Synthesis of Dinaphthofuranofuran and Dinaphthopyranopyran Derivatives

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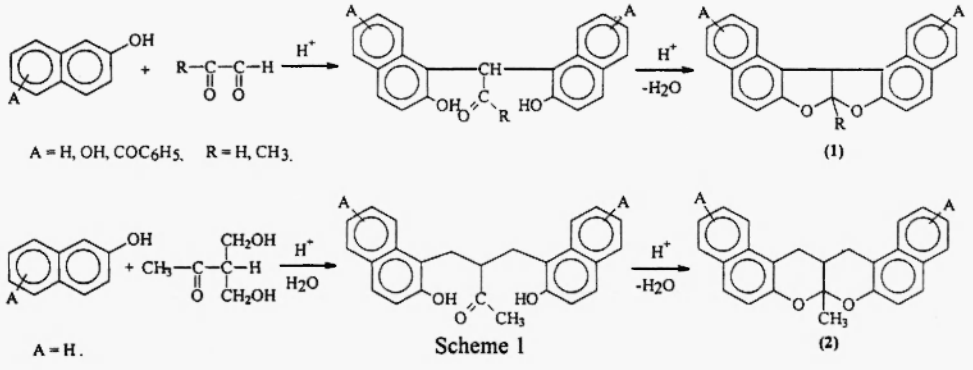
Abstract: Condensation reaction of carbonyl compounds [glyoxal, 1,3-dihydroxyacetone and 1,3-bis-(hydroxymethyl) acetone] with hydroxyaromatic compounds have been carried out and the structures of the products have been investigated. Naphthofuranonaphthofuran is modified by adding the functional groups which have been chosen from the compounds used for cancer and AIDS chemotherapy.

Introduction

In our recent reports we have described the synthesis of naphthofuranonaphthofuran (**1**) and naphthopyrano-naphthopyran (**2**) derivatives via the condensation reactions between carbonyl compounds with 2-naphthol and its derivatives.[1,2] (scheme 1)



Scheme 1

Some of the above mentioned product types have been tested for their potential anti-cancer and anti-HIV properties at the National Cancer Institute USA. However, only very weak biological activities have been observed.

Experimental

IR spectra were obtained for using Jasco 5300 instrument. ^{1}H-NMR Data were recorded on a Bruker 200 MHz and Bruker 250 MHz spectrometer. Chemical shifts were expressed as δ values from tetramethylsilane as an internal standard. Mass spectra were recorded with a VG-Zabspec double- focusing spectrometer at 70 eV (EI-MS)

Standard Method (For Compounds 1, 3, 6 and 9): Two moles of naphthol compound was dissolved in 98% formic acid and was heated to 50-60°C. Then one mole of glyoxalbisulphite[2] was added to the solution and stirred at that temperature for 4h. Reaction mixture was poured into water and the precipitated part was filtered and

washed with water till neutralizing occurred.The crude product was boiled with water to remove the unreacted naphthol.

Standard Method (For Compounds 5 and 7) : Two moles of naphthol compound and one mole of 1,3-dihydroxyacetone were dissolved in ethanol and then conc. H_3PO_4 was added into the mixture as a catalyst Reaction mixture was refluxed for 8 h and neutralized after cooling to room temperature. Precipitated inorganic salt was removed by filtration. The reaction mixture was concantrated by distillation of some alcohol. The mixture was allowed to stand for overnight in a refrigerator. Precipitated crude product was filtered and dried.

Standard Method (For Compounds 4, 8, 10 and 11) : 10 g of Amberlyst-15, 28 g of naphthol compound and 50 ml ethanol were placed in a three-necked round bottomed flask equipped with mechanical stirrer, condenser and a dropping funnel. The mixture was heated to 70°C with stirring.Then 9.7 g 1,3-bis-(hydroxymethyl)acetone[1] was added dropwise from the dropping funnel to the reaction mixture in 3 h. At the end of this period, Amberlyst-15 was filtered and the solution was allowed to stand overnight. Reaction products were purified by crystallization.

