of distillate composed of the following products: *m*-xylene (7 mmol.), V recovered (49 mmol.) and triaryls (7 mmol.). Recovered V had b.p. 144–150° at 7 mm., $n^{20}D$ 1.5640–1.5657. Its infrared spectrum was identical to that of the starting material except for a relatively weak 11.78 μ band which decreased in intensity in the higher boiling cuts. It is probable that some isomerization to 1-phenyl-1-(3,5-dimethylphenyl)-ethane occurred, the latter being responsible for the appearance of the 11.78 μ band (1,3,5-trisubstituted arenes are known to have bands in the 11.75–12.05 μ region[69]). The triaryl components boiled about 185° at 2 mm.; chromatography yielded purified material having $n^{20}D$ 1.5858. It was of interest that the infrared spectrum had a 5–6 μ pattern resembling that of a monosubstituted arene.

TABLE IX

REACTIONS OF II IN HYDROGEN FLUORIDE

Experiment B

Product (mmol.[a])	1	2[b]	3	4[c]
m-Xylene	0.1	..	0.6	2
1,3-Dimethyl-4-ethylbenzene (I)	5[d]	13	3	9
1,5-Dimethyl-2,4-diethylbenzene	1	3	0.2	0.7
1,3-Dimethyl-5-(1-methylcyclohexyl)-benzene	..	3	..	0.2
1,5-Dimethyl-2-ethyl-4-(x-methylcyclohexyl)-benzene	..	9	..	3
II recovered	21[e]	50	14	11
Methylcyclohexyl-(II)	..	6	..	..
Triaryldiethanes	7	6	..	..
1-Phenyl-1-(2,4-dimethylphenyl)-ethane (V)	..	..	3[f]	..

[a] Products on loss-free basis except in expt. B-3. [b] One mmol. of methylcyclohexene dimer also formed. [c] Methylcyclohexane (12 mmol.) was recovered. [d] Contained a small amount of the 5-ethyl isomer. [e] A minor amount of II underwent isomerization. [f] Includes a small amount of the 3,5-*dimethyl* isomer.

Anal. Calcd. for $C_{24}H_{26}$: C, 91.66; H, 8.34. Found: C, 91.70; H, 8.35.

D. Synthesis and Cleavage of 1-*p*-Tolyl-1-(2-methyl-5-ethylphenyl)-ethane (VI). 1. Synthesis of VI.—*p*-Methylacetophenone was prepared in 77% yield by the acetylation of toluene[4c]; it had b.p. 116–118° at 27 mm., $n^{20}D$ 1.5342 (lit.[4c] b.p. 108° at 18 mm., $n^{20}D$ 1.5348). The ketone was hydrogenolyzed in pentane at 230–260° and 101 atm. initial hydrogen pressure. Hypercal redistillation afforded a 78% yield of *p*-ethyltoluene, b.p. 161–162°, $n^{20}D$ 1.4948 (lit.[43e] b.p. 162.0°, $n^{20}D$ 1.4950), essentially free of the small amounts of *o*- and *m*-isomers (main bands at 13.27 and 12.80 μ,[48] respectively) initially detected in the roughly distilled product.

The reaction of *p*-ethyltoluene (60 g., 0.50 mole) with 4-methylcyclohexene (38.4 g., 0.40 mole) in the presence of 104 g. of hydrogen fluoride was carried out and the products isolated as previously reported.[4c] The physical constants of the individual products corresponded well with the recorded values.[4c] The following distribution was obtained (with moles in parentheses): methylcyclohexane (0.16), toluene (0.0032), *p*-ethyltoluene (0.20), dimethyldicyclohexyl (0.028), mono-unsaturated methylcyclohexene dimer (0.013), 4-ethyl-2-(x-methylcyclohexyl)-toluene (0.074), VI (0.080), methylcyclohexyl derivative of VI (0.031) and triaryls (0.016). The infrared spectrum of VI was identical to the published one.[4c]

