was demonstrated and the average dose rate of 1.24×10^{17} (100 ev/g hr) was used to calculate G values.

To determine G values (molecules of product formed per 100 ev absorbed), 20-g samples of solutions containing 2 moles of hydrocarbon/mole of CCl_4 were irradiated in the same reactor. The product formed was determined by vpc analysis. G values were calculated by dividing the number of molecules of product produced by the number of 100 ev [(1.24×10^{17})(20)(reaction time, hr)] absorbed.

Acknowledgment. The author wishes to thank Mr. J. J. Werner for his competent assistance.

Nuclear Magnetic Resonance. Influence of Substituents on the Long-Range Spin–Spin Coupling Constant between Benzylic and Ring Protons in the Orcinol Series[1a]

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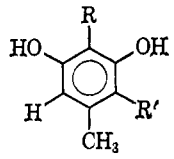
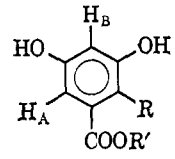
Abstract: Long-range spin–spin coupling between benzylic *ortho* and *para* ring protons in a number of substituted orcinol derivatives is discussed. The data show that coupling of methyl to *ortho* ring protons is not affected by the nature of the substituent introduced *para* to the methyl group. Introduction of CHO *ortho* to the methyl group causes an increase in the *ortho* coupling constant, a reflection of increased π-bond order between the carbons holding the methyl and *ortho* protons. Utilization of electron-withdrawing groups larger than CHO does not increase the π-bond order and the *ortho* coupling constant in this series because of steric inhibition of resonance.

Desire to obtain orcinol derivatives of the general structure I for metabolism studies prompted investigation of these compounds by means of nuclear magnetic resonance in order to confirm the direction of the substitution reaction utilized in their synthesis. During the course of these investigations long-range spin–spin coupling was observed between the Ar–CH_3 group and ring protons.



I, R = R′ = H
II, R = $COOCH_3$; R′ = H
III, R = COOH; R′ = H
IV, R = NO_2; R′ = H
V, R = $COOCH_3$; R′ = CHO
VI, R = H; R′ = CHO
VII, R = H; R′ = COOH
VIII, R = H; R′ = $COOCH_3$
IX, R = H; R′ = NO_2



X, R = R′ = H
XI, R = CHO; R′ = CH_3

Long-range coupling has been studied extensively in other systems but only during recent years has benzylic coupling received much attention.[2] Generally, side-chain ring coupling involving sp^3-hybridized carbon atoms has been observed in heterocyclic[2a,3] and some polycyclic[2a,4] aromatic ring systems. While Hoffman[5] was able to observe splitting of the proton and methyl resonances in mesitylene, spectra of *p*- and *o*-xylenes showed only single lines. Freeman[6] also reported that the methyl proton resonance of 3,5-di-*t*-butyl-4-hydroxytoluene exists as a triplet with $|J| = 0.60$ cps. This is in agreement with observations reported by Rottendorf and Sternhell[7] who studied a series of three isomeric tetrachlorotoluenes. The resonance assigned to the methyl group in the tetrachlorotoluene series indicated *ortho* and *para* coupling of methyl to ring protons to be equal ($|J| = 0.63$ cps), while *meta* coupling was considerably smaller (0.36 cps).

Hoffman[8] and others[9] have suggested such long-range couplings, presumably involving $\sigma-\pi$ configuration interactions,[2a,10] are evidence of hyperconjugation between the methyl group and π-electron orbitals. While hyperconjugation seems to be necessary for benzylic coupling, studies with polycyclic[2a,4,7] and heterocyclic[2a,3] compounds indicated the magnitude of the *ortho* coupling constant to be dependent upon the π-bond order between the carbons holding the methyl and *ortho* protons. Orcinol (I) derivatives are particularly suitable to a study of the magnitude of such long-range couplings relative to their dependence upon π-bond order since (1) hydroxyl groups prevent ad-

(1) (a) This research was supported by a grant from the Research Corporation. Presented at the 2nd Midwest Regional Meeting of the American Chemical Society, Lawrence, Kansas, Oct 1966. (b) Support by funds from the Graduate College of the University of Iowa is gratefully acknowledged.

