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Synthesis of Semi-tetracycline Backbone Through Diels-Alder Reaction of 2,3-Dimethylbutadiene or Cyclopentadiene With 1,4-Benzoquinones

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ABSTRACT

Two main semi-tetracycline systems were synthesized. The strategy of such synthesis depends on the transformation of aroyl-1,4-benzoquinone to aroylketal-1,4-benzoquinone causes a regiocontrol addition of cyclopentadiene and 2,3-butadiene to the unsubstituted side of the quinone. These ketal adducts were hydrolyzed using the acidic media; as a result deketalization and enolization in one step give the semi-tetracycline system. The structures of these compounds were confirmed by NMR, IR, MS and elemental analysis.

Keywords: - Diels-Alder, semi-tetracycline, Benzoquinone,Butadiene, Cyclopentadiene.

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INTRODUCTION

Substances with a conjugated double bond system, in particular 1,3-diene, are noted for their high reactivity and this is shon by their great tendency to undergo 1,4-cycloaddition reactions to for six membered rings through Diels-Alder reaction.

Due to the presence of two electron withdrawing groups, 1,4-benzoquinones is considered to be very effective dienophile towards variety of dienes in Diels-Alder reactions. Benzoquinone reacts with one molar ration of both butadiene and cyclopentadiene to give the mono adducts, while doubling the ratio will provide the bisadduct. The mode of reaction of mono substituted 1,4-benzoquinones was found to be mainly depend on the electronic feature of the substituent as well as the steric effect of the substituent.

Diels-Alder reaction of substituted benzoquinone bearing an electron withdrawing group was investigated by Norton[1] who reported that the addition normally occurs at the least hindered double bond. Tetracyclic skeleton antibiotic daunomycinones [2] are considered to be clinically useful drugs for the treatment of broad spectrum of human cancer.[3]

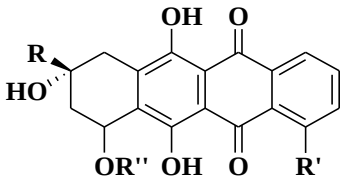


Figure 1:- General structure of tetracycline

These antibiotics have attracted the interest of organic chemists to assemble the tetracyclic skeleton of daunomycinones (**Figure 1)**. As result several regiospecific syntheses of such compounds have been reported.[4]

MATERIAL AND METHODS

Chemical and Instrument

^{1}H NMR spectra were recorded at 300 MHz on a Bruker DPX spectrometer and and ^{13}C NMR spectra at 75 MHz spectrometer. Chemical shifts are denoted in ppm (δ) relative to internal solvent standard (Me_4Si in the case of ^{1}H). The splitting patterns for NMR-spectra are designated as follows: s (singlet), d (doublet),dd (doublet of doublet), t (triplet),br (broad) and m (multiplet). Coupling constants (J) are designated in Hz. Infrared spectra were recorded using Perkin Elmer F.T.IR. SP-2000 spectrophotometer. Mass spectra were recorded using VG7070 E.G.C mass spectrophotometer. Melting points were determined on an uncalibrated electrothermal melting point apparatus. Elemental analyses were performed at M.H.W laboratories; Phoenix Arizona U.S.A. All the solvents and chemicals were used directly from Sigma-Aldrich vessel without

further purification.

Methods

Step 1:- Synthesis of 2,5-Dimethoxybenzohydrol (2)

A solution of 2,5-dimethoxybenzaldehyde (33.24 g) in dry ether (100 ml) was added to a stirred solution of phenylmagnesium bromide (0.25 mole) and magnesium turning (9.73 g) in ether (200 ml). Vigirous stirring was continued for another 2 hours. The mixture was then decomposed with concentrated NH_4Cl. The ether layer was separated and teh aqueous laye was extracted with ether (2X100 ml), the combined ether was washed with saturated $NaHSO_3$ solution then with water (2x40 ml) and dried over anhydrous $MgSO_4$. Evaporating off the solvent under vacuum afforded a crude oily product.

