E_{LEMO} alone would be that these molecules act as electron acceptors in the formation of a charge-transfer bond. Such a mechanism for quinine antimalarials has been supported by molecular orbital calculations;[27] however, no biochemical evidence supports this mechanism for naphthoquinones.

A third explanation of the observed structure-activity relationships might focus on the relationships between E_{LEMO} and σ (eq 2 and 4). If σ represents electronic effects on ionization of the hydroxyl group, then one might postulate that the acid-base properties of the group at the 2 position determine activity *vs.* inactivity of the molecule. Series no. **23** was synthesized on this basis and found to be inactive.[17] In addition, the naphthoquinones act in the lipid mileau of the mitochondrion which would suppress ionization and they are competitive with coenzyme Q which is not acidic. Thus, a consideration of the biochemistry eliminates two of the three explanations and leaves only the first.

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Further Side-Chain Modification of Antimalarial Phenanthrene Amino Alcohols

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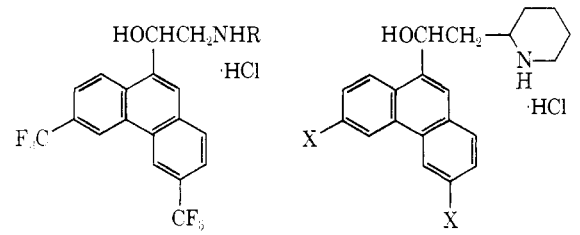
Several phenanthrene amino alcohols with specifically designed side chains attached to the 9 position have been synthesized and their structure-activity relationships in animal screening against *Plasmodium berghei* and *P. gallinaceum* have been studied. The shorter chain 3,6-bis(trifluoromethyl)-α-(alkylaminomethyl)-9-phenanthrenemethanols displayed activity at 10 mg/kg and are curative at 20 mg/kg against *P. berghei* with no toxicity to the host. Activity of the corresponding α-(2-piperidylmethyl) derivatives conforms with the postulated triangle pharmacophore for antimalarial activity.

In connection with our structure-activity relationship study on the side-chain modification of certain phenanthrene amino alcohols[1] and a comparison with 2-(*p*-chlorophenyl)-2-(4-piperidyl)tetrahydrofuran,[2] a triangle pharmacophore (composed of one nitrogen atom, one oxygen atom, and the center of an aromatic or heteroaromatic ring to which the side chain is attached) of definite parameters was uncovered among these antimalarial agents. It was also postulated that the nitrogen and the oxygen atoms are in close proximity and are linked by hydrogen bonds to form a five- or a six-membered ring with neighboring carbon atoms.[2] The proposed hydrogen-bond formation was subsequently confirmed by nmr studies.[3] Interestingly, a recent proposed triangulation feature for α-adrenergic receptors[4] is identical in every aspect with our proposed triangular feature. Some structurally similar 4-pyridylamino alcohols and corresponding quinoline derivatives have recently been reported to possess β-adrenergic blocking activity.[5,6]

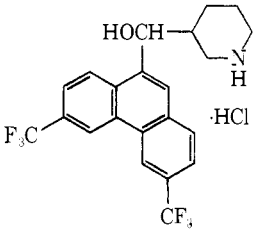
The foregoing information prompted us to synthesize several additional phenanthrene amino alcohols with specifically designed side chains in order to gain a better understanding of the mode of action of these antimalarial compounds. The outstanding antimalarial activity displayed by several 3,6-bis(trifluoromethyl)-α-(alkylaminomethyl)-9-phenanthrenemethanols[1] suggested the preparation of shorter α-alkylaminomethyl side chain derivatives **1a-c**. Compounds **1b** and **1c** are of particular interest since the side chain of **1b** and **1c** is identical with that of ephedrine (epinephrine, adrenaline) and norephedrine (norepinephrine, noradrenaline), respectively. The proposed hydrogen-bond feature prompted the preparation of compounds of type **2**, **3**, and **4**.