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Table I

Compd	Chemical shift, δ ppm: H_A	H_B	Other	Coupling constants, ±0.05 cps: $\lvert J_{AB}\rvert$	$\lvert J_{A\text{-CHO}}\rvert$	$\lvert J_{B\text{-CHO}}\rvert$	$\lvert J_{A\text{-CH}_3}\rvert$	$\lvert J_{B\text{-CH}_3}\rvert$	$\frac{1}{2}\lvert J_{A\text{-CH}_3}\rvert + \lvert J_{B\text{-CH}_3}\rvert$
I	6.14	6.14	Ar-CH_3 = 2.12	?	...	...	...	...	0.60
II	6.20	...	Ar-CH_3 = 2.19 Ar-$COOCH_3$ = 4.02	...	...	...	0.60	...	...
III	6.30	...	Ar-CH_3 = 2.23	...	...	...	0.60	...	...
IV	6.48	...	Ar-CH_3 = 2.32	...	...	...	0.60	...	...
V	6.40	...	Ar-CH_3 = 2.60 Ar-CHO = 10.22 Ar-$COOCH_3$ = 3.98	...	0.20	...	0.80	...	...
VI	6.28	6.20	Ar-CH_3 = 2.51 Ar-CHO = 10.06	2.35	0.20	0.55	0.77	0.57	...
VII	6.32	6.32	Ar-CH_3 = 2.54	?	...	...	...	...	0.60
VIII	6.28	6.28	Ar-CH_3 = 2.46 Ar-$COOCH_3$ = 3.92	?	...	...	...	...	0.60
IX	6.42	6.42	Ar-CH_3 = 2.50	?	...	...	...	...	0.60
X	7.00	6.56	Ar-$COOCH_3$ = 3.96	2.35	0.20	0.55	...	...	...
XI	6.92	6.47	...	2.35	...	...	...	...	...

ditional coupling of methyl to *meta* ring protons and do not couple with the *ortho* protons,[11] and (2) hydroxyl groups are in conjugation with electron-withdrawing groups at the site of R′. Therefore, if R′ is able to lie in the same plane as the ring the π-bond order between the carbons holding the methyl group and *ortho* proton should increase as the $-R$ effect for R′ increases.

Results and Discussion

Chemical shifts and coupling constants for all compounds studied are listed in Table I. The designation H_A refers to the proton *ortho* to the methyl group while H_B refers to the *para* proton. Coupling constants reported are accurate to ±0.05 cps. Analysis of the long-range coupling of methyl to ring protons in the orcinol series is most readily interpreted by first noting the spectra of the more highly substituted derivatives. This is because the A_2BX_3 spectrum (Figure 1) of orcinol is deceptively simple.[12]

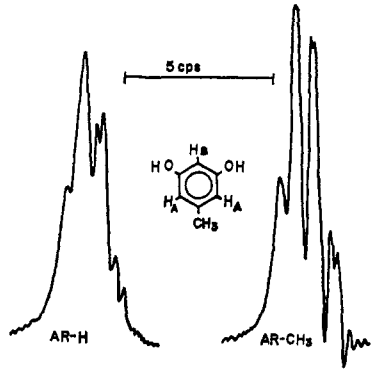

Figure 1.

For orcinol (I), decoupling[13] at frequencies of +240 and −243 cps afforded single lines for the aromatic and methyl proton resonances, respectively, indicating $(\nu_{H_A} - \nu_{H_B}) < 0.3$ cps. The results of first-order analysis show $\frac{1}{2}\lvert J_{CH_3\text{-}H_A}\rvert + \lvert J_{CH_3\text{-}H_B}\rvert = 0.60$ cps. Comparison with the analysis of the mesitylene spectrum reveals that $\lvert J_{CH_3\text{-}H_A}\rvert$ may or may not equal $\lvert J_{CH_3\text{-}H_B}\rvert$. While the major splittings of the mesitylene spectrum have been interpreted as indicating equal coupling of *ortho* and *para* protons with the methyl group,[5,7] Rottendorf and Sternhell[7] pointed out that a mathematical analysis[14] predicts that *ortho* and *para* side-chain ring coupling constants should differ (J_{ortho} = 0.89 cps; J_{para} = 0.45 cps).

