Reaction of 4-Vinylguaiacol Derivatives with Synthesis Gas in the Presence of Dicobalt Octacarbonyl. Hydroformylation and Cyclization of Coniferyl Alcohol into 3-(3-Methoxy-4-hydroxyphenyl)tetrahydrofuran

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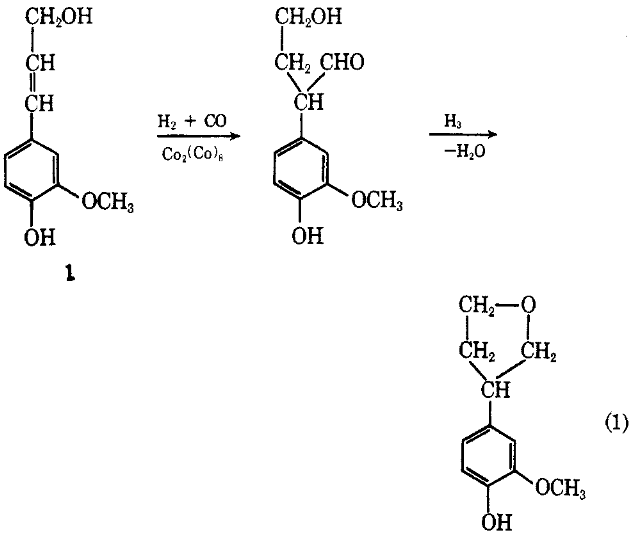
Coniferyl alcohol (1), ferulic acid, and ethyl ferulate were treated in benzene with an equimolar hydrogen-carbon monoxide mixture in the presence of dicobalt octacarbonyl, under conditions previously used for red spruce wood. Coniferyl alcohol gave 3-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran (2) in 25% yield by hydroformylation, followed by ring closure. 3-(3-Methoxy-4-hydroxyphenyl)propanol, 4-*n*-propylguaiacol, 3-methoxy-5,6,7,8-tetrahydro-2-naphthol, 4-ethylguaiacol, guaiacol, phenol, and probably 2-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran were other products; their formation mechanism is discussed. Ferulic acid and ethyl ferulate gave hydrogenation products; 3-(3-methoxy-4-hydroxyphenyl)propanoic acid, produced from ferulic acid, was partially esterified with ethanol formed from carbon monoxide and hydrogen.

In a previous study[1] on the reaction of lignin with carbon monoxide and hydrogen in the presence of dicobalt octacarbonyl, a compound was isolated and identified as 3-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran. Its formation could be explained by assuming the presence of a coniferyl alcohol structure in lignin and through hydroformylation of 1 (eq 1).



1

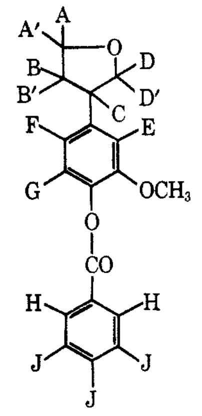
2

(1)

The finding of 3-(3-methoxy-4-hydroxyphenyl)-tetrahydrofuran in the product of oxo reaction of wood was unexpected. The formation of a tetrahydrofuran ring by hydroformylation of an unsaturated acyclic structure had been reported only in the case of 3-butene-1,2-diol,[2] and the double bond in 1, being conjugated with an aromatic ring, was expected to react predominantly by hydrogenation instead of hydroformylation. It was therefore of interest to verify the above hypothesis for the formation of 2 from lignin, by reaction of 1 under the conditions used for wood.

Ferulic acid and ethyl ferulate, which both contain a double bond conjugated with a guaiacol nucleus, were also allowed to react. The behavior of 3-(3-methoxy-4-hydroxyphenyl)propanoic acid under oxo conditions and that of ferulic acid in the absence of catalyst were investigated for a better understanding of the reactions involved. Compounds obtained from the oxo reaction of 1 and their yields are listed in Table I. Guaiacol, phenol, 4-ethylguaiacol, and 3-methoxy-5,6,7,8-tetrahydro-2-naphthol (8) could not be separated and were identified by vpc retention times; 4-*n*-propylguaiacol (4) and 3-(3-methoxy-4-hydroxyphenyl)propanol (3) were obtained pure and identified by vpc and tlc and through the benzoate and bis-*p*-nitrobenzoate, respectively; 2 was purified as its benzoate from the purest fractions obtained and was identified by nmr spectroscopy, melting point, elemental analysis, and methoxyl content.

