i> -Tolyl	83.0	150°	—	C ₂₆ H ₁₉ NO ₅	73.50	4.10	3.30	73.40	4.50	3.30	337	4.86
3.	<i>m</i> -Toluidine	3.24	5	<i>m</i> -Tolyl	80.5	160°	—	C ₂₆ H ₁₉ NO ₅	73.50	4.40	3.30	73.40	4.50	3.30	345	4.62
4.	<i>p</i> -Toluidine	3.09	5	<i>p</i> -Tolyl	66.0	176°	—	C ₂₆ H ₁₉ NO ₅	73.10	4.50	4.20	73.40	4.50	3.30	350	4.47
5.	<i>m</i> -Anisidine	3.46	4	<i>m</i> -Anisyl	67.0	167°	CHCl ₃	C ₂₆ H ₁₉ NO ₆	71.20	4.30	3.20	70.70	4.30	3.20	340	4.48
6.	<i>p</i> -Anisidine	3.4	5	<i>p</i> -Anisyl	96.7	162°	—	C ₂₆ H ₁₉ NO ₆	71.10	4.30	3.10	70.70	4.30	3.20	350	4.53
7.	<i>o</i> -Chloro-aniline	3.64	5	<i>o</i> -Chloro-phenyl	71.0	162°	—	C ₂₅ H ₁₇ ClNO ₅	66.90	3.50	3.10	67.30	3.60	3.10	330	4.45
8.	<i>m</i> -Chloro-aniline	3.99	5	<i>m</i> -Chloro-phenyl	58.3	172°	—	C ₂₅ H ₁₇ ClNO ₅	67.90	3.40	3.20	67.30	3.60	3.10	340	4.55
9.	<i>p</i> -Chloro-aniline	3.58	5	<i>p</i> -Chloro-phenyl	66.6	197°	—	C ₂₅ H ₁₇ ClNO ₅	67.00	3.60	3.10	67.30	3.60	3.10	350	4.71

TABLE 2. FORMATION OF N SUBSTITUTED 2,2-DIPHENYL-7-HYDROXY-4,5-DIOXO-6-PYRIDINO (4,3-D)-(1,3)-DIOXIN (III).

S.No.	7-Amino pyrano (1,3)-dioxin (I) R=	Quantity (g)	Sodium/phenol	Pyridino (4,3-d)-(1,3)dioxin(III)	Yield of III %	m.p. °C	Molecular formula	Analysis					
								Found			Requires		
								C	H	N	C	H	N
1.	Phenyl	4.0	1g/25ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6-phenyl.	57.5	182°	C ₂₅ H ₁₇ NO ₅	72.60	4.40	3.40	73.00	4.14	3.40
2.	<i>o</i> -Tolyl	2.5	0.6g/18ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>o</i> -tolyl.	80.0	181°	C ₂₆ H ₁₉ NO ₅	73.10	4.60	3.20	73.40	4.50	3.30
3.	<i>m</i> -Tolyl	2.5	0.6g/18ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>m</i> -tolyl	60.0	194°	C ₂₆ H ₁₉ NO ₅	73.50	4.60	3.30	73.40	4.50	3.30
4.	<i>p</i> -Tolyl	4.0	0.8g/25.8 ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>p</i> -tolyl.	45.0	207°	C ₂₆ H ₁₉ NO ₅	73.20	4.50	3.20	73.40	4.50	3.30
5.	<i>m</i> -Anisyl	2.5	0.5g/15 ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>m</i> -anisyl	100.0	198°	C ₂₆ H ₁₉ NO ₆	70.20	4.30	3.10	70.70	4.30	3.20
6.	<i>p</i> -Anisyl	6.0	1.25g/37.5 ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>p</i> -anisyl.	25.0	175°	C ₂₆ H ₁₉ NO ₆	71.10	4.40	3.20	70.70	4.30	3.20
7.	<i>o</i> -Chloro phenyl	1.2	0.24g/7.2ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>o</i> -chlorophenyl.	50.0	194°	C ₂₅ H ₁₇ ClNO ₅	66.10	3.50	3.20	67.30	3.60	3.10
8.	<i>m</i> -Chloro-phenyl	4.0	0.8g/24.4ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>m</i> -chlorophenyl.	41.2	161°	C ₂₅ H ₁₇ ClNO ₅	66.90	3.20	3.10	67.30	3.60	3.10
9.	<i>p</i> -Chloro-phenyl	3.0	0.7g/21ml	7-hydroxy-2,2 diphenyl 4,5-dioxo-6- <i>p</i> -chlorophenyl.	66.6	197°	C ₂₅ H ₁₇ ClNO ₅	66.90	3.60	3.10	67.30	3.60	3.10

refrigerator and the excess solvent was removed. The residue upon trituration with ether yielded a neutral product which showed no colouration with aq. FeCl_3 . The 7-methoxy-2,2-diphenyl-4,5-dioxo-6-*p*-anisyl-pyridino (4,3-d)-(1,3)-dioxin (IV, 0.3 g) m.p. 195.2° was crystallized from MeOH. (Found: C, 70.40; H, 4.7; N, 3.2% $\text{C}_{27}\text{H}_{21}\text{NO}_6$ requires: C, 71.20; H, 4.70; N, 3.1%.)

