The Structure of the Organomagnesium Complex in Carbonyl Bridge Indenones
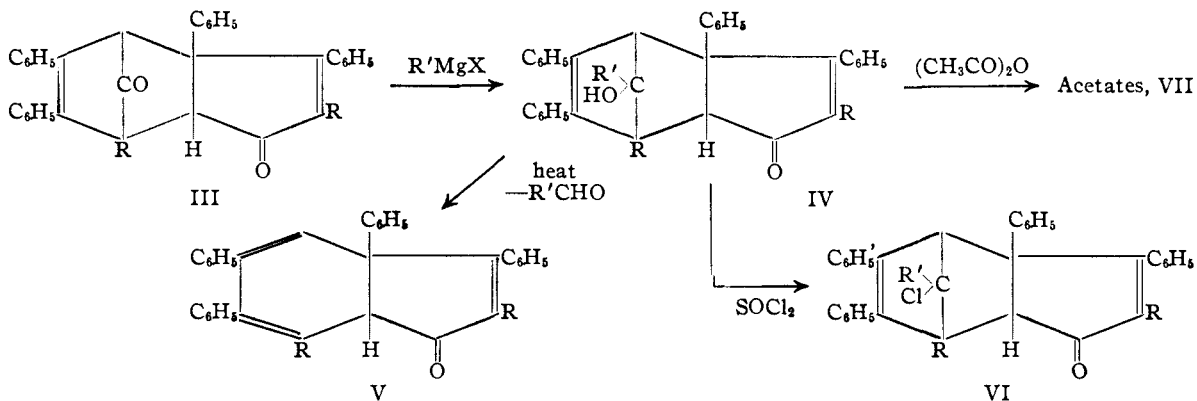
BY C. F. H. ALLEN AND J. A. VANALLAN

Carbonyl bridge compounds in the indene series unexpectedly show one active hydrogen and one addition when treated quantitatively with methylmagnesium iodide, unless they are completely substituted.[1] The presence of a hydrogen atom in the position *alpha* to the carbonyl bridge appeared to be essential for the evolution of methane. In view of this abnormal behavior, it was considered advisable to examine as many varieties of carbonyl bridge compounds as possible, ascertain the facts, and then write structures and devise mechanisms.

The bicyclic carbonyl bridge compound, I, differs from the indene series in showing one addition, without evolution of gas, in spite of having an enolizable *alpha* hydrogen. Camphorquinone,
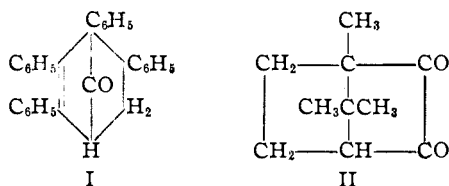
II, likewise evolves no gas, but shows two additions.[2] The absence of methane evolution here indicates that in the indene series the active hydrogen is not the one *alpha* to the carbonyl bridge.

binol bridge. It is known[4,5] that substances of this type give an aldehyde when heated. The ketocarbinol, IV (R' = C₆H₅), for instance, gives benzaldehyde and the dihydroindenone, V, under such treatment, conforming to the behavior of carbinol bridge compounds. The ketocarbinols resemble the latter in other respects, such as formation of chlorides and acetates when treated with thionyl chloride and acetic anhydride, respectively.[6] The formation of the same indenone from ketocarbinols which differ only in the nature of the radical, R', introduced by the Grignard reagent affords further proof that it is the bridge that has been lost.

