Lithium Aluminum Hydride Reactions in Pyridine Solution. II. The Role of Steric Effects in the Reductive Cleavage of Pinacolones

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The occurrence of carbon-carbon cleavage during the reduction of benzpinacolone and related ketones by lithium aluminum hydride in pyridine appears to depend, to some degree, on steric compression in the intermediate alkoxyaluminohydrides, as well as on the stability of the leaving group.

It has previously been observed that reduction of certain benzpinacolones with lithium aluminum hydride in pyridine results in surprisingly facile cleavage reactions, leading to triarylmethanes and benzyl alcohol.[3] The need for a highly stabilized carbanion as leaving group in this reaction, where no proton donor is available, is shown by the failure of phenyl benzhydryl ketone to undergo reductive cleavage.[3] Pyridine, by virtue of its excellent coordination properties, liberates the unassociated alkoxide ion from the initially formed alkoxyaluminohydride by nucleophilic displacement on aluminum.[3] The thermal cleavage of metal alkoxides to carbonyl compounds (which, in this instance, may undergo further reduction) and carbanions has been found to proceed most rapidly when the oxygen-metal bond is highly ionic,[4] thus explaining the role of pyridine in the present case. Since those alkoxides which cleave during reduction appear to suffer considerable steric compression, it appeared advisable to investigate the role of steric factors in promoting cleavage, in addition to the stability of the leaving group and the effect of the solvent.

A classical case of steric acceleration in free radical chemistry is the effect of *ortho* substituents on the ease of dissociation of hexaarylethanes into triarylmethyl radicals.[5] For example, hexa-*o*-tolylethane dissociates more readily than hexa-*p*-tolylethane; also, bis(9-phenyl-9-fluorenyl) dissociates less readily than hexaphenylethane, since two phenyl rings on each ethane carbon of the former compound are "tied back" and steric compression is partially relieved.[5] The cleavage of alkali metal salts of the highly branched diisopropylalkylcarbinols is also accelerated by increasing bulk in the primary alkyl group which is cleaved.[4a]

In order to gain information relating to possible steric acceleration of reductive cleavage, we have prepared two ketones which are isomeric with benzpinacolone, namely α-(*p*-biphenylyl)desoxybenzoin (I) and α-(*o*-biphenylyl)desoxybenzoin (II), and studied their behavior toward lithium aluminum hydride in pyridine. The cleaved carbanions would all have comparable resonance stability, and indeed the anions of 4-benzylbiphenyl and 2-benzylbiphenyl can be generated from their conjugate acids under the conditions of reduction (see below). Also, α-(1-naphthyl)desoxybenzoin (III) was reduced, although the cleaved anion would have only nine resonance forms, rather than ten as do the other species under consideration. Finally, methyl trityl ketone was compared with benzpinacolone in order to evaluate the effect of a smaller group in opposition to the neighboring phenyls of the trityl group.

Ketones I and II underwent normal reduction without any evidence of carbanion formation, as shown by the complete absence of characteristic orange to purple colors attributable to the anions. Also, product studies and infrared spectra showed that no cleavage products were present. Furthermore, it was observed that 1,2-diphenyl-2-*p*-biphenylylethanol was not cleaved by hot alcoholic sodium hydroxide, under conditions where benzpinacolyl alcohol was converted to triphenylmethane and benzaldehyde.[6] Reduction of III also gave only normal product. Regardless of which diastereomer would result in the reduction of these ketones, the intermediate alkoxyaluminohydride can achieve a conformation in which no aryl group is flanked by *two* aryl groups on the adjacent carbon.

Such nonbonded interaction of large groups, evident in the alkoxyaluminohydride from benzpinacolone (IV), causes considerable stretching and weakening of the carbon-carbon bond and may facilitate the cleavage reaction. Methyl trityl ketone (V) when subjected to reductive cleavage conditions, gave less than 10% yield of triphenylmethane, whereas IV had given 72% cleavage in a parallel experiment.[3] This difference can most satisfactorily be attributed to steric factors.[7]

(1) Taken in part from the B.S. thesis of J. R. Rogozinski, U. of Buffalo, June 1960.

(2) Participant in a summer research program for high school teachers of science in 1960, sponsored by the National Science Foundation (Grant G-10957).

