PUBLICATIONS

Synthetic Communications®, 35: 1715–1723, 2005

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1081/SCC-200061717

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Novel One-Pot Synthesis of Acetoxy-2,4-Cyclohexadienones

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Abstract: A new, simple, one-pot method for the oxidative acetylation of some substituted phenols leading to acetoxycyclohexa-2,4-dienones is described. A novel diacetoxycyclohexadienone **12** has also been prepared using the present method from 2-hydroxymethyl phenol (salicyl alcohol).

Keywords: Acetoxy-2,4-cyclohexadienones, *ortho*-quinols, oxidative acetylation

Cyclohexa-2,4-dienones of the type **1** are emerging as valuable intermediates in organic synthesis[1] because of their diverse chemical behavior. There are several elegant examples of efficient syntheses using them in a variety of reactions.[2] In general, these are prepared by oxidation of phenols with several reagents such as lead tetraacetate (LTA),[3] benzeneseleninic anhydride (BSA),[4] hypervalent iodide reagents,[5] and sodium metaperiodate.[6] Occasionally, diacyl peroxide[7] and trifluoro-peroxyacetic acid[8]

Received in India February 16, 2005
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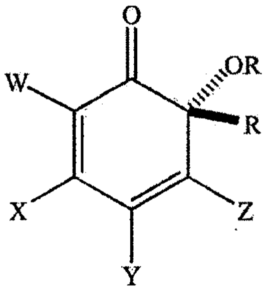
have also been used for their preparation. The oxidation of phenols with LTA, known as "Wessely oxidation," is a generally used method for their preparation.[3] However, it often proceeds in low yields and furnishes a mixture of products depending upon the nature of the substituents on the aromatic ring.[3] Alternatively, *ortho*-quinols **1a** can also be prepared in the dimeric form by the periodate oxidation of phenols as investigated by Adler et al.[6]

Wessely oxidation gives acetoxycyclohexadienones **1b** in one step, albeit in low yields. On the other hand, Adler's method gives relatively better yields but results in the formation of corresponding *ortho*-quinol dimer, which needs to be acetylated to the corresponding diacetate dimer. The dimeric diacetate needs to be pyrolyzed to furnish the corresponding acetate **1b**, which results in lower overall yield. The chemistry of *ortho*-quinols **1a** is dominated by their propensity toward [4 + 2] dimerization, which can be suppressed partially by converting them into acetates **1b** to exploit their synthetic potential (Figure 1).

With an appreciation of their utility as synthons, we set out to devise a general method for the preparation of **1b** with the hope that such a method might be useful in the synthesis. Toward the realization of this objective, we explored the reaction of phenols with periodate in acetic anhydride medium. We postulated that the oxidative acetylation of phenol would give corresponding acetoxy-2,4-cyclohexadienone **1b** directly in one step (Figure 1).

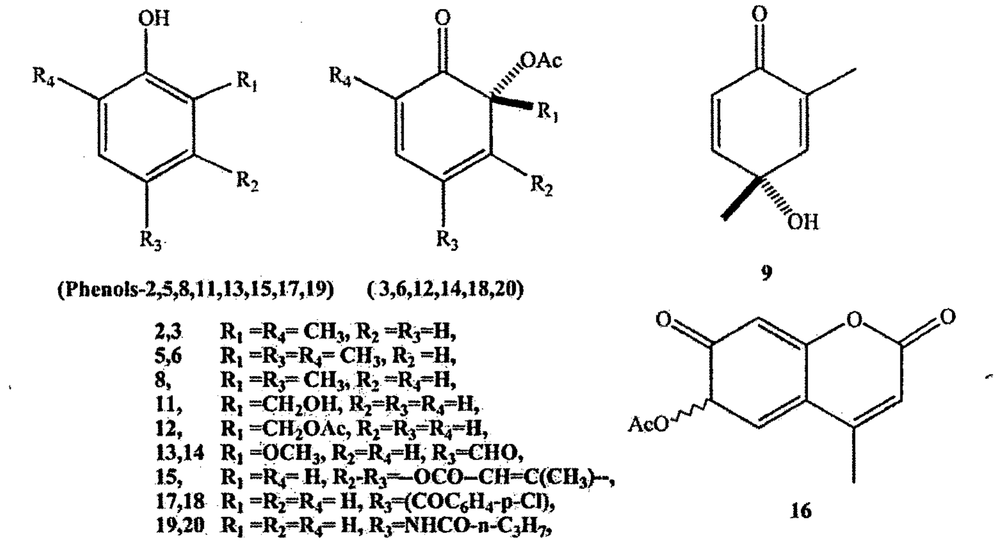
Thus, 2,6-dimethyl phenol **2** (Scheme 1) in acetic anhydride was treated with sodium metaperiodate (1.2 equiv.) added in portions, with stirring for 5 h at room temperature, which gave **3** and its dimer **4** in 32 and 36% yields, respectively, after usual workup and chromatography. All the physical and spectral characteristics of the compounds **3** and **4** were in full accordance with those reported in the literature.[6]

Encouraged by this observation, we attempted this procedure on other phenols. Accordingly, 2,4,6-trimethylphenol **5** was treated with 1.2 equivalent of sodium metaperiodate in acetic anhydride in similar way to obtain the corresponding acetoxycyclohexadienone **6** (30%) along with its dimer **7** (33%). All the physical and spectral characteristics of these compounds were also found to be in good agreement with those reported in literature.[6]



1a, R = H,
1b, R = Ac

Figure 1. Cyclohexa-2,4-dienones.



