thenic acid for the growth effect of pantothenic acid for *Lactobacillus casei* could be overcome by the addition of more pantothenic acid.

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Condensations by Sodium. XXVI. Metalation of Benzene, Toluene and Xylene. The Orienting Influence of Sodium and the Influence of Alkyl Groups on Metalation

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The purpose of this paper is to show (a) that benzene and toluene can be dimetalated so that the products after carbonation are exclusively iso- and homoisophthalic acids, (b) that *m*- and *p*-xylene can be dimetalated so that one sodium atom is introduced into each methyl group but that *o*-xylene is substituted to some degree in the nucleus and (c) that the three xylenes can be alkylated by the sodium-alkyl halide method, albeit with more difficulty than is met in the case of toluene. Formation of iso- and homoisophthalic acids will be interpreted from the viewpoint that sodium and, for that matter, other alkali metal substituents are *m*-orienting, and that the organometallic reagent behaves as an ion pair. The principles developed in connection with this orientating influence will be applied to interpretations of the reactions of amylsodium and like reagents. It will be shown that such agents can be classed as electrophilic. Finally, the decreased activity of the xylenes and of *o*-xylene in particular will be discussed in terms of the retarding influence which alkyl groups in general exert on metalation.

Dimetalations and Alkylation.—Previous work[1] has shown that benzene is readily monometalated and can be dimetalated to some extent by refluxing with amylsodium to give a mixture, the disodium content of which consists of 80% meta and 20% para phenylenedisodium. The present study shows that dimetalation can be made the principal reaction and can be caused to take place *exclusively* in the meta position. The change is brought about by restricting the amount of benzene used and by improving the stirring. Carbonation gives isophthalic acid in a yield of 51% based on the amyl chloride used in preparing amylsodium. The amount of monometalated product represented by benzoic acid is only 4.5%. Since these two products are the only ones obtained which are derived from benzene, it is apparent that about 85% of the benzene consumed in the reaction is dimetalated. The low yields calculated from the amyl chloride are due to the fact that there is about a 40% loss in preparing the amylsodium from the chloride and there is a small amount (about 2%) of amylsodium which does not participate in the reaction. As a preparative method the process is probably not as convenient as the permanganate oxidation of *m*-xylene[2] (95% yield of the hydrocarbon consumed), although that method has been reported[3] as being apt to give a contaminated product because of impurities in the *m*-xylene.

Toluene has previously[4] been found to be converted easily to benzylsodium with no trace of dimetalation. Under the improved conditions used in this study a second sodium atom is readily introduced. The dicarboxylic acid which results from carbonation is exclusively homoisophthalic acid and the yield is 40% based on the amyl chloride. The procedure is an excellent preparative one compared with the previous method[5] which requires six steps from 2-nitro-4-toluidine, itself produced from toluene, in three operations.

The three xylenes, which hitherto have not been studied in this series, undergo lateral metalation preferentially. The alkylation[6] reaction (amyl chloride dropped on sodium in hot xylene) shows that in all cases monosubstitution takes place exclusively in a methyl group giving the methylhexylbenzene in yields of 54, 32 and 22% (amyl chloride basis) for *p*-, *m*- and *o*-xylene, respectively. Dimetalation, by the method used with benzene and toluene, occurs on the two methyl groups exclusively in the case of *p*- and *m*-xylene

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(1) Morton and Fallwell, THIS JOURNAL, **60**, 1924 (1938).

(2) Ullmann and Uzbachian, *Ber.*, **36**, 1797 (1903).

(3) Schlenk and Brauns, *ibid.*, **48**, 661 (1915).

(4) Morton and Fallwell, THIS JOURNAL, **60**, 1426 (1938).

(5) Komppa and Hirn, *Ber.*, **36**, 3611 (1903); Komppa, Hirn, Rohrmann and Beckmann, *Ann.*, **521**, 242 (1936).

(6) (a) Morton and Fallwell, THIS JOURNAL, **60**, 1429 (1938); (b) Morton, Richardson and Hallowell, *ibid.*, **63**, 327 (1941).

and partly in the case of *o*-xylene. Carbonation yields 36, 37 and 19% of the corresponding phenylenediacetic acid. The *o*-xylene gives a by-product which shows that some metalation occurs in the nucleus. Preparation of the above three acids by older methods (Cl_2, KCN, H_2O) entails three steps and a much greater consumption of hydrocarbon.

