Pak. j. sci. ind. res., vol. 35, no. 9, September 1992

SYNTHESIS OF HETERO-BICYCLIC COMPOUNDS
Part -VIII. Formation of 6-Alkyl-2,2-Dimethyl-4, 5-Dioxo-7-Hyroxy-Pyridino [4,3-*d*][1,3]Dioxins

M.A. Butt*, R. Kemal, A. Salam and Ghazala Mumtaz
PCSIR Laboratories Complex, Karachi

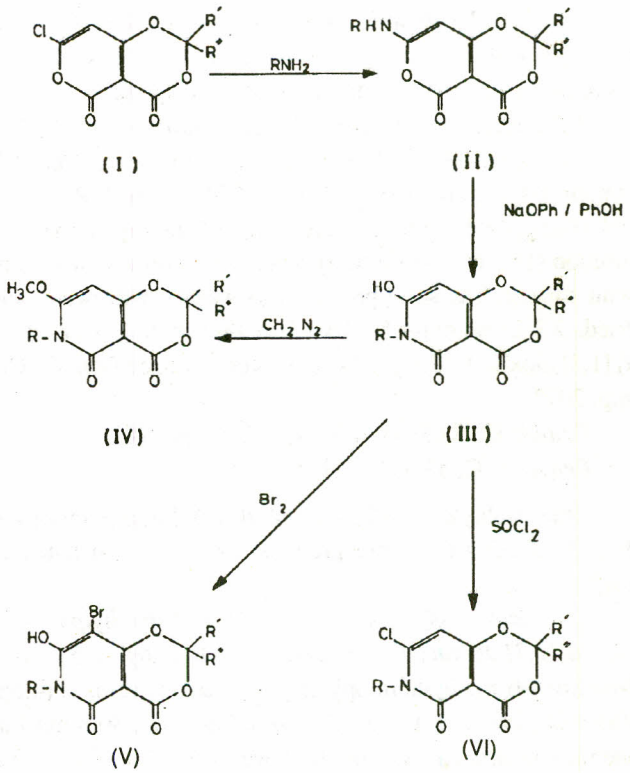
(Received July 9, 1992)

Aminopyranodioxins (II), derived from aliphatic amines, isomerise to yield the corresponding pyridino-dioxins (III). Chemical conversions and spectroscopic data are provided in support of their structure.

Key words. Pyrano-dioxin, Pyridino-dioxin, Aliphatic amines.

Introduction

Earlier it was reported [1] that the conversion of amino-pyranodioxins (II, R = alkyl) into the corresponding pyridino-dioxins (III, R' = R" = alkyl groups, same or different) was difficult to achieve except in case of iso-butylamine product (II, R = Isobutyl -). Re-investigation of this reaction with slightly altered conditions showed that it followed the same pattern as was reported in the case of aminopyranodioxins (II, R = aryl) derived from arylamines. For instance, the product 2,2- dimethyl-4, 5-dioxo-7-methylamino-pyrano [4,3-*d*][1,3] dioxin in the presence of sodium phenoxide in phenol formed the corresponding pyridinodioxin (III, R = R ' = R " = CH_3) $C_{10}H_{11}NO_5$, m.p. 174°, which had phenolic properties (it gave $FeCl_3$ test and dissolved in aqueous Na_2CO_3 solution), characteristic of such type of structures. Compounds prepared similarly are recorded in Table-1.



Experimental

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. U.V. and I.R. spectra were recorded on Beckman 36 and Perkin-Elmer 283 B spectrophotometers respectively.

Table 1. Formation of 7-Amino-2, 2-Dimethyl-4, 5-Dioxopyrano [4, 3-d][1,3] Dioxin.