2. VI in Hydrogen Fluoride.—Compound VI (11.9 g., 50 mmol.) was stirred with 8 g. of hydrogen fluoride and yielded the following products (total 10.9 g.): toluene (0.3 mmol.), *p*-ethyltoluene (10 mmol.), VI recovered (34 mmol.) and triaryls (7 mmol.). No isomerization of *p*-ethyltoluene or VI was detected. The highest boiling fraction (160–195° at 1 mm., $n^{20}D$ 1.5693) deposited a minute amount of yellow solid which melted in the range of 136–145° after recrystallization from ethanol. It was intensely yellow fluorescent in ultraviolet light and its infrared spectrum exhibited a strong 12.56 μ band (carbon disulfide solvent). The small amount precluded any further characterization of this compound which was probably an alkylanthracene. Chromatography of the distillation bottoms ($n^{20}D$ 1.582) failed to effect any separation of the triaryl components.

E. Synthesis and Cleavage of 1-(3,4-Dimethylphenyl)-1-(2,5-dimethylphenyl)-ethane (VII). 1. Synthesis of VII.—The compound was prepared in good over-all yield *via* the organolithium method followed by the usual steps (Tables V–VII).

2. VII in Hydrogen Fluoride.—Compound VII (23.8 g., 100 mmol.) was stirred with 10 g. of hydrogen fluoride and yielded 22.9 g. of distilled product consisting of the following compounds: *o*-xylene (0.8 mmol.), *p*-xylene (9 mmol.), VII recovered (79 mmol.) and bis-(α-xylylethyl)-xylenes (10 mmol.). Only a trace of *m*-xylene was detected in the xylene fraction and recovered VII cuts had infrared spectra identical to that of the starting material. The triaryl cut boiled at 190–195° at 1 mm. and the chromatographed material had $n^{20}D$ 1.5842. Its infrared spectrum strongly resembled that of VII.

Acknowledgment.—The authors wish to thank Miss H. Beck for the elemental analyses.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY]

Base-catalyzed Hydrocarbon Cleavage Reactions: A Novel Wurtz-type Reaction[1,2]

BY HERMAN PINES AND LUKE SCHAAP[3]

RECEIVED MARCH 10, 1958

The major products of the reaction of 3-methyl-3-phenyl-1-chlorobutane with potassium were found to be 2,5-dimethyl-2,5-diphenylhexane and ethylene which were formed by an elimination reaction followed by a Wurtz-type condensation. 3-Phenyl-1-chloropropane gave a much smaller yield of 1,4-diphenylbutane. Diarylalkanes such as 2-methyl-2,4-diphenylpentane and 2-methyl-2-phenyl-4-*p*-tolylpentane were cleaved by potassium at 180° to yield cumene and cumene with *p*-cymene, respectively, but were not cyclized to form indans. The mechanisms of the reactions are discussed.

The potassium-catalyzed ethylation of arylalkanes was previously reported to yield indans in addition to the expected ethylated products.[4] These probably were formed by the attack of the primary carbanion produced in the reaction on the aromatic nucleus as illustrated for the reaction of cumene.

In the course of the investigation of the cyclization reaction, 3-methyl-3-phenyl-1-chlorobutane (VI) was treated with potassium in refluxing cyclo-

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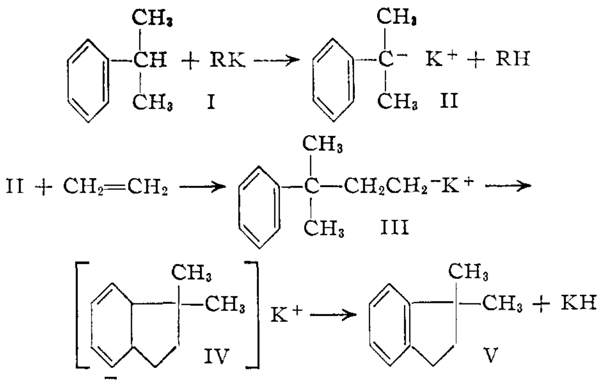
[1] Paper XIV of the series of Base-catalyzed Reactions. For paper XIII see H. Pines and L. Schaap, THIS JOURNAL, **80**, 3076 (1958).

