[Contribution from the Department of Chemistry, Massachusetts Institute of Technology]

Metalation of Cumene[1]

AVERY A. MORTON and EDWARD J. LANPHER

Received May 7, 1958

Amyl- and phenyl-potassium, prepared from potassium metal and amyl chloride or anisole, respectively, metalated cumene almost exclusively in the alpha position rather than on the nucleus. These results are contrasted with those obtained previously in this and other laboratories. The cation and associated salts have a greater influence upon the position attacked than does incipient acidity of the hydrocarbon.

Three different laboratories have obtained different results in the metalation of cumene, as has been noted in a recent review.[2] A reason for these differences should be understood because one of the laboratories[3] has maintained that the inductive and field effects of the substituent group determine the position attacked. This viewpoint has been reaffirmed in the review.[2] The differences cannot be credited to errors in the identification of the products of carbonation because the three laboratories agree about the properties of the respective acids. One feature, however, stands out clearly; each laboratory has in general prepared its metalating agent by a different method. This laboratory has used amylsodium,[4,5] prepared from amyl chloride and sodium; it metalated cumene almost exclusively on the nucleus. Bryce-Smith,[3] with one exception, used an alkylpotassium reagent which was made from potassium metal and an alkyllithium compound; it metalated 81 to 87% on the nucleus and the rest at the alpha carbon atom. Gilman and co-workers made only two experiments, one with a reagent derived from sodium and diethylmercury[6] and the other from potassium and the mercury compound[7]; both caused a large amount of lateral metalation with possibly some nuclear displacement also, although the separation of the acids corresponding to the latter did not occur easily.

If three different reagents caused three different results, another method of preparing a reagent might cause a still different result. This thought has, indeed, been realized with a preparation of amylpotassium made according to Equation 1 which parallels the preparation[4,5] of amylsodium from amyl chloride and sodium. This potassium reagent metalated cumene predominantly at the alpha position (2% on the nucleus) whereas Bryce-Smith's[3] amylpotassium had attacked the alpha position only 17% and amylsodium prepared as indicated in equation 1 had metalated laterally only 1%. The nearly exclusive nuclear metalation by amylsodium had already been demonstrated both here[4,5] and in the London[3] laboratory. Hence when the same materials were used for preparing the reagent, the results, as far as lateral versus nuclear attack was concerned, agreed despite the fact that the London laboratory did not use high speed stirring; and when unlike materials were used, as in the above cases, the results disagreed. Very clearly the reagent, rather than the hydrocarbon, determined the position attacked.

$$C_5H_{11}Cl + 2K(\text{or } Na) \longrightarrow C_5H_{11}K + KCl(\text{or } NaCl) \quad (1)$$

The idea of incipient acidity as the determinant of orientation is inconsistent also with the position attacked by phenylpotassium. That reagent, which was prepared in two ways according to Equations 2 and 3, attacked the alpha position predominantly (85% and possibly higher). According to the values for incipient acidity, as determined by Bryce-Smith,[3] nuclear attack should have occurred approximately four to one and metalation should have been slight because the attacking phenyl anion would have to remove a proton from the deactivated nucleus in cumene.

$$C_5H_{11}Cl + 2K + C_6H_6 \longrightarrow C_5H_{12} + KCl + C_6H_5K \quad (2)$$

$$C_6H_5OCH_3 + 2K \longrightarrow C_6H_5K + KOCH_3 \quad (3)$$

The present results emphasize the importance of the cation. When the cation was potassium, and no other cation but potassium was present in the associated salt, the preferred position of attack was at the alpha carbon atom. When sodium cations only were present the preferred position was on the nucleus. This preference of potassium for the alpha position accords also with the results from metalation by potassium metal[8] and sodium oxide. The sodium cation in the oxide salt did not alter the position taken by potassium, and the potassium cation remained at the alpha position during months of aging.[9] Incipient acidity had no control in these

---

[1] This work was performed as part of a research project sponsored by the National Science Foundation.