(3) P. T. Lansbury, *J. Am. Chem. Soc.*, **83**, 429 (1961).

(4) (a) H. D. Zook, J. Marsh, and D. F. Smith, *J. Am. Chem. Soc.*, **81**, 1617 (1959); (b) D. J. Cram *et al.*, *J. Am. Chem. Soc.*, **81**, 5740-5790 (1959).

(5) E. S. Gould, *Mechanism and Structure in Organic Chemistry*, Holt, Dryden, and Winston, Inc., New York, N. Y., 1959, p. 676.

(6) L. Ellison and J. Kenyon, *J. Chem. Soc.*, 779 (1954).
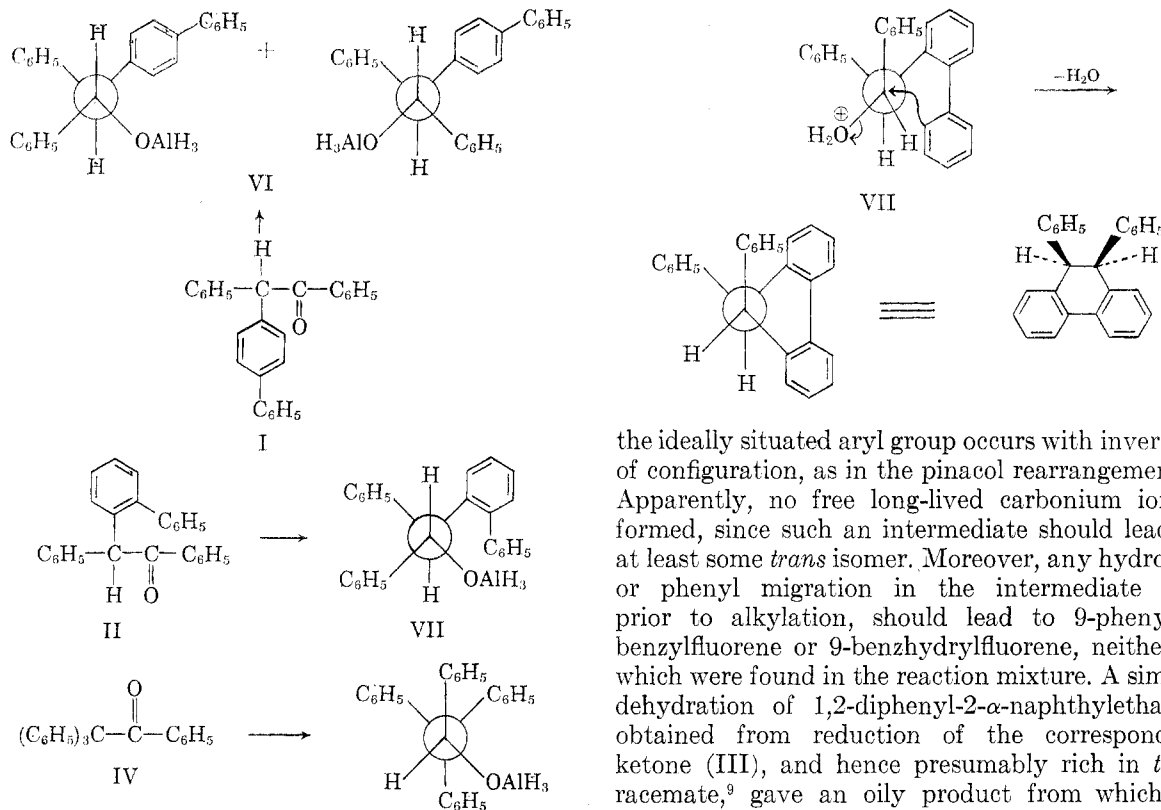
Ketones I, II, and III were prepared by the stereospecific addition of the appropriate organo-lithium compound to *dl*-benzoin, yielding the *dl*-erythro-triarylethylene glycols,[8] followed by pinacol rearrangement of the diols. The crude oily carbinols, VI and VII, resulting from reduction of I and II were shown to be free of ketone and cleavage products by infrared spectroscopy. Since I could undergo reduction equally well in either of two preferred conformations (assuming equal bulk for phenyl and *p*-biphenylyl),[9] it is not surprising that the crystallized product exhibited a broad melting range, suggesting a mixture of the two diastereomeric racemates. Although the carbinol from II could not be obtained in crystalline form, it was apparently quite pure *dl-threo* racemate, as predicted by Cram's rule.[9] This conclusion is based on the finding that cyclodehydration of the crude carbinol affords pure *cis*-9,10-diphenyl-9,10-dihydrophenanthrene[10] and none of the more stable *trans* isomer. In the dehydration step, the displacement of water from the protonated carbinol by

