Phosphorous Esters of 2,13-dihydroxy- 7a, 14c-dihydronaphtho[1',2':4,5]furo [3,2-d] furan

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Abstract : 2,13-dihydroxy-7a,14c-dihydronaphtho[1',2':4,5]furo[3.2-d]furan prepared from glyoxal bisulphite and 2,7-dihydroxynaphthalene was reacted with, $C_6H_5PCl_2$, $C_6H_5POCl_2$ and Br-$C_6H_4OPOCl_2$ to produce its phosphorous esters. The structures of the products were investigated by MS, FTIR, ^{1}H-NMR, ^{13}C-NMR, and ^{31}P-NMR. Although $C_6H_5PCl_2$ gave a compound with a new ring containing phosphorous atom, $C_6H_5POCl_2$ and Br-$C_6H_4OPOCl_2$ resulted acyclic phosphorous esters.

Introduction

2,13-dihydroxy-7a, 14c-dihydronaphtho[1',2':4,5]furo[3.2-d]furan 1 has been synthesized before by the reaction of 2,7-dihydroxynaphthalene with glyoxal (1,2). Naphtofuran derivatives with new functional groups have been synthesized in order to increase their possible biological activities. Attempts for acetylation or methylation of both hydroxyl groups of 1 have failed and only mono derivatives have been obtained even if high excess of corresponding reagents have been used (2). This has been suggested to be due to the steric hindrance of two naphthol rings , since two OH groups are very close to each other. In this work, the synthesis of phosphorous esters of 1 were aimed due to their possible biological activities. The phosphorous compounds containing two functional groups such as $C_6H_5POCl_2$, $C_6H_5PCl_2$, and Br- $C_6H_4OPOCl_2$ were used in order to obtain cyclic ester structure.

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Experimental

Analyses

FTIR spectra were recorded on Jasco FT-IR 5300 fourier transform infrared spectra. ^{1}H and ^{13}C NMR spectra were obtained in deuterated dimethyl sulfoxide, chloroform and acetone solution in a Bruker AMX (300 MHz) instrument using TMS as an internal standart. In case of ^{31}P-NMR , H_3PO_4 was used as internal standart. Mass spectra were recorded by DS-55 model instrument.

Glyoxal bisulphite and *2,13-dihydroxy 7a,14c-dihydronaphtho[1',2':4,5]furo[3.2-d]furan* **1**.

They were prepared as described before (1). The product **1** was purified by crystallization from ethanol and needle-like crystals were obtained.

Preparation of 26-phenyl-8, 10, 25, 25-tetra-26λ^5-phosphaheptacyclo [15, 7.3.0$^{4.23}$ 0$^{7.22}$. 0$^{9.21}$. 0$^{11.20}$.0$^{14.19}$]heptacosa-1,3,5,7(22),11(20),12,14,16,18,23-decaene **2** *:*

1 mole of **1** was dissolved in pyridine/dichloromethane (1/1) mixture and 1 mole of dichloro phenyl phosphine was then added slowly while stirring vigorously at room temperature under the nitrogen atmosphere. The temperature was increased to 100 °C[3], and kept at this temperature for 30 minutes while stirring, then the temperature was lowered and the stirring continued further for 10 h. The reaction mixture was precipitated by pouring into methanol and the product was filtered, washed several times with methanol and then purified by column chromatography (silica gel, acetone). The product was reprecipitated as white powder by pouring its ether solution into petroleum ether, and then dried at room temperature in vacuum. m.p.=340°C (decomp.), yield 72%. IR (KBr): 3030-2950, 1625, 1200, 830 cm^{-1}. ^{1}H – NMR (D_6-DMSO): δ ; 6.6 (1 H, d, J= 6.8 Hz, benzylic), 7.2 (1 H, d, J= 6.8 Hz acetalic proton), 7.1-8.0 (15 H, m, aromatics). ^{13}C-NMR (D_6-DMSO): δ ; 48, 110.83, 114.70, 117.38, 126.39, 126.55, 128.48, 129.70, 130.02, 130.41, 130.75, 131.56, 131.82, 154.51, 156.39. ^{31}P – NMR (D_6-DMSO): δ ; 160.6 and 163.6 . MS: M^+=448, m/e=342 (100%), 313, 239, 195, 171, 119, 64, 36.

