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Acid-catalyzed synthesis and thermal rearrangement of 3*H*-Spiro[1-benzofuran-2,1'-[3,5]cyclohexadien]-2'-one

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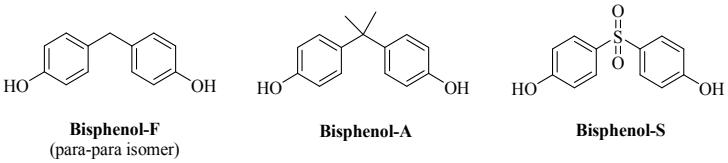
ABSTRACT

In this paper, at first a simple and efficient procedure for the synthesis of bisphenol F (BPF) (II) has been developed *via* one-pot condensation of phenol derivatives (I) with formaldehyde in the presence of phosphoric or sulfuric acid as a catalyst under solvent-free conditions. Then bisphenol F intermediate (II) was oxidized to 3*H*-Spiro [1-benzofuran-2,1'-[3,5]cyclohexadien]-2'-one intermediate (III) with potassium ferricyanide or sodium hypochlorite as oxidizing agent. In order to understand these reactions, the effect of replacing the carbonyl group in the five-membered ring by a methylene bridge was explored experimentally. In particular, it was hoped to determine the effect of a variety of substituents on the rearrangement pathways exhibited by spirobenzofurancyclohexadienone (III) and also to shed light on mechanistic processes which lead to those pathways. The study has shown that neat thermolysis of the spirobenzofurancyclohexadienone (III) produced a complex mixture of products from which only the bis phenol (II), the xanthone (IV) could be isolated and characterized. The structure of the xanthone (IV) was unequivocally established from both its spectral data and formation by oxidation of bis phenol (II). The synthesis of the benzophenone (V), which might be expected as products from thermal transformation of the Spiro benzofurancyclohexadienone (III) in view of the proposed mechanism, was attempted but was unfortunately unsuccessful. The acid- catalyzed rearrangement of the spirobenzofurancyclohexadienone was also studied. The obtained product was assigned the structure (VIII) although it was recognized that no clear-cut distinction could be made on basis of the spectral data between structure (VII) and structure (VIII).

Keywords: *Spiro benzofurancyclohexadienone, Diphenylmethane, Benzophenone, Rearrangment, Acid catalyzed.*

1. INTRODUCTION

Bisphenols (Figure 1) have attracted great interest because of their importance in organic chemistry. Bisphenol-A (BPA), for example, is a key monomer in the production of epoxy resins and in the most common form of polycarbonate plastic, which is used to make a variety of common products, including water bottles, sports equipment, medical and dental devices, CDs and DVDs and eyeglass lenses [1-4]. Bisphenol-F (BPF) mainly comprises bis (2-hydroxylphenyhmethane (ortho-ortho isomer), bis (4-hydroxylphenyl) methane (para-para isomer) and 4-hydroxylphenyl-2'-hydroxyphenyl methane (ortho-para isomer). It has been reported that bisphenol-F which contains a high concentration of bis (4-hydroxyphenyl) methane (para-para isomer content) provides superior viscosity and physical properties. It has been proved that para-para isomer content of bisphenol-F is preferably 33% or more when producing bisphenol-F type epoxy resin by reacting a diglycidyl ether of bisphenol-F with bisphenol-F. However, we have discovered that a higher proportion of ortho-phenol moieties in the bisphenol-F improves the melt/solution viscosity and physical properties of an epoxy resin. In other words, a higher content of bis (2-hydroxyphenyl) methane (ortho-ortho isomer) and 4-hydroxyphenyl-2'-hydroxyphenylmethane (ortho-para isomer) provides an epoxy resin having improved melt/solution viscosity and cured physical properties [5]. So bisphenol-F is used to make epoxy resins and coatings, especially for systems needing increased thickness and durability (i.e. high solid/high build systems), such as tank and pipe linings, industrial floors, road and bridge deck toppings, structural adhesives, grouts, coatings, and electrical varnishes [6]. BPF epoxy resins are also used for several consumer products such as lacquers, varnishes, liners, adhesives, plastics, water pipes, dental sealants, and food packaging [7]. Bisphenol-S (BPS) and bisphenol-F (BPF) have widespread consumer and commercial use. BPS is used for a variety of industrial applications including as a wash fastening agent in cleaning products, an electroplating solvent, and a constituent of phenolic resin [8]. BPS is also used as a developer in thermal paper including products marketed as "BPA-free paper" [9]. both of BPS and BPF them have been detected in many everyday products such as personal care products (e.g. body wash, hair care products, makeup, lotions, and toothpaste) [10], paper products (e.g. currency, flyers, tickets, mailing envelopes, and airplane boarding passes) [9], and food (e.g. dairy products, meat and meat products, vegetables, canned foods, and cereals) [11].



Bisphenol-F (para-para isomer) **Bisphenol-A** **Bisphenol-S**

Figure 1. Bisphenol structures (F, A, S).

Bisphenols are often prepared by the condensation reaction of phenols and aldehydes or ketones in the presence of various protonic or Lewis acids, such as boron trifluoride [12],

polyphosphoric acid [13], dry hydrochloric acid [14], acetic acid [15], trifluoro-methanesulfonic acid (TfOH) [16], cetyltrimethyl-ammonium chloride [17], metal cation-exchanged montmorillonites [18], heteropolyacid (HPA) and supported HPA [19]. Although these methods are suitable for the synthesis of bisphenols, many of them suffer from one or more drawbacks, such as long reaction times, low yield, use of toxic solvents, requirement of an excess of reagents/catalysts, hash reaction conditions, tedious work-up and multistep purifications. The search for milder and more environmentally benign conditions is, therefore, highly demanding for the synthesis of these compounds.