The structure of the dihydroindenones, V, appears clear, because they are obtained by the decarbonylation of the bimolecular products, III; the dihydroindenones will form the subject of a subsequent paper.
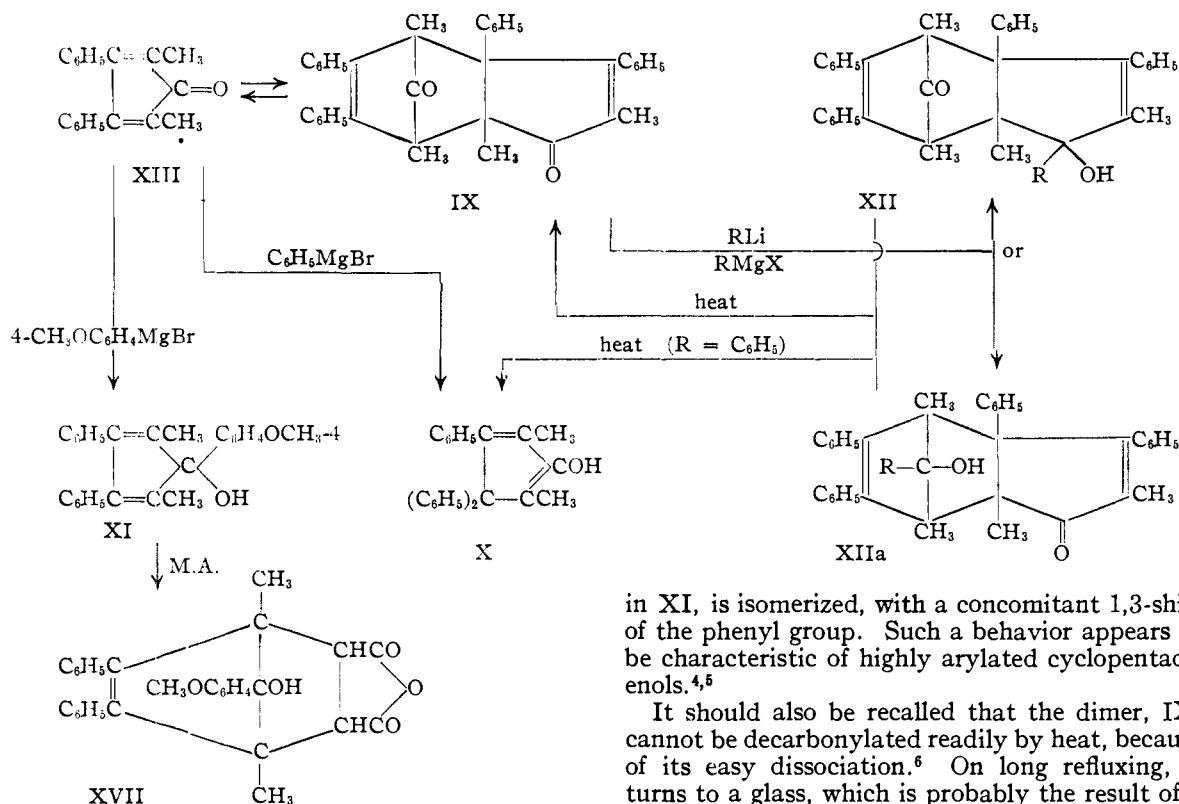
These ketocarbinols evolve two equivalents of methane when treated quantitatively with methylmagnesium iodide. One obviously comes from the carbinol bridge; the other must arise from enolization of the hydrogen atom on the carbon atom common to the two rings.

An observation, of which the interpretation is not yet clear, is the behavior of the chloride, VI (R' = CH₃), with methylmagnesium iodide; it evolves no gas but shows one addition. That is,

The bimolecular products, III, formed from monoalkylated anhydroacetonebenzils, likewise show one active hydrogen and one addition with methylmagnesium iodide. Four of these have been examined and all behaved alike. The product, after acidification, is a ketocarbinol, IV, which, in contrast to homologous Grignard products,[3] does not lose carbon monoxide when heated, indicating that the Grignard reagent has attacked the bridge. Therefore they contain a car-

replacement of the hydroxyl by chlorine has repressed the enolization tendency of the angular hydrogen *alpha* to the carbonyl group. A dichloro compound, VIII, the structure of which has not been determined, obtained from the action of phosphorus pentachloride on III, likewise shows one addition but no active hydrogen.

The bimolecular product, IX, from α,α'-dimethylanhydroacetonebenzil[7] reacts in two ways

(1) Allen, *Chem. Rev.*, **37**, 235 (1945).

(2) Allen, Jones and VanAllan, THIS JOURNAL, **68**, 708 (1946).

(3) Allen and Gates, *ibid.*, **64**, 2123 (1942).

(4) Allen and VanAllan, *ibid.*, **65**, 1384 (1943).

(5) Allen and VanAllan, *ibid.*, **66**, 8 (1944).

(6) Allen, Jones and VanAllan, *J. Org. Chem.*, **11**, 268 (1946).

(7) Allen and VanAllan, THIS JOURNAL, **64**, 1260 (1942).

