

the reagent over approximately 1 hour, the contents of the flasks were well stirred. After standing an additional hour at 0°, 10 cc. of water was added to destroy residual hydride, followed by addition of 50 cc. of 3 *N* sodium hydroxide and 50 cc. of hydrogen peroxide (30% solution). The temperature of the reaction mixture was kept below 50°. The reaction mixture was worked up in the usual way. After distillation there was obtained 13.7 g. (72% yield) of 2-(4-cyclohexenyl)-ethanol, b.p. 86–87° at 6 mm., n_D^{20} 1.4834; reported¹² b.p. 104.5° at 16 mm., n_D^{20} 1.4832.

The 3,5-dinitrobenzoate had m.p. 66–67°. *Anal.* Calcd. for $C_{15}H_{14}N_2O_6$: C, 56.24; H, 5.03; N, 8.79. Found: C, 56.57; H, 4.96; N, 8.80.

The unsaturated alcohol (30 mmoles) was hydrogenated in the presence of platinum oxide. The 2-cyclohexyl-ethanol obtained (79% yield) had b.p. 77–78° at 4 mm., n_D^{20} 1.4651 (reported¹³ b.p. 87–89 at 6 mm., n_D^{20} 1.4636). The 3,5-dinitrobenzoate had m.p. 71–72°, reported¹⁴ m.p. 70–70.5°.

Selective Hydroboration of *d*-Limonene.—To 0.165 mole of disiamylborane in diglyme at 0° was added 20.4 g. of *d*-limonene (0.15 mole, b.p. 174° at 742 mm., n_D^{20} 1.4730,

$[\alpha]_D^{25} + 125^\circ$; reported¹⁵ n_D^{20} 1.4725, $[\alpha]_D^{20} + 123^\circ$) over a period of 5 minutes. The reaction mixture was allowed to remain for ~3 hours at room temperature. The reaction mixture was oxidized by alkaline peroxide: 50 cc. of 3 *N* sodium hydroxide followed by 50 cc. of hydrogen peroxide (30%). The alcohol was worked up in the usual manner. By distillation, there was obtained 18.3 g. of primary terpineol (79% yield), b.p. 115–116° at 10 mm., n_D^{20} 1.4855, $[\alpha]_D^{20} + 99^\circ$ (*c* in benzene 4.2); reported¹² b.p. 67–69° at 0.6 mm. n_D^{20} 1.4853–1.4866.

The 3,5-dinitrobenzoate had m.p. 91–93° (sintered at 85°). *Anal.* Calcd. for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.78; N, 8.04. Found: C, 58.60; H, 5.89; N, 8.13.

Acknowledgment.—We are deeply indebted to Dr. Kenneth S. Greenlee of American Petroleum Institute Project 45 at the Department of Chemistry of Ohio State University, who generously made available several of the pure olefins used in this study. Without this invaluable assistance this study would have been greatly handicapped. We also wish to express our appreciation to The Upjohn Company and Parke Davis and Co. for generous grants which facilitated this investigation.

(15) G. Widmark, *Acta Chem. Scand.*, **9**, 938 (1955).

(12) K. Ziegler, F. Krupp and K. Zosel, *Ann.*, **629**, 241 (1960).

(13) G. S. Hiers and R. Adams, *J. Am. Chem. Soc.*, **48**, 2385 (1926).

(14) J. J. Bost, R. E. Kepner and A. D. Webb, *J. Org. Chem.*, **22**, 51 (1957).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE, DURHAM, N. H.]

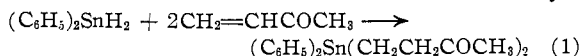
Reduction of Some Aldehydes and Ketones with Organotin Hydrides^{1,2}

BY HENRY G. KUIVILA AND O. F. BEUMEL, JR.

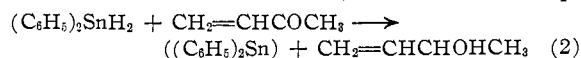
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Reductions of aldehydes and ketones with tri-*n*-butyltin hydride, triphenyltin hydride, di-*n*-butyltin dihydride, diphenyltin dihydride, *n*-butyltin trihydride and phenyltin trihydride have been investigated. In each case reduction can be achieved with certain compounds. The exclusive pathway for reduction involves transfer of hydrogen to the substrate; metal-oxygen bonds are not formed. The tin-containing products from the mono-, di- and trihydrides have the compositions R_3SnSnR_3 , R_2Sn and RSn , respectively. The double bond in α,β -unsaturated aldehydes and ketones is unaffected in the course of reduction. Stereoselectivity in the reduction of simple cyclohexanones is very similar to that exhibited by sodium borohydride. Nitrophenyl ketones suffer preferential reduction of the nitro group by diphenyltin dihydride.