Sr. No.	Primary amine	Quantity (g)	7-Chloro-2,2-dimethyl-4,5 dioxo-pyrano dioxin(I) (g)	Product II(R'= R"=CH_3) (R)	Yield (%)	m.p. °C	Molecular formula	Analysis Found (%) C	H	N	Requires(%) C	H	N	UV absorbance in MeOH λmax nm	logε
1.	Methyl amine	3.48	10.0	$-CH_3$	80.4	207	$C_{10}H_{11}NO_5$	53.2	4.9	6.2	53.3	4.9	6.2	330	4.62
2.	Ethyl amine	2.45	5.0	$-C_2H_5$	88.0	193	$C_{11}H_{13}NO_5$	55.0	5.4	5.6	55.2	5.4	5.6	327	4.05
3.	*n*-Pyropyl amine	5.17	10.0	*n*-C_3H_7-	76.6	189	$C_{12}H_{15}NO_5$	57.0	6.0	5.5	56.9	5.9	5.5	325	4.42
4.	Allyl amine	5.2	10.0	CH_2=CH-CH_2-	74.4	176	$C_{12}H_{13}NO_5$	57.2	5.5	5.5	57.4	5.2	5.6	330	4.57
5.	*n*-Hexyl amine	8.8	10.0	C_6H_{13}-	78.7	160	$C_{15}H_{19}NO_5$	61.0	6.9	4.5	61.0	7.1	4.7	336	4.70
6.	*n*-Butyl amine	3.8	6.0	*n*-C_4H_9-	85.6	179	$C_{13}H_{17}NO_5$	58.4	6.1	5.1	58.4	6.3	5.2	325	4.33

* Present Address: PCSIR Laboratories Complex, Lahore-54600

TABLE 2. FORMATION OF 6-ALKYL-2, 2-DIMETHYL-4, 5-DIOXO-7-HYDROXY-PYRIDINO [4, 3-d] [1,3] DIOXINS (III).

Sr. No.	7-Amino pyrano(1,3)-dioxin (II) R=	Quantity (g)	Sodium/ phenol (g/ml)	Pyridino [4,3-d][1,3] dioxin(III)	Yield (%)	m.p °C	Molecular formula	Analysis Found(%) C	H	N	Required(%) C	H	N
1.	CH_3-	4.5	1.8/60	2,2-Dimethyl-4,5-dioxo 7-hydroxy-6-methyl-	80.0	174	$C_{10}H_{11}NO_5$	53.2	4.9	6.2	53.3	4.9	6.2
2.	C_2H_5-	3.0	1.2/35	2,2-Dimethyl-4,5-dioxo-6-ethyl-7-hydroxy-	42.0	249	$C_{11}H_{13}NO_5$	55.3	5.5	5.7	55.2	5.4	5.8
3.	n-C_3H_7-	6.0	2.2/60	2,2-Dimethyl-4,5-dioxo-7-hydroxy-6-propyl-	72.8	168	$C_{12}H_{15}NO_5$	56.7	5.6	5.5	56.9	5.9	5.5
4.	CH_2=CH-CH_2-	4.5	1.7/50	6-Allyl-2, 2-dimethyl-4,5-dioxo-7-hydroxy-	93.0	169	$C_{12}H_{13}NO_5$	57.3	5.1	5.5	57.4	5.2	5.6
5.	n-C_6H_{13}-	6.0	2.0/60	2,2-Dimethyl-4,5-dioxo-6-hexyl-7-hydroxy-	48.6	127	$C_{15}H_{19}NO_5$	60.7	7.0	4.6	61.0	7.1	4.7
6.	n-C_4H_9-	3.7	1.3/40	6-Butyl-2,2-dimethyl-4,5-dioxo-7-hydroxy-	34.5	126	$C_{13}H_{17}NO_5$	58.2	6.2	5.0	58.4	6.3	5.2

7-Chloro-2,2-dimethyl-4,5-dioxo-pyrano [4,3-d][1,3] dioxin (I, R = R'R" = CH_3). The title compound was prepared according to the method of Davis and Elvidge [2].

