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A Simple One-Step Akylation of Orcinol Derivatives

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Boron trifluoride etherate on alumina catalyses the condensation of orcinol and monomethyl orcinol with cyclic allylic alcohols: in contrast to parallel reactions with boron trifluoride etherate in solution the products obtained undergo intramolecular cyclisations.

Introduction

The alkylation of phenols with monoterpenoid in Lewis acid has received some attention in the recent years. These investigations have been promoted by proposals of mechanism for the synthetic cannabinoids[1a,b], and they have been aimed to perform the alkylation in very mild media[1]. Thus most of the results concern isoprenylphenols.

In this paper we report a convenient single step synthesis of 2′-(1-methyl-cyclohexen-3-yl)-orcinol (**3**) in a yield of 21% from 1-methyl-2-cyclohexen-1-ol (**1**) and orcinol (**2**) in the presence of BF_3-etherate on alumina[1a].

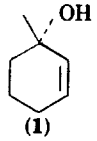
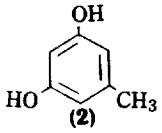
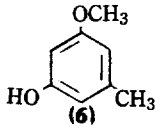
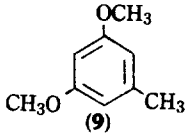
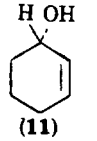
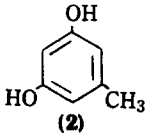
Two types of reactions were investigated as outlined in Table 1; **a)** condensation of 1-methyl-2-cyclohexzn-1-ol (**1**) with orcinol (**2**) and their mono and diethers (**6**) and (**9**) and **b)** condensation of 2-cyclohexen-1-ol (**11**) with orcinol (**2**).

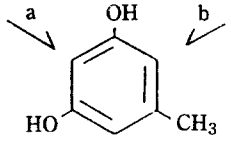
In these reactions described below three products were obtained: **a)** substitution ortho to both the hydroxy groups: **b)** substitution ortho to one of the hydroxy groups and to the methyl group: and **c)** double condensation (usually in a low yield). The compounds of type **b** are considerably more polar than those of type **a** as one of the acidic phenols is not hindered by an adjacent bulky alicyclic ring. In the compound of type **a** the two aromatic protons are equivalent in the NMR spectrum; in **b** they are not. These two criteria were used to differentiate between the two types of compound obtained. The double condensation products of type **c** are most probably substituted between the phenolic groups and between a phenolic group and the methyl group (Scheme 1).

Experimental

UV spectra were recorded on Varian techtron 635 UV-

Table 1. Condensation of Cyclic Allylic Alcohols with Orcinols by Catalysis with BF_3-etherate on Alumina

Cyclic allylic alcohol	Resorcinol	Product(s)	Yield	Ref.
 (1)	 (2)	(3)	21%	4
		(4)	33%	
		(5)	9%	
as above	 (6)	(7)	9%	4
		(8)	46%	
as above	 (9)	(10)	43%	4
 (11)	 (2)	(12)	30%	4,5
		(13)	46%	
		(14)	5%	



Substitution of type **a** and **b**

Scheme 1

VIS spectrophotometer. IR spectra were recorded on Perkin -Elmer 457 grating infrared spectrophotometer. H-NMR spectra were obtained on a Bruker WH-60, WH-200, and WH-300 pulsed FT spectrometer. Chemical shifts are given in parts per million downfield from Me_4Si internal standard. Mass spectra were recorded on Varian Mat, CH-5 mass spectrometer and LKB 2091-gas chromatograph-mass spectrometer. Chromatography; Analytical TLC was performed by using commercially available silica plates. Polygram sil N-HR/UV_{254} and the plates were visualized with fast blue phenol reagent or by charring with a solution of MeOH: H_2SO_4 (1:1). Medium pressure luquid chromatography was performed by ALTEX glass column, 1 meter long, internal diameter 9mm using FMI pump and silica gel 60 (230-400 mesh) purchased from Merck, collective fraction with LKB 2070 or LKB 7000 fraction collectors of 2-10 m*l*/min.

"Methylation in the usual way" means that compound was added to dimethylformamide, potassium carbonate and methyliodide; the mixture is left overnight, poured onto distilled water, extracted with ether, washed with saturated brine solution, then dried over anhydrous magnesium sulfate, followed by filtration and evaporation to dryness in vacuo.

Solvents and anhydrous reagents for the synthesis(e,g), dichloromethane, dimethylformamide, ether, ethylacetate, petroleum ether, were purified and dried according to established procedures by distillation under argon or nitrogen from an appropriate drying agent[2]. The solvents for other chromatography and general use were purified by distillation and filtration according to standard procedure. The deuterated NMR solvents were used without further purification. The spectroscopic solvents were purchased from Aldrich, or Merck.

Methyllithium was purchased from Aldrich. Orcinol was purchased from Aldrich or BDH and used without further purification or was synthesized by general procedures. BF_3 -etherate was purchased from Aldrich. Basic aluminum oxide (Woelm, grade I) was obtained from Merck. All reactions were run under an inert atmosphere of argon or nitrogen (oxygen free) and reaction requiring anhydrous conditions were performed in flame-dried apparatus.