[2] Taken in part from a dissertation submitted by L. Schaap in partial fulfillment of the requirements for the Ph.D. degree, August, 1957.

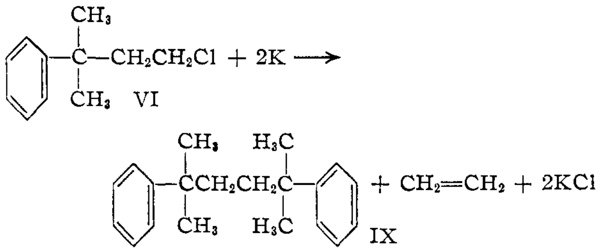
[3] Predoctoral fellow: Universal Oil Products Co., 1954–1955, 1956–1957; Standard Oil Co. (Indiana), 1955–1956.

[4] L. Schaap and H. Pines, THIS JOURNAL, **79**, 4967 (1957).

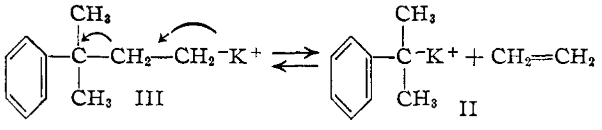


hexane. It was found that in this reaction only a small amount of 1,1-dimethylindan (V) was produced in addition to small amounts of *t*-pentylbenzene (VII) and 3-methyl-3-phenyl-1-butene (VIII). Hydrogen disproportionation which resulted in the formation of VII and VIII accompanies most Wurtz reactions.[5]

The major product of the reaction distilled at 200° at 20 mm. and the material has been identified as 2,5-dimethyl-2,5-diphenylhexane (IX), which was formed by



The reaction occurs through the formation of the primary carbanion III which on elimination of ethylene produces a more stable benzylic carbanion II



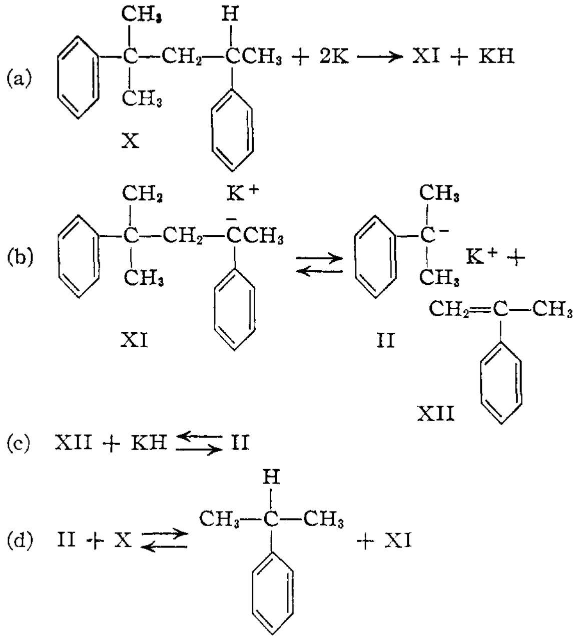
Ethylene was identified as the gas produced by the reaction along with some hydrogen which probably resulted from the olefin and indan forming reactions mentioned above. This elimination to form a benzylic carbanion and ethylene is the reverse of the addition of a benzylic carbanion to ethylene to form a primary carbanion which was proposed as the addition step in side-chain alkylation.[6] Wooster and Morse[7] have reported a similar cleavage for 3,3,3-triphenyl-1-iodopropane which reacts with sodium in liquid ammonia to yield the highly resonance stabilized triphenylmethyl carbanion.