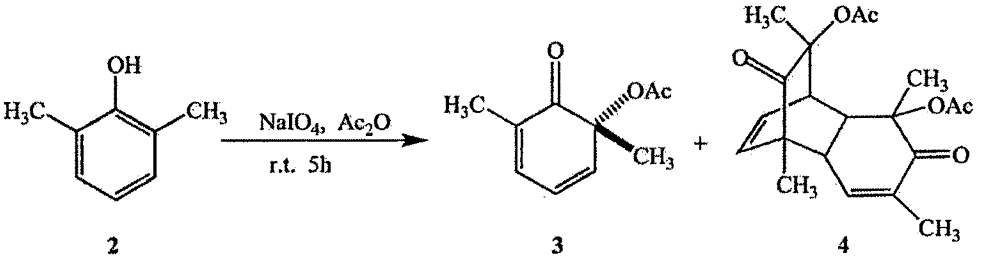
(Phenols-2,5,8,11,13,15,17,19) (3,6,12,14,18,20)

2,3 $R_1=R_4=CH_3, R_2=R_3=H$,
5,6 $R_1=R_3=R_4=CH_3, R_2=H$,
8, $R_1=R_3=CH_3, R_2=R_4=H$,
11, $R_1=CH_2OH, R_2=R_3=R_4=H$,
12, $R_1=CH_2OAc, R_2=R_3=R_4=H$,
13,14 $R_1=OCH_3, R_2=R_4=H, R_3=CHO$,
15, $R_1=R_4=H, R_2\text{-}R_3=\text{–OCO–CH=C(CH}_3\text{)–}$,
17,18 $R_1=R_2=R_4=H, R_3=(COC_6H_4\text{-p-Cl})$,
19,20 $R_1=R_2=R_4=H, R_3=NHCO\text{-n-}C_3H_7$,

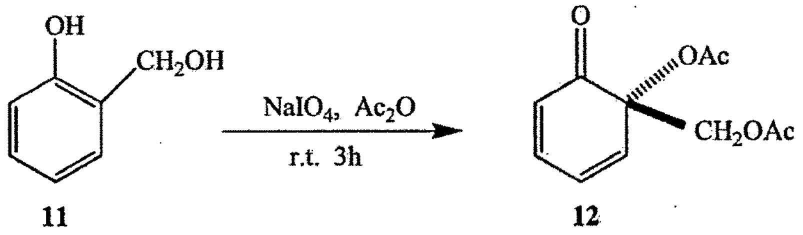
Figure 2. Substituted phenols and corresponding cyclohexadienones obtained by oxidative acetylation.

When 2,4-dimethyl phenol **8** was oxidized in similar manner, we obtained **9** (32%) along with the **10** (34%). The melting point, UV, IR, and elemental analysis of the compound **9** were in good agreement with those reported in the literature.[6] The compound **10** also gave matching spectral and analytical characteristics with those reported in the literature.[6] It should be mentioned here that the ^{1}H NMR spectrum of compound **10** was not reported earlier.[6] The ^{1}H NMR spectrum of **10** displayed signals at δ_H (200 MHz, $CDCl_3$): 6.21 (d, 1H at C_3) 6.0 (d, 1H at C_4), 5.5 (d, 1H at C_{12}, olefinic), 3.8 (s, O$\underline{H}$), 3.2 (s, 1H), 2.85 (d, 1H, bridgehead at C_1), 2.2 (s, O$\underline{H}$), 1.8 (s, 3H, olefinic $C\underline{H}_3$), 1.6 (s, 3H, $C\underline{H}_3$), 1.4 (s, 3H, $C\underline{H}_3$), 1.39 (s, 3H, $C\underline{H}_3$).

It was interesting to observe that when salicyl alcohol **11** was subjected to similar oxidation, a novel 1-(acetoxymethyl)-6-oxocyclohexa-2,4-dienyl acetate **12** was obtained in 53% yield (Scheme 2). The structure of **12** was fully discernible from its UV, IR, ^{1}H NMR, ^{13}C MR, mass spectra, and elemental analysis. It showed a strong band at 1740 cm^{-1} in addition to the characteristic carbonyl absorptions at 1625 and 1570 cm^{-1} in its IR spectrum. Its UV spectrum showed a band at 300 nm, indicating the



Scheme 1.



Scheme 2.

presence of a 2,4-cyclohexadienone ring system.[9] Its ^1H NMR spectrum showed signals at δ_H (200 MHz, $CDCl_3$): 7.51 (dd, $J_1 = 6$ Hz, $J_2 = 2$ Hz, 1H at C_2), 7.41 (dd, $J_1 = 8$ Hz, $J_2 = 6$ Hz, 1H at C_3), 7.35 (dd, 1H at C_4), 7.12 (d, 1H at C_5), 5.12 (s, 2H, methylene proton), 2.3 (s, 3H, $COC\underline{H_3}$), 2.1 (s, 3H, $COC\underline{H_3}$). The ^{13}C MR of **12** exhibited carbonyl resonances at δ_c 150.16 and two acetate carbonyls at δ_c 170.69 and 169.38. The olefinic carbons appeared at δ_c 130.62, 129.82, 128.45, and 126.36, the highly deshielded tetra-substituted carbon at δ_c 122.98, a methylene carbon at δ_c 61.90, and methyl carbons at δ_c 20.95. The mass spectrum of **12** gave following fragmentation patterns: M-43 (CH_3CO^+) and M-60 (CH_3COOH),[9] and was correctly analyzed for $C_{11}H_{12}O_5$.