Step 2:- Synthesis of 2,5-Dimethoxybenzophenone (3)

To a solution of 2 in ether (250 ml), a reagent (400 ml) made of $K_2Cr_2O_7$ (100 g). Conc. Sulphuric acid (75 ml) and water (500 ml) was added dropwise with vigrous stirring at room temperature. The mixture was stirred for six hours then the ether layer was separated and the combined ether was washed with saturated NaCl (3X500 ml), saturated $NaHCO_3$ (3X500 ml) and water (2X50 ml) then dried over anhydrous $MgSO_4$. Evaporating of the solvent under vacuum afforded solid powder that was recrystallized from heptane.

Step 3:- Synthesis of 2,5-Dihydroxybenzophenone(4)

2,5-Dimethoxybenzophenone derivative (0.01 mole) was dissolved in 200 ml of dry dichloromethane. The mixture was cooled to – 80 ^{o} C (N_2/ethyl acetate).ntribromide (0.33 mole) in borontribromide (0.33 mole) in dichloromethane was then added dropwise while stirring through a septum with the use of syringe. The mixture was stirred at this temperature for 15 mnutes. The cold bath was removed and the mixture was stirred for 30 minutesat room temperature, poured into ice water (200 ml), stirred for 30 minutes. The organic layer was separated and the combined ether was washed with saturated NaCl (3X500 ml), saturated $NaHCO_3$ (3X500 ml) and water (2X50 ml) then dried over anhydrous $MgSO_4$. Evaporating of the solvent under vacuum afforded solid powder that was recrystallized from carbontetrachloride.

Step 4:- Synthesis of 2,5-Dihydroxybenzophenone ethylene ketal (5)

A mixture of 2,5-dihydroxybenzophenone (0.165 mole), ethylene glycol (0.16 mole), toluene-p-sulphonic acid (0.1 mg) and benzene (200 ml) was vigorously refluxed using a Dean-Stark apparatus for about 36 hours. The mixture was cooled and dry ether ether (100 ml) was added. The solution was made alkaline by adding triethylamine (8 drops) then washed with saturated

$NaHCO_3$ (3X500 ml) and water (2X50 ml) then dried over anhydrous $MgSO_4$. Evaporating of the solvent under vacuum afforded solid powder that was recrystallized from hexane

Step 5:- Synthesis of 2-(benzoylethylene ketal)-1,4-benzoquinone (6)

A mixture of 2,5-Dihydroxybenzophenone ethylene ketal (0.002 mole), activated silver oxide (0.007 mole), anhydrous sodium sulphate (0.012 mole) and dry ether (15 ml) was stirred for 4 hours in the dark. The mixture was filtered off over celite. Removal of the solvent under vacuum afforded an orange oily product.

Step 6:- Reaction of 2-(benzoylethylene ketal)-1,4-benzoquinone with dienes towards the synthesis of (7) and (8)

2-(benzoylethylene ketal)-1,4-benzoquinone (0.002 mole) was dissolved in 25 ml of benzene , excess of the dienes (2,3-dimethylbutadiene or cyclopentadiene) (0.04 mole) was added and the solution was refluxed for 5 hours in the case of 2,3-dimethylbutadiene and 15 minutes in the case of cyclopentadiene. The solvent was removed affording yellow solid products that was recrystallized from hexane

Step 7:- Deketalizationand enolization of 2-(benzoylethylene ketal)-1,4-benzoquinone diene adduct towards the synthesis of (9) and (10)