13-hydroxy-7a,14c-dihydronaphto[2,1-b]naphtho[1',2':4,5]furo[3,2-d]furan-2-yl methyl phenyl phosphonate **3** *:*

This compound was obtained from the reaction of **1** with P,P-dichloro phenyl phosphine oxide. The reaction mixture was treated as explained in preparation of the compound **2**. It was purified by dissolving in ether and reprecipitating in petroleum ether. m.p.=300°C , yield: 70%. IR (KBr): 3300, 3030-2950, 1640, 1525, 1460, 1370, 1100, 1025, 770 cm^{-1}. ^{1}H – NMR ($(CD_3)_2CO$): δ , 3.7 (3H,

d, J=11 Hz, OCH_3), 7.2 (1 H, d, J= 6.8 Hz acetalic proton), 6.5-8.5 (15 H, m, aromatics). ^{31}P–NMR (D_6-DMSO): δ ;15-25. MS: M^+=496 (100%), m/e=356, 342, 324, 313, 239, 171, 119, 44, 18.

13-hydroxy-7a,14c-dihydronaphto[2,1-b]naphtho[1',2':4,5]furo[3,2-d]furan-2-yl hydrogen phenyl phosphonate **4** :

This compound was obtained from the reaction of **1** with P,P-dichloro phenyl phosphine oxide in pyridine/acetonitrile/dichloromethane (1/2/2) mixture as explained in the preparation of the compound **2** except the reaction mixture was poured into water. It was purified by dissolving in ether and reprecipitating in petroleum ether. m.p.=285 °C, yield: 72 %. IR (KBr): 3069, 1632, 1518, 1460, 1367, 1255, 1211, 1134, 1055, 966, 831 cm^{-1}. ^1H – NMR (D_6-DMSO): δ ; 5.5 (1H, d, J=6.2 Hz, benzylic), 7.2 (1 H, d, J= 6.8 Hz acetalic proton), 6.7-8.2 (15 H, m, aromatics) . ^{13}C-NMR (D_6-DMSO): δ ; 48, 105-160 (27 aromatic peaks). ^{31}P – NMR (D_6-DMSO): δ ; 5.3 . MS: M^+=482 (100%), m/e=384, 368, 342, 313, 285, 239, 160, 98, 44, 18.

4-bromophenyl (13-hydroxy-7a,14c-dihydronaphto[2,1-b]naphtho[1',2':4,5]furo[3,2-d]furan-2-yl) methyl phosphate **5** :