the ideally situated aryl group occurs with inversion of configuration, as in the pinacol rearrangement.[11] Apparently, no free long-lived carbonium ion is formed, since such an intermediate should lead to at least some *trans* isomer. Moreover, any hydrogen or phenyl migration in the intermediate ion, prior to alkylation, should lead to 9-phenyl-9-benzylfluorene or 9-benzhydrylfluorene, neither of which were found in the reaction mixture. A similar dehydration of 1,2-diphenyl-2-α-naphthylethanol, obtained from reduction of the corresponding ketone (III), and hence presumably rich in *threo* racemate,[9] gave an oily product from which no *cis*-1,2-diphenylacenaphthene could be obtained. The expected presence of both racemates in this alcohol mixture,[12] as well as the anticipated difficulty in forming the acenaphthene ring may well be responsible for the complexity of the dehydration product.

The acidity of triphenylmethane, 2-benzyl- and 4-benzylbiphenyl toward lithium aluminum hydride in pyridine is shown by the formation of typical highly colored carbanion solutions,[13] the first being blood red, the second orange, and the last deep violet. Since the three above carbanions can all be formed under reduction conditions, the cleavage of IV, versus normal reduction of I and II, appears to depend on steric compression due to phenyl-phenyl interaction in the alkoxyalumino-

(7) However, the resonance energy of acetaldehyde, which is obtained from cleavage of V, is not as great as benzaldehyde, from IV, and therefore the carbonyl-forming transition state from V may be less stabilized than that from IV.
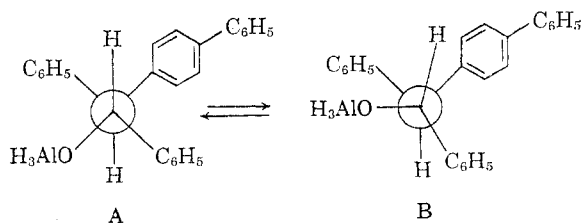
(8) D. J. Cram and K. Kopecky, *J. Am. Chem. Soc.*, **81**, 2748 (1959); D. Y. Curtin, E. E. Harris, and E. K. Meislich, *J. Am. Chem. Soc.*, **74**, 2901 (1952).

(9) D. J. Cram and F. A. Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952).

(10) E. D. Bergmann and Z. Pelchowicz, *J. Org. Chem.*, **19**, 1387 (1954).

(11) P. D. Bartlett and R. F. Brown, *J. Am. Chem. Soc.*, **62**, 2927 (1940).

(12) A. McKenzie and W. S. Dennler, *J. Chem. Soc.*, **125**, 2105 (1924). These workers observed a moderate degree of stereospecificity in the sodium-alcohol reduction of α-naphthylbenzoin oxime, the ratio of diastereomeric products being about 4:1.

(13) J. E. Leffler, *The Reactive Intermediates of Organic Chemistry*, Interscience Publishers, Inc., New York, N. Y., 1956, p. 177.

hydride ion from IV. When a neighboring phenyl is flanked on one side by a hydrogen atom, a small rotational adjustment toward the small group appears to relieve interference with the large group flanking the other side, as shown in conformation B for alkoxide VI.

The small amount of cleavage from methyl trityl ketone is due to the absence of severe phenyl-phenyl interactions in the alkoxide from V, and their replacement by the less effective phenyl-methyl interactions.