Orienting Influence of Sodium.—Evidences of meta orientation demonstrated in the above results are supplemented by the previous study[7] on metalation of naphthalene in which formation of 1,3-, 2,6- and 1,8-disodium compounds was observed. The last two products result from deactivation of one ring and heteronuclear[8] substitution, a phenomenon associated with meta directing groups. The dimetalation of acenaphthene[7] receives a satisfactory interpretation on the basis of a meta directing impulse from the first sodium atom, although the data in that case are not proof of the effect. The related lithium atom also appears to have a meta directing influence since the second lithium atom enters the other ring in the dimetalation of dibenzofuran by butyllithium.[9] All these results accord with the definite evidence reported in this paper that sodium causes the second atom to enter the meta position.

The effectiveness of sodium as a meta directing force appears to be as great as, if not greater than, that of any other agent. Direct comparison is not possible because the reagents employed necessarily differ with the group being tested. Yet it is interesting to note that the meta directing influence of the trimethylammonium group[10] falls from 100 to 88%, when a methylene group is interposed between the ring and the positive pole, and that of the nitro group falls from 93 to 48% as a result of the same change whereas sodium loses none of its specific meta directing character when moved to this more distant position.

Such an exclusive and powerful meta directing influence presents a problem of providing a rational explanation. Our present view is that the sodium ion is the directing force and that it functions as would a positive pole to effect meta substitution. This opinion is better appreciated by presenting a sequence of reasoning that leads to that conclusion. (a) Organosodium compounds are commonly regarded as salts. From the electronic viewpoint the bond between carbon and sodium must be ionic[11] because the octet of electrons about the sodium atom is already complete and the single valence electron of the metal must be a part of the eight electrons around carbon. (b) Though the sodium is bound to the organic ion by coulombic forces only, the non-dissociating solvent (petroleum) and the insolubility of the organosodium compound prevents any dissociation and therefore independent action of the two ions. If the sodium ion is thus prevented by its environment from leaving the organic ion, it must remain adjacent and exert some effect[12] in a manner quite comparable to that exerted by any other group or atom attached to the nucleus. This distinction between an ion pair and the dissociated ions is of great importance. (c) Positive poles adjacent to the nucleus have a meta orienting influence. This fact was originally suggested by Vorländer[13] and ably classified and extended by Ingold[10] and co-workers. (d) If the semipolar type of ion, *i. e.*, the nitro or sulfonic acid, and the onium type such as ammonium or phosphonium, promote meta orientation, it is reasonable to expect the same directive influence with still another class of ions, *viz.*, the metallic type for the accident that some poles happen to be bound to an aromatic nucleus by covalent links and others by a coulombic link should not invalidate the attraction which a positive pole has for an oppositely charged particle. (e) The great lack of balance between the two ions, phenyl and sodium (phenyl can readily be displaced by such weak acids as ammonia or water) makes very plausible the idea that the sodium ion can make its "general polarity influence"[14] felt in the phenyl nucleus as a whole as well as at the point of attachment. The result would be that the electrons in the ring are rendered less available for combination or, as it is sometimes expressed, the electron density in the ring is reduced with consequent decrease in substitution by cationoid reagents. Meta substitution would follow.

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[7] Morton, Davidson and Gibb, THIS JOURNAL, **64**, 2250 (1942).

[8] Gilman, "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, p. 141.

[9] Gilman and Bebb, THIS JOURNAL, **61**, 109 (1939); Gilman, Stuckwisch and Kendall, *ibid.*, **63**, 1758 (1941).

[10] Ingold, "Annual Reports," **23**, 129 (1926); Goss, Hanhart and Ingold, *J. Chem. Soc.*, 250 (1927); Goss, Ingold and Wilson, *ibid.*, 2440 (1926); Baker and Ingold, *ibid.*, 2462 (1926).

[11] Carothers and Coffman, THIS JOURNAL, **51**, 588 (1929).

[12] Fajans, "Chemical Forces," The George F. Baker Lectures, at Cornell University, McGraw-Hill Book Company, 1931, p. 68, in a discussion of inorganic ions, points out that "the actions of the forces which ions exert upon one another may lead to a more or less pronounced deformation of the ions, particularly of the anion under the influence of the cation."

[13] Vorländer, *Ber.*, **52**, 263 (1919).

[14] Waters, "Physical Aspects of Organic Chemistry," D. Van Nostrand, New York, N. Y., 1936, p. 241.

The effect of the undissociated character of the ion pair under the conditions of our experiments can be judged by considering the case of benzylsodium. Had the medium and solubility favored dissociation, the electrons on the methylene group, no longer bound by the attraction of a strong adjacent positive pole, would surely have increased the electron density of the phenyl group even as do the unbound electrons in the phenoxy ion. Ortho and para substitution would then result. Instead, the sodium ion remains attached, attracts firmly the two electrons at the junction point and immobilizes those in the ring so that meta substitution occurs. If the less effective lithium ion had been employed, it is quite possible that ortho or para substitution might have resulted. Ingold has already shown that the comparatively weak nitro and phosphonium groups[10] lose much of their influence as a methylene group is interposed between the ring and the seat of ion activity and therefore permit much ortho and para substitution.