Vanillin, upon similar oxidation, also gave the expected acetate dienone **14** whose ^1H NMR spectrum exhibited singlets at δ_H 9.91 and 3.88, indicating the presence of aldehyde and methoxy groups respectively among other signals. 4-Methyl-7-hydroxy coumarin **15**, however, gave rise to only one regioisomer **16** exhibiting a doublet at δ_H 7.59 and a singlet at 7.10 for one proton each in its ^1H NMR spectrum, ruling out the possibility of presence of other isomers. 4-Hydroxy-4′-chlorobenzophenone **17** furnished 3-(4-chlorobenzoyl)-6-oxocyclohexa-2,4-dienyl acetate **18** under similar conditions, which was evident because the mass spectrum of **18** displayed a base peak at M-140, which suggests loss of the $C_6H_4ClCO^+$ ion, among other characteristic signals. Oxidation of 4-hydroxy butyranilide **19** also led to similar observation producing **20**, whose ^1H NMR spectrum revealed a doublet at δ_H 1.60 for a single proton in addition to other supporting evidence. 4-Methoxy phenol, thymol, and o-, m-, and p-cresols gave rise to complex mixtures under reaction conditions.[10] Various acetoxy-2, 4-cyclohexadienones prepared by the present method are listed in Table 1, which summarizes the reaction temperature, yields, and mp of various products obtained from the oxidative acetylation of various substituted phenols.

EXPERIMENTAL

Melting points were recorded in open capillary tubes and are uncorrected. Ultraviolet spectra were recorded on a Perkin-Elmer Lambda-19 spectrometer. Infrared spectra were recorded on a Perkin-Elmer PC-16 FTIR

Table 1. Yields of products of oxidative acetylation of substituted phenols

Phenol (mols)	Reaction temp. (°C)	Cyclohexadienone (% yield)	Mp (°C)	Reported mp[6] (°C)	Dimer (% yield)	Mp (°C)	Reported Mp[6] (°C)
2 (0.032)	Ambient	**3** (32)	32–35	34–35	**4** (36)	158–159	159–160
5 (0.029)	Ambient	**6** (30)	80–82	82–84	**7** (33)	164–166	162–163
8 (0.032)	Ambient	**9**[a] (32)	53–55	53–54	**10**[a] (34)	225–228	225–228
11 (0.032)	Ambient	**12** (53)	235	—	—	—	—
13 (0.013)	60	**14** (59)	85	—	—	—	—
15 (0.011)	85	**16** (52)	171	—	—	—	—
17 (0.002)	70	**18** (60)	134	—	—	—	—
19 (0.004)	Ambient	**20** (52)	102	—	—	—	—

[a] Corresponding hydroxy compounds isolated.

spectrophotometer. ^{1}H NMR (200/300 MHz) spectra and ^{13}CMR (50 MHz) were recorded either on a Bruker-200 FT-NMR or on a Bruker-300 FT-NMR using $CDCl_3$ as solvent containing tetramethylsilane as an internal standard. Mass spectra were recorded on a Shimadzu QP-5050-A mass spectrometer. Microanalyses were performed on a Perkin-Elmer 2400 series II laser instrument.

Column chromatography was performed using Acme's silica gel (60–120 mesh size), and the elution was done using light petroleum and ethyl acetate mixtures. The percent yields are reported based on the isolated material after column chromatography. Thin-layer chromatography was performed using Acme's silica gel for TLC, and spots were visualized in iodine vapor.

General Procedure for the Oxidative Acetylation of Substituted Phenols

To a stirred solution of phenol in acetic anhydride (15–20 mL) was added sodium metaperiodate (1.2 mol, excess) in portions over a period of 1 h. Stirring was further continued for 4–5 h either at room or at elevated temperatures in cases of phenols **13, 15,** and **17**. The reaction mixture was then poured into a saturated solution of sodium bicarbonate and stirred vigorously to neutralize excess acetic acid. The aqueous layer was extracted with ethyl acetate (4 x 25 mL) and combined organic extracts were washed successively with saturated sodium bicarbonate (25 mL), water (25 mL), and brine solution (20 mL), followed by drying over anhydrous sodium sulphate. Removal of solvent under reduced pressure furnished a residue, which was chromatographed using mixtures of light petroleum and ethyl acetate to give corresponding acetoxycyclohexadienones. The corresponding dimeric diacetates were also obtained additionally in cases of phenols **2**, **5**, and **8**.