We were interested in the preparation of tin compounds containing appropriate functional groups in two side chains so that cyclization could be effected in a subsequent step.³ One reaction which offered such a possibility was the newly-observed addition of organotin monohydrides to double bonds.⁴ If the reaction were undergone by dihydrides it might be possible to carry out the reaction between diphenyltin dihydride and methyl vinyl ketone (eq. 1). Cyclization of the resulting diketone could then lead to a tin heterocycle.



When the reactants were allowed to stand in ether solution, a reaction did occur, but as shown in eq. 2.



The products were easily separated by virtue of the fact that the diphenyltin was insoluble in ether.

(1) Support of this research by the Office of Ordnance Research, U. S. Army, is gratefully acknowledged.

(2) (a) A preliminary account of this work has been published: H. G. Kuivila and O. F. Beumel, Jr., *J. Am. Chem. Soc.*, **80**, 3798 (1958). (b) Based on the doctoral dissertation of O. F. Beumel, Jr., May, 1960.

(3) H. G. Kuivila and O. F. Beumel, Jr., *J. Am. Chem. Soc.*, **80**, 3250 (1958).

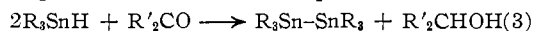
(4) G. J. M. van der Kerk, J. G. Noltes and J. G. A. Luijten, *J. Applied Chem.*, **7**, 356 (1957).

Pure methylvinylcarbinol was isolated in 59% yield.⁵

This reaction is apparently unique among metal hydride reductions in the fact that *two hydrogens are transferred to the substrate directly*; the formation of an intermediate metal alkoxide is avoided. Consequently a hydrolysis step is not needed, and acidic or basic conditions need not exist in the reaction medium at any time. This might be of importance in the reduction of certain types of sensitive compounds. A practical disadvantage lies in the fact that one mole of dihydride reduces only one mole of ketone, whereas the alkoxide mechanism would lead to the reduction of two moles. Because of its unusual character we began a study of the scope and mechanism of the reaction. In this paper, we report the results obtained in a survey of the reactions of organotin mono-, di- and trihydrides, one aromatic and one aliphatic in each case, with several aldehydes and ketones with particular emphasis on the stereochemistry whenever it was pertinent.

(5) In the interim van der Kerk and his co-workers have reported the addition of organotin di- and trihydrides to certain olefins. However, the reaction is not general (G. J. M. van der Kerk and J. C. Noltes, *J. Appl. Chem.*, **9**, 106 (1959)). These investigators find that even triphenyltin hydride does not add to methyl vinyl ketone or to phenyl vinyl ketone. In each case reduction occurs instead, the products being the alcohol and hexaphenyldistannane. See also M. C. Henry and J. G. Noltes, *J. Am. Chem. Soc.*, **82**, 558, 561 (1960).

General Considerations.—The phenyl and the *n*-butyl derivatives of each class of hydride were prepared by the reduction of the appropriate chloride with lithium aluminum hydride. The monohydrides are the most stable thermally, and can be purified by distillation at reduced pressure. They react with aldehydes and ketones according to eq. 3. This reaction is quite as remarkable as



that involving the dihydride, and has been observed independently by van der Kerk and Noltes.⁵

The reductions of cyclohexanones by triphenyltin hydride which were carried out required temperatures above 100° (without solvent), causing the hexaphenylditin to decompose partially to tetraphenyltin and metallic tin. Although benzaldehyde could be reduced by tri-*n*-butyltin hydride in 86% yield to benzyl alcohol in 15 hours at 140°, essentially no reduction of cyclohexanones occurred with triphenyltin hydride under comparable conditions. Therefore, this hydride was not examined further.