Spiro compounds having cyclic structures fused at a central carbon are of recent interest due to their interesting conformational features and their structural implications on biological systems. The asymmetric characteristic of the molecule due to the chiral spiro carbon is one of the important criteria of the biological activities. spirocyclicbenzofuranone is a privileged synthetic motif that constitutes a large family of natural products and clinical pharmaceuticals [20]. These compounds have been shown to exhibit a broad range of biological activities [21]. For example, abietanediterpenoids such as rosmadial [22], carnosol [23] and isoromanol [24] (Figure 2.), isolated from aerial parts of *Salvia pachyphylla* and *S.clevelandii*, have displayed effects against human cancer cells [25]. The most common methodologies for the synthesis of spirocyclic compounds involve alkylation methods, transition- metal based processes, rearrangement based approaches, ring closure of geminally substituted compounds, radical cyclizations, cleavage of bridged ring systems or cycloaddition reactions [26]. Benzofuran systems are found in many naturalsubstances of plant and microbial such as Griseofulvin is used in medicine as an anti-fungus.

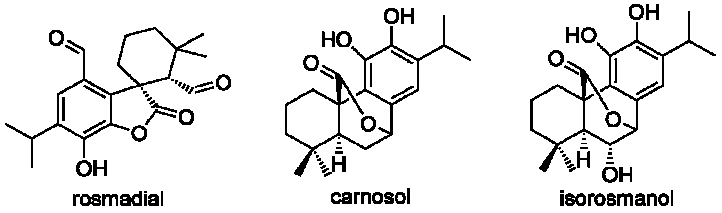


Figure 2. Spirocyclicbenzofuranone-type natural products.

Xanthones are biologically active tricyclic molecules characterized by a dibenzo-γ-pyrone nucleus or 9*H*-xanthen-9-one (Figure 3) [27, 28].

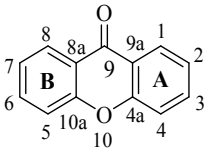


Figure 3. Xanthone basic skeleton.

The diversity of xanthone derivatives is possible due to the variation of the nature and position of substituents on the A and B rings. According to that, natural xanthones may be categorized into: simple oxygenated, glycosylated, prenylated and their derivatives (xanthone dimers, xanthonolignoids, and miscellaneous). On the other hand, the synthetic xanthones can have simple groups such as hydroxyl, methoxyl, methyl, carboxyl, as well as more complex substituents such as epoxide, azole, methylidenebutyrolactone, aminoalcohol, sulfamoyl, methylthiocarboxylic acid and dihydropyridine in their scaffold [27].

Natural xanthones of higher plants mainly occur in two families, Guttiferae and Gentianaceae, and can also be found in microorganisms as fungi and lichens [29]. The majority of these compounds were obtained from Garcinia mangostana Linn, being the most abundant and frequently studied the α-mangostin, β-mangostin, γ-mangostin, garcinone E and gartanin [30].

Xanthones have shown remarkable biological/ pharmacological activities linked with their tricyclic scaffold, depending on the nature and/or position of the diverse constituents [28]. As xanthones from natural origin are quite limited in type and position of the substituents due to the biosynthetic pathways, the syntheses of new xanthones can attempt to alter or improve their activity by having different nature and positions of the substituents on the nucleus of these compounds [31].

Xanthenes and benzoxanthenes are important intermediates in organic synthesis due to their wide range of biological and pharmaceutical properties, such as antiviral [32], antibacterial [33], and anti-inflammatory [34] activities. The other useful applications of these heterocycles include their utilization as dyes [35], as fluorescent materials for the visualization of biomolecules [36] and in laser technologies [37].

Benzophenone is used as a flavor ingredient, a fragrance enhancer, a perfume fixative and an additive for plastics, coatings and adhesive formulations; it is also used in the manufacture of insecticides, agricultural chemicals, hypnotic drugs, antihistamines and other pharmaceuticals [38]. Benzophenone is used as an ultraviolet (UV)-curing agent in sunglasses, and to prevent UV light from damaging scents and colors in products such as perfumes and soaps. Moreover, it can be added to plastic packaging as a UV blocker, which allows manufacturers to package their products in clear glass or plastic rather than opaque or dark packaging. It is also used in laundry and household cleaning products [39]. Benzophenone is widely used as a photoinitiator for inks and varnishes that are cured with UV light. In addition to being a drying catalyst, benzophenone is an excellent wetting agent for pigments; it can also be used in printing to improve the rheological properties and increase the flow of inks by acting as a reactive solvent. [No data were available to the Working Group on the use of benzophenone in sunscreens, whereas data were available on the use of one of its derivatives (3-benzophenone, 2-hydroxy- 4-methoxybenzophenone) in such products.

In this study, we have attempted to synthesize Spiro benzofuran (3*H*) dienonedrivatives using simple methods, cheap materials available and low risk of catalysts and solvents. The rearrangement of cyclohexadienone and their derivatives, particularly those which involve catalysis by acids, cover a vast area and no attempt will therefore be made at comprehensive account of this subject [40, 41]. The thermal migration of one of the alkyl (R) substituents in cyclohexa-2,4-dienone can be done, if

this group is alkyl or benzyl, lead to either of products arising from rearrangements or can lead to the phenol which would be formed by [1,5] transposition. Similarly, thermolysis of *para*-cyclohexadienone in which the two 4-substituents are the same could give rise to the two compound by [1,3] and [1,5] rearrangement respectively. This type of migration has been generally termed the "dienon-phenol" rearrangement [40]. The acid catalyzed migration of alkyl groups generally involves [1,2] shifts. Thus, historically the first established dienone-phenol rearrangement was treatment of santonin with acid to give the phenol desmotroposantonin [42].

Although the area of dienone- phenol rearrangements is intimately associated with the study of natural products [41, 43], this type of behavior is also exhibited by simple cyclohexadienones [44]. Thus a variety of monocyclic cyclohexa-2,4-dienones of the type have been shown to rearrange on treatment with acid to the phenols [45].

2. EXPERIMENTAL SECTION

2.1. Materials and Instruments.

All materials were purchased from Sigma-Aldrich and Merck Company. The infrared spectra by IR Spectrometer Thermo Scientific Nicolet FT-IR 8700 with KBr tablet taken and frequencies of vibration transmission is in wave number unit (Cm^{-1}). Nuclear magnetic resonance spectra ^{1}H-NMR, ^{13}C-NMR, by the spectrometer Bruker Ultra 500 MHz in the solvent DMSO-d_6 and $CDCl_3$ in the presence of TMS as standard is measured. Electro thermal 9100 melting point is measured by the device. The reaction solvent was evaporated by rotary STRIKE 202 models, the characteristics of which are as follows: STEROGLASS s.r.l. PERUGIA ITALY 230 Vac 50/60 Hz 700VA FUSE 5A. All synthetic methods to develop reaction and purification of the product by thin layer chromatography (TLC) and TLC with aluminum plates with silica gel 60 with UV at a wavelength of 365-254 nm was observed with a fluorescence reagent.

