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SYNTHESIS OF MUCONIC ACIDS BY PERACETIC ACID OXIDATION OF CATECHOLS

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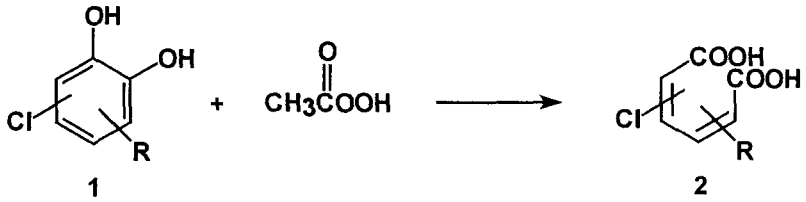
Abstract: Monomeric and dimeric muconic acids were prepared in 30-83% yield by oxidation of catechols with peracetic acid in acetic acid.

Muconic acids (2,4-hexadienedioic acids) were recently identified in effluent from the bleaching of wood pulps[1]. In order to determine their behaviour and facilitate further identification work, a simple, general procedure was required for the preparation of a muconic acids having a variety of substituents. Reported synthetic methods include chemical or enzymatic oxidation of phenols, catechols or quinones[2-6]. Chemical procedures reported vary with respect to time of reaction, temperature, yield, mole ratio of reactants and inclusion of catalysts.

This paper describes the preparation of muconic acids **2** by a simple one-step oxidation of catechols **1** with peracetic acid in acetic acid according to the scheme:



1 2

R = H, CH_3 R = H, CH_3

The reaction was performed on a variety of monomeric alkyl and chlorocatechols **1** as well as some dimeric catechols (Tables I and II). Yields of muconic acids ranged from 30-83%, products being a mixture of geometric or cyclized lactone isomers, depending on the nature and position of the substituents. Reaction were performed simply by adding a 4 mole ratio of 32% peracetic acid in acetic acid to a stirred solution/suspension of the catechol in acetic acid. The mixture of the catechol and peracetic acid was then placed in an ice bath and stirred for 48-72 h, allowing the ice to melt of its own accord over the first few hours.

In the case of catechol **1a**, the pure Z,Z-isomer **2a** crystallized from the reaction mixture in 10% yield and was removed by filtration. The filtrate contained a 2:1 ratio of the ZZ:ZE isomers **2a** and **2b**. Pure methyl ester derivatives of each isomer were obtained by methylation and fractionation on silica gel. The major product from 3-methylcatechol **1b** was the lactonized muconic acid **2c** as previously reported[7]. The isomeric 2-chloromuconic acids **2e** and **2f** obtained from 3-chlorocatechol **1c** were separated directly by fractionation on silica gel. In the case of 4-methylcatechol **1d**, the major product was the

Table I: Preparation of monomeric muconic acids by peracetic acid oxidation of catechols