$C_6H_5C\!=\!\cdot CCH_3$
$C_6H_5C\!=\!CCH_3$ $\quad\rangle\!C\!=\!O \rightleftarrows$

XIII

4-$CH_3OC_6H_4MgBr$

$\qquad$ C_6H_5MgBr

$C_6H_5C\!=\!CCH_3 \quad C_6H_4OCH_3\text{-}4$
$C_6H_5C\!=\!CCH_3 \quad OH$ $\quad\rangle\!C\!\langle$

XI

$\downarrow$ M.A.

(Structure **XVII**: $CH_3OC_6H_4COH$ ring with C_6H_5C, C_6H_5C, CH_3, CHCO, CHCO, O)

XVII

$C_6H_5C\!=\!CCH_3$
$(C_6H_5)_2C\!-\!CCH_3$ $\quad\rangle\!COH$

X

(Structure **IX**: CH_3 C_6H_5 ... C_6H_5, CO, C_6H_5, CH_3, CH_3 ... C_6H_5, CH_3, O)

IX

heat (R = C_6H_5)

(Structure **XII**: CH_3 C_6H_5 ... C_6H_5, CO, C_6H_5, CH_3, CH_3, R, OH ... C_6H_5, CH_3)

XII

$\dfrac{RLi}{RMgX}$

heat   or

(Structure **XIIa**: CH_3 C_6H_5 ... C_6H_5, R—C—OH, C_6H_5, CH_3, CH_3 ... C_6H_5, CH_3, O)

XIIa

with organometallic compounds. When examined quantitatively with methylmagnesium iodide, it shows one addition. In ether, this reagent gives a product that has one active hydrogen, presumably a carbinol (XII or XIIa—no attempt has been made to distinguish between these structures). Phenyllithium under forced conditions also gives a carbinol (incorrectly called a diol on p. 1267 of ref. 7). The dimer also reacts by addition[8] with one equivalent of phenyl- or p-methoxyphenylmagnesium bromide under forced conditions but, in this instance, the products, X and XI, are derived from the monomeric cyclopentadienone formed by dissociation; thus, this behavior parallels that of the bimolecular product with other reagents.[7]

The carbinols (XII or XIIa), formed by the action of methylmagnesium iodide and phenyllithium, however, are unusual, in that when heated they regenerate the bimolecular product, IX; the yield of the latter is about 20%. When the phenylated carbinol (XII, R = C_6H_5) is employed, a second product, the enol, X, can be isolated. This gives a clue as to the nature of the heat treatment. The carbinol is dissociated into its components, cleavage occurring in accordance with the double-bond rule[1]; the dienone part, XIII, then dimerizes to IX. The second part, which would be expected to be the carbinol of the type shown

(8) The statement on p. 1267 of ref. 7, that "the bimolecular product IV failed to react" is incorrect; at that time the reaction was attempted at the boiling point of ether; reaction occurs when the ether is replaced by benzene and the temperature is raised.

in XI, is isomerized, with a concomitant 1,3-shift of the phenyl group. Such a behavior appears to be characteristic of highly arylated cyclopentadienols.[4,5]

It should also be recalled that the dimer, IX, cannot be decarbonylated readily by heat, because of its easy dissociation.[6] On long refluxing, it turns to a glass, which is probably the result of a slow decarbonylation.

The evidence for the structures of the Grignard products, X and XI, is as follows: molecular weight determinations show that they must be derived from the monomolecular form, XIII. The methoxylated substance is the carbinol, XI, formed by 1,2-addition, for it shows one active hydrogen, adds maleic anhydride to give XVII, and gives a deep blue-violet color with concentrated sulfuric acid. The substance, X, however, appears to be an enol, formed by 1,4-addition; it shows one active hydrogen, does not add maleic anhydride, gives a yellow color with concentrated sulfuric acid, and furnishes benzophenone upon oxidation. These properties parallel those of analogous substances.[5]

From this behavior with organometallic compounds it is thus possible to arrange the bimolecular products in three groups: (1) those derived from symmetrical dialkylated anhydroacetonebenzils, (2) those from the monoalkylated homologs, and (3) those from anhydroacetonebenzil itself. Members of the last two groups show one active hydrogen and one addition when treated quantitatively with methylmagnesium iodide, whereas with the first only addition can be detected. The Grignard products from the third group are indenols, still having a carbonyl bridge; in those from the second group, the bridge has been converted to a carbinol, while the indenone carbonyl is left free. Upon being heated, the carbinols of the third group form hydrocarbons in the indene series, that retain the radical introduced by

the Grignard reagent. On the contrary, carbinols of the second group lose this radical, and give dihydroindenones. When carbinols of the first group are heated, the original bimolecular product from which the carbinols were prepared is always formed; the second product can be identified only in favorable instances.

