

CONDENSATIONS BY SODIUM. XXXVIII. THE METALATION OF
tert-BUTYLBENZENE BY AMYLSODIUM AND THE EFFECTS OF
ASSOCIATED SALTS^{1, 2}

AVERY A. MORTON, CHESTER E. CLAFF, JR., AND FRANCES W. COLLINS

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INTRODUCTION

This work was intended to be a study of the metalation of the benzene nucleus under the directing influence of an alkyl group which could not itself be metalated, but steric factors probably limit the scope of polar influence. No *ortho* metalation occurs. Only one dimetalation, the *m, m'*, can take place because of the hindrance at the two *ortho* positions and the failure of sodium to attack a position adjacent to another sodium ion on the ring. Nevertheless some excellent demonstrations of the effects of associated salts, which is one of the special aspects of the work in this laboratory, have been achieved.

MONO- AND DI-METALATION

The experimental method in all cases was to prepare amylsodium from amyl chloride and sodium. If the effect of an alkoxide was to be tested, an alcohol then was allowed to react with part of the amylsodium, or an alkoxide, prepared separately from the metal and an alcohol, was added. If the effect of a metal halide was to be tested, some alkyl halide was allowed to react with part of the amylsodium or granular metal halide was added. Finally *tert*-butylbenzene was added and the mixture was maintained at a stipulated time and temperature. Carbonation of the mixture gave carboxylic acids corresponding to the sodium compounds. Analyses were made by conventional methods of crystallization, titration, and infrared absorption of these acids.

Table I gives the results of monometalation. No alkoxide was present in the first three experiments where the highest proportion of *para* substitution took place. In the remaining experiments, the trend was toward a *meta* attack, six out of the eleven tests being 50% or more in that direction. As in other cases (1, 2), potassium alkoxides (experiments 5 K, 7 K, and 10 K) caused more activity than the corresponding sodium salts (Nos. 5, 7, and 30) the total metalation being doubled or more.

Table II lists the results of dimetalation at 60° in the order of increasing quantity of dicarboxylic acid, column 3. An abrupt increase in this acid at Exp. No. 35 divides the table naturally into two parts but the average amounts (182 and 188 milliequivalents) of total organosodium compound, as measured by the total

¹ This work was performed as a part of the research project sponsored by the Reconstruction Finance Corporation, Office of Synthetic Rubber, in connection with the Government Synthetic Rubber Program.

² A portion of this paper was presented at the Boston Meeting of the American Chemical Society, 1951.

TABLE I
MONOMETALATION^a OF *tert*-BUTYLBENZENE BY AMYLSODIUM

Exp. ^b No.	Alcohol	Temp., ^c °C.	Yield of Acids ^d		Para subs. ^e %
			Benz., %	Cap., %	
1	None	15	9	65	76
2	None	15 ^f	10	54	82
3	None	20	4		97
4	2-Prop.	20	38		44
5	<i>n</i> -Pent.	15	5	62	46
5 K	<i>n</i> -Pent.	15	12	27	70
6	<i>n</i> -Pent.	20	26		51
7	2-Pent.	15	3	29	58
7 K	2-Pent.	15	64 ^g	23	57
8	2-Pent.	20	46		29
9	<i>tert</i> -Pent.	5	13	28	37
10	<i>tert</i> -Pent.	15	16	37	50
10 K	<i>tert</i> -Pent.	15	34	14	50
11	<i>tert</i> -Pent.	25	5	36	47

^a The reaction time was five hours unless otherwise stated. The amount of amylsodium in each case would have been 0.3 mole if the reaction of amyl chloride with sodium had given a quantitative yield of this reagent. ^b The letter K signifies that the potassium alkoxide was used. ^c The experiments at 5, 15, and 25° were by C. E. C., those at 20° were by F. W. C. ^d Benz. refers to the mixture of *tert*-butylbenzoic acids; cap. refers to caproic acid. ^e These analyses were by infrared absorption. Because the two experimentalists used different methods for isolating the *tert*-butylbenzoic acids, the values at 20° are a little higher in *para* and those at the other temperatures are higher in *meta* than are the true amounts. ^f The reaction mixture was transferred to a bottle after the usual five hours and was allowed to stand 91 more hours before carbonating. The yield of *tert*-butylbenzoic acids was not appreciably increased during this additional time but some dimetalation (1.2 g. or 2.4%) took place. ^g A trace (0.1 g.) of dimetalated product was formed in this reaction.

carboxyl groups in *tert*-butylisophthalic acid, *tert*-butylbenzoic acids, and caproic acid and recorded in the last column, are approximately equal in the two divisions. In the first group there was, as a rule, a smaller transfer of sodium from amyl to *tert*-butylphenyl (89 m.e. on the average) and of that amount only 24% was for dimetalation. In the second group, the transfer averaged 148 m.e. of acid, 42% of which was in dimetalation.

