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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[8] G. Galingaert, *Chem. Rev.*, **2**, 43 (1925).

[9] M. E. Griffing, A. Rozek, L. J. Snyder, and S. R. Henderson, *Anal. Chem.*, **29**, 190 (1957).

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

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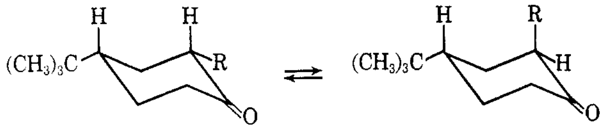
Secondary isotope effects arising from replacement of hydrogen by deuterium have been attributed by some workers to hyperconjugative effects[2] and by others to steric effects.[3] Recently this problem has been examined[4] in an attempt to obtain a quantitative estimate of both effects in a given reaction. 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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[2] A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958); E. S. Lewis, *Tetrahedron*, **5**, 143 (1959); V. J. Shiner, Jr., *ibid.*, **5**, 243 (1959).

[3] (a) L. S. Bartell, *Tetrahedron Letters*, No. 6, 13 (1960); *J. Am. Chem. Soc.*, **83**, 3567 (1961); (b) K. Mislow, R. Graeve, A. J. Gordon, and G. H Wahl, Jr., *ibid.*, **86**, 1733 (1964); (c) H. C. Brown and G. J. McDonald, *ibid.*, **88**, 2514 (1966); (d) H. C. Brown, M. E. Azzaro, J. G. Koelling, and G. J. McDonald, *ibid.*, **88**, 2520 (1966).

[4] G. J. Karabatsos, G. C. Sonnichsen, C. G. Papaioannou, S. E. Scheppele, and R. L. Shone, *ibid.*, **89**, 463 (1967).

[5] K. Mislow, R. E. O'Brien, and H. Schaefer, *ibid.*, **82**, 5512 (1960); **84**, 1940 (1962).

[6] A. Horeau, A. Nouaille, and K. Mislow, *ibid.*, **87**, 4957 (1965).

[7] M. M. Green, M. Axelrod, and K. Mislow, *ibid.*, **88**, 861 (1966).

[8] (a) N. L. Allinger and H. M. Blatter, *ibid.*, **83**, 994 (1961); (b) N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *ibid.*, **88**, 2999 (1966); (c) W. D. Cotterill and M. J. T. Robinson, *Tetrahedron*, **20**, 765 (1964).

methyl-d_3-4-*t*-butylcyclohexanone) were prepared and then were equilibrated and analyzed under identical conditions. The method of synthesis was similar to that used by Allinger and co-workers[8a,b] and involved alkylation of 2-carboethoxy-4-*t*-butylcyclohexanone with either methyl iodide or methyl-d_3 iodide followed by hydrolysis and decarboxylation. The two ketones were purified by gas chromatography prior to equilibration. The results of the equilibration studies are shown in Table I. Our results for 2-methyl-4-*t*-butylcyclohexanone do not differ materially from those of Allinger and Blatter.[8a]

TABLE I
EQUILIBRIUM DATA FOR 2-ALKYL-4-*t*-BUTYLCYCLOHEXANONE IN METHANOL WITH METHOXIDE

2-Alkyl group	Temp, °C	% *cis*[a]
Methyl	25	93.04 ± 0.26
	64	91.68 ± 0.28
Methyl-d_3	25	93.15 ± 0.34
	64	91.15 ± 0.47

[a] Each of these values represents the average of three separate equilibrations. Each equilibration was analyzed five times.

If the methyl-d_3 group is smaller than the methyl group, then the 2-methyl-d_3 ketone should show a smaller amount of *cis* isomer at equilibrium since the *cis* isomer has the 2-alkyl group in an equatorial configuration. While this appears to actually occur at 64°, the difference appears to be at the limits of experimental error. From the observed precision a difference of greater than ±0.5% in the *cis* and *trans* isomers at equilibrium in going from the 2-methyl to the 2-methyl-d_3 ketone would have been required in order to be reliably observed. In order to set the limits of error in thermodynamic quantities which our method could observe, it can be calculated that an error of ±0.5% in the *cis* and *trans* isomers at equilibrium corresponds to an error of approximately ±0.05 kcal/mole in ΔF, and an error of ±1.0% in the *cis* and *trans* isomers corresponds to an error of approximately ±0.10 kcal/mole in ΔF.

It appears that in the degree of steric crowding in the axial position of a cyclohexanone ring the methyl and methyl-d_3 groups do not show a difference in steric size of greater than about 0.05 kcal/mole relative to the equatorial position. It is not clear whether the method used here is simply not sensitive enough to detect a difference in size of a methyl and methyl-d_3 groups or whether as Mislow has suggested[5] a more sterically crowded situation is required before a difference in size can be detected.