2,2-Dimethyl-4,5-dioxo-7-methylamino-pyrano[4,3-d][1,3] dioxin (I, R = R'R"= CH_3). A solution of 7-chloro-2,2-dimethyl-4, 5-dioxopyrano-[4,3-*d*] [1,3] dioxin (I, R' = R" = CH_3) (10 g, 43.4 mmol) in $CHCl_3$ (15 ml), methylamine 25% solution (11.5 ml, 86.8 mmol) was added dropwise with constant stirring. The solid product was washed with water and dried. 2,2-Dimethyl-4,5-dioxo-7-methylamino-pyrano [4,3-*d*] [1,3] dioxin (I) (7.8 g, 80.4%) was crystallized from $CHCl_3$, m.p. 207°.

Found: C, 53.5; H, 4.9; N, 6.2; $C_{10}H_{11}NO_5$
Requires: C, 53.3; H, 4.9; N, 6.2%

Other 7-alkylamino-2,2-dimethyl-4, 5-dioxo-pyrano [4,3-d] [1,3] dioxins (II) were prepared as above and listed in Table 1.

2,2-Dimethyl-4, 5-dioxo-7-hydroxy-6-methylpyridino [4,3- d][1,3] dioxin (III, R = CH_3). 2-2-Dimethyl-4, 5-dioxo-7-hydroxy-6-methylaminopyrano [4,3- *d*][1,3] dioxin (4.5g, 20m mol) was added to a solution of Na (1.8g, 80m mol) in phenol (60 ml) and the mixture was heated at 120° for 2 minutes. The solution was cooled, diluted with water and extracted with ether to recover excess of phenol. The ethereal layer was extracted with water and the combined aqueous extracts (150 ml) were acidified with HCl (3N). The solid product, 2,2-dimethyl-4, 5-dioxin-7-hydroxy-6-methylpyridino [4,3-*d*][1,3]dioxin (R = R' = R" = CH_3), (III, 4.0g, 88%) was crystallized from MeOH, m.p. 174°. It produced reddish brown colour with aq. $FeCl_3$ and effervescence with aq. $NaHCO_3$.

Found: C, 53.2; H, 4.9; N, 6.2; $C_{10}H_{11}NO_5$
Requires: C, 53.2; H, 4.9; N, 6.2%

The products III obtained as a result of the reaction of alkyl aminopyranodioxins (II) with sodium phenoxide in phenol are listed in Table 2.

2,2-Dimethyl-4,5-dioxo-7-methoxy-6-methylpyridino [4,3- d][1,3]dioxin (IV, R = CH_3). An ethereal solution of diazomethane was added in portions to 2,2-dimethyl-4,5-dioxo-7-hydroxy-6-methylpyridino [4,3-*d*] [1,3]dioxin (0.5g) suspended in ether (20 ml) until the yellow colour persisted. The solution was kept for 2 hr. in a refrigerator and the solvent was removed. The residue showed no colouration with aq. $FeCl_3$. 2,2-Dimethyl-4, 5-dioxo-7-methoxy-6- methylpyridino [4,3-*d*][1,3]dioxin (IV, 0.2g, 38%), m.p. 143°, was crystallized from MeOH.

Found: C, 55.4; H, 5.4; N, 5.7. $C_{11}H_{13}NO_5$
Requires: C, 55.2; H, 5.4; N, 5.8%.

8-Bromo-2, 2-dimethyl-4, 5-dioxo-7-hydroxy-6-methylpyridino [4,3-d] [1,3] dioxin (V, R = R ' = R" = CH_3). The compound (III, R = R' = R" = CH_3) (0.5g) was dissolved in $CHCl_3$ (20 ml) and bromine in $CHCl_3$ was added dropwise, till an orange colour persisted. The reaction mixture was kept at room temperature for 2 hr. and the solvent was removed. The solid bromo product (V, 0.4g, 59%) was crystallized from MeOH, m.p. 160°.