Three distinct relationships between reactivity of amylsodium and the structure or composition of the associated salts, are evident. For example, *tert*-alkoxides, as a rule, increased metalation and favored disubstitution, as shown by the fact that every salt in group 2, except for 17 K, is tertiary and the three such salts in group 1 caused higher than average metalation. Second, the potassium ion, even more than *tert*-alkoxides, increased both metalation and disubstitution to a degree sufficient to change one alkoxide from group 1 to group 2 (17 to 17 K). Third, the cyclic systems in cyclopentyl and cyclohexyl caused a reduction in the proportion of dimetalation. Six of the eight uses of such rings fell in group 1, and the exceptions are rationalized on the ground that No. 35, in group 2, has a tertiary alkoxide and No. 17 K has a potassium ion.

TABLE II
EFFECT OF ALKALI METAL SALTS ON THE DIMETALATION OF *tert*-BUTYLBENZENE

Exp. ^a No.	Added Salt ^b	Yields and Distribution of Carboxyls ^c				
		Diacid, m.e.	Monoacid, m.e.	Total met., %	Dist. Di, %	Total RNa m.e.
12	NaNHCHMe ₂	5				123
13	None	6	14	7	30	237
14	None	8	16	8	33	228
15	NaOCMe ₂ CHMe ₂	8	96	35	8	144
16	NaN ₂ C ₆ H ₁₀	9	47	19	16	99
17	NaOCyHex	14	79	31	15	186
18	NaI	14				159
19	NaOCyPen.	16	130	49	11	210
20	NaOH	17	63	27	22	123
21	NaOCHMe ₂	19				183
22	NaBr	19				192
23	NaOCyHex-4Me	20	94	38	18	195
24	NaOCMeEtPr.	21	79	33	21	147
25	NaOMe	23	46	23	30	219
26	NaCl	25				210
27	NaSCMe ₂	26	35	20	42	192
28	NaODec- <i>n</i>	26	41	22	39	171
29	NaOCCyHexMe ₂	26	103	43	20	144
30	NaOCyHex-3Me	27	111	46	19	201
31	NaOCyHex-2Me	27	70	32	28	198
32	NaOEt	30	117	49	20	216
33	NaSCHMe ₂	30				183
34	NaCl	31	57	29	35	261
Averages ^d		19	70	30	24	182
35	NaOCyHex-1Me	45	64	36	41	153
36	NaOCMe ₂ Et	46	98	48	34	189
37	NaOCMe ₂ Pr	46	89	45	34	165
38	NaOCMe ₂	48				189
39	NaOCMe ₂ Et	49	85	45	34	174
40	NaOCEt ₂ Pr	54	79	44	41	162
41	NaOCMeEt ₂	60	93	51	39	183
17 K	KOCyHex	62	107	56	37	219
42	NaOCMe ₂ Pen.	64	71	45	47	168
43	NaOCEt ₃	71				183
44	(NaOCMe ₂ -) ₂	77	63	47	55	225
45	NaOCMe ₂ Pen.	86	121	69	42	237
36 K	KOCMe ₂ Et	98	76	58	56	195
Averages ^d		62	86	49	42	188

^a The letter K attached to the number signifies that the potassium salt was used in an experiment otherwise identical with the previous experiment where the sodium alkoxide was used. ^b The abbreviations are typical for organic groups, *e.g.*, Me, Et, Pr, Pen, Hex, Dec, signifying Methyl, Ethyl, Propyl, Pentyl, Hexyl, Decyl respectively, and Cy signifies the cyclic system. In No. 16, NC₆H₁₀ means the piperidyl group. The quantity of alkoxide or other salt was 0.2 mole except for three halides, where the amount was 0.1 mole. ^c All values are calculated in terms of carboxyl groups. For instance, for the diacid the milliequivalents of carboxyl would be divided in half to give the millimoles of the diacid. The monoacid is the total of the two *tert*-butylbenzoic acids. The total metalation calculated in column 5 refers to the percentage of sodium transferred from amyl to *tert*-butylphenyl on the assumption that 0.3 mole of amylsodium had originally been present. Actually the yield of amylsodium from amyl chloride was never 100%. The sixth column records the percentage of carboxyls in the isophthalic acid per total carboxyls on a benzene ring. The last column records the total sodium compound at the end of the reaction as measured by the number of carboxyl groups. ^d These averages are for each column. The absence of some data in certain experiments has probably not changed the average values greatly.