EXPERIMENTAL[14]

Preparation of α-(p-biphenylyl)hydrobenzoin. A solution of p-biphenylyllithium was prepared, according to the procedure of Gilman and Dunn,[15] from 1.34 g. (0.19 g.-atom) of lithium, 20.9 g. (0.089 mole) of p-bromobiphenyl, and 400 ml. of anhydrous ether. The gradual addition of 5.30 g. (0.025 mole) of benzoin led to the appearance of an olive-green color. After setting overnight, the reaction mixture was hydrolyzed with saturated ammonium chloride solution and the resulting ether layer washed with sodium bicarbonate solution, dried over sodium sulfate, and subsequently evaporated nearly to dryness. The remaining paste was stirred with ligroin and the resulting solid filtered and dried. This crude material showed no carbonyl absorption in the infrared (Nujol mull). Recrystallization from ethanol gave three crops of the desired carbinol, totaling 6.55 g. (72%) and melting at 205–218°. The analytical sample of the alcohol had m.p. 220.5–221.5° (from ethanol).

Anal. Calcd. for $C_{26}H_{22}O_2$: C, 85.2; H, 6.1. Found: C, 84.4; H, 6.0.

Preparation of α-(p-biphenylyl)desoxybenzoin. Five grams of the above glycol was dissolved in 25 ml. of hot acetic acid, which contained a few drops of sulfuric acid, and refluxed for 5 min. The solution was then cooled, poured into ice water, and the white precipitate removed by filtration, washed with water, dilute bicarbonate, and dried. This crude material was free of glycol, as judged by infrared. Recrystallization from ethanol (Norit) gave 2.2 g. of the ketone (I), m.p. 146–149°, from which an analytical sample was obtained, m.p. 147–149°. The yield of I was 46%, although more impure ketone could be isolated from the filtrates.

Anal. Calcd. for $C_{26}H_{20}O$: C, 89.6; H, 5.9. Found: C, 89.4; H, 5.8.

The ketone showed a strong carbonyl band at 1685 cm.$^{-1}$ in its infrared spectrum (Nujol mull).

Reduction of α-(p-biphenylyl)desoxybenzoin (I) with lithium aluminum hydride in pyridine. A half gram of I (1.4 mmoles) was dissolved in 10 ml. of dry pyridine and 0.11 g. of lithium aluminum hydride (2.9 mmoles) added, whereupon an exothermic reaction ensued and a pale green color appeared. The reaction mixture was allowed to stand for 3 hr. in a stoppered Erlenmeyer flask, then poured into excess 5% hydrochloric acid. The acidic slurry was extracted two times with ether and the extracts were washed with sodium bi-

carbonate solution, salt solution, and finally dried over magnesium sulfate. Removal of the ether left an oil whose infrared spectrum showed strong hydroxyl absorption at 3600–3300 cm.$^{-1}$, no absorption in the carbonyl region, and no band at 855 cm.$^{-1}$, where 4-benzylbiphenyl, the product which would result from reductive cleavage, displays a medium intensity band. The crude product was taken up in ethanol, from which several crops of alcohol (VI) melting in the range 111–130° were obtained, yield: 0.39 g. (78%). For analysis, a sample of VI, containing both diastereomeric racemates, was obtained as fluffy crystals, m.p. 125–130° (from ethanol).

Anal. Calcd. for $C_{26}H_{22}O$: C, 89.1; H, 6.3. Found: C, 89.2; H, 6.3.

Reduction of α-(1-naphthyl)desoxybenzoin (III) with lithium aluminum hydride in pyridine. The ketone (III) was prepared according to the procedure of McKenzie and Roger,[16] by rearrangement of the pinacol prepared from 1-naphthylmagnesium bromide and benzoin. In our hands, the glycol had m.p. 181–183° (from ethanol or benzene) whereas McKenzie reported m.p. 205°, and claimed the isolation of a 180–181° epoxide from acid-catalyzed rearrangement of the glycol, in addition to III. Our glycol showed strong hydroxyl absorption at 3600–3400 cm.$^{-1}$ and therefore could not be an epoxide.

One half gram of III, m.p. 107–108°, was reduced with excess lithium aluminum hydride in pyridine as described above for ketone I. The crude oily product showed strong hydroxyl absorption (3650–3400 cm.$^{-1}$) and only a trace of ketone at 1685 cm.$^{-1}$ Trituration with cold ethanol afforded 0.15 g. (30%) of crystals melting at 108–124° and showing an infrared spectrum essentially identical with that of the above oil, except that carbonyl absorption was completely absent. From this diastereomeric mixture, an analytical sample was obtained, m.p. 126–132° (ethanol).