Whether these general considerations of comparative strength of the cation attached to the benzyl ion have any bearing on the "allylic rearrangement"[15] which occurs when benzyl-lithium[16] or -magnesium halide[15] is treated with formaldehyde cannot at this writing be affirmed but it is interesting to note that the change, leading to *o*-tolylcarbinol, does not take place when benzylsodium is treated with trioxymethylene.[6a] These results are in accord with the possibility that the lithium or magnesium halide cation is too weak to intervene in any substitution reaction which the benzyl ion[17] might undergo, but that the stronger sodium ion decreases the availability of the electrons in the nucleus and therefore favors the normal change to phenylethyl alcohol. In any event, it is reasonable to suppose that as far as introduction of substituents in the ring is concerned the reactions of benzylsodium and benzyllithium will frequently differ because of the difference in the influence which the respective cations are able to exert.

One viewpoint only might appear to cloud the simplicity of the above explanation for a meta directing influence. How can one reconcile the fact that in the periodic table sodium in group I has electrons to donate whereas chlorine in group VII appropriates electrons? It might, in fact, be assumed that the sodium in benzylsodium and the halogen atoms in benzotrichloride would have opposite rather than parallel directive influences. This seeming conflict is easily reconciled. When sodium donates an electron it does not lose all attraction for that particle. The fitting of that electron into the octet of another atom merely causes the sodium ion to attract the mass to which the electron has become attached for there is a difference in charge between the nucleus and electron shell of the cation. Each chlorine atom in benzotrichloride, however, has taken up an electron, not because of any difference in charge between the nucleus and outer shell, but merely because there is a vacant position in its shell, the filling of which is eminently desirable, possibly from a standpoint of symmetry. Both the sodium ion and the chlorine atom, therefore, attract an electron. The orientation of benzylsodium and of benzotrichloride is accordingly in the same direction but with different intensity, the ion apparently having the stronger effect.

Apart from the novelty involved in a meta directing force attached by an ionic rather than a covalent bond, there are a few other interesting features to which attention should be drawn. Sodium, representing a class of substituents, is the only meta orienting agent which consists of one atom only. It is also the only one which has an octet of unshared electrons in its outer shell, although of course such electrons are not of the valence type which can resonate with those in the ring. Finally, the phenomenon is realized by the reaction of the insoluble amylsodium with the insoluble phenyl- or benzyl-sodium. The crystal lattice structure that may prevail in these solid reagents does not interfere with the exhibition of orienting influence. This last point does not apply of course to the lithium compounds which are soluble in ether and frequently so in petroleum ether.

Reactions of Amylsodium.—The foregoing section has shown that an organosodium compound acts as an ion pair and that the metal ion has such a dominating influence that it controls the position at which a metal substituting agent attacks an aromatic nucleus. It is the purpose of this section to observe whether these two principles can be applied to other reactions of amylsodium and related compounds. In other words, is it possible to view the reactions of organometal-

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[15] Gilman and Kirby, THIS JOURNAL, **54**, 345 (1932); **51**, 1571 (1929).

[16] Gilman and Breuer, *ibid.*, **56**, 1127 (1934).

[17] Johnson, *ibid.*, **55**, 3029 (1933).

lic compounds as those in which the two ions are adjacent to each other with the sodium playing the dominant role, if any preference exists?

If such an opinion is applicable, it would follow that amylsodium, representing a class of substances, is an electrophilic reagent, particularly in metalation processes. The original definition[18] for this class, *viz.*, that they "acquire electrons or a share in electrons previously belonging to a foreign molecular ion" needs merely to be extended to include reagents which introduce substituents that acquire electrons by a strong attractive force only, a full acquisition or sharing in the octet sense being impossible because an octet about sodium is already complete. Unless the mechanism of metalation is complicated, it would appear difficult to arrive at any other conclusion without denying to the ion, which is entering the nucleus, the same power of attracting electrons that it shows as an orienting agent. This opinion does not necessarily conflict with an earlier classification[19] of organometallic reagents as nucleophilic, since that assignment was made on the basis of the reaction of the alkyl portion. It would be helpful, however, to show that the process of metalation was really initiated by the entrance of the metal ion rather than by abstraction of a proton by the anion.