The carbanion II reacts then with more of the original chloride VI to yield 2,5-dimethyl-2,5-diphenylhexane (IX). This condensation is similar to that which has been found to take place between benzylsodium and alkyl halides.[8]

A similar elimination–condensation reaction was reported by Hurd and Wilkinson[9] for the reaction of alkyl (or aryl) 2-chloroethyl sulfides with sodium which yielded sodium chloride, the alkyl (or aryl) sodium sulfide, ethylene and the 1,2-bis-(alkylthio)-ethane. The reaction scheme which was proposed is the same as that discussed above for the aralkyl chloride.

When 3-phenyl-1-chloropropane was treated with potassium in refluxing cyclohexane, only small yields of 1,4-diphenylbutane and ethylene were produced in addition to *n*-propylbenzene. This probably is due to the fact that this chloride has benzylic hydrogens which may be metalated, and condensation reactions of the chloride with these benzylic carbanions may result in higher boiling products. The higher boiling material from this reaction was not investigated.

The elimination reaction is not limited to the halides only. It was found that diarylalkanes such as 2-methyl-2,4-diphenylpentane (XI) react with potassium at 180–184° to yield cumene. This reaction may also result from an elimination of the benzylic carbanion formed to yield another benzylic carbanion.



Some of the α-methylstyrene (XII) formed in the elimination reaction (b) must have undergone hydrogenation by an addition of a hydride as shown in steps c and d. This type of hydride transfer reaction involving α-methylstyrene was discussed previously.[10]

A similar cleavage accompanied by a hydride transfer was found in the reaction of 2-methyl-2-phenyl-4-*p*-tolylpentane (XIII) with potassium. About 37% of the XIII reacted to yield 36% of isopropylbenzene and 13% of *p*-cymene. The remainder of the product consisted of higher boiling hydrocarbons, which probably were formed by the condensation of the isopropenylarenes described previously.[10] The formation of *p*-cymene from

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[5] A. A. Morton, *Chem. Revs.*, **35**, 1 (1944).

[6] H. Pines, J. A. Vesely and V. N. Ipatieff, THIS JOURNAL, **77**, 554 (1955).

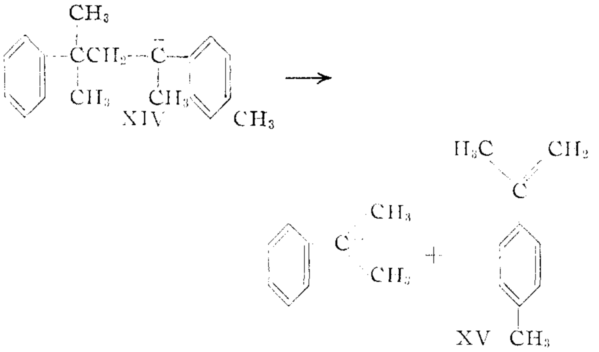
[7] C. B. Wooster and R. A. Morse, *ibid.*, **56**, 1735 (1934).

[8] A. A. Morton and F. Fallwell, Jr., *ibid.*, **60**, 1429 (1938).

[9] C. D. Hurd and K. Wilkinson, *ibid.*, **71**, 3429 (1949).

[10] M. Kolobielski and H. Pines, *ibid.*, **79**, 5820 (1957).

XIV is a further indication that the intermediate alkenylarenes produced from the cleavage reaction underwent hydrogenation through a hydrogen transfer reaction as already indicated.[10] The primary product of cleavage of XIV must have been *p*-isopropenyltoluene (XV).


