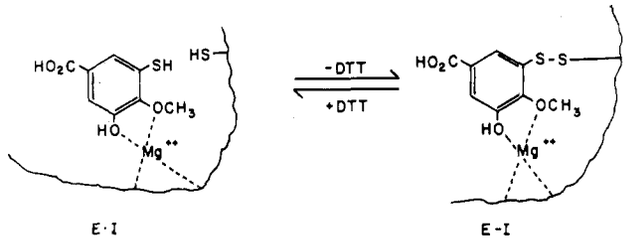

Figure 3. Proposed mechanism for the inactivation of COMT by 5-hydroxy-3-mercapto-4-methoxybenzoic acid.

shown in Figure 3 is modified after that proposed by Lutz et al.,[2] to explain the inactivation of COMT by 3-mercaptotyramine. Borchardt and Thakker[5] had previously provided evidence for two sulfhydryl groups at the active site of COMT. These groups could be selectively modified by functional-group reagents or affinity-labeling reagents.[6] In the case of compound **5** and COMT, the ligand–protein disulfide bond probably forms because of the close juxtaposition of the sulfhydryl groups of the inhibitor and protein during the initial reversible binding process. It would appear that an active-site sulfhydryl group is involved because of the fact that the inhibitory effects of compound **5** can be partially prevented by inclusion of the catechol substrate (data not shown). Therefore, 5-hydroxy-3-mercapto-4-methoxybenzoic acid (**5**) can be added to the list of affinity-labeling reagents that modify a sulfhydryl group at the active site of COMT.[6]

Experimental Section

Materials. *S*-Adenosyl-L-(*methyl*-^{14}C)methionine (SAM-$^{14}CH_3$, New England Nuclear Corp., 50–60 mCi/mmol) was diluted to a concentration of 8.8 μCi/mL and stored at −20 °F. SAM chloride (Sigma Chemical Co.) was stored as a 10 mM aqueous stock solution at the same temperature. 3,4-Dihydroxybenzoic acid was obtained from Aldrich Chemical Co., and dithiothreitol (DTT) was obtained from Sigma Chemical Co.

COMT Purification and Assay. COMT was purified from rat liver (male, Sprague–Dawley, 180–200 g) using a modification[7,8] of the procedure described by Nikodejevic et al.[9] The enzyme preparation used in the kinetic experiments was purified through the calcium phosphate step, resulting in a 48-fold increase in specific activity as compared to the crude supernatant. This enzyme preparation had a specific activity of 49.6 nmol of product (mg of protein)$^{-1}$ min^{-1} using 3,4-dihydroxybenzoic acid as the substrate. The enzyme activity was determined using SAM-$^{14}CH_3$ (55 Ci/mol) and 3,4-dihydroxybenzoic acid as substrates according to a previously described radiochemical assay.[7] Upon prolonged storage, some loss of enzyme activity was detected. Therefore, prior to use, COMT was routinely reactivated by preincubation for 40 min at 37 °C in phosphate buffer (pH 7.6) containing 4 mM DTT.

Preparation of 5-Hydroxy-3-mercapto-4-methoxybenzoic Acid (5). A mixure of 3-acetoxy-4-methoxy-5-nitrobenzoic acid (1;[4] 510 mg, 2 mmol) and PtO_2 (100 mg) in absolute EtOH (100 mL) was hydrogenated (40 psi) for 1.5 h in a Parr shaker. The reaction mixture was then filtered, and the product was isolated as the HCl salt: mp 168 °C; NMR of the free base of **2** (acetone-d_6) δ 2.3 (s, 3, OAc), 3.7 (s, 3, OMe), 5.75 (NH_2, exchanges with D_2O), 6.9 and 7.4 (2 d, 1 each, Ar H). The material was sufficiently pure to be used in subsequent synthetic conversions.