The above differences are not a consequence of any variation in the total amount of metalation in the presence of individual alkoxides but are the result of specific effects. For example, sodium cyclopentoxide, No. 19 in group 1, and sodium pinacoloxide, No. 44 in group 2, permitted nearly equal amounts of metalation (49 and 47% respectively) but only 11% of the former was for dimetalation as compared with 55% of the latter, which was well above the average for group 2. Also sodium 2,3-dimethylbutoxide-2, which is No. 15, in group 1, induced a total metalation of 35%, almost the same as the 36% yield obtained with sodium 1-methylcyclohexoxide, No. 35 in the second group, but the respective proportions of dimetalation were 8 and 41%.

A few salts caused unusually large losses of amylsodium without a corresponding increase in a phenyl to sodium bond, presumably because the sodium reagent and the compound being metalated were not always in proper juxtaposition for a metal-hydrogen switch. For instance, in Nos. 16 and 12 with the two nitrogen-containing salts, only 123 and 99 milliequivalents of total organo-

TABLE III

COMPARISON OF THE EFFECT OF SODIUM CYCLOHEXOXIDE WITH SODIUM *tert*-PENTOXIDE ON THE METALATION OF *tert*-BUTYLBENZENE

Exps. No.	Cond. ^a	Cyclohexoxide					<i>tert</i> -Pentoxide				
		Distribution of carboxyls			Diacid, m.e.	Total acid, %	Distribution of carboxyls			Diacid, m.e.	Total acids, %
		Disub., %	Mono-sub., %	Cap., %			Disub., %	Mono-sub., %	Cap., %		
17, 38	A	8	43	42	14	62	28	49	18	49	58
46	B	8	57	26	15	61					
47, 48	C	7	53	33	15	73	31	55	0	57	63
49, 50	D	11	56	29	23	71	26	41	20	20	65
51, 52	E	17	46	35	34	67	53	32	4	115	72
53	F						17	40	13	40	34
54, 55	G	11	25	40	21	64	17	26	34	33	64
56, 57	H	6	74	21	12	61	17	70	6	29	58
58	I						42	25	15	101	80
Average ^b		10	50	33	20	66	29	46	14	51	63

^a The conditions are as shown below. A. Same conditions as in Table II. B. The amount of alkoxide was 0.40 mole, twice the usual quantity. C. The rate of stirring was 2500 r.p.m. instead of the usual 5000. D. The stirring in these two experiments was 6500 and 7250 r.p.m. respectively. E. The reaction temperature was 75° instead of the usual 60°. F. The reaction temperature was 85° and the time was only two hours instead of the usual five hours. G. The amount of *tert*-butylbenzene was 0.078 mole instead of the usual 0.15 mole. H. The amount of *tert*-butylbenzene was 0.30 mole. I. The theoretical amount of amylsodium was 0.45 instead of 0.30 mole, the temperature was 80° and the time was 2.5 hours. ^b Only those experiments which can be compared in the two series are averaged. The three other experiments are included in the table to show the products obtained under some special conditions.

sodium compounds were present. These quantities represent losses of 47% and 57% respectively from 233 milliequivalents which is the average for Nos. 13 and 14, the control experiments where no additional salt was present. Actually, in Table II, there are only three experiments, Nos. 34, 44 and 45, where the transfer of sodium from amyl to *tert*-butylphenyl was made without some loss, only a part of which can be credited to the formation of small amounts of ketone or tertiary carbonol during carbonation.

CONSISTENCY OF ALKOXIDE INFLUENCE

The general consistency of these effects by added salts was certified by comparing sodium cyclohexoxide as a representative from group 1, Table II, with sodium *tert*-pentoxide from group 2 over a wide variation of conditions which cover the rate of stirring, the temperature and the concentration. The results, in Table III, show that the relative effects of these two alkoxides were always the same. On the average only one di- to every five mono-substitutions was permitted by sodium cyclohexoxide, whereas one to every 1.6 was the rule in the presence of sodium *tert*-pentoxide. In one pair of experiments, Nos. 56 and 57, the proportion of dimetalation was drastically reduced but the relative effects of the two alkoxides were still evident. To this list of variations in conditions can be added the two experiments, 17 K and 36 K in Table II, where the same relative effects were experienced with the corresponding potassium salts.