Although rigorous proof of this point is difficult to offer, it can be shown that the position occupied when metalation takes place in a system containing a directive group is the same as that taken in the nitration, sulfonation, chlorination and other well known electrophilic processes. For example, the ortho and para orienting methoxy and dimethylamino groups cause metalation in the ortho position, whether the agent is amylsodium,[20] butyllithium[21] or the Grignard reagent.[22] Phenyl and alkyl groups which direct nitration to the ortho or para position direct metalation in a similar way for both amylsodium[22] and butyllithium[21] metalate biphenyl in the para position, and amylsodium metalates isopropylbenzene[23] in the para position. The sodium carboxyl group, present in sodium benzoate, which Ingold[24] has pointed out is ortho directing when chlorinated in alkaline solution (because the sodium ion destroys the polarity of the carbon atom) is, in fact, ortho directing with amylsodium[1] also. Obedience to the influence of the common meta directing groups such as nitro, carbethoxy and the like is not realized, because amylsodium reacts with the group itself. However, the influence of one metal ion on the entrance of a second is in agreement with the opinion that the reagent is electrophilic.

According to such a classification, it is reasonable to expect other instances where typical reactions of organo-alkali compounds are found in electrophilic reagents as well. In this connection, it is worth mentioning that the metal-halogen[25] interchange which has been studied so extensively with lithium compounds is indeed paralleled by a nitro-halogen[26] interchange. Both types of reactions occur in compounds where the halogen atom is labilized by the same type of group, *viz.*, a methoxy or ether linkage. The latter is not so well known and has been studied less merely because it is less unexpected and perhaps less useful.

This similarity between nitration and metalation, that is, between an acid and an alkaline reagent is not so impossible as it might at first seem. Ingold[18] has already pointed out that in substitution reactions the nitric acid is not functioning in the manner which might be expected from its role as an acid but rather is undergoing a change as if the division were into hydroxyl and nitro ions HO^- and NO_2^+. Ri and Eyring,[27] likewise, infer that nitric acid may dissociate into a positive nitro and a negative hydroxyl ion, particularly in a complex. So also does sulfuric acid function as if it were HO^- and SO_3^+. It would appear therefore that various electrophilic reagents could have much more in common than might be inferred from the different *p*H values which result from their reaction with water. They represent various types of ionization, incipient or complete, into negative and positive ions. All of these considerations therefore are in agreement with the opinion that organoalkali reagents can be considered as electrophilic.

Disproportionation in the Wurtz reaction is

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(18) Ingold, *Chem. Rev.*, **15**, 268 (1934).

(19) Robinson, "Solway Reports," 1931, p. 434, *cf.* ref. 14.

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

(21) Gilman and Bebb, *ibid.*, **61**, 109 (1939); Gilman and Brown, *ibid.*, **62**, 3208 (1940).

(22) Challenger and Miller, *J. Chem. Soc.*, 894 (1938).

(23) Unpublished research.

(24) Ingold, Ingold and Shaw, *J. Chem. Soc.*, 817 (1927).

(25) Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938); Gilman, Willis and Swislowsky, THIS JOURNAL, **61**, 1371 (1939); Langham, Brewster and Gilman, *ibid.*, **63**, 545 (1941).

(26) Jackson and Dunlap, *Am. Chem. J.*, **18**, 117 (1896); Birosel, *Uni. Philippines, Natural Applied Sci. Bull.*, **I**, 145 (1931); *C. A.*, **26**, 972 (1932); Hodgson and Nixon, *J. Chem. Soc.*, 1085 (1930).

(27) Ri and Eyring, *J. Chem. Phys.*, **8**, 433 (1940).

another phenomenon, the interpretation of which is interesting in the light of the concepts being discussed. This process has already been formulated in terms of an ion-pair.[28] An alternative suggestion[29] that it is the action of the organo ion, a "hydrocarbo base," on the alkyl halide was almost simultaneously made. The latter proposal would appear to bring this reaction in line with current mechanisms[30] used to express the elimination reactions that occur when organic halides are treated with alcoholic sodium hydroxide or alcoholate, or with piperidine.[31] The evidence presented in this paper of the dominating role of the sodium over the organic ion, is easily accommodated to the ion-pair mechanism. The differences between the Wurtz reaction and the common elimination process are clearly visible. In the former, the paired character of the reagent insures a simultaneous action of both ions or, if either ion acts faster, necessitates that the dominating sodium ion be pried loose by another force—the halide—before the anion can function. In the latter, each molecule of solvent is capable of furnishing an electron which provides an object for the attractive power of the sodium ion, so that the alkali metal ion is solvated and the ethoxy ion is left free to initiate the elimination process. The solvent, in other words, plays the role of freeing the anion from the influence of the cation by offering so many molecules (mass action) with exposed electrons that the sodium ion no longer dominates the organic ion. The processes in both cases are somewhat similar save for the manner in which the influence of the cation is removed.