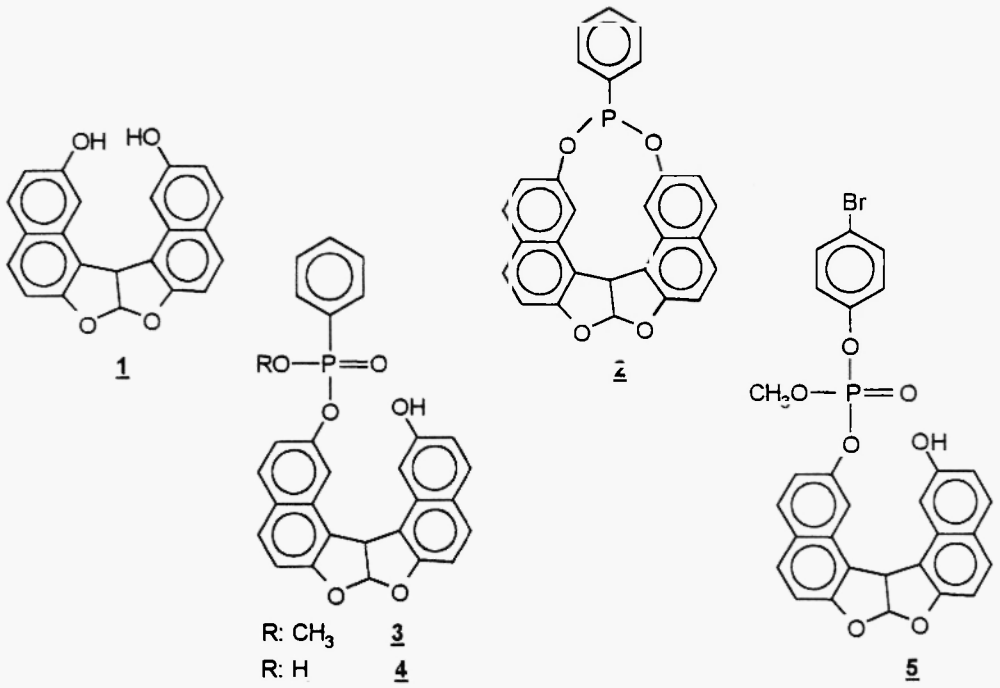
This compound was obtained from the reaction of **1** with 4-bromophenyl dichloro phosphate. The reaction mixture was treated as explained in preparation of the compound **2**. It was purified by dissolving in ether and reprecipitating in petroleum ether.

m.p.=310 °C (decomp.), yield: 74 %. IR (KBr): 3300, 3096, 2131, 1726, 1631, 1583, 1504, 1487, 1458, 1369, 1329, 1258, 1211, 1132, 1080, 1044, 966, 918, 829, 748, 679, 603, 569, 495 cm^{-1}.

^1H – NMR (D_6-DMSO): δ ; 2.3 (3H, d, J= 2Hz, OCH_3), 5.5 (1H, d, J=6 Hz, 14c-H), 7.1 ppm (1H, d, J= 6 Hz, 7a-H), 6.7-8.2 (15 H, m, aromatics), 9.8 (1H, s, -OH). ^{13}C-NMR (D_6-DMSO): δ ; 20, 48, 105.4, 105.9, 108.4, 112.3, 114.5, 114.61, 115.9, 116.7, 117.3, 118.2, 119.6, 119.8, 119.9, 124.8, 125.8, 126.4, 129.6, 130, 131.7, 131.9, 156.2, 156.3, 157.4 . ^{31}P –NMR (D_6-DMSO): δ ,-12. MS: M^+= 512, m/e= 496, 384, 368, 342, 325, 313, 295, 268, 255, 239, 226, 213, 184, 171, 134, 119, 107, 90, 80, 77, 65.

Results and Discussion

The compound **1** was reacted with phenyl phosphorous dichloride under anhydrous and oxygen free conditions and the product **2** was obtained. ^{31}P-NMR spectrum of **2** showed two peaks with about the same integration intensities at about 160 ppm. This is due to the product **2** being a mixture of two streoisomers about equal amount. Similar reaction was carried out with $C_6H_5POCl_2$ and the cyclic structure could not be produced instead the compound **3**, was obtained.



If the work-up changed, i.e. the reaction mixture was poured into water instead of methanol, the product **4** was formed. Even if two moles of phenyl phosphorous oxychloride for one mol of the compound **1** was used only the compound **3** was obtained. Furthermore, the compound **5** was formed when the reaction mixture of the compound **1** and 4-bromophenyl dichloro phosphate was poured into methanol. The compounds **3**, **4** and **5** had no stereoisomers. These results suggest that trivalent phosphorous compound, phenyl phosphorous dichloride, easily forms cyclic product **2** while pentavalent phosphorous compounds such as phenyl phosphorous oxydichloride and 4- bromo phenyl dichloro phosphate could not form cyclic products containing phosphorous atom in the ring. This may be due to steric effect of pentavalent phosphorous atom which inhibites intramolecular reaction between hydroxyl and P-Cl groups.

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