Chemistry. The 3,6-bis(trifluoromethyl)-α-(alkylaminomethyl)-9-phenanthrenemethanols **1a-c** were prepared by the interaction of 3,6-bis(trifluoromethyl)-9-phenanthryloxirane[1,7] (**5a**) with a primary amine or ammonia. 3,6-Dichloro-α-(2-piperidylmethyl)-9-phenanthrenemethanol



1a, R = C_2H_5
b, R = CH_3
c, R = H

2a, X = Cl
b, X = CF_3



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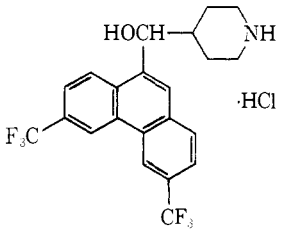
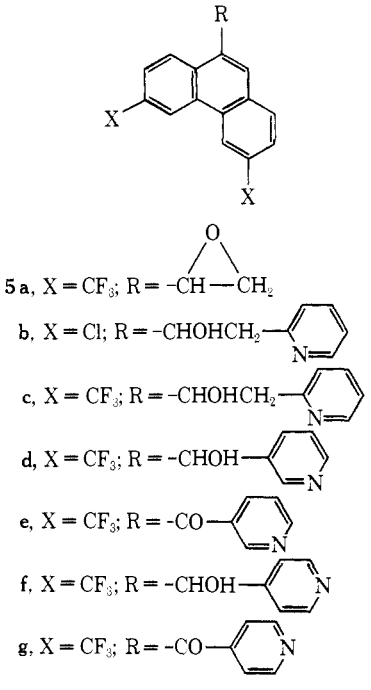


4

(2a) and the corresponding 3,6-bis(trifluoromethyl) compound **2b** were obtained by treatment of the appropriate 9-phenanthrenecarboxaldehyde[1] with 2-lithiopicoline followed by hydrogenation of the resulting pyridine intermediates **5b** and **5c**. 3,6-Bis(trifluoromethyl)-α-(3-piperidyl)-9-phenanthrenemethanol (**3**) was prepared as follows. Condensation of the lithiopyridine, prepared by treatment of 3,5-dibromopyridine with 1 equiv of butyllithium, and phenanthrene-9-carboxaldehyde, followed by hydrogenolysis yielded 3,6-bis(trifluoromethyl)-α-(3-pyridyl)-9-phenanthrenemethanol (**5d**). It was then hydrogenated catalytically in the presence of Adams catalyst to yield **3**. Compound **3** can be alternatively prepared by catalytic hydrogenation of the ketone **5e**, the latter being obtained by CrO_3 oxidation of **5d**. In both courses, a mixture of two isomers (**3a** and **3b**) was invariably formed. 3,6-Bis(trifluoromethyl)-α-(4-piperidyl)-9-phenanthrenemethanol (**4**) was prepared in a similar manner from either the alcohol **5f** or the ketone **5g**. As expected from the stereoisomeric consideration, only one product was isolated.



5a, X = CF_3; R = -CH(O)CH$_2$
b, X = Cl; R = -CHOHCH$_2$-(2-pyridyl)
c, X = CF_3; R = -CHOHCH$_2$-(2-pyridyl)
d, X = CF_3; R = -CHOH-(3-pyridyl)
e, X = CF_3; R = -CO-(3-pyridyl)
f, X = CF_3; R = -CHOH-(4-pyridyl)
g, X = CF_3; R = -CO-(4-pyridyl)

Biological Activity. Antimalarial testing results of the aforementioned compounds are given in Table I. Excellent antimalarial activity against *P. berghei* was observed (active at 10 mg/kg, curative at 20 mg/kg, and no toxicity at 640 mg/kg) with both 3,6-bis(trifluoromethyl)-α-(alkylaminomethyl)-9-phenanthrenemethanols 1a and 1**b**. It appears that compounds **1a**, **1b**, and the corresponding propylaminomethyl analog[1] are the most active ones in this series against *P. berghei* as well as against *P. gallinaceum*. The activity diminished abruptly when the terminal amino group is unsubstituted (**1c**).