The general procedure is as follows: BF_3-etherate (0.2 m*l*) was added under nitrogen to a stirred suspension of basic aluminum oxide (Woelm, grade I) (2 g) in dichloromethane (10 m*l*). Cyclic allylic alcohols (1 mmol) and orcinols (1 mmol) in dichloromethane (3 m*l*) were added to the solution via syringe and the mixture was stirred for 5 min at room temperature. The reaction was quenched with 10% aqueous solution of sodium bicarbonate (10 m*l*). Ether (50 m*l*) and an additional portion of sodium bicarbonate solution (50 m*l*) were added. The organic layer was washed with brine, dried and evaporated to dryness. The oil obtained was separated by medium pressure liquid chromatography (MPLC) (230-400 mesh ASTM, silica gel 60 for column chromatography, elution with ethylacetate to petroleum ether 2.5:97.5).

Preparation of 1-methyl-2-cyclohexen-1-ol (1)[3]. To an excess of CH_3Li in ether (100 m*l*) at -78°C was added via syringe 2-cyclohexen-1-one (4 g, 41.6 mmol), stirred till at room temperature. The reaction mixture was quenched with saturated sodium bicarbonate solution, washed with brine, dried and evaporated to dryness. The oil obtained was separated by medium pressure LC (elution with ethylacetate to petroleum ether 5:95) to give 3.67 g (79%) of 1-methyl 2-cyclohexen-1-ol (1) NMR ($CDCl_3$) δ 1.26(3H, S, CH_3), 5.62 (2H, brs, olefinic); IR(film), 3400, 3040, 1440, 1375, 1332 cm^{-1}.

Preparation of 2-cyclohexen-1-ol (11)[5]. To a suspension of excess lithium aluminum hydride in 100 m*l* ether was added a solution of 2-cyclohexen-1-one (5 g, 52 mmol). The mixture was stirred for 30 min at room temperature. The excess reagent was destroyed with a saturated solution of sodium sulphate. The reaction mixture was extracted three times with ether, washed with brine, dried and evaporated. The obtained oil was separated by medium pressure LC to give 1.72 g (34%) of 2-cyclohexen-1-ol, an oil NMR ($CDCl_3$) δ 4.11 (1H, br, OH), 5.72(2H, brs, olefinic); IR(film), 3350, 3035, 1430, 1385cm^{-1}.

Preparation of compounds (3), (4), and (5). Under the conditions of general procedure three compounds were obtained. The first compound eluted was 2′,4′-bis-(1-methylcyclohexen-3-yl)-orcinol (**5**) (55 mg, 9%), an oil, UVmax (EtOH), 276 sh (ε 1790), 282 nm (1840); NMR ($CDCl_3$) δ 1.78 (6H, brs, CH_3), 2.22 (3H, s, CH_3), 3.86 (2H, br, C-3H), 5.63 (2H, brs, C-2H), 6.26 (1H, brs, arom H); MS (20°C), m/e 312 (M^+, 100), 297(26), 284(21), 269(64), 244(51); IR (film), 3450, 1625, 1585, 1450cm^{-1}. Methylation with methyliodide and potassium carbonate in DMF led to 2′,4′-bis-(1-methylcyclohexen-3-yl)-1′,3′-dimethylorcinol (**5a**), an oil, NMR($CDCl_3$) δ 1.85 (6H, brs, CH_3), 2.30 (3H, s, CH_3), 3.63 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 5.33 (2H, brs, C-2H), 6.45 (1H, s, arom H); MS (20°), m/e 340 (M^+ 100), 326(56), 313(18), 310(13), 298(16), 273(18), 259(28), 244(24); IR(film), 2910, 1594, 1567, 1440cm^{-1}. The second compound eluted was 2′-(1-methylcyclohexen-3-yl)-orcinol (**3**) (90 mg, 21%), an oil, UVmax (EtOH), 275 sh (ε 1550), 280(1720), 290 sh nm (1020); NMR ($CDCl_3$) δ 1.75(3H, brs, CH_3), 2.16 (3H, s, CH_3), 3.77 (1H, br, C-3H), 5.59 (1H, brs, C-2H), 6.17 (2H, brs, arom H); MS (20°), m/e 218 (M^+, 90), 203(23), 190(19), 175(100), 150(86), 137(42); IR(film), 3430, 1630, 1590, 1450 cm^{-1}. The third compound eluted was 4′-(1-methylcyclohexen-3-yl)-orcinol (**4**) (142 mg, 33%) as the major product, an oil, UVmax (EtOH), 281 nm (ε 2700); NMR ($CDCl_3$) δ 1.78 (3H, brs, CH_3), 2.21 (3H, s, CH_3), 3.54 (1H, br, C-3H), 5.61 (1H, brs, C-2H), 6.21 (2H, brs, arom H); MS (20°), m/e 218 (M^+, 81), 203(16), 190(16), 175(100), 150(58), 138(22); IR(film), 3430, 1620, 1598, 1465cm^{-1}. Methylation with methyliodide and potassium carbonate in DMF led to 4′-(1-methylcyclohexen-3-yl)-1′3′-dimethyl orcinol (**4a**), an oil, NMR ($CDCl_3$) δ 1.92 (3H, brs, CH_3), 2.28 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 5.28 (1H, brs, C-2H), 6.29 (2H, brs, arom H); MS (20°), m/e 246 (M^+, 100), 231(38), 218(50), 203(75), 188(21); IR(film), 2920, 1585, 1450, 1416 cm^{-1}.