XIV

XV

The carbanion XIV apparently does not cyclize to form 1,1,3-trimethyl-3-phenylindan. This is probably due to the fact that the benzylic carbanion is too stable to attack the aromatic nucleus as primary or secondary resonance non-stabilized carbanions will.[4]

Experimental

The Reaction of 3-Methyl-3-phenyl-1-chlorobutane with Potassium.—The apparatus used consisted of a 500-ml. creased flask equipped with an oil-sealed stainless steel stirrer, dropping funnel and reflux condenser. The chloride (10 g., 0.55 mole) was dissolved in 50 ml. of cyclohexane (free of benzene) and was added during a period of 5 hr. to 2.19 g. (0.056 g. atom) of potassium in 200 ml. of refluxing cyclohexane. Reflux temperature was maintained for an additional 4.5 hours while stirring, at which time the blue color faded to gray. Then the flask was cooled while the contents were blanketed with a nitrogen atmosphere. Water was added and the organic layer was separated and washed with water and distilled. Unreacted starting material, 0.83 g. (8.3%), was recovered. The C_{11}-fraction, b.p. 75–91.8° at 20 mm., 1.08 g., when selectively hydrogenated with a 10% palladium-on-charcoal catalyst, consisted of 47% of 1,1-dimethylindan and 53% of *t*-pentylbenzene. The method of infrared analysis used for these compounds has been reported in a previous publication.[4] The hydrogenation showed 18% unsaturation to be present, and removed the 10.92 μ infrared absorption band indicating that a terminal olefin was hydrogenated. This olefin is assumed to be 3-methyl-3-phenyl-1-butene. The yields of these compounds based on the chloride reacted are: 7.0% of 1,1-dimethylindan, 2.7% of 3-methyl-3-phenyl-1-butene and 5.1% of *t*-pentylbenzene.

The last three distillation cuts, b.p. 197.9–200° at 20 mm., $n^{20}D$ 1.5412, 3.47 g., solidified on standing to yield white crystals, m.p. 62–63° when recrystallized from methanol. A Rast molecular weight determination gave a value of 275. This compound was shown to be identical with a synthetic sample of 2,5-dimethyl-2,5-diphenylhexane by mixed melting point and identical infrared spectra. The yield of this material was 51% based on reacted halide.

A similar experiment was carried out with 9.00 g. (0.0493 mole) of the chloride and 1.95 g. (0.05 g. atom) of potassium. The gases produced were collected and amounted to 0.022 mole. Ethylene and hydrogen were produced in a ratio of 3 to 1. A 13% yield of C_{11}-fraction was obtained and 2.13 g. (33%) of 2,5-dimethyl-2,5-diphenylhexane was crystallized out of the higher boiling distillation cuts.

The Reaction of 3-Phenyl-1-chloropropane with Potassium.—Two reactions of this chloride (10.0 g., 0.0647 mole), with 2.54 g. (0.065 g. atom) of potassium were carried out in the apparatus described previously. Both yielded 1.5 g. (19%) of *n*-propylbenzene. One of these reactions in which the chloride was added rapidly in 1 hr. yielded 0.0135 mole of gas which contained ethylene and a yield of 0.28 g. (4%) of 1,4-diphenylbutane, m.p. 52–52.5° (recrystallized from methanol), was crystallized out of the fraction boiling at 193–200° at 20 mm. In the other experiment in which the chloride was added during a period of 2 hours, only 0.0042 mole of gas was obtained and no solid material could be crystallized from the fraction boiling at 214° at 23 mm.

The identification of the solid obtained in the first experiment was based on a mixed melting point and identical infrared spectrum with a synthetic sample.

The Reaction of 2-Methyl-2,4-diphenylpentane with Potassium.—This reaction was carried out in a 250-ml. Magne-Dash autoclave.[11] The diarylalkane (23.8 g., 0.10 mole) in 100 ml. of purified cyclohexane was treated with 1 g. (0.027 g. atom) of potassium at 180–184° for 5 hours. Distillation of the resulting product and infrared analysis of the cuts showed a yield of 2.18 g. of cumene (12% if two moles of cumene are produced for each mole of the diarylalkane reacted) to be produced. The rest of the distilled material, b.p. 169° at 13 mm., $n^{20}D$ 1.5476, 18.01 g., consisted of unreacted starting material (76%). A residue of 1.2 g. was not investigated. No 1,1,3-trimethyl-3-phenylindan was found.