Of the compounds containing a piperidyl side chain, compounds **2a**, **2b**, and **3**a were found to have antimalarial activity in animal screening. These results indicate that insertion of a $-CH_2-$ linkage between the carbinol carbon and the nitrogen atom does not appreciably alter the original activity, thus substantiating the proposed hydrogen bonding *vs.* activity relationship of this type of antimalarial compounds.[2] Again, diastereomerism was shown to play an important role with regard to biological activity.[1] This is indicated by the lack of activity of compound **3b** in contrast to the activity displayed by its diastereomer 3a. Lack of antimalarial activity of compound **4** may be attributed to unfavorable molecular conformation of **4**, which precludes the formation of the desired triangle pharmacophore.

Experimental Section

All melting points (corrected) were taken on a Thomas-Hoover melting point apparatus. The uv and ir absorption spectra have been taken and were as expected. Where analyses are indicated only by symbols of the elements, analytical results obtained for these elements were within ±0.4% of the theoretical values.

3,6-Bis(trifluoromethyl)-α-(ethylaminomethyl)-9-phenanthrenemethanol Hydrochloride (1a). A mixture of 5.34 g (0.015 mol) of 3,6-bis(trifluoromethyl)-9-phenanthryloxirane (**5a**) and 100 g of anhydrous ethylamine was heated at 125° in a pressure vessel for 14 hr. Excess ethylamine was evaporated by air stream and the residue was triturated with methanol. The solid was filtered to give 3.4 g of the free base of the desired product as white crystals, mp 174–176° (57% yield). Its hydrochloride was prepared by treatment of the free base with ethanolic hydrogen chloride and was recrystallized from methanol as white crystals, mp 272–274° dec. *Anal.* ($C_{20}H_{17}F_6NO$·HCl) C, H, N.

3,6-Bis(trifluoromethyl)-α-(methylaminomethyl)-9-phenanthrenemethanol Hydrochloride (1b). This compound was prepared from the oxirane **5a** and a large excess of anhydrous methylamine in the same manner as described above. The free base was obtained as white crystals, mp 183–185° (MeOH) (68% yield). *Anal.* ($C_{19}H_{15}F_6NO$) C, H, N.

The hydrochloride, also obtained as white crystals, has a melting point of 265–267° dec (MeOH). *Anal.* ($C_{19}H_{15}F_6NO$·HCl) C, H, N.

3,6-Bis(trifluoromethyl)-α-(aminomethyl)-9-phenanthrenemethanol Hydrochloride (1c). The free base of this compound was obtained in 94% yield by the reaction of the oxirane **5a** and liquid ammonia under pressure at 100°. It was converted into the hydrochloride in the usual manner: white crystals; mp 277–279° dec (EtOH–$CHCl_3$). *Anal.* ($C_{18}H_{13}F_6NO$·HCl) C, H, N.

3,6-Dichloro-α-(2-picolyl)-9-phenanthrenemethanol (5b). A solution of 2.79 g (0.03 mol) of 2-picoline in 20 ml of anhydrous Et_2O was added, in 10 min with stirring, into a solution of 19 ml (0.03 mol) of BuLi in 100 ml of Et_2O at room temperature under N_2. After being stirred for 40 min, the mixture was cooled to −50° while a THF solution (180 ml) of 3,6-dichloro-9-phenanthrenecarboxaldehyde (5.50 g, 0.02 mol) was added in 1 hr. Stirring was continued for 30 min as the red color of the reaction mixture gradually faded. Tlc indicated the presence of unreacted aldehyde. A fresh 2-lithiopicoline (0.03 mol) solution was then prepared in a separated flask and added to the reaction mixture. After 20 min, the mixture was cautiously treated with H_2O (100 ml) and the organic layer separated. It was washed (H_2O), dried ($MgSO_4$), and evaporated. The residue was recrystallized three times from Me_2CO to afford 1.6 g (22% yield) of **5b** as white needles, mp 168–170°. *Anal.* ($C_{21}H_{15}Cl_2NO$) C, H, N.