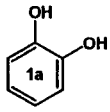
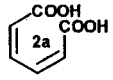
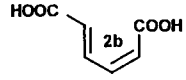
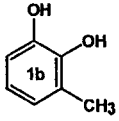
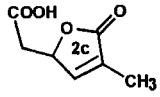
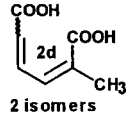
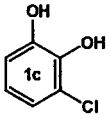
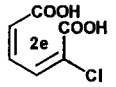
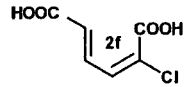
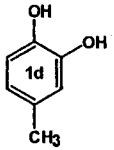
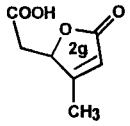
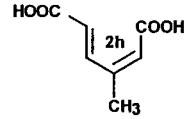
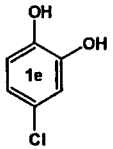
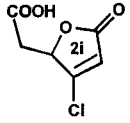
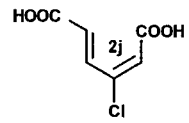
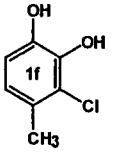
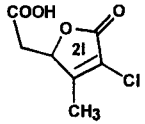
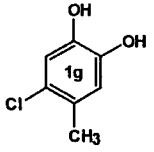
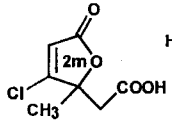
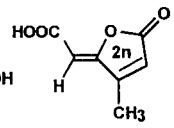
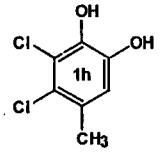
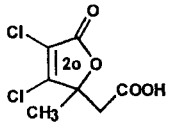
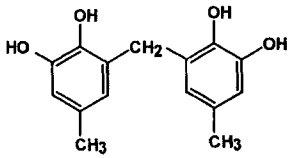
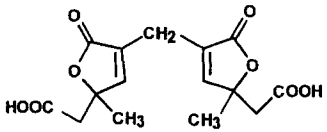
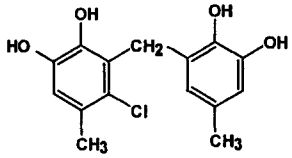
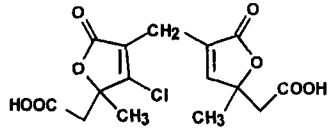
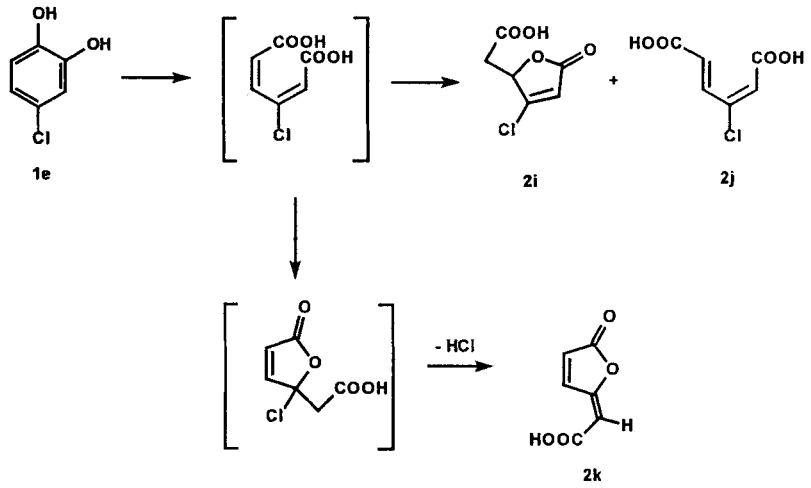
Catechol	Muconic acids	Ratio	Yield
	 	5:2	70
	  2 isomers	2:1	50
	 	2:1	83
	 	15:1	45
	 	2:1	40
		—	60
	 	1:1	45
		—	45

Table II: Preparation of dimeric muconic acids by peracetic acid oxidation of catechols

Catechol	Muconic acid	Yield
 1i	 2p	50
 1j	 2q	30

lactonized muconic acid **2g**, previously obtained by the oxidation of a variety of substrates[8]. (2E, 4E)-3-chloro-2,4-hexadienedioic acid **2j** precipated in 10% yield from the reaction of 4-chlorocatechol **1e**. The major product from this reaction was the cyclized muconic acid **2i,** which has been previously reported as the major product of cyclization of (2E,4Z)-3-chloro-2,4-hexadienedioic acid in concentrated hydrochloric acid[9]. Cyclization and dehydrohalogenation, as previously reported[9,10], to form predominantly the diene lactone **2k** as shown in the scheme below, and as might have been expected at the pH of the reaction, did not occur.



Whereas 3-chloro-4-methylcatechol **1f** gave the cyclized chloromuconic acid **2l**, 4-chloro-5-methylcatechol **1g** gave a mixture of the products **2m** and **2n** which result from both modes of cyclization as shown in the scheme above. The lactonized muconic acid **2o** was the only product obtained from 3,4-dichloro-5-methylcatechol **1h**.

The dimeric catechols **1i** and **1j** were included because formation of methyline linkages between the aromatic rings of lignin probably occurs during pulping[11,12]. Oligomeric muconic acids could therefore form during bleaching, analogous to the formation of monomeric muconic acids. Spectral data and information about the properties of dimeric muconic acids is useful for interpreting information obtained on high molecular weight material resulting from pulp bleaching.

The dimeric cyclized muconic acids **2p** and **2q** were obtained from catechols **1i** and **1j** respectively. In the case of **2p**, analysis of the methylated

product by gas chromatography (GC) and nmr spectroscopy showed equal amounts of the two possible stereoisomers were present. Two closely eluting peaks were obtained on GC and double sets of nmr signals were present in the ^{1}H nmr spectrum. The nmr spectrum of **2q** was more complicated because the presence of a chlorine atom on one of the rings makes the two lactone rings different in any case.