The Reaction of 2-Methyl-2-phenyl-4-*p*-tolylpentane with Potassium.—The reaction of this diarylalkane (25.0 g., 0.10 mole) with 1.0 g. (0.027 g. atom) of potassium in 100 ml. of cyclohexane at 183–194° for 5 hr. was carried out in the Magne-Dash autoclave. Distillation of the recovered liquid and infrared analysis showed it to consist of 1.18 g. (9.8% yield) of cumene, 0.50 g. (3.7% yield) of *p*-cymene, and 15.94 g. (63%) of recovered diarylalkane. A distillation residue of 4.9 g. was not investigated. The analytical infrared bands used for this and the previous experiment are listed in Table I. Photographs of the spectra of these compounds and others mentioned in this work may be found in the Ph.D. thesis of L. A. Schaap, Northwestern University, August, 1957.

TABLE I

ANALYTICAL INFRARED BANDS

Compound	Wave length, μ
Cumene	10.85, 11.03
p-Cymene	7.67, 13.75
2-Methyl-2,4-diphenylpentane	11.90
2-Methyl-2-phenyl-4-*p*-tolylpentane	6.20, 7.90
1,1,3-Trimethylindan	7.60

Synthesis of 3-Methyl-3-phenyl-1-chlorobutane.—3-Methyl-3-phenylbutanoic acid was prepared in a yield of 61.96 g. (67%) by the hypochlorite oxidation of 4-methyl-4-phenyl-2-pentanone (90 g., 0.51 mole), which had been prepared using the procedure of Hoffman.[12] The hypochlorite solution was prepared according to the method of Newman and Holmes[13] and the reaction was carried out at 55–60° for 2 hours. The acid boiled at 156.5–160° at 10 mm., m.p. 58–59° (reported[14] b.p. 155° at 10 mm., m.p. 58–59°). It was reduced to 3-methyl-3-phenyl-1-butanol with lithium aluminum hydride.[15] Starting with 61.9 g. (0.347 mole) of the acid and 16.6 g. (0.436 mole) of lithium aluminum hydride in 1130 ml. of ether, the alcohol produced amounted to 44.26 g. (77%), b.p. 127–127.5° at 10 mm., $n^{20}D$ 1.5227.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.98; H, 9.90.

3-Methyl-3-phenyl-1-chlorobutane was prepared from 41 g. (0.249 mole) of the above alcohol by reaction with 39.3 g. (0.33 mole) of thionyl chloride in 22.1 g. (0.28 mole) of anhydrous pyridine at 80–90° for 3 hours. The yield of product was 15.78 g. (29%), b.p. 104.5–105° at 9 mm., $n^{20}D$ 1.5191, d^{20}_4 1.022; *MR*D calcd. 54.264, found 54.26.

Anal. Calcd. for $C_{11}H_{15}Cl$: C, 72.13; H, 8.28. Found: C, 72.12; H, 7.93.

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[11] Autoclave Engineers, Inc., Erie, Pa.

[12] A. Hoffman, THIS JOURNAL, **51**, 2542 (1929).

[13] M. S. Newman and H. L. Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 428.

[14] C. F. Koelsch and C. D. LeClaire, *J. Org. Chem.*, **6**, 516 (1941).

[15] R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 2548 (1947).

The Preparation of 3-Phenyl-1-chloropropane.[16]—3-Phenyl-1-propanol (100 g., 0.735 mole) was allowed to react with thionyl chloride (120 g., 1.0 mole) in 64 g. (0.80 mole) of anhydrous pyridine using the conditions described for 3-methyl-3-phenyl-1-chlorobutane. The product was obtained in a yield of 81.4 g. (52.8%), b.p. 85° at 8 mm., $n^{20}_{\rm D}$ 1.5207 (reported[17] b.p. 89–93° at 6 mm., $n^{20}_{\rm D}$ 1.5160).