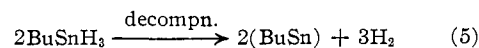
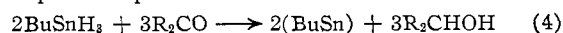
Diphenyltin dihydride was convenient to use. Since it decomposes rapidly above 100°, no attempt was made to isolate it by distillation. The ether solution obtained from the lithium aluminum hydride reduction of diphenyltin dichloride was hydrolyzed with water and used without further treatment. Reductions usually occurred readily at room temperature, and the excess hydride which was used in each reaction could be decomposed by addition of diethylamine, which also catalyzed the conversion of the diphenyltin to a less soluble modification. The fact that amines, or any strong bases, catalyze the decomposition of diphenyltin dihydride to hydrogen and diphenyltin imposes a restriction on the use of the reagent. Its thermal instability also limits application to relatively low temperatures.

Although dibutyltin dihydride was not used as extensively in this investigation, it might prove to be of greater utility than the diphenyl compound. The one drawback observed thus far is the appearance of complications in reactions with unsaturated carbonyl compounds described below. Its advantages are higher thermal stability, which makes possible reactions at higher temperatures, it can be stored under nitrogen for relatively long periods without significant decomposition; and it is essentially unaffected by amines at room temperature. The dibutyltin which is formed in the course of reductions with this hydride is an oil from which the reduction product is removed by distillation. Alternatively the dibutyltin can be allowed to oxidize and the product extracted from the oxide with ether.

Phenyltin trihydride was prepared, but decomposed at room temperature. It was possible to show that reductions could be effected with it, but they were not particularly fast nor were they complete. Ketones which underwent partial reduction were cyclohexanone, 4-*t*-butylcyclohexanone and (–)-menthone.

Butyltin trihydride was somewhat more stable, but it also decomposed at room temperature. However, by using large excess in reduction reac-

tions, high yields of ketone-free alcohols were obtained in the two cases tried: 4-methylcyclohexanone (82%) and 4-*t*-butylcyclohexanone (91%). The other product of the reaction was a deep red substance which, after removal of all volatile compounds, remained as a glass. When finely divided, it ignited spontaneously in the air. Because of this ease of oxidation considerable difficulty was experienced in obtaining a reasonably pure analytical sample. Its empirical formula was C₄H₉Sn. Since it was formed partly by hydrogen transfer to ketone and partly by simple decomposition, the course of the individual reactions cannot be definitely formulated, but eq. 4 and 5 represent possibilities.



In summary, all three classes of organotin hydrides follow the same general course of reaction with aldehydes and ketones, namely by transfer of two hydrogens to the carbonyl group.⁶

Scope of Reductions with Dihydrides.—As implied above, the dihydrides proved to be the most convenient to use in a survey of the reduction of simple aldehydes and ketones. The yields of alcohols obtained in nineteen cases using diphenyltin dihydride and in twelve cases using di-*n*-butyltin dihydride are gathered in Table I. The simple aldehydes and ketones gave uniformly good yields of alcohol. In these cases we believe that the reductions were essentially quantitative and that the lower actual yields were due to mechanical losses in the isolation.

TABLE I
REDUCTIONS OF ALDEHYDES AND KETONES WITH DIPHENYL-
TIN DIHYDRIDE AND DI-*n*-BUTYL TIN DIHYDRIDE

Carbonyl compound	% alcohol with—	
	(C ₆ H ₅) ₂ SnH ₂	<i>n</i> -Bu ₂ SnH ₂
Cyclohexanone	82	..
Benzophenone	59	85
2-Methylcyclohexanone	83	94
4-Methylcyclohexanone	82.5	76.5
4- <i>t</i> -Butylcyclohexanone	85.5	93.5
<i>l</i> -Menthone	81.5	81.5
<i>d</i> -Carvone	83.5	70.5
<i>dl</i> -Camphor	^a	^b
Benzaldehyde	62	..
Methyl vinyl ketone	59	31, 12.5
Cinnamaldehyde	75	..
Crotonaldehyde	59	43.5
Mesityl oxide	60	..
Chalcone	75	..
Benzoquinone	59	66
Anthraquinone	^c	..
Benzil	87.5	93
Acetone	^c	..
Dimethyldihydroresorcinol	^c	..
2-Acetylcyclohexanone	^c	..

^a Partial reduction along with considerable hydride decomposition. ^b About 50% reduction upon refluxing in diisopropyl ether for 15 hr. ^c Only decomposition of the hydride appeared to occur.

(6) This leads to an amusing paradox. In the case of an organotin dihydride, for example, the tin is originally in the "stannic" state, and is converted into the "stannous" state in the course of the reduction. Thus it is "reduced," even though it is acting as a reducing agent.

