Pak. J. Sci. Ind. Res. 2003 ***46****(6) 406 - 408*

SYNTHESIS OF HETERO-BICYCLIC COMPOUNDS
PART-X. FORMATION OF 2H,4H,5H 2,2-DIPHENYL-4, 5-DIOXOPYRIDO [4, 3-d] 1,3 DIOXIN

Abdul Salam and Ausaf Akhtar*

PCSIR Laboratories Complex, Karachi-75280, Pakistan

(Received May 24, 2002; accepted December 14, 2002)

Aminopyranodioxin derived from benzophenone isomerize to yield 6 substituted 1, 2-dihydropyridodioxins **(III)**,whose structures were determined by chemical conversions and spectroscopic studies.

Key words: Pyranodioxin, Pyridodioxin, Hetero-bicyclic compound.

Introduction

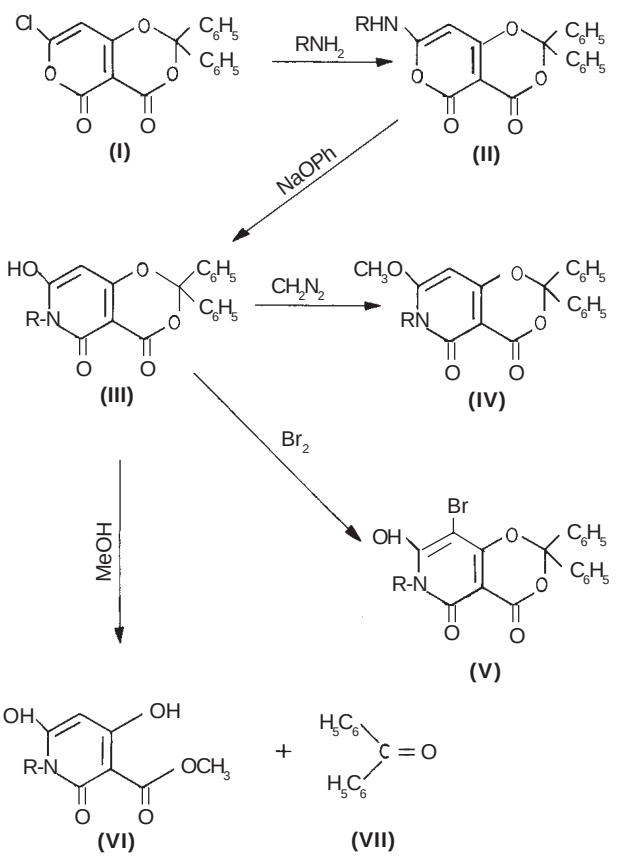
The reaction of acetone with malonyl chloride yields chloropyranodioxins (Davis and Elvidge 1952). These chloropyranodioxins react with amines to produce aminopyranodioxins (Butt *et al* 1992). The aminopyranodioxins isomerize to the corresponding pyridodioxins in the presence of sodium phenoxide (Butt and Akhtar 1965). This study was extended to the reaction of ketones other than acetone with malonyl chloride and the subsequent reaction with amines followed by isomerization to yield pyridodioxins (Butt *et al* 1997). Benzophenone yields similar chloro product with malonyl chloride which reacted with aromatic amines and isomerized then gives the corresponding 2,2-diphenyl 4,5-dioxopyrido (4, 3-d) (1,3) dioxins (Butt *et al* 1990). In the present study, 2,2-diphenyl chloropyranodioxin has been reacted with aliphatic amines to yield the amino compound, which undergo rearrangement under the action of sodium phenoxide to the corresponding aminopyridodioxins. The title compound was characterized by elemental analysis supported by degradations to known product, formation of derivatives and spectroscopic studies.

Materials and Methods

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. UV Spectra were recorded on Perkin Elmer UV visible spectrophotometer λ 4C.

*7-Chloro-2,2-diphenyl-4,5-dioxopyrano[4,3-d]1,3 dioxin **(I)***. The title compound **(I)** was prepared by heating benzophenone (0.1 mole, 3.7 g) and malonyl chloride (0.2 moles, 4.0 ml) on a water bath until the mass is solidified. Trituration of the product with ether gave 7-chloro-2,2-diphenyl-4,5-dioxopyrano [4, 3-d] 1,3 dixoin **(I)**, which crystallized from benzene, m.p 179°C. Found: C, 64.1; H, 3.3; Cl, 9.8% For $C_{19}H_{11}O_5Cl$ requires: C, 64.3; H, 3.1; Cl, 10.0%.