The performance of these two alkoxides was checked in yet another manner, namely, by changing the amount used progressively from one to the other under the same conditions as were employed for Table II. The results are recorded in Table IV and show once more a general trend toward more metalation and a higher proportion of dimetalation with the *tert*-pentoxide. Included also in this table are the data for the proportion of *para* to *meta* metalation.

TABLE IV
EFFECT OF CHANGING FROM SODIUM CYCLOHEXOXIDE TO SODIUM *tert*-PENTOXIDE IN THE METALATION OF *tert*-BUTYLBENZENE AT 60°

Exp. No.	Alkoxides		Distribution of Carboxyl Groups in the Acids			Diacid, m.e.	Total Acid, %	Mono Substitu.		Ratio <i>p/m</i>
	CyONa, moles	<i>tert</i> -AmONa, moles	Di, %	Mono, %	Cap., %			<i>Meta</i> , %	<i>Para</i> , %	
17	0.20	0.00	8	43	42	14	62	15	28	1.4
59	.19	.10	8	47	38	15	62	13	34	2.0
60	.17	.03	9	47	34	14	53	18	29	1.3
61	.14	.06	12	41	34	17	48	15	26	1.3
62	.10	.10	17	37	45	34	67	14	23	1.0
63	.06	.14	19	45	26	35	61	16	29	1.1
64	.03	.17	20	53	18	31	52	15	38	1.4
38	.00	.20	28	49	18	49	58	14	35	1.3

^a One of the *meta* metalations leading to the diacid is included in this calculation.

DISCUSSION

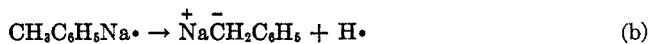
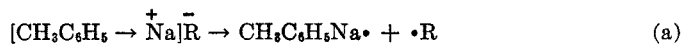
An interpretation of these results can be made on the basis that the change from one organosodium reagent to a more stable salt goes through a biradical transition state. This idea may seem to violate chemical intuition but actually the underlying reasons for its adoption are in full accord with chemical tradition. For instance, radicals are assumed to be present in many Grignard reactions and such intermediates should be more common with the thermally more unstable sodium reagents. Already this idea of radicals has proven very useful, perhaps essential, for the interpretation of the pyrolysis of amylsodium (3), of the polymerization of butadiene by Alfin catalysts (4, 5), and of the cleavage of ethers (6). With plausible assumptions the concept accords with the calculations of potential energy for a reagent of this class. Baughan, Evans, and Polanyi (7) show that the energy diagrams for ionic and homopolar methylsodium intersect. An increase in bond distance under conditions unfavorable to stabilization of ions could, therefore, lead easily to the biradical state. An important contributor³ to bond strain or increased bond distance between ions is the coordination which occurs between the organic compound, C, and the cation of the organosodium reagent, $\text{Na}^+\bar{\text{R}}$, to give $[\text{C} \rightarrow \text{Na}]^+\text{R}^-$. This initial or electrophilic (8) stage of reaction can be likened to classical concepts of the formation and reactivity of cobaltamines where coordination about cobalt displaces the halogen of cobalt chloride, CoCl_3 , to an outer or ionizable sphere to give the coordinated salt, $[(\text{NH}_3)_6\text{Co}]^+\bar{\text{Cl}}_3$. The halogen, which has a great attraction for electrons, can maintain its ionic status very easily, but carbon has no such affinity and requires unusual conditions for stabilization of the carbanion such as are provided for sodium triphenylmethide by numerous contributors to resonance or for sodium ethide in zinc diethyl by complexing with the solvent. No such aids are present for the reactions of these sodium reagents. Hence as the carbanion is pried away from the cation by coordination, an electron is lost to sodium and a transitory condition consisting of atomic sodium adjacent to an organic compound, CNa^\cdot , and a carbyl radical, R^\cdot , is formed. These two

