[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 170]

Condensations by Sodium. XII. Mechanism of Formation of Phenylmalonic Acid and the Syntheses of Butyl- and Phenylmalonic Acids from Monocarboxylic Acids

BY AVERY A. MORTON, FRANKLIN FALLWELL, JR., AND LEON PALMER

Phenylmalonic acid has been reported[1] as one of the products of the carbonation of a sodium exchange reaction between toluene and phenylsodium. We are now submitting evidence that its synthesis, beginning with amyl chloride and sodium, can occur by a series of steps involving the presence of benzylsodium, sodium phenylacetate, and sodium sodiophenylacetate according to the equations

$$C_5H_{11}Cl + 2Na + C_6H_6 \longrightarrow C_5H_{12} + C_6H_5Na + NaCl \quad (1)$$

$$C_6H_5Na + C_7H_8 \longrightarrow C_7H_7Na + C_6H_6 \quad (2)$$

$$C_7H_7Na + CO_2 \longrightarrow C_6H_5CH_2COONa \quad (3)$$

$$C_6H_5CH_2COONa + C_7H_7Na \longrightarrow C_6H_5CH(Na)COONa + C_7H_8 \quad (4)$$

$$C_6H_5CH(Na)COONa + CO_2 \longrightarrow C_6H_5CH(COONa)_2 \quad (5)$$

That monosodium compounds are present prior to introducing carbon dioxide is indicated, for equation 1, by carbonating before addition of toluene and obtaining therefrom benzoic but no phthalic acid (this equation has also been balanced with respect to the pentane content) and for equation 2, by substituting methyl iodide or butyl chloride[2] for carbon dioxide in the next step and finding thereby considerably more benzylsodium—disclosed as ethylbenzene or amylbenzene—than is revealed in the form of phenylacetic acid by the carbonation process. This difference indeed was so sizable and so contrary to all of our previous experience as to stimulate our search for secondary reactions which might consume sodium phenylacetate. Support for the remaining steps, 3, 4, and 5 in the above mechanism is deduced from (a) the highly significant dependence of the relative amounts of di- and monocarboxylic acids on the slowness with which carbon dioxide is admitted, the yield of phenylmalonic acid being increased at the expense of phenylacetic acid as the rate of carbonation is decreased, and (b) the production of phenylmalonic acid by carbonation of the resultant of interaction between sodium phenylacetate and phenylsodium (same as equation 4 except for use of phenyl- instead of benzylsodium) in the absence of toluene, a synthesis explicable only on the ground that sodium had been substituted for a hydrogen atom alpha to the carboxyl group.

Facts related to formation of butylmalonic acid had led us earlier to a conclusion that the best interpretation required a belief in the occurrence of amylidene disodium as a primary intermediate. With the proven role of sodium phenylacetate as an intermediate in preparation of phenylmalonic acid before us, it was advisable to make a careful reivew of the possibility that the course of synthesis of butylmalonic acid lay through sodium caproate. Yet every experiment which was successful in the case of sodium phenylacetate failed to assign a parallel part to sodium caproate. Thus butyl chloride[3] has not given a product in excess of the monocarboxylic acid formed on carbonation, carbonating at a slow rate caused not the slightest increase in the yield of butylmalonic acid, and sodium caproate was barely metallated, if at all, by amylsodium even at the boiling point (about 45°) of the petroleum ether used as the solvent in these preparations. Nothing from these results encourages the opinion that sodium sodiocaproate has been formed during the usual preparations of butylmalonic acid.

Though unsuccessful in causing amylsodium to react with sodium caproate under the above-named conditions, we have nevertheless effected this exchange with phenylsodium at a higher temperature. In boiling benzene the two react yielding sodium sodiocaproate which in turn is carbonated to give butylmalonic acid. This reaction is of great interest because it demonstrates the potency of this reagent which will react with a hydrogen atom activated solely by a carboxyl rather than by the conjunction of a phenyl and carboxyl group. We are engaged in a further study of this type of activity.