3,12-Dibenzoyl-7a,14c-dihydronaphtho[2,1-b]naphtho[1',2'; 4,5] furo[3,2-d] furan (3): This compound was obtained from the reaction of 6-benzoyl-2-naphthol with glyoxalbisulphite and purified by recrystallization from toluene-acetone (1/1) mixture. 38% yield. M.p=264°C. IR(KBr): 3100, 1657, 1616, 1280, 1089 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 6.1(1H, d, J=6.0 Hz, H_{14c}), 7.3 (1H, d, J=6.0 Hz, H_{7a}), 7.2-8.4 ppm (20H, m, Ar-H), MS(%): M^+=518(75), m/z:437(65), 416(63), 393(55), 305(53), 249(62), 219(100), 201(42). (Found: C, 83.2; H,4.0 ; $C_{36}H_{22}O_4$; requires; C, 83.4; H,4.3 %)

3,12-Dibenzoyl-7a,15a-dihydro-7a-methyl-naphtho [2,1-b] naphtho [1',2';5,6] pyrano [3,2-e] pyran (4) : This compound was obtained from the reaction of 6-benzoyl-2-naphthol with 1,3-bis-(hydroxymethyl)acetone and purified by recrystallization from methanol-water (3/1) mixture. 35% yield. M.p=209°C. IR(KBr): 3100, 2980, 1651, 1631, 1288, 1226 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 2.2 (3H, s, CH_3), 2.8 (1H, t, H_{15a}), 2.9 (2H, d,d J=17.1 Hz, J:6.3 Hz H_{15eq}, H_{16eq}), 3.4 (2H, d,d J=17.2 Hz, J:6.1 Hz H_{15ax}, H_{16ax}), 7.2-8.2 ppm (20H, m, Ar-H), MS(%): M^+=560(40), m/z:523(53), 514(35), 490(44), 453(45), 429(58), 413(62), 387(70), 377(83), 363(100). (Found: C, 83.5; H,4.8 ; $C_{39}H_{28}O_4$; requires; C, 83.6; H,5.0 %)

3,12-Dibenzoyl-7a,14c-dihydro-7a-methyl-naphtho[2,1-b]naphtho[1',2'; 4,5]furo[3,2-d] furan (5): This compound was obtained from the reaction of 6-benzoyl-2-naphthol with 1,3-dihydroxyacetone and purified by recrystallization from methanol. 32% yield. M.p=192°C. IR(KBr): 3200, 2950, 1651, 1263, 1059 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 2.2 (3H, s, CH_3), 5.6 (1H, s, H_{14c}), 7.2-8.2 ppm (20H, m, Ar-H) MS(%): M^+=532(35), m/z:517(52), 481(82), 437(87), 393(85), 349(60), 307(38), 265(43), 219(100). (Found: C, 83.4; H,4.8 ; $C_{37}H_{24}O_4$; requires; C, 83.4; H,4.5 %)

3,12-Dibromo-7a,14c-dihydronaphtho[2,1-b]naphtho[1',2';4,5]furo[3,2-d]furan (6): This compound was obtained from the reaction of 6-bromo-2-naphthol with glyoxalbisulphite and purified by recrystallization from toluene-ethanol (3/1) mixture. 69% yield. M.p=290°C. IR(KBr): 3100, 1622, 1257, 1079, 508 cm^{-1}. ^{1}H-NMR (d_1-chloroform) δ; 5.5 (1H, d, J=5.95 Hz, H_{14c}), 7.1 (1H, d, J=5.9 Hz, H_{7a}), 7.3 (2H, d, J=5.8 Hz, H_1-H_{14}), 7.5 (2H, dd, J=9.0 Hz, J=1.8 Hz, H_2-H_{13}), 7.6 (2H, d, J=1.8 Hz, H_4-H_{11}), 7.7 (2H, d, J=8.9 Hz, H_5-H_{10}), 8.1 ppm (2H, d, J=8.9 Hz, H_6-H_9), MS(%): M^++2=470(45), M^+=468(100),m/z: 466(45) , 439(15), 359(15), 279(12), 250(23), 125(23), 113(15). (Found: C, 56.5; H,2.5 ; Br,34.3; $C_{22}H_{12}O_2Br_2$; requires; C, 56.4; H,2.6 ; Br, 34.2 %)

3,12-Dibromo-7a,14c-dihydro-7a-methyl-naphtho[2,1-b]naphtho [1',2'; 4,5] furo[3,2-d] furan (7): This compound was obtained from the reaction of 6-bromo-2-naphthol with 1,3-dihydroxyacetone and purified by recrystallization from the ethanol-water (3/1) mixture. 45% yield. M.p=217°C. IR(KBr): 3100, 2950, 1628, 1265, 1066, 508 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 2.8 (3H, s, CH_3), 5.6 (1H, s, H_{14c}), 7.3 (2H, d, J=6.0 Hz, H_1-H_{14}), 7.5 (2H, d, J=9.0 Hz, H_5-H_{10}), 7.8 (2H, d, J=2.1 Hz, H_4-H_{10}), 8.0 (2H, d, J=9.0 Hz, H_6-H_9), 8.2 ppm (2H, dd, J=6.5 Hz, J=2.0 Hz, H_2-H_{13}), MS(%): M^++2=484(44), M^+= 482(65), m/z:480(48), 439(20), 437(15), 359(10), 332(42), 276(40), 251(38), 222(50), 152(74), 113(100), 63(70). (Found: C, 57.0; H,2.7 ; Br,33.1; $C_{23}H_{14}O_2Br_2$; requires; C, 57.3; H,2.9 ; Br, 33.2 %)

