98-83-9; AP, 98-86-2; S, 588-59-0; BZ, 100-52-7; BA, 100-51-6; $PhC^+(CH_3)_2$, 16804-70-9; $PhC\cdot(CH_3)_2$, 4794-07-4; $(NH_4)_2S_2O_8$, 7727-54-0; $S_2O_8^{2-}$, 15092-81-6; $PhCH(OH)CH_2Ph$, 614-29-9; $PhCH_2Cl$, 100-44-7; $PhCH(NHAc)CH_2Ph$, 21511-90-0; CH_3CN, 75-05-8; $4\text{-}HOC_6H_4CH{=}CHPh$, 3839-46-1; $4\text{-}CH_3C_6H_4CH_2Br$, 104-81-4; $4\text{-}CH_3C_6H_4CH(OH)CH_2C_6H_4\text{-}4\text{-}CH_3$, 54881-85-5; $4\text{-}CH_3C_6H_4CH_2Cl$, 104-82-5; $4\text{-}CH_3C_6H_4CH(NHAc)CH_2C_6H_4\text{-}4\text{-}CH_3$, 89165-04-8; $4\text{-}CH_3C_6H_4CH_2CH_2C_6H_4\text{-}4\text{-}CH_2OH$, 89165-05-9; *cis*-$4\text{-}ClC_6H_4CH{=}CHC_6H_4\text{-}4\text{-}CH_3$, 89165-06-0; *trans*-$4\text{-}ClC_6H_4CH{=}CHC_6H_4\text{-}4\text{-}CH_3$, 3041-83-6; $(C_6H_5)_3P$, 603-35-0; $4\text{-}CH_3C_6H_4CH_2P^+(C_6H_5)_3Br^-$, 2378-86-1; $4\text{-}ClC_6H_4CHO$, 104-88-1; $4\text{-}CH_3C_6H_4CH_2CH_2C_6H_4\text{-}4\text{-}Cl$, 89165-07-1; $4\text{-}CH_3C_6H_4CH_2CH_2C_6H_4\text{-}4\text{-}CO_2H$, 89165-08-2; $4\text{-}CH_3OC_6H_4CH(OH)CH_2Ph$, 5422-47-9; $4\text{-}CH_3OC_6H_4CHO$, 123-11-5; $4\text{-}CH_3C_6H_4CH(OH)CH_2Ph$, 20498-63-9; $PhCH(OH)CH_2C_6H_4\text{-}4\text{-}CH_3$, 20498-68-4; $PhCH{=}CHC_6H_4\text{-}4\text{-}CH_3$, 4714-21-0; $4\text{-}CH_3OC_6H_4COCH_2Ph$, 1023-17-2; $Fe(ClO_4)_2$, 13933-23-8; $Cu(ClO_4)_2$, 13770-18-8; Cu^{2+}, 15158-11-9; $C_6H_5CH_3$, 108-88-3; $C_6H_5CH_3^{+\cdot}$, 34504-47-7; $2\text{-}CH_3C_6H_4OH$, 95-48-7; $3\text{-}CH_3C_6H_4OH$, 108-39-4; $4\text{-}CH_3C_6H_4OH$, 106-44-5; $4\text{-}CH_3C_6H_4CH_2CH_2C_6H_4\text{-}4\text{-}CH_3$, 538-39-6; $4\text{-}CH_3C_6H_4CH_2CH_2C_6H_4\text{-}4\text{-}CH_3^{+\cdot}$, 89196-12-3; $4\text{-}CH_3C_6H_4CHO$, 104-87-0; $4\text{-}CH_3C_6H_4CH_2OH$, 589-18-4; $4\text{-}CH_3C_6H_4CH_2CH_2Ph$, 14310-20-4; $4\text{-}CH_3C_6H_4CH_2CH_2Ph^{+\cdot}$, 89165-03-7; $PhCH_2CH_2C_6H_4\text{-}4\text{-}CH_2OH$, 34224-29-8; $4\text{-}CH_3OC_6H_4CH_2CH_2Ph$, 14310-21-5; $4\text{-}CH_3OC_6H_4CH_2CH_2Ph^{+\cdot}$, 89165-01-5.

Migrations in Oxidations of Mesidine

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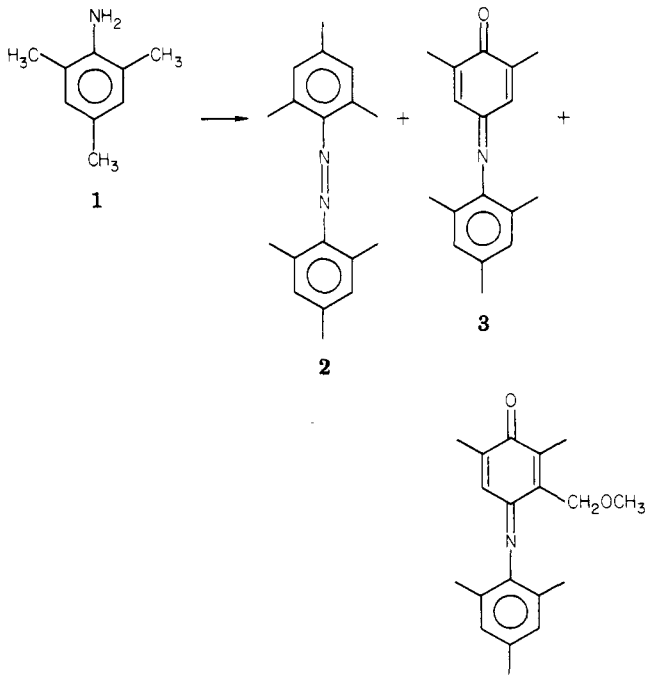
The oxidation of mesidine in methanolic media by ferricyanide, dichromate, and persulfate afforded an anil **4** containing a shifted methoxymethyl group in addition to the principal anil **3** formed by oxidative dealkylation. Possible intermediates **6**, **7**, and **8** were prepared and oxidized to the product anils. Oxidations of related anilines **9**, **10**, and **13** did not parallel those of mesidine but afforded analogues of **3**. There is significant spectral evidence for anils with alkyl shifts but little for anils analogous to **4**.

In a prior communication we reported the unusual formation and migration of a methoxymethyl group during the oxidation of 2,4,6-trimethylaniline (mesidine) in methanolic media.[1] Herein we describe details, extensions, and certain limitations of this reaction.

The oxidations of mesidine (**1**) in methanol–water mixtures afford usually three products, whose formations are influenced by the acidity of the media. The azo compound **2** is the principal product in basic systems; anil **3** [2,6-dimethyl-*p*-benzoquinone 4-(2,4,6-trimethylanil)] is the principal product in acidic systems with or without methanol; anil **4** [2,6-dimethyl-3-(methoxymethyl)-*p*-benzoquinone 4-(2,4,6-trimethylanil)] is a significant product in acidic systems containing methanol. The mechanism of removal or shifts of the methyl groups has been postulated to involve *para*-imino methides which add water to form hydroxymethyl groups or methanol to form methoxymethyl groups.[2] The hydroxymethyl groups can be eliminated in a subsequent coupling step as formaldehyde. The hydroxymethyl groups cannot be eliminated after coupling and migrate to the adjacent carbon to restore aromaticity. An analogous mode of dealkylation through a quinone methide has been shown for 2,4,6-trimethylphenol (mesitol).[3] Although migrations in methanolic media were not observed for mesitol, such reactions have been reported extensively for enzymatic oxidations of tyrosine and related compounds and are called commonly the NIH shift.[4]



Results and Discussion

Oxidizing Agents. The formation of the anil **4** in the oxidation of mesidine was observed initially with a solution of potassium ferricyanide and ammonium acetate in a water and methanol (volume ratio, 6:1) mixture. The range of acidity of such systems was 6.4 to 6.7. The reaction times were slow—five to ten days to achieve full conversion of mesidine to compounds **2**, **3**, and **4** in yields of 2%, 54%, and 17%, respectively. The ferricyanide to mesidine ratio was 7.6 to 1. The importance of the acidity level was

(1) Goldstein, S. L.; McNelis, E. *J. Org. Chem.* **1973**, *38*, 183.

(2) Saunders, B. C.; Wodak, J. *Tetrahedron* **1967**, *23*, 473.
(3) McNelis, E. *J. Am. Chem. Soc.* **1966**, *88*, 1074.
(4) Jerina, D. M.; Daly, J. W.; Landis, W.; Witkop, B.; Udenfriend, S. *J. Am. Chem. Soc.* **1967**, *89*, 3347.

0022-3263/84/1949-1613$01.50/0

demonstrated by a ferricyanide oxidation of mesidine in methanol–water containing potassium hydroxide, wherein the selectivity of azomesitylene **2** was 79% on an 89% conversion. Anil **3** was formed in 1% selectivity and no anil **4** was detected.

