precluded the collection of accurate data with these products. Intact ferrichrome, in contrast to the iron-free molecule, is only very slowly attacked by periodic acid.

*Determination of active acyl function.* Exactly 10 mg. (100 μmoles) of succinic anhyride was dissolved in a mixture of 0.2 ml. each of 4*M* *N*-methylhydroxylamine·hydrochloride and 3.5*N* sodium hydroxide. The solution was diluted to 2.0 ml. and a 0.2 ml. volume was placed on a 5 × 60 mm. column of analytical grade Dowex 50W4H. Water was washed through the column to give an effluent volume of 5.0 ml. Aliquots of 0.1, 0.2, and 0.3 ml. were analyzed with 0.5 ml. of 0.05% periodic acid solution and a drop of glycerol in a final volume of 3.0 ml. as described above. Separate aliquots of 0.5, 1.0, and 1.5 ml. were analyzed with 1.5 ml. of the ferric ion reagent[18] in a final volume of 3.0 ml. A second 10 mg. quantity of succinic anhydride was dissolved in a mixture of 0.2 ml. each of 4*M* hydroxylamine hydrochloride and 3.5*N* sodium hydroxide and after dilution to 50 ml., 0.5, 1.0, and 1.5 ml. were analyzed by use of 1.5 ml. of the iron reagent in a final volume of 3.0 ml. The results given in Fig. 1 show that the periodic acid method is about 5 times as sensitive as the ferric hydroxamate procedure. As 2 moles of alkylhydroxylamine are required per mole of dimer, this number agrees with the ratio of maximum extinction coefficients of the two colored species, namely, (10,000/2)/1000.[19]

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(18)(a) F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945); (b) E. R. Stadtman, *Methods in Enzymology*, III, 228 (1957).

(19) A. Kornberg and W. E. Pricer, *J. Biol. Chem.*, **204**, 345 (1953).

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# Hydrogenolysis of Substituted Phenolic Mannich Bases

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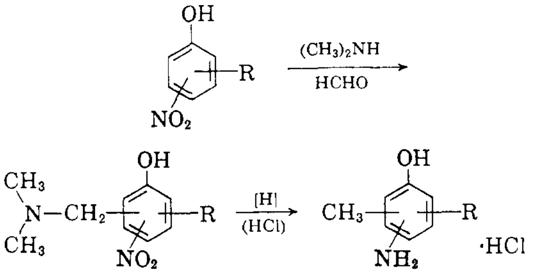
The preparation of cresols by hydrogenolysis of phenolic Mannich bases has usually involved high pressures and temperatures.[1,2] Low pressure hydrogenation of other reducible groups on such molecules have generally left the Mannich bases intact. Thus we have hydrogenated 2-dimethylaminomethyl-4-phenyl-6-chlorophenol at two atmospheres of hydrogen, over 10% palladium-on-barium sulfate, and succeeded only in removing the chlorine. We have also reduced 4-nitro-2-dimethylaminomethylphenol in ethanol solution under similar conditions to the corresponding anilino compound. This is in agreement with the results of Burckhalter,[3] who hydrogenated 4-nitro-2-diethylaminomethylphenol to the corresponding amino-Mannich base.

We have now found that phenolic Mannich bases having a nitro group *meta* to the aminomethyl group are readily reduced to the aminocresols at low pressures under controlled acidic conditions. In practice we have found the reaction to go best when we use about 0.85 equivalents of mineral acid per mole of Mannich base. When more than one equivalent of acid is present, there is virtually no debenzylation. When we replace the nitro group by methoxyl, phenyl, or amino debenzylation does not occur under these conditions. Hydrogenolysis would seem to take place, therefore, before the nitro group has been completely reduced.



The aminocresols formed are readily oxidized in air, hence they are advantageously isolated as their hydrochloride salts.

## EXPERIMENTAL

*Mannich bases.* One equivalent of the nitrophenol, 1.1 equivalents of 37% aqueous formaldehyde, 1.1 equivalents of 25% aqueous dimethylamine, and a small amount of ethanol were refluxed 1 hr. on the steam bath. The mixture was cooled, the product separated and crystallized. Physica data are summarized in Table I.