The nmr spectrum of the benzoate of 2 (Figure 1) has been already described and discussed:[1] the structural formula proposed as the most probable was confirmed in the present work through spin decoupling. A peak at τ 6.26, corresponding to the three protons of the methoxyl, partially overlapped a broad band between 5.80 and 6.40 which accounted for two methylene groups adjacent to an oxygen (protons A, A′, D, and D′). The benzylic proton C produced a band between τ 6.46 and 6.80 showing it to be not adjacent to the oxygen. Double irradiation of D and D′ at τ 5.88 revealed coupling with proton C. Double irradiation of A or A′, respectively, at τ 6.08 and 6.25 showed them to be coupled with B and B′, producing a band between 7.45 and 8.20. Positions of bands corresponding to aromatic protons were at τ 1.75–1.90 for H and 2.35–2.65 for J; a quartet between 2.90 and 3.02 was due to G; the complex structure between 3.07 and 3.27 was due to F and E, the last at 3.14 as shown by decoupling. The



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[1] L. S. Nahum, *Ind. Eng. Chem., Prod. Res. Develop.*, 4, 71 (1965).

[2] I. Wender, H. W. Sternberg, R. A. Friedel, S. J. Metlin, and R. E. Markby, "Chemistry and Catalytic Properties of Cobalt and Iron Carbonyls," U. S. Bureau of Mines, Washington, D. C., 1962.

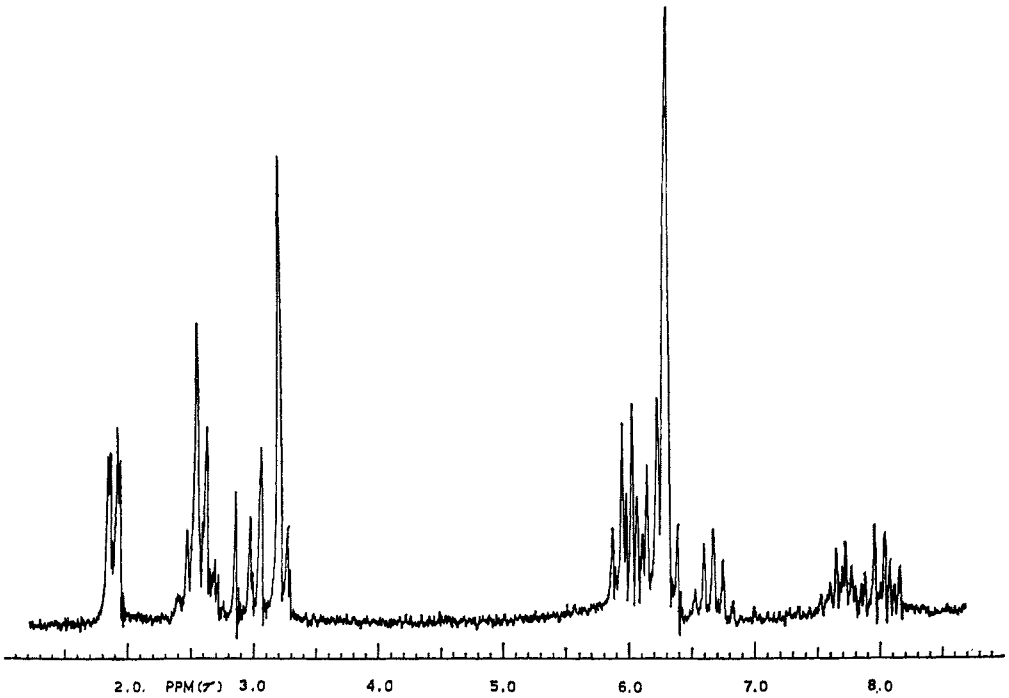


Figure 1.—Nmr spectrum of 3-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran (**2**).