2.2. Synthesis method.

2.2.1. Preparation of di(2-hydroxy-3-tert-butyl-5-methylphenyl) methane: (173).

A suspension of 2-*tert*-butyl-4-methylphenol (254) (100g, 0.6mol) in a mixture of conc. hydrochloric acid (20g, 0.55mol) and 37% aqueous formaldehyde solution (20 g, 0.66 mol) was stirred at room temperature. After about one hour a yellow solid was produced. After stirring for 24 h the reaction mixture was filtered and residual solid washed with water and crystallized from aqueous acetic acid, giving di(2-hydroxy-3-*tert*-butyl-5-methylphenyl) methane (65g, 63%) as colorless crystals, m.p. 133-134℃ (Found: M^+. 340. $C_{25}H_{32}O_2$ requires M, 340), υ_{max} ($CHCl_3$) 3500-3580, 2840-3010, 1715, and 865 cm^{-1}; δ($CDCl_3$) 6.93(4H, s, 2 * H-C4, 2 * H-C6), 5.3-6.3 (2H, broad s, 2 * $OH_)$, 3.86 (2H, s, CH_2), 2.23 (6H, s, 2 * CH_3) and 1.37 (18H, s, 2 * *tert*-butyl).

Selected data:

Bis (2-hydroxy -3-nitrophenyl) methane: Yellow, crystal, m.p: 48-50 °C, yield: 97%, FT-IR(υ_{max}, KBr): 3447 (O-H), 3240 (C-H aromatic), 3114 (C-H aliphatic), 1478-1589 (C = C), 1532, 1374 (NO_2), 1266 (C -O) Cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ= 2.41 (CH_2, 2H, s), 6.93-7.56 (H-Ar, 6H, m), 7.82 (OH, 2H, s, D_2O Exchangeable) ppm. ^{13}C-NMR (DMSO-d_6): δ=36.7(C-CH_2), 119-152 (C-Ar) ppm.

Bis (2-hydroxy- 3,5-dinitrophenyl) methane: Yellow crystal, m.p:116-118 °C, yield: 98%, FT-IR (υ_{max}, KBr): 3271 (O-H), 3109 (C-H aromatic), 2958 (C-H aliphatic), 1432 (C = C), 1540, 13338 (NO_2), 1253(C -O) Cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ= 2.4 (CH_2, 2H, s), 7.2-8.2 (H-Ar, 4H, s), 8.6 (OH, 2H, s, D_2O Exchangeable) ppm; ^{13}C-NMR (DMSO-d_6): δ=36.7(C-CH_2), 120-158 (C-Ar) ppm.

2.2.2. Preparation of some 3H-Spiro[1-benzofuran-2,1'-[3,5]cyclohexadien]-2'-one derivatives with potassium ferricyanide.

To a stirred solution of di-(2-hydroxy-3-*tert*- butyl-5-methylphenyl) methane (2.0 g, 5.8 mmol) in methanol **(**50 mL) was added slowly a solution of potassium ferricyanide (10.0g, 30 mmol) and sodium hydroxide (10.0 g ,0.25 mol) in water (50 mL) under nitrogen atmosphere at room temperature for 6 h. the solution was then extracted with ethyl acetate and the organic layer was washed with water, dried by $MgSO_4$, and concentrated. The residual solid was approved by ^{1}H-NMR and TLC to consist solely of the starting material.

Selected data:

Spiro [7-nitro benzofuran-2 (3H)-1'(3'- nitro) cyclohexa -3',5' dien -2'-one]: Yellow crystal, mp: 34-38 °C**,** yield: 97%, FT-IR (υ_{max}, KBr): 3167 (C-H aromatic), 2878 (C-H aliphatic), 1666 (C=O), 1518, 1386 (NO_2), 1452-1597(C=C), 1286 (C-O) Cm^{-1}. ^{1}H-NMR($CDCl_3$): δ=2.4(CH_2, 2H, s), 7.02-7.64 (H-Ar, 6H, m) ppm.

Spiro [5,7-dinitro benzofuran-2 (3H)-1' (3',5'- dinitro) cyclohexa-3',5' dien-2'one]: Yellow crystal, m.p:98-100 °C, yield: 98%, FT-IR (υ_{max} , KBr**)**:3109 (C-H aromatic), 2924 (C-H aliphatic), 1672 (C=O), 1540, 1347 (NO_2), 1599-1433 (C=C), 1255 (C-O) Cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ=2.4(CH_2, 2H, s), 7.37-8.51 (H-Ar, 4H, s) ppm.

2.2.3. Another method for preparation of some 3H-Spiro[1-benzofuran-2,1'-[3,5]cyclohexadien]-2'-one derivatives withpotassium ferricyanide:(207).

To a stirred solution of di(2-hydroxy-3-methyl-5-trityl-phenyl) methane (209) (20 g, 0.028 mol) in boiling benzene(150 mL) was added slowly over 30 min a solution of potassium ferricyanide (100.0 g, 0.3 mol) and potassium hydroxide (60.0 g, 1.07 mol) in water (800 mL) under nitrogen atmosphere at room temperature. After addition, the solution was stirred for 3h during which time it first became green and then yellow. The solution was then extracted with ether and ether phase washed with water and dried by $MgSO_4$. Concentration yielded a yellow solid which was purified by column chromatography on silica using chloroform: 40/60 ligroin=4:96 eluents to give, after crystallization from acetone, Spiro[7-methyl-5-tritylbenzofuran-2(3H),1'-(3'-methyl-5'-tritylcyclohexa-3'-5'-dien-2'-one)] (207) (10.0g, 50%) as yellow crystals, m.p. 118-119˚C) (Found: C. 89.8,

H, 5.7; M^+, 712. $C_{53}H_{42}O_2$ requires C. 89.8, H, 5.9% M, 710), υ_{max} ($CHCl_3$) 3000-3100, 1680, 965, and 640 cm^{-1}; δ($CDCl_3$) 7.0-7.4 (30H, m, 2 * trityl), 6.74(1H, s) and 6.72 (1H, s) (H-C4, H-C6), 6.45(1H, d, J = 2Hz, H-C6'),6.33 (1H, d, J = 2Hz, H-C4'),3.35 and 3.04 (2H, AB system, J_{AB} 16 Hz, CH_2), 2.10 (3H, s, CH_3-C7), 1.74(3H, s, CH_3-C_3').