3,12-Dibromo-7a,15a-dihydro-7a-methyl-naphtho[2,1-b]naphtho[1',2';5,6]pyrano[3,2-e]pyran(8): This compound was obtained from the reaction of 6-bromo-2-naphthol with 1,3-bis-(hydoxymethyl)acetone and purified by recrystallization from ethanol-water (3/1) mixture. 35% yield. M.p=230°C. IR(KBr): 3200, 2930, 1622, 1410, 1265, 1115, 1064, 518 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 1.8 (3H, s,CH_3), 2.8 (1H, t, H_{15a}), 2.9 (2H, d,d J=17.1 Hz, J:6.7 Hz H_{15eq}, H_{16eq}), 3.4 (2H, d,d J=17.1 Hz, J:6.1 Hz H_{15ax}, H_{16ax}), 7.2 (2H, d, J=9.0 Hz, H_5-H_{10}), 7.6 (2H, d,d J=8.9 Hz, J=2.0Hz, H_2-H_{13}), 7.7 (2H, d, J=8.9 Hz, H_1-H_{14}), 7.9 (2H, d, J=9.0 Hz, H_6-H_9), 8.05 ppm (2H, d, J=2.0 Hz, H_4-H_{11}),

MS(%): M^++2=512(10). M^+=510(20), m/z: 508(10),439(44), 415(25), 361(25), 279(27), 275(35), 222(100), 152(38), 128(60), 55(50). (Found: C, 58.9; H,3.5 ; Br,31.3; $C_{25}H_{18}O_2Br_2$; requires; C, 58.8; H,3.5 ; Br, 31.4 %)

6a,12b-Dihydro-indano[5,6-b]indano[6',5'; 4,5] furo[3,2-d] furan (9): This compound was obtained from the reaction of 5-indanol with glyoxalbisulphite and purified by recrystallization from ethanol. 65% yield. M.p=198°C. IR(KBr): 3100, 2957, 1626, 1257, 1140, 1039 cm^{-1}. ^{1}H-NMR (d_6-benzene) δ; 1.8 (4H, td, J=7.3 Hz, J=1.8 Hz H_3-H_{10}), 2.5 (4H, t, J=8.1 Hz, H_2-H_{11}), 2.6 (4H, t, J=8.2 Hz, J:2.9 Hz H_4, H_9), 4.3 (1H, d, J=6.23 Hz, H_{12b}), 6.6 (1H, d, J=6.3 Hz, H_{6a}), 6.7 (2H, s, H_1-H_{12}), 7.0 ppm (2H, s,H_5-H_8), MS(%): M^+=290(20), m/z:256(22), 221(22), 219(28), 177(50), 133(100), 117(25), 89(100), 87(100), 73(100), 59(62). (Found: C, 82.6; H,6.3 ; $C_{20}H_{18}O_2$; requires; C, 82.7; H,6.3 %)

6a, 13a-Dihydro-6a-methyl-indano[5,6-b]indano[6',5'; 5,6]pyrano[3,2-e]pyran (10): This compound was obtained from the reaction of 5-indanol with 1,3-bis-(hydroxymethlyl)acetone and purified by recrystallization from ethanol-water (3/1) mixture. 45% yield. M.p=186-187°C. IR(KBr): 3100, 2922, 1645, 1271, 1167, 1097 cm^{-1}. ^{1}H-NMR (d_6-benzene) δ; 1.6 (3H, s, CH_3), 1.9 (1H, t, J=6.35 Hz, H_{13a}), 2.6 (4H, t, J=7.6 Hz, H_4-H_9), 2.7 (4H, t, J=7.2 Hz, H_3-H_{11}), 2.9(4H,m,H_3-H_{10}), 3.4 (4H,dd,H_{13}-H_{14}), 6.9 (2H,s,H_5-H_8), 6.7 ppm (2H,s,H_1-H_{12}), MS(%): M^+=332(28), m/z:280(18), 185(72), 147(75), 69(53), 59(100). (Found: C, 83.3; H,7.0 ; $C_{23}H_{24}O_2$; requires; C, 83.1; H,7.3 %)