Experimental Section

Methyl-d_3 Iodide.—The methyl-d_3 iodide was prepared by thermal decomposition of trimethyl-d_9-sulfoxonium iodide according to the procedure of Cotton and co-workers[9] and had bp 41° (760 mm) (lit.[9] bp 41°).

2-Alkyl-4-*t*-butylcyclohexanones.—Since reduction using a hydrogenation catalyst was not feasible with a methyl-d_3 compound the method of Allinger and co-workers[8a,b] involving alkylation of 2-carbethoxy-4-*t*-butylcyclohexanone (bp 125–128° (6 mm); $n^{25}\text{D}$ 1.4781) with methyl iodide or methyl-d_3 iodide followed by hydrolysis and decarboxylation was used. The 2-methyl-4-*t*-butylcyclohexanone had bp 77° (3.5 mm) and the 2-methyl-d_3-4-*t*-butylcyclohexanone had bp 80–81° (4 mm). In each case the products appeared to be contaminated with 4-*t*-butylcyclohexanone. They were therefore purified by gas chromatography on a 2-m column of 25% tricyanoethylation product of glycerine on firebrick prior to equilibration. The purified 2-methyl-d_3-4-*t*-butylcyclohexanone was analyzed by combustion[10] and showed 14.5 atom % excess deuterium, or 2.9 deuteriums per molecule. This indicates the compound is about 90% d_3 and 10% d_2.

Equilibrations.—Both sets of ketones, the 2-methyl and 2-methyl-d_3, were equilibrated and analyzed under identical conditions. Equilibration was carried out by dissolving 170 mg of sodium in 30 ml of dry methanol and then adding 200 mg of purified ketone. The resulting solution was then maintained at 64° for 30 hr or 25° for 72 hr. The equilibrated ketones were isolated by pouring the methanol solutions onto ice, and extraction with benzene. After drying the benzene solutions and removal of most of the solvent under reduced pressure the resulting ketone mixture was analyzed on a 2-m column of 25% tricyanoethylation product of glycerine on firebrick using an F & M Model 500 gas chromatograph. Each ketone was equilibrated three times at each temperature and each equilibration was analyzed five times. Analysis of the gas chromatograms was carried out by cutting out each peak and weighing it. The results are shown in Table I. It was assumed that the two isomers of the 2-methyl ketone would show the same relative thermal response as the two isomers of the 2-methyl-d_3 ketone. This was necessary because difficulty of isolating a sufficient quantity of the pure *trans* ketones precluded the possibility of preparation of standards. The assumption made appears to be a safe one and should not affect the validity of the results.

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[9] F. A. Cotton, J. H. Fassnacht, W. D. Horrocks, Jr., and N. A. Nelson, *J. Chem. Soc.*, 4138 (1959).

[10] Deuterium analysis was performed by J. Nemeth, University of Illinois, Urbana, Ill.

Alkylation of 2-Carbethoxycyclopentanone in Dimethyl Sulfoxide[1]

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In the course of other work we had occasion to alkylate 2-carbethoxycyclopentanone. In general, alkylations of this β-keto ester are carried out in refluxing benzene or toluene,[2] solvents in which high molecular weight ion pair aggregates of the metal enolate are formed.[3] The reactivity of such aggregates is considerably less than that of the "free" enolate ion.[3] We have found that interaction of the potassium salt of 2-carbethoxycyclopentanone with an appropriate alkyl halide in dimethyl sulfoxide at room temperature (25–30°) provides good yields of alkylated keto ester and probably constitutes the best method of alkylating this β-keto ester.[2,4] Our results are summarized in Table I.

Rhoads[5] has found that alkylation of the sodium salt of 2-carbethoxycyclopentanone in dimethyl sulfoxide with isopropyl iodide led to appreciable O-alkylation. Our repetition of this work gave identical results. On the other hand we were unable to detect

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[1] We thank the donors of the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation for support of this research.

[2] H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., p 172; see also p 170, footnote 20.

[3] H. E. Zaugg, B. W. Horrom, and S. Borgwardt, *J. Am. Chem. Soc.*, **82**, 2895 (1960).

[4] See D. Martin, A. Weise, and H. J. Niclas, *Angew. Chem. Intern. Ed. Engl.*, **6**, 318 (1967), for leading references.

[5] S. J. Rhoads and R. W. Hasbrouck, *Tetrahedron*, **22**, 3557 (1966).