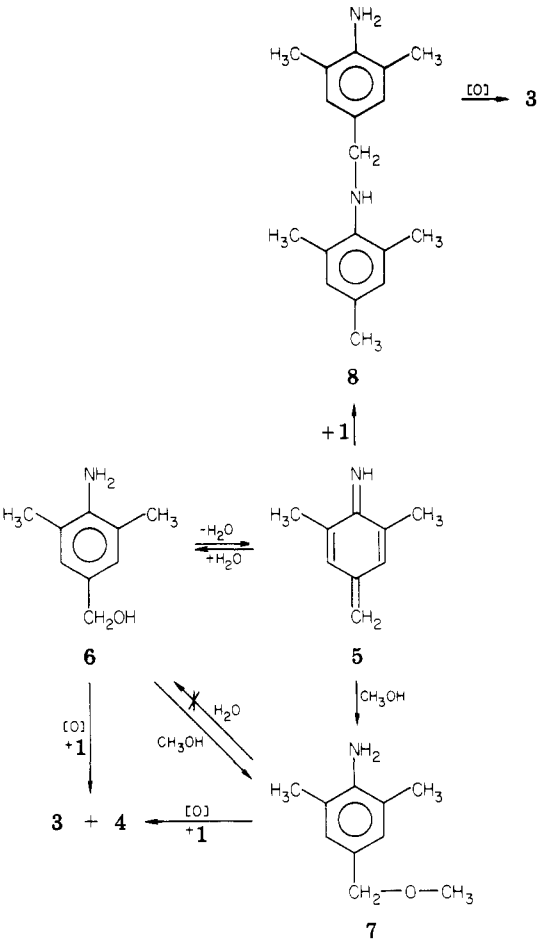
Attempts to decrease reaction times succeeded when the oxidizing compound was changed to potassium dichromate in a solvent mixture of water, methanol, and acetic acid (volume ratio, 10:2:1). At conversions in excess of 85%, the selectivities to compounds **2**, **3**, and **4** were 3%, 70%, and 12%, respectively, within 4 h. Inverse addition of oxidant was required for such selectivities in these reactions whose pH values were 1.8 to 2.2 and whose oxidizer to substrate molar ratios were 1:1. Another homogeneous system consisted of ammonium persulfate or potassium persulfate with silver nitrate (molar ratio, 10:1) in water–methanol (volumetric ratio, 5:2). The reaction time was also 4 h; the conversion was 91%; the selectivities for **2**, **3**, and **4** were 3%, 49%, and 10%, respectively. Slow addition of the persulfate solution to mesidine was used. The pH values ranged from 1.7 to 2.0.

The narrow range of conditions for an oxidation of mesidine can be further indicated by the reaction of activated manganese dioxide with mesidine in benzene. If mesidine were in excess, the nonbasic reaction products were azomesitylene (75%), uncharacterized tars, and a trace of anil **3**. Another heterogeneous oxidizing agent, sodium bismuthate, behaved similarly. It is known that the bismuthate forms a strong base during oxidation[5] and activated manganese dioxides, formed usually by the reduction of permanganate in base, have residual basic sites formed during preparation.[6] Another basic oxidation of mesidine, silver carbonate on Celite, has been reported to give high yields of azomesitylene.[7] In such systems the concentration of the mesidinyl radical increases at the expense of the protonated form and the probability of nitrogen coupling increases as in the case of the basic ferricyanide systems.

Intermediates. In the proposed reaction path there is present an imino methine **5** that adds water to give aniline **6** or methanol to give aniline **7**. Both anilines have been synthesized and shown to lead to their respective anils with mesidine under the usual conditions of the ferricyanide system (pH 6.7). The yield of anil **3** from **6** and mesidine was 55%; than of anil **4** was 22%. When tetrahydrofuran was substituted in place of methanol the yield of anil **3** rose to 75%. Similarly, aniline **7** and mesidine in the methanolic system afforded a 61% yield of anil **4** whereas in the tetrahydrofuran-containing system the yield of anil **4** was 35% and of anil **3** was 13%.

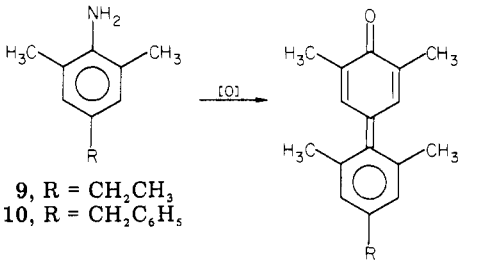
There is a conversion of aniline **6** to **7** independent of oxidizing agent. Aniline **6** was stirred in methanol–water (volumetric ratio, 1:6) with ammonium acetate for five days and converted to a mixture of **6** and **7** in a molar ratio of 3 to 1, as determined by ^{1}H NMR. A similar treatment of aniline **7** gave no reaction.

The presence of mesidine (**1**) in mixtures containing the imino methine **5** raised the possibility of an addition reaction to afford aniline **8**. This material was not detected but its synthesis and oxidation was undertaken. With tetrahydrofuran as a cosolvent in a ferricyanide oxidation anil **3** was formed in 78% yield along with 1% azomesitylene. Such a cleavage is interesting since it does not conform to afford cleavage to aldehydes.[8] The cleavage



of the carbon nitrogen bond could proceed if the benzylic nitrogen protonated due to a greater basicity compared to the primary nitrogen, which would be the side of oxidation to a cation radical.

Mesidine Analogues. The oxidations of two variations of mesidine were undertaken. When the 4-ethyl-*m*-xylidine **9** was oxidized with the methanolic dichromate system, anil



9, R = CH_2CH_3
10, R = $CH_2C_6H_5$

11, R = CH_2CH_3
12, R = $CH_2C_6H_5$

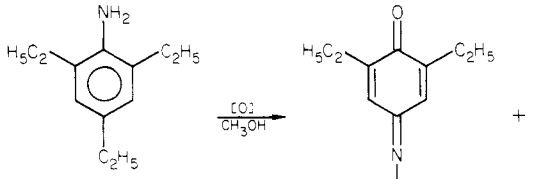
11 was formed in 73% yield. The anil was identified by comparison with material prepared by the condensation of 2,6-dimethyl-1,4-benzoquinone and aniline **9**. A small amount of impure anils was isolated but not characterized. A strong peak in the mass spectrum of impure material displayed base peaks at 295 (suggestive of an ethyl group rather than a methoxyethyl group (325)), analogous to anil **4**. The ^{1}H NMR had one peak at 6.4 ppm and none at 7.1 ppm, characteristic of anils substituted at the 3 position as in anil **4**. There were no peaks in the 3.0 to 3.5 ppm region characteristic of methoxyl protons. We infer from these data that there is an ethyl shift rather than a methoxyethyl shift. When the oxidation was carried out

(5) Kon, E.; McNelis, E. *J. Org. Chem.* **1975**, *40*, 1515.
(6) Evans, R. M. *Quart. Rev. (London)* **1959**, *13*, 61.
(7) Hedayatulla, M.; Dechatre, J. P.; Denivelle, L. *Tetrahedron Lett.* **1975**, 2039.
(8) Audeh, C. A.; Lindsay-Smith, J. R. *J. Chem. Soc. B* **1971**, 1741.

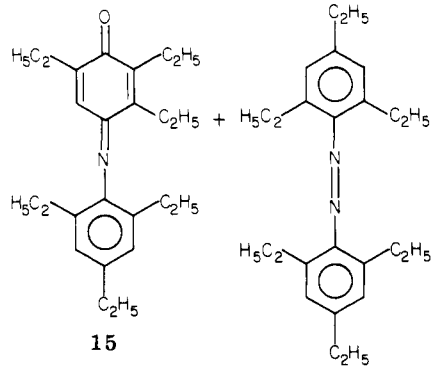
without the use of any cosolvent in the dichromate system, the yield of anil 11 was 86% and no shifted anil was detected.

The aniline 10 was subjected to oxidation with the methanolic ferricyanide system. Here again at least two anils were formed in addition to benzaldehyde, the end product of the eliminated benzyl group, and the azo compound (7%). The melting point of anil 12 was undepressed upon admixture of the product from aniline 10 and 2,6-dimethyl-1,4-benzoquinone. Its yield was 40%. Again another anil fraction seemed to be a mixture of shifted products. The presence of a methoxylated product was suggested by a base peak of 451 in the mass spectrum of the purple oil after it had been reduced by ascorbic acid to white crystals, mp 107–108 °C. However, no methoxy hydrogens were seen in the ^{1}H NMR which featured the characteristics of a shifted anil—one peak at 6.4 ppm. Since the mass spectrum of the reduced mixture of anils had a peak at 421 (70%), consistent with a 3-benzyl group, the major portion of the shifted anils would be from a benzylic group migration.