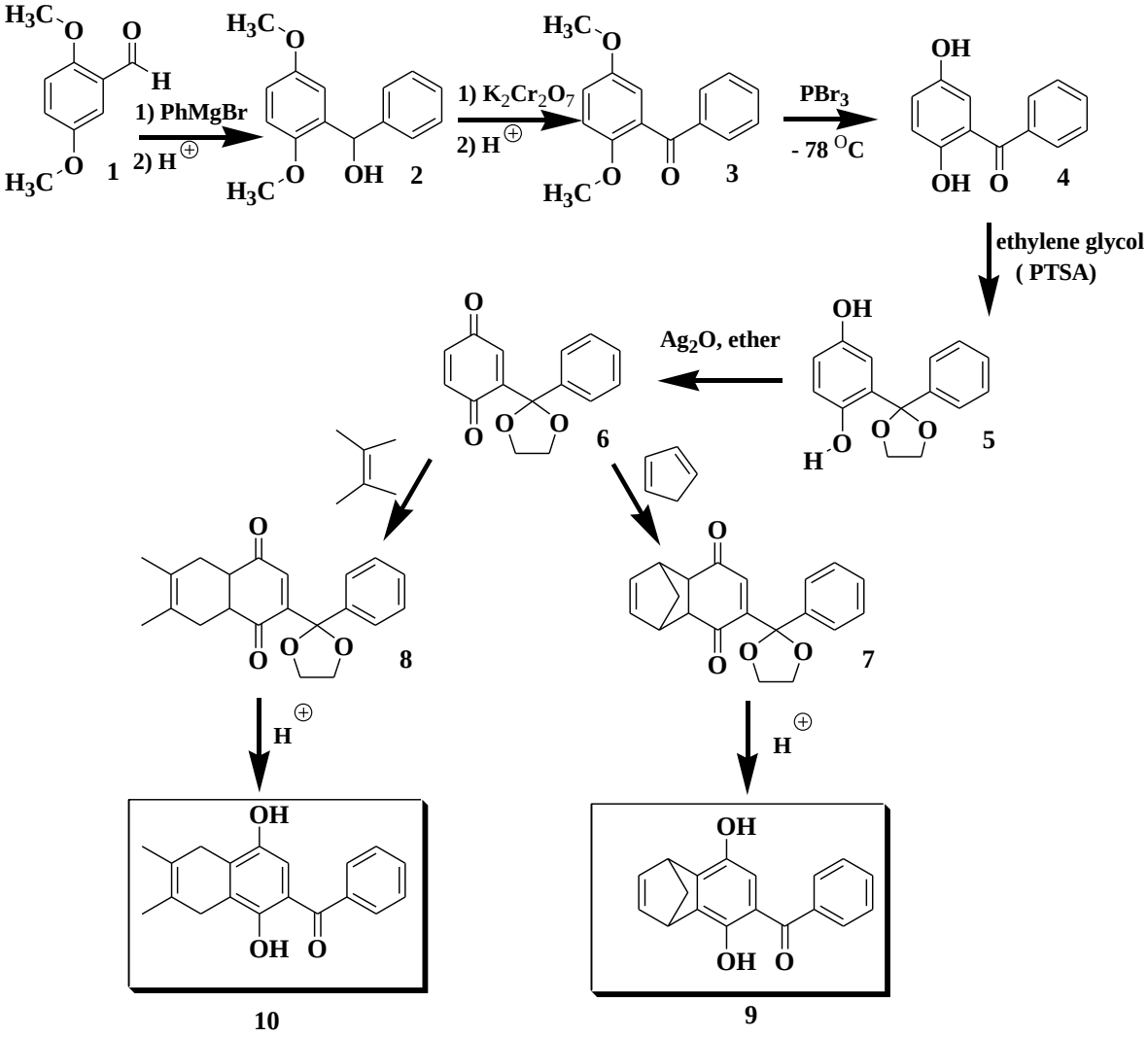
0.25 mole of Ketal adducts (**7**) and (**8**), acetone (10 ml) and conc. HCl (7 drops) were refluxed on a steam bath for about 2 hours, after cooling, the solvent was removed under vacuum affording yellow solid products that was recrystallized from pentane

RESULTS AND DISCUSSION

Since it was realized that daunomycinone compounds are of biological importance, the partial or complete synthesis of the tetrcyclic system was the aim of many organic chemists. Our interest was to synthesize at least the same as Bruce's but through Diels-Alder reaction[5]; which includes reaction of specifically synthesized substituted 1,4-benzoquinonewith dienes to inverse method to that of Bruce method. This required quinone that contains a protected benzoyl group in which its electronwithdrawal is decreased and it can be easily recovered by hydrolysis.