3,6-Dichloro-α-(2-piperidylmethyl)-9-phenanthrenemeth-

Table I. Antimalarial Activity[a] of Phenanthrene Amino Alcohols

Compd	Dosage, mg/kg						
	10	20	40	80	160	320	640
1a	10.1	3C	5C	5C	5C	5C	5C
	(0.0)	(6.0)	(10.0)	(10.0)	(12.0)	(12.2)[b]	
1b	6.9	2C	4C	5C	5C	5C	5C
	(4.2)	(5.6)	(6.2)	(10.8)	(16.8)	(17.0)[b]	
1c		0.1	0.1	0.1	0.1	0.1	0.1
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)[b]	
2a	0.5	0.6	11.4	4C	5C	5C	5C
	(0.0)	(0.0)	(2.4)	(5.4)	(9.2)	(11.8)[b]	
2b	3.9	12.2	3C	5C	5C	5C	5C
	(0.0)	(0.0)	(2.6)	(4.4)	(6.4)	(6.6)[b]	
3a		0.5	5.7	5C	5C	5C	5C
3b	0.0	0.1	0.1	0.1	0.1	0.3	0.3
4	0.0	0.0	0.0	0.0	0.0	0.0	

[a] Antimalarial tests were performed by Dr. Leo Rane and results were provided through the Walter Reed Army Institute of Research. Increase in mst (mean survival time) of the control group is reported: mst for controlled mice infected with *P. berghei*, 6.5 ± 0.5 days; C (curative) = the number of mice surviving at 60 days postinfection; T (toxic) = the number of deaths occurring on days 2–5 after infection. For details of test results, see T. S. Osdene, P. B. Russell, and L. Rane, *J. Med. Chem.*, **10**, 431 (1967). [b] Test data (increase in mst) of chicks infected with *P. gallinaceum* are listed in parentheses; mst for controlled chicks infected with *P. gallinaceum*, 4 days; T (toxic) = the number of deaths occurring within 2 days after injection.

anol Hydrochloride (2a). A mixture of 1.6 g of 5b and 100 ml of EtOH was hydrogenated at 5 kg/cm² in the presence of PtO_2 and 2 ml of concentrated HCl for 7 hr. The resulting mixture was heated on a steam bath to dissolve the precipitated solid and immediately filtered to remove the catalyst. The filtrate was evaporated to dryness and the residue recrystallized from EtOH to give 1.0 g (56% yield) of 2a as a white solid, mp 275–277°. *Anal.* ($C_{21}H_{21}Cl_2NO \cdot HCl$) C, H, N.

3,6-Bis(trifluoromethyl)-α-(2-piperidylmethyl)-9-phenanthrenemethanol Hydrochloride (2b). To a stirred solution of 3.72 g (0.04 mol) of 2-picoline in 100 ml of anhydrous Et_2O was added dropwise 25 ml (0.04 mol) of BuLi in hexane at room temperature. The resulting orange-colored solution was stirred for 30 min. It was then cooled to −50° and a solution of 3.42 g (0.01 mol) of 3,6-bis(trifluoromethyl)-9-phenanthrenecarboxaldehyde and 100 ml of Et_2O was added slowly with stirring. After the addition was complete, the reaction mixture was allowed to warm to −10° in 30 min with continued stirring. Excess lithiopicoline was decomposed with 50 ml of H_2O and the Et_2O layer separated. It was washed with H_2O, dried ($MgSO_4$), and evaporated. The residue 5c was taken up in 100 ml of EtOH and the resulting solution was cooled in an ice bath for 30 min. This was treated with 3 ml of concentrated HCl and then shaken overnight under H_2 in a Parr hydrogenator in the presence of PtO_2. After removal of the catalyst, the solution was evaporated to dryness. The residue was triturated with Me_2CO and Et_2O, and the solid was filtered to give 1.0 g of the desired product, mp 310–312°. An analytical sample was prepared by recrystallization from MeOH–Me_2CO as white needles, mp 317–319°. *Anal.* ($C_{23}H_{21}F_6NO \cdot HCl$) C, H, N.