Attention should be called to the increase in yield of caproic and butylmalonic acids as the boiling point of the hydrocarbon solvent is lowered. Thus butane is the best solvent and Nujol the poorest so far noted for using in preparing the intermediate alkylsodium compounds. Another

---

(1) Morton and Hechenbleikner, THIS JOURNAL, **58**, 2599 (1936).

(2) Experiments with butyl chloride are reported in the succeeding paper.

(3) Morton and Fallwell, THIS JOURNAL, **59**, 2387 (1937).

interesting solvent effect is the absence of phthalic acids when the reaction is carried out in benzene, long refluxing of the phenylsodium so formed followed by carbonating in the usual manner producing but a trace of dicarboxylic acid. It will be recalled[1] that adding benzene to the organosodium compounds formed from amyl chloride and sodium in petroleum ether as a solvent, and subsequently refluxing the mixture, never failed to produce weighable amounts of phthalic (iso- and tere- mixture) acids.

A possibility of complexes in exchange reactions was observed when toluene was added to phenylsodium at room temperature. Though addition of methyl iodide to this reaction mixture yielded ethylbenzene, an evidence of the presence of benzylsodium, the introduction of carbon dioxide gave almost entirely benzoic acid, indicating that the reagent was still phenylsodium. Exchange to benzylsodium was completed partially by two hours of warming at 60° but not until the mixture was heated for some time at 75° did the carbonation process yield the expected carboxylic acids in quite equivalent amount. A similar heating of phenylsodium in the absence of toluene was without appreciable effect upon the yield of benzoic acid (except for the formation of a trace of a phthalic acid). The effect of heat in the exchange reaction therefore was not to increase the quantity of phenylsodium but to set the sodium atom on the tolyl radical.

Experiments

The reactions were carried out in the usual manner, namely, by gradual addition of the alkyl chloride to sodium suspended in a solvent at a temperature near 15–20°. The apparatus was the customary three-necked, one-liter flask with triple addition tube providing inlets for the necessary mercury sealed stirrer, thermometer, nitrogen or carbon dioxide tube, reflux condenser, and dropping funnel. Sodium sand was made up in stock quantity, a half kilo at a time. Technical amyl chloride, E. K. Co. grade, was used. Thiophene-free benzene and sulfur-free toluene were always used. The products were decomposed by addition of ice, the organic layer distilled through a fractionating column (8 or 17 theoretical plates as required) and the aqueous layer acidified. Monocarboxylic acids were extracted with petroleum ether, and malonic acids with ordinary ether. All yields are calculated on the basis of the amyl chloride used, one carboxyl group being equivalent to one chloride atom. Specific conditions and variations from the above are noted for each experiment.

Benzylsodium and the Rate of Carbonation (by F. F.).—Phenylsodium was prepared by gradual addition of 75 ml. of amyl chloride dissolved in 75 ml. of benzene to a suspension of 35 g. of sodium sand in 100 ml. of solvent over a period of two and one-half hours at 15–20°, more solvent being added as the mixture thickened until the total volume was about 500–600 ml. Stirring was continued for one and one-half hours longer after which 75 ml. of toluene was added. The temperature was next raised to 75° for a period of four hours and then allowed to fall to 45°, at which level carbon dioxide was passed in slowly. Heat did not cease to be evolved until after two hours but the gas was passed in for one hour longer. On cooling, decomposing, and separating the products, phenylacetic acid, phenylmalonic acid, and decane were obtained in 8, 24, and 4 g. (10, 43, and 10%) lots, respectively. In a control experiment using the ordinary rate of carbonation (heat rise over in about twenty minutes and total time one hour) the corresponding quantities were 19, 16, and 4 g. (23, 29, and 9%). Using 100 ml. of toluene and heating the mixture at 75° for eight hours instead of four hours and carbonating at the usual rate, the yields were approximately the same, namely, 18, 17, and 4 g. (22, 30, and 9%) each. In each of these three experiments the combined yield of mono- and dicarboxylic acids is approximately the same, 52–53%, although the relative proportions depend on the rate of admitting carbon dioxide.