Thus, oxidation of 2,6-dimethyl phenol **2** gave 1,5-dimethyl-6-oxocyclohexa-2,4-dienyl acetate **3**, as a pale yellow thick liquid (32%), mp 32–35°C. ν_{max}: 3020, 1739, 1674, 1346, and 1226 cm^{-1}. UV (λ_{max}): 295 nm. Elemental analysis: Found C, 65.96%; H, 6.43%; requires C, 66.66%; H, 6.66% for $C_{10}H_{12}O_3$ along with 6,9-diacetoxy-1,4,6,9-tetramethyltricyclo[6.2.2.0^{2,7}]dodeca-3,11-dien-5,10-dione **4**, as a white crystalline solid (36%), mp 158–159°C. ν_{max}: 3007, 2982, 1744, 1698, 1654, 1456, 1368, 1232 and 700 cm^{-1}. UV (λ_{max}): 241 nm. δ_H (200 MHz, $CDCl_3$): 6.26 (d, 1H at C_{12}), 6.15 (dd, 1H at C_{11}), 5.61 (d, 1H at C_3), 3.78 (d, 1H at C_8, bridgehead), 3.44 (d, 1H at C_2), 3.0 (dd, 1H at C_7), 2.2 (s, 3H, CH_3, at $COC\underline{H}_3$), 2.1 (s, 3H, CH_3 at $COC\underline{H}_3$), 1.82 (s, 3H, $C\underline{H}_3$, olefinic), 1.72 (s, 3H, $C\underline{H}_3$), 1.49 (s, 3H, $C\underline{H}_3$), and 1.39 (s, 3H, $C\underline{H}_3$). MS m/z: 361(M + 1), 300 (M–CH_3COOH), 241[M-($2CH_3COOH$)], and 181[(M + 1)-monomer]. Elemental analysis: Found C, 67.12%; H, 6.67%; requires C, 66.66%; H, 6.66% for $C_{20}H_{24}O_{16}$.

Similarly, oxidation of 2,4,6-trimethylphenol **5** gave 1,3,5-trimethyl-6-oxocyclohexa-2,4-dienyl acetate **6** as a white solid (30%), mp 80–82°C.

ν_{max}: 3078, 2855, 1745, 1719, 1693, and 1621 cm^{-1} along with 6,9-diacetoxy-1,2,4,6,9,11-hexamethyltricyclo[6.2.2.0^{2,7}]dodeca-3,11-diene-5,10-dione **7**, as a white crystalline solid (33%), mp 164–166°C. ν_{max}: 3033, 2982, 2876, 1735, 1695, 1651, 1540, 1258, 1180, 1080, 834, and 725 cm^{-1}. UV (λ_{max}): 241 nm. δ_H (200 MHz, CDCl$_3$): 5.91 (s, 1H, olefinic), 5.12 (d, 1H at C$_7$), 3.53 (d, 1H, bridgehead), 3.0 (s, 1H, olefinic), 2.2 (s, 3H, CH$_3$, at $COC\underline{H}_3$), 2.1 (s, 3H, CH$_3$ at $COC\underline{H}_3$), 1.79 (d, 3H, $C\underline{H}_3$, olefinic), 1.73 (d, 3H, $C\underline{H}_3$), 1.70 (s, 3H, $C\underline{H}_3$), 1.54 (s, 3H, $C\underline{H}_3$), 1.26 (s, 3H, $C\underline{H}_3$) and 1.09 (s, 3H, $C\underline{H}_3$). MS m/z: 389 (M + 1), 329 (M–CH$_3$COOH), 269 [M-(2CH$_3$COOH)], and 194 [(M + 1)-monomer)]. Elemental analysis: Found C, 67.89%, H, 7.54%, requires C, 68.04%; H, 7.21% for $C_{22}H_{28}O_{16}$.

Oxidation of 2,4-dimethyl phenol **8** furnished 4-hydroxy-2,4-dimethylcyclohexa-2,5-dienone **9**, as a white crystalline solid (33%), mp 53–55°C. ν_{max}: 3456, 1662, 1631, 1292, 1130, and 1095 cm^{-1}. UV (λ_{max}): 239 nm. δ_H (200 MHz, CDCl$_3$): 6.87 (d, 1H at C$_6$), 6.81 (d, 1H at C$_5$), 6.67 (m, 1H at C$_3$, olefinic), 2.45 (s, OH), 1.89 (d, 3H, $C\underline{H}_3$), and 1.5 (s, 3H, $C\underline{H}_3$). δ_c (50 MHz, CDCl$_3$): 16.20 (methyl carbon), 27.52 (olefinic methyl carbon), 68.11 (carbon at OH), 152.67, 148.32, 134.28, 127.61 (four olefinic carbon), and 186.83 (keto carbon). Elemental analysis: Found C, 69.65%; H, 7.96%; requires C, 69.56%; H, 7.24%, for $C_8H_{10}O_2$ along with 6,9-dihydroxy-2,6,9,11-tetramethyltricyclo[6.2.2.0^{2,7}]dodeca-3,11-diene-5,10-dione **10** as a white solid (32%), mp 225–228°C. ν_{max}: 3425, 1720, 1681, and 1643 cm^{-1}. UV (λ_{max}): 230 nm. δ_H (200 MHz, CDCl$_3$): 6.21 (d, 1H at C$_3$), 6.0 (d, 1H at C$_4$), 5.5 (d, 1H at C$_{12}$, olefinic), 3.8 (s, $O\underline{H}$), 3.2 (s, 1H), 2.85 (d, 1H, bridgehead at C$_1$), 2.2 (s, $O\underline{H}$), 1.8 (s, 3H, olefinic $C\underline{H}_3$), 1.6 (s, 3H, $C\underline{H}_3$), 1.4 (s, 3H, $C\underline{H}_3$), 1.39 (s, 3H, $C\underline{H}_3$). Elemental analysis: Found C, 69.53%; H, 8.87%; requires C, 69.56%; H, 7.30% for $C_{16}H_{20}O_4$.