The structure of the organomagnesium derivatives of groups 2 and 3 would appear to be represented by the structure XV, in view of the following facts: (a) the non-enolization of ketones I and II by Grignard reagents; (b) the formation of a series of ketocarbinols in the monoalkylated series which yield the same dihydroindenone on heating. A previous assumption,[1] involving a supposed exception to Bredt's rule,[9] is no longer tenable.

XV

XVI
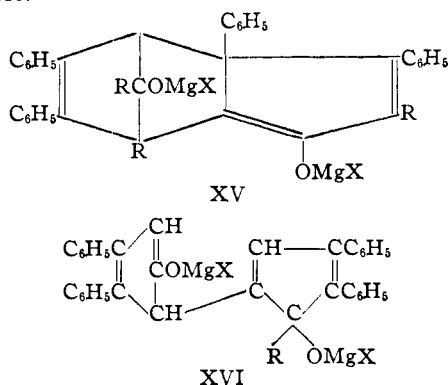
Such a structure cannot be applied to magnesium derivatives of the indenols which retain the group introduced by the Grignard reagent. These, however, are formed from a rearranged bimolecular product; in this instance it is believed[10] that the ring is opened under the influence of the Grignard reagent, and that the magnesium complex has the structure shown in XVI. This accounts satisfactorily for the fact that both stereoisomeric forms of the bimolecular product give the same carbinol with phenylmagnesium bromide.[11]

It now appears that in the indenones the necessary hydrogen atom for enolization is not the one *alpha* to the carbonyl bridge, but the one on the angular carbon atom common to both rings, and *alpha* to the indenone carbonyl group.

The proof of structure for the ketone, I, was obtained by reactions now known to be characteristic for carbonyl bridge compounds, cleavage of the bridge with alkali,[2,6] decarboxylation by permanganate,[2,12] and dehydrogenation with bromine.[2] The known 1,2,3,4-tetraphenylbenzene[13] produced showed the mode of addition of styrene.

Experimental

7-Keto-1,2,3,6-tetraphenyl-1,4-methano-1,4,5,6-tetrahydrobenzene, I, was obtained by refluxing for three

(9) Bredt, *Ann.*, **437**, 1 (1924).

(10) See ref. 1, pp. 236, 237.

(11) Allen and Gates, THIS JOURNAL, **64**, 2439 (1942).

(12) Allen and Gates, *ibid.*, **64**, 2120 (1942).

(13) Dilthey and Hurtig. *Ber.*, **67**, 2004 (1934).

hours a mixture of 13.2 g. of 2,3,4-triphenylcyclopenten-3-olone,[13] 18 cc. of styrene, 70 cc. of acetic acid and two drops of concentrated sulfuric acid, and removing the solvent *in vacuo* until crystals appeared. The product was recrystallized from isopropyl alcohol; the yield was 9.5 g.; m. p. 155°.

Anal. Calcd. for $C_{31}H_{24}O$: C, 90.3; H, 5.8. Found: C, 90.6; H, 6.2; act. H, 0; addn., 1.1.

Proof of Structure.—Cleavage of the bridge by alkali was brought about by four hours' refluxing of 4.1 g. of the ketone, I, 3 g. of potassium hydroxide and 30 cc. of aldehyde-free absolute ethanol. The red solution was poured into water, acidified, and extracted with benzene. The liquid acid was dissolved in dilute potassium carbonate solution and stirred for one hour on the steam-bath during which time 12 g. of potassium permanganate was gradually added. After acidification, the mixture was extracted with benzene, the extract shaken with sodium bicarbonate solution, and, after removal of the solvent, heated *in vacuo* as long as any distillate came over. The latter solidified in the receiver, and melted at 125–132° after one recrystallization from ligroin. This crude dihydro compound was taken up in carbon tetrachloride and 0.5 cc. of bromine was added; hydrogen bromide was evolved copiously. After evaporation of the solvent, the residue was crystallized from a benzene–methanol mixture. It was identified by comparison with an authentic specimen of 1,2,3,4-tetraphenylbenzene at hand; there was no depression of melting point on admixture. A chlorinated product, thought to be 1,1-dichloro-8-keto-2,7-di-methyl-3,3a,5,6-tetraphenyl-4,7-methano-3a,4,7,7a-tetrahydroindene, VIII, was produced on refluxing for two and one-half hours a mixture of 4.6 g. of the dimethylated bimolecular product,[14] m. p. 230° (III, R = CH₃), 6.2 g. of phosphorus pentachloride, and 20 cc. of benzene, pouring the mixture into water, and working up by suitable manipulation; it was recrystallized from cymene, after which it had the melting point of 290°.