8-Bromo-2,2 diphenyl-7-hydroxy-4,5-dioxo-6-*p*-anisyl-pyridino-(4,3-d)-(1,3)-dioxin (V, R=*p*-anisyl, R'=R''=Ph). The compound (III, R=*p*-anisyl) (0.5g) was dissolved in CHCl_3 (20ml) and bromine in CHCl_3 was added dropwise till an orange colour persisted. The reaction mixture was kept at room temperature for 1 hr. and subsequently the solvent was removed. The solid bromo-product (0.4 g, 68%) (V, R=*p*-anisyl, R'=R''=Ph) was recrystallized from MeOH. m.p. 175°. (Found: C, 60.3; H, 3.50; N, 2.80% Requires: C, 60.0; H, 3.50; N, 2.70).

Morpholinium salt of 7-hydroxy product (VI, R=*p*-anisyl, R'=R''=Ph). The compound (0.5g) (III, R=*p*-anisyl, R'=R''=Ph) in CHCl_3 and morpholine (0.5ml) was refluxed for 3 mins. The solvent was removed under vacuum. The residue obtained (0.4g, 67.7%) was recrystallized from MeOH (VI, R=*p*-anisyl, R'=R''=Ph), m.p. 178°. (Found: C, 67.50; H, 5.30; N, 5.30; $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_7$ requires: C, 68.2; H, 5.3; N, 5.3%.)

aryl- substituted pyridinodioxins of the general formula (III, R=aryl, R=R=Ph), similar to those described earlier. For instance, the compound 7-Anilino-4,5-dioxo 2,2-diphenylpyrano (4,3-d)-(1,3)- dioxin (II, R=R=R=Ph) on reacting with phenoxide in phenol, produced $\text{C}_{25}\text{H}_{17}\text{NO}_5$, (III, R=R=Ph), m.p. 182 (decom), enolic in nature (FeCl_3 test) and dissolved in aq NaHCO_3 solution, isomeric with the starting material. It is moderately stable towards alcohols and is decomposed on boiling. Various other arylamino-dioxins (II) yielded similar isomeric products (III).

These products (III) absorb characteristically in the UV region 310-315 μ (Table 3) closely resembling pyridinodioxins. Substituent at position 1, apparently has no effect on the UV absorption, I.R. absorption peak due to ester carbonyl at position 4 appears at (1696-1750) cm^{-1} while that due to carbonyl at position 5, appear at (1620-1663) cm. The OH group at position 7, was methylated into the product (IV R=*p*-anisyl, R=R=Ph), max 300 (log 4.0) and max 275, (log 4.2). Similarly, morpholinium salt of the product (III, R=*p*-anisyl, R=R=Ph), absorbed max 310. (log 9.93). Bromo derivative (V, R=*p*-anisyl, R=R=Ph) had max 330, (log 4.87). Finally the structure (III) for these new products was confirmed by boiling it (III, R=R=R=Ph) in methanol to form a known methyl ester pyridine[3] (VII, R=Ph) and benzophenone (VIII).

TABLE 3. UV AND IR SPECTRA OF PYRIDINO-(4,3-D)-(1,3)-DIOXIN (III R'=R''=PH).

S. No.	Pyridino (4,3-d)-(1,3)-dioxins (III, R=R''=ph) R	UV light absorption (95% methanol)		IR absorption max (cm^{-1}) mainly for the 3-6,7 μ region, (KBr disc)	
		λ max μ	log ϵ	$\nu\text{C-O}(4)$ cm^{-1}	$\nu\text{C-O}(5)$ cm^{-1}
1	Phenyl	315	4.50	1750s	1625s
2	<i>o</i> -Tolyl	310	4.66	1730s	1650s
3	<i>m</i> -Tolyl	312	4.17	1745s	1627s
4	<i>p</i> -Tolyl	312	4.64	1710s	1665s
5	<i>m</i> -Anisyl	315	4.63	1740s	1620s
6	<i>p</i> -Anisyl	315	4.38	1696m	1656s
7	<i>o</i> -Chloro phenyl	312	4.38	1770s	1650s
8.	<i>m</i> -Chloro phenyl	310	4.36	1730s	1650s
9.	<i>p</i> -Chloro phenyl	310	4.64	1718m	1663s

Degradation of III with methanol. The compound (III, R=R'=R''=Ph) (0.5g) was refluxed with MeOH (25ml) for 6 hrs. The solution upon concentration in vacuum yielded (VII, R=Ph) (0.2g) which crystallized from MeOH, m.p. 210°. (Found = C, 59.90; H, 4.1; N, 5.40; Requires: C, 59.80; H, 4.20; N, 5.40). From the filtrate benzophenone was isolated and characterized as the 2,4 dinitrophenyl-hydrazone derivative.

Results and Discussion

7-arylamino-2,2-diphenyl-4,5-dioxo-pyrano (4,3-d)-(1,3) dioxins (II, R=aryl, R=R=Ph) isomerise smoothly into

The latter was characterised as 2,4 dinitrophenyl hydrazone.

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References

1. S.J. Davis and J.A. Elvidge, J. Chem. Soc., 4109 (1952).
2. M.A. Butt and I.A. Akhtar, Tetrahedron, 1917 (1965).
3. M.A. Butt, J.A. Evidge and A.B. Foster, J. Chem. Soc., 3069 (1963).