EXPERIMENTAL PART

Melting points were determined on a Fisher Johns apparatus and are uncorrected. Column chromatography was performed on silica gel, 80-200 mesh. Gas chromatography (GC) was done on a Hewlett Packard 5890 Gas Chromatograph equipped with a 25m HP-1 capillary column and gas chromatography/mass spectrometry (GCMS) on a Hewlett Packard 5890 Chromatograph equipped with a 30m DB-5 capillary column coupled to a Fisons 70-250S high resolution mass spectrometer operating in the electron impact mode. ^{1}H nmr and ^{13}C nmr were recorded on a Varian UNITY plus 500MHz spectrometer. Signal positions are given in ppm (δ) relative to Me_4 Si. Starting catechols were either purchased from chemical supplies or prepared by literature methods. The dimeric catechol **1j** was prepared by chlorination of **1i** with sulfuryl chloride in acetic acid at 50^{0}C for 1½ h. The product was cooled, poured into water and filtered. Crystallization from methanol/water initially gave a mixture of **1j** and the dichloroderivative. Concentration of the mother liquor then gave **1j**,

m.p. 207-209°C. ^{1}H nmr ($(CD_3)_2SO$): 1.96 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 3.90 (s, 2H, CH_2), 5.81, 6.40 and 6.67 (s, 3H, ArH); mass spectrum m/z (%): 296 ($M^+ + 2$, 31), 294 (M^+, 71), 257 (43), 171 (78), 170 (71), 160 (41), 158 (87), 137 (79), 124 (100).

General Procedure for Oxidation to Muconic Acids

A 4 mole ratio of 32% peracetic acid in acetic acid was added over a few minutes to a stirred solution/suspension of the catechol **1** (0.01-0.02 moles) in acetic acid (5-10 mL). The flask containing the mixture was then placed in an ice bath and stirring continued for 48-72h allowing the mixture to come to room temperature of its own accord. Crystals which were deposited were filtered and characterized by physical and spectroscopic properties. The filtrate was poured into water, excess peracetic acid destroyed by adding sodium bisulfite, sodium chloride added and the product extracted with ethyl acetate. The extracts were washed with small amounts of water, dried over anhydrous magnesium sulfate, and evaporated to get the product **2**. Characterization involved separation of isomers, normally by fractionation on silica gel and elution with hexane:ethyl acetate mixtures containing 5% acetic acid, and comparison of spectral properties with reported values. Purity of silica gel fractions was determined by GC. Methyl esters, also used for characterization, were prepared by methylation with diazomethane.

Catechol **1a**: (2Z, 4Z)-2,4-Hexadienedioic acid **2a**, crystallized from the reaction mixture, m.p. 194-196°C (lit.[13] 194-195°C). The dimethyl esters of **2a**

and **2b** were obtained by methylation of the filtrate from **2a** and fractionation on silica gel. The dimethyl ester of **2a**, crystallized from hexane, m.p. 72-73°C (lit.[13,14] 73°C). ^{1}H nmr ($(CD_3)_2CO$): 3.73 (s, 6H, 2 x $COOCH_3$), 6.06 (m, 2H, 2 x $\underline{CH}COOCH_3$), 7.88 (m, 2H, 2 x $\underline{CH}$=$CHCOOCH_3$). The dimethyl ester of **2b** had m.p. 72-73°C (lit.[13,14] 75°C). ^{1}H nmr ($(CD_3)_2CO$): 3.74 (s, 6H, $COOCH_3$), 6.06 (d, J 11.2Hz, 1H, $C\underline{H}COOCH_3$), 6.28 (d, J 15.6Hz, 1H, $C\underline{H}COOCH_3$), 6.87 (dd, J 11.5, 11.1Hz, 1H, $C\underline{H}$=$CHCOOCH_3$), 8.42 (dd, J 15.6, 11.7Hz, 1H, $C\underline{H}$=$CHCOOCH_3$); mass spectra **2a** and **2b** methyl esters m/z (%): 170 (M^+, 20), 155 (M^+-15, 5), 139 (M^+-31, 35), 123 (15), 111 (M^+-59, 100), 79 (20), 59 (15).

3-Methylcatechol **1b**: Fractionation of the product on silica gel gave the lactonized muconic acid **2c**[7] (30% yield). Mass spectrum m/z (%): 156 (M^+, <1), 110 (M^+-46, 100), 97 (35). Methylation gave the dimethyl ester of **2c**. ^{1}H nmr ($CDCl_3$): 1.94 (s, 3H, CH_3), 2.62 (dd, J 16.3, 6.9Hz, 1H, $C\underline{H}COOCH_3$), 2.80 (dd, J 16.3, 7.3Hz, 1H, $C\underline{H}COOCH_3$), 3.75 (s, 3H, $COOCH_3$), 5.28 (m, 1H, CH-O), 7.18 (s, 1H, olefinic H); mass spectrum m/z (%): 170 (M^+, 8), 110 (100), 97 (76), 69 (72). Two isomeric muconic acids **2d** were byproducts (20% yield) which could not be purified. The dimethyl esters of **2d** had m/z (%): 184 (M^+, 5), 169 (M^+-15, 5), 153 (M^+-31, 10), 137 (15), 125 (M^+-59, 100), 93 (20), a pattern analogous to that of the dimethyl esters **2a** and **2b**.