*7-Ethylamino-2,2-diphenyl-4,5-dioxopyrano [4,3-d]-1,3 dioxin **(II)** R=ethyl.* To a solution of **(I)** (5.0g, 0.02 mole) in chloroform (10 ml), ethylamine (2.3 ml, 0.04 mole) in 10



Scheme 1

*Author for correspondence

ml chloroform was added with constant stirring. The solid product obtained was washed with water and dried. 7-ethylamino-2, 2-diphenyl-4, 5-dioxopyrano [4, 3-d] 1, 3-dioxin (4.2g) was crystallized from methanol, m.p. 162˚C. Found: C, 69.2; H, 4.4; N, 3.6; $C_{21}H_{17}O_5N$ requires: C, 69.4; H, 4.6; N, 3.8%. Other 7-amino 2, 2-diphenyl-4, 5-dioxopyrano [4, 3-d] 1, 3 dioxins **(II)** prepared as above are listed in Table 1.

Reaction of 4,5 dioxo-2,2-diphenyl 7-ethylamino [4,3-d]1,3 dioxin with sodium phenoxide in phenol. 4, 5 dioxo-2, 2-diphenyl 7-ethylamino [4, 3-d] 1, 3 dioxin (2.5 g, 0.01 mole) was added to a solution of sodium (0.7 g.) in phenol (20 ml) and the mixture was heated at 120˚C for two minutes. 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 2N HCl. The solid product obtained 4, 5-dioxo-2, 2-diphenyl-6-ethyl-7-hydroxy pyrido [4, 3-d] 1, 3 dioxin **(III)** R = ethyl, 2.1g was crystallized from methanol, m.p. 198˚C. It produced reddish brown colour with aq. $FeCl_3$ and gave effervescence with aq. sodium bicarbonate. Found: C, 69.3; H, 4.6; N, 3.7% for $C_{21}H_{17}O_5N$ requires: C, 69.4; H, 4.6; N, 3.8%.

Table 1
7-Amino-2, 2-diphenyl-4, 5-diphenyl-4, 5-dioxopyrano [4, 3-d]-1, 3-dioxins **(1)**

S. No.	Primary amine	Quantity ml	7-Chloro-2-2-diphenyl, 4, 5-dioxopyrano-[4,3-d] 1,3 dioxing	Product IR	Yield %	M.P ˚C	Solvent for crystallization	Molecular formula	Analysis Found C H N	Analysis Requires C H N	UV Light absorption in methanol λ_{Max}	Log
1	Methyl amine	3.90	5	Methyl	82.0	165˚C	CH_3OH+$CHCl_3$	$C_{10}H_{15}O_5N$	68.8, 4.1, 3.8	68.7, 4.2, 4.0	305	4.57
2	Ammonia	1.00	5	Hydrogen	53.0	270˚C	CH_3OH	$C_{19}H_{13}O_5N$	67.9, 3.7, 4.3	68.0, 3.8, 4.1	314	4.51
3	Ethyl amine	2.27	5	Ethyl	68.0	162˚C	$CHCl_3$+ CH_3OH	$C_{21}H_{17}O_5N$	69.2, 4.4, 3.6	69.4, 4.6, 3.8	302	4.54
4	Propyl amine	2.29	5	Propyl	66.0	148˚C	CH_3OH	$C_{12}H_{19}O_5N$	69.4, 4.8, 3.3	70.0, 5.0, 3.7	325	4.54
5	*n*-Butyl amine	2.80	5	*n*-Butyl	71.0	164˚C	CH_3OH	$C_{23}H_{21}O_5N$	70.8, 5.3, 3.5	70.5, 5.3, 3.5	305	4.57
6	Benzyl amine	3.00	5	Benzyl	58.3	170˚C	$CHCl_3$	$C_{26}H_{19}O_5N$	73.9, 4.3, 3.15	73.4, 4.4, 3.2	315	4.56

Table 2
N-Substituted 4, 5-dioxo, 2-2-diphenyl-7-hydroxy-6-pyrido [4, 3-d] 1, 3 dioxins **(III)**