Preparation of compounds (7) and (8). Under the conditions of general procedures two compounds were obtained. The first compound eluted was 2′-(1-methylcyclohexen-3-yl) -3′-methylorcinol (**7**) (56 mg, 9%), an oil, UVmax (EtOH), 275 nm (ε 1310); NMR ($CDCl_3$) δ 1.78 (3H, brs, CH_3), 2.27 (3H, s, CH_3), 3.77 (3H, s, OCH_3), 5.60 (1H, brs, C-2H), 6.23 (1H, s, arom H), 6.29 (1H, brs, arom H); MS (20°), m/e 232 (M^+, 96), 217(28), 204(22), 189(100), 164(71); IR(film), 3455, 1615, 1590, 1460cm^{-1}. The second compound eluted was

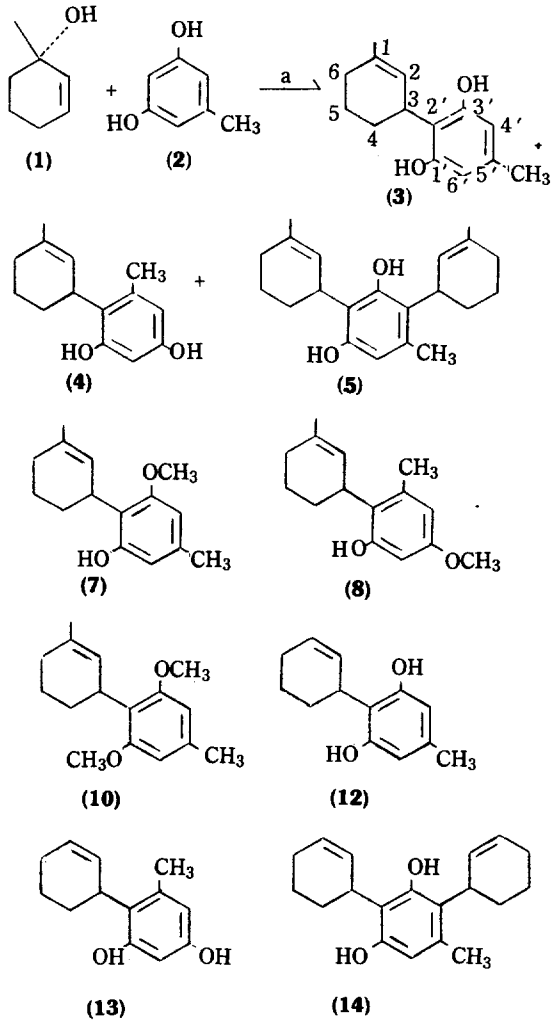
6′-(1-methylcyclohexen-3-yl)-3′-methylorcinol (**8**) (215 mg, 46%), an oil, UVmax (EtOH), 227 sh (ε 15970), 277(4090), 282 sh nm (3960); NMR ($CDCl_3$) δ 1.78 (3H, brs, CH_3), 2.25 (3H, s, CH_3), 3.48 (1H, br, C-3H), 3.72 (3H, s, OCH_3), 5.61 (1H, brs, C-2H), 6.18 (1H, brs, arom H), 6.27 (1H, brs, arom H); MS (20°), m/e 232 (M^+, 64), 217(18), 204(20), 189(100), 164(50); IR(film), 3450, 1620, 1586, 1500, 1455cm^{-1}. Methylation with methyliodide and potassium carbonate in DMF led to 6′-(1-methylcyclohexen-3-yl)-1′,3′-dimethyl-orcinol (**8a**), an oil, NMR ($CDCl_3$) δ 1.67 (3H, s, CH_3), 2.29 (3H, s, CH_3), 3.75 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 3.91 (1H, br, C-3H), 5.30 (1H, s, C-2H), 6.28 (1H, d, J = 1Hz, arom H), 6.32 (1H, d, J = 1Hz, arom H); MS (20°), m/e 246 (M^+, 100), 231(36), 218(43), 203(79), 187(19), 165(17); IR(film), 2992, 2923, 1600, 1585, 1484, 1460, 1450, 1413cm^{-1}.

Preparation of 2′-(1-methylcyclohexen-3-yl)-1′, 3′-dimethylorcinol (10). Under the conditions of general procedures compound (**10**) was obtained. (210 mg, 43%), an oil, UVmax (EtOH), 280 nm (ε 2610); NMR ($CDCl_3$) δ 1.68 (3H, brs, CH_3), 2.29 (3H, s, CH_3), 3.75 (6H, s, OCH_3), 5.30 (1H, brs, C-2H), 6.30 (2H, brs, arom H); MS (20°), m/e 246 (M^+, 100), 231(33), 218(44), 203(47); IR(film), 2930, 1588, 1456cm^{-1}.