Table I

Products of Oxo Reaction

Compound	Retention time, minutes		R_f	Yields (% based on starting material)		
	Carbowax 20M 235°	BDS 220°	(thin layer silica gel)	From coniferyl alcohol	From ferulic acid	From ethyl ferulate
Guaiacol (**5**)	2.2			Trace	Trace	Trace
Phenol (**6**)	2.8	0.6		Trace	Trace	Trace
4-Ethylguaiacol (**7**)	3.3	0.8		Trace	0.8	1.6
4-*n*-Propylguaiacol (**4**)	4.0	0.9	0.57	11.3	Trace	Trace
3-Methoxy-5,6,7,8-tetrahydro-2-naphthol (**8**)	11.2	2.6	0.55	1.1		
3-(3-Methoxy-4-hydroxyphenyl)tetrahydrofuran (**2**)	20.9	5.2	0.37	23.3		
2-(3-Methoxy-4-hydroxyphenyl)tetrahydrofuran (**9**)	21.7	6.3	0.30	0.3		
Ethyl 3-(3-methoxy-4-hydroxyphenyl)propanoate	22.2	6.1	0.41		14.4	85.4
3-(3-Methoxy-4-hydroxyphenyl)propanol (**3**)	33.9	7.8	0.09	45.5	Trace	Trace
3-(3-Methoxy-4-hydroxyphenyl)propanoic acid			0.04		59.9	3.9
			Total	81.5	75.1	90.9

agreement of nmr data with qualitative and quantitative analytical results and ir and uv spectra was previously pointed out.[1]

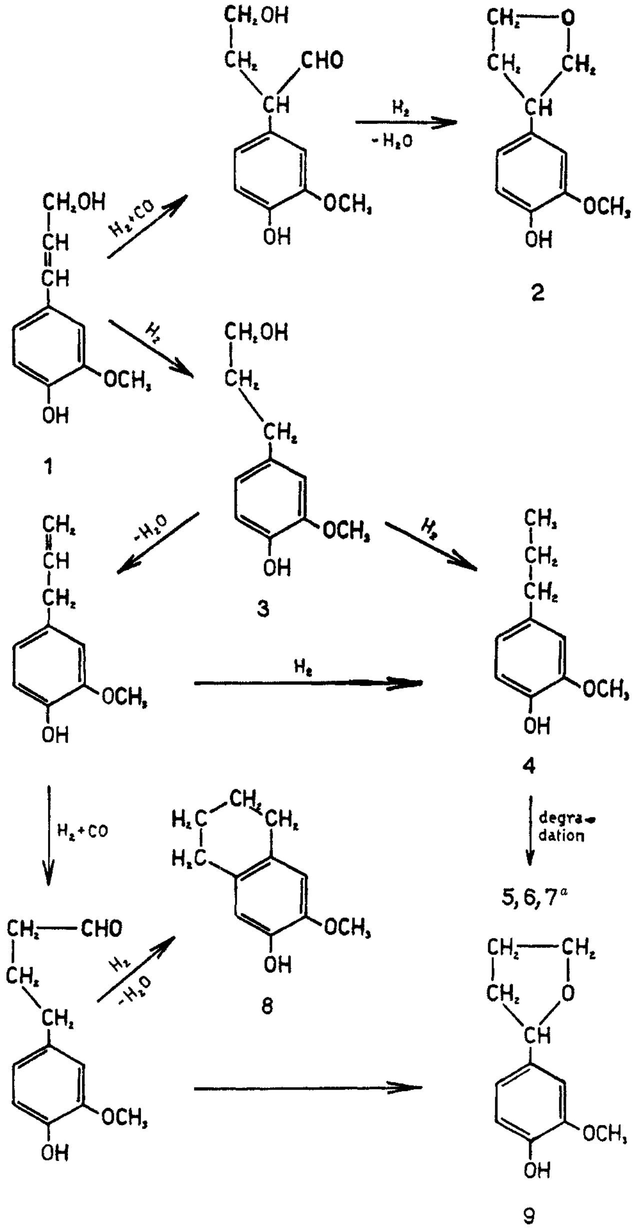
Compound **9**, for which the formula 2-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran is suggested, could not be separated from **2**, by either fractional distillation or column chromatography on alumina or silica gel, nor could its yield be accurately estimated because of overlapping peaks in the gas chromatograms. On treating a mixture of **2** and **9** with benzoyl chloride, only the benzoate of the most abundant component **2** was isolated. However, the nmr spectrum of a mixture of **2** and **9** gave useful information about the structure of **9**. It showed that **9**, like **2**, was a *para*-substituted guaiacol. The substituent had an alicylic structure, since no methyl band was present, apart from the methoxyl of the guaiacol nucleus, and because no other oxygenated terminal functions could be detected in the mixture. Relative amounts of **2** and **9** in the mixture considered were found to be 70 and 30% by integration of the phenolic hydroxyls peaks, which were completely separated. It was thus possible to subtract from the integrals of bands the portions due to **2**. Residual intensities of bands accounted for three aromatic protons (τ 3.10–3.45), the hydroxyl (peak at τ 4.28, disappearing on exchange with deuterium oxide), the methoxyl and the other three protons linked to a carbon adjacent to an oxygen (a complex band between τ 5.80 and 6.42 overlapping a peak at 6.28), and two methylene groups not adjacent to the oxygen (τ 7.10–8.25). From elemental analysis and methoxyl contents of the mixture, **2** and **9** must have been isomers.