[2] A. R. Benkeser, D. J. Foster, D. M. Sauve, and J. F. Nobis, *Chem. Revs.*, 57, 867 (1957).

[3] D. Bryce-Smith, *J. Chem. Soc.*, 1079 (1954).

[4] A. A. Morton, J. T. Massengale, and M. L. Brown, *J. Am. Chem. Soc.*, 67, 1620 (1945).

[5] A. A. Morton and E. L. Little, *J. Am. Chem. Soc.*, 71, 487 (1949).

[6] H. Gilman and R. V. Young, *J. Am. Chem. Soc.*, 62, 1519 (1940).

[7] H. Gilman and L. Tolman, *J. Am. Chem. Soc.*, 68, 522 (1946).

[8] C. E. Claff, Jr., and A. A. Morton, *J. Org. Chem.*, 20, 981 (1955).

[9] A. A. Morton and J. E. Eisenmann, *J. Org. Chem.*, 23, 1469 (1958).

cases. The frequent failure of incipient acidity as a guiding rule in these reactions has been noted earlier.[10]

To chemists who wish to interpret and predict all things by a simple anionic concept, which has been derived from the reactions of dissolved and dissociated reagents, this situation possibly seems distressing; but to those who think in terms of reactions of complexes and associated salts and particularly of reactions at the surfaces of solids, these results are quite in order. Organic compounds are adsorbed or chemisorbed on the solids as the first step of reaction and their accessibility to the reagent determines the reaction. A change in the cation or the association of other solids with the reagent changes the number and position of the places where adsorption can occur. Consequently the degree and sometimes the type of reaction change. Already these ideas have been certified in five separate fields—polymerization,[11] alkylation,[12] metalation,[13] ether cleavage,[14] and pyrolysis.[15] The effect was very striking in the polymerization of butadiene[11] where the association of sodium isopropoxide and sodium chloride with allylsodium changed the process from the 1,2-chain growth, universally credited to anionic reagents, to a 1,4-growth which became as high as was found in free radical polymerization.

The wide variety of results obtained because the reagents were prepared differently must not obscure the fact that broadly the conclusions and opinions are the same when the separate factors are measured. For instance the two laboratories which have studied the effect of some variables agree that the anion has no appreciable influence on orientation; this laboratory because amyl- and phenyl-potassium behaved alike in metalating cumene at the alpha position and the London laboratory[3] because ethyl-, propyl-, and amyl-potassium gave the same meta/para ratio in metalation at the nucleus. Also both laboratories agree that the cation does have an influence; the former because amyl-sodium and -potassium metalated primarily at the nucleus and side chain, respectively, and the latter[3] because amyl-sodium and -potassium gave different meta/para ratios in metalation at the nucleus. However, Bryce-Smith[3] did not think that the difference was great enough to alter his opinion about the mechanism being anionic with the position of attack controlled by the incipient acidity of the hydrogen atoms. Unfortunately his comparison of cation influence was with two reagents prepared by different methods. When the comparison was with two reagents made by the same method, as has been observed with the amyl-sodium and -potassium reported in this paper, the difference is too large to ignore.

The real disagreement between the two laboratories is concerned with the influence of associated salts upon metalation. This feature is new and is not recognized generally. Indeed, the recent reviewers[2] of this field have given considerable weight to the adverse opinion of Bryce-Smith[5] and have suggested that still more evidence is required.[16] Actually the difference is one of fact versus opinion. Over many years this laboratory has shown that associated salts can exert an influence[11–15] in a variety of reactions and specifically has shown that a lithium alkoxide can affect the orientation in the dimetalation of benzene.[17] Bryce-Smith[3] stated that any effect by an alkoxide was "unlikely" but made no tests. In a previous paper[18] he had acknowledged that his potassium reagent probably contained a lithium compound (39%) and had suggested a composition of the type $(RLi)_x(RK)_y$. Apparently an inactive salt, such as an alkoxide or alkyllithium compound, which could not itself metalate a hydrocarbon, was supposed to be incapable of affecting the action of the metalating agent. Hence no control test was made of metalation in the absence of such a compound. The experiments reported in this paper show that in the absence of a lithium compound, metalation by a potassium reagent is chiefly lateral rather than nuclear.