For *p*-orsellenic acid (III) the methyl resonance (Figure 2) occurs as a triplet and the *ortho* aromatic

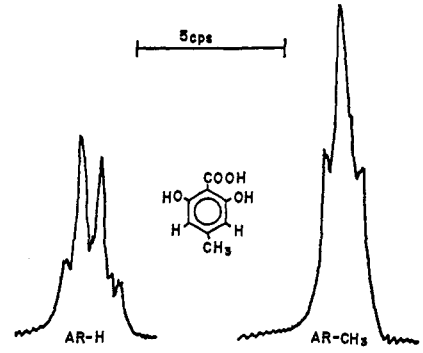

Figure 2.

proton resonance is observed as a quartet with $\lvert J\rvert$ = 0.60 cps. Methyl *p*-orsellinate (II) and 3,5-dihydroxy-4-nitrotoluene (IV) exhibit the same coupling pattern with $\lvert J\rvert$ = 0.60 cps in accord with the *ortho* coupling constant observed in the tetrachlorotoluene series.[7]

By means of a modified Gatterman reaction[15] methyl 2-formyl-*p*-orsellinate (V) is prepared from methyl *p*-orsellinate (II) in 95% yield. Insertion of the carbonyl function causes a slight downfield shift for the resonances of the aromatic methyl and *ortho* aromatic proton with a concomitant increase in the coupling constant (Figure 3, $\lvert J_{CH_3\text{-}H}\rvert$ = 0.80 cps). As expected, no coupling is observed between the formyl proton and the aromatic proton. This is because hydrogen bonding of the carbonyl oxygen to the neighboring hydroxyl

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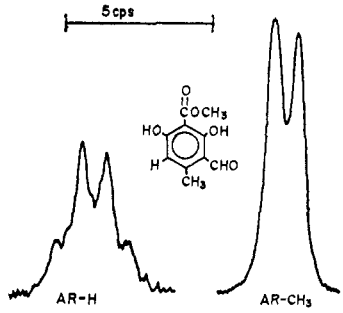

Figure 3.

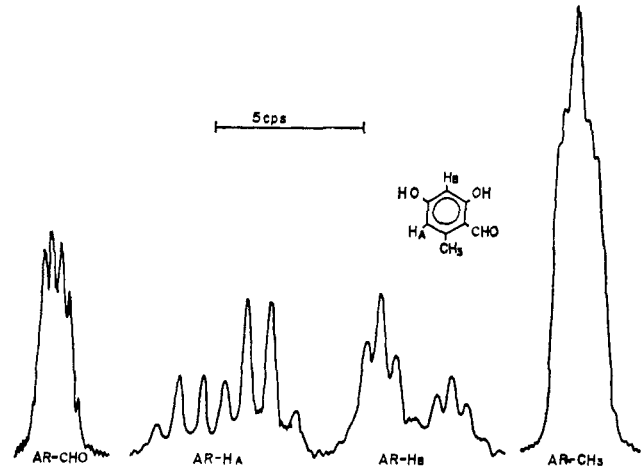

Figure 4.

group causes the two protons involved to assume a cisoid relationship. That a transoid relationship is necessary for such coupling to occur was recently discussed by Karabatsos and Vane[16] and is further substantiated by the fact that coupling of the formyl proton in methyl 3,5-dihydroxy-2-formylbenzoate (XI) mainly takes place with the H_B proton ($|J_{CHO-H_B}| = 0.55$ cps).

In the case of orcylaldehyde [4,6-dihydroxy-2-methylbenzaldehyde (VI)] the formyl, aromatic, and methyl hydrogens couple in a $YABX_3$ pattern (Figure 4) with $|J_{H_A-H_B}| = 2.35$ cps. This is essentially the same magnitude observed for *meta* splitting in α-resorcylic acid (XII) and methyl 3,5-dihydroxy-2-formylbenzoate (XI). Decoupling of the methyl protons utilizing a frequency of +220 cps afforded an unsymmetrical quartet for H_A-H_B in which the inner and outer lines, owing to the H_A resonance, exhibited half-widths of 0.7–0.8 cps. The inner and outer lines, owing to the H_B resonance, exhibited half-widths of 1.6–1.7 cps. The H_B resonance observed during the decoupling procedure could only be partially resolved because of the high noise level. Sufficient resolution was obtained to indicate $|J_{CHO-H_B}| = 0.55$ cps. This is in agreement with the results found for the H_B resonances of methyl 3,5-dihydroxy-2-formylbenzoate (XI). Utilizing $|J_{H_A-H_B}| = 2.35$ cps and $|J_{CHO-H_B}| = 0.55$ cps the 16-line spectrum which best fits the observed spectrum for the H_B resonance yields $|J_{CH_3-H_B}| = 0.57 \pm 0.05$ cps. The resonance for the H_A proton exists as a septet owing to coupling with the *o*-methyl protons. In this case $J_{CHO-H_A} \sim 0$ and the septet results from overlap of the center lines of each quartet of the H_A resonance of the AB part of the spectrum. Therefore, $|J_{CH_3-H_A}| = 0.77$ cps is in agreement with the *o*-methyl to ring proton coupling observed for methyl 2-formyl-*p*-orsellinate (V) and is approximately 0.15 cps greater than *para* coupling of methyl and H_B protons.