Similar findings were obtained for 2,4,6-triethylaniline (13) which upon oxidation with methanolic dichromate led



13 14

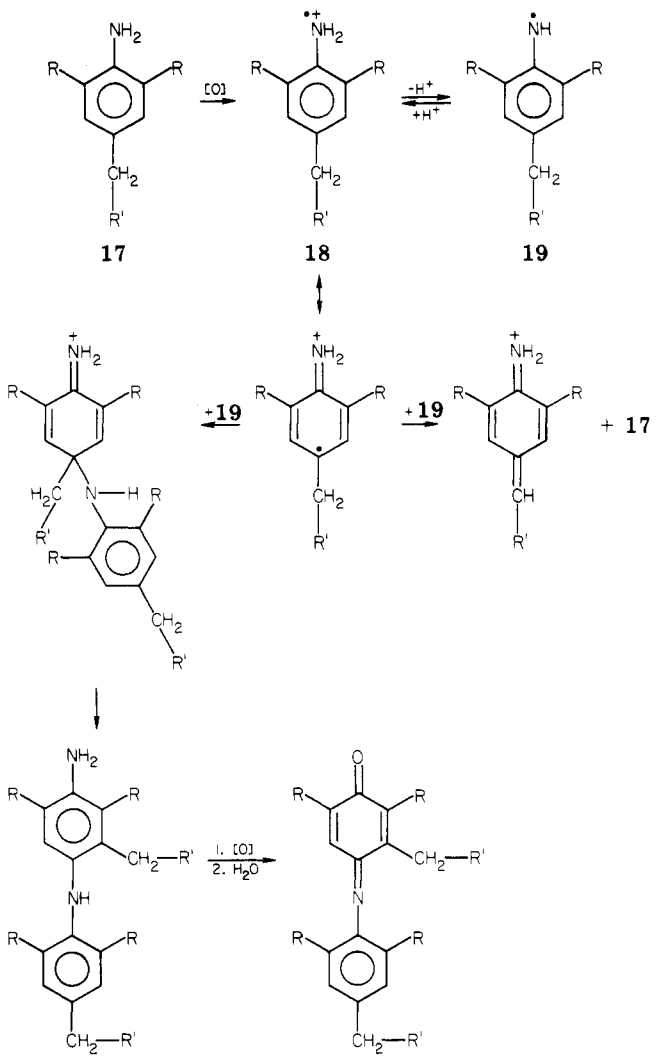


15 16

to anil 14 in 55% yield. It was identified by hydrolysis to its components, a mass spectrum with a base peak at 323 (M^+), an infrared spectrum similar to anil 3, and a ^{1}H NMR spectrum with two olefinic protons at 6.4 and 7.1 ppm. A small amount of anil-like material showed the single peak at 6.4 ppm and no methoxyl absorption in the ^{1}H NMR. The mass spectral base peak was at 351, ascribable to a 3-ethyl anil 15 with a small peak (20%) at 380, an ($M^+ - 1$) for a 3-methoxyethyl anil analogous to anil 4. The azo compound 16 was the sole product of oxidation of 13 with methanolic ferricyanide.

Anils 11, 12, and 14 were prepared by condensations of the parent anilines and the appropriate quinones. The preparation of anil 4 and aniline 7 were outlined previously.[1] The details are given in the Experimental Section. These experiments with three analogues of mesidine afforded no evidence for a general methoxyalkyl migration. The anils formed by oxidative dealkylation predominated.

Scheme I



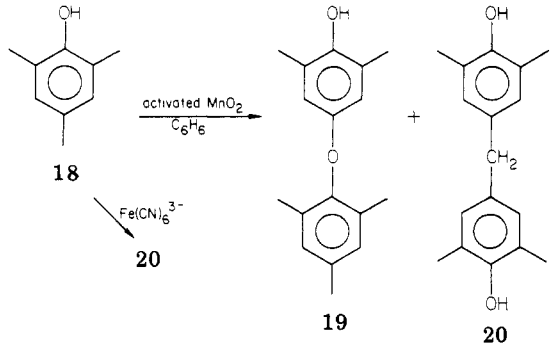
There might be a relation between the relative rates of addition of methanol and water to the intermediate amino methides. As the bulk of the methide center increases, the addition of water would be preferred to the addition of methanol. The inference of alkyl shift also can be related to a slowing in the rate of benzylic abstraction by an aniline radical to give an imino methide and to a coupling of the radical and cation radical as shown in Scheme I.

These indications of alkyl shifts have some precedence in the extensive work of the Saunder's group with vegetable peroxidases and anilines. Their first report of the shifted alkyl group was a methyl shift in 2,4-dimethylaniline's oxidation whereby a small amount of a bisanil with a central 2,5-dimethyl-*p*-benzoquinone was isolated.[9] Later, a most striking case was reported for 4-cyclohexyl-2,6-dimethylaniline in which oxidation by peroxidase led to a shifted anil, 3-cyclohexyl-2,6-dimethyl-*p*-benzoquinone 4-(4-cyclohexyl-2,6-dimethylanil), in 64% yield.[10] An analogous anil was isolated after the oxidation of 4-*tert*-butyl-2,6-dimethylaniline in 6% yield. No shift was observed for the corresponding 4-isopropyl isomer, which did undergo a mesidine-like oxidative dealkylation as the sole reaction path.

Comparison with Phenolic Oxidations. In the oxidative dealkylation of mesitol 18 with activated manganese

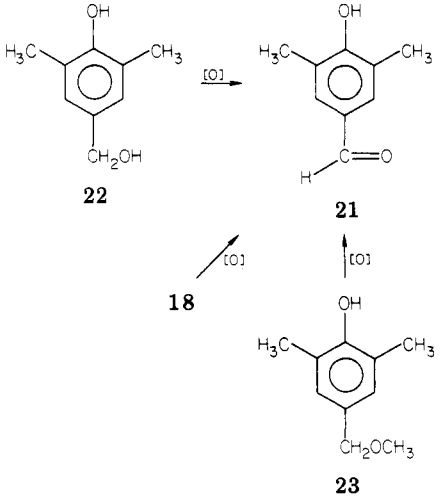
(9) Holland, V. R.; Roberts, B. M.; Saunders, B. C. *Tetrahedron* **1969**, *25*, 2291.
(10) Baker, P. B.; Holland, V. R.; Saunders, B. C. *Tetrahedron* **1973**, *29*, 85.

dioxide, quinone methides were formed and reacted with water to give a *p*-hydroxybenzyl alcohol, suitable for loss of formaldehyde after a subsequent coupling step.[3] Unlike



the mesidine case, the reaction could proceed by either O–C coupling to give phenol **19** or by C–C coupling to give the bisphenol **20**. The possibility of C–C coupling in mesidine is not ruled out but no evidence for the formation of a bisaniline analogue of **20** or an oxidized form has been obtained.

When mesitol was treated with the methanolic ferricyanide system the bisphenol **20** was isolated in 55% yield. Some phenol **19** was detected with its polymeric forms in less than 10% yield. With the methanolic dichromate oxidizing mixture the sole isolated product (70% yield) was 3,5-dimethyl-4-hydroxybenzaldehyde (**21**). Oxidative



dealkylation with the dichromate did not take place even with 2,6-dimethyl-4-(hydroxymethyl)phenol (**22**) which was converted to the aldehyde **21** in 90% yield. A similar high yield (89%) of aldehyde **21** was obtained with a possible candidate for a shift reaction, 2,6-dimethyl-4-(methoxymethyl)phenol (**23**). These results suggest that the ferricyanide oxidation proceeded in a one-electron oxidation fashion whereas the dichromate behaved in the two-electron mode via a phenolic chromate ester. Saunders reported that vegetable peroxidases oxidized mesitol to the aldehyde **21** and its corresponding alcohol rather than the products of the one-electron systems, phenol **19** and bisphenol **20**.[11]

These results with phenolic oxidations suggest that the chromium system is a better model than ferricyanide for the iron-containing peroxidases. The similarity between the chromium and the enzyme may be due to their abilities to span more than one oxidation change unlike ferricyanide which is limited to one change. Peroxidases' iron atoms range from iron(III) to an oxoiron(V) porphyrin formed by peroxides to an oxoiron(IV) prophyrin formed by reductants.[12] What is interesting in these comparisons is that the same enzyme and the two different inorganic oxidants react with mesidine to give the same products in non-methanolic media. The similarity of products obtained with the two oxidants of mesidine might suggest that both are one-electron oxidants. The vast difference in reaction rates and the results with mesitol argue against that possibility. The key imino methine intermediate can be reached by both processes. For the one-electron process a cation radical is formed first. It can lose a proton to give the neutral aniline radical which abstracts a benzylic hydrogen from another cation radical to give the imino methine as shown in Scheme I. A two-electron mode would start with a nitrogen chromium bond, whose heterolytic cleavage would promote the loss of a benzyl proton to give the neutral imino methine. The methine is protonated in the acidic media to obtain the same protonated species that resulted from the bimolecular process of the one-electron system. Another two-electron oxidation of the product from the addition of water in a 1,6-fashion affords a cation susceptible to attack by mesidine. The loss of formaldehyde proceeds and is followed by further oxidation to the anil. Indeed, this is the mechanism proposed in 1967 by Saunders for the oxidation of mesidine with horse radish peroxidase.[2] Another observation in support of this path was the need for inverse oxidant addition in the dichromate system. This suggests that the cationic form would be attacked by solvents to give cyclohexadienimino products. Such a product is formed if mesidine is oxidized by sodium periodate in aqueous methanol.[13] If the para position is not occupied, such periodate oxidations lead to imino quinones suitable for 1,4-additions and further oxidations and hydrolyses.[14] Products such as these are likely components of the seemingly intractible melange obtained with dichromate or persulfate oxidations without the inverse addition technique designed to keep mesidine available for attack on the positive species.