The α,β -unsaturated carbonyl compounds were reduced selectively to the unsaturated alcohols. However, yields were much lower with dibutyltin dihydride than with diphenyltin dihydride. This is probably due to the addition of the hydride to the double bond of the alcoholic product.

A rather high sensitivity to steric bulk is reflected in the low reactivity of camphor. Diphenyltin dihydride gave very little reduction at room temperature. Refluxing for 15 hours with dibutyltin dihydride led to only about 50% reduction.

Benzil, an α -diketone, was reduced very readily with two moles of hydride to hydrobenzoin. Dimethyldihydroresorcinol and 2-acetylcyclohexanone, β -diketones, merely facilitated the decomposition of diphenyltin dihydride. Benzoquinone was reduced in good yield to hydroquinone, but anthraquinone was not reduced. Whether these results were due to rapid decomposition of the hydride alone or to this factor combined with very slow reduction was not determined.

In addition to the compounds listed in Table I, *m*-nitrobenzaldehyde, *p*-nitrobenzaldehyde and *m*-nitroacetophenone were allowed to react with diphenyltin dihydride. In the first case a 62.5% yield of *m*-aminobenzaldehyde was obtained. The other two compounds also suffered reduction at the nitro group in preference to the carbonyl.

Stereochemistry of Reductions.—In all reductions which we have carried out, in which stereochemistry was pertinent, the composition of the isomeric alcohol mixture was determined. Results are listed in Table II. Data reported in the litera-

hydrides studied is barely outside of the experimental error involved in determining the compositions of the mixtures. In the two cases where comparison with sodium borohydride is possible the results are identical. Lithium aluminum hydride, on the other hand, gives a higher proportion of the more stable equatorial isomer in every case.

The product obtained in the reduction of benzil was exclusively the *meso*-hydrobenzoin.

These results show that the stereochemical course of the reduction is independent of the number of organic groups attached to the tin atom, and that the moderate difference in bulk between the phenyl and *n*-butyl groups has no effect. Rather large variation in rate of reaction exists among the hydrides, the order of decreasing reactivity being $(C_6H_5)_2SnH_2 > n-Bu_2SnH_2 > n-BuSnH_3 > (C_6H_5)_3SnH > n-Bu_3SnH$. The rate at which a given hydride reacts with carbonyl compounds depends on the nature of the carbonyl group. For example, diphenyltin dihydride reduced camphor very slowly whereas it reduced benzaldehyde in a rapid exothermic reaction; triphenyltin hydride reduced benzaldehyde in high yield upon heating on a steam-bath for 15 hours, whereas cyclohexanone was not completely reduced under the same conditions in two days.

Although much more information will be necessary before detailed mechanisms for these reactions can be given, certain characteristics can be deduced from the above observations. One mechanism which is definitely ruled out is a rate-determining dissociation of the hydride. If this were the case each carbonyl compound would be reduced at the same rate by a given hydride. It is hoped that further work which is in progress will provide more information regarding the mechanisms involved.

Experimental

Organotin Hydrides.—The hydrides were prepared by reduction of the appropriate organotin chlorides with lithium aluminum hydride.⁷ Our procedures differed somewhat from those described by van der Kerk and his co-workers.^{8,9}

Triphenyltin Hydride.—To 150 ml. of anhydrous ether in a three-neck flask, which was cooled in an ice-water-bath and fitted with a nitrogen inlet tube, a dropping funnel and stirrer, was added 1.56 g. (40.9 mmoles) of lithium aluminum hydride and 38.5 g. (100 mmoles) of triphenyltin chloride. The mixture was stirred at the bath temperature for 15 minutes, and then at room temperature for 3 hours. It was slowly hydrolyzed with 100 ml. of water with cooling by the ice-water-bath. The ether layer was washed with two 100-ml. portions of ice-water and dried over magnesium sulfate. The ether was distilled off and the hydride distilled very rapidly, using an oil-bath preheated to 200°. The yields amounted to 27–29 g. (77–85%), b. p. 162–168° (0.5 mm.). Because of the thermal instability of the hydride, low distillation pressures with a high-capacity vacuum pump are desirable.

Tri-*n*-butyltin hydride prepared in the same way, b. p. 68–74° (0.3 mm.), was obtained in 87% yield.

(7) A. E. Finholt, A. C. Bond, Jr., K. E. Wilzbach and H. I. Schlie-singer, *J. Am. Chem. Soc.*, **69**, 2692 (1947).