The HCl salt of **2** (410 mg, 1.47 mmol) was dissolved in a mixture of 1–2 g of ice and 0.15 mL (1.8 mequiv) of concentrated HCl. When dissolution was complete, 135 mg (1.95 mmol) of $NaNO_2$ in 1.4 mL of cold water was added slowly so that the temperature remained below 10 °C. Addition of the $NaNO_2$ was stopped when an aliquot of the reaction mixture turned starch–iodine paper blue. Meanwhile, a separate solution containing 270 mg (1.7 mmol) of potassium ethyl xanthate in 0.70 mL of H_2O and 210 mg of sodium carbonate (2.0 mmol) in 1.4 mL of H_2O was prepared under N_2 and heated to 70 °C. The diazonium solution was maintained in the cold for 15 min and then filtered through glass wool into the hot, well-stirred xanthate solution. Stirring at 75 °C was continued for 1 h, after which 310 mg (7.8 mmol) of NaOH in 1.4 mL of H_2O was added. The mixture was refluxed for 3 h and then cooled in ice and acidified. Extraction with Et_2O (3 times) and evaporation of the Et_2O extract gave 70 mg (mp 170 °C) of crude product. Further extraction of the aqueous phase with EtOAc (2 times) gave 100 mg of additional product. Sublimation (130–150 °C, 0.01 mm) of a 70-mg sample of the crude material afforded 42 mg of a light yellow solid, mp 172–177 °C. The product exhibited a single spot (R_f 0.2) on thin-layer chromatography (silica gel; solvent: 95% CH_3Cl saturated with formic acid, 5% EtOH). When the thin-layer plates were sprayed with Ellman's reagent,[10] a characteristic yellow color developed: NMR (acetone-d_6) δ 7.5 and 7.35 (2 d, J = 3 Hz, 1 each, Ar H), 9.0–6.0 (br, 2, exchanges with D_2O, SH, OH), 3.85 (s, 3, OCH_3); IR (KBr) 3400, 2580, 1700, 1580 cm^{-1}; mass spectrum, m/e 200 (M^+). MS peak matching: calcd, 200.01427; found, 200.01415.

Acknowledgment. This work was supported by a grant from the National Institute of Neurological and Communicative Disorders and Stroke (NS-10918). The authors gratefully acknowledge the support provided by the Center for Biomedical Research, University of Kansas.

(5) R. T. Borchardt and D. R. Thakker, *Biochim. Biophys. Acta*, **445**, 498 (1976).
(6) R. T. Borchardt, "Biochemistry and Function of Monoamine Enzymes", E. Usdin and N. Weiner, Eds., Marcel Dekker, New York, 1977, p 707.
(7) R. T. Borchardt, *Methods Enzymol.*, **77**, 267 (1981).
(8) R. T. Borchardt, C. F. Cheng, and D. R. Thakker, *Biochem. Biophys. Res. Commun.*, **63**, 69 (1975).
(9) B. Nikodejevic, S. Senoh, J. W. Daly, and C. R. Creveling, *J. Pharmacol. Exp. Ther.*, **174**, 83 (1970).
(10) G. L. Ellman, *Arch. Biochem. Biophys.*, **82**, 70 (1959).

Antiestrogenic Properties of Substituted Benz[*a*]anthracene-3,9-diols

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The antiestrogenic potency of benz[*a*]anthracene-3,9-diol, as well as its 7- and 12-methyl derivatives, was evaluated by measuring the inhibition in the onset of estrus brought about by this compound in ovariectomized rats treated with 17β-estradiol. At a dose of 0.5 mg the 7,12-dimethyl derivative caused a decrease in the percentage of rats in estrus from 78 to 44%. This decrease is identical with that caused by 0.05 mg of nafoxidine.

There is much evidence to support the concept that estrogen is of primary importance in the development and growth of rat mammary cancer and that at least a part of these biochemical events occurs directly in the target or-