Special attention is directed to the method of analysis of the products of metalation. Infrared measurements[19] of phenyl-sodium and -potassium, of benzyl-sodium and -potassium, of *p*-tolylpotassium, and of cumenylsodium and phenylisopropylpotassium show distinctive absorption for the aryl ions at 1210 cm.$^{-1}$ and for the benzyl type ions at 1165 cm.$^{-1}$ The two absorptions are sharply characteristic. The method has proven unusually valuable in following chemical changes, for instance in the metalation of cumene by phenylpotassium. It is superior to the usual carbonation process because any secondary changes during carbonation cannot become involved. For example some car-

---

[10] A. A. Morton and C. E. Claff, Jr., *J. Org. Chem.*, **21**, 736 (1956).

[11] A. A. Morton, I. Nelidow, and E. Schoenberg, *Proc. 3rd Rubber Tech. Conf.*, (1948) 108; A. A. Morton, *Advances in Catalysis*, IX 743 (1957), Academic Press Inc., New York.

[12] A. A. Morton and A. E. Brachman, *J. Am. Chem. Soc.*, **73**, 4363 (1951).

[13] A. A. Morton, C. E. Claff, Jr., and F. W. Collins, *J. Org. Chem.*, **20**, 428 (1955).

[14] A. A. Morton and A. E. Brachman, *J. Am. Chem. Soc.*, **76**, 2973 (1954).

[15] A. A. Morton and E. F. Cluff, *J. Am. Chem. Soc.*, **74**, 4056 (1952).

[16] On page 873, line 24, of the recent review[2] the yield should be 17% instead of 48%. The original report[5] gave 48% as the total yield of acids obtained by carbonation, but pointed out that 64.5% of the total acid was caproic acid, representing unchanged amylsodium which had not participated in metalation. This result therefore does not constitute an exception to the alkoxide effect.

[17] A. A. Morton and C. E. Claff, Jr., *J. Am. Chem. Soc.*, **76**, 4935 (1954).

[18] D. Bryce-Smith and E. E. Turner, *J. Chem. Soc.*, 861 (1953).

[19] E. J. Lanpher, *J. Org. Chem.*, **21**, 830 (1956); *J. Am. Chem. Soc.*, **79**, 5578 (1957).

boxyl might be introduced into the nucleus during carbonation of phenylisopropylpotassium because of a rapid change of one radical (or ion) into the other during carbonation as shown in Equation 4.

$$C_6H_5C(CH_3)_2\cdot \longrightarrow \cdot C_6H_4CH(CH_3)_2 \quad (4)$$

For this reason the tests[5] by oxidation of the crude acid product by chromic acid or permanganate can be open to some question although that method was used twice in the present work and gave roughly confirmatory results.

EXPERIMENTS

Direct determination of the metalation product by infrared absorption. Nujol mulls[19] were prepared from 5-ml. samples of each suspension as obtained from a reaction mixture. Excess solvent was removed by evaporation under vacuum. The grease-like residue of Nujol and organometallic compound was smeared between salt plates under dry box conditions. The film was adjusted to proper thickness. Excellent spectra were obtained in these cases. The bands were sharp with strong absorption at numerous positions as would be expected for aromatic compounds. All preparations used in establishing the facts that the aryl ion absorbed at 1210 cm.$^{-1}$ and the benzyl-type ion absorbed at 1165 cm.$^{-1}$ were carried out by methods which have been shown by carbonation to give primarily or exclusively the type of acid corresponding to the carb anion in question.