Ethylbenzene and the Pentane Balance (by F. F.).—Using a Davis fractionating column and dry-ice trap to catch all pentane and pentene, the experiment was carried out in exactly the same manner described in the first experiment up to the addition of carbon dioxide. To the benzylsodium thus formed was added 30 ml. of methyl iodide in 30 ml. of benzene during thirty-five minutes. The mixture was decomposed in the usual manner, the organic layer separated, and dried over calcium chloride and fractionated. The portion boiling from 132–136° was ethylbenzene; yield 27.5 g. or 42%. Other products obtained by fractionation were pentene 2.8 g. (6.6%) which was determined in the 30–40° fraction (caught in the trap during heating at 75°) by addition of bromine; pentane 35 g. (79%); decane 4 g. (9%); a 174–205° liquid (density 0.85) 2.8 g.; and a 205° boiling liquid, density 0.88, 7.3 g. The pentane and decane recovered account for 95% of the amyl chloride originally added.

Phenylmalonic Acid from Sodium Phenylacetate (by F. F.).—Sodium phenylacetate was prepared by adding 17 g. of phenylacetic acid to 25 g. of sodium suspended in benzene in the usual reaction flask. The preparation of phenylsodium was then carried out in the customary manner by gradual addition of 47 ml. of amyl chloride. Presence of sodium phenylacetate in no wise hindered formation of phenylsodium. In fact, the reaction appeared to start more readily than usual. After heating for two hours at 75° to effect metallation, the brick-red colored mixture was allowed to cool to about 45° before carbonation. Yields: phenylmalonic acid, 14 g. (60% calculated on the phenylacetic acid used); decane 3 g. (7).

In another preparation, employing 41 g. of phenylacetic acid, 45 g. of sodium sand, and 75 ml. of amyl chloride, the mixture became so thick during the heating period necessary for formation of sodium sodiophenylacetate that stirring was impossible. The total quantity of phenylmalonic acid, 25 g., was larger than before, but the percentage yield (47) was less. The percentage of decane was the same. Preparation of sodium phenylacetate by neutralizing an aqueous solution of phenylacetic acid with sodium hydroxide, evaporating to dryness, and powdering prior to addition to the flask in which phenylsodium was to be prepared, was not very satisfactory (6% yield of phenyl malonic acid from 54 g. of sodium salt).

Butylmalonic Acid from Sodium Caproate (by F. F.).—Freshly distilled caproic acid, 20 g., was added to 45 g. of sodium sand in 100 ml. of benzene. When formation of the sodium salt had been completed, 75 ml. of amyl chloride was added gradually as in the usual conditions for preparing phenylsodium. The mixture was stirred for one hour after addition of amyl chloride was completed and was then heated for three hours at 70°. Carbonation at 45° resulted in the formation of 5 g. (17% based on the caproic acid added) of butylmalonic acid. The yield of decane was 3.5 g. (8%).

When a similar experiment was carried out with 20 g. of caproic acid, 45 g. of sodium sand, and 75 ml. of amyl chloride, using petroleum ether rather than benzene as the solvent, the temperature at vigorous refluxing did not exceed 45°. Caproic acid 43 g. and butylmalonic acid, 10 g. (20%), were obtained after the usual carbonation. When corrected for the amount of caproic acid used in the experiment, the yield of this acid is 23 g. (32%). These figures are within the error usually observed in these experiments, the average of a considerable number being for caproic acid 30 ± 2%; for butylmalonic acid 17 ± 2%.

Slow carbonation for a period of two and one-half hours (usually this step is completed in fifteen to twenty minutes) of the product of the action of 75 ml. of amyl chloride in 75 ml. of solvent on 35 g. of sodium sand in petroleum ether as in the usual preparation gave practically no change in the amount of acids usually obtained. Yields: caproic acid 24 g. (33%); butylmalonic acid 8 g. (16%).