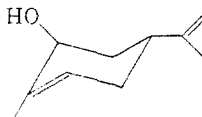
(8) J. G. Noltes and G. J. M. van der Kerk, "Functionally Substituted Organotin Compounds," Tin Research Institute, Greenford, England, 1958.

(9) G. J. M. van der Kerk, J. G. Noltes and J. G. A. Luijten, *J. Appl. Chem.*, **7**, 366 (1957).

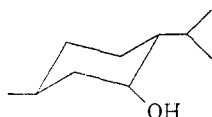
TABLE II

STEREOCHEMISTRY OF REDUCTION OF CYCLOHEXANONES BY ORGANOTIN HYDRIDES, COMPLEX METAL HYDRIDES AND ALUMINUM ISOPROPOXIDE

Reducing agent	% <i>trans</i> -alcohol obtained in the reduction of		(% I) from carvone	(% II) from methone
	4- <i>t</i> -Butyl-cyclohexanone	4-Methyl-cyclohexanone		
<i>n</i> -BuSnH ₂	92	73		
<i>n</i> -Bu ₂ SnH ₂	88	75	94.7	
(C ₆ H ₅) ₂ SnH ₂	87	76	97.1	48
(C ₆ H ₅) ₃ SnH	87	70		
LiAlH ₄	91–93 ^a	79–81 ^a	94	71 ^b
NaBH ₄		75		49
Al(Opr- <i>i</i>) ₃	77–81	67	58 ^c	30
Equilibrium	77–81 ^a	69–71 ^a		



I



II

^a E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 5992 (1957). ^b A. K. Macbeth and J. S. Shannon, *J. Chem. Soc.*, 2852 (1952). ^c R. H. Reitsem, *J. Am. Chem. Soc.*, **75**, 1996 (1953).

ture on reduction of the same compounds with lithium aluminum hydride, sodium borohydride and aluminum isopropoxide, along with equilibrium compositions of the epimeric alcohol mixtures, are included for comparison. The variation in the selectivity of the organotin hydrides is seen to be small. In fact, the total variation among the four

Diphenyltin dihydride was prepared as previously described,¹⁰ the wet ether solutions being used. Treatment of aliquots with acid yielded amounts of hydrogen corresponding to 95–100% yields of the hydride.

Di-*n*-butyltin dihydride, obtained 95–100% yields, was also used in the wet ether solution.

Phenyltin trihydride was prepared by adding phenyltin trichloride to the ether suspension of lithium aluminum hydride cooled to -70° and then allowed to warm up to -20° before hydrolysis at 0° . The ether layer contained 59% of hydride. Distillation provided 30%, b.p. 35° (2.5 mm.).

n-Butyltin trihydride⁹ (b.p. 34° (0.5 mm.)) was prepared under the same conditions used for phenyltin trihydride.

Reduction with Triphenyltin Hydride.—In these, as in all of the reductions, a nitrogen atmosphere was maintained over reaction mixtures as long as hydride was present. All of the reaction products were characterized by comparison of their infrared spectra with those of authentic samples.

Benzaldehyde.—Triphenyltin hydride (13.5 g., 38.0 mmoles) was added to 1.48 g. (14.0 mmoles) of freshly distilled benzaldehyde in a small Claisen flask. The mixture was heated on the steam-bath for 15 hours, by which time the mixture had become a wet, crystalline mass. Distillation yielded 1.2 g. (85%) of benzyl alcohol, b.p. 65° (0.8 mm.).

The residue in the flask, hexaphenylditin, was recrystallized from chloroform; m.p. 230 – 232° .

Anal. Calcd. for $C_{36}H_{50}Sn_2$: Sn, 33.91. Found: Sn, 33.76.

4-Methylcyclohexanone was reduced by the same procedure yielding 84% of 4-methylcyclohexanol containing $70 \pm 2\%$ *trans* isomer and $30 \pm 2\%$ *cis*.¹¹

4-*t*-Butylcyclohexanone was reduced in a long test-tube, and the alcohol was removed as it deposited as fine long needles near the top of the tube; yield, 62% containing $87 \pm 2\%$ *trans* and $13 \pm 2\%$ *cis*.¹¹

Reduction of Benzaldehyde with Tri-*n*-butyltin Hydride.—To 1.59 g. (15.0 mmoles) of freshly distilled benzaldehyde in a small Claisen flask was added 11.1 g. (38.0 mmoles) of tri-*n*-butyltin hydride. After heating at 140° for 15 hours, a clear, yellow solution containing a gray precipitate, presumably metallic tin, resulted. Distillation yielded 1.9 g. (86%) of benzyl alcohol, b.p. 49 – 50° (0.3 mm.), and a small amount of a colorless liquid, b.p. 137 – 145° (0.5 mm.), apparently tetrabutyltin.