3,6-Bis(trifluoromethyl)-α-(3-pyridyl)-9-phenanthrenemethanol (5d). To a stirred solution of 11.9 g (0.05 mol) of 3,5-dibromopyridine in 400 ml of anhydrous Et_2O was added dropwise, under N_2, 32 ml of 1.6 *M* BuLi in hexane (0.05 mol) at −30°. Stirring was contined for 1 hr at that temperature. A solution of 5.13 g (0.015 mol) of 3,6-bis(trifluoromethyl)-9-phenanthrenecarboxaldehyde in 350 ml of anhydrous Et_2O was then introduced in 20 min. The reaction mixture was stirred for 1 hr and the excess organolithio reagent was decomposed with H_2O (50 ml). The Et_2O layer was separated, thoroughly washed with H_2O, dried ($MgSO_4$), and evaporated. The residue was taken into 150 ml of EtOH and hydrogenated at 5 kg/cm² in the presence of Pd on C and 3 ml of Et_3N for 10 hr. The catalyst was removed and the solution concentrated to 50 ml. It was initially acidified with dilute HCl and then made basic with 10% NaOH. The product was extracted with Et_2O (3 × 100 ml). The combined Et_2O solution was washed, dried, and evaporated. The residue was triturated with MeOH and the solid product collected by filtration. More precipitate was formed in the mother liquor and was also collected (1.9 g, 30% yield). A small amount of product was obtained when the mother liquor was chromatographed over silica gel. An analytical sample (white crystals) was prepared by recrystallization of the crude product from MeOH, mp 267–269°. *Anal.* ($C_{22}H_{13}F_6NO$) C, H, N.

3,6-Bis(trifluoromethyl)-α-(3-piperidyl)-9-phenanthrenemethanol Hydrochloride (3). Method A. 3,6-Bis(trifluoromethyl)-α-(3-pyridyl)-9-phenanthrenemethanol (5d), 1.5 g, was hydrogenated in 150 ml of EtOH and 4 ml of concentrated HCl over Adams catalyst in a Parr hydrogenator at 5 kg/cm² for 14 hr. After removal of the catalyst, the solution was evaporated to dryness. The residue was triturated with absolute EtOH and evaporated again to dryness. The solid product thus obtained melted at 170–195°. It was recrystallized three times from MeOH–H_2O to give 0.16 g (10% yield) of the desired product as a white solid, mp 290–293°. Further recrystallization of this material raised the melting point to 293–295°. *Anal.* ($C_{22}H_{19}F_6NO \cdot HCl$) C, H, N.

From the mother liquors of the first two recrystallizations, there was isolated 0.3 g (20% yield) of white crystals. It was purified by recrystallization from MeOH–H_2O, mp 189–191°. *Anal.* ($C_{22}H_{19}F_6NO \cdot HCl$) C, H, N.

Method B. An AcOH solution (100 ml) of 4.21 g (0.01 mol) of 3,6-bis(trifluoromethyl)-α-(3-pyridyl)-9-phenanthrenemethanol (5d) was treated with a concentrated aqueous solution of CrO_3 (2.0 g, 0.02 mol). The reaction mixture was allowed to stand at room temperature overnight. After the excess oxidizing agent was destroyed by the addition of 5 ml of MeOH, the mixture was diluted with 300 ml of H_2O and extracted with $CHCl_3$ (5 × 40 ml). The aqueous phase was made alkaline with sodium hydroxide solution and extracted with Et_2O (4 × 100 ml). The combined Et_2O extract was washed with H_2O, dried, and evaporated. The $CHCl_3$ extracts were worked up similarly. There was obtained a total of 3.4 g of 3,5-bis(trifluoromethyl)-9-phenanthryl 3-pyridyl ketone (5e), mp 150–162°. A small sample was recrystallized from MeOH as off-white crystals, mp 163–165°.