Preparation of compounds (12), (13) and (14). Under the conditions of general procedures three compounds were obtained. The first compound eluted was 2′,4′-bis-(1-cyclohexen-3-yl)-orcinol (**14**) (13 mg, 5%), an oil, UVmax (EtOH), 281 nm (ε 2620); NMR ($CDCl_3$) δ 2.23 (3H, s, CH_3), 3.78 (2H, m, C-3H), 5.78 (2H, brs, C-1H), 6.06 (2H, brd, J = 5Hz, C-2H), 6.24 (1H, q. J = 2.6Hz, arom H); MS (20°), m/e 284 (M^+, 100), 269(17), 256(39), 241(50), 231(26), 204(36); I (film), 3470, 1620, 1582, 1450cm^{-1}. Methylation with methyliodide and potassium carbonate in DMF led to 2′,4′-bis-(1-cyclohexen-3-yl)-1′,3′-dimethylorcinol (**14a**), an oil, NMR ($CDCl_3$) δ 2.35 (3H, s, CH_3), 3.66 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 5.63 (2H, brs, C-1H), 5.69 (2H, brs, C-2H), 6.46 (1H, brs, arom H); MS (180°), m/e 314 (M^+, 100), 297(47), 284(28), 296(14), 244(16), 229(17), 216(14); IR (Nujol), 1595, 1450cm^{-1}. The second compound eluted was 2′-(1-cyclohexen-3-yl)-orcinol (**12**) (61 mg, 30%), an oil, UVmax (EtOH), 280 nm (ε 6410); NMR ($CDCl_3$) δ 2.21 (3H, brs, CH_3), 3.86 (1H, br, C-3H), 5.36 (2H, brs, OH), 5.90 (1H, brs, C-1H), 6.00 (1H, brd, J = 3Hz, C-2H), 6.22 (2H, brs, arom H); MS (20°), m/e 204 (M^+, 100), 189(19), 176(32), 161(95), 150(22), 137(25), 124(23); IR(film), 3435, 1596, 1468 cm^{-1}. The third compound eluted was 4′-(1-cyclohexen-3-yl)-orcinol (**13**) (93 mg, 46%), an oil, UVmax (EtOH), 281 nm (ε 2050) NMR ($CDCl_3$) δ 2.24 (3H, s, CH_3), 3.59 (1H, br, C-3H), 5.97 (1H, brs, C-1H), 6.10 (1H, brs, C-2H), 6.23 (2H, brs, arom H); MS (20°), m/e 204 (M^+, 72), 189(12), 180(21), 176(40), 161(100); IR(film), 3448, 1615, 1590, 1460cm^{-1}. Methylation with methyliodide and potassium carbonate in DMF led to 4′-(1-cyclohexen-3-yl)-1′,3′-dimethyl-orcinol (**13a**), an oil, NMR ($CDCl_3$) δ 2.31 (3H, s, CH_3), 3.73 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 5.63 (2H, brs, C-1H and C-2H), 6.29 (2H, brs, arom H); MS (20°), m/e 232 (M^+, 100), 217 (29), 204(57), 189(50); IR(film), 2920, 1584, 1450cm^{-1}.

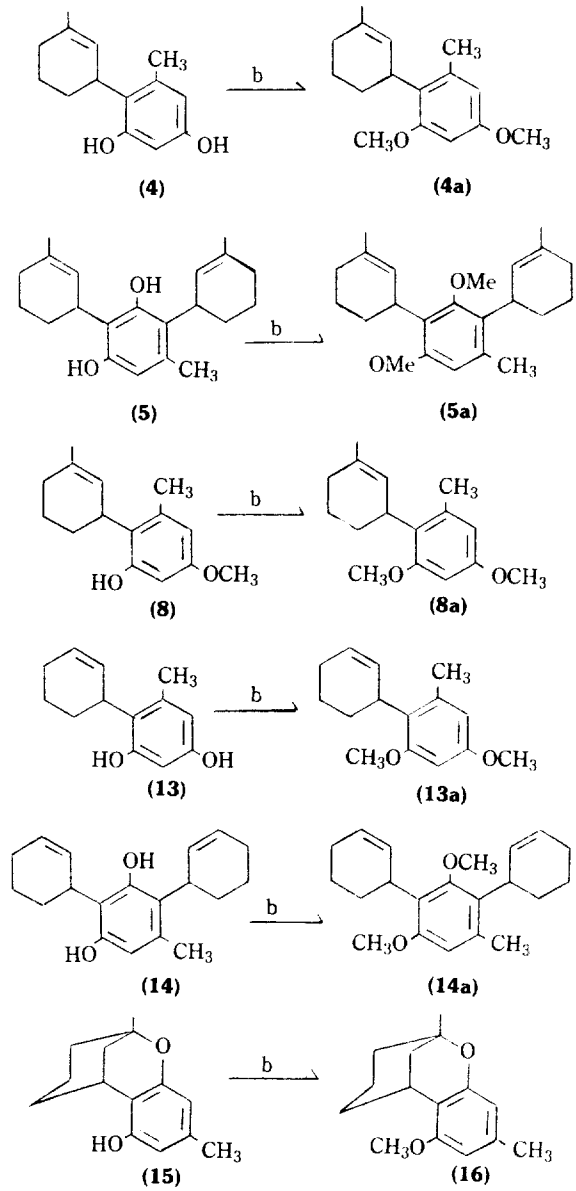
Preparation of 3,4,5,6-tetrahydro-7-hydroxy-2,9-dimethyl-2.6-methano-2H-1-benzoxocin (15). Under the conditions of general procedures in the absence of alumina compound (**15**) was obtained. (80 mg, 37%), an oil, UVmax (EtOH), 277 sh (ε 1410), 281 nm (1440); NMR ($CDCl_3$) δ 1.33 (3H, s, CH_3), 2.20 (3H, s, CH_3), 3.31 (1H, brs, C-6H), 4.79 (1H, br, OH), 6.12 (1H, brs, arom H), 6.25 (1H, brs, arom H); MS (20°), m/e 218 (M^+, 77), 203(13), 175(57), 150(100), 138(21); IR(film), 3430, 1625, 1590, 1455cm^{-1}.

