THE COMPARATIVE REACTIVITY OF SOME ESTERS OF BENZOIC ACID WITH ANILINE

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INTRODUCTION.

The reaction studied in this research may be represented by the general equation

$$C_6H_5COOR + HNH.C_6H_5 = C_6H_5CO.NH.C_6H_5 + HOR$$

in which "R" represents either an aliphatic or an aromatic radicle. The purpose of the investigation was to determine if the reaction would take place, and if so something of the comparative reactivity of some of the esters under different conditions of temperature and length of time of heating. It was suggested also that esters of ring-substitution products of benzoic acid be tried in this reaction in order to learn what effect the nature of the entering group and its position in the ring might have on the reactivity of the ester, but time did not permit that part of the work to be started.

So far as could be learned by reference to the literature this particular type of reaction had not been tried before. The nearest approach to it that could be found is the familiar hydrolysis of esters with concentrated ammonia solution or alcoholic ammonia with

the formation of the amide of the acid and an alcohol. This latter reaction has been tried with a great many esters, substituting liquid ammonia for the ammonia solutions, by Professor Edward Bartow at the University of Kansas, but he was entirely unsuccessful in bringing about any reaction whatsoever. The use of a primary amine in place of ammonia in this reaction with the consequent formation of a substituted amide has apparently not been attempted before.

Four esters of benzoic acid were used, the methyl, the ethyl, the normal butyl, and the phenyl. From the wide variation found in the reactivity of these four, it would seem desirable to try a few more esters, but again time did not permit this work to be attempted.

The experimental work carried out falls naturally into three main divisions; first, the preparation and purification of the esters and aniline, second, the preliminary trials to learn if the reaction is possible and if so under what conditions, and third, quantitative determination of the amount of reaction under accurately known conditions of temperature and length of time of heating. The third division represents the really important part of the work, and is briefly summarized in the table of results at the end of this paper.

The writer wishes to express his appreciation to Dr. R. Q. Brewster, the director of this work, for his valuable assistance, and to Dr. F. B. Dains for his many helpful suggestions.

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PREPARATION OF METHYL BENZOATE.

Materials:

Benzoic acid - - - - - - - - - -	300 gm.
Methyl alcohol - - - - - - - - -	500 cc.
Sulfuric acid (Conc.)- - - - - -	250 gm.

Method:

The methyl alcohol was placed in a large round-bottomed flask, and the sulfuric acid added carefully, the flask being kept cold meanwhile. The benzoic acid was added to the cold solution, and the flask then heated on a water bath under a reflux condenser for two hours. The mixture boiled gently and became very dark in color. At the end of the two hours the liquid was observed to separate into two distinct layers, and after separating the two in a funnel each was poured into a large volume of cold water. The lighter liquid gave a large quantity of a brown oil, which was washed with water by decantation and neutralized with sodium carbonate to remove benzoic acid. Ether was added to the mixture to make the oil separate rapidly, and the water removed by means of a separatory funnel.

The heavier liquid, which was chiefly sulfuric acid and alcohol, gave a small quantity of oil when poured into water, which was treated in the same way

as the other and then combined with it. The ether was distilled off on a water bath, and the oil then distilled with a free flame, an air condenser being used. The ester distilled at 194° C.; the recorded boiling point is 199°. The yield, calculated from benzoic acid, was 80 per cent.

Several trial preparations of methyl benzoate had been made previously, using small quantities but varying the proportions. The proportions used above were found to give the best results.

PREPARATION OF ETHYL BENZOATE.

Materials:

Benzoic acid - - - - - - - - -	300 gm.
Ethyl alcohol (95%)- - - - - -	500 cc.
Sulfuric acid (Conc.)- - - - -	250 gm.

Method:

The sulfuric acid was added to the alcohol in a large round-bottomed flask slowly with cooling, and the benzoic acid added to the cold solution. The flask was heated on a wire gauze under a reflux condenser for 3½ hours at such a temperature that it boiled

gently. The liquid remained clear and practically colorless, but separated into two distinct layers as in the case of the methyl benzoate. The lighter fraction was neutralized with sodium carbonate solution, and the oil separated from the water with a separatory funnel. The heavier fraction was poured into a large volume of cold water, the small quantity of oil which separated out washed by decantation, neutralized with sodium carbonate, and then added to the main portion of the ester. The oil was distilled, boiling at a constant temperature of 207° C. The recorded boiling point is 213° C. The yield, calculated from benzoic acid, was 84 per cent.