2,13-Dihydroxy-7a,15a-dihydro-7a-methyl-naphtho[2,1-b]naphtho[1',2';5,6]pyrano[3,2-e]pyran (11): This compound was obtained from the reaction of 2,7-dihydroxy naphthalene with 1,3-bis-(hydroxymethyl)acetone and purified by recrystallization from toluene.35% yield. M.p=290°C.. IR(KBr): 3427, 2920, 1622, 1286, 1136, 1064 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 1.7 (3H, s,CH_3), 2.8 (1H, t, J=5.9 Hz, H_{15a}), 2.9 (2H, d,d J=16.5 Hz, J:6.05 Hz H_{15eq}, H16eq), 3.3 (2H, d,d J=16.5 Hz, J:5.93 Hz H_{15ax}, H_{16ax}), 6.8 (2H, d, J=8.9 Hz, H_5-H_{10}), 7.0 (2H, dd, J=8.8 Hz, J=2.2Hz, H_2-H_{13}), 7.1 (2H, d, J=2.2 Hz, H_1-H_{14}), 7.6 (2H, d, J=8.9 Hz, H_6-H_9), 8.7 (2H, d, J=8.8 Hz, H_4-H_{11}), 8.9 ppm (2H, s, OH) MS(%): M^+=384(3), m/z:369(5), 351(100), 349(18), 275(35), 210(80), 181(32), 152(32), 77(14). (Found: C, 78.2; H,5.0 ; $C_{25}H_{20}O_4$; requires; C, 78.1; H,5.2 %)

3,12-Dinitro-7a,14c-dihydro-naphtho[2,1-b] naphtho [1',2'; 4,5] furo[3,2-d] furan (12): 3 g of Compound (1) was dissolved in 10 ml acetic acid and heated to 50-60°C on the water bath. Mixture of HNO_3/H_2SO_4 1.5ml/2.5ml was added dropwise to the mixture at this temperature. After the end of the addition, reaction mixture was stirred additional 1 h and then poured into 100 ml cold water. The yellow precipitate was filtered, washed with water several times. Then, the solid material was put into 10% sodium hydroxyde solution and stirred for 15 min. Filtered and washed with water. Dried solid product was boiled with 150 ml ethanol. Undissolved part was separated by filtration and purified by recrystallization from dioxan. 40% yield. M.p=285°C. IR(KBr): 3100, 2920, 1626, 1606, 1600, 1340, 1260, 1120, 1061, cm^{-1}. ^{1}H-NMR (d_6-dimethyl sulfoxide) δ; 6.2 (1H, d, J=6.0 Hz, H_{14c}), 7.4 (1H, d, J=5.9 Hz, H_{7a}), 7.5 (2H, d, J=9.0 Hz, H_6-H_9), 8.2 (2H, d, J=2.3 Hz, H_4-H_{11}), 8.3 (2H, d, J=8.1 Hz, H_5-H_{10}), 8.4 (2H, dd, J=8.1 Hz, J=2.4 Hz, H_2-H_{13}), 8.6 ppm (2H, d, J=8.2 Hz, H_1-H_{14}), MS(%): M^++2=402(100), M^+=400(30), m/z:384(12), 380(15), 355(22), 259(18), 211(20), 167(50), 132(20), 113(30), 74(60), 57(100), 29(90). (Found: C, 66.0; H,3.1 ; N,6.9; $C_{22}H_{12}N_2O_6$; requires; C, 66.0; H,3.0; N,7.0 %)

3,12-Diamino-7a,14c-dihydro-naphtho[2,1-b] naphtho [1',2'; 4,5] furo[3,2-d] furan (13): 200 mg of Compound **12** was dissolved in 20 ml dioxan and 0.7 g Zn powder was put into this solution. 3 ml con. Hydrochloric acid was added dropwise in the period of 15 min and stirred futher for 15 min. At the end of this period, the mixture was poured into 200 ml 5% hydrochloric acid solution. Unreacted nitro compound was filtered off. The solution was made slightly basic by adding 5% NaOH solution. The precipitated amino compound was filtered, washed with water several times and dried. The dried solid product was boiled with 150 ml acetone and added 0.5 g activated carbon. After filtration, 50 ml hot water was added to the solution, then cooled.The solid precipitated was purified by recrystallization from acetone-water (3/1) mixture. 25% yield. M.p=240°C. IR(KBr): 3400, 2930, 1651, 1625, 1217, 1089 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 4.7 (4H, s, N-H), 5.6 (1H, d, J=5.86 Hz, H_{7a}), 6.9(2H, d, J=2.1 Hz, H_4-H_{11}), 7.0 (1H, d, J=5.9 Hz, H_{14c}), 7.2 (2H, dd, J=9.04 Hz, J=2.2 Hz, H_2-H_{13}), 7.3 (2H, d, J=8.8 Hz, H_5-H_{10}), 8.2 (2H, d, J=8.9 Hz, H_6-H_9), 8.4 ppm (2H, d, J=8.35 Hz, H_1-H_{14}), MS(%): M^+=340(41), m/z:322(32), 308(20), 252(18), 226(5), 222 (8), 57(50). (Found: C, 77.6; H,4.8 ; N,8.0; $C_{22}H_{16}N_2O_2$; requires; C, 77.7; H,4.7; N,8.2 %)