The ketone thus obtained was dissolved in 150 ml of EtOH and 3 ml of concentrated HCl and hydrogenated in the presence of PtO_2 in a Parr hydrogenator at 5 kg/cm² for 14 hr. After removal of the catalyst, the solution was concentrated to 30 ml, neutralized with 10% NaOH, and extracted with Et_2O (3 × 100 ml). The Et_2O extracts were washed, dried, and evaporated. The residue was dissolved in EtOH (100 ml) and treated with 2 g of $NaBH_4$ for 1 hr. Excess $NaBH_4$ was decomposed with 400 ml of H_2O and the mixture extracted with Et_2O. The washed and dried Et_2O solution was treated with anhydrous HCl in EtOH. The resulting precipitate was collected by filtration to yield 0.92 g (20% overall yield) of the desired product, mp 285–290° dec. The compound was shown to be identical with that prepared by method A.

3,6-Bis(trifluoromethyl)-α-(4-pyridyl)-9-phenanthrenemethanol (5f). 4-Bromopyridine hydrochloride (12 g, 0.062 mol) was dissolved in 100 ml of H_2O and made basic with dilute NaOH. The free base was extracted with 250 ml of anhydrous Et_2O. After being thoroughly dried ($MgSO_4$), the ether solution was cooled to −75° and to this solution was added dropwise, with stirring, 0.05 mol of BuLi in hexane in 15 min under N_2. The mixture was then stirred for 1 hr at the same temperature and a solution of 6.84 g (0.02 mol) of 3,6-bis(trifluoromethyl)-9-phenanthrenecarboxaldehyde in 40 ml of THF was introduced over a period of 15 min. Stirring was continued for 90 min while the temperature of the reaction mixture was allowed to reach −40°. Excess organolithi-

um compound was then decomposed with H_2O (100 ml). The Et_2O layer was separated, washed with H_2O, and concentrated. The solid was collected by filtration to give 3.3 g (40% yield) of the desired product, mp 217–220°. Recrystallization from acetone–cyclohexane yielded analytically pure **5f** as white crystals, mp 218–220°. *Anal.* ($C_{22}H_{13}F_6NO$) C, H, N.

3,6-Bis(trifluoromethyl)-9-phenanthryl 4-Pyridyl Ketone (5g). A solution of 2.1 g (0.005 mol) of **5f** in 100 ml of AcOH was treated with a saturated solution of CrO_3 (2.0 g, 0.02 mol) in H_2O. The reaction mixture was allowed to stand overnight at room temperature, and excess oxidizing agent was then destroyed by the addition of MeOH. The resulting mixture was made basic with aqueous NaOH. The product was isolated by Et_2O extraction (frequent filtration was required to break up the emulsion). On evaporation of the Et_2O solution there was obtained 1.26 g (60% yield) of crude **5g**, mp 157–159°. An analytical sample was obtained as white needles upon recrystallization from MeOH, mp 162–164°. *Anal.* ($C_{22}H_{11}F_6NO$) C, H, N.

3,6-Bis(trifluoromethyl)-α-(4-piperidyl)-9-phenanthrenemethanol Hydrochloride (4). A solution of 1.8 g of **5f** in 250 ml of EtOH and 1 ml of HCl was hydrogenated in the presence of Adams catalyst at 5 kg/cm² for 4 hr. The reaction mixture was then heated to dissolve the precipitated solid product and filtered to remove the catalyst. The filtrate was evaporated to dryness *in vacuo* and the residue recrystallized from MeOH to give **4** as white crystals, mp 323–325° dec. The combined yield of pure **4** from two similar runs was 2.35 g (60%). This compound could also be prepared by hydrogenation of 3,6-bis(trifluoromethyl)-9-phenanthryl 4-pyridyl ketone (**5g**) under the same reaction conditions. *Anal.* ($C_{22}H_{19}F_6NO\cdot HCl$) C, H, N.