Anal. Calcd. for $C_{24}H_{20}O$: C, 88.9; H, 6.3. Found: C, 88.9; H, 6.2.

A portion of the oily carbinol from III was refluxed for 15 min. with glacial acetic acid, containing a small amount of p-toluenesulfonic acid. Cooling and dilution did not give any crystalline product.

Preparation of α-(o-biphenylyl)hydrobenzoin. o-Biphenylyllithium was prepared according to the procedure of Gilman and Dunn,[15] using 1.34 g. (0.19 g.-atom) of lithium wire, 20.9 g. (0.088 mole) of 2-bromobiphenyl, and 300 ml. of anhydrous ether. Benzoin (5.3 g., 0.025 mole) was added in portions to the lithium reagent and the mixture then allowed to stand overnight. Work-up of the product followed the procedure used for the p-biphenylyl analog (above), yielding 6.41 g. of crude glycol, m.p. 145–173°, yield: 57%. The first crop of material, m.p. 166–173°, was examined by infrared and found to be free of carbonyl absorption. Recrystallization of this material from ethanol-benzene provided an analytical sample, m.p. 173–174°.

Anal. Calcd. for $C_{26}H_{22}O_2$: C, 85.2; H, 6.1. Found: C, 85.1; H, 6.0.

The known α-(o-biphenylyl)desoxybenzoin (II) was prepared from the above glycol by treatment with iodine-acetic acid in the usual manner. Fractional recrystallization from ethanol separated the crude product into 9,10-diphenylphenanthrene, m.p. 234–235° and mixed m.p. 234–235°, which results from the slow cyclodehydration of II[17] and the desired ketone, m.p. 94–98° (reported[17] m.p. 98–99°).

Reduction of α-(o-biphenylyl)desoxybenzoin (II) with lithium aluminum hydride. One half gram of II (1.4 moles) was dissolved in 10 ml. of pyridine and treated with 0.11 g. (2.9 mmoles) of lithium aluminum hydride. As in the reduction of ketones I and III, no bright colors attributable

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(14) Melting points were taken in a "Mel-temp" capillary melting point apparatus which was checked with known compounds, and are uncorrected. Infrared spectra were obtained with a Perkin-Elmer model 21 spectrometer equipped with sodium chloride optics. Solids were examined as Nujol mulls and oils were smeared between salt plates. Elemental analyses were performed by Dr. Alfred Bernhardt, Max Planck Institute, Mulheim, Germany. The technique employed for running lithium aluminum hydride reductions in pyridine is essentially the same as that reported previously.[3]

(15) H. Gilman and G. E. Dunn, *J. Am. Chem. Soc.*, **73**, 5078 (1951).

(16) A. McKenzie and B. Roger, *J. Chem. Soc.*, **125**, 853 (1924).

(17) C. K. Bradsher and L. J. Wissow, *J. Am. Chem. Soc.*, **68**, 1094 (1946).

to carbanions were noted. Work-up in the usual manner gave an oil whose infrared spectrum indicated complete reduction of the ketone (no absorption at 1685 cm.$^{-1}$) but which resisted crystallization. Stirring with cold ethanol allowed the separation of a few milligrams of 9,10-diphenyl-phenanthrene, m.p. 233–235°, which apparently was a minor contaminant in II. When further attempts to crystallize the oil failed, it was treated with hot acetic acid, which contained a small amount of p-toluenesulfonic acid. After 15 min. of reflux, the solution on cooling yielded pure cis-9,10-diphenyl-9,10-dihydrophenanthrene, m.p. 169–171°, in 70% yield. The reported[10] m.p. is 168–169°. The ultraviolet spectrum of this product, taken in ether solution, was identical with the reported curve,[10] showing λ_{max} 269 mμ and log ϵ = 4.05.

Further proof of the structure of the dehydration product was gained by dehydrogenation to 9,10-diphenylphenanthrene. This was accomplished by refluxing the dihydro compound (0.2 g.) with an equimolar quantity of N-bromosuccinimide (0.11 g.) in carbon tetrachloride for 2 hr., under conditions where the monobromo derivative readily loses hydrogen bromide.[18] The expected amount of succinimide was recovered by filtration of the cooled solution, which was then evaporated down on a steam bath. Recrystallization of the crude product, m.p. 197–213°, from acetic acid, containing a little potassium acetate afforded pure 9,10-diphenylphenanthrene, m.p. 234–236°, weight 0.13 g. The possibility that the dihydro compound was the trans isomer was precluded by the lower reported melting point of 130–131°.[19]

Repetition of the reduction of II, followed by dehydration of the crude carbinol, gave cis-9,10-diphenyl-9,10-dihydrophenanthrene as the only isolable product.