3,12-Dihydroxy-7a,14c-dihydro-naphtho[2,1-b] naphtho [1',2'; 4,5] furo[3,2-d] furan (14): 85 mg of Compound **13** was dissolved in 200 ml 5% HCl solution and cooled in ice-bath to 5°C. 35 mg $NaNO_2$ was dissolved 10 ml water and added to amin solution while stirring. The solution was allowed to stand 10 min and diazonium salt was precipitated. Then the reaction mixture was heated to 50°C for 45 min and stand overnight. Solid product was filtered and dissolved in 5% NaOH solution. Undissolved part was filtered off. When the solution was acidified, dihydroxy compound began to fall down. The product was filtered, washed with water and dried. The solid precipitate was purified

by recrystallization from acetic acid. 18% yield. M.p=295°C. IR(KBr): 3450, 3100, 1633, 1606, 1222, 1057 cm^{-1}. ^{1}H-NMR (d_6-acetone) δ; 5.8 (1H, d, J=5.9 Hz, H_{14c}), 7.1 (1H, d, J=5.9 Hz, H_{7a}), 7.2 (2H, dd, J=7.04 Hz, J=2.0 Hz, H_2-H_{13}), 7.4 (2H, d, J=7.9 Hz, H_1-H_{14}), 7.6 (2H, d, J=8.78 Hz, H_5-H_{10}), 8.4 (2H, d, J=8.5 Hz, H_6-H_9), 8.6 ppm (2H, s, O-H). MS(%): M^+=342(88), m/z:313(18), 297(14), 184(75), 160(100), 114 (40), 77(18), 63(15), 51(15). (Found: C, 77.5; H,4.2 ; $C_{22}H_{14}O_4$; requires: C, 77.2; H,4.1; %)

4,11-Di(thiomethoxymethyl)-3,12-dihydroxy-7a,14c-dihydro-naphtho[2,1-b] naphtho[1',2'; 4,5] furo[3,2-d] furan (15): 200 mg of Compound **14** and 1.2 g DCC were put together into the 1 ml dried benzene. 65 ml DMSO and 0.5ml H_3PO_4 were added and stirred overnight. The reaction mixture was washed with 5% NaOH solution. Benzene layer was dried over anhydrous Na_2SO_4 and the solid product was crystallizated from carbontetrachloride. 23% yield M.p=267-269°C. IR(KBr): 3350, 2920, 2850, 1620, 1580, 1320, 1250, 1050 cm^{-1}. ^{1}H-NMR (d_6-dimethylsulphoxide) δ: 2.4 (6H, s, CH_3), 3.6 (4H, s, CH_2), 4.95 (1H, d, J=5.6 Hz, H_{7a}), 6.8 (1H, d, J=5.6 Hz, H_{14c}), 8.0-7.0 ppm (8H, m, Ar-H details were given for compound **14**), 9.6 ppm (2H, s, O-H). MS(%): M^+=462(3), m/z:446(25), 355(25), 326(30), 310(100), 281 (60), 252(30), 239(13). (Found: C, 67.8; H,4.5 ; S,14.0; $C_{26}H_{22}O_4S_2$; requires; C, 67.5; H,4.8; S,13.9 %)