2.2.4. Preparation of some 3H-Spiro[1-benzofuran-2,1'-[3,5]cyclohexadien]-2'-one derivatives with sodium hypochlorite.

To a cooled solution (-5 ^{O}C) of Di-(2-hydroxy -3-*tert*-butyl-5-methylphenyl) methane (7.0 g, 20 mmol) in methanol (80 mL) was added dropwise 10% aqueous sodium hypochlorite solution (3.0 g, 0.04 mol). The resulting yellow-red solution was stirred for 24 h and then diluted with ethyl acetate and saturated aqueous sodium metabisulfite solution. The organic and aqueous layers were separated and then organic layer was washed with water, dried by $MgSO_4$, and evaporated. The resulting reddish yellow oil was purified by column chromatography on silicagel using 60/80 ligroin as eluent. The yellow fraction eluted first from the column was further purified by preparative TLC using ethyl acetate: 60/80 ligroin=1:9 as eluent and the yellow major b and (R_f= 0.8) collected and crystallized from methanol to give Spiro [7- tertbutyl-5-methylbenzofuran-2(3H)-1'-(3'- *tert*-butyl-5'-methylcyclohexa-3',5' dien -2'-one] (1.7 g, 24%) as a yellow crystalline solid, m.p. 119-121° C) (Found: M^+. 338. $C_{23}H_{30}O_2$ requires M, 338), υ_{max} (Nujol) 1710-855 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ = 6.1-6.9 (4H, m, H-C_4, H-C_6, H-C_4', H-C_6'), 3.20(2H, AB, J_{AB} 17 Hz, H_2-C_3), 2.23(3H, s, CH_3-C_5),1.89 (3H, s, CH_3-C_5'), 1.35 (9H, s), 1.15 (9H, s) (2 * *tert*-butyl).

2.2.5.Thermolysis of spiro[7-tert-butyl-5-methylbenzofuran-2(3H)-1'-(3'-tert-butyl-5'methylcyclohexa-3',5'dien-2'-one].

Spiro[7-*tert*-butyl-5-methylbenzofuran-2(3H)-1'-(3'-*tert*-butyl-5'methylcyclohexa-3',5'dien-2'-one] was heated neat at 180-185° C for 3h. the cooled dark brown melt was then separated by preparative TLC using ethyl acetate: 80/100 ligroin= 1:9 as eluent into two broad fractions:

Fraction 1: (R_f= 0.6-0.8) was again separated into two components by preparative TLC using acetone 60/80 ligroin = 1:4 as eluent.

Component 1: (R_f= 0.8, blue fluorescence under ultra violet illumination) gave, after crystallization from methanol, 4,5-di-*tert*- butyl-2,7-dimethyl- (9H)-xanthen-9-one (225) (30mg, 3%) as colorless crystals, m.p. 196-199° C (Found: M^+. 336. $C_{23}H_{28}O_2$ requires M, 336), υ_{max} ($CHCl_3$) 2930, 2840, 1715, 1610, 1365, and 1710 cm^{-1}; δ ($CDCl_3$) 8.12(2H, d, *J*= 2Hz, H-Cl, H-C_8), 7.58(2H, d, J2 Hz, H-C_3, H-C_6), 2.45(6H, s, 2 * CH_3),1.63 (18H, S, 2 * tert-but). Treatment of small portion of this compound (225) with either concentrated sulphuric acid produced in each case a yellow fluorescence under ultra-violet illumination.

Component 2: (R_f= 0.6) gave, after crystallization from acetic acid/water, di(2-hydroxy-3-tert-butyl-5-methylphenyl) methane (250 g, 25%) as a colorless solid, m.p. 133-134° C, which was identified by comparison with authentic material(TLC, ^{1}H-NMR, and mixed m.p.).

This fraction also contained a large number of minor bands which were not further investigated.

Fraction 2: (R_f= 0.3-0.5) was again separated into two components by preparative TLC using acetone 80/100 ligroin = 1:3 as eluent:

Component 1: (R_f= 0.5) gave approximately 25 mg of a dark red solid which was shown by ^{1}H-NMR and TLC to contain several compounds and which was not further investigated.

Component 2: (R_f= 0.3) gave 140 mg of a dark red solid which was shown by analytical TLC to contain several compounds and which was not further investigated.

This fraction also contained a large number of minor bands which were not further investigated.

2.2.6. Neat thermolysis of spiro [7-methyl-5-tritylbenzofuran-2(3H),1'-(3'-methyl-5'-tritylcyclohexa-3'-5'-dien-2'-one)]: (207).

The spiro [7-methyl-5-tritylbenzofuran-2(3H),1'-(3'-methyl-5'-tritylcyclohexa-3'-5'-dien-2'-one)] (3.0g, 4.2mmol) was heated neat at 180-185℃ for 3h. the resulting red liquid solidified on cooling and analytical TLC using chloroform: 40/60 ligroin = 1:1 as an eluent revealed it to contain a number of distinct compounds. The mixture was separated into three broad fractions by column chromatography using chloroform: 40/60 ligroin = 1:4 as eluant:

Fraction 1 was again separated into three components by preparative TLC using chloroform: 40/60 ligroin= 1:4 as eluant:
Component 1 (R_f= 0.8) gave, after crystallization from methanol, triphenylmethane (250 g, 25%) as colorless crystals, m.p. 89-90° C, (Found: M^+. 244. calculated for $C_{19}H_{16}$ M, 244), υ_{max} (Nujol695 and 655 cm^{-1}. This compound was shown by ^{1}H.N.M.R and TLC comparison and mixed m.p. to be identical with an authentic sample of triphenylmethane(211).