Finally, the application of these two principles, *viz.*, the ion pair and the sodium ion influence, to metathetical reactions would suggest a note of caution in the growing practice of writing reactions of organic ions as if they were entirely independent of the presence of the inorganic one or of regarding the participation of the inorganic component of the salt as being any more fundamental than or providing some energy of crystallization which may act as a driving force. It would appear that such views do slight justice to the true role that the inorganic ion can play in such reactions. For it is difficult on the one hand to accept the fact that sodium, though detached as an ion, is still sufficiently attached to control entirely the position which an entering group can take in the phenyl nucleus and at the same time deny that at the point of attachment of this force the influence in a reaction is nil. It might indeed be more reasonable to assume that if electrons in a distant nucleus, as in benzylsodium, are unavailable for reaction they are even less available at the point where the coulombic forces are centered until some force approaches which is capable of offering a more suitable affinity for the metal or unless the solvent will *assuredly* permit sufficient dissociation to allow independent action.

Effect of Alkyl Groups on Metalation.—Attention should be called to the many independent evidences of decreased reactivity caused by two adjacent methyl groups in *o*-xylene as compared with that found in *p*- and *m*-xylene, as witnessed by (a) the lower yield of methylhexylbenzene from that isomer; (b) the lower yield of phenylenediacetic acid and the correspondingly larger quantity of unreacted amylsodium (detected as caproic acid) present at the end of the reaction; and (c) the fact that the *o*-xylene is the only one of the three isomers in which the reactivity of the methyl hydrogen has been reduced to such a low level that nuclear metalation can occur. These results may have a bearing on the interesting observation of Bartlett and Jones[32] on the inactivity of the hydrogen attached to the central carbon atom of tri-*o*-tolylmethane; for if the last compound be considered as three ortho xylenes with one of the methyl groups held in common by the three phenyl systems, then the inactivity in the two cases would appear to have a common origin, accentuated in the case of the larger compound because the effect of three methyl groups can be concentrated on one atom.

The cause of such decreased activity is not clear. It may well be that a steric factor is somehow involved. There are, however, many examples which show that the introduction of an alkyl or methyl group into any position about an aromatic hydrocarbon decreases the ease with which a given hydrogen atom is replaced by metal. For example, amylbenzene[6a] can be used as a solvent during preparation of amylsodium under conditions where toluene is attacked at once; alkylation[6] of toluene by propyl chloride and sodium results in introducing the first propyl group

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[28] Morton, Davidson and Hakon, THIS JOURNAL, **64**, 2242 (1942).

[29] Whitmore and Zook, *ibid.*, **64**, 1783 (1942).

[30] Bateman, Cooper, Hughes and Ingold, *J. Chem. Soc.*, 925 (1940); Hughes, Ingold, Masterman and McNulty, *ibid.*, 899 (1940).

[31] Drake and McElvain, THIS JOURNAL, **56**, 1810 (1934).

[32] Bartlett and Jones, THIS JOURNAL, **64**, 1837 (1942).

on the methyl carbon but further alkylation at that position meets such resistance that the second propyl group enters the nucleus[33]; introduction of two methyl groups into toluene to form isopropylbenzene[23] so inactivates the methyl (tertiary) hydrogen atom that metalation in the para position takes place; alkylation of the three xylenes reported in this paper requires a higher temperature than is necessary for toluene. In brief, it appears that alkyl or methyl groups, whether placed on a methyl group whose hydrogen atoms have previously displayed activity or located on a benzene nucleus, make the metalation that previously occurred in a side chain more difficult. This effect might be expected to be at a maximum when the alkyl group is adjacent to the position being attacked and might alone be sufficient to account for the phenomena previously mentioned, although the possibility of complicating influence of steric hindrance is not eliminated. It is worth noting that a similar influence of alkyl groups is present in other reactions that involve a proton transfer to a negative ion, namely, in the degradation of methylated ammonium salts[34] and the decomposition of dialkyl sulfones[35] and that Ingold[34] has referred to it very aptly as a reduction of "incipient ionization" caused by the electron-donating capacity of the methyl or alkyl groups.

The question might be raised as to how well the previous discussion on the ion-pair and dominant sodium ion fits with the increased resistance which alkyl or electron donating groups impart to the metalation of the side chain. It must be remembered that the process of metalation is essentially that of a reaction of a salt, amylsodium, with that of an acid, toluene, to form a new and more stable salt, benzylsodium. Unlike the metalation of the aromatic ring, when an orienting group is present, there appear to be no data available which would indicate for toluene whether the process parallels that of nucleophilic or electrophilic reagents. If the former, the anion presumably abstracts the proton, and thereby exposes a position which is filled by the cation; if the latter, the cation, ejects the proton, which is simultaneously, or nearly so (ion-pair reaction), taken up by the anion. On the latter basis, the sodium ion displaces a proton because it will thereby acquire a more stable position than formerly. If the affinity with which benzyl holds the proton is increased by introduction of an alkyl group, the displacement occurs with more difficulty. An interpretation can therefore be made which is adequate and consistent with the viewpoint presented earlier in this paper.