Reductive cleavage of methyl trityl ketone. One gram (3.5 mmoles) of methyl trityl ketone[20] in 20 ml. of pyridine was treated with 0.20 g. of lithium aluminum hydride, whereupon an exothermic reaction ensued and a blood red coloration soon developed. After 3 hr., the reaction mixture was hydrolyzed and worked up in the usual manner, yielding a pale yellow oil whose infrared spectrum showed strong hydroxyl absorption in the 3600–3400 cm.$^{-1}$ region and generally resembled that of pure methyltritylcarbinol. Chromatography of the oil over alumina yielded an initial fraction of crude triphenylmethane (0.10 g.; 12% yield) having m.p. 65–79°, which was eluted with benzene. Recrystallization from methanol afforded 0.06 g. of triphenylmethane which had m.p. 85–90°. Further elution with benzene and then 1:1 benzene-ethanol, gave 0.82 g. (82%) of methyltritylcarbinol, m.p. 94–97° (reported[21] m.p. 93–95°)

after combination of the several fractions which had fairly sharp melting points in the range 86–98°. A mixed melting point of the alcohol with triphenylmethane was strongly depressed and the spectra of the two compounds were wholly different.

Attempted cleavage of 1,2-diphenyl-2-biphenylylethanol with ethanolic sodium hydroxide. The alcohol (0.15 g.; m.p. 125–130°) was dissolved in 10 ml. of 95% ethanol and a pellet of sodium hydroxide added. The resulting solution was refluxed for 15 min., then diluted with water and allowed to cool. Two crops of crystals (0.15 g.) were obtained, m.p. 113–116° and 109–112°, which amounted to an essentially quantitative recovery of the alcohol. The infrared spectrum of the combined crystals was identical with that of the starting diastereomeric alcohol mixture. A portion of the filtrates was made acidic and tested with 2,4-dinitrophenylhydrazine, resulting in a negative test for benzaldehyde.

Metalation of triphenylmethane, 2-benzylbiphenyl, and 4-benzylbiphenyl by means of lithium aluminum hydride in pyridine.[22] When small quantities of triphenylmethane (1.0 to 2.0 g.) were dissolved in pyridine and ca. two molar equivalents of lithium aluminum hydride added, the evolution of gas was evident, as well as the appearance of the blood red color of triphenylmethide ion.[3,13] The resulting carbanion solutions were allowed to stand for 1–2 hr. in stoppered flasks, then poured onto a crushed Dry-Ice-ether slurry. After evaporation of excess Dry Ice, the mixture was hydrolyzed with 5% hydrochloric acid and the ether layer separated and extracted with 5% sodium hydroxide. Acidification of the alkaline extract afforded triphenylacetic acid, m.p. 255–265° (with prior softening). Yields of the acid were as high as 19% using this method of carbonation; bubbling carbon dioxide gas into stirred carbanion solutions gave decidedly inferior yields.

Several exploratory reactions of 4-benzylbiphenyl, carried out as above, yielded deep purple colored solutions of the carbanion. Difficulty was experienced in preparing the carboxylic acid, however. The anion of 2-benzylbiphenyl was also similarly obtained as a deep orange solution. It should be noted that these intense colors constitute convincing evidence for the presence of resonance-stabilized carbanions,[13] and their appearance is not confusable with the pale orange-green coloration noted when lithium aluminum hydride interacts with pyridine.

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(18) R. A. Barnes, *J. Am. Chem. Soc.*, **70**, 145 (1948).

(19) W. Schlenk and E. Bergmann, *Ann.*, **463**, 89 (1928).

(20) Kindly furnished by Professor H. D. Zook.

(21) V. Prelog, E. Philbin, E. Watanabe, and M. Wilhelm, *Helv. Chim. Acta*, **39**, 1086 (1956).

(22) Several of these experiments were performed by Dr. N. Simmons.