Component 2 (R_f= 0.7) gave approximately 30 mg of a dark yellow oil which was shown by analytical TLC to contain several components and it was not further investigated: (Found: M^+. 262), δ($CDCl_3$) 7.1-7.4(6H, m,), 6.75(1H, dd, J 17 Hz, J11 Hz), 6.46(1H, d, J 17 Hz),6.28(1H, dd, J 16 Hz, J11 Hz),5.81(1H, dt, J 16 Hz, J7 Hz), 2.95 (2H, d, J 7 Hz) and 2.20 (5H, s).

Component 3 (R_f= 0.6) gave, after crystallization from acetone, a compound of unknown structure (40 mg) as colorless crystals, m.p. 145-146 C (Found: M^+. 337); δ($CDCl_3$) 6.9-7.3(3OH, m), 6.43(2H, s), 3.48(1H, s) and 1.8-2.21 (8H, m).

Fraction 2 was further separated into three components by preparative TLC using chloroform: 40/60 ligroin = 3:2 as eluant:

Component 1 (R_f= 0.5 shows bright blue fluorescence under ultra violet illumination) gave, after recrystallization from ethyl acetate, 4,5-di- dimethyl-2,7—dityrityl- (9H)-xanthen-9-one(210) (0.60g, 20%) as pale yellow crystals,. m.p. 242-243° C (Found: C. 89.8, H, 5.6; M^+, 708. $C_{53}H_{40}O_2$ requires C. 89.8, H, 5.6% M, 708), υ_{max} ($CHCl_3$) 3060,2920, 1655, 1610 and 875 cm^{-1}; δ($CDCl_3$) 8.12(2H, d, J 2Hz , H-Cl, H-C_8), 7.38(2H, d, J2 Hz, H-C_3, H-C_6), 7.05-7.33(3OH, m, 2x trityl), and 2.40 (6H, s, 2x CH_3). δ ^{13}C($CDCl_3$) 177.5 s(C9), 152.8 s, 146.3 s, 139.0 d, 130.9 s, 127.6, 126.0, 125.3 d, and 120.4 s (aromatic C), 64.6 s (CPh_3) and 15.9 q (CH_3).

Component 2 (R_f= 0.4) gave, after crystallization from acetic acid, di(2-hydroxy-3-methyl-5-tritylphenyl)methane(209) (200 mg, 7%), m.p. 252-253 ° C, which was shown by ^{1}H.N.M.R and TLC comparison to be identical to an authentic sample.

Component 3 (R_f= 0.3) gave approximately 10 mg of a dark yellow solid which was shown by analytical TLC to contain several components and it was not further investigated.

Fraction 3 was again separated into two components by preparative TLC using chloroform as eluant:

Component 1 (R_f= 0.2) gave approximately 4 mg of a dark yellow solid which was shown by analytical ^{1}H.N.M.R to contain several components and which was not further investigated.

Component 2 (R_f= 0.0-0.1) was 0.33 g of a colorless solid which after purification by preparative TLC using chloroform: ethyl acetate = 1:1 as eluant, gave di(2-hydroxy-3-methyl-5-tritylphenyl)methane(209) (200 mg, 7%), as a colorless solid, which was shown by ^{1}H.N.M.R and TLC comparison to be identical to an authentic sample.

2.2.7. Reaction of di(2-hydroxy-3-tert-butyl-5-methylphenyl) methane (173) with selenium dioxide.

A mixture of di-(2-hydroxy-3-*tert*-butyl-5-methylphenyl) methane (173) (1.0 g, 2.94 mmol) and selenium dioxide (1.0 g, 8.96 mmol) was heated under solvent-free conditions at 140℃ for 1h, allowed to cool to room temperature, diluted with water, and extracted into diethyl ether. the ether layer was dried by $MgSO_4$ and evaporated to give a red dark solid which was separated by preparative TLC using acetone:80/100 ligroin = 1:9 as eluent into three fractions.

Fraction 1: (R_f= 0.9) gave the compound (258) as a yellow tar (150 mg) which resisted all attempts at crystallization (Found: M^+. 416. $C_{23}H_{28}O_2Se$ requires M, 416), δ ($CDCl_3$) 8.23(2H, d, J= 2Hz, 2 * H-C3), 7.38(2H, d, J = 2Hz, 2 * H-C5), 2.54(6H, s, 2 * CH_3) and 1.53 (18H, s, 2 * *tert*-butyl).

Fraction 2: (R_f= 0.6) gave a brown solid (250 mg) which was shown by ^{1}H-NMR to contain a number of products, one of which appeared to be the starting diphenylmethane (173).

Fraction 3: (R_f= 0.3) gave a dark red tar (80 mg) which was shown by ^{1}H-NMR to contain a number of products, one of which appeared to be the starting diphenylmethane (173).

2.2.8. Acid-catalyzed rearrangement of spiro [7-methyl-5-tritylbenzofyran-2(3H)-1'-(3'-methyl-5-tritylbenzofuran-2(3H), 1'-(3'-methyl-5-tritylcyclohexa-3',5'-dien-2'-one)]: (207).

Concentrated sulphuric acid (4 drops) was added to a suspension of spiro[7-methyl-5-tritylbenzofyran-2(3H)-1'-(3'-methyl-5-tritylbenzofuran-2(3H), 1'-(3'-methyl-5-tritylcyclohexa-3',5'-dien-2'-one)] (207) (100 mg, 0.14 mmol) in acetic anhydride (5ml) and the mixture was stirred at room temperature for 24 h. the mixture was poured into ice – water, stirred for 2 h, and extracted into ether. The ethereal extract was washed twice with saturated aqueous sodium bicarbonate solution and once with water, dried ($MgSO_4$), and concentrated. The residual dark yellow solid was separated by preparative TLC using ethyl acetate: 60/80 ligroin = 1:9 as eluant into 2 components:

Fraction 1 (R_f= 0.8) gave starting deoxygrisan(207) (45 mg, 45%) as a yellow crystalline solid which was %)(R_f= 0.8) comparison to be identical to authentic material.

Fraction 2 (R_f= 0.6) gave, after recrystallization from acetic acid, the acetoxyxanthene (252) (35 mg, 33%) as colorless crystals, m.p. 255-257 ° C (Found: C. 87.6, H, 6.1; M, 752), υ_{max} (Nujol) 2800-3000, 1770, 742 and 705 cm^{-1}; δ($CDCl_3$) 7.0-7.25(3OH, m, 2x trityl), 6.80(1H, d, J2 Hz, H-C_6), 6.29(1H, d, 2 Hz, H-C8), 6.67 (1H, s, H-C2), 2.48 (2H, s, CH_2), 2.37 (3H, s, CH_3CO), 2.17(3H, s), and 2.06(3H, s)(CH_3-C3, CH_3-C6).