Compounds, obtained by reaction of ferulic acid and ethyl ferulate under the same conditions described for **1**, were identified as reported in the Experimental Section; yields are listed in Table I. Ferulic acid subjected to the same conditions in absence of catalyst was partially decarboxylated yielding 34.5% 3-methoxy-4-hydroxystyrene, which was identified by methoxyl and double-bond determinations; 43.8% of the starting material was recovered unchanged. When 3-(3-methoxy-4-hydroxyphenyl)propanoic acid was subjected to oxo conditions, 91.0% was recovered unchanged; 2.1% ethyl 3-(3-methoxy-4-hydroxyphenyl)propanoate, <0.1% 4-ethylguaiacol, and traces of guaiacol and phenol were identified by vpc.

Discussion

SCHEME I

ROUTES FOLLOWED IN THE FORMATION OF PRODUCTS DURING REACTION OF CONIFERYL ALCOHOL (1) WITH SYNTHESIS GAS IN THE PRESENCE OF DICOBALT OCTACARBONYL



[a] Formation of traces of guaiacol (5), phenol (6), and 4-ethylguaiacol (7) from 4 was experimentally confirmed; other labile intermediates may also contribute.

The trend toward exclusive hydrogenation under oxo conditions of a double bond conjugated with a guaiacol nucleus, shown by ferulic acid, ethyl ferulate, and previously[3] by isoeugenol, appears to be altered by the adjacent alcoholic function in **1**, 25% of which reacted by hydroformylation to yield **2**. Scheme I illustrates a flow sheet of the reaction of **1**. The portion of **1** which did not undergo hydroformylation was reduced to **3**. Part of **3** was further reduced to **4**, one-fifth of **4** (2.2% of **1**) probably being produced through the intermediate formation of eugenol by dehydration of **3**, whereas the remaining four-fifths came directly from **3**. This was deduced from finding, among the products, 1.1% **8**, which is known[3] to originate from eugenol under oxo conditions together with **4** in a ratio of about 1:2. The partial transformation of **3** into **4** was verified by reaction of **3** under the conditions used for coniferyl alcohol. Most of **3** was recovered unchanged, but about 5% was reduced to **4**. Traces of **5**, **6**, **7**, and **8** were also produced.

The intermediate formation of eugenol may also explain the formation of **9** by hydroformylation followed by ring closure. If this interpretation were correct, **9** should also have been present in the oxo reaction product of eugenol.[3] Reexamination of the high boiling fraction by vpc did in fact confirm the presence of **9**.

An unexpected result was the formation of 14.4% ethyl 3-(3-methoxy-4-hydroxyphenyl)propanoate in the oxo reaction of pure ferulic acid. Esterification must have occurred in the course of the reaction with some ethanol catalytically synthesized from carbon monoxide and hydrogen, as ethanol is known[2] to be the major oxygenated product in the Fischer–Tropsch process. Naturally no ethyl ferulate was obtained from ferulic acid in the absence of catalyst. Since 3-(3-methoxy-4-hydroxyphenyl)propanoic acid, subjected to oxo conditions, gave only 2.1% ester, esterification appears to be favored by the adjacent double bond and to compete with hydrogenation. As expected the double bond favored decarboxylation too: 34.5% 3-methoxy-4-hydroxystyrene was obtained from ferulic acid in the absence of catalyst, whereas only 0.8% 4-ethylguaiacol was produced in the presence of dicobalt octacarbonyl.

Experimental Section

Apparatus and Techniques.—An adiabatic column was used to distil reaction products. The number of theoretical plates was 35, and the hold up volume was less than 1 ml.

Vpc was carried out using a Perkin-Elmer Model 800, equipped with a flame-ionization detector and 6-ft columns (0.125-in. diameter, packed with 8% BDS (butanediol succinate polyester) or 30% Carbowax 20M on 80–100 mesh Chromosorb W, HMDS treated). The nitrogen flow was 60 cc/min.