Experiments

Metalation of Benzene, Toluene and Xylenes (by E. L.).—The procedure for preparing amylsodium in *n*-octane was in general the same as described[28] before in which the high speed stirrer[36] and special flask were used. The hydrocarbon, sulfur-free in every case, was then added and the mixture heated. The organosodium compound was carbonated by pouring it on solid carbon dioxide. The general method of separating the acids was a combination of extraction with petroleum ether and with ether and of filtering the insoluble product. Formation of the dicarboxylic acids was first observed with toluene when an attempt was made to effect a complete conversion of a small quantity of toluene to benzylsodium by warming to 50–55° with high speed stirring. The quantity of homoisophthalic acid obtained was sufficiently large to draw attention to the method as a preparative one. From a considerable number of experiments a suitable proportion of reagents and other conditions was found (see Table I) which gives a satisfactory yield. The high temperature used for toluene in the experiment listed is not of course obligatory. At 50–55° (metalation time 4.3 hours) the yield of homoisophthalic acid from 0.145 mole of toluene was a trifle higher (0.289 mole) but there was a considerable quantity of unused amylsodium (0.028 mole of caproic acid) present. The addition time in that experiment was sixty minutes. No phenylacetic acid was found. Naturally the yield of homoisophthalic acid fell as the quantity of toluene was increased. For example, an experiment identical with the one above but using twice the amount of toluene (0.29 mole) caused a small decrease in the homoisophthalic acid to 0.025 mole and the formation of 0.015 mole of phenylacetic acid where none had been found before, and a smaller quantity (0.01 mole) of caproic acid representing unused amylsodium. An experiment practically identical with that recorded for toluene in the table but with over eleven times the quantity of toluene (0.87 mole) gave only 0.0056 mole of homoisophthalic acid but 0.092 mole of phenylacetic acid with no unused amylsodium. Formation of the disodium compound can of course be largely avoided by using still larger amounts (1.015 mole) of toluene, and by operating at a lower temperature (30–35°). After three hours at this temperature, carbonation gave 0.104 mole of phenylacetic acid and only 0.0004 mole of homoisophthalic acid.

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(33) In that experiment the product was a mixture of meta (chiefly) and *p*-methylbutylbenzenes. The results of the present study provide a very simple explanation for the two products. The meta isomer is derived from the reaction of a disodium intermediate *m*-$NaC_6H_4CH_2Na$ with propyl chloride; the para isomer from the para metalation of the primarily formed butylbenzene to give *p*-$NaC_6H_4C_4H_9$ followed by the Wurtz reaction with propyl chloride. Both reactions are very likely to occur simultaneously under the conditions of the experiment.

(34) Hanhart and Ingold, *J. Chem. Soc.*, 997 (1927); Ingold and Vass, *ibid.*, 3125 (1928).

(35) Fenton and Ingold, *ibid.*, 2338 (1929).

(36) Morton, Darling and Davidson, *Ind. Eng. Chem., Anal. Ed.*, **14**, 734 (1942).

Isophthalic acid was identified by its melting point (346–347° uncor.), neutralization equivalent 84.5. The absence of any appreciable quantity of terephthalic acid was shown by converting to the di-*p*-bromophenacyl derivative (m. p. 179–179.5° cor.). This ester was put in chloroform. When half was dissolved, the melting point of the residue was found to be the same as that of the crystals from the dissolved part. Any derivative of a terephthalic acid should have been observed under these conditions.[1]

TABLE I

METALATION OF HYDROCARBONS BY AMYLSODIUM

Constant conditions. Except for benzene, the quantities of reagents in each experiment were: amyl chloride 15.5 g. or 0.145 mole, sodium 10 g. or 0.44 g. atom, hydrocarbon 0.073 mole. The amounts used with benzene were 31 g. (0.28 mole); 20 g. (0.87 g. atom) and 0.145 mole, respectively. The addition time for the hydrocarbon was thirty minutes in each case except for toluene, where it was 75–80°. The time for metalation at these temperatures was 1.3 hours for benzene, 2.5 hours for toluene and 3 hours for the xylenes.