3,12-Di[2-(diethylamino)ethoxy]-7a,14c-dihydro-naphtho [2,1-b] naphtho [1',2'; 4,5] furo[3,2-d] furan (18): 35 mg of Compound **14** and 23 mg sodiumcarbonate were dissolved in 15 ml ethylacetate and refluxed for 8 h. After cooling, the solution was washed with 10 ml cold water. Ethylacetate layer was dried and evaporated. The solid material was crystallized from acetic acid. 16% yield. M.p=246°C. IR(KBr): 2851, 1620, 1580, 1250, 1110 cm^{-1}. ^{1}H-NMR (d-chloroform) δ; 1.0 (12H, t, CH_3), 1.5-2.0 (12H, m, CH_2-N), 3.5 (4H, t, CH_2O), 5.6 (1H, d, J=5.9 Hz, H_{7a}), 7.0 (1H, d, J=5.9 Hz, H_{14c}), 7.1-7.8 ppm (10H, m, Ar-H details were given for compound **14**). MS(%): M^+=540(5), m/z:530(80), 525(35), 446(44), 432(74), 405 (100), 394(32). (Found: C, 75.6; H,7.3 ; N,5.0; $C_{34}H_{42}N_2O_4$; requires; C, 75.5; H,7.5; N,5.2 %)

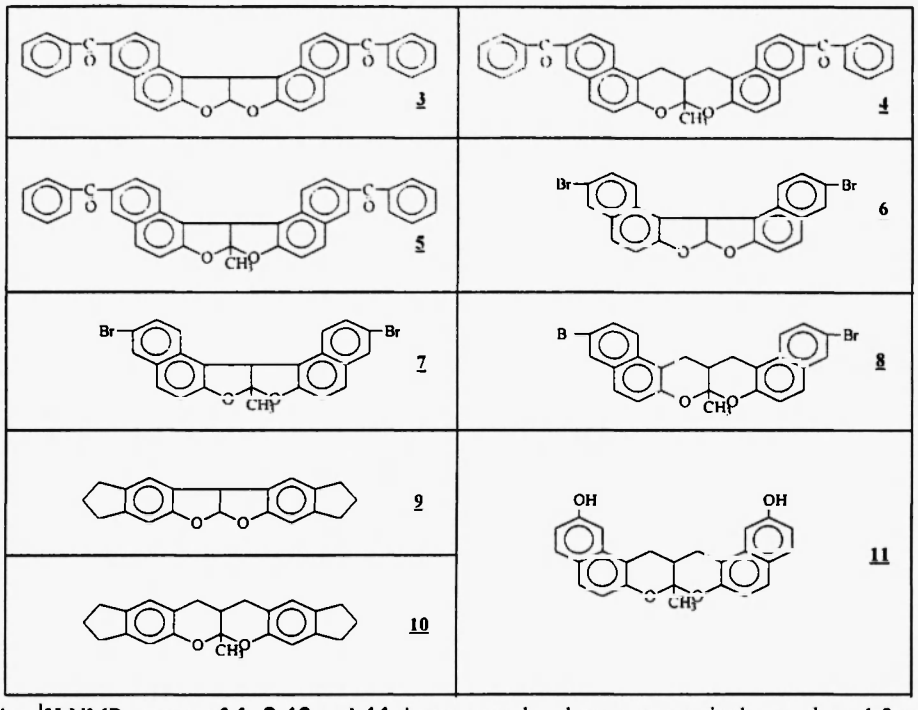
3,12-Di[3-(diethylaminopropanoyl)amino]-7a,14c-dihydro-naphtho [2,1-b] naphtho [1',2'; 4,5] furo[3,2-d] furan (19): 340 mg of Compound **13** and 225 mg 3-diethylaminopropanoic acid were dissolved in 10 ml dimethylformamide and cooled to 0°C, then 400 mg DCC was added.The mixture was stirred at this temperature for 1 h and then at room temperature for 4 hours. Precipitated dicyclohexylurea was removed by filtration. Solution was poured into 50 ml water, pricipitate was filtered and dissolved in acetone. 0.5 g Silicagel was added to the acetone solution in order to absorb the product. Silicagel was filtered and dried.The powder was mixed with DMF to dissolve the product. DMF solution was poured into water and the diamide compound was collected. The solid material was crystallized from acetone-water (4/1) mixture. 38% yield. M.p=230°C. IR(KBr):3300, 2934, 1631, 1232 cm^{-1}. ^{1}H-NMR (d-chloroform) δ; 1.2 (12H, t, CH_3), 2.5-3.0 (16H, m, CH_2), 5.5 (1H, d, J=5.5 Hz, H_{7a}), 7.0 (1H, d, J=5.5 Hz, H_{14c}), 8.4-7.2 (10H, m, Ar-H details were given for compound **13**), 11.5 ppm (2H, s, NH) MS(%): M^+=594(13), m/z:565(33), 521(28), 448(60), 379(93), 368(100). (Found: C, 72.5; H,7.0 ; N,9.5; $C_{36}H_{42}N_4O_4$; requires; C, 72.7; H,7.1; N,9.4 %)