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A General Method for Modifying the 2-Methyl Group of Pyridoxol. Synthesis and Biological Activity of 2-Vinyl- and 2-Ethynylpyridoxols and Related Compounds†

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In order to explore the bulk tolerance indicated in the 2 position of vitamin B_6 for enzymes both dependent on the vitamin and metabolizing it, we have developed a general method for modifying the 2 position. To this end, formation of cyclic ketals from acetone and pyridoxol or α^2-hydroxypyridoxol has been studied, using various amounts of catalyst, principally *p*-toluenesulfonic acid. With a limited amount of catalyst, ketal formation occurs across the α^4- and α^5-OH groups, without involving the phenolic OH. When the ratio of acid catalyst to substrate is increased (*e.g.*, to 4:1), acetone condenses with the 3- and α^4-OH groups in these compounds but not with the 3- and α^2-OH groups in α^2-hydroxypyridoxol. By blocking the 3-OH group in α^2-hydroxypyridoxol with benzyl, and the α^4- and α^5-OH groups with acetone, a generally useful intermediate for modifying the 2 position was obtained. An alternative, more efficient method for synthesizing the compound was developed, starting from 3-*O*-benzylpyridoxol, converting it to the α^4,α^5 cyclic ketal, N-oxidizing that, rearranging the *N*-oxide with trifluoroacetic anhydride, and hydrolyzing the 2-(trifluoroacetyl) group. The 2-CH_2OH group of this intermediate was oxidized to 2-CHO, which on mild hydrolysis gave 2-formyl-2-norpyridoxol. The 2-CHO groups of the blocked intermediate were converted by Wittig reactions to 2-CH=CH_2 and 2-CH=CHCl groups; dehydrochlorination of the latter gave the 2-C≡CH derivative. The blocking groups in all of these compounds were readily hydrolyzed with acid, and the resulting analogs were tested as inhibitors of the growth of mouse mammary adenocarcinoma (TA-3) cells *in vitro*. 2-Vinyl-2-norpyridoxol, with an ID_{50} of 9×10^{-6} *M*, was the best inhibitor in this series. In contrast to the inhibition caused by the 4-vinyl analog of pyridoxal, readily reversed by pyridoxal, that caused by the 2-vinyl analog of pyridoxol could not be reversed by the vitamin.

Analogs of vitamin B_6[2] modified in the 2 position, such as α^2-methylpyridoxol (**1**, R_2 = Et), have been of considerable biochemical interest in the development of ideas in regard to pyridoxal catalysis[3] and the mode of binding of the cofactor analogs,[4] and in studies of the active sites of enzymes metabolizing vitamin B_6.[5] Generally, the analogs that were studied had the 2-methyl group replaced either with 2-CH_2OH (**1**, R_2 = CH_2OH) or with various other alkyl groups. The results of these studies indicated that there is a certain bulk tolerance in the 2 position with respect to several enzymes requiring pyridoxal phosphate and also with respect to enzymes involved in metabolic interconversions of different forms of vitamin B_6. In order to exploit this bulk tolerance in the design of potential antagonists of vitamin B_6, we had to develop a method for modifying the 2-methyl group of pyridoxol in such a way that the method would also be suitable for the introduction of reactive groups. The present paper describes the synthesis of a blocked intermediate that satisfies these requirements. The utility of this intermediate parallels that of α^4,3-*O*-isopropylidenepyridoxol for modifying the 5-CH_2OH group[6] and that of 3,α^5-*O*-dibenzylpyridoxol for modifying the 4-CH_2OH group.[1a,7]

Initially, we investigated the acetonation of α^2-hydroxypyridoxol (Scheme I). The latter compound was prepared from tri-*O*-acetylpyridoxol by a simplified version of the

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