Oxidation of salicyl alcohol **11** furnished 1-(acetoxymethyl)-6-oxocyclohexa-2,4-dienyl acetate **12**, as a pale yellow liquid (53%), bp 237°C (dec.), UV (λ_{max}): 300 nm, ν_{max}: 1740, 1625, 1570, 1491, 1369, 1226 and 753 cm^{-1}, δ_H (200 MH$_z$, CDCl$_3$): 7.51 (dd, $J_1 = 6$ Hz $J_2 = 2$ Hz, 1H at C$_2$), 7.41 (dd, $J_1 = 8$ Hz, $J_2 = 6$ Hz, 1H at C$_3$), 7.35 (dd, 1H at C$_4$), 7.12 (d, 1H at C$_5$), 5.12 (s, 2H, methylene proton), 2.3 (s, 3H, $COC\underline{H}_3$), 2.1 (s, 3H, $COC\underline{H}_3$). δ_c (50 MHz, CDCl$_3$): 20.95 (sp^3 carbon), 61.90 (–CH$_2$– carbon), 122.98 (tetra-substituted carbon), 126.36, 128.45, 129.82, and 130.62 (four olefinic carbon), 170.69, 169.38 (two acetate carbonyls), 150.16 (keto carbon). MS m/z: M-43 (M–CH$_3$CO$^+$) and M-60 (M–CH$_3$COOH). Elemental analysis: Found C, 57.99%; H, 5.51%; requires C, 58.92%; H, 5.35% for $C_{11}H_{12}O_5$.

Oxidative acetylation of vanillin **13** gave 3-formyl-1-methoxy-6-oxocyclohexa-2,4-dienyl acetate **14** as a white crystalline solid (59%), mp 85°C, ν_{max}: 3018, 1757, 1690, 1678, 1647, 1155 cm^{-1}, UV (λ_{max}): 320 nm. δ_H (300 MHz, CDCl$_3$): 9.91 (s, 1H $C\underline{H}O$), 7.48 (s, 1H at C$_2$), 7.44 (d, $J = 6$ Hz, 1H at C$_4$), 7.21 (d, $J = 6$ Hz, 1H at C$_5$), 3.88 (s, 3H, $-OC\underline{H}_3$), 2.32 (sharp s, 3H, $-COC\underline{H}_3$). δ_c (50 MHz, CDCl$_3$): 20.36 ($OCO\underline{C}H_3$), 55.87 ($O\underline{C}H_3$), 110.57 (tetra subst., $-O\text{-}\underline{C}-O-$ type), 135, 144, 151, 168 (four olefinic C), 190.8, 191.2, 206.5 (three carbonyl C), MS m/z: 210 (M^+), 196, 168, 154, 104, 97, 89, 80. Elemental analysis: Found C, 57.21%; H, 4.68%, requires C; 57.14%; H, 4.76% for $C_{10}H_{10}O_5$.

Oxidation of 4-methyl-7-hydroxy coumarin **15** gave 4-methyl-2,7-dioxochroman-6-yl acetate **16** as a white crystalline solid (52%), mp 171°C, ν_{max}: 3053, 2968, 1765, 1726, 1713 cm^{-1}, UV (λ_{max}): 280 nm, δ_H (300 MHz, $CDCl_3$): 7.59 (d, 1H at C_5), 7.10 (s, 1H at C_8), 6.25 (s, 1H, olefinic H at C_3), 2.42 (sharp s, 3H, $-COC\underline{H}_3$), 2.33 (sharp s, 3H, olefinic $-C\underline{H}_3$), 1.72 (broad s, 1H at C_6), δ_c (50 MHz, $CDCl_3$): 20.9 ($-OCO\underline{C}H_3$), 63.6 (olefinic -$\underline{C}H_3$), 96.4 (C_6), 110.4, 114.4, 118.0, 125.4, 132.2, 140.3 [six olefinic C (sp^2 type)], 154.1, 160.5, 168.8 (three carbonyl C), MS m/z: 234 (M^+), 217, 207, 192, 175, 165, 100, 77. Elemental analysis: Found C, 60.98%; H, 4.19%; requires C, 61.53%; H, 4.27% for $C_{12}H_{10}O_5$.

Similarly, oxidation of 4-hydroxy-4′-chlorobenzophenone **17** furnished 3-(4-chlorobenzoyl)-6-oxocyclohexa-2,4-dienyl acetate **18** as a white crystalline solid (60%), mp 134°C, ν_{max}: 3051, 1757, 1694, 1683, 759 cm^{-1}, UV (λ_{max}): 300 nm, δ_H (300 MHz, $CDCl_3$): 7.79 (d, $J = 8$ Hz, 2H, aromatic ring p-substituted), 7.82 (d, $J = 8$ Hz, 2H, aromatic ring p-substituted), 7.45 (d, $J = 11$ Hz, 2H at C_4 and C_2), 7.49 (merged with signal of C_2-olefinic proton), 7.24 (d, $J = 12$ Hz, 1H at C_5), 2.35 (sharp s, 3H, $-COC\underline{H}_3$), 1.63 (sharp s, 1H at C_6). δ_c (50 MHz, $CDCl_3$): 21.1 ($OCOCH_3$), 65.1(C_6), 101.9, 121.4, 121.6, 121.9 (four olefinic C), 128.9, 131.3, 131.8, 134.7, 135.8, 138.9 (six aromatic C), 154.1, 168.9, 194.3 (three carbonyl C), MS m/z: $M^+ = 292.6$, $M+2 = 294.6$ (of 1/3 intensity of M^+), M-140 (loss of $C_6H_4ClCO^+$), and M-60 ($M-CH_3COOH$). Elemental analysis: Found C, 61.88%; H, 3.83%; requires C, 61.96%; H, 3.78% for $C_{15}H_{11}O_4Cl$.