Preparation of compounds (16) and (17). Under the conditions of general procedure in the absence of alumina two tricyclic compounds were obtained. The first compound eluted was 3,4,5,6-tetrahydro-7-methoxy-2,9-dimethyl-2,6-methano-2H-1-benzoxocin (**16**) (139 mg, 60%) as the major product, an oil, UVmax (EtOH), 272 (ε 1520), 280 nm (1410) NMR ($CDCl_3$) δ 1.33 (3H, s, CH_3), 2.27 (3H, s, CH_3), 3.35 (1H, brs, arom H), 3.78 (3H, s, OCH_3), 6.21 (1H, brs, arom H), 6.29 (1H, brs, arom H); MS(20%), m/e 232 (M^+, 100), 217(17), 204(15), 189(62), 164(94), 149(32); IR(film), 2950, 1623, 1593, 1456, 1422cm^{-1}. The second compound eluted was an isomer (**17**) of compound (**16**) were obtained. (78 mg, 34%), an oil, UVmax (EtOH), 225 sh (ε 13550), 276(4290), 286 nm (4080); NMR ($CDCl_3$) δ 1.33 (3H, s, CH_3), 2.20 (3H, s, CH_3), 3.18 (1H, br, C-6H), 3.72 (3H, s, OCH_3), 6.24 (2H, brs, arom H); MS (20°), m/e 232 (M^+, 88), 217(17), 204(13), 189(84), 164(100); IR(film), 2942, 1615, 1595, 1492, 1455, 1430cm^{-1}.



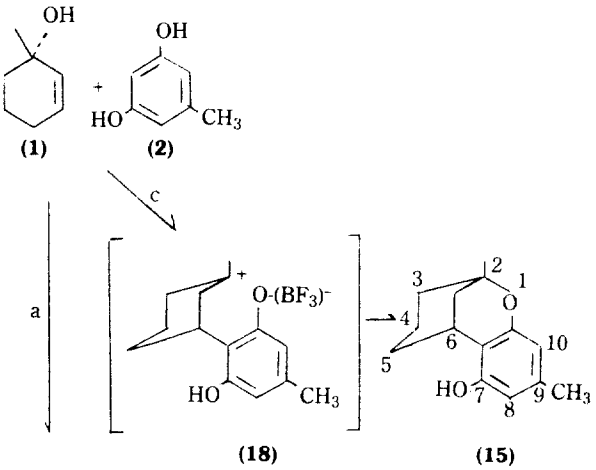
a) BF_3-etherate, Alumina, CH_2Cl_2

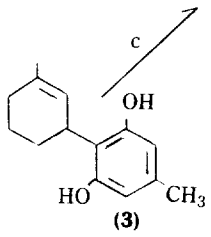
Scheme 2



b) CH_3I, K_2CO_3, DMF

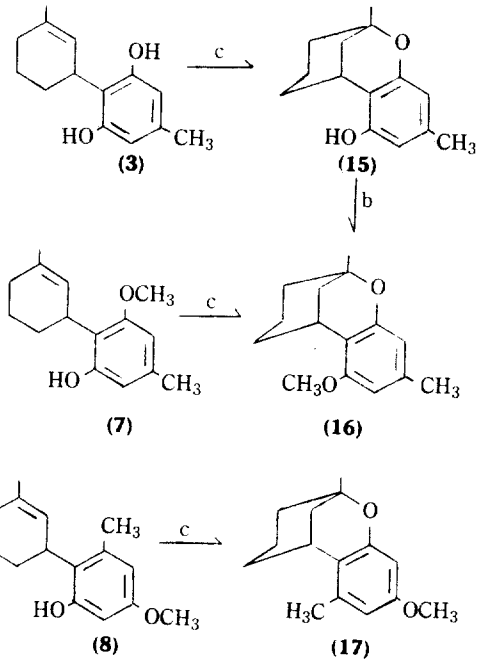
Scheme 3





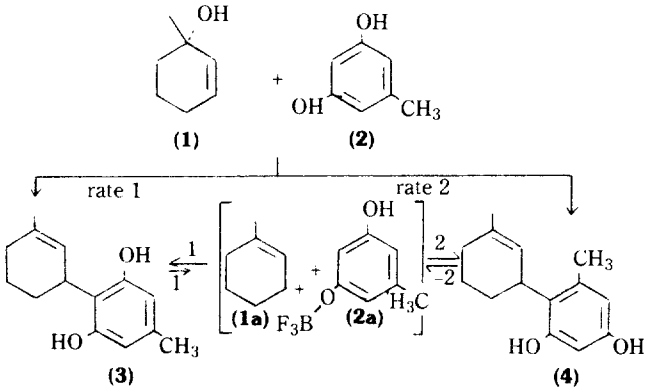
a) BF_3-etherate, Alumina, CH_2Cl_2
c) BF_3-etherate, CH_2Cl_2