Tlc was carried out on silica gel using cyclohexene, chloroform, and acetic acid (8:1:1 v/v) as an irrigant. The spots on the developed chromatograms were located by examination in uv light and/or by coupling with diazotized benzidine.

Nmr spectra were carried out in deuteriochloroform using a 100-Mc Varian spectrometer using TMS as the internal reference.

Melting points are uncorrected.

Reagents and Reference Compounds.—Ethyl ferulate, bp 157–159° (0.4 mm), and coniferyl alcohol, mp 74–76°, were prepared according to a method described by Freudenberg and Hübner.[4] Ferulic acid was prepared from vanillin and malonic acid;[5] 3-(3-methoxy-4-hydroxyphenyl)propanoic acid was prepared by hydrogenation of ferulic acid with Raney alloy;[3] 4-*n*-propylguaiacol was prepared by catalytic hydrogenation of eugenol.[6] Authentic samples of 3-methoxy-5,6,7,8-tetrahydro-2-naphthol, 3-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran, and 3-(3-methoxy-4-hydroxyphenyl)propanol were obtained in the course of previous work.[1,3] Other reference compounds were purchased.

Oxo Reaction of Coniferyl Alcohol.—Coniferyl alcohol (10 g) in benzene (250 ml) and cobaltous carbonate (2.5 g, 50% Co) were charged into a 500-ml oscillating autoclave. Hydrogen and carbon monoxide (1:1) were compressed to 100 atm and the autoclave was heated to 170° and maintained at this temperature for about 24 hr. After cooling the gas was discharged. Hydrogen was compressed to 100 atm, and the autoclave was heated to 150° for 3 hr to decompose the catalyst. After cooling, the

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[3] F. Gaslini and L. S. Nahum, *J. Org. Chem.*, **29**, 1177 (1964).

[4] K. Freudenberg and H. H. Hübner, *Chem. Ber.*, **85**, 1181 (1952).

[5] R. Adams, *Org. Reactions*, **1**, 250 (1947).

[6] D. E. Levin and A. Lovy, *J. Amer. Chem. Soc.*, **55**, 1955 (1933).

solution was discharged, refluxed for 2 hr, extracted with dilute hydrochloric acid to remove cobalt, washed with water, dried over anhydrous sodium sulfate, and filtered, and the solvent was evaporated, yielding 9.5 g of a brown viscous liquid. The cumulated raw product (25 g) was distilled. The distillate, up to 170° at 0.6 mm (21.4 g), was collected in four fractions. A sample of the residue injected into the gas chromatograph did not show any peaks. Each one of the four fractions was fractionated in an adiabatic column and each fraction obtained was refractionated. Compounds were identified as specified above. The following derivatives were prepared.

The benzoate of 4-*n*-propylguaiacol had a mixture melting point of 72.5–73° (from dilute ethanol) with an authentic specimen.

Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71; OCH_3, 11.49. Found: C, 75.80; H, 6.68; OCH_3, 11.12.

The benzoate of 3-(3-methoxy-4-hydroxyphenyl)tetrahydrofuran had mp 109–110° (from ligroin).

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08; OCH_3, 10.41. Found: C, 72.98; H, 6.02; OCH_3, 10.36.

The bis-*p*-nitrobenzoate of 3-(3-methoxy-4-hydroxyphenyl)-propanol had a mixture melting point of 119.5–120.5° (from ethanol) with an authentic sample.

Anal. Calcd for $C_{24}H_{20}O_9N_2$: C, 60.00; H, 4.20. Found: C, 59.61; H, 4.16.

Yields of **2**, **3**, and **4** were determined by weighing the pure fractions obtained; additional amounts of the above compounds present in impure fractions were determined by weighing the area covered by each peak in the gas chromatograms. Yields of **8** and **9** were similarly determined by vpc.

Oxo Reaction of Ferulic Acid.—Ferulic acid (10 g, mp 168–170°) reacted under the same conditions described for **1**. The recovered crude product weighed 7.5 g. Yields of 3-(3-methoxy-4-hydroxyphenyl)propanoic acid and ethyl 3-(3-methoxy-4-hydroxyphenyl)propanoate were determined on different samples by acidic and saponification equivalents; the remainder was dissolved in chloroform and extracted with a saturated solution of sodium bicarbonate. The aqueous extract was acidified and extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulfate and filtered, and the solvent was evaporated. The residue was crystallized from water and identified as 3-(3-methoxy-4-hydroxyphenyl)propanoic acid. Mixture melting point with a synthetic sample was 91–92°.