Anal. Calcd. for $C_{18}H_{38}Sn$: Sn, 34.19. Found: Sn, 33.63.

Reductions with Diphenyltin Dihydride.—The ether solutions of diphenyltin dihydride were adjusted to 1 *M* on the assumption of quantitative yields in its preparation. Generally 50 ml. of this solution was added to 45.0 mmoles of carbonyl compound, the 10% excess being used in case yields were not quantitative, and to ensure complete reduction, particularly in those cases where the isomeric composition of the product alcohol was to be determined. Within about 5 minutes a white precipitate appeared; after standing overnight the precipitate was yellow, covered by a colorless supernatant. Diethylamine (1 ml.) was added in order to destroy the remaining hydride, and further polymerize the diphenyltin and thus diminish its solubility. If the amine was not added more diphenyltin precipitated as the reaction product was worked up. For maximum recovery of product, since the volume of the diphenyltin was substantial, the reaction mixture was transferred into a Soxhlet cup and extracted with ether for 2 hours or more. The extract was then concentrated and the product recovered by distillation or crystallization. The products were characterized by melting point when convenient and by comparison of their infrared spectra with those of authentic materials. Yields given in Table I refer to products with narrow distillation ranges or sharp melting points.

This procedure was used without essential modification in the reductions of benzaldehyde, cinnamaldehyde, crotonaldehyde, 4-*t*-butylcyclohexanone and 4-methylcyclohexanone. In the cases of anthraquinone, dimethyldihydroresorcinol and 2-acetylcyclohexanone, only rapid decomposition of the hydride occurred and the spectrum of the reaction product showed no indication of hydroxyl absorption.

(10) H. G. Kuivila, A. K. Sawyer and A. G. Armour, *J. Org. Chem.*, in press.

(11) Infrared spectral data in chloroform for the individual pure isomers and mixtures, recorded in the doctoral dissertation of Roland S. Ro, University of Notre Dame, were used in these determinations.

dl-Camphor was reduced only partially in 15 hours, and considerable decomposition of the hydride occurred.

Benzhydrol was recrystallized from 60– 90° petroleum ether, and the reduction product of chalcone from ethyl ether. Hydroquinone was recovered by addition of benzoquinone and the quinhydrone which precipitated was collected.

Preliminary experiments with the nitro compounds indicated that the nitro group was reduced preferentially. Consequently, 150 ml. of the diphenyltin dihydride solution was used with 47.0 mmoles of the substrate. *m*-Nitrobenzaldehyde yielded *m*-aminobenzaldehyde. The product from *o*-nitrobenzaldehyde was an oil from which the pure aminoaldehyde was not isolated, and *m*-nitroacetophenone yielded a polymeric material which did not melt below 225° .

Since methyl vinyl ketone was the first ketone reduced, the methylvinylcarbinol obtained was characterized by conversion to the allophanate, m.p. 148 – 149° , lit.¹² m.p. 151 – 152° . An analysis of the diphenyltin was made.

Anal. Calcd. for $C_{12}H_{10}Sn$: Sn, 43.49. Found: Sn, 43.22.

Benzil yielded *meso*-hydrobenzoin which was recrystallized from acetone; m.p. 134 – 35° . The product from carvone had $[\alpha]_D^{25} +29.4^{\circ}$ (*c* 2, chloroform). From the known specific rotations at 25° of $+22.8^{\circ}$ for the *d*-*cis*-alcohol, and $+202^{\circ}$ for the *d*-*trans*-alcohol,¹³ the product mixture was estimated to contain 97.1% of *d*-*cis*-alcohol. From *l*-menthone there was obtained alcohol with $[\alpha]_D^{25} -14.0^{\circ}$ (*c* 2, chloroform). This was estimated to contain 49% of *l*-menthol and 51% *d*-neomenthol on the basis of the rotations at 25° of -50.1° and $+20.7^{\circ}$, respectively, for the pure isomers.¹⁴