3-Chlorocatechol **1c**: Fractionation of the product on silica gel gave initially **2e**[4]. ^{1}H nmr ($(CD_3)_2CO$): 6.05 (dd, J 11.5, 1.3Hz, 1H, CHCOOH), 7.61 (dd, J 11.7, 11.7Hz, 1H, $C\underline{H}$=CHCOOH), 8.27 (dd, J 11.7, 1.3Hz, 1H,

CH=CClCOOH) followed by **2f**[4]. ^{1}H nmr ($(CD_3)_2CO$): 6.29 (dd, J 15.5, 0.8Hz, 1H, CHCOOH), 7.22 (dd, J 11.7, 0.9Hz, 1H, CH=CClCOOH), 8.18 (dd, J 15.5, 11.7, 1H, CH=CHCOOH). Mass spectra **2e** and **2f** methyl esters m/z (%): 204 (M^+, 5), 189 (M^+-15, 8), 173 (M^+-31, 17), 169 (M^+-35, 100), 157 (18), 145 (M^+-59, 60).

4-Methylcatechol **1d**: (2Z,4E)-3-methyl-2,4-hexadienedioic acid **2h** crystallized from the reaction mixture and had m.p. 190-193^{o}C (Lit.[8] various including 190-191^{o}C. ^{1}H nmr ($(CD_3)_2SO$): 1.99 (d, J 1.3Hz, 3H, CH_3), 5.96 (q, J<1Hz, 1H, C2-H), 6.15 (d, J 16Hz, 1H, C4-H), 8.43 (d, J 16Hz, 1H, C5-H); mass spectrum m/z (%): 156 (M^+, 7), 138 (M^+-18, 13), 111 (M^+- 45, 100), 110 (43), 97 (27), 69 (35). The major product **2g** from **1d** was isolated by fractionation of the reaction product on silica gel and elution with hexane:ethyl acetate 1:1 containing 5% acetic acid. Crystallization from acetone/hexane gave m.p. 119-121 ^{o}C (Lit.[8] 129-130 ^{o}C). ^{1}H nmr ($(CD_3)_2SO$): 2.32 (s, 3H, CH_3), 2.71 (dd, J 16, 8Hz, 1H, CHCOOH), 3.18 (dd, J 16, 8Hz, 1H, CHCOOH), 5.46 (m, 1H, CH-O); 6.03 (m, 1H, olefinic H); mass spectrum m/z (%): 156 (M^+, 9), 138 (M^+-18, 20), 111 (22), 110 (M^+- 46, 100), 97 (59), 96 (34), 69 (85).

4-Chlorocatechol **1e** : (2E,4E)-3-chloro-2,4-hexadienedioic acid **2j** crystallized from the reaction mixture and had m.p. 228-231^{o}C (Lit. 229-231^{o}C[15], 232^{o}C[16]). ^{1}H nmr (CD_3OD): 6.39 (s, 1H, CHCOOH), 6.50 (dd, J 15.2, 0.4Hz, 1H, CHCOOH), 8.58 (dd, J 15.2, 0.6Hz, 1H, CH=CHCOOH); mass spectrum *m/z*

(%): 176 (M^+, 5), 159 (M^+-17, 8), 141 (M^+-35, 15), 133 (M^++2-45), 131 (M^+-45), 95 (19), 75 (22). The major product **2i**[9] was isolated by fractionation of the reaction product on silica gel and elution with hexane:ethyl acetate 2:1 containing 5% acetic acid. ^{1}H nmr (CD_3OD): 2.66 (dd, J 16.9, 7.9Hz, 1H, CHCOOH), 3.06 (dd, J 16.8, 3.7Hz, 1H, CHCOOH), 5.42 (m, 1H, CH-O), 6.34 (d, J 1.7Hz, olefinic H); mass spectrum **2i** methyl ester m/z (%): 190 (M^+, 8), 158 (M^+-32, 27), 132 (M^++2-60, 25), 130 (M^+-60, 80), 119 (29), 117 (100).