Anal. Calcd for $C_9H_{11}O_2COOH$: C, 61.21; H, 6.17; COOH, 22.95. Found: C, 60.96; H, 6.20; COOH, 22.75.

The carboxymethyl ether was prepared: mp 142–142.5°.

Anal. Calcd for $C_{10}H_{12}O_2(COOH)_2$: C, 56.69; H, 5.55; COOH, 35.42. Found: C, 56.30; H, 5.50; COOH, 35.45.

The first chloroform phase, which had been extracted with sodium bicarbonate solution, was dried and filtered, and the solvent was evaporated. Samples of the residue obtained were analyzed by vpc. Another sample of the residue was saponified with alcoholic potassium hydroxide, by refluxing for 1 hr. The solution obtained was concentrated, diluted with water, saturated with carbon dioxide, extracted with chloroform, acidified with hydrochloric acid, and extracted again with chloroform. The second extract was dried and filtered, and the solvent was evaporated. The residue was crystallized from ligroin and identified as 3-(3-methoxy-4-hydroxyphenyl)propanoic acid as described above.

Oxo Reaction of Ethyl Ferulate.—Ethyl ferulate (10 g) reacted under the same conditions. The recovered product weighed 9.1 g. Yields of 3-(3-methoxy-4-hydroxyphenyl)-propanoic acid and ethyl 3-guaiacylpropanoate were determined on different samples by acidic and saponification equivalents; the remainder (7.6 g) was saponified by adding 150 ml of alcoholic potassium hydroxide and refluxing for 1 hr. The solution was concentrated, diluted with water, saturated with carbon dioxide, and extracted with chloroform. The extract was dried and filtered, and the solvent was evaporated. The residue (0.2 g) was analyzed by vpc. The aqueous phase was acidified with hydrochloric acid and extracted with chloroform. The extract was dried and filtered, and the solvent evaporated. The residue (6.2 g) was crystallized from ligroin and identified as 3-(3-methoxy-4-hydroxyphenyl)propanoic acid, as described for the product from ferulic acid.

Reaction of Ferulic Acid in Absence of Catalyst.—Ferulic acid (10 g) was heated under pressure of hydrogen and carbon monoxide, under the same conditions without cobalt catalyst. The crude product recovered after evaporation of the solvent weighed 7.9 g: unreacted ferulic acid was determined by alkali titration of a sample; another sample, used for a saponification equivalent determination, consumed the same amount of alkali, within experimental error, required to neutralize the free acid; the remainder of the product (7.0 g) was dissolved in chloroform and extracted with a saturated solution of sodium bicarbonate. Th organic phase was dried and filtered, and the solvent was evaporated. On the residue (3.1 g) the double-bond equivalent was determined by bromination.[7]

Anal. Calcd for $C_6H_3(OCH_3)(OH)CH{:}CH_2$: double-bond equivalent, 150.2; OCH_3, 20.60. Found: double-bond equivalent, 153.0; OCH_3, 20.30.

The sodium bicarbonate solution extract was acidified and extracted with chloroform; the chloroform extract was dried and filtered; and the solvent was evaporated. The residue (3.2 g) was identified as unreacted ferulic acid, mp 160–163° (mp 168–170°, after recrystallization from ligroin, not depressed by mixing with an authentic specimen).

Treatment of 3-(3-Methoxy-4-hydroxyphenyl)propanoic Acid under Oxo Conditions.—3-(3-Methoxy-4-hydroxyphenyl)propanoic acid (10 g) reacted under the same conditions described for **1**. The crude product obtained weighed 9.4 g. Separation and identification of recovered 3-(3-methoxy-4-hydroxyphenyl)propanoic acid were carried out as described for the ferulic acid oxo reaction. The extract containing the nonacidic products was analyzed by vpc. Yields of 3-(3-methoxy-4-hydroxyphenyl)-propanoic acid and ethyl 3-(3-methoxy-4-hydroxy-phenyl)-propanoate were determined on samples of the raw product as described for the ferulic acid oxo reaction.

Registry No.—**1**, 458-35-5; **2**, 3579-89-3; dicobalt octacarbonyl, 10210-68-1; benzoate of **2**, 17182-71-7; 3-(3-methoxy-4-hydroxyphenyl)propanoic acid carboxymethyl ether, 17182-72-8.

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(7) S. Siggia, "Quantitative Organic Analysis *via* Functional Groups" John Wiley and Sons, Inc., New York, N. Y., 1949.