Reductions with Di-*n*-butyltin Dihydride.—The procedure was the same as that followed with diphenyltin dihydride. Reactions with aldehydes were fairly vigorous and exothermic; with ketones slight warming was usually noted. A change in color to a light yellow was the only visual change observed when ether was used as the solvent. If no solvent was used the di-*n*-butyltin separated out as a yellow oil. Ether was used in all cases except those noted specifically below. Although the dibutyltin was an oil, its molecular weight apparently was high enough that no difficulties were encountered in separating liquid products from it by distillation. A reduction of acetone was conducted. After standing overnight the isopropyl alcohol was distilled off and the di-*n*-butyltin which remained was analyzed.

Anal. Calcd. for $C_8H_{18}Sn$: Sn, 50.96. Found: Sn, 48.55.

This unsatisfactory analysis may be the result of incomplete removal of alcohol and partial oxidation.

In another experiment the di-*n*-butyltin residues from several reductions were combined, covered with methanol, warmed to 45 – 50° , and air was bubbled through for a day. Methanol was added from time to time. The methanol solution was then decanted from the oil still remaining and concentrated. Colorless crystals which appeared were recrystallized twice from methanol; m.p. 113 – 116° . This material showed hydroxyl absorption in this infrared, and its analysis corresponds, surprisingly, to di-*n*-butyltin dihydroxide. Its structure remains to be examined in more detail.

Anal. Calcd. for $C_8H_{20}SnO_2$: C, 35.99; H, 7.55; Sn, 44.47. Found: C, 35.67; H, 7.23; Sn, 43.63.

Crotonaldehyde, methyl vinyl ketone, 4-*t*-butylcyclohexanone and 4-methylcyclohexanone were reduced uneventfully by the standard procedure.

In the case of benzophenone, no solvent was used, and the mixture of reactants was heated at 40 – 60° for 3 hours before being allowed to stand overnight at room temperature. The product was then allowed to stand exposed to the air for 12 days and extracted with ether, from which the benzhydrol was recovered and recrystallized from 60– 90° ligroin.

Camphor showed no evidence of being reduced after standing in ether solution with the hydride for 15 hours. The ethyl ether was distilled off and replaced with diiso-

(12) I. M. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, 1953, p. 526.

(13) R. G. Johnson and J. Read, *J. Chem. Soc.*, 233 (1934).

(14) J. Read, *Chem. Revs.*, 7, 1 (1930).

propyl ether. After refluxing for 24 hours a clear, yellow solution containing metallic tin resulted. The ether was distilled and the product sublimed. Infrared analysis indicated approximately 50% reduction.

Reduction of benzoquinone was vigorous and exothermic, leading initially to the precipitation of quinhydrone, which redissolved as it in turn was reduced completely within 2 hours. The product hydroquinone was converted to quinhydrone by addition of more benzoquinone for isolation.

The *meso*-hydrobenzoin from reduction of benzil was isolated after the di-*n*-butyltin had been converted to the oxide by the addition of 30% hydrogen peroxide.

Isomeric alcohol mixtures obtained from *d*-carvone and *l*-methanol had specific rotations (*c* 2, chloroform) of +34.0° and -21.31°, respectively, from which the compositions reported in Table II were estimated.

Reductions with Phenyltin Trihydride.—To 2.94 g. (30.0 mmoles) of cyclohexanone was added 50 ml. of ether containing 25.5 mmoles of phenyltin trihydride. The reaction flask was cooled in an ice-bath. A pale yellow solid began to form in the orange solution and precipitation continued for several hours. The mixture was then allowed to stand at room temperature for 4 days. An infrared spectrum indicated about one-third reduction of the ketone and the presence of considerable hydride. Upon warming, decomposition of the hydride occurred, but further reduc-

tion of ketone did not seem to take place. The cyclohexanol was not isolated. Similar results were observed with 4-*t*-butylcyclohexanone and *l*-menthone.

Reductions with Butyltin Trihydride. 4-*t*-Butylcyclohexanone.—To 1.54 g. (10.0 mmoles) of 4-*t*-butylcyclohexanone in a long test-tube was added 4.6 g. (25.0 mmoles) of butyltin trihydride. The mixture was allowed to stand at room temperature for a day. Since the reaction was incomplete, the mixture was heated at 40–50° for 4 hours whence the reduction was complete. Heating at 75° for 2 hours destroyed the remaining hydride, leaving a solid red mass in the bottom of the tube. Heating on the steam-bath caused the alcohol to sublime and deposit near the top of the tube where 91% was collected. The procedure for reduction of 4-methylcyclohexanone was essentially the same.