Oxidation of 4-hydroxy butyranilide **19** gave 3-butyramido-6-oxocyclohexa-2,4-dienyl acetate **20** as a white crystalline solid (52%), mp 102°C, ν_{max}: 3310, 2945, 1763, 1661, 1532, 1366, 1221, 904, 835 cm^{-1}, UV (λ_{max}): 300 nm, δ_H (300 MHz, $CDCl_3$): 7.55 (d, 1H at C_2), 7.30 (s, 1H, $N\underline{H}CO$), 7.15 (d, 1H at C_4), 7.00 (d, 1H at C_5), 2.35 (t, merged with $-OCOCH_3$ signal, 2H, $NHCOC\underline{H}_2-$), 2.30 (s, 3H, $-OCOCH_3$), 1.75 (m, 2H, $-C\underline{H}_2-CH_3$), 1.60 (d, 1H at tetra-substituted carbon), 1.00 (t, 3H, $-C\underline{H}_3$). δ_c (50 MHz, $CDCl_3$): 13.3, 18.4, 21.2, 39.3 (methyl and methylene C), 97.4 (tetra-substituted C), 121.1, 122.0, 135.8, 146.6 (four olefinic C), MS m/z: 237 (M^+), 220, 178. Elemental analysis: Found C, 50.69%; H, 6.28%; N, 6.10%; requires C, 50.53%; H, 6.33%; N, 5.90% for $C_{12}H_{15}NO_4$.

CONCLUSION

We have demonstrated a new, simple, one-pot method for the preparation of acetoxy-2,4-cyclohexadienones. A novel 1-(acetoxymethyl)-6-oxocyclohexa-2,4-dienyl acetate **12** was also obtained. Application of this method for the synthesis of various carbocyclic systems is underway.

ACKNOWLEDGMENTS

The authors thank V. B. Valodkar and S. P. Sahoo for their help.

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Synthetic Communications®, 36: 673–678, 2006

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910500408928

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Oxidative Acetylation of Tetramethyl Bisphenol-F

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Abstract: Oxidative acetylation of tetramethyl bisphenol-F (**2**) using two different reagents is described. The reaction of (**2**) with $NaIO_4$ in acetic anhydride furnished a novel triacetate (**3**) and its reaction with lead tetraacetate (LTA) in dry benzene resulted in the formation of a novel bis-cyclohexadienone (**4**).

Keywords: Bis(3,5-dimethyl-4-hydroxyphenyl)methane, bis(3,5-dimethyl-3-acetoxy-4-oxocyclohexa-1,5-dienyl)methane, cyclohexa-2,4-dienones, oxidative acetylation

Cyclohexa-2,4-dienones are useful intermediates for preparing a variety of complex natural products.[1–4] We have recently reported a one-pot synthesis of acetoxy-2,4-cyclohexadienones by treatment of substituted phenols with sodium metaperiodate in acetic anhydride.[5] Our continued efforts in this area prompted us to synthesize tetramethyl bisphenol-F (**2**) and investigate its reaction with LTA[6] as well as with sodium metaperiodate in acetic anhydride.[5]

Received in India August 22, 2005

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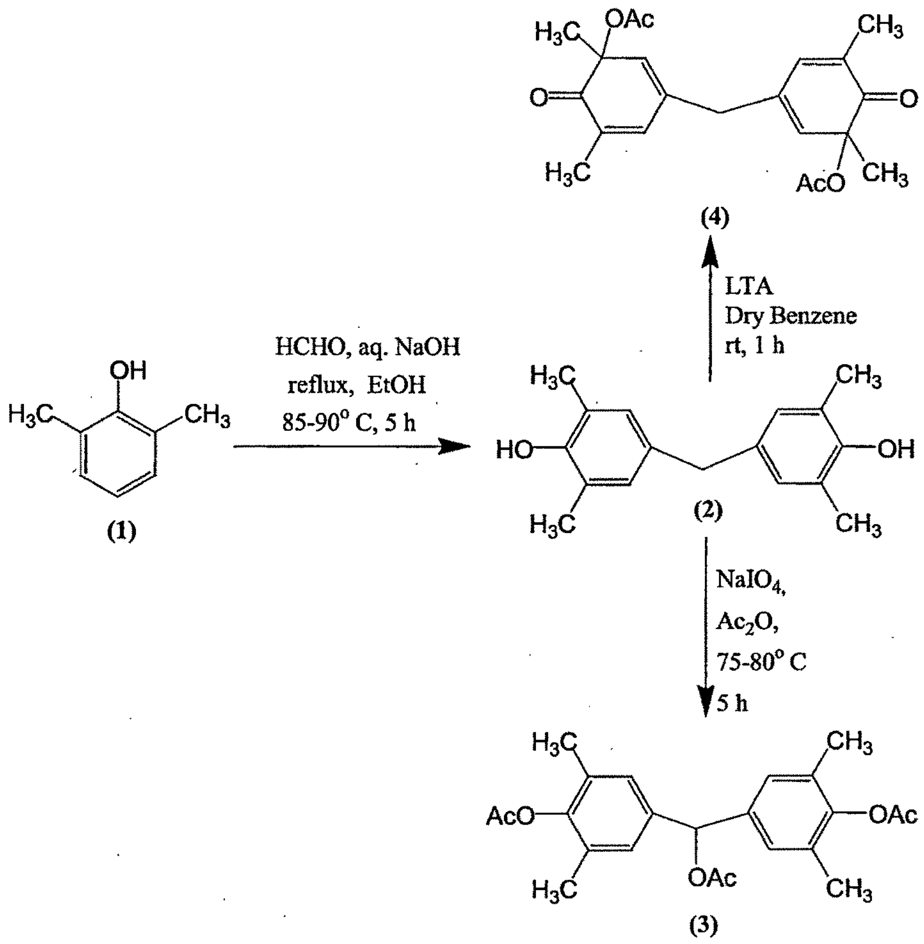
The bisphenol-F (**2**) was prepared from 2,6-dimethylphenol (**1**) by modifying the procedure of Kharasch et al. reported for the preparation of 3,3′,5,5′-tetra-*tert*-butyl-4,4′-dihydroxy diphenyl methane.[7] Thus, treatment of 2,6-dimethylphenol (**1**) with formaldehyde solution (37% w/v) in the presence of aqueous sodium hydroxide at 85°C for 5 h resulted in the formation of tetramethyl bisphenol-F (**2**) in 52% yield (Scheme 1) The structure of (**2**) was readily established through its spectral and analytical data. Its ^{1}H NMR spectra exhibited a singlet at δ_H 3.7 for two protons and a broad singlet at 2.2 for twelve protons on methyl groups along with a singlet at 4.5 for two exchangeable protons, indicating the presence of two phenolic OH groups. The ^{13}C NMR of (**2**) displayed diagnostic signals at δ_C 16.49 for four methyl carbons and a signal at 40.16 for the methylene carbon, among other characteristic signals for aromatic carbons. Its mass spectrum was also consistent with the structure that showed the molecular ion peak at 258 and a base peak at 135 (M-121).