Scheme 4



b) CH_3I, K_2CO_3, DMF
c) BF_3-etherate

Scheme 5



Scheme 6

Results and Discussion

We think that the postulated carbonium ion (**1a**) or congeners can be produced by Lewis acid treatment of any cyclic allylic alcohol (Scheme 6). The compound (**3**) obtained in this reaction may be converted to compound (**4**) with BF_3-etherate by a retro-Friedel-Crafts reaction, followed by recombination[1b].

The products is readily separated by medium pressure liquid chromatography. The products formed may be primary alkylation products (noncyclised) and secondary products obtained by acid-induced cyclization. The linkage occurs always between carbon **3** of the cyclic allylic alcohol moiety and the position 2′ or 4′ of the orcinol. It is shown that alkylations of orcinols take place preferentially at the C-4′ position.

The condensation of 1-methylcyclohexen-1-ol with orcinol gave three compounds under the conditions of general procedures; 2′-(1-methylcyclohexen-3-yl)-orcinol (**3**) in 21% yield, an isomer (**4**) of compound (**3**) as the major product in 33% yield and the product of double condensation (**5**) in 9% yield.

In (**3**) the NMR spectrum indicates that the two aromatic protons (at $\delta = 6.17$) are magnetically equivalent. In (**4**) this spectrum shows two nonequivalent aromatic protons (at $\delta = 6.21$). Methylation (Scheme 3) on compound (**4**), (**4a**) was obtained. As expected, the aromatic methoxy groups (at $\delta = 3.72$ppm and $\delta = 3.76$ppm) in (**4a**) are not magnetically equivalent. In (**5**) the aromatic proton is centered at 6.26ppm and the area of this signal corresponds to one proton. Methylation (Scheme 3) on compound (**5**), (**5a**) was obtained. As shown, the aromatic methoxy groups (at $\delta = 3.63$ppm and $\delta = 3.71$ppm) in (**5a**) are not magnetically equivalent. In the three compounds the UV spectra show the absence of conjugation with the benzene ring, and as an olefinic methyl group seen in the NMR spectra the double bond is at the C-1 position. The methyl group on the aromatic ring is deshielded (see experimental section). These findings are compatible with structures (**3**), (**4**) and (**5**).

The BF_3-etherate on alumina catalysed condensation reaction takes place also with monomethyl orcinol.

The condensation of 1-methylcyclohexen-1-ol with 3-methylorcinol gave two compounds; 2′-(1-methylcyclohexen-3-yl)-3′-methylorcinol (**7**) as the minor product in 9% yield, an isomer (**8**) in 46% yield. Compound (**7**) is less polar than isomer (**8**), and the product of double condensation was not yielded.

The UV spectra of (**7**) and (**8**) indicate that the double bond is not conjugated with the aromatic ring. The NMR spectra show the presence of only one aromatic methoxy group and two methyl groups which are either on the aromatic or the vinylic. This observation places the double bond in the C-1 position. As indicated, the two aromatic protons are not equivalent; $\delta = 6.18$ppm and $\delta = 6.27$ppm for (**8**); $\delta = 6.23$ppm and $\delta = 6.29$ppm for (**7**). A further difference between the positional isomer (**8**) and 2′-(1-methylcyclohexen-3-yl)-3′-methylorcinol (**7**) is in the chemical shift of the aromatic methoxy and methyl groups; $\delta = 3.72$ppm and $\delta = 2.25$ppm for (**8**); $\delta = 3.77$ppm and $\delta = 2.27$ppm for (**7**). In order to establish the positional methylation of compound (**8**), the compound (**8a**) was synthesized. Methylation (Scheme 3) on compound (**8**), (**8a**) was obtained. As shown the aromatic methoxy groups (at $\delta = 3.77$ppm and $\delta = 3.73$ ppm) and the aromatic protons (at $\delta = 6.32$ppm and $\delta = 6.28$ppm) in (**8a**) are not magnetically equivalent. When the compound (**7**) was reacted with BF_3-etherate, intramolecular cyclisation took place. As expected, this tricyclic product (**16**) was obtained (Scheme 5). The structures of compounds (**8**) and (**7**) are deduced thus from their spectral data.

The structure of (**10**) was determined as follows; The UV spectrum shows the absence of conjugation. The NMR spectrum shows the presence of only one olefinic methyl group (at $\delta = 1.68$ppm); two aromatic methoxy groups, a broad singlet olefinic proton ($\delta = 5.30$ppm), and two magnetically equivalent aromatic protons ($\delta = 6.30$ppm). The equivalence of the aromatic protons indicates that the substitution is symmetrical.

A second group of condensations which we investigated were these of 2′-cyclohexen-1-ol (**11**) with orcinol.