S. No.	7-Amino pyrano (1,3) dioxin	Quantity (g)	Sodium/ phenol	Pyridino (4, 3-d) 1, 3-dioxin **(III)**	Yield %	MP ˚C	Molecular formula	Analysis Found C	H	N	Analysis Requires C	H	N
1.	Methyl amino	4.0	0.65g/ 3.2 ml	4, 5-dioxo 2,2-diphenyl hydroxy 6-methyl	50	201˚C	$C_{20}H_{15}O_5N$	68.9	4.3	3.9	68.7	4.2	4.0
2.	Ammonia	2.5	0.70g/ 20 ml	6-amine 4, 5 dioxo 2, 2-diphenyl 7-hydroxy	48	210˚C	$C_{19}H_{13}O_5N$	67.9	3.7	3.9	68.0	3.8	4.1
3.	Ethyl amino	2.5	0.70g/ 20 ml	4, 5-dioxo 2, 2-diphenyl 6-ethyl 7-hydroxy	61	280˚C	$C_{21}H_{17}O_5N$	69.3	4.6	3.7	69.4	4.6	3.8
4.	*n*-Propyl amino	2.5	0.60g/ 18 ml	4, 5-dioxo 2, 2-diphenyl 7-hydroxy 6-propyl	70	228˚C	$C_{22}H_{19}O_5N$	69.4	5.1	3.9	70.0	5.0	3.7
5.	*n*-Butyl amino	2.0	0.70g 21 ml	6-butyl 4, 5 dioxo 2, 2-diphenyl 7-hydroxy	45	214˚C	$C_{23}H_{21}O_5N$	70.1	5.0	3.2	70.7	5.1	3.5
6.	Benzyl amino	4.0	0.86g/ 25.8 ml	6-benzyl 4, 5 dioxo 2, 2-diphenyl 7-hydroxy	60	198˚C	$C_{26}H_{19}O_5N$	73.1	4.3	3.1	73.4	4.4	3.2

Other alkylamino pyranodioxins **(II)** were reacted similarly with sodium phenoxide in phenol and the products obtained by formula **(III)** are listed in Table 2.

*Both 4,5-dioxo-2,2-diphenyl 6-ethylamino 7-methoxy pyrido [4,3-d] 1,3 dioxin **(IV)***. To 0.5g **(III)** R = ethyl 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 refrigerator and the excess solvent was removed. The residue upon trituration with ether yielded a neutral product, which showed no colouration with aq $FeCl_3$ **(IV)** 0.3 g obtained was crystallized from methanol, m.p 183˚C Found: C, 69.9; H, 4.9; N, 3.8% for $C_{22}H_{19}NO_5$ requires: C, 70.0; H, 5.0; N, 3.7%.

*8-Bromo 4,5-dioxo 2,2-diphenyl-6-ethylamino-pyrido [4,3-d]-1,3 dioxin **(V)** R = ethyl.* The compound **(III)** R = ethyl (0.5 g) was dissolved in chloroform (20 ml) and bromine in chloroform was added dropwise till an orange colour persisted. The reaction mixture was kept at room temperature for 1 h and subsequently, the solvent was removed. The solid bromo product (0.5 g, 75%) **(V)** R = ethyl was re-crystallized from methanol, m.p. 189˚C. Found: C, 57.0; H, 3.6; N, 3.1% requires: C, 56.8; H, 3.8; N, 3.1% for $C_{21}H_{16}O_5N$ Br.

*Degradation of **(III)** with methanol*. The compound **(III)** R = ethyl (0.05g) was refluxed with methanol (25 ml) for 6 h. The solution upon concentration in vacuum yielded **(VI)** 0.3 g which was crystallized from MeOH, m.p 221˚C. Found: C, 50.5; H, 5.3; N, 6.3% requires: C, 50.7; H, 5.1; N, 6.5 %. From the filtrate benzophenone was isolated and characterized as 2,4 dinitrophenyl - hydrazone derivative for $C_9H_{11}NO_5$.

Results and Discussion

Isomerization of 7-alkylamino 4, 5-dioxopyrano 2, 2-diphenyl [4, 3-d] 1, 3 dioxins **(II)** under the influence of sodium phenoxide to the corresponding alkyl substituted pyridodioxins **(III)** has been studied. For instance, 7-ethylamino 4, 5 dioxo 2, 2-diphenyl 6-ethylamino pyrano [4, 3-d] 1, 3 dioxin **(II)** on reacting with phenoxide in phenol produced $C_{21}H_{17}O_5N$ **(III)** R-C_2H_5, m.p. 198˚C (Scheme 1). This product is enolic in nature ($FeCl_3$ test) dissolves in aq. sodium bicarbonate solution and is isomeric with the starting material. It is moderately stable towards alcohol and is decomposed on boiling. The other alkylamino pyranodioxins yield similar isomeric products upon treatment with sodium phenoxide in phenol. These products **(III)** absorb in the UV region 310-315 mμ. Table 3 closely resembling pyridodioxins.

The OH group at position 7, was methylated into the product **(IV)** R = ethyl, λ_{max} 300 log ∈ 4.0 (λ_{max} 275, log ∈ 4.2). Similarly, bromo derivative **(V)** R = ethyl had (λ_{max} 300 log ∈ 4.87). Finally, the structure **(III)** for these new products was confirmed by boiling it **(III)** R = ethyl in methanol to form pyridine methyl ester **(VI)** R = ethyl and benzophenone **(VII)**.

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