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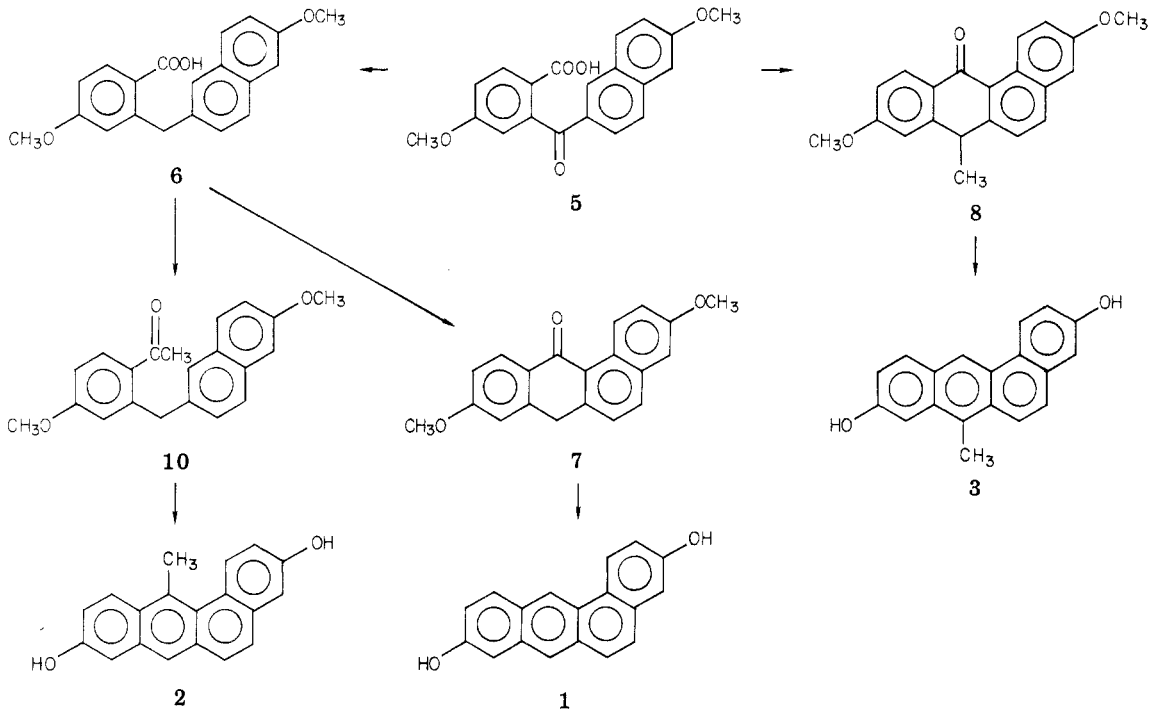
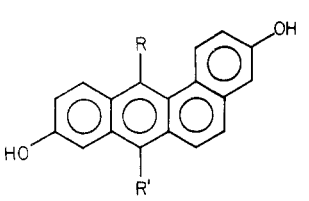
Scheme I



gan.[1] It is known that 7,12-dimethylbenz[*a*]anthracene (DMBA) causes mammary cancer in the rat under a variety of conditions[2-4] and that this mammary cancer mimics the human disease in a variety of ways. In particular, the experimental rat summary cancer is sensitive to hormonal conditions much like hormone-dependent human breast cancer.[5-7] Antiestrogens are known to antagonize the growth of estrogen-dependent tissue, but their mode of action is difficult to assess because there seems to be little or no correlation of structure and physiological properties. Investigations leading to the acquisition of new compounds with antiestrogenic properties that may not possess the deleterious effects of conventional estrogens have not only theoretical interest by leading to a better understanding of the mechanism of estrogenic action but also possible practical value by contributing to knowledge of modes of treatment of breast cancer by antiestrogens. The diphenols **1**–**4** described in this work were selected



1, R = R′ = H
2, R = CH_3; R′ = H
3, R = H; R′ = CH_3
4, R = R′ = CH_3

because they represent possible metabolites of the corresponding parent hydrocarbons and because molecular models show that their phenolic groups are superimposable with the hydroxy groups of the natural estrogen 17β-estradiol.

Table I. Antiestrogenic Properties of Substituted Benz[*a*]anthracenes

test compd	dose, mg	% inhibn of estrus	affinity constant: K_a, M^{-1}
1	5	12	3.0×10^7
2	5	44	4.3×10^7
3	5	22	1.8×10^9
4	5	74	1.7×10^8
4 diacetate	5	67	
4	0.5	44	
nafoxidine	0.05	44	
estradiol			0.7×10^{10}

Chemistry. The substituted benz[*a*]anthracene-3,9-diols were prepared from 2-(6-methoxy-2-naphthoyl)-4-methoxybenzoic acid (**5**) (Scheme I). Reduction of this keto acid afforded the benzylic derivative **6** which readily cyclized in HF to the tetracyclic anthrone **7**. Aromatization of this anthrone and deprotection gave an alternate and more convenient source of compound **1**, which had previously been prepared from deoxyanisoin in a Stobbe condensation.[8]

The benzylic acid **6** when treated with methyllithium, gave the acetophenone derivative **10**, which easily cyclized in polyphosphoric acid to 3,9-dimethoxy-12-methylbenz[*a*]anthracene from which the free diol **2** was obtained by cleavage with BBr_3.