*2-Methoxy-4-amino-6-methylphenol hydrochloride.* A mixture of 13.3 g. of 2-methoxy-4-nitro-6-(dimethylaminomethyl)phenol, 125 ml. of 95% ethanol, and 17.5 ml. of 3*N* hydrochloric acid was heated on the steam bath until the solid was completely dissolved. Four grams of 10% palladium-on-barium sulfate was added to the warm (50°C) solution, and the mixture was hydrogenated on a standard Parr apparatus under 30 p.s.i. of hydrogen. Uptake of hydrogen was complete in 25 min., the drop in pressure corresponding stoichiometrically to 100% nitro reduction plus 80% debenzylation. The reduction mixture was acidified immediately on opening with 10 ml. of concd. hydrochloric acid and the catalyst was filtered off. The filtrate was concentrated *in vacuo* to about $^1/_5$ its original volume, at which point white crystals began to separate. Fifty milliliters of concd. hydrochloric acid was added, and the mixture was then chilled and filtered. The precipitate was washed with acetone, then with ether. The product melted at 267° with decomposition; yield was 69%.

*Anal.* Calcd. for $C_8H_{12}ClNO_2$: C, 50.7; H, 6.4; Cl, 18.7; N, 7.4. Found: C, 50.6; H, 6.4; Cl, 18.4; N, 7.4.

*2-Methyl-4-aminophenol hydrochloride.* Hydrogenation of 2-dimethylaminomethyl-4-nitrophenol under the same conditions gave an 89% yield of white crystals, m.p. 263–266° dec.

*Anal.* Calcd. for $C_7H_{10}ClNO$: C, 52.7; H, 6.3; Cl, 22.2; N, 8.8. Found: C, 52.7; H, 6.2; Cl, 22.5; N, 8.7.

*2-Amino-4-methylphenol hydrochloride.* A warm suspension of 7.7 g. of 2-nitro-4-dimethylaminomethyl-6-chlorophenol in 200 ml. of ethanol was hydrogenated over 4 g. of 10% palladium-on-barium sulfate.[4] Five equivalents of hydrogen

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(1) W. T. Caldwell and T. R. Thompson, *J. Am. Chem. Soc.*, **61**, 765 (1939).

(2) W. J. Burke *et al.*, *J. Org. Chem.*, **26**, 4669 (1961).

(3) J. H. Burckhalter *et al.*, *J. Am. Chem. Soc.*, **70**, 1363 (1948).

(4) In this case the acid required for the debenzylation was generated *in situ* by the hydrogenolysis of the chlorine.

TABLE I

| Mannich Base | M.P.[a] | Recryst. Solvent[b] | Yield, % | Carbon[c] |  | Hydrogen |  | Nitrogen |  |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| 2-Dimethylaminomethyl-4-nitrophenol | 168–170 | A | 48 | 55.1 | 55.3 | 6.2 | 6.4 | 14.3 | 14.4 |
| 2-Dimethylaminomethyl-4-nitro-6-methoxyphenol | 198–200 | B | 76 | 53.1 | 53.3 | 6.2 | 6.2 | 12.4 | 12.4 |
| 2-Dimethylaminomethyl-4-phenyl-6-chlorophenol | 75–76 | C | 68 | 69.0 | 69.0 | 6.1 | 5.9 | 5.3 | 5.4 |
| 2-Dimethylaminomethyl-4-phenylphenol | 84.5–86 | D | 82 | 79.3 | 79.0 | 7.5 | 7.6 | 6.2 | 6.2 |
| 2-Nitro-4-dimethylamino-methyl-6-chlorophenol | 210 | B | 67 | 46.9 | 46.8 | 4.8 | 4.7 | 12.1 | 11.9 |

[a] Melting points are uncorrected and were taken on a Mel-Temp capillary melting point apparatus. [b] Recrystallization solvent; A, water; B, not recrystallized; C, ethanol; D, hexane. [c] We are indebted to Dr. Carol Fitz of Needham, Mass., for the microanalyses.

were taken up in 15 min. The product was worked up as above to give 2.4 g. of white crystals (45%), m.p. 198–200°, reprecipitated twice from methanol–ether.