3-Chloro-4-methylcatechol **1f:** The lactone **2l**[17] was isolated by fractionation of the reaction product on silica gel and elution with hexane: ethyl acetate 2:1 containing 5% acetic acid. ^{1}H nmr ($(CD_3)_2CO$): 2.15 (d, J 1.1Hz, 3H, CH_3), 2.7 (dd, J 16.7, 7.9Hz, 1H, CHCOOH), 3.1 (dd, J 16.7, 3.9Hz, 1H, CHCOOH), 5.39, (m, 1H, CH-O); mass spectrum m/z (%): 190 (M^+, 12), 172 (M^+-18, 18), 146 (M^++2-46, 32), 144 (M^+-46, 100), 103 (55), 97 (36), 75 (48).

4-Chloro-5-methylcatechol **1g**: Fractionation of the product on silica gel and elution with hexane:ethyl acetate 2:1 containing 5% acetic acid gave **2m** followed by **2n.** The methyl ester of compound **2m** was identical to a sample of material previously obtained from the reaction of 4-methylguaiacol with chlorine dioxide[17] and had ^{1}H nmr ($CDCl_3$): 1.62 (s, 3H, CH_3), 2.83 (d, J 15.7Hz, 1H, $CHCOOCH_3$, 2.93 (d, J 15.7Hz, 1H, $CHCOOCH_3$), 3.68 (s, 3H, $COOCH_3$), 6.13 (s, 1H olefinic H); mass spectrum (%): 169 (M^+-35, 10), 133 (32), 131 (100). The methyl ester of **2n** was identical to a sample of material prepared previously[17] by the Wittig reaction of methylmaleic anhydride with methoxycarbonylmethylene-

triphenylphosphorane[18,19] and had m.p. 90-92°C (Lit.[17] 94-95°C). ^{1}H nmr ($CDCl_3$): 2.20 (d, J 1.5Hz, 3H, CH_3), 3.83 (s, 3H, $COOCH_3$), 5.5 (d, J 0.9Hz, 1H, olefinic H), 6.18 (m, 1H, olefinic H); mass spectrum m/z (%): 168 (M^+, 15), 137 (M^+-31, 100), 69 (95).

3,4-Dichloro-5-methylcatechol **1h**: The cyclized dichloromuconic acid **2o** was isolated by fractionation of the product on silica gel and elution with hexane: ethyl acetate 2:1 containing 5% acetic acid. The compound had ^{1}H nmr ($CDCl_3$): 1.66 (s, 3H, CH_3), 2.91 (d, J 17Hz, 1H, CHCOOH); 3.01 (d, J 17Hz, 1H, CHCOOH); mass spectrum m/z (%): 226 (M^+ + 2, 10), 224 (M^+, 14), 189 (14), 188 (15), 167 (70), 165 (100), 146 (25); high resolution: M calc'd: 223.9643; found: 223.9650.

Dimeric Catechol **1i** : The dimeric cyclized muconic acid **2p** was isolated as a mixture of two stereoisomers by fractionation of the product on silica gel and elution with ethyl acetate containing 5% acetic acid. Derivatization with diazomethane gave the dimethyl esters. ^{1}H nmr ($CDCl_3$): 1.55 (2s, 6H, 2 x CH_3), 2.72 (dd, J 15.7, 15.7Hz, 2H, CH_2COOCH_3), 2.87 (dd, J 15.7, 15.7Hz, 2H, CH_2COOCH_3) 3.28 (s, 2H, CH_2), 3.68 (s, 6H, 2 x $COOCH_3$), 7.41 (t, J 1.3Hz, 1H, olefinic), 7.42 (t, J 1.3Hz, 1H, olefinic); mass spectrum m/z (%): 352 (M^+, 36), 279 (91), 229 (56), 205 (100), 183 (47), 127 (54), 97 (70), 59 (77); high resolution: M calc'd: 352.1158; M found: 352.1168.

Dimeric Catechol **1j**: Similar isolation and derivatization gave the dimeric cyclized muconic acid **2q** as the dimethyl esters. ^{1}H nmr ($CDCl_3$): 1.55 (s, 3H,

CH_3), 1.60 (s, 3H, CH_3), 2.68 (d, 1H, $CHCOOH_3$), 2.86 (3d, 3H, $CHCOOCH_3$ and CH_2COOCH_3), 3.33 (d, J 1.5Hz, 2H, CH_2), 3.65 (s, 3H, $COOCH_3$), 3.68 (s, 3H, $COOCH_3$), 7.49 (dd, J 1.5Hz, 1H, olefinic); mass spectrum m/z (%): 386 (M^+, 10), 351 (52), 313 (58), 239 (100); high resolution: M calc'd: 386.0768; M found: 386.0769.

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