These results fully confirm those obtained by infrared analysis. Any equilibrium I $\rightleftarrows$ II must lie very far to the right at the total concentrations used for infrared and nuclear magnetic resonance measurements. It is not impossible that at much lower concentrations, such as those used for ultraviolet spectroscopy, the relative concentration of I may become more significant.

The formation of an oxime of phthalaldehydic acid in acidic solution[6] suggested the presence of some I in these conditions. When the compound was dissolved in 2 *N* hydrochloric or sulfuric acid, the nmr spectrum was practically identical with that recorded in water. However, when the concentration of acid was increased, the spectrum changed in a manner analogous to that observed in alkaline solution. The 6.75-ppm signal in water was at 7.18 in 50% sulfuric acid, 8.48 in 80% acid, 9.12 in 90% acid, and 9.45 ppm in pure sulfuric acid. In comparison, the 4-carboxybenzaldehyde showed a sharp singlet at 9.95 ppm and phthalide, a singlet at 5.05 ppm in the same conditions, indicating no drastic effect of the strong acid on the spectrum of these compounds. No good model compound was available for judging the possible effect on the nmr spectrum of protonation of II or formation of a carbonium ion derived from it.[10] We noted, however, that, whereas all the compounds mentioned above gave colorless sulfuric acid solutions, intense colors were observed when benzhydrol or benzylic acid were dissolved in this acid. Furthermore in these last two spectra the benzylic protons did not appear at a field lower than that of the aromatic ones. We believe, therefore, that our results indicate a rapid equilibrium between the open and cyclized forms of phthalaldehydic acid in strong acid, favoring the open form. In pure sulfuric acid, the equilibrium probably has close to 95% of the open form.

It is clear that in general the name 2-carboxybenzaldehyde should be avoided in designating phthalaldehydic acid, best described as 3-hydroxyphthalide, except in strong acids or in basic media. Furthermore, the claim that the deuterated acid III was easily isolated[7] is not supported by the results of either infrared or nmr spectroscopy. Although the structure of the described products may not be affected, the mechanistic discussions found in that article deserve a more critical evaluation.

Experimental Section

The starting material used in this work was purchased as 2-carboxybenzaldehyde from Aldrich Chemical Co., Milwaukee, Wis. After recrystallization from water, it melted at 97°. The sulfuric acid (95–98%) and all solvents for nmr determinations were reagent grade and were used without further purification.

The nmr spectra were determined on a Varian A60-A spectrometer, using a tetramethylsilane standard. In the case of the water and sulfuric acid solutions, the general position of the peaks being more important than their precise location, the standard was used externally.

3-Ethoxyphthalide was obtained by irradiating II in ethanol-containing chloroform.[11]

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[10] The study of 3-ethoxyphthalide in concentrated sulfuric acid shed no light. Immediate hydrolysis took place and the spectrum was identical with that of an equimolar mixture of II and ethanol.

[11] J. Kagan, unpublished results.

Synthesis of Organolead Compounds from Lead Tetraacetate

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The reactions of divalent lead salts with organometallic alkylating agents have been thoroughly studied.[1,2] The most frequently used laboratory preparation of tetraorganolead compounds is the reaction of lead dichloride with an organomagnesium or organolithium reagent (eq 1). The reactions of organometallic alkylating agents and tetravalent lead salts have been studied by several investigators.[3,4] The interest in tetravalent lead salts arises because one might expect them to be converted quantitatively to the desired tetraorganolead compound without formation of any by-product lead metal (eq 2). Previous investigations have found no advantage in using tetravalent lead salts with Grignard or lithium reagents since substantial reduction of the tetravalent lead by the organometallic occurred.[5]

$$4RM + 2PbCl_2 \rightarrow R_4Pb + Pb + 4MCl \qquad (1)$$

$$4RM + PbX_4 \rightarrow R_4Pb + 4MX \qquad (2)$$

This study was undertaken to investigate further the reaction of lead tetraacetate with Grignard reagents and attempt to find reaction conditions under which no by-product lead is obtained. Tetramethyllead and tetraethyllead were prepared in 89 and 94% yield, respectively, according to eq 2. Unexpectedly it was found that the most critical factors in obtaining these high yields is the order in which the reactants are mixed and the solvent used. The preferred method, resulting in no by-product lead formation, is the addition of lead tetraacetate to the Grignard reagent in tetrahydrofuran (THF). Higher yields are obtained by performing the reaction at lower temperature (5°) as compared to ambient temperature (25°). These three modifications of reaction conditions account for the success of these experiments and the failure of earlier workers in obtaining high yields without production of lead metal. Because of the availability of lead tetraacetate and ability to obtain high yields in short reaction times, this reaction is particularly useful for synthesis of many tetraalkyllead compounds.

An attempt to form tetraneopentyllead from the reaction of neopentylmagnesium chloride and lead tetraacetate at 5° resulted in a 50% yield of hexaneopentyldilead. Previous attempts in preparing tetraneopentyllead by several methods have also met with failure.[6,7] It was found that reaction of neopentyl-

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magnesium chloride and lead dichloride gives hexaneopentyldilead and trineopentyllead chloride; however, the yield of hexaneopentyldilead was considerably less than that obtained in this work from lead tetraacetate.