Preparation of 2-Methyl-2,4-diphenylpentane.—The olefin from the dehydration of 4-methyl-2,4-diphenyl-2-pentanol was obtained using the method of Bergmann, Taubadel and Weiss.[18] The olefin which boiled at 165° at 9 mm., $n^{20}_{\rm D}$ 1.5682 (reported[18] b.p. 170–171° at 17 mm.) was produced in an over-all yield of 54% based on the starting 4-methyl-4-phenyl-2-pentanone.

This olefin (50.0 g., 0.231 mole) was selectively hydrogenated using 5 g. of copper–chromite catalyst at 116–154° in a 450-ml. rotating autoclave with an initial hydrogen pressure of 115 atm. The yield of 2-methyl-2,4-diphenylpentane was 36 g. (65%), b.p. 158° at 9.5 mm., $n^{20}_{\rm D}$ 1.5471.

Preparation of 1,1,3-Trimethyl-3-phenylindan.—This compound was prepared from 10 g. of the above-described olefin, by allowing it to stand for 24 hr. with 1 g. of stannic chloride.[18] The yield of product was 7.26 g. (73%), b.p. 161–165° at 12 mm., m.p. 52–53° (recrystallized from methanol) (reported[18] b.p. 166–167° at 25 mm., m.p. 52–53°).

Preparation of 2-Methyl-2-phenyl-4-*p*-tolylpentane.[19]—The method of preparation of this hydrocarbon, b.p. 139° at 3 mm., $n^{20}_{\rm D}$ 1.5431, was identical with that for 2-methyl-2,4-diphenylpentane except for the substitution of *p*-tolylmagnesium bromide for phenylmagnesium bromide in the reaction with 4-methyl-4-phenyl-2-pentanone.

Preparation of 2,5-Dimethyl-2,5-diphenylhexane.—β-Chloro-*t*-butylbenzene (neophyl chloride) was prepared in a yield of 69% using hydrogen fluoride as a catalyst.[20] The material boiled at 126° at 40 mm., $n^{20}_{\rm D}$ 1.5244 (reported[21] b.p. 97° at 13 mm., $n^{20}_{\rm D}$ 1.5250). 2,5-Dimethyl-2,5-diphenylhexane cannot be prepared by a Wurtz reaction of this chloride[21] nor can it be prepared by coupling of neophyl radicals[22] because rearrangements take place, although Urry and Kharasch did isolate some dimer of uncertain structure, m.p. 129°, from the cobaltous chloride-catalyzed dimerization of neophylmagnesium chloride.[22] On attempted coupling the tosylate of neophyl alcohol (prepared by bubbling oxygen into neophylmagnesium chloride) with neophylmagnesium chloride gave only a trace of high boiling material. It was found, however, that the reaction of neophyl chloride with magnesium did give some of the desired product. Neophyl chloride (135 g., 0.80 mole) was allowed to react with 9.72 g. (0.40 g. atom) of magnesium in 200 ml. of anhydrous ether, and the mixture was refluxed for 72 hours. There is no evidence, however, that additional reaction of the chloride with the Grignard reagent takes place during this period. Then 9.72 g. of magnesium was added to react with the excess chloride and the solution was refluxed for an additional 3 hours. The products consisted of *t*-butylbenzene, b.p. 167–169°, $n^{20}_{\rm D}$ 1.4923, 90.2 g. (84%), and the desired product, b.p. 175–177° at 10 mm., $n^{20}_{\rm D}$ 1.5395, 3.41 g. (3.2%). This material solidified on cooling and melted at 62–63° when recrystallized from methanol.

Anal. Calcd. for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 89.78; H, 9.87.