Effect of Solvent on the Yield of Caproic Acid (by L. P.).—Sodium sand, 35 g., with 25 g. of cleaned and dried ordinary sand as an abrasive (actually little benefit could be observed from its use) was put into a square-shaped bottle with 200 ml. of solvent. Stirring in this bottle was much better than in the ordinary round-bottomed flask judged from the uniform suspension of sand seen in preliminary trials. A large rubber stopper was bored to carry the inlets required for the reaction. Amyl chloride, 75 ml., in 75 ml. of solvent, was added gradually over a three-hour period at 10–17°. More solvent was added as the mixture thickened so that the final volume varied from 375 to 450 ml. One hour of stirring at room temperature or less followed the addition period. Carbonation was carried out at room temperature or lower. For the run in butane correspondingly lower temperatures were of course needed. Difficulty experienced in starting the reaction in Nujol was overcome by preparing the sand in the bottle in the presence of 2 ml. of amyl chloride. Even with this active surface the temperature during the addition had to be maintained around 30°. The solvents were technical butane, petroleum ether, 35–60°, ligroin (90–120°), turpentine, and Nujol. Corresponding yields of caproic acid in each of these solvents were 24, 14, 10, 5, and 3 g. (40, 34, 14, 7, and 4%); of butylmalonic acid 4.8, 5.5, 0.1, 0.5, and 1.6 g. (19, 11, 0.2, 1, and 3%); of decane.., 5, 10, 11, 30 g. (.., 12, 23, 25, 68%). Removal of the olefins from petroleum ether and from ligroin by treatment with fuming sulfuric acid, followed by washing with alkali and distilling over sodium, caused some increase in the quantities of acids, particularly in the case of ligroin. Yields for this purified petroleum ether and ligroin were, respectively: of caproic acid 25, 18 g. (34, 25%); of butylmalonic acid, 7, 5 g. (14, 9%). In an experiment where the quantity of solvent, petroleum ether, was kept constant but that of the reagents was halved, the yield of caproic acid was 11 g. (29%); that of butylmalonic acid was 4.7 g. (19%), values which do not differ from the usual amounts obtained by more than mechanical losses.

Phenyl-tolyl-sodium Exchange (by F. F.).—Phenylsodium was prepared in the manner given in the first experiment. Toluene, 150 ml., was then added to the blue suspension and stirred for two hours at 25–30°. When 30 ml. of methyl iodide in 30 ml. of benzene was added to the now green solution over a period of forty minutes and the product was decomposed in the usual manner, 15 g. (23%) of ethylbenzene was obtained together with 4 g. (9%) of decane, and 3.5 g. of liquid, b. p. 180–250°. If carbonation instead of methylation was carried out, 24 g. (32%) of crude benzoic acid, m. p. 100–110°, 0.5 g. (0.6%) of phenylacetic acid, and 3.0 g. (5.4%) of phenylmalonic acid were recovered.

When the reaction mixture was heated to 60° for two hours before carbonation, 18 g. (22%) and 10 g. (17%) of phenylacetic and phenylmalonic acids, respectively, were obtained. Exchange at 75° as in the first experiment in this paper gave the maximum yields.

Effect of Heating Phenylsodium (by F. F.).—Phenylsodium was prepared as in the first experiment. The mixture was then heated and stirred four hours at 75°. After carbonating at 45°, 37 g. (49%) of benzoic acid, 0.2 g. of a phthalic acid, m. p. above 360°, presumably tere-, 3 g. (7%) of decane, and 1 g. (2%) of triphenylcarbinol together with 4 g. of a high-boiling liquid were obtained. In a blank experiment where the four-hour stirring was carried out at room temperature, 36 g. (47%) of benzoic acid, 2.7 g. (6%) of decane, 1 g. (2%) of triphenylcarbinol, and 4 g. of high-boiling liquid were found.

Summary

Synthesis of phenylmalonic acid by carbonating the product of interaction between phenylsodium and sodium phenylacetate has been shown to be possible.

Butylmalonic acid can be prepared in a similar way from phenylsodium and sodium caproate in boiling benzene but in petroleum ether amylsodium has little if any effect on this salt.

Yields of phenylmalonic acid from benzylsodium are increased at the expense of phenylacetic acid as the rate of carbonation is reduced, but a similar relationship between caproic and butylmalonic acids is not observed.