This reaction was repeated as above by the addition of concentrated sulphuric acid (12 drops) to a to a suspension of spiro [7-methyl-5-tritylbenzofyran-2(3H)-1'-(3'-methyl-5-tritylbenzofuran-2(3H), 1'-(3'-methyl-5-tritylcyclohexa-3',5'-dien-2'-one)] (207) (300 mg, 0.42 mmol) in acetic anhydride (15 ml). after work-up as described above, the residual solid was separated by preparative TLC using ethyl acetate: 60/80 ligroin = 1:9 as eluant into the starting deoxygrisan (207) (60 mg, 20%)(R_f= 0.8) as a yellow crystals and the acetoxyzanthene (252) (150 mg, 46%) (R_f= 0.6) as a colorless crystals (both products were identified by ^{1}H-NMR and TLC and mixed m.p. comparison with authentic material).

Concentrated sulphuric acid (3ml) was added to a suspension of spiro [7-methyl-5-tritylbenzofyran-2(3H)-1'-(3'-methyl-5-tritylbenzofuran-2(3H), 1'-(3'-methyl-5-tritylcyclohexa-3',5'-dien-2'-one)] (207) (2 g, 2.8 mmol) in acetic anhydride (50 ml) and the mixture stirred at room temperature for 3 days. the mixture was poured into ice – water, stirred for 4 h, and extracted into ether. The ethereal extract was washed twice with saturated aqueous sodium bicarbonate solution and once with water, dried ($MgSO_4$), and concentrated. The residual dark yellow solid was separated by preparative TLC using ethyl acetate: 60/80 ligroin = 1:9 as eluant into three components:

Component 1 (R_f= 0.8) gave, after recrystallization from methanol, triphenylmethane(211) (0.4 g) as a colorless crystals, m.p. 91-92 ° C, which was identified by ^{1}H-NMR and TLC comparison to be identical to authentic material.

Component 2 (R_f= 0.6) gave 30 mg of a dark red oil which was shown by analytical TLC to contain several components and it was not further investigated.

Component 3 (R_f= 0.4) gave 20 mg of a dark brown solid which was shown by analytical TLC to contain several components and it was not further investigated.

3. RESULTS SECTION

Our goal in this work were five folds: a) The synthesis of ring systems via a methylene bridge, b) synthesis of polycyclic heterocyclic with oxygen atoms, c) Synthesis of Spiro derivatives, d) pharmaceutical, agricultural, color, and so it is of practical purposes, e) the most important synthesis of these compounds having antimicrobial properties.

Bis (2-hydroxy -3-nitrophenyl) methane: 3447 Cm^{-1} peak observed in the area stretching frequency of phenolic OH is

strong. Aromatic C-H stretching absorption in the aliphatic C-H 3240 Cm^{-1} and 3114 Cm^{-1} has appeared in the area. C = C bond stretching vibration 1589-1478 Cm^{-1} is the area stretching two strong uptake in areas of 1374 Cm^{-1} and 1532 Cm^{-1} is related to NO_2. C-O bond stretching frequency in the area is 1266 Cm^{-1}. In ^{1}H-NMR of this compound, peak of the two methylene hydrogen as a singlet peak is observed in 2.4 ppm. Six aromatic hydrogens as three multiple peaks has appeared in 6.9 -7.5 ppm. OH peak for a singlet peak with the under area peak 2 is observed in 7.8 ppm. Methylene carbon peak is observed in 36.7 ppm. Aromatic carbon peak has appeared in 119 ppm up to 152 ppm. The peak of carbon attached to the methylene carbon is in 119 ppm. The carbon peaks in C-H are 120 ppm and 125 ppm and 136 ppm, respectively.C-NO_2 peak is in the 137 ppm and C-OH peak is observed in 152 ppm.

Bis (2-hydroxy- 3,5-dinitrophenyl) methane: 3271 Cm^{-1} peak observed in the area stretching frequency of phenolic OH is strong. Aromatic C-H stretching absorption in the aliphatic C-H 3109 Cm^{-1} and 2958 Cm^{-1} has appeared in the area. C = C bond stretching vibration 1432 Cm^{-1} is in the area of attracting strong traction in areas 1338 Cm^{-1} and 1540 Cm^{-1} is related to NO2. C-O bond stretching frequency in the area is 1253Cm^{-1} . In ^{1}H-NMR of this compound, Peak of the two methylene hydrogen as a singlet peak is observed in 2.4 ppm. Four aromatic hydrogens as two singlet peaks have appeared in 7.2-8.2 ppm. OH peak as a singlet peak with the under area peak 2 is observed in 8.6 ppm.Methylene carbon peak is observed in 36.7 ppm. Aromatic carbon peak has appeared 120 ppm up to 158 ppm. The peak of carbon attached to the methylene carbon is in 120 ppm. The carbon peaks in C-H are 122 ppm and 130 ppm, respectively. C-NO_2 peak is the 137 ppm and 139 ppm.C-OH peak is observed in 158 ppm.

Spiro [7 - nitro benzofuran -2 (3H) - 1' (3'- nitro) cyclohexa - 3',5' dien -2'one]: Aromatic C-H stretching absorption in 3167 Cm^{-1} and the aliphatic C-H has appeared in the 2878 Cm^{-1} area. Stretching absorption in the carbonyl group is 1666 Cm^{-1}. Two strong tension absorption in areas 1386 Cm^{-1} and 1518 Cm^{-1} is related to NO_2. C = C bond stretching vibration area is 1597-1452 Cm^{-1}. C-O bond stretching frequency is in the area of 1286 Cm^{-1}. Peak of the two methylene hydrogens as a singlet peak are observed in 2.4 ppm. Six aromatic hydrogens as three multiple peaks has appeared in 7.02-7.64 ppm.