*Anal.* Calcd. for $C_7H_{10}ClNO$: C, 52.7; H, 6.3; Cl, 22.2; N, 8.8. Found: C, 52.4; H, 6.3; Cl, 22.0; N, 9.0.

*2-Dimethylaminomethyl-4-phenylphenol.* A warm solution of 7.84 g. of 2-dimethylaminomethyl-4-phenyl-6-chlorophenol in 150 ml. of 95% ethanol over 3 g. of 10% palladium-on-barium sulfate readily absorbed one equivalent of hydrogen on the Parr shaker. The solution gave a positive test for chloride ion, indicating hydrogenolysis of the chlorine. The filtered solution was evaporated to dryness *in vacuo,* the residue dissolved in water, and neutralized with sodium carbonate solution. The product that separated was filtered, dried, and crystallized from hexane to give 2-dimethylamino-4-phenylphenol (see Table I).

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## Reaction of the 2-Cyano-2-propyl Radical with Elemental Sulfur

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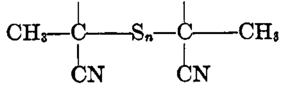
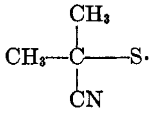
During the course of other work in this laboratory, it became desirable to know the nature and extent of the reaction between elemental sulfur and the 2-cyano-2-propyl radical derived from thermal decomposition of azobisisobutyronitrile (AIBN). The decomposition of AIBN at 80° in benzene containing dissolved sulfur gave a mixture of products I, III, and IV resolved by elution from aluminum oxide with pentane and ether. The new compound III has been characterized by elemental analysis, infrared absorption spectrum, and hydrolysis to the corresponding dicarboxylic acid. Compound III was also prepared for comparison by the reaction of *alpha*-chloroisobutyronitrile and sodium disulfide. The chromatogram shows there is no detectable amount of monosulfide II eluted between the I and III fractions. Zechmeister and Cholnoky have shown for several diverse types of compounds that when a homologous series of adsorbates is eluted from a chromatographic column, the order of elution is strictly that of increasing molecular complexity.[1] Therefore, the nonappearance of monosulfide II between dinitrile I and disulfide III in the chromatogram strongly suggests that none is formed in the reaction of AIBN and sulfur.

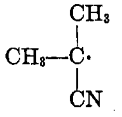

$CH_3{-}\overset{CH_3}{\underset{CN}{C}}{-}S_n{-}\overset{CH_3}{\underset{CN}{C}}{-}CH_3$

I. $n = 0$
II. $n = 1$
III. $n = 2$
IV. $n = 3$ or more

We may then speculate that the monothio radical V does not exist as an intermediate in the reaction of VI and sulfur, for if it did, we should expect II to be formed along with I and III.[2] It has been widely noted previously that the fragments from the breakup of the $S_8$ ring contain sulfur in multiples of two atoms.[3]


$CH_3{-}\overset{CH_3}{\underset{CN}{C}}{-}S\cdot$

V


$CH_3{-}\overset{CH_3}{\underset{CN}{C}}\cdot$

VI

Hammond, Sen, and Boozer[4] have studied the decomposition of 0.2*M* AIBN in solvents containing similar concentrations of 1-butanethiol. Comparison of their data with the present results indicates that elemental sulfur and 1-butanethiol are approximately equal in efficiency as scavengers for 2-cyano-2-propyl radicals. In both cases only about a 20% yield of I was formed, perhaps by reaction of primary radicals within a solvent cage.

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(1) L. Zechmeister and L. Cholnoky, *Principles and Practice of Chromatography,* Wiley, New York, 1941, pp. 24–41.

(2) A system in which equal concentrations of radicals V and VI react in a random manner would give products I, II, and III in the ratio 1:2:1. Since I and III are formed in about the same yields (20% and 16%, respectively) the yield of II should be 30–40% in such a system.

(3) For example, E. H. Farmer and F. W. Shipley, *J. Chem. Soc.,* 1519 (1947); G. F. Bloomfield, *J. Soc. Chem. Ind.,* **67,** 14 (1948).

(4) G. S. Hammond, J. N. Sen, and C. E. Boozer, *J. Am. Chem. Soc.,* **77,** 3244 (1955).