When 2-cyclohexen-1-ol (**11**) was condensed with orcinol under the conditions of general procedures a mixture of three products was obtained which was separated by medium pressure liquid chromatography. The isomer (**13**) as the major product (46% yield) which was the most polar component, 2′-(1-cyclohexen-3-yl)-orcinol (**12**) in 30% yield, and the double condensation product (**14**) in 5% yield.

The UV spectra of the three compounds indicate the absence of conjugation. The NMR spectra show the presence of two olefinic protons and two aromatic protons (at $\delta = 6.22$ppm for (**12**); $\delta = 6.23$ppm for (**13**)), four olefinic protons in (**14**), only one aromatic methyl group (at $\delta = 2.21$ ppm for (**12**); $\delta = 3.59$ppm for (**13**); $\delta = 3.78$ppm for (**14**)). Methylation (Scheme 3) on compound (**13**), (**13a**) was obtained. As expected, the aromatic methoxy groups (at $\delta = 3.73$ ppm and $\delta = 3.76$ppm) in (**13a**) are not magnetically equivalent. Methylation (Scheme 3) on compound (**14**), (**14a**) was obtained. As Anticipated, the aromatic methoxy groups (at $\delta = 3.66$ppm and $\delta = 3.74$ppm) in (**14a**) are not magnetically equivalent. In (**13**) the aromatic methyl group apparently pushes the C-3 proton somewhat out of the plane, thus causing a dimunition of the deshielding effect[6].

In none of the above described reactions intramolecular cyclisations were not observed by the addition of one of the hydroxy groups to a suitably placed double bond. This is undoubtedly due to the "mildness" of the BF_3-etherate on alumina reagent which catalyses a Friedel-Crafts type reaction but apparently does not attack olefins (or attacks them at a low rate) to form a cationic center.

When the above described reactions are undertaken with BF_3-etherate the condensation reaction was followed by cyclisation (see Scheme 4 and Table 2)[7,8,9]. In the above reaction (Scheme 4) a benzoxocin ring is formed. BF_3-etherate in methylene chloride initiates the ring closure which probably proceeds by the mechanism indicated through the hypothetical intermediate cation (**18**). The cyclohexane ring is expected to exist predominantly in a chair conformation[10,11,12]

When the noncyclized condensation products (e.g. 7 or 8) were reacted with BF_3-etherate, intramolecular cyclisation took place by the addition of one of the hydroxy groups to a suitably placed double bond (Scheme 5)[1c,8,9].

When 1-methyl-2-cyclohexen-1-ol was condensed with orcinol derivatives under the conditions of general procedure in the absence of alumina, the expected products (**15, 16** and **17**) were obtained. The structures of (**15**), (**16**) and (**17**) were established on the basis of their molecular weight (mass spectra) and NMR spectra (see experimental section), and by cyclisation of the appropriate open compounds (**3,7,8**) (Scheme 5). Methylation (Scheme 5) groups (at $\delta = 3.78$ppm for 16) was shown.

Under the reaction conditions of procedure in the absence

Table 2. Condensation of 1-methyl-2-cyclohexen-1-ol with Orcinols by Catalysis with BF_3 Etherate

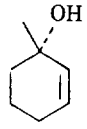
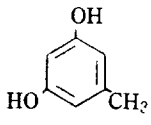
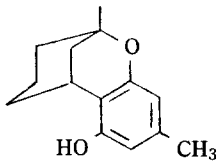
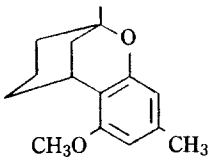
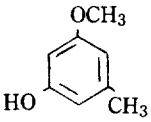
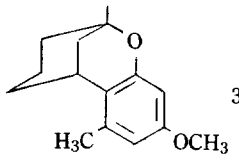
1-Methyl-2-cyclohexen-1-ol	Resorcinol	Product(s)	Yield	Ref.
 (1)	 (2)	 (15)	37%	4,6
		 (16)	60%	4,6
	 (6)	 (17)	34%	

Table 3. NMR spectra of 3,4,5,6-tetrahydro-7-methoxy-2,9-dimethyl-2,6-methano-2H-1-benzoxocin and Its Isomer[a]

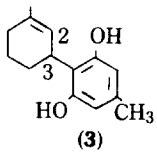
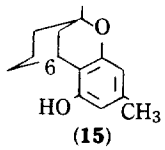
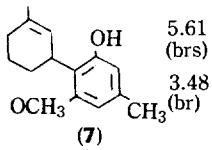
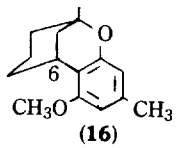
Type of proton	C-6	Aromatic	
16	3.35 (br) (1)	6.21 (brs) (1)	6.29 (brs) (1)
17	3.18 (br) (1)	6.24 (brs) (2)	

[a]Spectra were determined on a Bruker WH-60 spectrometer in deuteriochloroform. Values given in ppm relative to tetramethylsilane as internal standard. Number in parentheses denote the number of protons, determined by integration of areas. Letters in parentheses denote singlet (s) and broad (br).

of alumina, 1-methyl-2-cyclohexen-1-ol and 3,5-dimethylresorcinol gave a 2:1 mixture of compound (**16**) and (**17**). Compound (**16**), the major product, was less polar than (**17**).