Treatment of (**2**) with sodium metaperiodate in acetic anhydride at 75–80°C for 5 h resulted in the formation of a novel triacetate (**3**) whose



Scheme 1.

structure was fully established through its spectral and analytical data. It showed a characteristic band at 1749 cm^{-1} for the carbonyl absorption in its IR spectrum. It also displayed singlets for methyl groups at δ_H 2.14 (12H) along with 2.15 (3H) and 2.26 (6H). Its ^{13}C NMR spectrum showed signals at δ_C 170.1 and 168.9 for acetate carbonyls along with 21.6 and 20.7 for acetate methyls. The mass spectrum of (**3**) showed a molecular ion peak at 398 and a base peak at 339 (loss of acetic acid) in addition to other diagnostic signals. It was evident that acetylation of the two phenolic OH groups and at the benzylic position led to the formation of the triacetate (**3**).

The compound (**2**) was then treated with LTA in dry benzene for 1 h at room temperature (~27°C). Usual workup and chromatography over silica gel furnished the novel bis(3,5-dimethyl-3-acetoxy-4-oxocyclohexa-1,5-dienyl)methane (**4**) in 45% yield. The structure of the compound (**4**) was confirmed through its spectral and analytical characteristics. The bis-cyclohexadienone (**4**) showed a characteristic band at 1669 cm^{-1} in its IR spectrum for cyclohexadienones.[8] Its ^{1}H NMR spectrum displayed signals at δ_H 1.37, 1.92, and 2.06 each for 6H along with singlets at 3.05 (2H) and 5.86 (2H) for methylene and olefinic protons respectively. The ^{13}C NMR spectrum of (**4**) was also consistent with the proposed structure and exhibited resonances at δ_C 15.90, 21.07, and 24.63 for methyl carbons and a signal at 40.51 for the methylene carbon in addition to other characteristic signals. Its mass spectrum showed a molecular ion peak at 372 and a base peak at 313 (M-59) indicating loss of acetate ion and was correctly analyzed for $C_{21}H_{24}O_6$. It was interesting to observe that both the aromatic rings participated in the oxidation leading to the novel bis-cyclohexadienone (**4**). It is also noteworthy that although the oxidative acetylation of tetramethyl bisphenol-F could lead in principle to the formation of several addition products through inter- and intramolecular modes of cycloaddition, the reaction only furnished a single product (**4**). To study its possible intra- as well as intermolecular cycloaddition reactions, the bis-dienone (**4**) was also heated under reflux in o-xylene for 5 h with stirring. We observed that the bis-dienone (**4**) is stable under the reaction conditions and remained unchanged.[9] It is also worthwhile to mention here that the tetramethyl bisphenol-F (**2**) was found to be stable toward oxidation with $NaIO_4$ in water even at 80°C and did not yield any cyclohexadienone.[9,10]

Further investigation on the reactivities of the novel acetates (**3**) and (**4**) is currently under way.

EXPERIMENTAL

IR spectra were recorded on a Perkin–Elmer PC-16 FTIR spectrophotometer. NMR spectra were recorded on either a Bruker-200 FT-NMR or Bruker-300 FT-NMR spectrophotometer. Mass spectra were obtained on a Shimadzu QP-5050A mass spectrophotometer with quadrupole detector. Microanalyses were performed on a Perkin–Elmer 2400 CHN/S Analyzer instrument. Column chromatography was performed using Acme's silica gel (60–120 mesh size) and spots on TLC were visualized in iodine vapor.