³ One of the referees has very kindly discussed the effect of alkoxides upon bond distance from the interesting viewpoint that the alkoxide exerts an effect comparable to solvation. The distance between ions would thus be increased but the ionic potential energy minimum might also be lowered and provide easier dissociation of the carbanion. If the energy of the "solvated" system did rise, however, to a value where the homopolar state is preferred over the ionic condition, the alkyl and sodium radicals would promptly revert to the sodium cation of a new salt and to the products of radical interaction, all of which would set free sodium alkoxide for action upon another molecule of sodium reagent. In short, the sodium alkoxide would act as a catalyst and small amounts should suffice for the conversion of all. His suggestion is very interesting. However, in pentane the organosodium reagents are insoluble, the alkoxides are only slightly soluble—around .03 *N* or less (unpublished research with Dr. E. Schoenberg) and probably highly associated—and the alkoxide remains associated in the aggregate with the salt-like product of the reaction. All these facts decrease the chances of a small amount of alkoxide ever serving as a catalyst for the rapid conversion of all of the reagent.

radicals change quickly to a new sodium salt ($\text{Na}^+\bar{\text{C}}\text{R}$ if addition occurs), so quickly, indeed, as to create the impression usually of chemical changes evolving about a cation pivot; but the assumption that the distance between the ionic centers affects the separation to a biradical state in which atomic metal functions briefly, fits nicely with the well-known order of reactivity of potassium, sodium, and lithium reagents. According to the old concept (9) the special role of these cations was judged to be catalytic.

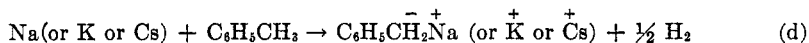
For the reactions described in this paper no proof for a biradical transition state is offered, but for that matter no proof for an ionic state can be given.⁴

⁴ After this paper was written, Bryce-Smith, Gold, and Satchell reported in the *Journal of the Chemical Society*, 2743 (1954), that deuterated benzene and toluene reacted more slowly with an organoalkali metal reagent, ethylpotassium, than did their hydrogen isotopes. Accordingly they judged the rate-determining step to be the removal of a proton or deuteron by the anion and claimed support for a "protophilic" mechanism. Actually their results accord beautifully with the concept of biradical behavior of the sodium reagent as developed in this laboratory. This alternative process is illustrated below for toluene in three separate steps, although in reality they will be as simultaneous as circumstances permit. In the first step (a) the salt, with toluene coordinated on the cation, dissociates to two radicals. In the second (b) hydrogen is expelled from the sodio radical as a new salt is formed. In the third, the hydrogen and alkyl radicals join to terminate the process. A



deuterated toluene should react slower than toluene itself, even if the only dynamic phase of the process were as in (b) and the amyl radical gave no help by pulling upon the hydrogen.

This second step is in principle identical with the reaction of an alkali metal with the hydrocarbo acid, toluene, as written in (d) but with the advantage of providing a unique way of putting the sodium into a favorable position for reaction. The London workers



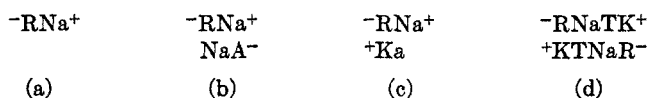
point out that toluene can, indeed, be classed as an acid which evolves hydrogen in reaction with caesium metal. The same possibility exists for its reaction with ethylpotassium if the process is written analogously to (b). They credited the metal ion as being a coordinating agent solely and assigned the dynamic role exclusively to the anion which serves to extract a proton. The radical-pair concept attributes a dynamic role to both components of the salt.

The concluding step (c) in the radical-pair scheme is written separately in order to emphasize the extreme condition if the steps could be defined sharply. In reality both radicals from step (a) cooperate to the maximum extent that conditions permit in effecting the reaction. The sequence is written in the above order because toluene is presumed to be attached already to the cation by coordination and therefore to be subject instantly to the sodium at the moment of dissociation. Whatever difference exists in timing between the two radicals should clearly favor the metal component.

In an earlier paper Bryce-Smith (*J. Chem. Soc.*, 1079 (1954)) pointed out that the order of metalation at the α -position (toluene > ethylbenzene > isopropylbenzene) is the reverse to that found for the abstraction of hydrogen atom. This order, however, is also that of

The presentation as a biradical is made on the usually accepted basis that the best interpretation is one which requires the least modification to be applicable to all facts in that field. The biradical concept fulfills this condition better than the ionic, all facts presently known being considered.