These data are in agreement with theoretical concepts proposed by McConnell[17] who derived an equation[18] based on empirical data on hyperfine splittings in aromatic free radicals. McConnell has shown that the contribution of π electrons to proton–proton nuclear spin–spin couplings is such that $J_{NN'}^{\pi}$ is proportional to the square of the π-bond order connecting carbon atoms N and N′. In long-range spin–spin coupling contribution to J is largely a factor of the π electrons since their influence is not rapidly attenuated by increasing the distance between the involved protons. In the case of compounds II, III, and IV it is observed that the substituent inserted *para* to the methyl group has no effect upon the coupling constant between the methyl and *ortho* aromatic protons. However, insertion of the aldehyde function *ortho* to the methyl group as in compounds V and VI causes an increase in the π-electron density between the carbons holding the methyl and *ortho* proton. A corresponding increase in the coupling constant is observed. Such an insertion has no effect on the *para* coupling constant.

Substitution of carboxy, carbomethoxy, and nitro groups (compounds VII, VIII, IX, respectively) *ortho* to the aromatic methyl again yields deceptively simple spectra[12] since $|J_{AB}| > (\nu_{H_A} - \nu_{H_B})$. In each of these spectra the resonance for the methyl group appears as a triplet and the resonance for the aromatic protons appears as a quartet. First-order analysis again shows $^1/_2|J_{CH_3-H_A} + J_{CH_3-H_B}| = 0.60$ cps. While this is the only value which is experimentally accessible, data obtained with other compounds in this series substantiate the proposal $|J_{CH-H_A}| = |J_{CH-H_B}| = 0.60$ cps. Therefore, the experimental results are not in agreement with the mathematical analysis[14] which predicted unequal coupling of methyl to *ortho* and *para* protons in mesitylene. Further, these data represent strong support for steric inhibition of resonance when functional groups larger than -CHO are inserted between hydroxyl and methyl groups.[19]

Experimental Section

Nmr spectra were recorded utilizing a Varian A-60 spectrometer. Decoupling experiments were carried out with the Varian Model V-6058 attachment. Coupling constants and chemical shifts were determined in hexadeuterioacetone with concentrations of 10–30% utilizing trimethylsilane as an internal standard.

Orcinol (I) was purchased from Fisher Scientific Co. and recrystallized from water, mp 106–108° (lit.[20] mp 107.5°).

***p*-Orsellenic acid (III)** was synthesized by the method of St. Pfau; mp 179–180° (lit.[21] mp 179–180°).

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(18) $J_{NN'}^{\pi} = (\beta Q \eta_{NN'})^2/h\Delta E$, where β is the Bohr magneton, Q is a hyperfine splitting constant, $\eta_{NN'}$ is the bond order connecting carbon atoms N and N′, h is Planck's constant, and ΔE is an effective electronic excitation energy.

(19) M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp 429, 437, 162, 174, 175; J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 63; E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, Inc., New York, N. Y., 1959, pp 70, 236, 455.

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Methyl *p*-Orsellinate (II). *p*-Orsellinic acid (5.05 g, 0.03 mole) was dissolved in 50 ml of ether. To the solution was added 1.68 g (0.04 mole) of diazomethane in ether.[22] The mixture was allowed to stand at room temperature for a period of 2 hr. Dilute acetic acid was added to decompose the excess diazomethane. The ether layer was separated and extracted with two 25-ml portions of sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure affording a white solid. Recrystallization from hot water yielded a solid (3.5 g, 70%) identical in all respects with the ester obtained in 10% yield from the Fisher esterification of *p*-orsellinic acid, mp 96–98° (lit.[15] mp 97°).