Results and Discussion

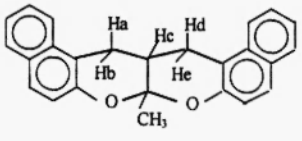
In this work, naphthofuranonaphthofuran, 7a-methyl naphthofuranonaphthofuran and 7a-methyl naphtho-pyranonaphthopyran derivatives with new functional groups, selected from, biologically active compounds used for chemoterapy, have been synthesized in order to improve the biological activities of this class of compounds. For this purpose, two methods have been considered. First method was based on the condensation reaction of carbonyl compounds with 2-naphthol derivatives as given in scheme 1 and the second method involved modifications of 7a,14c-dihydronaphtho[2,1-b]naphtho[1',2'; 4,5]furo- [3,2-d]furan (**1**) (A=H) in order to add the new functional groups with appropriate reagent.

Compounds **3, 6** and **9** were obtained from glyoxalbisulphite and appropriate phenolic compounds by the method mentioned previously.[2] Compounds **4, 8,10** and **11** were produced by the condensation of two moles of the 2-naphthol derivative with one mole of 1,3-bis -(hydroxymethyl)acetone which was obtained from one mole of acetone and two moles of formaldehyde by Claisen-Schmidt reaction[1]. The reaction proceeded via Friedel-Crafts alkylation and intramolecular acetalization. Compounds **5** and **7** were obtained from 1,3-dihydroxyacetone which was converted insitu methylglyoxal in acidic media[3]. In the case of compound **5** and **7** the reaction proceeded via condensation of two moles of the appropriate derivative of naphthol with the aldehyde group of methylglyoxal followed by intramolecular acetalization reaction.[4]

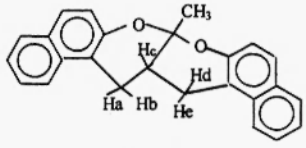
Table 1 The Reaction Products of Carbonyl Compounds with Naphthols



From the ^{1}H-NMR spectra of **4, 8,10 and 11**, it was seen that there was one singlet at about 1.8 ppm for angular methyl group. This result indicated the presence of only one stereoisomer. Although trans isomer of these compounds was reported to be highly strained [5] and although the energy of the trans isomer was found higher than that of the cis isomer (from Desktop Molecular Modelling Program), in this study the configuration of these compounds were identified as trans from their ^{1}H-NMR spectra. Two doublet-doublet (J=17 Hz, J=6.7 Hz) which were belonging to the axial and equatorial protons of pyran rings at 3.4 ppm and 2.5 ppm were determined respectively. Because the trans structure has a plane of symmetry, two axial or two equatorial protons appeared at the same chemical shifts and the spectra was simple. If it had been a cis structure, we would have been obtained more complex spectrum due to the absence of plane of symmetry.

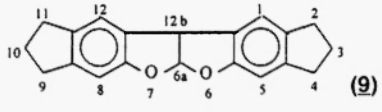


(Trans isomer)

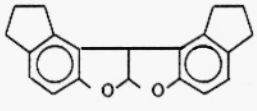


(Cis isomer)

Although it was possible to have two kind of isomers from 5- indanol, we obtained only one type of isomer 9_ and **10.** This result was attributed to the more hindrence of 4-position then the 6-position of 5-indanol.



(9)



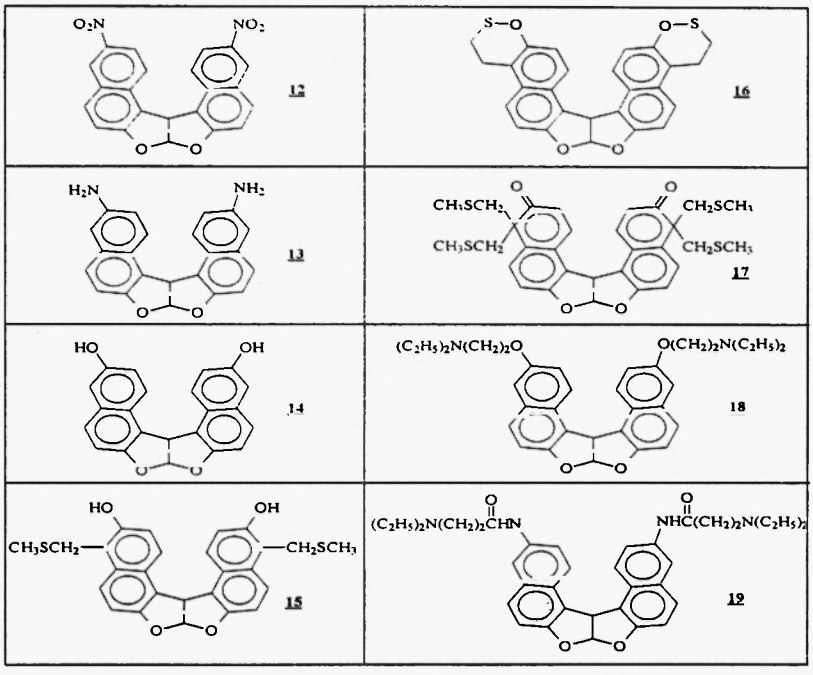
The second part of this work involves the modification of the compound 1 (A=H) by introducing certain groups which are popular in cancer research. For this purpose, compound 1 (A=H) was nitrated and a dinitro compound **12** was isolated with 40% yield.