Found: C, 39.3; H, 3.2; N, 4.6. $C_{10}H_{10}NO_5Br$
Requires: C, 39.4; H, 3.2; N, 4.63%

7-Chloro-2,2-dimethyl-4,5-dioxo-6-methylpyridino [4,3-d][1,3]dioxin (VI, R = R''= R" = CH_3). 2,2-Dimethyl-4,5-dioxo-7-hydroxy-6-methylpyridino [4,3- *d*][1,3] dioxin (III, R = R' = R" = CH_3) (0.5g) was added thionyl chloride (4.0 ml) and the mixture was refluxed under anhydrous conditions for 15 min. Thionyl chloride was removed *in vacuo* and the residue was washed with water to yield the chloro product (VI, 0.4g, 68%). 7-Chloro-2, 2-dimethyl-4,5-dioxo-6- methylpyridino [4,3-*d*][1,3] dioxin (VI) was crystallized from MeOH, m.p. 300° decomp.

Found: C, 49.8; H, 4.1; N, 5.8. $C_{10}H_{10}NO_4$
Requires: C, 49.2; H, 4.1; N, 5.7%

Results and Discussion

It has been reported earlier that pyrano-dioxins derived from aliphatic amines, except isobutylamine, produced intractable phenolic materials when subjected to phenoxide rearrangements [3]. Reinvestigation of the isomerization of pyrano-dioxins (II) with sodium phenoxide in phenol resulted in pyridino-dioxins (III, R = R' = R" = alkyl). for instance, 7-methylamino-4, 5- dioxo-2, 2-dimethyl pyrano [4,3-*d*][1,3] dioxin (II, R = R' = R" = CH_3) on reacting with sodium phenoxide in phenol gave an isomeric product, $C_{10}H_{11}NO_5$ (III, R = R'= R" = CH_3), m.p. 174°, phenolic in nature (it gave $FeCl_3$ test and dissolved in aqueous $NaHCO_3$ solution). Other alkylamino dioxins (II) yielded the corresponding isomeric products (III).

These pyridino-dioxins (III) showed characteristic absorbance in the UV region 300 - 310 nm (Table 1). The substitution at position I, therefore, has apparently no effect on the UV absorption. An examination of IR spectra of the pyridino-dioxins showed absorbance at 1700 - 1740 cm^{-1} due to the lactone carbonyl at position 4 and absorption peaks at 1580 - 1615 cm^{-1} due to the amide carbonyl group at position 5.

The OH group at position 7 was methylated into the product (IV, R = R' = R" = CH_3), λmax 310 nm (log ε 4.15) and λmax 276 nm (logε, 4.10). Similarly the bromo derivative (V, R = R' = R" = CH_3) absorbed at λmax. 317 nm (logε 4.54). These observations are in conformity with the structures assigned to the products represented by formula III.

TABLE 3. UV AND IR SPECTRA OF PYRIDINO- [4,3-d][1,3] DIOXINS(III).

Sr. No.	Pyridino [4,3-d] [1,3] dioxin (III, R'=R"=CH_3) R	UV Light absorption (95% methanol) λmax (nm)	log ε	IR absorption max (cm^{-1}) mainly for the 3-6, 7u region, (KBr disc) υ C = 0(4) (cm^{-1})	υ C = 0 (5) (cm^{-1})
1.	Methyl	308	4.28	1725	1615
2.	Ethyl	300	3.94	1735	1610
3.	*n*-Pyropyl	310	4.25	1710	1580
4.	Allyl	308	4.23	1705	1600
5.	*n*-Hexyl	310	4.36	1700	1595
6.	*n*-Butyl	308	4.21	1740	1605

References

1. M.A. Butt, R. Kemal, A. Salam and A. Akhtar, Pak. j. sci. ind. res., 33, 27 (1990).
2. S.J. Devis and J.A. Elvidge, J. Chem. Soc., 4109 (1952).
3. Aslam Butt, I.A. Akhtar and M. Khurshid, Pak. j. sci. ind. res., 9, 335 (1966).