Spiro [5,7-dinitro benzofuran -2 (3H) - 1' (3',5'- dinitro) cyclohexa - 3',5' dien -2'one]: aromatic C-H stretching absorption in 3109 Cm^{-1} and the aliphatic C-H has appeared in the 2924 Cm^{-1} area. Stretching absorption in the carbonyl group is 1627 Cm^{-1}. Two strong tension absorption in areas 1347 Cm^{-1} and 1540 Cm^{-1} is related to NO2. C = C bond stretching vibration area is 1599-1433 Cm^{-1}. C-O bond stretching frequency is in the area of 1255 Cm^{-1}.Peak of the two methylene hydrogens as a singlet peak are observed in 2.4 ppm. Four aromatic hydrogens as two singlet peaks has appeared in 7.37-8.51 ppm.

Spiro benzofurancyclohexadienone (III) is prepared by the oxidative coupling of the corresponding dihydroxydiphenylmethane, typically using potassium ferricyanide [$K_3Fe(CN)_6$] as the oxidant. In all but one case the product formed has been a Spiro benzofurancyclohexadienone and the oxidant use [$K_3Fe(CN)_6$]. Thus in 1914 cherbuliez prepared the Spiro benzofurancyclohexadienone (III) by oxidizing the dinaphtylmethane (II) while the compound was prepared very recently in similar fashion. A series of Spiro benzofurancyclohexadienone which contain two bulky tert-buthyl groups have also been prepared in good yield using this method. However, oxidation of the diphenylmethane (II) with sodium hypochlorite has been claimed to give good yield of desired Spiro benzofurancyclohexadienone (III).

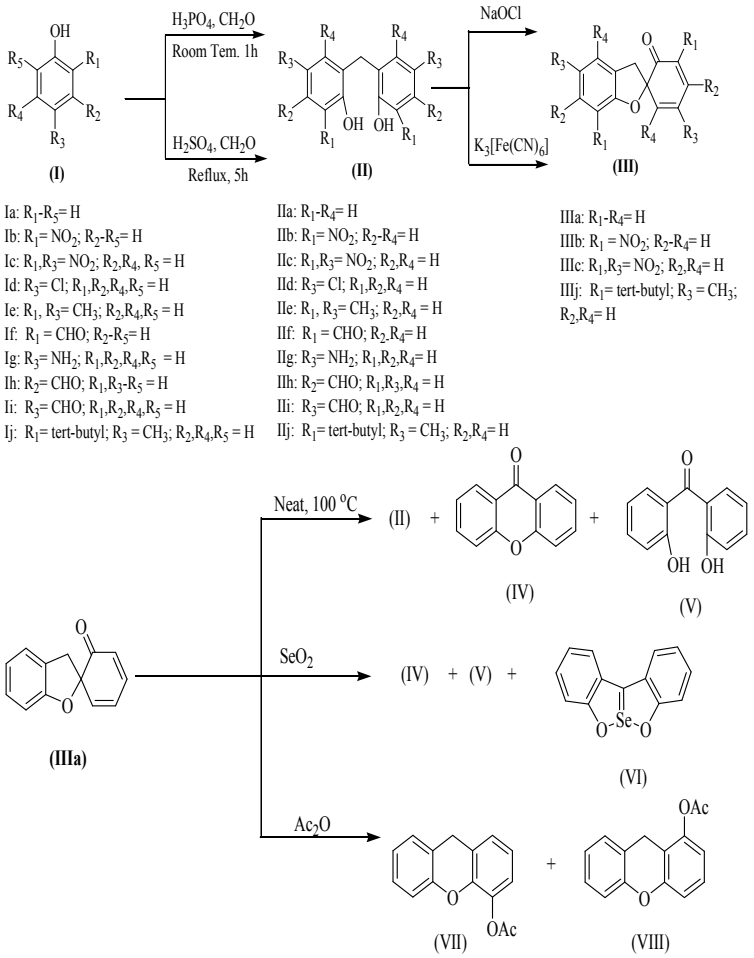
The spectral data for this product is compatible with it being a Spiro benzofurancyclohexadienone. Thus, its elemental analysis is consistent with the molecular formula $C_{53}H_{42}O_2$ which confirmed by the presence in its mass spectrum of a molecular ion at m/e 710. Infra-red spectrum of the spirobenzofurancyclohexadienone has an absorption maximum at 1680 cm^{-1} which is consistent with the presence of a cyclohexa-2,4-dien-1-one group and shows the complete absence of hydroxyl stretching bands. The ^{1}H-N.M.R. spectrum of the Spiro benzofurancyclohexadienone contains four signals in the region δ= 6.3-6.8, indicating that the two six-membered rings are no longer equivalent. In addition, a broad multiplet in the region δ= 7.0-7.4, with an integrated intensity of thirty protons is present arising from the two trityl groups. That one of the rings is no longer aromatic is evidenced by the fact that two signals are present in the ^{1}H-N.M.R. spectrum of this compound at δ= 1.74 and 2.10 which are attributable to an olefinic methyl group and aromatic methyl group, respectively. Furthermore, the fact that methylene protons are no longer magnetically equivalent and give rise to an ABsystem(δ_A= 3.35, $\delta_{B=}$ 3.04, J_{AB}= 16 Hz) indicates generation of chiral center in the product. All this spectral data is consistent with the Spiro benzofurancyclohexadienone structure.

The Spiro benzofurancyclohexadienone was heated neat at 180-185℃ for 3h. the resulting melt, which was shown to be a complex mixture of products were isolated and identified as (i) 4,5-dimethyl-2,7-ditrityl-(9H)0xanthen-9-one, di(2-hydroxy-3-methyl-5-tritylphenyl) methane, and (iii) triphenylmethane. The compound assigned the xanthone structure (20% yield) exhibited a blue fluorescence on TLC under ultra-violet illumination. The xanthones and have been reported to exhibit a similar fluorescence. The presence of a plane of symmetry in the compound was apparent from its ^{1}H-NMR spectrum. The presence of double (J=1.5 Hz) at δ= 8.12 in its ^{1}H-NMR. The additional presence of a doublet at δ=7.38 attributable to the protons on the 3- and 6- positions, a multiplet at δ= 7.05-7.33 with an integrated intensity of thirty groups, and singlet at δ= 2.40 arising from two aromatic methyl groups in the ^{1}H-NMR spectrum is compatible with the xanthone structure. The presence of am absorption maximum at 1648 cm^{-1} in the infra-red spectrum of the Spiro benzofurancyclohexadienone is in agreement with the observation that most xanthones possess a carbonyl stretching frequency in their infra-red spectra in the region 1622-1657 cm^{-1}. Further confirmation of xanthone structure for Spiro benzofurancyclohexadienone came from its ^{13}C-NMRspectrum which showed the presence of high field signal at δ= 177.5 ppm which was assigned to the carbonyl atom since xanthones are known to exhibit signals in the region δ= 175.7-185.4 ppm in their ^{13}C-NMR spectra for the carbonyl carbon atom. The xanthone could, however, be successfully reduced to the xanthene using sodium borohydride in boiling isopropanol while the use milder conditions led to recovery of the starting material. For this reason,