Easily the outstanding feature of this work is the effect produced by associated salts. They shift the amount and position of metalation, and the former particularly can be rationalized with the general principles stated above by assuming that (I) they increase the number of places where reaction is initiated and (II) they change the bond strengths. A single ion pair, $^-\text{RNa}^+$, pictured in (a) below, has only one bond which can separate to the radicals, $\text{R}\cdot$ and $\text{Na}\cdot$ adjacent to the organic compound, but a four ion aggregate with sodium alkoxide, NaA , as in (b) has, on one hand, more RNa bonds per R and therefore



a greater chance of forming radicals that initiate a reaction, and has, on the other hand, different bond distances. If the alkoxide is a potassium salt as in (c) the greater diameter of the potassium ion facilitates cleavage of RK in preference to RNa , other factors being equal. Similarly a tertiary alkoxide, KT , as in the aggregate (d) also affects both the number and energy of the separations. Variations in the facility of adsorption and effect of the organic compound, C , on these aggregates are superimposed on these factors.

An increase in activity by these means should produce less selectivity in the position of attack as well as more reactivity, somewhat in the manner that an increase in temperature affects such matters in homogeneous systems. If steric factors on the aggregate are disregarded, the general trend would be in the direction of an equal amount of metalation at the two *meta* and one *para* positions available for attack. That is to say, the yield of *meta* should reach 67% and would not exceed this amount unless some steric factor in the aggregate, unusually successful at blocking the *para* position or favoring the *meta* position,

decreasing acidity of the hydrocarbo acid. Hence the reaction expected with atomic sodium or potassium, such as is represented in equation (b), is in the order actually found.

This concept of a radical-pair does not do away necessarily with all of the suggestions of ion-pair effects which were made at the beginning of the efforts in this laboratory to credit the cation of these reagents with specific and important roles in reactions. Where conditions are favorable for dissociation as ions the chance that the process can be that of an ion-pair or even of the anion only is not denied. However the assumption of a radical-pair seems eminently desirable, possibly essential for the cleavage of ethers and for Alfin catalysis, and the application of such a view to the other reactions of these highly reactive agents assigns a dynamic role to both parts of the reagent and provides a very rational explanation for the great changes in degree and often product of reaction when the cation component of the organoalkali metal salt is changed. All facts so far known can be interpreted easily on the basis that these very reactive organoalkali salts act as radical-pairs and some facts appear to be more plausible on such a basis than on any other presently known idea.

intervened. In the numerous experiments carried out so far, this two-thirds proportion has barely been exceeded in the 71 % yield in experiment 8, Table I, and has been approached in the 63 % yield in No. 9. Both values are within the limits of accuracy.

This failure to rise above the level of two-thirds *meta* substitution must not be construed as proposing a limit. Steric and orienting effects in these insoluble reagents are at a maximum and a complete change is sometimes possible by changes in the composition of the aggregate as witnessed by the changes which occur in the dimetalation of benzene (10) when different alkoxides are used, and in the alfin polymerization where highly specific effects, applicable almost solely to butadiene are realized.

EXPERIMENTS

The experiments on monometalation are by Frances W. Collins and Chester E. Claff, Jr., those on dimetalation are by Chester E. Claff, Jr.

General conditions. The apparatus and general technique used in this study are the same as are regularly employed (1, 2, 3, 11) in this program of work. The usual procedure was to prepare amylsodium from 0.5 mole of *n*-amyl chloride and 1 g.-atom of sodium at -10° , then add 0.2 mole of alcohol, and finally add 0.3 mole of *tert*-butylbenzene if monometalation was desired or 0.15 mole if dimetalation was the object. Accordingly, 0.5 mole of Wurtz sodium chloride was present in all of the metalation experiments, except for those where halide salt only was present, and where some variation seemed unavoidable in order to get the desired amount of sodium chloride or of amylsodium (0.3 mole theoretically but actually about 0.25 mole). For instance, in No. 13, the reagent was prepared from 0.3 mole of amyl chloride and 0.6 g.-atom of sodium metal but 0.2 mole of granular sodium chloride was added in order to make the total amount equal to 0.5 mole. The comparison experiment, No. 14, was the same as No. 13, except that no granular salt was added. In Nos. 18, 22, and 26, the reagent was made from 0.5 mole of amyl chloride and 1.0 g.-atom of sodium metal, as usual, but 0.2 mole of the respective amyl halide (to give a Wurtz sodium halide) then was added. Hence the total amount of sodium halide in each of these experiments was 0.7 mole. In No. 34, the reagent was made from 0.4 mole of amyl chloride and 0.8 g.-atom of sodium and an additional 0.1 mole of amyl chloride then was added.