Anal. Calcd. for $C_{36}H_{28}Cl_2O$: C, 79.0; H, 5.1; Cl, 13.0. Found: C, 79.0; H, 5.4; Cl, 12.7; act. H, 0; addn., 0.9.

The carbinols, IV, were all prepared in the same way; a hot benzene solution of the carbonyl bridged compound was added to the Grignard reagent as fast as the reaction permitted, after which the mixture was refluxed one and one-half to two hours. A yellow solid slowly separated. This was cautiously decomposed by the addition, at 5–10°, of a solution of 35 cc. of acetic acid in 200 cc. of water. The insoluble carbinol was collected and recrystallized from a large volume of solvent; there is a strong tendency to retain solvent of crystallization. The phenylated carbinol, m. p. 229°, was never obtained in an analytically pure condition, but its derivatives all gave correct values. The yields were 90–98%. Their properties are given in Table I.

The chlorides, VI, were obtained by refluxing for one and one-half hours a mixture of 2 g. of the carbinol and 10 cc. of thionyl chloride, removing the unused solvent *in vacuo*, and triturating the residue with ligroin (b. p. 90–120°); cymene was employed for recrystallization. Their properties are collected in Table I.

The acetates, VII, were prepared by dissolving 3 g. of the carbinol in 25 cc. of hot acetic anhydride, cooling to 30°, and adding one drop of concentrated sulfuric acid; the acetate (2.9 g.) separated quickly; cymene was used for recrystallization. With the methyl carbinol (IV, R′ = CH₃), dioxane was added to the acetic anhydride to effect solution. The properties of the acetates are given in Table I.

The carbinols, XII (except where R = CH₃), were obtained under forced conditions. The bimolecular product, IX, was dissolved in hot benzene or butyl ether, and after it had been added to the ethereal solution of the organometallic compound, the ether was distilled, and the residual mixture heated, with stirring, on the steam-bath for six to

(14) Japp and Meldrum, *J. Chem. Soc.*, **79**, 1024 (1901).

Table I

Properties of Bridged Compounds

No.		Substance	M. p., °C.	Empirical formula	Calcd. C	H	Cl	Mol. wt.	Found C	H	Cl	Mol. wt.	Act. H
IV	R, R' = CH₃	Methylated carbinol	286–288ᵃ	$C_{37}H_{32}O_2$	87.4	6.3			87.5	6.5			2
IV	R = CH₃, R' = C₆H₅	Phenylated carbinol	229ᵇ	$C_{42}H_{34}O_2$	88.5	6.0							2
IV	R = CH₃, R' = 4-CH₃OC₆H₄	Anisylated carbinol	258ᶜ	$C_{43}H_{36}O_3$	86.0	6.0		600	86.1	6.3		540ᵉ	2
IV	R = n-C₅H₁₁, R' = C₆H₅	Phenylated carbinol	180–181ᵈ	$C_{50}H_{50}O_2$	88.0	7.3			87.6	7.2			2
VI	R, R' = CH₃	Methylated chloride	235	$C_{37}H_{31}ClO$			6.8	527			6.6	569ᶜ	1
VI	R = CH₃, R' = C₆H₅	Phenylated chloride	198–199ᵈ	$C_{42}H_{43}ClO$			6.0	588			6.0	508ᶜ	0ʰ
VII	R, R' = CH₃	Methylated acetate	199ᵃ	$C_{39}H_{34}O_3$	85.0	6.2		550	85.1	6.2		543ᵉ	
VII	R = CH₃, R' = C₆H₅	Phenylated acetate	281ᶠ	$C_{44}H_{36}O_3$	86.3	5.9			86.7	5.8			
VII	R = CH₃, R' = 4-CH₃OC₆H₄	Anisylated acetate	270ᵍ	$C_{45}H_{38}O_4$	84.3	5.9			84.3	6.2			
XII	R = CH₃	Methylated carbinol	206	$C_{39}H_{36}O_2$	87.3	6.7		536	87.0	6.5		543ᵉ	1ⁱ
XII	R = C₆H₅	Phenylated carbinol	223	$C_{44}H_{38}O_2$	88.3	6.4			88.2	6.4			
XVII		Anhydride	210–212ᵃ	$C_{30}H_{26}O_6$	77.2	5.6			77.1	5.6			