The keto acid **5** is also a source of the anthrone **8**, via 3-methyl-3-(6-methoxy-2-naphthyl)-5-methoxyphthalide as described previously.[9] Reduction of this benzanthrone

(1) Leung, B. S.; Sasaki, G. H.; Leung, J. S. *Cancer Res.* **1975**, *35*, 621.
(2) Huggins, C.; Grands, L. D.; Brillantes, F. P. *Nature (London)* **1961**, *189*, 204.
(3) Sinha, D.; Dao, T. L. *J. Natl. Cancer Inst.* **1974**, *53*, 841.
(4) Dao, T. L. *Science* **1969**, *165*, 810.
(5) Dao, T. L.; Sunderland, J. *J. Natl. Cancer Inst.* **1959**, *23*, 567.
(6) Dao, T. L. *Cancer Res.* **1962**, *22*, 937.
(7) Dao. T. L. *Prog. Exp. Tumor Res.* **1964**, *5*, 124.
(8) Morreal, C. E.; Alks, V. *J. Org. Chem.* **1975**, *40*, 3411.
(9) Morreal, C. E.; Bronstein, R. E. *J. Chem. Eng. Data* **1978**, *23*, 354.

with Zn–Cu gave the 7-methyl derivative from which the free diol **3** was obtained.

Biological Results

The percentage inhibition in estrus is shown in Table I. In 32 h, 6 μg of 17β-estradiol induces estrus in 78% of the animals. A dose of 0.5 mg of compound **4** shows a 44% inhibition of estrus. This reduction in the number of animals in estrus can be compared to a similar reduction noticed with 0.05 mg of nafoxidine. In this respect, nafoxidine is 10 times stronger an antiestrogen than **4**. With 5-mg doses of the test compounds, the influences of the 7- and 12-methyl groups in the molecule can be observed. In compound **1**, with no substitution at the 7 and 12 positions, there is very little inhibition (12%). Introduction of a methyl group into the 7 position doubles the inhibition to 22% as shown in compound **3**. A methyl group in position 12, as in compound **2**, shows a still greater inhibition of estrus (44%). In compound **4**, which contains methyl groups in both the 7 and 12 positions, there is a 74% inhibition of estrus. This magnitude of inhibition is only slightly affected by conversion to the diacetate.

Although all of the compounds **1–4** show affinity for the specific estrogen receptor, the degree of this competition is no criterion for antiestrogenic activity, as Table I shows. These results support the views expressed by Rochefort describing a lack of correlation between antiestrogenic activity and binding affinity with the estrogen receptor.[10]

The monophenols in the 3 and 9 positions of the benz[*a*]anthracene ring system have been shown to be metabolites of the parent hydrocarbons,[11,12] but as yet, the 3,9-diol has not been reported as a metabolite of benz[*a*]anthracene or its methylated derivatives. The formation in vivo of such a compound would indicate the possibility that hormone dependency in polycyclic hydrocarbon induced tumors could be internally influenced by metabolic products.

Experimental Section

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The IR spectra of all compounds were consistent with the proposed structures. Elemental analyses (C and H) within ±0.4% of the theoretical values were submitted for review and were performed by Atlantic Microlab, Atlanta, GA. Nafoxidine hydrochloride was a gift from Upjohn Co., Kalamazoo, MI.