The IR spectra of (**16**) and (**17**) are similar but not identical. In addition to minor differences in all parts of the 7.2-12.5 region, the compound (**16**) has two bands which are absent in the (**17**), namely two strong peak at 8.72 μ and at 12.0 . In the NMR spectra the two protons of aromatic ring in (**16**) are determined by comparison of their NMR spectra with those of (**17**). In compound (**16**) these protons appear as two broad singlets centered at 6.21ppm and 6.29 ppm while in (**17**) the aromatic protons shows a broad singlet centered at 6.24ppm. In both the compounds the area of the this signal corresponds to two protons and we assign them to the hydrogens on the aromatic ring. The proton at C-6 in (**16**) appears as a broad signal centered at 3.35ppm. In (**17**) this

Table 4. NMR Spectra of new Compounds formed from Cyclic allylic Alcohols and Orcinols[a]

Compound	C-2H C-3H	Ref.	Compound	C-6H	Ref.
 (3)	5.59 (brs) 3.77 (br)	4	 (15)	3.31 (brs)	4,6
 (7)	5.61 (brs) 3.48 (br)	4	 (16)	3.35 (br)	4,6

[a]Spectra were determined on a Bruker WH-60 spectrometer in deuteriochloroform. Values given in ppm relative to tetramethylsilane as internal standard. Number in parentheses denote the number of protons, determined by integration of areas. Letters in parentheses denote singlet (s) and broad (br).

broad signal is centered at 3.18ppm. Apparently the methoxy group is too far to cause significant changes in the shifts of any cyclohexane protons. As both (**16**) and (**17**) are rigid systems, we suggest that the NMR data fit to (**16**), the peak at 3.35ppm being due to the proximity of a methoxy group, which causes the additional deshielding contributions.

The structures of the new compounds were determined on the basis of their mass spectra and in particular the NMR spectra. When the alicyclic compound was 1-methyl-2-cyclohexen-1-ol the cyclisation invariably took place at the tertiary position as expected from the prefered tertiary carbonium ion formed with BF_3-etherate. The relative positions of the free hydroxy group and the methyl group could be determined chemically.

The products formed by the condensation of cyclic allylic alcohols with orcinols by catalysis with BF_3-etherate are presented in Table 2 and 3.

The noncyclised products (e,g, 7) contain double bond which are on the cyclohexene ring. As the ultraviolet spectra eliminate the possibility of conjugation with either the double bond or the aromatic ring, the cyclohexene double bond has to occupy position C-1. This position is supported additional-indicated that it is deshielded by both the double bond and the aromatic ring. Such an effect is possible only if the double bond occupies the C-1 position[13].

In the cyclized products (e,g, 16) the corresponding benzylic C-6 proton is shielded. Molecular models show that this proton is out of the plane of the aromatic ring. It is of interest to compare the chemical shifts of the C-3 and C-6 protons in the noncyclized and the cyclized compounds, respectively. The C-3 proton in the noncyclized compounds is deshielded as compared to the corresponding C-6 proton in the cyclized compounds. In the open structures the aromatic ring, which can rotate freely, is most probably in the same plane as the C-3 hydrogen, which is therefore deshielded[13,14].

The above correlations are tabulated on Table 4.

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Determination of Chromium(VI) by Differential-Pulse Polarography with a Sodium Borate Supporting Electrolyte

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A suitable choice of supporting electrolyte medium for trace level determinations of chromium(VI) by differential pulse polarography is described. A comparative study suggests that sodium borate buffer is superior to ammonium acetate, ammonium tartrate, and especially to NaF which was recently known to be one of the most proper medium for the purpose. With 0.01 M borate, the best combination of high sensitivity, well-defined base line, and freedom from common interferents was attained. With 5.0×10^{-7}M Cr(VI), tenfold excesses of Cu(II) and Fe(III), and a five hundred-fold excess of Cl^- do not change the peak current by more than about 1%. And the detection limit was 5.0×10^{-8}M Cr(VI).

Introduction

The development of an analytical method suitable for the trace level Cr(VI) species is a continuing problem. Because Cr(VI) has a significantly higher toxicity than Cr(III),[1] it is desirable to perform trace level determinations, which yield directly the former species. Atomic absorption spectrometry has the required sensitivity, but it does not distinguish between the oxidation states unless it is coupled with a separation step.[2]

Polarographic techniques, however, can determine directly Cr(VI) in the presence of Cr(III). Most of the recent work on this subject has focused on the differential-pulse polarography (DPP) in a suitable supporting electrolyte.[3,4] A variety of neutral and basic buffers have been suggested as supporting electrolytes for the polarographic reduction of Cr(VI), involving ammonium chloride/ammonia buffer, ammonium tartrate, and sodium hydroxide solutions[5]; ammonium acetate/acetic acid buffer[6], sodium hydrogen carbonate solution[7], sodium sulfate[8], sodium fluoride solution[3] and phosphate buffered solution.[4] Two common concerns which these suggestions share are to improve analytical detection limits and to avoid or alleviate interferences from the various metal ions, especially copper, a common substance in a diversity of analytical samples, whose reduction wave coincides with or appear near that of Cr(VI) in