The diamino derivative 13 (A=NH_2) was obtained by reduction of nitro groups . Replacement of diamino groups with OH groups was realized by hydrolysis of diazonium derivative of **13**. Because, the synthesis of 3,12- dihydroxy substituted compound could not be carried out by using 2,6-dihydroxynaphthalene due to the formation of polymeric products between dicarbonyl compounds and 2,6-dihydroxynaphthalene under experimental conditions. During the

replacement reaction the diazonium salt was also reacted with the starting material and gave deep red coloured azo compound as byproduct.

Although the products involving two -OH groups in 1,14- and 2,13- positions could be synthesized easily by the condensation reaction of 2,7- and 1,7-dihydroxynaphthalenes with glyoxal, these compounds could not be modified due to the very close of two OH groups to each other . On the other hand, the compounds involving two OH groups at 3,12- positions led to the new substituted products. (Table 2)

Table 2. The Reaction Products Which are Synthesised by the Modification of Dinaphthofuranofuran



Reaction between compound **14** and dimethylsulphoxide in the presence of DCC gave mainly a product having OH and a thioether groups **15** . Reaction mechanism can be explained by nucleophilic attack of the naphthol oxygen upon the sulphonium isourea leading to the naphthoxysulphonium derivative.[7] The sulphonium compound readily lose a proton giving a ylide, the carbanion which can migrate to o-position with [2,3]-sigmatropic shift giving to 4,11-di(thiomethoxy-methyl-7a,14c-dihydronaphtho[2,1-b]naphtho[1',2';4,5]furo-[3,2-d] furan. In this reaction, compound **14** behaved quite abnormally from the 1-naphthol and 2-naphthol and gave compound **15** as major product. Because under similar conditions 1 and 2-naphthols resulted the ketones 1,1 -di(thiomethoxymethyl)-2-(2H) naphthalenone and 2,2-di(thiomethoxymethyl)-1-(2H) naphthalenone as the major products.[8] However ,similar compounds **16** and **17** formed in the reaction but they could not be isolated in pure states. 3,12-Di-(2-diethylaminoethoxy)-7a,14c-dihydronaphtho[2,1-b]naphtho[1',2';4,5] furo[3,2-d]furan **18** was prepared by the reaction of compound **14** and 2-(diethylamino)ethyl chloride. Moreover, the damide derivative **19** was synthesized from the reaction of diamino compound **13** and 3-diethyl-aminopropanoic acid, using DCC as catalyst , in good yield.[9]

Acknowledgements: The authors are grateful to ITU Research Foundation for financial support.

References

1. N.Talinli, A.Akar and A.C.Aydogan, Tetrahedron ***43***, 3505-3508 (1987)
2. A.Acuner Tunca, N.Talinli and A.Akar, Tetrahedron ***51***, 2109-2116 (1995)
3. S.K.Gupta, J.Org.Chem. ***41*** ,No:15,2642-2646 (1976)
4. N.Talinli, Unpublished results
5. D.W.Cotteril, M.Iqbal, R. Livingstone and M.V. Walshaw, J. Heterocyclic Chem. ***11***, 283 (1974)
6. A. Acuner Tunca, O. Sirkecioglu ,N. Talinli and A.Akar,Eur. Polym. J. ***31***, 9-14 (1995)
7. M.G.Burdon and J. G. Moffatt, J. Amer. Chem. Soc. ***89***, 4725-4735 (1967)
8. M.G.Burdon and J. G. Moffatt, J. Amer. Chem. Soc. ***88***, 5855-5864 (1966)
9. J.C. Sheeran and D. H. Yang, J. Amer. Chem. Soc. ***80***, 1154 (1958)

Received on August 5, 2000