Methyl 2-Formyl-*p*-orsellinate (V). Methyl *p*-orsellinate (5.0 g, 0.027 mole) and aluminum chloride (11.0 g, 0.082 mole) were dissolved in 200 ml of ether, with continuous stirring. The solution turned cloudy in 10 min. Zinc cyanide (5.0 g, 0.065 mole) was added, and gaseous hydrochloric acid was introduced into the stirred mixture for a period of 8 hr. Water (100 ml) was added, and the mixture was heated on a steam bath for 1.5 hr. On cooling, a solid (4.7 g, 94%) precipitated and was removed by filtration. Recrystallization from hot water afforded white crystals, mp 146–148° dec.

Anal. Calcd for $C_{10}H_{10}O_5$: C, 57.15; H, 4.76. Found: C, 57.47; H, 4.98.

Orcylaldehyde [4,6-dihydroxy-2-methylbenzaldehyde (VI)] was prepared according to the method of Adams and Levine, mp 179–181° (lit.[23] mp 178–180°).

(22) H. A. Blatt, Ed., "Organic Synthesis," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1955, p 165.

***o*-Orsellinic acid (VII)** was prepared from orcylaldehyde (VI) by a reaction sequence developed by Hoesch,[24] mp 194–196° (effervescence) [lit.[25] mp 176° (effervescence)].

Methyl *o*-orsellinate (VIII) was prepared in the same manner as methyl *p*-orsellinate (II), mp 138–140° (lit.[26] mp 140°).

2-Nitroorcinol [3,5-dihydroxy-2-nitrotoluene (IV)] and 4-nitroorcinol [3,5-dihydroxy-4-nitrotoluene (IX)] were prepared by nitration of orcinol according to the method of Henrich and Meyer: for IV, mp 119–121° (lit.[27] mp 122°); for IX, mp 126–127° (lit.[27] mp 127°).

Methyl 3,5-dihydroxy-2-formylbenzoate (XI) was prepared from the methyl ester of 3,5-dihydroxybenzoic acid (X) according to the method of Birkinshaw and Bracken, mp 164–165° (lit.[28] mp 163.5°).

Acknowledgments. We are grateful to Professor Robert Barker for making the nmr spectrometer in the biochemistry department available for our use. We wish to thank the referee for helpful suggestions.

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(25) O. Hesse, *Ann.*, **139**, 22 (1866).
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An Ionic Aromatization of Steroidal Dienones

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Abstract: Treatment of a 9α,11β-dichloro or 9α,11β-halohydrin steroid in refluxing dimethylformamide or refluxing pyridine afforded a ring AB aromatic compound. It was further shown that the C-19 methyl group was expelled as the appropriate methyl halide. A mechanism, based on these facts, is discussed.

The preparation of a steroidal ring AB aromatic compound from simpler aromatic or nonaromatic systems has been of interest principally to provide "equilenin"-type compounds. Apart from total synthetic methods,[1] most of the published procedures depended upon (a) dehydrogenation of a suitable ring A[2–4] or ring B[3] aromatic precursor, (b) dehydrogenation of a Δ^6-ring A aromatic system,[5] (c) dehydrogenation of a $\Delta^{3,5}$-19-nor system,[6] and (d) acid elimination of an allylic hydroxyl group in a suitably unsaturated system.[7] Ionic processes that provide aromatization with concomitant expulsion of the C-19 methyl group have generally been applied to prepare ring A aromatic compounds only.[8] This paper is concerned with the preparation of ring AB aromatic steroids from nonaromatic intermediates by a new ionic method[9] with elimination of the C-19 methyl group. The method, moreover, may be generalized so that the preparation of ring AB aromatic steroids with a variety of substituents may be devised.

The method may be illustrated by the following experiment. 21-Acetoxy-9α,11β-dichloro-17α-hydroxypregna-1,4-diene-3,20-dione (Ia)[10] was refluxed in DMF for 30 min to produce at least three products as indicated by thin layer chromatography. One of the products was not in sufficient quantity to be isolated. A second product had the ultraviolet[11] and infrared spectra characteristic of a ring AB aromatic system and was assigned the structure 21-acetoxy-3,17α-dihydroxy-19-

(1) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 481.
(2) A. Butenandt, A. Wolff, and P. Karlson, *Chem. Ber.*, **74**, 1308 (1941).
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(11) L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).