Reagents. *tert*-Butylbenzene was obtained from Eastman Kodak Company and was fractionated through a three-foot Vigreux column before use.

Methanol, ethanol, isopropanol, *n*-decanol, *tert*-butanol, *tert*-pentanol, *L*-menthol, and cyclopentanol were obtained from commercial sources. All except the first two were refractionated before use and all had constants which agreed with published values. *n*-Pentanol, 2-pentanol, 3-ethyl-3-pentanol, 2-methylcyclohexanol, 3-methylcyclohexanol, 4-methylcyclohexanol, pinacol, isopropylamine, piperidine, isopropyl mercaptan, and *tert*-butyl mercaptan were obtained from Eastman Kodak Company. They were usually fractionated before use. Other alcohols were prepared by Grignard reactions and the constants have been certified in the literature. In this group were 2-cyclohexyl-2-propanol (12) from cyclohexylmagnesium chloride and acetone, 2,3-dimethyl-2-butanol (13) from isopropylmagnesium chloride and acetone, 3-ethyl-3-hexanol (14) from *n*-propylmagnesium and diethyl ketone, 1-methylcyclohexanol (15) from methylmagnesium iodide and cyclohexanone, 3-methyl-3-hexanol (16) from *n*-propylmagnesium chloride and butanone-2, and 3-methyl-3-pentanol (13) from ethylmagnesium bromide and methyl ethyl ketone. 2-Methyl-2-heptanol was prepared from *n*-amylmagnesium bromide and acetone by the method of Whitmore and Williams (15), after purification of a sample, made from amylsodium and acetone, proved difficult. The latter material was, however, used in experiment 45 and gave excellent results in total metalation and dimetalation, possibly because a

pinacol was present as an impurity from that preparation of carbinol and a pinacoloxide in experiment 44 was found to have a pronounced effect.

Separation of products and determination of the yields. In the early part of the work, the analysis did not always include the four acids that might be present or the total number of carboxyl groups. The complete process, developed later, is described here and variations from that procedure will be mentioned as necessary.

At the conclusion of each experiment the contents of the reaction flask were forced onto solid carbon dioxide. The next day a few more lumps of carbon dioxide were added, followed by 450 ml. of water in order to decompose bits of sodium metal and to dissolve the sodium carboxylates. The clear aqueous portion then was extracted with ethyl ether, saturated with sodium chloride, acidified with hydrochloric acid, and then extracted with ethyl ether. In all of these operations, as also in subsequent extractions, the volumes were maintained constant and several extractions were made in order to avoid losses. The ether extracts of the acids were dried over calcium sulfate and partially evaporated on a steam-bath. The solution then was filtered into a graduated flask and made up to a given volume. A titration of an aliquot of this solution gave the total number of carboxyl groups. The remainder of the ether solution was evaporated on the steam-bath and petroleum ether was added to the residue in order to dissolve caproic and the two *tert*-butylbenzoic acids. This treatment with petroleum ether was done several times and the clear petroleum ether was separated each time by decantation. The insoluble isophthalic acid next was dissolved in alkali; the aqueous solution was decolorized at 100° with carbon, and was filtered, cooled and finally acidified with hydrochloric acid. The solid acid then was collected on a filter, washed with water, and dried under a vacuum at 40°. A calculation from the weight, corrected for the aliquot originally removed, and the milliequivalents of base consumed, gave the amount of 5-*tert*-butylisophthalic acid.

The petroleum ether extract which had been removed by decantation was evaporated on a steam-bath and the residue was left in a vacuum desiccator over calcium chloride-calcium sulfate overnight. The weight and neutralization equivalent of this dried product were then used very often to calculate the respective quantities of caproic and the mixture of the two *tert*-butylbenzoic acids. When the proportions of *meta* and *para tert*-butylbenzoic acids were determined, the caproic acid was removed by vacuum distillation and the two benzoic acids were collected. An analysis by infrared absorption (to be described later) enabled these two isomeric acids to be differentiated.

This simple procedure was always carried out in the same manner, with the same volumes of solvent and with all other precautions to insure as correct a determination as possible. As Table V shows, the method was sufficiently accurate for the purposes of this work. The greatest losses are in the caproic acid but no significance is attached to the amount of that material. Most of that loss occurred when the mixture of mono acids was dried in the vacuum desiccator.