Experimental Section

All reactions were carried out under an argon atmosphere. Tetrahydrofuran was distilled from lithium aluminum hydride before use. Lead tetraacetate was obtained from Matheson Coleman and Bell, Norwood, Ohio. Before use it was washed several times with pentane to remove excess acetic acid. The reactions were carried out in a 500-ml three-necked flask equipped with condenser (dewar filled with Dry Ice–acetone) and paddle stirrer. In all experiments the lead salt was added from a 50-ml round-bottom flask connected to the reaction vessel by a short piece of Gooch tubing.

At the end of the reaction residual Grignard reagent was destroyed with dilute HCl (1.0%). The organolead products were either collected and weighed or the organic layer was analyzed without physical separation by iodimetric titration[8] or spectrophotometrically by dithizone method.[9] The lead alkyls were identified by nuclear magnetic resonance (nmr) and vapor phase chromatography.

Tetramethyllead.—Methylmagnesium chloride was prepared from 6.0 g (0.25 g-atom) of magnesium metal and an equivalent amount of methyl chloride in 200 ml of THF. The solution was then cooled to 5° in an ice bath and 22.2 g (0.05 mole) of lead tetraacetate added over a 20-min period. The ice bath was then removed and stirring was continued at ambient temperature for 15 min. The excess Grignard was hydrolyzed and the organic layer yielded 11.78 g (89% yield) of tetramethyllead. No lead metal was formed in the reaction mixture.

Tetraethyllead.—Ethylmagnesium chloride was prepared from 8.0 g (0.32 g-atom) of magnesium metal and an equivalent amount of ethyl chloride in 200 ml of THF. The solution was then cooled to 5° in an ice bath and 22.2 g (0.05 mole) of lead tetraacetate was added over a 40-min period. The ice bath was then removed and stirring was continued at ambient temperature for 15 min. The reaction mixture was hydrolyzed and the THF layer was separated. The aqueous layer was then extracted several times with THF. The combined THF extracts were distilled and 14.5 g (90% yield) of tetraethyllead was obtained. In a similar experiment the organic layer was diluted to volume in a volumetric flask. The organic lead content as determined by titration was 15.11 g (94% yield). No lead metal was observed. When ethyl ether was substituted for THF under the same conditions, the yield of tetraethyllead decreased to only 12.5%.

Hexaneopentyldilead.—A Grignard solution was prepared from 5.0 g (0.2 g-atom) of magnesium metal and 22.0 g (0.2 mole) of neopentyl chloride in 300 ml of THF. The Grignard was cooled to 5° in an ice bath and 22.2 g (0.05 m) of lead tetraacetate was added over a 30-min period. The ice bath was removed and the greenish-brown solution was stirred at ambient temperature for 15 min. The solution was hydrolyzed and the THF was removed by distillation. The yellow solid which floated on the aqueous layer was extracted into petroleum ether (bp 37–54°). Evaporation of the ether yielded 21 g (50% yield) of hexaneopentyldilead. The product was identified from its nmr spectrum and melting point. The nmr spectrum of the crude product indicated the presence of a small amount of trineopentyllead chloride. No lead was formed in the reaction.

Registry No.—Lead tetraacetate, 546-67-8; tetramethyllead, 75-74-1; tetraethyllead, 78-00-2; hexaneopentyldilead, 5573-80-8.

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Conformational Analysis. I. The Relative Size of Methyl and Methyl-d_3 Groups[1]

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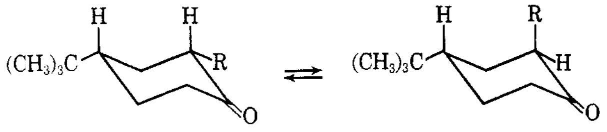
Secondary isotope effects arising from replacement of hydrogen by deuterium have been attributed by some workers to hyperconjugative effects[2] and by others to steric effects.[3] Recently this problem has been examined[4] in an attempt to obtain a quantitative estimate of both effects in a given reaction. In virtually every case investigated the position being examined has been adjacent to an aromatic ring or reaction center such that hyperconjugative effects could not be excluded. Even in those cases where a difference in size of deuterium and hydrogen was proven, the possibility of hyperconjugative effects could not be totally excluded.

In three cases where totally saturated systems were used different results were found. In a Meerwein–Ponndorf–Verley reduction[5] no evidence for difference in size of a methyl and methyl-d_3 was observed. However, in the alcoholysis of α-phenylbutyric anhydride[6] and in the generation of sulfoxides[7] from optically active alcohols a methyl and methyl-d_3 appear to show a difference in steric size.

We wanted to examine the relative size of deuterium and hydrogen in an equilibrium reaction in a case where hyperconjugative effects could be excluded. We chose to compare the relative size of a methyl and methyl-d_3 group in a steric situation which involved equilibration between the axial and equatorial 2 position of 4-*t*-butylcyclohexanone. Steric effects are relatively well understood in cyclohexanone systems[8] and this appeared to offer an opportunity to determine what factors were needed to cause deuterium and hydrogen to show different steric sizes.



cis *trans*

Since a high degree of accuracy was needed, both compounds (2-methyl-4-*t*-butylcyclohexanone and 2-

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[1] This investigation was supported in part by Research Grant HE 07050 from the National Heart Institute, U. S. Public Health Service.

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