Thus as scheme (1) shows the reaction of 2.5 dimethoxy benzaldehyde with aryl magnesium bromide was conducted which afford the corresponding alcohol **2**, all the products were oily and many attempts to solidify them were failed. The i.r spectra of products show the presence of strong absorption at 3350 cm^{-1} due to OH group as well as at 1660 cm^{-1} due to unreacted aldehyde, while the H-NMR spectra show the two singlets in the range of δ3. 6-3.8 due to two OCH_3, one proton broad doublet exchanged to singlet on addition of D_2O at 86.3 due to the

benzylic proton, the resonated aromatic protons in the range of δ6.9- 7.6 and a broad absorption at δ2.9 exchanged with D_2O due to the hydroxyl group. Oxidation of the previous alcohols with $K_2Cr_2O_7/H^+$ in ether afforded the corresponding dimethoxybenzophenone derivative **3**. Its structure was confirmed from their i.r spectra through the presence of a strong absorption at 1640 cm^{-1} and the absence of the hydroxyl absorption which confirmed complete oxidation. The ^{1}H-NMR spectra showed two singlets in the range of δ 3.66-3.67 and δ 3.77-3.79 due to the two methoxy groups. The downfield one could be attributed to that at position 2, affected by the carbonyl group through anisotropic effect. The aromatic protons appear in their expected range.



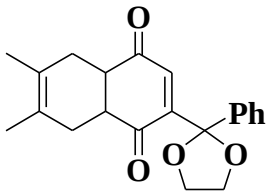
Scheme 1:- Total route of semi-tetracycline synthesis

The mass spectra of compound **3** showed the molecular ion peak. The peak at (M/z) = 165 due to the loss of 2.5 dimethoxy benzoyl ion.

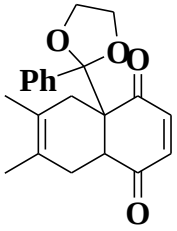
Demethylation of these dimethoxybenzophenone derivative **3** was achieved using borontribromide in dichloromethane at -80^{0}C. Demethylation occurred smoothly and afford in