Experimental Section

The following instruments were used: a Varian A-60 NMR spectrometer, a Perkin-Elmer 137 IR spectrometer, and a Perkin-Elmer 202 UV/vis spectrophotometer. Mass spectra were taken on a Varian M-66 spectrometer operated by Charles H. Strom. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, MI. Melting points were determined by the use of a Thomas-Hoover Unimelt apparatus, which was checked periodically with standards supplied by A.H. Thomas Co.

Mesidine was obtained from the Aldrich Chemical Co. and purified by distillation over zinc dust through a Vigreux column. The fraction boiling at 229–230 °C was collected and stored under nitrogen. Activated manganese dioxide was obtained from Beacon Chemical Co. Sodium bismuthate was obtained from Fisher Scientific Co. Other chemicals were reagent grade from J.T. Baker Chemical Co. Solvents were distilled and dried over molecular sieves (4 Å) for at least two days.

Preparation of Anilines. Preparation of 4-(Hydroxymethyl)-2,6-dimethylbenzenamine (6). Nitromesitylene (20 g) prepared by the method of Powell and Johnson was dissolved in acetic acid (50 mL) and added to a slurry of CrO_3 (40 g) in acetic acid (450 mL).[15] After 2 h the reaction mixture was added to

(11) Booth, H.; Saunders, B. C. *J. Chem. Soc.* **1959**, 940.

(12) Dunford, H. B.; Stillman, J. S. *Coord. Chem. Rev.* **1976**, *19*, 187.

(13) Robbins, S.; McNelis, E., unpublished results, New York University.

(14) Rao, M. P.; Sethuram, B.; Rao, T. N. *Indian J. Chem.* **1979**, *17A*, 52.

(15) Powell, G.; Johnson, F. R. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. 3, p 449.

water to precipitate an acid which was dissolved in base. The basic solution was washed with ether and acidified to give a white powder, mp 170–173 °C. To the dried 3,5-dimethyl-4-nitrobenzoic acid (19.5 g) was added a suspension of $NaBH_4$ (5.6 g) in THF (300 mL) followed by BF_3 etherate (28.2 g) in THF (30 mL). The mixture was added to water and extracted with ether, which was dried and removed to a yellow oil (16 g): bp 140–142 °C (0.05 torr). The oil crystallized on standing to yellow prisms (13.5 g, 75%): mp 39–40 °C; IR (KBr) 3400 (s), 2930 (m), 1610 (m), 1540 (s), 1370 (s), 1090 (m), 1060 (s), 860 (m), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.22 (s, 6 H, Ar CH_3), 3.72 (s, 1 H, OH), 4.60 (s, 2 H, Ar CH_2), 7.10 (s, 2 H, Ar H); MS, *m/e* (%) 181 (M^+, 80), 164 (100), 134 (25). Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.59; H, 6.09; N, 7.69.

A portion (3 g) of the 2,6-dimethyl-4-nitrobenzyl alcohol was added to a solution of NaOH (3 g) in water (2 mL) and 95% ethanol (50 mL). The solution was refluxed while zinc dust (9 g) was added in small portions over 0.5 h. After a further refluxing of 1 h, the mixture was filtered and the zinc was washed with two 50-mL portions of hot ethanol and ether (25 mL). Sodium dithionate (0.5 g) was added to the washings. A brown solid was collected and crystallized twice from chlorobenzene as white needles (**6**, 64% yield): mp 93–94 °C (lit.[3] 94.5 °C); IR (KBr) 3150 (s), 2890 (m), 1610 (m), 1490 (s), 1360 (m), 1300 (m), 1240 (m), 1150 (s), 1030 (s), 990 (s), 870 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.11 (s, 6 H, Ar CH_3), 3.10 (br, 3, NH_2, OH), 4.47 (s, 2 H, Ar CH_2–O), 6.92 (s, 2, Ar H); MS, *m/e* (%) 151 (M^+, 80), 134 (65), 114 (40), 112 (100).

Preparation of 4-(Methoxymethyl)-2,6-dimethylbenzenamine (7). A solution of the above 2,6-dimethyl-4-nitrobenzyl alcohol (12.7 g) and PBr_3 (9.5 g) in ether (150 mL) was stirred overnight, washed with ice water, and dried. The ether was evaporated to a crude benzyl bromide to which was added sodium methoxide (15 g) in dry methanol (150 mL). The mixture was refluxed for 5 h and added to water (50 mL). The mixture was extracted with ether which was evaporated to a yellow oil (10 g, 73%): bp 96–8 °C (0.05 torr); IR (film) 2890 (m), 1610 (m), 1540 (s), 1450 (m), 1360 (s), 1210 (m), 1130 (s), 870 (m), 840 (s) cm^{-1}; ^1H NMR (CCl_4) δ 2.21 (s, 6 H, Ar CH_3), 3.33 (s, 3 H, O–CH_3), 4.32 (s, 2 H, Ar CH_2O–), 7.05 (s, 2 H, Ar H); MS, *m/e* (%) 195 (M^+, 100), 180 (30), 178 (70). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.47; H, 6.59; N, 7.00.

This 4-(methoxymethyl)-2,6-dimethylnitrobenzene was reduced with zinc and base as before. An etheral solution of the amine was dried and cooled to −50 °C. Gaseous HCl was passed through the solution and the hydrochloride was collected as white plates. Anal. Calcd for $C_{10}H_{16}ClNO$: C, 59.19; H, 7.88; N, 6.91. Found: C, 59.37; H, 7.93; N, 7.07.

Some of the salt was converted to the free amine **7** with NH_4OH: IR (film), 3400 (m), 2900 (m), 1660 (m), 1610 (m), 1490 (m), 1470 (s), 1440 (m), 1370 (s), 1280 (m), 1170 (m), 1100 (s), 1070 (s), 910 (m), 810 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (s, 6 H, Ar CH_3), 3.25 (s, 3 H, Ar–O–CH_3), 3.45 (s, 2 H, Ar NH_2), 4.25 (s, 2 H, Ar–CH_2–O), 6.86 (s, 2 H, Ar–H); MS, *m/e* (%) 165 (M^+, 70), 134 (100), 120 (40). The benzamide of **7** was prepared: mp 155–156 °C. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.89, H, 7.11; N, 5.26.

Preparation of *N*-(4-Amino-3,5-dimethylbenzyl)-2,4,6-trimethylbenzenamine (8). A 2 M solution of ceric ammonium nitrate (52 mL) was mixed with a solution of 3,5-dimethyl-4-nitrobenzyl alcohol (9 g) in acetic acid (50 mL). The red solution was heated on a steam bath for 0.5 h and then poured into iced water (500 mL). A white solid was collected and dissolved in $CHCl_3$ for drying over $MgSO_4$. It crystallized from a reduced volume of $CHCl_3$ and petroleum ether (30–60 °C) to white needles (8 g, 90%): mp 49–50 °C; IR (KBr) 2840 (w), 1710 (s), 1610 (m), 1530 (s), 1370 (m), 1300 (m), 1160 (m), 1080 (m), 870 (m), 840 (s) cm^{-1}; ^1H NMR (CCl_4) δ 2.38 (s, 6 H, Ar CH_3), 7.62 (s, 2 H, Ar H), 9.96 (s, 1 H, –C–H); MS, *m/e* (%) 179 (M^+, 80), 162 (100). Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.22; H, 5.04; N, 7.82.

To a solution of mesidine (1.4 g) in acetic anhydride (15 g) and 90% formic acid (27 g) was added the above 3,5-dimethyl-4-nitrobenzaldehyde. The solution was refluxed for 3 h. Water was then added to a cloud point and the solution was allowed to stand overnight. The product was isolated and recrystallized from aqueous acetic acid to give white needles (2.6 g, 85%): mp 160–161 °C); IR (KBr) 2900 (m), 1610 (m), 1530 (s), 1470 (m), 1430 (m), 1370 (s), 1220 (s), 930 (m), 860 (s), 830 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.28 (s, 15 H, Ar CH_3), 4.09 (s, 2 H, Ar CH_2N), 6.95 (s, 4 H, Ar H); MS, *m/e* (%) 297 (M^+ − 1,100), 147 (60), 117 (40).

This material was reduced with Zn/NaOH as described above to give a white powder which was recrystallized from petroleum ether (30–60 °C) to white needles: mp 118–119 °C; IR (KBr) 3400 (m), 2950 (s), 1640 (s), 1490 (s), 1450 (m), 1360 (m), 1320 (m), 1250 (m), 1210 (m), 1150 (s), 1120 (s), 1030 (m), 870 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (s, 9 H, Ar CH_3), 2.17 (s, 6 H, Ar CH_3), 3.25 (br s, 3 H, NH), 3.95 (s, 2 H, Ar CH_2N), 6.78 (s, 4 H, Ar H); MS, *m/e* (%) 268 (M^+, 15), 135 (100), 120 (65). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.39; H, 8.91; N, 10.31.