PREPARATION OF NORMAL BUTYL BENZOATE.

Materials:

Benzoic acid - - - - - - - - - - -	200 gm.
Butyl alcohol- - - - - - - - - - -	180 gm.
Sulfuric acid (Conc.)- - - - - - -	50 gm.

Method:

The sulfuric acid was added to the alcohol in a round-bottomed flask slowly with cooling, and the benzoic acid added to the cold acid solution. The mix-

ture was boiled gently under a reflux condenser for four hours. As in the cases of the preparation of the methyl and the ethyl esters the fluid mixture separated into two layers. The whole was poured into a large volume of cold water, the oil which separated out was washed by decantation, and was neutralized with sodium carbonate. The ester was separated from the alkaline solution and purified by distillation. The boiling point was 243° C. The recorded boiling point is 249° C. The yield, calculated from benzoic acid, was 90 per cent.

PREPARATION OF PHENYL BENZOATE.

Materials:

Phenol - - - - - - - - - - - - - 80 gm.
Benzoyl chloride - - - - - - - -120 gm.
Sodium hydroxide sol. (10%)-

Method:

Benzoyl chloride was first prepared by the usual method of reacting molar quantities of benzoic acid and phosphorus pentachloride, and fractionation of the liquid product.[1] Phenyl benzoate was prepared by the Schotten-Baumann reaction.[2] The phenol was melt-

[1] Perkin and Kipping, Organic Chemistry, Page 472.

[2] Perkin and Kipping, Organic Chemistry, Page 473.

ed and poured into water, and enough of the sodium hydroxide solution added to dissolve it. The solution was cooled in an ice bath and kept cold during the entire reaction. Benzoyl chloride and sodium hydroxide were added alternately in small quantities and stirred in, care being taken to keep the solution alkaline in reaction. After standing two hours the odor of benzoyl chloride had entirely disappeared. The ester separated out as a pure white solid, which was filtered by suction and recrystallized from alcohol. The melting point was the same as the recorded, 71° C. A very good yield of the ester was obtained.

PURIFICATION OF REAGENTS.

The aniline, methyl, ethyl, and butyl esters were all redistilled before trying their reactions in order to have fractions with a constant boiling point. Fractions of the following boiling points were used:

	Boiling Point	Recorded Boiling Point
Aniline	179°	182°
Methyl benzoate	194-195°	198.6
Ethyl benzoate	207	212.9
Butyl benzoate	241-243	249

PRELIMINARY TRIALS WITH ANILINE AND METHYL BENZOATE.

In order to determine something of the conditions under which the reaction being studied takes place, a number of trials were made heating mixtures of molar quantities of aniline and methyl benzoate from two to four hours in test tubes at 125°, 150°, 175°, and finally at 185° C. The presence of benzanilid was tested for by diluting the sample with gasoline, in which aniline and the ester are soluble but benzanilid is insoluble. In no case was any cloudiness or precipitate formed, indicating that no reaction had taken place. Finally the reaction mixture was heated to boiling under a reflux air condenser and kept at that temperature for two hours, during which time the temperature at which it boiled remained constantly at 191° C., indicating again that no reaction was taking place.

It then seemed necessary to determine if the reaction would take place under any conditions, and in order to determine this molar quantities of the aniline and the ester were heated in a closed tube for two hours at 225° C. After cooling, the tube was opened

and found to contain a mass of dark, shiny crystals, which, after being washed with gasoline, melted at 158° C. The recorded melting point of benzanilid is 160° C.

Having thus demonstrated that the reaction could be made to take place, an attempt was made to carry it out in an apparatus in which the pressure as well as the temperature could be measured, but this attempt was abandoned when it was found that pressure was not necessary for the formation of benzanilid. It was thought that the reaction might take place at the boiling temperature if the mixture were only heated long enough, and in order to test out this point the sample which had previously been boiled for two hours was heated once more to boiling. After about three hours more of heating the boiling temperature began gradually to rise, and then more rapidly, going from 195° to 225° C. in less than an hour. This was sufficient proof that the reaction could be carried out without the application of pressure, and the tests under pressure were abandoned.