most of the cases a complete demethylation. The hydroquinone prepared **4** using this method was pure enough. Its structure was confirmed from their analytical and spectral data. The i.r spectra of compound **4** showed a strong absorption in the range of 3100- 3393 cm^{-1} due to strong hydrogen bonded OH and 1598- 1608 cm^{-1} due to the carbonyl group, the low absorption can be attributed to the presence of strong hydrogen bond. On the other hand their ^{1}HNMR ($CDCl_3$) showed the presence of two exchangeable hydroxyl groups at δ4.47 and δ11.54 The down field one is attributed to OH located at position 2. The aromatic protons appear in their expected position as a multiplet for compound **4** in the range of (7.30- 7.81). The other three protons (H3, H4 and H6) appeared as a singlet with fine splitting in the range of (6.95-7.09). The mass spectra of compound **4** showed the exact molecular ion peaks and peaks at (M/z) = 105 due to the loss of benzoyl. After the achievement of 2- aroyl–1,4- hydroquinone **4**; ketalization of the carbonyl group was the next step to be attempted since such reaction will decrease the electronwithdrawal and increase the steric effect at the carbon atom attached to the hydroquinone. ketalization process was realized through refluxing a solution of 2- aroyl-1-4- hydroquinone in benzene containing excess of ethyleneglycol and p-toluence sulfonic acid as a catalyst using Dean Stark apparatus for about 48 hr is the best condition for the ketalization of these hydroquinones. The structure of the obtained ketal **5** was confirmed from the analytical and spectral data. The i.r spectra of this compound show the absence of the absorption due to carbonyl group and the presence of strong absorption in the range of (3090- 3590 cm-1) due to hydroxyl group and in the range of (1054- 1069) cm^{-1} due to the ether linkage of the ketal group. On the other hand the 1H-NMR ($CDCl_3$) showed the common peaks in the expected regions, for example, four protons as unidentified multiplet in the range of (4.00- 4.17) due to the ketal methylene groups, one singlet at 7.00 due to H3, two singlets in the range of (6.75- 6.93) due to H5 and H6. Oxidation of the ketal **5** with sliver oxide in ether under anhydrous condition and in the dark afforded the corresponding quinone **6** in a good yield as a crystallizable solid product. It was realized that such quinone is slightly unstable and hydrolyzed or polymerized in air. The structure of this quinone was confirmed from their spectral data. The i.r spectra show the following absorption 1656 (enedione). 1593 (C=C) and 1060 cm^{-1} (ethane linkage). There was no sign of any hydroxyl absorption indicated that complete oxidation occurred. On the other hand the ^{1}H- NMR ($CDCl_3$) spectra of compound **6** showed the ketal group in the range of δ4.05–4.08 as a singlet in compounds. The quinonoid protons were not identical H-3 appears as a double with fine splitting in the range of (7.00- 7.13) while H-5 and H-6 Hz. The aromatic protons appear as a multiplet in the range of (7.31- 7.6). After success in handling the reactive quinone, the next step in our

synthesis was to react them with dienes through Diles Alder reaction. For this purpose 2,3-dimethyl butadiene as an acyclic diene and cyclopentadiene as a cyclic diene were chosen. The later has to be prepared freshly to avoid dimerization. The mode of addition of these dienes as a symmetrical diene to the mentioned quinone as an unsymmetrical dienophile can in principle give rise to two structurally different adducts **(Figure 2)**. The first type resulted from the addition to the unsubstituted side of the quinone, on the basis that aroyl ketal group, being a bulky group, giving rise to non angular adduct of type (**X**) . The second type resulted from the addition to the substituted side of the quinone, if the aroyl ketal group is still electron withdrawing group, giving rise to the angular adduct of type (**Y**).



X



Y

Figure 2:- Angular and non-angular adducts

Spectroscopic tools especially HNMR can easily distinguish between the two types of products, those of type (**X**) can clearly show one enedione proton to two olefinic protons in the range of δ6.7-7.00 and δ5.5-6.7 respectively, while those of type (**Y**) should clearly show H4 as one proton doublet, in case of cyclopentadiene or one proton doublet or triplet, in case of acyclic dienes in the range of δ3.0-3.5, while those of type (**X**) should give multiplets for two protons in the same range.

Since the Diels-Alder adducts are known to be unstable to heat and retro reaction can occur at high temperature, the reactions of quinone **6** was conducted either at room temperature; with cyclopentadiene, as a reactive diene or as it was realized in boiling benzene in case of 2.3-dimethy butadiene as less reactive diene. Thus the Diels-Alder reaction of quinine **6** with 2.3-dimethyl butadiene in refluxing benzene afforded as a solid crystallizable product. Spectral data confirm the structure since the i.r. shows the presence of the following absorption in the range of 1656, 1593 and 1066 cm^{-1}due to enedione (C=O), (C=C) and (C-O) groups respectively. The ^{1}H-NMR ($CDCl_3$) spectral data clearly shows the presence of one proton doublet with fine splitting in the range of δ6.65-7.12 due to the W type coupling of the enedione proton H-3 with H-4a, two protons "triplets" in the range of δ 2.98-3.6 due to the bridge head protons. These data indicate that the addition of diene occurs to the unsubstituted side giving the non angular adducts