Preparation of 4-Ethyl-2,6-dimethylbenzenamine (9). The acetate of 2,6-xylenol (41 g, 250 mmol) was treated with $AlCl_3$ (40 g, 300 mmol) at 120 °C overnight. The mixture was added to ice (250 g) and concentrated (50 g). A tan powder (40 g, 96%) was isolated by filtration, mp 148–150 °C. A sample was recrystallized from ethanol, mp 150–151 °C (lit.[16] 150–151 °C). The rest of the 4-acetyl-2,6-xylenol was reduced to 4-ethyl-2,6-xylenol by the Clemmensen method of Read and Wood:[17] bp 107–110 °C (15 torr) [lit.[16] 229–230 °C (760 torr)]. The liquid crystallized on standing to give white prisms (83%): mp 36–37 °C (lit.[12] 36–37 °C); IR (KBr) 3500 (s), 2950 (s), 1490 (s), 1460 (m), 1320 (m), 1200 (s), 1150 (s), 1020 (m), 930 (m), 870 (s) cm^{-1}; ^1H NMR ($CDCl_4$) δ 1.13 (t, 3 H, J = 8, Ar CH_3), 208 (s, 6 H, Ar CH_3), 2.43 (q, 2 H, J = 8, Ar CH_2–CH_3), 4.78 (s, 1 H, Ar OH), 6.67 (s, 2 H, Ar H); MS, *m/e* (%) 150 (M^+, 35), 135 (100).

Sodium hydride (5 g) was added to a solution of 4-ethyl-2,6-xylenol (15 g, 100 mmol) in dry diglyme (35 mL). After hydrogen evolution, additional NaH (6.5 g) was added. The mixture was stirred for 5 min and 4-chloro-2-phenylquinazoline (24 g, 100 mmol) was added.[18] The mixture was stirred and heated to 110 °C for 0.5 h whereupon it was quenched in iced water (500 mL). A white powder (33 g, 96%) was collected by filtration: crude mp 110–112 °C; crystallized from ethanol, mp 112–113 °C; IR (KBr) 2950 (m), 1620 (m), 1570 (s), 1480 (m), 1380 (s), 1350 (s), 1190 (s), 1160 (m), 1140 (m), 930 (m), 860 (m), 770 (s) cm^{-1}; ^1H NMR (CF_3COOH) δ 1.34 (t, 3 H, J = 8, Ar–CH_2–CH_3), 2.21 (s, 6 H, Ar, CH_3), 2.75 (q, 2 H, J = 8, Ar–CH_2–CH_3), 7.12 (s, 2 H, Ar H), 7.58–8.34 (m, 9 H, Ar H); MS, *m/e* (%) 354 (M^+, 100), 339 (20), 206 (30).

This product, 4-(4-ethyl-2,6-dimethylphenoxy)-2-phenylquinazoline, was heated under nitrogen at 325 °C for 1.5 h to a brown solid which was crystallized from ethanol (30 g, 90%): mp 140–141 °C; IR 1700 (s), 1560 (m), 1340 (m), 870 (m), 780 (s), 770 (s) cm^{-1}. This quinazolinone was treated with KOH (64 g) in ethylene glycol (330 mL) at reflux for 3 days. After cooling the solution was added to water 1.5 L) and extracted with ether. The ether was dried over $MgSO_4$ and evaporated to a tan liquid **9** (10.3 g, 69%): bp 80–82 °C (2 torr) [lit.[19] 104–105 °C (10 torr)]; IR (film) 3500 (m), 2950 (s), 1640 (s), 1490 (s), 1340 (m), 1250 (m), 1150 (m), 870 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (t, 3 H, J = 8, Ar CH_2CH_3), 2.07 (s, 6 H, Ar CH_3), 2.47 (q, 2 H, J = 8, Ar CH_2–CH_3), 3.27 (s, 2 H, Ar NH_2), 6.72 (s, 2 H, Ar H).

The aniline was used and stored as the hydrochloride. Anal. Calcd for $C_{10}H_{16}ClN$: C, 64.84; H, 8.68; N, 7.54. Found: C, 64.60; H, 8.60; N, 7.52.

The benzamide was crystallized from ethanol as white needles, mp 183–184 °C. Anal. Calcd for $C_{19}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.61; H, 7.52; N, 5.53.

Preparation of 4-Benzyl-2,6-dimethylbenzenamine (10). 3,5-Dimethyl-4-nitrobenzoic acid (20 g) prepared as in the preparation of **6** was refluxed with $SOCl_2$ (50 g) for 3 h. After excess $SOCl_2$ was evaporated the residual oil was distilled and crystallized on standing (18 g, 82%): bp 120–122 °C (0.3 torr); mp 53–54 °C; IR (KBr) 1750 (s), 1550 (s), 1360 (s), 1300 (m), 1180 (s), 1100 (s), 1040 (m), 980 (m), 840 (s) cm^{-1}.

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The acid chloride (18 g, 85 mmol) was added to dry benzene (80 mL). The solution was cooled and $AlCl_3$ (13.3 g, 100 mmol) was added slowly. The mixture was refluxed for 1 h and then added to ice (500 g) and concentrated HCl (150 mL). After extraction with benzene and ether and evaporation of solvents a yellowish brown solid was isolated (20 g, 78%). It was crystallized from ethanol as pale yellow plates: mp 102–103 °C; IR (KBr) 1660 (s), 1610 (m), 1630 (s), 1370 (m), 1330 (s), 1320 (m), 1240 (s), 1100 (m), 900 (m), 860 (s), 800 (m) cm^{-1}; ^1H NMR (CCl_4) δ 2.37 (s, 6 H, Ar CH_3), 7.44–7.49 (m, 5 H, Ar H), 7.67 (d, 1 H, J = 2, $HArNO_2$), 7.74 (d, 1 H, J = 2, $HArNO_2$); MS, m/e (%) 255 (M^+, 100), 238 (50), 178 (30), 105 (85). Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.67; H, 5.24; N, 5.63.

3,5-Dimethyl-4-nitrobenzophenone (10 g, 40 mmol) was dissolved in hot ethanol (50 mL) and $NaBH_4$ (0.8 g, 50 mmol) was added. After the initial reaction the mixture was heated on a steam bath for 0.5 h and then added to water. Ether extraction followed. The dried ether contained a brown oil (8 g) which was dissolved in $CHCl_3$ and put onto a dry alumina column. A front band was collected and crystallized from petroleum ether (30–60 °C) to yellow prisms (6 g, 60%): mp 68–69 °C; IR (KBr) 3200 (s), 1610 (m), 1530 (s), 1440 (m), 1360 (s), 1270 (m), 1070 (m), 1040 (s), 1030 (m), 920 (m), 880 (s), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (s, 6 H, Ar CH_3), 3.25 (d, 1 H, J = 3, Ar–C–OH), 5.63 (d, 1 H, J = 3, Ar–CH(OH)–), 7.10 (s, 2 H, Ar–H), 7.30 (s, 5 H, Ar–H); MS, m/e (%) 257 (M^+, 70), 178 (45), 105 (100). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.04; H, 5.71; N, 5.55.

3,5-Dimethyl-4-nitrobenzhydrol (5 g) in ethanol (150 mL) was hydrogenated in the presence of 10% Pd/C (0.5 g) and concentrated HCl (15 mL). The catalyst was removed by filtration through Celite and the residue was washed with hot ethanol. The filtrate and washings were evaporated to the cruve amine **10** hydrochloride. It crystallized from ethanol–ether as white plates (4 g, 80%): ^1H NMR (CF_3COOH) δ 2.35 (s, 6 H, Ar CH_3), 3.90 (s, 2 H, Ar–CH_2), 7.0 (s, 2 H, Ar–H), 7.23 (s, 5 H, Ar–H). Anal. Calcd for $C_{15}H_{18}ClN$: C, 72.72; H, 7.32; N, 5.65. Found: C, 72.50; H, 7.59; N, 5.62.

Some of the salt was converted to the free amine **10** with aqueous NH_3: IR (film) 3400 (m), 2950 (m), 1640 (s), 1610 (m), 1490 (s), 1460 (m), 1750 (m), 1150 (m), 1070 (m), 1030 (m), 870 (br m) cm^{-1}; MS, m/e (%) 211 (M^+, 10), 155 (100), 120 (70).

The benzamide of **10** crystallized from aqueous ethanol as white needles: mp 190–191 °C. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.72; H, 6.52; N, 4.42.