Amylpotassium and cumene. Amyl chloride (30 ml. or 0.25 mole) was added dropwise during 1 hr. at −10° to a suspension of 19.5 g. (0.5 atom) of potassium sand in heptane which contained 60 g. (0.5 mole) of cumene. The conditions were in general similar to those regularly used in the preparation of amylsodium.[20] The product showed no band at 1205 cm.$^{-1}$ characteristic for an aryl ion but absorbed strongly at 1165 cm.$^{-1}$ as is typical for phenylisopropylpotassium. In order to determine traces of nuclear metalation the crude solid, low melting, water-soluble phenylisobutyric acid (2.5 g.) from a 100-ml. aliquot of the reaction mixture was oxidized by chromic acid.[8] By this procedure an aromatic acid (any *m*- or *p*-cuminic acid) would be oxidized to an isophthalic or terephthalic acid which would be insoluble in water. The yield of insoluble acid thereby obtained was 53 mg. corresponding to only 2% of the total product.

Phenylpotassium from amyl chloride and benzene. In a typical preparation potassium (39 g., 1 mole) was added to 400 ml. of heptane and 150 ml. of benzene, both liquids having been dried over sodium hydride. The temperature was raised to 95° and the mixture stirred at 5000 r.p.m. in the high speed stirring apparatus commonly used in preparations of organoalkali metal reagents in this laboratory. The mixture was cooled to −10°. Amyl chloride (61 ml., 0.5 mole) was added dropwise to the potassium sand during 1 hr. The infrared absorption at 1205 cm.$^{-1}$ was strong. The carbonated product was solely benzoic acid (m.p. 121–122°) and the yield was 34 g., or 55% based upon the amyl chloride.

Phenylpotassium from anisole. Potassium sand (19.5 g., 0.5 atom) was prepared in 500 ml. of heptane at 95° in the high speed stirring apparatus. The addition of 0.5 ml. of anisole at this time often facilitated dispersion of the metal and gave a finer sand. The mixture was allowed to cool to room temperature. Anisole (27 g. or 0.25 mole) was added dropwise over a period of 1 hr. while the mixture was stirred at 5000 r.p.m. The temperature was maintained at 25–30°. The infrared absorption from a sample of this preparation showed strong absorption at 1210 cm.$^{-1}$ typical for the phenyl ion. Carbonation by forcing the light colored suspension onto solid carbon dioxide yielded benzoic acid (m.p. 122–123°) in a yield of 60%.

Phenylpotassium and cumene. To 100-ml. suspension of phenylpotassium prepared from amyl chloride, benzene, and potassium was added 150 ml. (1 mole) of cumene which previously had been dried over sodium hydride. During five days at room temperature the infrared absorption at 1210 cm.$^{-1}$ gradually disappeared while strong absorption developed at 1165 cm.$^{-1}$ The yield of crude acid was 6.7 g. (75%). The crystals from hot water melted at 77–78°, close to that recorded[21] (80–81°) for phenylisobutyric acid and identical with a sample from a previous preparation[10] in this laboratory.

A preparation of phenylpotassium made from potassium metal and anisole showed a similar change in infrared absorption when cumene was added.

The crude carbonated product from this metalation was oxidized by permanganate according to the method of Bryce-Smith.[5] The yield of 0.55 g. (m.p. 77–78°) from 0.65 g. of crude acid corresponded to 85% phenylisobutyric acid according to the procedure prescribed.[5]

Acknowledgments. The authors are indebted to Marianne Taylor for infrared analyses and to James Howard for assistance in many of the preparations.

CAMBRIDGE 39, MASS.

---

(20) A. A. Morton, F. D. Marsh, R. D. Coombs, A. L. Lyons, S. E. Penner, A. E. Ramsden, V. B. Baker, E. L. Little, Jr., and R. L. Letsinger, *J. Am. Chem. Soc.*, 72, 3785 (1950).

(21) K. Ziegler and H. Thielmann, *Ber.*, 56, 1740 (1923).