7 the rest of ^{1}H-NMR ($CDCl_3$) spectra shows six protons singlet at δ1.58 due to the two methyl groups at C6 and C7, four protons mutiplet in the range of δ 1.83-2.31 due to 2H5 and 2H8, the appearance of these protons ad a multiplet is due to the coupling between them as well as with the bridge head protons, four protons either a singlet with fine splitting or as a doublet in the range of δ4.03-4.10 due to the ketalic protons; the coincidence of these protons may be attributed to the planarity of the molecule.

On the other hand the Diels-Alder reaction of quinone **6** with cyclopentadiene was carried out at room temperature to assure the formation of the kinetically controlled endo products, since dissociation- recombination at high temperature facilitate the formation of the thermally stable exo-adducts. Thus when the reaction is conducted, a change in the orange color was noticed immediately; working up afforded a solid product.

The i.r spectra (KBr) of the products show the presence of the following absorptions in the range of 1665, 1621 and 1067. The ^{1}H-NMR ($CDCl_3$) shows the presence mainly of two peaks at δ7.00 as a singlet and two sets of multiplets in the range of δ7.22-7.63 integrating 1:2 protons respectively. These result indicates clearly that the addition of cyclopentadiene with quinones **6** occurs at the unsubstituted side giving the non angular adducts **7** respectively, the mentioned peaks in the ^{1}H-NMR spectra are clearly due to H-3, H-6 and H-7 respectively. The rest of the spectra shows the following absorptions: two protons multiplet in the range of δ1.25-1.57 due to methylene protons (2H9), two protons multiplet in the range of δ3.02-3.28 due to the bridge head protons H4a and H8a, two protons multiplets in the range of δ3.29-3.63 due to H5 and H8, the appearance of each set of these protons as identical, clearly agrees with the fact that the addition occurs at the unsubstituted side of the quinones. The remaining protons in the spectra are due to the ketalic four protons which appear as a singlet in the range of δ4.02. The aromatic protons appear as a multiplet in the range of δ7.22-7.63. The mass spectra shows the exact molecular ion peaks. After the selective achievement in the Diels-Alder addition of dienes to the unsubstituted side of quinone **6** and the safe handling of the adducts **7** and **8**, the next step in the synthesis is the hydrolysis of the ketal group and the enolization of the quinonoid ring to achieve the required product. For this step many ways have been tried. In all of them each adduct was refluxed either in conc. H_2SO_4 or conc. HCl, with different organic solvent for several hours. It was found that the optimum condition was refluxing the compound in acetone in the presence of catalytic amount of conc. HCl for about (2.5) hours. Thus when this reaction was conducted with 2,3-dimethybutadiene adducts **8** and working up it afforded a solid crystallizable product. The i.r spectra showed the presence of a strong absorption in the range of 3125-3457 cm^{-1} due to OH