Preparation of 2,4,6-Triethylbenzenamine (13). 1,3,5-Triethylbenzene was prepared from benzene, $AlCl_3$, and bromoethane by the method of Norris and Rubinstein:[20] bp 212–216 °C; IR (film) 3050 (s), 1670 (s), 1540 (s), 1430 (m), 1380 (m), 1120 (m), 900 (m), 870 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.19 (t, 9 H, J = 8, Ar–CH_2–CH_3), 2.55 (q, 6 H, J = 8, Ar–CH_2–CH_3), 6.80 (s, 3 H, Ar H); MS, m/e (%) 162 (M^+, 60), 147 (100), 133 (60).

The triethylbenzene was nitrated by the procedure of Powell and Johnson.[21] The crude material was purified by fractional distillation to a pale yellow liquid (70%): bp 100–102 °C (2 torr); IR (film) 3050 (s), 2960 (m), 1620 (s), 1540 (s), 1470 (s), 1380 (s), 1100 (m), 1070 (m), 1060 (m), 910 (m), 880 (s), 840 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.19 (t, 9 H, J = 8, Ar–CH_2–CH_3), 2.55 (q, 4 H, J = 8, 2/6-Ar–CH_2–CH_3), 2.62 (q, 2 H, J = 8, 4-Ar–CH_2–CH_3), 7.04 (s, 2 H, Ar–H).

2,4,6-Triethylnitrobenzene (15 g) was hydrogenated in the presence of 5% Pd/C (1 g) in ethanol. After catalyst removal and ethanol evaporation, a residual oil was taken up in ether and dried over $MgSO_4$. Dry HCl was bubbled through the solution to form the hydrochloride as white plates (12.5 g, 80%): ^1H NMR (CF_3COOH) δ 1.28 (t, 3 H, J = 8, 4-Ar–CH_2–CH_3), 1.33 (t, 6 H, J = 8, 2/6-Ar–CH_2–CH_3), 2.74 (q, 2 H, J = 8, 4-Ar–CH_2–CH_3), 2.83 (q, 4 H, J = 8, 2/6-Ar–CH_2–CH_3), 7.22 (s, 2 H, Ar H).

Some of the salt was converted to the amine **13** with NH_4OH: IR (film) 3400 (m), 3050 (s), 2950 (m), 1640 (s), 1480 (s), 1460 (s), 1360 (m), 1320 (m), 1290 (m), 1240 (m), 1150 (m), 1060 (m), 880 (s) cm^{-1}; MS, m/e (%) 177 (M^+, 50), 162 (100); acetanilide mp 148–149 °C (lit.[22] 149.5 °C); benzamide mp 180–181 °C (lit.[22] 181.3 °C).

Preparation of Anils. Preparation of 2,6-Dimethyl-*p*-benzoquinone 4-(2,4,6-Trimethylanil) (3). Mesidine (0.52 g, 3.8 mmol) was added to a solution of 2,6-dimethylbenzoquinone (0.55 g, 4.0 mmol) in water (50 mL) containing acetic acid (0.5 mL). The mixture was stirred for one day and allowed to stand for ten days. The supernatant liquid was decanted. The residue was suspended in water and filtered. A purple solid was recrystallized from aqueous methanol as lustrous purple plates (0.22 g, 70%): mp 96–97 °C (lit.[23] mp 97 °C); IR (KBr) 2970 (m), 1650 (s), 1610 (m), 1470 (m), 1320 (m), 1220 (s), 1210 (m), 1130 (m), 1040 (m), 1030 (m), 940 (m), 920 (s), 860 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.89 (s, 6 H, 2/6-*N*-Ar–CH_3), 1.90 (s, 3 H, 4-*N*-Ar–CH_3), 2.08 (d, 3 H, J = 1, anti CH_3), 2.28 (s, 3 H, syn CH_3), 6.34 (m, 1 H, syn H), 6.79 (s, 2 H, Ar H), 7.08 (m, 1 H, anti H); MS, m/e (%) 253 (M^+, 100), 224 (40).

Anil **3** (0.17 g) was dissolved in 50% aqueous methanol (20 mL). Ascorbic acid (1 g) was added and the color faded to a pale yellow. The volume of the solution was reduced until a precipitate formed (0.13 g, 75%). It was recrystallized to white plates: mp 120 °C; IR (KBr) 3400 (s), 2920 (s), 1610 (m), 1500 (s), 1470 (s), 1220 (s), 1030 (m), 850 (m), 840 (m) cm^{-1}; MS, m/e (%) 255 (M^+, 100), 238 (10).

Preparation of 2,6-Dimethyl-3-(methoxymethyl)-*p*-benzoquinone 4-(2,4,6-Trimethylanil) (4). Aluminum chloride (44.3 g, 0.33 mmol) was added slowly with cooling to a solution of 2,6-dimethylnitrobenzene (50 g, 0.33 mmol) and chloromethyl ether (26.6 g, 0.33 mmol). The mixture was stirred for 1 h while the temperature was kept below 20 °C and then added to ice (500 g) and concentrated HCl (200 mL). The aqueous layer was decanted and extracted with ether. The remaining solid was digested with ether. The ether extracts were combined, dried over $MgSO_4$ and evaporated to a clear oil (50 g). The oil (2,4-dimethyl-3-nitrobenzyl chloride) was distilled at reduced pressure. The distillate crystallized and was recrystallized from methanol as white prisms: mp 61–62 °C; IR (KBr) 2950 (m), 1530 (s), 1450 (m), 1370 (s), 1260 (m), 1180 (m), 1030 (m), 960 (m), 880 (s), 840 (s), 800 (s) cm^{-1}; ^1H NMR (CCl_4) δ 2.25 (s, 3 H, Ar CH_3), 2.27 (s, 3 H, Ar CH_3), 4.55 (s, 2 H, Ar CH_2Cl), 7.08 (d, 1 H, J = 8, 3-Ar H), 7.33 (d, 1 H, J = 8, 2-Ar–H); MS, m/e (%) 201 (M^+, 20), 199 (M^+, 100), 184 (30), 182 (90), 164 (40), 146 (30). Anal. Calcd for $C_9H_{10}ClNO_2$: C, 54.14; H, 5.05; N, 7.01. Found: C, 54.20; H, 5.02; N, 7.35.

A mixture of the benzyl chloride (20 g), sodium methoxide (20 g), and absolute methanol (150 mL) was refluxed for 24 h and added to ice (600 g). The mixture was extracted with benzene. The dried benzene was evaporated to an oil (20 g). Vacuum distillation at 0.1 torr gave three fractions at 100–105 °C, 105–109 °C, and 109–112 °C. The second and third fractions were combined and crystallized from methanol as white prisms (7 g, 37%) of 2,6-dimethyl-3-(methoxymethyl)nitrobenzene: mp 46–47 °C; IR (KBr) 2950 (m), 1540 (s), 1450 (m), 1370 (s), 1210 (s), 1120 (s), 1050 (m), 1040 (m), 990 (m), 830 (s), 810 (m) cm^{-1}; ^1H NMR (CCl_4) δ 2.13 (s, 3 H, Ar CH_3), 2.20 (s, 3 H, Ar CH_3), 3.33 (s, 3 H, –OCH_3), 4.37 (s, 2 H, Ar CH_2–OCH_3), 7.07 (d, 1 H, J = 8, 5-Ar H), 7.28 (d, 1 H, J = 8, 4-Ar–H); MS, m/e (%) 195 (M^+, 30), 180 (30), 163 (100), 146 (50). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.67; H, 6.74; N, 7.24.

This nitrobenzene (3 g) was added to a solution of H_2O (2 mL) and 95% ethanol (50 mL) containing NaOH (3 g). The solution was refluxed while zinc dust (9 g) was added in small portions over 0.5 h. After an additional refluxing for 1 h, the mixture was filtered and the zinc was washed with 2 portions (50 mL) of boiling ethanol and ether (25 mL). The filtrate and washings to which was added sodium dithionate (0.5 g) were heated until most of the ethanol was removed. A white solid formed. The 2,6-dimethyl-3-(methoxymethyl)aniline was collected and crystallized from aqueous methanol as white plates (2.4 g, 94%): mp 61–62 °C; IR (KBr) 3400 (s), 2950 (s), 1660 (s), 1580 (m), 1500 (m), 1470 (s), 1430 (s), 1370 (s), 1330 (m), 1280 (s), 1260 (m), 1180 (s), 1170 (m), 1100 (s), 1070 (s), 950 (m), 900 (s), 810 (s), cm^{-1}; ^1H NMR

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($CDCl_3$) δ 2.15 (s, 3 H, Ar CH_3), 2.17 (s, 3 H, Ar CH_3), 3.37 (s, 3 H, OCH_3), 3.60 (m, 2 H, D_2O exch, NH_2), 4.44 (s, 2 H, Ar–CH_2–OCH_3), 6.70 (d, 1 H, J = 8, 5-Ar, H), 6.97 (d, 1 H, J = 8, 4-Ar–H); MS, m/e (%) 165 (M^+, 100), 133 (90), 120 (20). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.75; H, 9.22; N, 8.56.