Preparation of 1,4-Diphenylbutane.[16]—1,4-Diphenyl-1-butanol was prepared by the Grignard method using 15.4 g. (0.10 mole) of 3-phenyl-1-chloropropane and 2.6 g. (0.11 g. atom) of magnesium with 10.6 g. (0.10 mole) of benzaldehyde in 150 ml. of anhydrous ether. The yield of product was 12.2 g. (55%), b.p. 175.5° at 5 mm., m.p. 45.5–47° (reported[23] m.p. 45–46°).

1,4-Diphenylbutane was prepared from the above alcohol, (11.8 g., 0.052 mole) by means of hydrogenolysis using 1 g. of copper-chromite catalyst at 211–239° in a 114-ml. rotating autoclave with an initial hydrogen pressure of 105 atm. The yield of product was 8.8 g. (80%), m.p. 52–52.5° (reported[24] 52–52.5°).

Acknowledgment.—The authors wish to express their appreciation to Miss H. Beck for the elemental analysis and to Professor D. F. Mason of the Chemical Engineering Department, Northwestern University, for the mass spectral gas analysis.

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[16] This preparation was carried out by Mr. H. L. Golding, Jr., at this Laboratory.

[17] S. S. Rossander and C. S. Marvel, THIS JOURNAL, **50**, 1491 (1928).

[18] E. Bergmann, H. Taubadel and H. Weiss, *Ber.*, **64**, 1493 (1931).

[19] This compound was synthesized by Dr. H. Alul at this Laboratory.

[20] W. S. Calcott, J. M. Tinker and V. Weinmayr, THIS JOURNAL, **61**, 1010 (1939).

[21] F. C. Whitmore, C. A. Weisgerber and A. C. Shabica, Jr., *ibid.*, **65**, 1468 (1943).

[22] W. H. Urry and M. S. Kharasch, *ibid.*, **66**, 1438 (1944).

[23] R. Stoermer and F. Schenck, *Ber.*, **61**, 2320 (1928).

[24] G. Egloff, "Physical Constants of Hydrocarbons," Vol. III, Reinhold Publishing Corp., New York, N. Y., 1946.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE WESTERN UTILIZATION RESEARCH AND DEVELOPMENT DIVISION, AGRICULTURAL RESEARCH SERVICE, U. S. DEPARTMENT OF AGRICULTURE]

Synthesis of Coumestrol, 3,9-Dihydroxy-6H-benzofuro[3,2-c][1]benzopyran-6-one[1]

BY O. H. EMERSON AND E. M. BICKOFF

RECEIVED MARCH 10, 1958

A practical synthesis of coumestrol is described. 2,4-Dimethoxyphenylacetonitrile is condensed with resorcinol to give α-(2,4-dimethoxyphenyl)-2,4-dihydroxyacetophenone. Treatment of this compound with methyl chloroformate yields 3-(2,4-dimethoxyphenyl)-4,7-dihydroxycoumarin which, on heating with aniline hydrochloride, yields coumestrol in an over-all yield of about 17%. Coumestrol is easily acetylated to give the diacetate, m.p. 235–236°, which crystallizes well from acetonitrile or acetic acid, and from which coumestrol can be regenerated readily. An improved preparation of 2,4-dimethoxyphenylacetonitrile from 2,4-dimethoxybenzaldehyde and rhodanine is reported also, giving an over-all yield of about 62%.

Previous work in this Laboratory[2–4] resulted in the isolation of an estrogen from ladino clover and alfalfa which was shown to have the empirical formula $C_{15}H_8O_5$, and for which structural formula I and the name coumestrol were proposed. It was felt most desirable to synthesize the substance, both to confirm the structure and to make it accessible for pharmacological study.

Although the substance is new, a number of closely related compounds are well known. Thus

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[1] We wish to thank Dr. Leonard T. Capell of the staff of "Chemical Abstracts" for the systematic name.

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