		Yields of acids from				
		Benzene	Toluene	*o*-Xylene	*m*-Xylene	*p*-Xylene
Caproic acid	grams	5		3	1	2
	mole	0.004	0	0.026	0.0086	0.0173
Per cent. yield		1.5		1.8	5.9	11.9
Monocarboxylic acid	grams	1.6[a]	0.9[b]			1.8[c]
	mole	0.013	0.0066	....	.....	4.7
Dicarboxylic acid	grams	12.2[d]	4.5[e]	2.7[f]	5.2[g]	5.1[h]
	mole	0.074	0.025	0.014	0.027	0.027
Per cent. yield		51	40	19	37	36

[a] Benzoic acid. [b] Phenylacetic acid. [c] *p*-Tolylacetic acid. [d] Isophthalic acid. [e] Homoisophthalic acid. [f] *o*-Phenylenediacetic acid, 0.0072 mole of a dicarboxylic acid, in which one carboxyl group is attached to the ring, was also obtained. [g] *m*-Phenylenediacetic acid. [h] *p*-Phenylenediacetic acid.

Homoisophthalic acid was identified by its melting point (183.4–183.9° cor., reported[37] value 184–185°), a mixed melting point with an authentic sample, neutralization equivalent 90, and the diamide derivative which has a melting point of 227.5–228.5° cor. (reported 228°[37]) and a nitrogen analysis of 15.8% (calcd. 15.9%). Oxidation with alkaline permanganate yielded isophthalic acid which was identified as its di-*p*-bromophenacyl derivative.

o-Phenylenediacetic acid melted at 147–148° (cor.). The recorded[38] value is 148.5–149°. It had the correct neutralization equivalent (97.2° observed) and gave a diamide derivative that melted at 196–197° (cor.) in agreement with the reported[39] value of 198°. Oxidation of the diacid with alkaline permanganate gave phthalic acid identified by the anhydride.

m-Phenylenediacetic acid was similarly identified by its melting point (169–170° observed; 170° reported)[40] and its neutralization equivalent. The diamide, hitherto not prepared, melted at 213–214° cor. and had the correct analysis. *Anal.* Calcd. for $C_{10}H_{12}O_2N_2$: N, 14.58. Found: N, 14.61 and 14.88.

p-Phenylenediacetic acid melted at 243–244.5° (reported[40] value 244°) and the correct neutralization equivalent. Its dimethyl ester melted at 56–57° (reported[41] value 56.5–57°). Oxidation of the diacid with alkaline permanganate gave terephthalic acid which was identified by the melting point of its dimethyl ester.

The acid by-product from the reaction with *o*-xylene consisted of 1.4 g. of an acid which melted from 235–239.5° and could not be separated by recrystallization from water, acetic acid, alcohol, acetone or benzene. The calculated neutralization equivalent for a dicarboxylic acid was 97. The observed value was 88, indicating that some tricarboxylic acid (neut. eq., 79.3) was present. Oxidation gave trimellitic acid identified by neutralization equivalent and m. p. 226–227°; recorded[42] value 228°. The acid from the reaction therefore was substituted in the nucleus as well as the side chain.

Alkylation Experiments (by W. O. S.).—Alkylation was carried out in the manner previously recorded[6] except that no inert atmosphere was maintained and the temperature had to be raised to 100°. The special creased flask was used but the stirrer had a moderate velocity (3000 r. p. m.) only. The alkyl halide was added dropwise during a period of one hour. The products were fractionated in a jacketed Vigreux column of about seven plates. The process was checked by an experiment with amyl chloride and toluene and was found to give at 70° the customary yield of 60% of hexylbenzene. The structure of each product was confirmed by alkaline permanganate oxidation which yielded benzoic acid only in the case of hexylbenzene and the expected dicarboxylic acid only from the products of the reaction with the three xylenes.

p-Xylene (85 cc.) containing 15 g. of sodium in suspension was thus treated at 100° with 25 cc. of *n*-amyl chloride. 1-Methyl-4-hexylbenzene was collected between 236–238°. The yield was 10.5 g. or 54%. The sulfonamide melted at 76.5°. *Anal.* Calcd. for $C_{13}H_{21}O_2SN$: N, 5.5. Found: N, 5.2. In like manner, 300 cc. of *m*-xylene with 30 g. of sodium and 50 cc. of *n*-amyl chloride yielded 12.2 g. (32%) of 1-methyl-3-hexylbenzene which boiled from 235–238°. Half of this quantity of reagents at 105° gave 6.1 g. or 32% of the same compound. Likewise 300 cc. of *o*-xylene, 30 g. of sodium and 50 cc. of *n*-amyl chloride at 100° gave 10.4 g. or 27% of 1-methyl-2-hexylbenzene boiling 236–238°. The sulfonamide melted at 75.5% and contained 5.3% of nitrogen. Half the quantity of reagents gave 4.3 g. or 22% of the same compound. Some higher boiling fractions corresponding to dimetalation were obtained in all of the above experiments.