This aniline (4.34 g, 26 mmol) in acetone (100 mL) was added to Fremy's salt (30 g) in 0.17 M NaH_2PO_4 (400 mL) and water (600 mL).[24] The solution was stirred for 1.5 h and extracted with $CHCl_3$. The solvent was evaporated to yield a reddish yellow oil (4.5 g) which was chromatographed on alumina with $CHCl_3$ as eluant. The leading yellow band was collected and evaporated to a yellow oil (3.8 g). The oil was sublimed at 60 °C (0.5 torr) to give 2,6-dimethyl-3-(methoxymethyl)-*p*-benzoquinone (2.9 g, 61%) as yellow needles: mp 33 °C; IR (KBr) 2950 (m), 1660 (s), 1380 (m), 1320 (m), 1260 (s), 1190 (m), 1120 (s), 1080 (s), 990 (m), 950 (m), 920 (m), 880 (m), 800 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.07 (d, 3 H, J = 1.5, 6-CH_3), 2.15 (s, 3 H, 2-CH_3), 3.38 (s, 3 H, –OCH_3), 4.33 (s, 2 H, C–CH_2–OCH_3), 6.67 (q, 1 H, J = 1.5, vinyl H); MS, m/e (%) 180 (M^+, 100), 165 (60), 151 (40), 137 (40). Anal. Calcd for $C_{10}H_{12}O_2$: C, 66.65; H, 6.71. Found: C, 66.82; H, 6.65.

Anil **4** (0.30 g, 1 mmol) in 3 N H_2SO_4 (100 mL) was refluxed for 10 min and then steam distilled until the distillate was colorless. The distillate was extracted with ether. The ether was evaporated to an oil which was sublimed at 60 °C (0.5 torr) to yellow prisms (42 mg, 25%), mp 33 °C. This material's melting point was undepressed with the 2,6-dimethyl-3-(methoxymethyl)-*p*-benzoquinone synthesized as above. The mesidine in the acidic distilland was recovered as the benzamide, mp 204 °C, undepressed with authentic material.[25]

Formation of anil **4** by the condensation procedure given above for anil **3** was not successful.

Anil **4** was isolated by wet chromatography (alumina with $CHCl_3$ as eluant) of oxidation mixtures of mesidine. It is a viscous purple oil: IR (film) 2950 (s), 1640 (s), 1540 (m), 1470 (s), 1430 (m), 1350 (m), 1260 (m), 1230 (s), 1180 (m), 1150 (m), 1110 (s), 1070 (s), 1030 (m), 990 (m), 950 (m), 920 (m), 890 (m), 850 (s), 790 (m), 750 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.97 (s, 9 H, Ar CH_3), 2.10 (s, 3 H, 2-CH_3), 2.32 (br s, 3 H, 6-CH_3), 3.44 (s, 3 H, –OCH_3), 4.75 (s, 2 H, –CH_2–OCH_3), 6.44 (q, 1 H, J = 1.5, vinyl H), 6.88 (s, 2 H, Ar H); MS, m/e (%) 297 (M^+, 50), 282 (100), 266 (30), 252 (35); UV/VIS λ_{max} (log ε) 209 (4.35), 277 (4.35), 515 (3.15) nm. Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76974; H, 7.80; N, 4.71. Found: C, 76.39; H, 7.60; N, 4.79.

Preparation of 2,6-Dimethyl-*p*-benzoquinone 4-(4-Ethyl-2,6-dimethylanil) (11). The procedure used for anil **3** was used in a reaction between 2,6-dimethylbenzoquinone (0.55 g, 4 mmol) and 4-ethyl-2,6-dimethylbenzenamine (0.60 g, 4 mmol) in water (50 mL) and acetic acid (0.5 mL). The anil was purified by dry column chromatography (alumina) to a purple oil (0.59 g, 63%) which could not be crystallized: IR (film) 2950 (s), 1650 (s), 1620 (m), 1580 (m), 1460 (s), 1440 (m), 1370 (m), 1320 (s), 1220 (s), 1130 (m), 1020 (m), 940 (s), 910 (s), 870 (s), 780 (m) cm^{-1}; ^1H NMR (CCl_4) δ 1.22 (t, 3 H, J = 8, Ar–CH_2–CH_3), 1.90 (d, 3 H, J = 1.5, syn CH_3), 1.97 (s, 6 H, 2,6-Ar CH_3), 2.08 (d, 3 H, J = 1.5, anti CH_3), 2.58 (q, 2 H, J = 8, Ar–CH_2–CH_3), 6.47 (q, 1 H, J = 1.5, syn vinyl), 6.88 (s, 2 H, Ar H), 7.17 (q, 1 H, J = 1.5, anti vinyl); MS, m/e (%) 267 (M^+, 100), 252 (75), 238 (40).

Preparation of 2,6-Dimethyl-*p*-benzoquinone 4-(4-Benzyl-2,6-dimethylanil) (12). A reaction of 2,6-dimethyl-*p*-benzoquinone (0.28 g, 2.1 mmol) and 4-benzyl-2,6-dimethylbenzenamine (0.42 g, 2 mmol) was carried out as for anil **3**. A purple solid from the dry chromatography was crystallized from aqueous methanol to purple needles (0.33 g, 50%): mp 114–115 °C; IR (KBr) 2950 (m), 1650 (s), 1610 (m), 1560 (m), 1490 (m), 1470 (m), 1450 (m), 1350 (m), 1320 (m), 1220 (s), 1130 (m), 1020 (m), 940 (m), 910 (s), 870 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08 (d, 3 H, J = 1.5, syn CH_3), 2.17 (s, 6 H, 2,6-Ar–CH_3), 2.22 (d, 3 H, J = 1.5, anti CH_3), 3.87 (s, 2 H, Ar–CH_2–), 6.62 (q, 1 H, J = 1.5, syn vinyl), 6.80 (q, 1 H, J = 1.5, anti vinyl), 6.86 (s, 2 H, Ar–H), 7.30 (s, 5 H, Ar H); MS, m/e (%) 329 (M^+, 100), 314 (20), 300 (25).

Preparation of 2,6-Diethyl-*p*-benzoquinone. A mixture of 2,6-diethylaniline (1.49 g, 10 mmol), acetone (50 mL), Fremy's salt (6 g), 0.17 M KH_2PO_4 (100 mL), and water (200 mL) was stirred for 1.5 h. The solution was extracted with chloroform, which was evaporated to a dark oil and subjected to dry column chromatography. The first band was collected and evaporated to give a yellow solid, which was crystallized from petroleum ether (30–60 °C) as yellow needles (0.51 g, 30%): mp 34–35 °C (lit.[26] 35 °C); IR (KBr) 2950 (m), 1650 (s), 1610 (m), 1450 (m), 1280 (s), 1180 (m), 920 (s), 860 (s), 820 (m) cm^{-1}; ^1H NMR (CCl_4) δ 1.16 (t, 6 H, J = 8, CH_3), 2.48 (q, 4 H, J = 8, CH_2), 6.48 (s, 2 H, Ar H); MS, m/e (%) 164 (M^+, 85), 136 (40), 121 (100).

Preparation of 2,6-Dimethyl-4-(methoxymethyl)phenol (23). Mesitol (8.16 g, 60 mmol) was dissolved in dry methanol (300 mL). As the solution was agitated by a stream of nitrogen, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (3.6 g, 60 mmol) was added in small portions. The nitrogen was stopped and the flask was stoppered. The solution was stirred overnight and then the methanol was evaporated. Two portions (100 mL) of boiling benzene were added to the residue. The benzene, after filtration, was evaporated to a tan semisolid which was subjected to dry column chromatography (alumina/chloroform) to afford a colorless oil. The oil was distilled, bp 82–84 °C (2 torr), but crystallized on cooling to white prisms (5.4 g, 55%): mp 52–53 °C (lit.[3] 54–55 °C); IR (KBr) 3500 (s), 2950 (s), 1490 (s), 1380 (m), 1320 (m), 1220 (s), 1160 (s), 1080 (m), 1030 (m), 990 (s), 880 (m), 850 (m), 820 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21 (s, 6 H, Ar CH_3), 3.34 (s, 3 H, OCH_3), 4.30 (s, 2 H, Ar CH_2O), 5.00 (br s, 1 H, Ar OH), 6.92 (s, 2 H, Ar H); MS, m/e (%) 166 (M^+, 65), 135 (100), 121 (45).

Oxidation Procedures. (a) Ferricyanide. A mixture of the aniline (10 mmol), ammonium acetate (80 g), potassium ferricyanide (25 g), water (600 mL), and cosolvent (methanol or THF, 100 mL) was stirred for ten days at 45 °C. The mixture was extracted with benzene which was washed with 1 M HCl. The benzene was evaporated and the residue was separated into components by wet or dry column chromatography on alumina.[27] The acidic layer was made basic and extracted with ether after cooling. The ether was dried over $MgSO_4$ and evaporated to a residue examined for starting aniline by IR.