2-[(6-Methoxy-2-naphthyl)methyl]-4-methoxybenzoic Acid (6). A solution of 17.1 g (51 mmol) of 2-(6-methoxy-2-naphthoyl)-4-methoxybenzoic acid (**5**) in 855 mL of 10% KOH was added to Zn–Cu couple prepared from 102.6 g of Zn and 350 mg of $CuSO_4$ in 13 mL of water, and the solution was refluxed for 18 h. Removal of the zinc by filtration and acidification of the filtrate gave a white solid, which was dissolved in ethyl acetate that was washed with water, dried with $MgSO_4$, and evaporated. The residue was recrystallized from ethyl acetate–heptane to give 11.6 g (71%) of reduced acid **6**, mp 188–190 °C. Anal. ($C_{20}H_{18}O_4$) C, H.

3,9-Dimethoxybenz[*a*]anthr-12-one (7). A solution of 6 g (19 mmol) of acid **6** in 45 mL of anhydrous HF, after standing at 24 °C for 30 min, was poured into water and extraced with ethyl acetate, and the organic layer was washed with water, saturated $NaHCO_3$, and again with water. The dried ($MgSO_4$) solution was evaporated, and the solid was crystallized from benzene–heptane to give 2.3 g (41%) of the tetracyclic ketone **7**, mp 141–143 °C. Anal. ($C_{20}H_{16}O_3$) C, H.

Benz[*a*]anthracene-3,9-diol (1). To 3.83 g of Zn–Cu couple prepared from 3.5 g of Zn and a solution of 28 mg of $CuSO_4$ in 10 mL of water was added 2.3 g (7.56 mmol) of the substituted anthrone **7**, 60 mL of xylene, and a solution of 3.83 g of NaOH in 60 mL of water. The mixture was refluxed for 18 h, filtered, acidified with concentrated HCl (10 mL), and extracted with ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to about 40 mL. The dimethoxy compound, an orange crystalline material (1.2 g, 55%), had a mp of 190–192 °C.[8] Anal. ($C_{20}H_{16}O_2$) C, H. Cleavage of the ether with boron tribromide gave 76% of the diol **1**, mp 255–265 °C with decomposition.[8]

12-Methylbenz[*a*]anthracene-3,9-diol (2). A solution of 18.9 g (58.6 mmol) of acid **6** in 30 mL of THF was treated dropwise with 112 mL of 1.3 M methyllithium in heptane at 24 °C. After 3 h, a solution of 17 mL of concentrated HCl in in 100 mL of water was added, and the THF removed in vacuo. The residue was dissolved in ethyl acetate, washed with saturated $NaHCO_3$, and evaporated. Elution of the dark oil from alumina with benzene gave 7 g (37%) of 2-[(6-methoxy-2-naphthyl)methyl]-4-methoxyacetophenone (**10**) as a yellow oil, which was chromatographically pure by TLC but did not crystallize.

The acetophenone derivative (7.9 g, 24.7 mmol) was dissolved in 200 mL of polyphosphoric acid, heated to 50 °C, and stirred for 4 h. The dark viscous solution was dissolved in water and extracted with ethyl acetate, which was then washed with saturated $NaHCO_3$, followed by water. Evaporation of the ethyl acetate and crystallization from benzene gave 4.4 g (60%) of 3,9-dimethoxy-12-methylbenz[*a*]anthracene, mp 233–235 °C. Anal. ($C_{21}H_{18}O_2$) C, H.

The free diol **2** (mp 262–265 °C dec) was prepared in 30% yield by cleavage of the dimethoxy compound in a benzene solution of boron tribromide. Anal. ($C_{19}H_{14}O_2$) C, H.

7-Methylbenz[*a*]anthracene-3,9-diol (3). A mixture of 1 g (3.14 mmol) of 3,9-dimethoxy-7-methylbenz[*a*]anthr-12-one (**8**),[9] 1.6 g of Zn–Cu, 30 mL of xylene, 1.6 g of NaOH, and 30 mL of water was refluxed for 18 h. An additional 1.6 g of Zn–Cu was added, and the mixture again was refluxed for 18 h. The decanted liquid was extracted with benzene that was washed with dilute HCl followed by water. The benzene solution was concentrated to give 3,9-dimethoxy-7-methylbenz[*a*]anthracene (**9**) as a yellow, crystalline solid (670 mg, 71%), mp 184–186 °C. Anal. ($C_{21}H_{18}O_2$) C, H.