group and 1605-1621cm^{-1} due to hydrogen bonded benzophenone carbonyl group. These data indicate that deketalization and enolization occurred to afford compounds **10**. The ^{1}H-NMR ($CDCl_3$) of this compound shows the presence of two hydroxy1 groups, exchanged with D_2O in the range of δ12.12-12.40 and δ4.38-4.45, the former one: highly deshielded, can be attribute to the hydroxyl group attached to C-1, deshielded by strong hydrogen bonding, while the other was found in its normal position due to OH-C4, one proton singlet in the range of δ6.82-6.87 due to H3. The rest of NMR showed six protons singlet in the range of δ1.79-1.86 due to the methyl groups at C6 and C7, four protons appear as a singlet in the range of δ3.19-3.2; due to H_5 and H_8 their appearance as a singlet can be attributed to the absence of bridge head protons H4a and H8a. The aromatic protons appear as a multiplet in compound **10** in the range of δ7.25-7.75 integrate for five and four protons respectively. On the other hand the cyclopentadiene adducts **7** when hydrolyzed and enolized afforded a solid crystallizable product. The i.r spectra of the product showed the presence of a strong absorption in the range of 3175-3425 cm^{-1} due to OH group and 1632-1637 cm^{-1} due to hydrogen bonded bezophenone carbonyl group, these data indicate that deketalization and enolization occurred to afford compounds **9**. The ^{1}H- NMR ($CDCl_3$) spectra of this compound showed the presence of two hydroxyl groups exchanged with D_2O in the range of δ11.46-11.68 and δ4.47-4.83, the former one can be attributed to the hydroxyl group attached to C-1 deshielded by strong hydrogen bonding while the other is due to shielded OH-C4.The H-3 appear as a singlet in the range of δ 6.45-6.73, the rest of NMR spectra, the two protons of (H9) appear as a multiplet in the range of δ1.31-1.18, two protons appear as a doublet in the range of δ 4.-4.33 due to H-5 and H-8, the two protons H6 and H7 appear as two sets of multiplet in the range of δ6.8-6.92. The aromatic protons appear as a mutiplet in the range of δ 7.10-7.79. The mass spectra of the compounds **9** and **10** showed the molecular ion peaks clearly as well as a base peaks.

EXPERIMENTAL

2,5-Dimethoxybenzophenone (3)

^{1}H NMR (300MHz, DMSO) δ 3.66 (s,3H), 3.79(s,3H), 6.80-7.00 (d, 2H), 7.25 (s, 1H), 7.31-7.92 (m, 5H). ^{13}C NMR (75MHz, DMSO) δ 51.4(CH_3), 56.9 (CH_3), 167.8 (C=O). IR υ_{max} cm $^{-1}$, 1074 (C-O), 1651 (C=O).

2,5-Dihydroxybenzophenone(4)

^{1}H NMR (300MHz, DMSO) δ 4.47 (s,OH), 6.95-7.09 (m, 3H), 7.30-7.81 (m, 5H), 11.54 (s, OH). ^{13}C NMR (75MHz, DMSO) δ 171.0 (C=O). IR υ_{max} cm $^{-1}$,1603 (C=O), 3100-3393 (OH).

2,5-Dihydroxybenzophenone ethylen ketal (5)

^{1}H NMR (300MHz, DMSO) δ 4.00-4.17 (m,4H), 5.44 (s, OH), 6.75 (s, 1H), 6.93 (s, 1H), 7.00 (s, 1H), 7.26-7.62 (m, 6H). ^{13}C NMR (75MHz, DMSO) δ 55.5 (CH_2). IR υ_{max} cm $^{-1}$,1054 (C-O), 3090-3590 (OH).

2-(benzoylethylene ketal)-1,4-benzoquinone (6)

^{1}H NMR (300MHz, DMSO) δ 4.07 (s,4H), 6.50-6.78 (dd, 2H), 7.00-7.13 (d, 1H), 7.31-7.60 (m, 5H). ^{13}C NMR (75MHz, DMSO) δ 59.1 (CH_2), 174.9 (C=O). IR υ_{max} cm $^{-1}$,1593(C=C), 1060 (C-O), 1656 (C=O).

2-(benzoylethylene ketal)-4a,5,8,8a-tetrahydro-6,7-dimethyl-1,4-naphthaquinone (7)

^{1}H NMR (300MHz, DMSO) δ 1.58 (s,6H), 1.83-2.34 (m, 4H), 2.98-3.25 (t, 2H), 4.03-4.10 (d,4H), 7.07-7.12 (d, 1H), 7.27-7.69 (m, 5H). ^{13}C NMR (75MHz, DMSO) δ 30.91 (CH_3), 57.4 (CH_2), 174.9 (C=O). IR υ_{max} cm $^{-1}$,1593(C=C), 1066 (C-O), 1656 (C=O).