ᵃ From xylene. ᵇ From n-octane. ᶜ From butanol. ᵈ From chloroform–methanol. ᵉ In benzene. ᶠ From cymene. ᵍ From toluene. ʰ One addition. ⁱ Insoluble in reagent.

eighteen hours. The products were handled by suitable operations. The properties of the two bridged products are given in Table I.

1-p-Methoxyphenyl-2,5-dimethyl-3,4-diphenylcyclopentadienol, XI, resulted when p-methoxyphenylmagnesium bromide reacted with the dimer, IX, by the procedure just described; it crystallized well from benzene, toluene and butanol; and has the melting point of 193–194°. It gives a bluish-violet solution, tinged with red, when dissolved in concentrated sulfuric acid.

Anal. Calcd. for $C_{26}H_{24}O_2$: C, 84.7; H, 6.5; act. H, 1. Found: C, 84.9; H, 6.5; act. H, 1.

The anhydride, XVII, of 3,6-dimethyl-4,6-diphenyl-7-p-methoxyphenyl-7-hydroxy-3,6-methano-1,2,3,6-tetrahydrobenzene-1,2-dicarboxylic acid was formed by the addition of maleic anhydride to the carbinol, XI, equal weights of the components being heated for two hours at 200°. It was also obtained by two hours' refluxing a benzene solution of the components; any acidic material was extracted by shaking with aqueous sodium carbonate. The properties are given in Table I.

The product from the action of phenylmagnesium bromide upon the dimer, IX, was distilled *in vacuo*, b. p. 197–201° (2 mm.). After recrystallization from i-propyl alcohol or heptane, the white 2,5-dimethyl-3,3,4-triphenylcyclopentadienol-1, X, has a melting point of 137–138°; nothing else could be obtained from the yellow solution. The enol gives a yellow solution, with a slight greenish fluorescence, in concentrated sulfuric acid.

Anal. Calcd. for $C_{25}H_{22}O$: C, 88.7; H, 6.6; mol. wt., 338; act. H, 1; addn., 0. Found: C, 88.7; H, 6.5; act. H, 1; addn., 0.25; mol. wt., 304 (in C₆H₆).

It was oxidized by chromic acid and the benzophenone formed was identified in the usual way.[4]

When the phenylated carbinol, (XII, R = C₆H₅), was distilled, there was some decomposition. The solid distillate was triturated with methanol, followed by extraction with hot ligroin (b. p. 90–100°). The latter removed the enol, X, which was identified by a mixed melting point. The insoluble portion was crystallized from benzene-ligroin, and identified ·by comparison with an authentic specimen of the bimolecular product, IX, and also with its 2,4-dinitrophenylhydrazone. The dimer, IX, was also identified after the other carbinols in the series (XII) had been heated, but the remainder of the material failed to crystallize.

Summary

All three types of bimolecular products formed by the dehydration of anhydroacetonebenzils under acidic conditions have been compared with respect to their behavior with Grignard reagents. They fall into three groups, each having characteristic properties.

The structures which are postulated for the organomagnesium complex of each group appear to account satisfactorily for the behavior.

Rochester 4, New York Received May 17, 1946

[Contribution from the Department of Chemistry of The University of Rochester]

Analogs of Pyridoxine. I. Some Hydroxymethylpyrimidine Derivatives[1]

By G. E. McCasland,[2] D. Stanley Tarbell, R. B. Carlin[3] and Nancy Shakespeare[4]

The synthesis of analogs of pyridoxine (I) for testing as antimalarials was suggested by the work of Seeler,[5] who found that large doses of pyridoxine counteracted the effects of atebrine or quinine on

P. lophurae in ducks. This might mean that pyridoxine was necessary for growth of the parasites, and hence that its action might be antagonized by a compound differing slightly from it in structure. Accordingly, we attempted the preparation of compounds in which the characteristic groups of pyridoxine are attached to a different heterocyclic ring[6] than the pyridine ring.

There are seven different ways in which the four characteristic groups of pyridoxine might be attached to the four carbon atoms in the pyrimidine ring. The most promising route for any of