In the early stages of this research, such a complete analysis was not deemed necessary. Also, in the experiments by F. W. Collins at 20°, in Table I, the petroleum ether extract of the acids was evaporated on a steam-bath and the residue was heated under a vacuum in a Claisen flask in order to remove the caproic acid. The remaining acid mixture, which still contained traces of caproic, was recrystallized from *n*-hexane prior to the infrared analysis. Small losses of *meta-tert*-butylbenzoic acid may occur in this procedure.

Examination of the combined solid products. The combined acids from the petroleum ether extractions of about 30 experiments amounted to 543 g. This material was examined carefully for the presence of any *ortho* acid or other material not included in the other tests. Filtration and vacuum distillation yielded 196 g. of liquid which by fractionation, esterification followed by fractionation, and by measurement of refractive indices proved to be caproic acid with traces of unsaturated acid such as would be derived from the metalation of pentene. The 343 g. of solid acid, when recrystallized from ligroin, yielded 7 g. of 5-*tert*-butylisophthalic acid, 125 g. of *p-tert*-butylbenzoic acid, 48 g. of a mixture of 38% *p-tert*-butylbenzoic acid and 62% of the *meta* isomer, and 100 g. of tar. The tar was divided

TABLE V

ANALYSIS OF A MIXTURE OF THE FOUR ORGANIC ACIDS PRESENT IN THE REACTION PRODUCT

Carboxylic acids	Milliequivalents of carboxyl group		
	Known	Found	Error, %
Total Acids	207.8	204.0	1
5- <i>tert</i> -Butylisophthalic	32.7	30.4	7
5- <i>tert</i> -Butylbenzoic	30.8	28.6	7
Caproic	144.5	128.5	11
Total Identified Acids	207.8	187.5	
	Per Cent Distribution of Carboxyl Groups		
5- <i>tert</i> -Butylisophthalic	15.7	14.9	5
<i>tert</i> -Butylbenzoic	14.8	14.0	6
Caproic	69.5	63.0	9
	Composition of <i>tert</i> -Butylbenzoic Acid Mixture		
<i>Meta</i>	51	52	2
<i>Para</i>	49	48	2

into 10 fractions by multiple fractional extraction and samples from the separate fractions were further purified by steam-distillation, hot water extractions, and esterification followed by distillation. Numerous mixtures of crystals were thereby obtained, all of which proved by infrared analysis to consist only of the *para* and *meta* isomers of *tert*-butylbenzoic acid. Eventually all of the remaining residues were esterified and distilled. The methyl esters thereby obtained also proved by boiling point and infrared analyses to be mixtures of the two isomers from *tert*-butylbenzoic acid. The cause for the original tarry condition of a mixture which proved to consist almost entirely of two acids is not clear but it was not because of the presence of appreciable amounts of the *ortho* isomer or the products from the metalation of alkoxides.

Identification of the acids. *m-tert*-Butylbenzoic acid melted at 127.0–127.5° [reported (17) 127.0–127.6°] and had N.E. 178.0 (Calc'd 178.2). The *para* isomer melted at 167.0° [reported (18) 165.0–165.6°] and had N.E. 178.5. The 5-*tert*-butylisophthalic acid, after being converted to the dimethyl ester, melted at 94.2–95.7° [reported (17) 97°].

*Infrared analyses of mixtures of *t*-butylbenzoic acids.* The majority of the measurements were made on a Baird apparatus. Carbon tetrachloride was used as the solvent. The absorption bands at 9.2 and 11.7 microns were used for the *meta* and *para* isomers respectively. Known mixtures were used as the reference standard and the absorption *vs.* composition relationship was found to deviate a small amount from linear. Appropriate correction was made. For the earlier work by F. W. C., we are greatly indebted to Mr. McDonald of Professor Lord's laboratory for observations on a Beckman IR₂ apparatus. The solvent was dioxane and the absorptions were at 13.18 and 12.84 respectively. A linear relationship was assumed to exist.

SUMMARY

The metalation of *tert*-butylbenzene at 20° and below occurs chiefly in the *para* position, but in the presence of sodium and potassium alkoxides, it shifts toward the *meta* position. At 60° dimetalation in the 3,5-positions takes place. Some alkoxides, notably tertiary alkoxides and potassium alkoxides, favor

dimetalation, but others which contain cyclic systems favor monometalation. With nearly all alkoxides some loss of sodium reagent occurs.

CAMBRIDGE 39, MASS.

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