the xanthone was heated under reflux in isopropanol with sodium borohydride to give, after two days, the xanthene in good yield. An intimate mixture of the diphenylmethane and selenium dioxide was heated at 210-220℃ for three hours, from which, after separation of the melt, the xanthone (24% yield) was obtained together with another product in approximately 17% yield as a yellow solid. It was noted that this minor product was somewhat un stable in the presence of air, being slowly converted into xanthone. Thus its ^{1}H-NMR spectrum exhibits signal at δ=11.31(exchangeable with D_2O) and δ=9.64 each arising from two protons, a multiplet in the aromatic region(δ=7.0-7.3) arising from 30-35 protons, and a singlet at δ=2.15 arising from six protons. It is apparent from this spectrum that the aromatic rings are magnetically equivalent. The infra- red spectrum of this product (in $CHCl_3$) shows a carbonyl stretching frequency at 1655 cm^{-1} but no appreciable absorption maximum attributable to hydroxyl groups while its mass spectrum contains aa distribution pattern characteristic of the presence of one selenium atom. It must be noted that this mass spectrum shows no evidence for existence of a molecular ion at m/e = 726 arising from the benzophenone while the molecular weight observed equals that required for the structure. However, the remaining spectral data is not compatible with either the benzophenone or the compound (227). Thus the presence of a signal at δ= 9.64 which does not exchange with D_2O in the ^{1}H-NMR spectrum and molecular ion in the mass spectrum are incompatible with the benzophenone structure. Similarly the presence of a carbonyl stretching frequency in infra-red spectrum is variance with the structure (227) as is ^{1}H-NMR spectrum. Thus, in analogy with the compounds (225) and (227) which give rise to signals at δ= 8.41 and 8.47, the compound (227) would be expected to contain a signal in its ^{1}H-NMR spectrum in the region δ= 8.0-8.5 arising from two aromatic protons. Furthermore, the presence of signals at δ= 9.64 and 11.31 ppm cannot be explained in terms of the structure (227).

In an attempt to obtain the benzophenone, the oxidation of the diphenylmethane with selenium dioxide was also performed in solution. Heating the diphenylmethane with selenium dioxide in pyridine under reflux gave the zanthone (20% yield) together with approximately 20% of a yellow solid which was shown by ^{1}H-NMR to contain the previously obtained unknown product and at least two other unidentifiable products. Repeating this reaction in acetic acid solution gave the xanthone (20% yield) together with together with approximately 30% of a yellow solid whose composition appeared to be very similar by ^{1}H-NMR to that of the product obtained from the reaction in pyridine solution. Similarly, conducting the oxidation in toluene solution gave 15% of the xanthone and approximately 35% of a yellow solid whose composition was again similar to those of the previously obtained product. All attempts to separate these yellow solids into their pure component were singularly unsuccessful. Indeed, some evidence was obtained (by TLC) that this product was converted, at least partially, into the xanthone on exposure to the atmosphere. Heating a solution of the diphenylmethane with selenium dioxide in ethanol solution under reflux led to recovery of starting material. It is unfortunate that none of the desired benzophenone could be obtained from the reactions of selenium dioxide with either of diphenylmethanes and (222).

Treatment of the Spiro benzofurancyclohexadienone (0.42 mol) in acetic anhydride (15 ml) with concentrated sulphuric acid (12 drops) at room temperature 24 hours gave, after work-up and chromatography, 46% of a colorless crystalline solid, melting point 225-257℃, together with 20% of the starting material(207). That this product corresponded to one of the two possible acid-catalyzed rearrangement products (252) or (253) was apparent from its spectral data. Thus, the ^{1}H-NMR spectrum of this product contained two meta-coupled doublets (J=2Hz) at δ= 6.8 and 6.29 and a singlet at δ= 6.67 attributable to three aromatic protons, a multiplet in the region δ=7.0-7.5 arising from two trityl groups, a two proton singlet at δ= 2.84 assignable to the methylene protons on the 9-position, and three singlets at δ= 2.37 (arising from the acetoxy methyl group) and δ= 2.17 and 2.06 (arising from the aromatic methyl groups). The infra-red spectrum of this, product possessed a carbonyl absorption frequency at 1770 cm^{-1} while its mass spectrum showed the presence of a molecular formula - $C_{55}H_{44}O_3$. From this data it is apparent that the product formed from the acid catalyzed rearrangement of the Spiro benzofurancyclohexadienone has one of the structures (252) or (253). The structure (252) would arise from migration of the carbon-carbon bond in the compound (251), which is formed by acetylation of the Spiro benzofurancyclohexadienone, followed by deprotonation while the structure (253) would similarly arise from corresponding migration of the carbon-oxygen bond.



Scheme 1. Synthesis, thermal rearrangement and acid-catalyzed of Spiro benzofurancyclohexadienone.

4. CONCLUSIONS

In the present study, we used simple methods, available and cheap raw materials. The use of catalysts and solvents which are low-risk. shorter reaction times by the same method of synthesis. The evaluation of different catalysts to increase efficiency and reduce time. The purification method is simple and is ideal ethanol was used as solvent and the product was of high purity. phenol derivatives withelectron withdrawing substituent such as nitro which are products with higher efficiency compared to the electron donating substituent. In the first stage of the reaction, the reflux of long reaction time but the products were synthesized with high efficiency. But the products are solvent-free method reduces reaction time but their efficiency are lower than reflux. In the second stage high-efficiency products were synthesized.

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