Yields of caproic and butylmalonic acids are increased as hydrocarbon solvents of lower boiling point are employed.

The product of addition of toluene to phenylsodium at room temperature will yield ethylbenzene with methyl iodide but benzoic acid with carbon dioxide. Higher temperatures are needed to fix the sodium to the tolyl radical.

CAMBRIDGE, MASS. RECEIVED JANUARY 13, 1938

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 171]

Condensations by Sodium. XIII. The Wurtz–Fittig Synthesis of Amylbenzene and Some Reactions of Benzylsodium

BY AVERY A. MORTON AND FRANKLIN FALLWELL, JR.

Previous work[1] has demonstrated that an important and possibly a sole cause of the Wurtz synthesis, namely, that phase involving the reaction between an organosodium compound and an alkyl halide, is by no means quantitative with respect to coupling. With a view of sifting the intermediates involved in a typical Wurtz–Fittig synthesis we have conducted an experimental inquiry into formation of amylbenzene. Amylsodium and chlorobenzene form chiefly a polymer and the phenylsodium and chlorobenzene pair react incompletely. Simultaneous addition of chlorobenzene and amyl chloride to metallic sodium, a circumstance which might favor combinations as free radicals, did not alter the above findings. Evidently the reactions involved in this particular Wurtz–Fittig synthesis may proceed through intermediate organosodium stages, yet give poor yields and a diversity of products.

As a means of arriving at a satisfactory preparation we have utilized a by-pass from phenyl- to benzylsodium and thence with butyl chloride to amylbenzene according to the sequence

$$C_5H_{11}Cl \xrightarrow[C_6H_6]{\text{Na in}} C_6H_5Na \xrightarrow{C_7H_8}$$

$$C_6H_5CH_2Na \xrightarrow{C_4H_9Cl} C_5H_{11}C_6H_5$$

Yields of 56% calculated on the amyl chloride used testify to the the success of this round-about procedure. Substitution of toluene for benzene in the first step of the above chain is impractical as a means of stopping the reaction at the benzylsodium stage (10% yield) but serves admirably for synthesizing hexylbenzene (61%), particularly if the reaction is carried out at 75°. Similar application to the amylbenzene synthesis using butyl chloride gave a 70% yield. Where the alkyl chloride is expensive it is preferable to prepare benzylsodium first via the amyl chloride–benzene–toluene route and then decolorize with the desired alkyl halide so that its conversion is practically quantitative. Incidentally, benzylsodium, in contrast to amyl- and phenylsodium, is the only one of those so far studied at length in this series which has consistently given the expected products with methyl iodide, ethyl bromide, amyl chloride, or methylene dichloride. In general its use is recommended for a Wurtz–Fittig reaction wherever the nature of the product permits.

Examination of the polymer from amylsodium and chlorobenzene showed that it consisted of one amyl and three phenyl residues. Possibility of its source from any secondary reaction involving amylbenzene was eliminated by an independent experiment (No. 7). Absence of free benzene suggested that the amyl and phenyl radicals had disproportionated giving pentane and phenylene, the doubly unsaturated radical then becoming the chief agent in polymerization.

The lack of complete reactivity exhibited by phenylsodium to amyl chloride is not a general behavior of this organometallic compound toward all substances for its reactions with toluene, iodine, and carbon dioxide have led to entire consumption of the reagent. Even chlorobenzene appears to react more readily with phenylsodium than does amyl chloride. Neither is benzylsodium outstandingly reactive toward all substances, for in an additional comparison with another reagent, namely, trioxymethylene, the three organometallic reagents in question yielded hexyl alcohol, benzyl alcohol and phenylethyl alcohol in 28, 19 and 17% yields, respectively.

Experiments

The general method of carrying out these reactions was the same as that previously described. Specific details are included in the tables or in the accounts of separate experiments. In all experiments a carbonation was performed as the last step in order to determine the amount of unconsumed reagent.

---

[1] Morton and Fallwell, THIS JOURNAL, 59, 2387 (1937).