Tetramethyl Bisphenol-F [Bis(3,5-dimethyl-4-hydroxyphenyl)methane] (2)

An aqueous solution of sodium hydroxide (22 mL, 23% w/v, 0.126 mol) was added to a stirred mixture of 2,6-dimethyl phenol (**1**) (10.0 gm, 0.082 mol) in ethyl alcohol (30 mL) and formaldehyde (15 mL, 37% w/v, 0.185 mol) over a period of 15 min. The reaction mixture was heated at 85–90°C for 5 h under continuous stirring. The reaction mixture was then allowed to cool down to room temperature and was diluted ten times its volume with water and stirred for 15 min. The solid thus obtained was filtered and washed thoroughly with water and dried at 85–90°C under vacuum. The solid mass thus obtained was dissolved in ethyl acetate (100 mL), and the solution was dried over anhydrous sodium sulphate. Column chromatography of the residue over silica gel and elution (light petroleum/ethyl acetate, 95 : 5) furnished (**2**) as a white crystalline solid (52%). Mp 180–182°C, ν_{max} (neat) 3463, 3007, 2915, 2847, 1629, 1608, 1484, 1304, 1227, 1186, 1145, 1013, 882, 774, 730, and 5765 cm^{-1}. δ_H (200 MHZ, $CDCl_3$); 2.2 (s, 12H, methyl), 3.7 (s, 2H, methylenes), 4.5 (s, 2H, exchangeable, phenolic OH), 6.8 (s, 4H, aromatic H). δ_C (50 MHZ, $CDCl_3$): 16.49, 40.16, 124.02, 128.37, 132.62, 151.02. M/z: 256 (M^+), 135 (M-121) (base peak: loss of 2,6-dimethyl phenol). Elemental analysis found: C, 79.80%; H, 7.94%; requires C, 79.69%; H, 7.81% for $C_{17}H_{20}O_2$.

Bis(4-acetoxy-3,5-dimethylphenyl)methyl Acetate (3)

Sodium metaperiodate (1.5 gm, 0.007 mol, excess) was added to a stirred solution of bis(3,5-dimethyl-4-hydroxyphenyl)methane (**2**) (0.50 gm, 0.00195 mol) in acetic anhydride (15 mL) in portions over a period of 1 h. Stirring was continued for 5 h while maintaining the reaction temperature between 75 and 80°C. The reaction mixture was allowed to cool down to room temperature and then poured into a vigorously stirred saturated solution of sodium bicarbonate (125 mL) to neutralize excess acid. The aqueous layer was then extracted with ethyl acetate (3 x 25 mL) and combined organic extracts were successively washed with saturated sodium bicarbonate solution (20 mL), water (20 mL), and brine solution (20 mL). Drying over anhydrous sodium sulphate followed by removal of solvent under reduced pressure furnished a dark brown residue, which was chromatographed using a mixture of light petroleum and ethyl acetate (95 : 5) to furnish the acetylated product (**3**) as a white crystalline solid (0.414 gm, 51.28%). Mp 139°C, (λ_{max}): 250 nm; ν_{max} (neat) 3469, 3016, 2929, 1749, 1607, 1370, 1144 cm^{-1}. δ_H (300 MHZ,

$CDCl_3$); 2.14 (sharp s, 12H, $-C\underline{H}_3$ on aromatic rings), 2.15 (s, 3H, $-OCOC\underline{H}_3$ on the central tetra-substituted carbon), 2.26 (sharp s, 6H, acetate methyl protons), 6.75 (s, 1H, methane proton), 7.02 (s, 4H, aromatic Hs). δ_C (75 MHZ, $CDCl_3$): 170.1, 168.9, 148.0, 137.6, 130.5, 127.5, 76.1, 21.6, 20.7, 16.6. M/z: 398 (M^+), 339 (base peak, M-60, loss of acetic acid), 297 (loss of CH_3CO), 255 (loss of another CH_3CO). Elemental analysis found: C, 68.93%; H, 6.43%; requires C, 69.34%; H, 6.53% for $C_{23}H_{26}O_6$.

Bis(3,5-dimethyl-3-acetoxy-4-oxocyclohexa-1,5-dienyl)methane (4)

LTA (2.66 gm, 0.006 mol) was added to a solution of bis(3,5-dimethyl-4-hydroxyphenyl)methane (**2**) (0.5 gm, 0.002 mol) in dry benzene (30 mL) in portions with constant stirring. The reaction mixture was stirred for 1 h at room temperature (~27°C) after which it was diluted with ethyl acetate (150 mL) and stirred further for 15 min. Removal of the residue by filtration and concentration of the filtrate furnished a pale yellow liquid, which was chromatographed over a column of silica gel. Elution of the column (light petroleum/ethyl acetate 95 : 5) gave (**4**) as a light yellow crystalline solid (45%). Mp 183–184°C, ν_{max} (neat): 2994, 2919, 1734, 1669, 1437, 1371, 1253, 1225, 1060, 859, and 762 cm^{-1}. δ_H (200 MHZ, $CDCl_3$); 1.37 (s, 6H, methyl protons), 1.92 (s, 6H, olefinic methyl protons), 2.06 (s, 6H, acetate methyl protons), 3.05 (s, 2H, methylene protons), 5.86 (s, 2H, olefinic H), 6.59 (s, 2H, olefinic H). δ_C (50 MHZ, $CDCl_3$): 15.90, 21.07, 24.63, 40.51, 78.93, 131.26, 134.61, 137.03, 139.85, 169.91, 199.31. M/z: 372.0 (M^+), 313 (M-59) (loss of acetate ion, base peak), (M-119) (loss of two acetate ions). Elemental analysis found: C, 67.71%; H, 6.44%; requires C, 67.74%; H, 6.45% for $C_{21}H_{24}O_6$.

ACKNOWLEDGMENTS

We thank Madhusudanan (CDRI), Lucknow, India, for his help in providing spectral analysis.

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