Characterization of the Tin-containing Product from Butyltin Trihydride Reductions.—The product remaining in the test-tube after the above experiments was pyrophoric. In order to obtain the product in an analytically pure state reductions were carried out with acetone with extreme precautions taken to exclude air. From one such reduction a deep red amorphous solid was isolated.

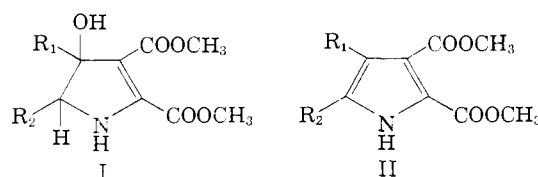
Anal. Calcd. for C₈H₉Sn: C, 27.31; H, 5.16; Sn, 67.52. Found: C, 27.23; H, 5.21, Sn, 66.57.

COMMUNICATIONS TO THE EDITOR

A NEW HETEROCYCLE SYNTHESIS: PYRROLES AND QUINOLINES

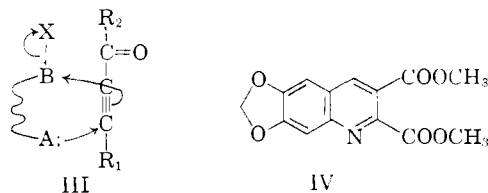
Sir:

Impelled by an interest in providing a better synthesis of pyrroles, we were led to consider Michael addition of amines to acetylenic ketones as a means of affording the enamine moiety of these heterocycles. In particular the appropriate amines should be α -amino-ketones so that the enamine, once formed, could be cyclized and dehydrated to complete the synthesis of the pyrrole ring. α -Amino-ketones, however, dimerize readily to dihydropyrazines and are stable only as their salts.¹ It was deemed reasonable, however, that in the presence of a relatively weak base the salts would generate a concentration of free base low enough to hamper the bimolecular dimerization but suitable for Michael addition to the acetylenic carbonyl compound. Accordingly, when equimolar quantities of α -aminopropiophenone hydrochloride, sodium acetate, and dimethyl acetylenedicarboxylate were boiled in methanol, NaCl deposited over several minutes and after ten minutes, filtration and evaporation afforded an 80% yield of I ($R_1 = C_6H_5$; $R_2 = CH_3$), m.p. 108°, which was converted readily to II ($R_1 = C_6H_5$; $R_2 = CH_3$), m.p. 182–183°, on boiling half an hour with a little HCl/CH₃OH and recrystallizing. The infrared spectra and analyses confirmed these formulations (infrared I, 2.85, 2.95, 5.80, 5.92, 6.21 μ ; II, 2.85, 5.80, 5.92 μ). Isolation of the intermediate I was of course not necessary and these pyrroles were prepared in the indicated yields without isolation of intermediates: II ($R_1 = R_2 = C_6H_5$), m.p. 192°, 44%; II ($R_1 = C_6H_5$, $R_2 = CH_3$),



m.p. 182–183°, 81%; II ($R_1 = R_2 = CH_3$), m.p. 142–143°, 20%. In each case the analyses were consistent with these formulations. Of these only the diethyl ester of II ($R_1 = R_2 = CH_3$) previously has been prepared, by Fischer² by the Knorr synthesis, m.p. 110°; prepared in the present procedure using diethyl acetylenedicarboxylate, the same diethyl ester had m.p. 112–113°.

The great ease and relatively high yields of this synthesis prompted us to a consideration of the extension of the approach to other heterocycles. The synthetic conception may be generalized as in III to indicate its broad potential for the production of heterocyclic nuclei; it should be noted that the acetylenic carbonyl reactant provides asymmetric directionality so that only a single isomer will



form and also affords one unit of unsaturation toward the ultimate heteroaromatic system. We have demonstrated this expanded scope in the production of the quinoline IV, m.p. 178–179°, from

(1) A. H. Corwin, "Heterocyclic Compounds," Vol. 1, p. 287, ed. R. C. Elderfield, John Wiley and Sons, New York, N. Y., 1950.

(2) H. Fischer and W. Kutscher, *Ann.*, **481**, 199 (1930).