(b) Dichromate. An oxidizing solution was prepared by dissolving potassium dichromate (3.0 g) in water (50 mL) and acetic acid (5 mL). Half of the solution was added slowly to a stirred solution of aniline (10 mmol), water (50 mL), acetic acid (5 mL), and cosolvent (20 mL). After the mixture was stirred at room temperature for 2 h, the remaining oxidizing solution was added dropwise. Additional stirring was carried out for 2 h. The mixture was extracted with benzene, which was washed with 5% $NaHCO_3$. The benzene was evaporated to a residue which was analyzed by wet or dry column chromatography on alumina.

(c) Persulfate. Ammonium or potassium persulfate (20 mmol) in 50 mL of water was added to a solution of amine (10 mmol), $AgNO_3$ (0.5 g), 20 mL of methanol, and 50 mL of water. After a stirring for 2 h, additional persulfate (10 mmol) in 20 mL of water was added. Stirring continued for two more hours. Extraction followed with benzene, which was washed with 1 M HCl, 5% $NaHCO_3$, and water. After the evaporation of benzene the residues were separated as above.

Oxidation of 2,4,6-Triethylbenzenamine (13). Aniline **13** (10 mmol) was treated with concentrated NH_4OH (20 mmol) and oxidized with the methanolic ferricyanide system. The residue after workup was subject to dry column chromatography to give **13** (29% recovery) and azotriethylbenzene as a red oil (48%): IR (film) 2950 (s), 1490 (s), 1440 (s), 1350 (m), 1320 (m), 1260 (m), 1080 (s), 1060 (s), 870 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.20 (m, 18 H, –CH_3), 2.73 (m, 12 H, Ar CH_2), 7.01 (s, 4 H, Ar H); MS, m/e (%) 350 (M^+, 65), 335 (85), 209 (50), 190 (100), 161 (50), 148 (55), 132 (50).

The hydrochloride of aniline **13** (5.7 mmol) was treated with 1 M NaOH (5.8 mL) and oxidized with methanolic dichromate. The benzene extracts were separated by wet column chromatography (alumina). The anil compound was isolated as a purple oil (55% yield): IR (film) 3000 (s), 1640 (s), 1610 (m), 1570 (m),

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1450 (s), 1370 (m), 1330 (s), 1250 (m), 1210 (s), 1140 (m), 1060 (m), 920 (s), 870 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.1 (m, 15 H, CH_3), 2.3 (m, 10 H, CH_2), 6.43 (m, 1 H, syn vinyl H), 6.88 (s, 2 H, Ar H), 7.14 (m, 1 H, anti-vinyl H); MS, *m/e* (%) 323 (M^+, 100), 308 (70), 294 (85), 280 (40).

A small amount (3%) of another purple oil was isolated by means of chromatography: IR (film) 3000 (s), 1640 (s), 1610 (m), 1570 (m), 1440 (s), 1370 (m), 1330 (m), 1310 (m), 1280 (m), 1260 (m), 1210 (s), 1150 (m), 1060 (s), 920 (m), 900 (m), 870 (s) cm^{-1}; ^1H NMR (CCl_4) δ 1.15 (m, 18 H, CH_3), 2.45 (m, 12 H, $-CH_2$), 6.35 (m, 1 H, syn vinyl H), 6.87 (s, 2 H, Ar H); MS, *m/e* (%) 380 (20), 351 (M^+, 100), 336 (10), 323 (20).

Anil **14** (0.34 g, 1 mmol) was hydrolyzed in refluxing 3 N H_2SO_4 with concurrent steam distillation. 2,6-Diethyl-*p*-benzoquinone (0.090 g, 50%) was isolated from the distillate: mp 34–35 °C, undepressed with authentic quinone. The acidic distilland was made basic to form **13** which was characterized as the benzamide (195 mg, 70%): mp 180–181 °C, undepressed with authentic benzamide of **13**.[22]

Oxidations of Phenols. Oxidation of Mesitol with Ferricyanide. Mesitol (4.08 g, 30 mmol) was oxidized with the methanolic ferricyanide system as used above for the oxidations of anilines. The reaction mixture was extracted with four protions (100 mL) of benzene. The benzene extracts were washed with 5% NaOH (4 × 100 mL). The base was acidified with concentrated HCl and the resultant mixture was filtered. The filtrate was extracted with ether and its residue was combined with the precipitate for treatment with dry column chromatography (alumina/chloroform). A mobile band was evaporated to a white solid (2.1 g, 55%), crystallized from aqueous methanol, mp 173–174 °C, undepressed with authentic (4,4′-dihydroxy-3,3′,5,5′-tetramethyldiphenyl)methane.

Oxidation of Mesitol with Dichromate. Mesitol (1.36 g, 70 mmol) was oxidized with the methanolic dichromate system as used before for the oxidations of anilines. After 2 h a large amount of a precipitate had formed. After 4 h, the mixture was filtered and the solid was crystallized from aqueous methanol as white prisms (1.04 g, 70%): mp 113–114 °C, undepressed with authentic 3,5-dimethyl-4-hydroxybenzaldehyde (**21**).

Oxidation of 2,6-Dimethyl-4-(hydroxymethyl)phenol (22). Phenol **22** (1.52 g, 10 mmol) was oxidized with the methanolic ferricyanide system. After 4 h he mixture was filtered to afford a tan solid, mp 111–114 °C. The solid was crystallized from aqueous methanol to give white prisms (1.35 g, 90%): mp 113–114 °C, undepressed when mixed with authentic **21**.

Oxidation of 2,6-Dimethyl-4-(methoxymethyl)phenol (23). Phenol **23** (1.66 g, 10 mmol) was oxidized with the ferricyanide system without methanol as cosolvent. Ether extracts of the reaction mix were evaporated to a tan solid, which was crystallized from benzene to white prisms (1.27 g, 82%): mp 114–115 °C, undepressed with authentic **21**.

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Registry No. **1**, 88-05-1; **1** (benzamide), 4476-12-4; **3**, 14033-86-4; **4**, 40113-57-3; **6**, 89210-26-4; **7**, 40113-63-1; **7**·HCl, 89210-29-7; **7** (benzamide), 89210-30-0; **8**, 89210-27-5; **9**, 40813-99-8; **9**·HCl, 89210-34-4; **9** (benzamide), 89210-35-5; **10**, 16819-52-6; **10**·HCl, 89210-38-8; **10** (benzamide), 89210-39-9; **11**, 89210-41-3; **12**, 89210-42-4; **13**, 19779-32-9; **13**·HCl, 89210-40-2; **13** (benzamide), 19779-32-9; **14**, 89210-43-5; **22**, 4397-14-2; **23**, 5048-02-2; 2,6-dimethyl-4-nitrobenzyl alcohol, 89210-28-6; 4-(methoxymethyl)-2,6-dimethylnitrobenzene, 40113-64-2; 2,6-dimethyl-4-nitrobenzyl bromide, 89210-31-1; 4-acetyl-2,6-xylenol, 5325-04-2; 4-ethyl-2,6-xylenol, 10570-69-1; 4-(4-ethyl-2,6-dimethylphenoxy)-2-phenylquinazoline, 89210-32-2; 2-phenyl-3-(4-ethyl-2,6-dimethylphenyl)-4(3*H*)-quinazolinone, 89210-33-3; 3,5-dimethyl-4-nitrobenzoyl chloride, 3558-73-4; 3,5-dimethyl-4-nitrobenzophenone, 89210-36-6; 3,5-dimethyl-4-nitrobenzhydrol, 89210-37-7; 1,3,5-triethoxybenzene, 102-25-0; 2,6-dimethyl-4-(2,4,6-trimethylamino)phenol, 89231-62-9; 2,4-dimethyl-3-nitrobenzyl chloride, 40113-60-8; 2,6-dimethyl-3-(methoxymethyl)nitrobenzene, 40113-61-9; 2,6-dimethyl-3-(methoxymethyl)aniline, 40113-62-0; 2,6-dimethyl-3-(methoxymethyl)-*p*-benzoquinone, 40113-58-4; 4-benzyl-2,6-dimethylbenzenamine, 40113-62-0; (4,4′-dihydroxy-3,3′,5,5′-tetramethyldiphenyl)methane, 5384-21-4; ferricyamide, 13408-62-3; persulfate, 15092-81-6; dichromate, 13907-47-6; ammonium persulfate, 7727-54-0; potassium persulfate, 7727-21-1; potassium dichromate, 7778-50-9; 3,5-dimethyl-4-nitrobenzoic acid, 3095-38-3; 2,6-xylenol acetate, 876-98-2; 4-chloro-2-phenylquinazoline, 6484-25-9; benzene, 71-43-2; bromoethane, 74-96-4; 2,4,6-triethylnitrobenzene, 13402-30-7; 2,6-dimethylbenzoquinone, 527-61-7; L-ascorbic acid, 50-81-7; 2,6-dimethylnitrobenzene, 81-20-9; chloromethyl ether, 542-88-1; methanol, 67-56-1; 2,6-diethylaniline, 579-66-8; 2,6-diethyl-*p*-benzoquinone, 50348-20-4; mesitol, 527-60-6; potassium ferricyanide, 13746-66-2; 3,5-dimethyl-4-hydroxybenzaldehyde, 2233-18-3; nitromesitylene, 603-71-4.