The free diol **3** was prepared by adding 2 mL of boron tribromide to a stirred suspension of 200 mg (0.7 mmol) of the dimethoxy compound **9** in 20 mL of dry benzene at 24 °C. The dark red solution was then refluxed for 1.25 h, changing to a light yellow color. The solution was poured into a mixture of ice and ether, which was agitated by bubbling nitrogen gas into the solution. The ether layer was washed with water four times, dried over $MgSO_4$, and concentrated under nitrogen to 5 mL at 35–40 °C. The tan solid (170 mg, 94%) had a mp of 185–190 °C dec. Anal. ($C_{19}H_{14}O_2$) C, H.

7,12-Dimethyl-3,9-diacetoxybenz[*a*]anthracene. A mixture of 3,9-dimethoxy-7,12-dimethylbenz[*a*]anthracene[9] (2 g, 6.3 mmol) and 16 mL of boron tribromide in 200 mL of benzene was refluxed for 1 h and poured into a mixture of ice–water and ether. The organic layer was washed with water six times, dried over $MgSO_4$, and evaporated in vacuo. A mixture of 30 mL of pyridine and 25 mL of acetic anhydride was added, and the red solution was heated over steam for 1 H. Following evaporation in vacuo, the dark residue was eluted from a silica gel column with benzene–ethyl acetate to give an oil, which crystallized from ethyl acetate–ether to give 620 mg (26%) of orange-yellow crystals, mp 185–191 °C. Anal. ($C_{24}H_{20}O_4$) C, H.

Biological Studies. The antiestrogenic properties were assessed in randomly distributed ovariectomized female Sprague–Dawley rats following a modification of the technique of Lerner et al.[13] Rats were ovariectomized at 7 weeks and were randomly distributed into groups containing ten rats each. Five days after

(10) Rochefort, H.; Garcia, M.; Borgna, *J. Biochem. Biophys. Res. Commun.* **1979**, *88*, 351.
(11) Thakker, D. R.; Levin, W.; Yagi, H.; Ryan, D.; Thomas, P. E.; Karle, J. M.; Lehr, R. E.; Jerina, D. M.; Conney, A. H. *Mol. Pharmacol.* **1978**, *15*, 138.
(12) Gentil, A.; Lasne, C.; Chouroulinkov, I. *Xenobiotica* **1977**, *7*, 221.
(13) Lerner, L. J.; Holthaus, Jr., F. J.; Thompson, C. R. *Endocrinology* **1958**, *63*, 295.

ovariectomy, each rat was subcutaneously injected with 6 μg of 17β-estradiol in 0.1 mL of corn oil at time 0. The test compound in corn oil was injected subcutaneously twice, at time 0 and at 8 h, with 2.5 mg of test compound in 0.2 mL of corn oil. Vaginal smears were obtained at 32 h, and rats showing smears with cornified epithelial cells were considered to be in estrus. The optimum conditions were established with compound 4 at 0, 8, 24, 32, 48, 56, and 72 h. Thereafter, smears were taken at 32 h for compounds 1–3. Details of the procedures describing the competitive binding to the estrogen receptor protein are outlined in previous publications.[14,15]

Acknowledgment. This investigation was supported by Grant CA 22001, awarded by the National Cancer Institute, Department of Health, Education and Welfare.

(14) Schneider, S. L.; Alks, V.; Morreal, C. E.; Sinha, D, K.; Dao, T. L. *J. Natl. Cancer Inst.* **1976**, *57*, 1351.
(15) Morreal, C. E.; Schneider, S. L.; Sinha, D. K.; Bronstein, R. E. *J. Natl. Cancer Inst.* **1979**, *62*, 1585.