Summary

Metalation of benzene, or toluene, with amylsodium can be made to give either a mono- or a dimetalation product depending on the quantity of reagent employed, the temperature, and effectiveness of stirring. Carbonation of the dimetalated products gives isophthalic and homoisophthalic acids, respectively.

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(37) Reinglass, *Ber.*, **24**, 2417 (1891).

(38) Baeyer and Pape, *ibid.*, **17**, 447 (1884).

(39) Moore and Thorpe, *J. Chem. Soc.*, **93**, 175 (1908).

(40) Kipping, *ibid.*, **53**, 21 (1888).

(41) Zincke and Klippert, *Ber.*, **9**, 1767 (1876).

(42) Ruzicka, de Graaff and Hosking, *Helv. Chim. Acta*, **14**, 237 (1931).

Save for *o*-xylene the three xylenes are attacked on the methyl groups exclusively. Alkylation of the mono-products gives the corresponding methylhexylbenzene. Carbonation of the dimetalated compounds gives the corresponding phenylene diacetic acids. *o*-Xylene undergoes some nuclear metalation, presumably after one sodium atom has been introduced in the methyl group. Alkylation and metalation of the xylenes occurs with more difficulty than the corresponding reaction of toluene.

The products of dimetalation of benzene and toluene are meta substituted exclusively. A reasonable interpretation of this result is that the mono-metalated product is a salt and acts as an ion-pair with the sodium ion so close to the anion that it exerts a meta directing influence, *i. e.*, the cation dominates the position taken by a substituent in the anion. This opinion is shown to be consistent with other experimental facts and with current theories.

The substitution, disproportionation, and metathetical reactions which amylsodium and like reagents undergo with various other compounds are discussed from the viewpoint of the findings in the orientation study, *viz.*, that an organosodium compound may act as an ion-pair with the metal ion having the leading role, if any preference is to be considered. The reactions are shown to be consistent with such a view. A comparison with electrophilic reagents is possible.

The difficulty of alkylating or metalating the three xylenes and *o*-xylene in particular is correlated with the general retarding effects of alkyl groups on metalation. These results may likewise be interpreted in the light of an ion-pair mechanism with the sodium ion having an equal or more dominant role.

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Condensations by Sodium. XXVII. Furylene Disodium. Comments on the Aromatic Properties of Furan

BY AVERY A. MORTON AND G. HAROLD PATTERSON

While endeavoring to prepare furylsodium by the action of amylsodium on excess furan, we discovered, after pouring the mixture on solid carbon dioxide, that an appreciable quantity of α,α'-furandicarboxylic acid was present. Furan had obviously been metalated twice. Although no attempt was made to find conditions for optimum yields as was done in the case of benzene and toluene,[1] the generally greater ease of substitution in furan as compared with benzene suggests that the process is capable of giving large amounts of material in one step.

Since the sodium ion has a strong meta-directing influence,[1] this result constitutes one more of the failures of such groups[2] in general to exert any influence in the furan nucleus. Since it is reasonable to assume that the properties which cause sodium to be meta-directing in the benzene nucleus are inherent in the metal, it is logical to look for a reason why this influence is set aside when the same type of reaction is carried out in another system. Now a meta-directing group can fail to operate even in an aromatic system, chiefly when opposed by an ortho-para directing force such as an ether (methoxy) group. It is, therefore, necessary to look only to the ether group in furan to observe a cause for the failure of meta-directing groups in general to function in this heterocyclic system.

A transfer of the seat of activity from a point outside to one inside the ring is by no means an unusual occurrence. The C=N system in pyridine has the properties of an ammono aldehyde[3]; the imide (ammono phenol[3]) function in pyrroles[4] and in indoles[5] serves as an imino phenolic group and participates with varying degrees of success in such reactions as the Kolbe or Reimer synthesis; the amidine function is evident in imidazoles. Even in such a resonating molecule as benzene the additive character of the double bonds is not entirely suppressed. Finally, in the case of furan itself, the ether function still has, to an advanced degree in fact, the property of easy

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[1] Morton, Little and Strong, THIS JOURNAL, **65**, 1339 (1943).

[2] Kohler, Westheimer and Tishler, *ibid.*, **58**, 264 (1936).

[3] Franklin and Bergstrom, *Chem. Rev.*, **16**, 305 (1935).

[4] Ciamician, *Monatsh.*, **1**, 624 (1880); Ciamician and Silber *Ber.*, **17**, 1437 (1884).

[5] Ellinger, *ibid.*, **39**, 2515 (1902).