2-(benzoylethylene ketal)-4a,8a-dihydro-5,8-methano-1,4-naphthaquinone (8)

^{1}H NMR (300MHz, DMSO) δ 1.25-1.57 (m,2H), 3.02-3.28 (m, 2H),), 3.29-3.63 (m, 2H), 4.02 (s,4H), 5.66-6.23 (d, 2H), 7.00 (s, 1H). 7.22-7.63 (m,5H). ^{13}C NMR (75MHz, DMSO) δ 51.4 (CH_2), 170.6 (C=O). IR υ_{max} cm $^{-1}$, 1067 (C-O), 1621(C=C), 1665 (C=O).

2-(benzoyl)-5,8-dihydro-1,4-dihydroxy-6,7-dimethyl-naphthalene (9)

^{1}H NMR (300MHz, DMSO) δ 1.86 (s,6H), 3.25(s, 4H), 4.38 (s, OH), 6.82 (s,1H), 7.35-7.75 (m, 5H), 12.14 (s, OH). ^{13}C NMR (75MHz, DMSO) δ 31.5 (CH_2), 170.8 (C=O). IR υ_{max} cm $^{-1}$, 1621 (C=O), 3125-3425 (OH)

Table 1:- Physiochemical parameters of the novel synthesized compounds

Sr. No	Molecular Formula and Molecular Mass	Yield %	Melting point(^{0}C)	(Cryst. Solvent)	Elemental Analysis % Calcd./ Found
1	$C_{15}H_{14}O_3$ 242	87	56-66	Heptane	C, 74.36 (74.32); H, 5.82 (5.85); O, 19.81(19.82)
2	$C_{13}H_{10}O_3$ 214	92	128-129	Carbon tetrachloride	C, 72.89 (72.93); H, 4.71 (4.69) ; O, 22.41 (22.39)
3	$C_{15}H_{12}O_4$ 256	62	78-80	Hexane	C, 70.31 (70.33); H, 4.72 (4.73); O, 24.97 (24.94)
4	$C_{21}H_{22}O_4$ 338	81	104-105	Hexane	C, 74.54 (74.55); H, 6.55 (6.56) ; O, 18.91 (18.89)
5	$C_{20}H_{18}O_4$ 322	60	102-104	Hexane	C, 74.52 (74.50); H, 5.63 (5.64) ; O, 19.85 (19.86)
6	$C_{19}H_{18}O_3$ 294	73	153-155	Pentane	C, 77.53 (77.55); H, 6.16 (6.18) ; O, 16.31 (16.27)
7	$C_{18}H_{14}O_3$ 278	78	156-157	Pentane	C, 77.68 (77.65); H, 5.07 (5.08); O, 17.25 (17.27)

2-(benzoyl)-1,4-dihydroxy-5,8-methano-naphthaquinone (10)

^{1}H NMR (300MHz, DMSO) δ 1.32-1.81 (m,2H), 4.13-4.33 (d, 2H),), 4.83 (s, OH), 6.7 (s,1H),

6.92-7.05 (m,2H), 7.45-7.79 (m, 5H), 11.49 (s,OH). ^{13}C NMR (75MHz, DMSO) δ 51.4 (CH_2), 170.6 (C=O). IR υ_{max} cm $^{-1}$, 1637 (C=O), 3175-3400 (OH)

CONCLUSION:-

This research involves semitetracyclic structure synthesis through several simple steps starts with derivatized p-dimethyl benzyl alcohol synthesis followed by oxidation affording the benzophenone derivative which was ketalized as a protective step. Demethylation of the p-dimethylbenzophenone provided the corresponding p-hydroquinone which is the precursor for p-benzoquinone through oxidation. The arising bezoquinone was treated with 1,4-diene such as cyclopentadiene and 2,3-dimethylbutadiene to afforded tricycline system after the step of acidic hydrolysis that causes deketalization as well as enolization that restore the aromatic feature

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