N-Aralkyl Substitution of 2-Amino-5,6- and -6,7-dihydroxy-1,2,3,4-tetrahydronaphthalenes. 2. Derivatives of a Hypotensive-Positive Inotropic Agent[1]

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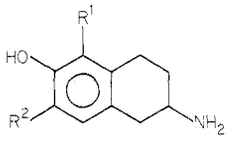
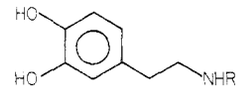
Seven derivatives of 2-[[2-(3,4-dihydroxyphenyl)-1-methylethyl]amino]-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene, an inotropic agent which also causes a decrease in blood pressure, were synthesized and tested for inotropic potency, cardioselectivity, and inotropic selectivity. The derivatives were designed to explore whether catechol moieties and rigid rotamers of dopamine are necessary for the activity which was found in the parent compound. The derivatives had phenolic functions in place of catechols, and they had phenethylamine in place of the tetrahydronaphthalene moiety. In no case was the profile of activity of the parent compound duplicated in the derivatives.

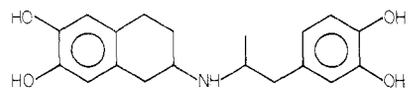
In a previous paper we described the cardiovascular properties of a series of *N*-aralkyl-substituted rigid analogues of dopamine,[2] where 2-amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene (A-5,6-DTN, **1**) and 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (A-6,7-DTN, **2**) served as rigid forms of dopamine. One goal of that research was to prepare a selective inotropic agent which was superior to either dopamine (**3**) or dobutamine (**4**). Indeed, one compound, **5**, proved to be at least as potent and inotropic selective as the standards and, unlike compounds of similar structure which increased blood pressure,[2] it caused a decrease in blood pressure at inotropic doses. This combination of hypotensive and inotropic activities has found clinical application in the treatment of congestive heart failure using the two drugs nitroprusside and dopamine.[3] We were intrigued by the unique pharmacological profile exhibited by this compound and, therefore, set out to examine the effect of structural modification on pharmacological activity.



1, R^1 = OH; R^2 = H
2, R^1 = H; R^2 = OH



3, R = H
4, R = $CH(CH_3)CH_2$-Ph-OH



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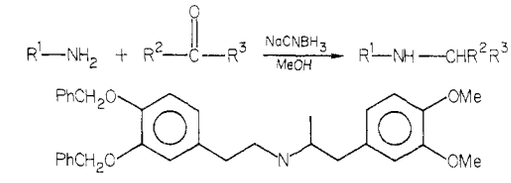
(1) This paper has been presented. See "Abstracts of Papers", 182nd National Meeting of the American Chemical Society, New York, Aug 1981; American Chemical Society: Washington, DC, 1981; Abstr MEDI 8.
(2) Gorczynski, R. J.; Anderson, W. G.; Stout, D. M. *J. Med. Chem.* **1981**, *24*, 835.
(3) Miller, R.; Awan, N.; Joye, J.; Maxwell; DeMaria, A.; Amsterdam, E.; Masson, D. *Circulation* **1977**, *55*, 881.

Scheme I



13

Our earlier work[2] explored two structural parameters necessary for potency, cardioselectivity and inotropic selectivity, in *N*-aralkyl-substituted rigid dopamine analogues. One parameter was the rotation of the phenyl ring relative to the ethylamine side chain (A-5,6-DTN vs. A-6,7-DTN) and the other was the chain length and branching of the aralkyl function attached to the tetralin amine. Compound **5** demonstrated that the A-6,7-DTN moiety coupled with a 2-propyl-3-(3′,4′-dihydroxyphenyl) group afforded the best spectrum of activity in the series. The present study examined the effects of the hydroxyl groups on the aromatic rings and the necessity of a rigid form of dopamine in the molecule.

Chemistry. The products (Table I) were formed by reductive amination of the 6-methoxy- and 6,7-dimethoxy-2-aminotetralin or dopamine *O*-methyl ether with the corresponding ketones using the method of Borch (Scheme I).[4] The hydroxyl groups were then deblocked in refluxing 48% hydrobromic acid. In the case of **12**, the hydroxyl groups were protected as benzyl ethers (**13**) with deblocking accomplished by hydrogenolysis. The dihydroxytetralin products were unstable in aqueous solution over a few hours; however, the compounds were stable for several hours in aqueous bisulfite solution.

Because of the sensitivity of the catechol products to air, the products were isolated after deblocking simply be removing the hydrobromic acid in vacuo, dissolving the re-

(4) Borch, R.; Bernstein, M.; Durst, H. *J. Am. Chem. Soc.* **1971**, *93*, 2897.

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