It was suggested that the reaction might be speeded up by the presence of a catalyzer, and to test this out two samples of the mixture were prepared, one

containing some very finely divided copper powder, the other without any catalyzer. By accident these samples were allowed to reflux for 48 hours, at which time the tubes both contained a solid mass of benzanilid. The attempts to catalyze the reaction were given up until later.

It having thus been proven by the preliminary tests that the reaction could be carried out, it became necessary before proceeding with the quantitative study of the reaction to find a method for freeing the benzanilid formed from the unchanged aniline and ester. The esters and the aniline are all volatile in steam while benzanilid is not, and a test was made to determine if the product might not be purified by steam distillation. A mixture of aniline and methyl benzoate containing a weighed quantity of benzanilid was steam distilled until no more oil came over, and the benzanilid, which remained in the distillation flask, was filtered out by suction, dried, and weighed. The recovery was 100 per cent. An attempt was also made to purify the benzanilid by extracting the oils with gasoline, but the benzanilid seemed to be somewhat soluble and the precipitate was very sticky and hard to handle. Purification by steam distillation was therefore adopted for all the quantitative determinations of benzanilid.

PROCEDURE IN CARRYING OUT COMPARATIVE REACTIVITY DETERMINATIONS.

The reaction mixtures in all the following determinations were made up in the proportions of 1.00 mole of aniline to 1.25 moles of ester. The samples were heated in long tubes made by sealing two large eight inch test tubes together after cutting the bottom off one. The reason for using these long tubes was in order that the tube itself should act as a reflux condenser and thus eliminate any action of the hot vapors on the cork in the top of the tube. A short glass tube was inserted through the cork in the top of the reaction tubes to act as an additional condenser and also to prevent the circulation of air in the reaction tubes. Samples of each of the four esters were heated at the same time, all four tubes being placed in the same metal bath in order to insure identical conditions. The composition of the alloy in this bath was equal parts of lead and tin and about ten per cent of mercury; its melting point was in the neighborhood of 130° C. The surface of the bath was covered with a layer of charcoal to prevent oxidation. The bath sat on top of a stoneware wind shield inside of which the burner was

placed, thus assuring an unvarying temperature to the bath after an adjustment of the flame had once been made.

The samples were made up by weighing the proper proportions of aniline and ester in a test tube of known weight, pouring the mixture into the reaction tube, weighing the tube again, and determining the weight of sample by difference. The tubes were placed deep enough in the bath so that the sample was entirely surrounded by the melted alloy, and the bath quickly adjusted to the proper temperature. After heating the required length of time, the tubes were removed from the bath, and their contents washed into 250 cc. long-necked flasks with hot alcohol. The flasks were attached to the steam distillation apparatus, and a rapid current of steam passed through until there were no more drops of oil present in the distillate, the length of time required varying from one to three hours. Soon after the distillation started, the benzanilid if present began to precipitate out of the solution in the solid form, a factor which increased very materially the length of time required to complete the distillation. After distillation was completed, the flasks were removed from the apparatus, the contents cooled, and the benzanilid filtered out by suction in a buchner funnel. Filter paper and

benzanilid were removed from the funnel, wrapped up in another filter paper, and dried in an oven at 100° C. The dry benzanilid and first filter paper were weighed on horn pan balances which were counter-poised with a filter paper of equal size and weight, thus making the weights on the pan the true weight of the benzanilid. The percentage yield was calculated from the weight of aniline used in the sample.

TEN HOUR HEAT AT 150° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.93	2.95	2.97	3.08
Wt. of ester	5.41	5.93	7.11	7.83
Wt. of benzanilid	.10	Trace	.06	5.01
Theoretical yield	6.20	6.24	6.29	6.52
% yield	1.6	- --	.95	76.8

It was observed that soon after the heating was started that the liquids in all the tubes darkened to a very deep mahogany. After the steam distillation the precipitated benzanilid was darkened to different shades of red and gray. It is believed that this change in color is due to a slight oxidation of the aniline.

TEN HOUR HEAT AT 200° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.96	2.95	2.96	2.95
Wt. of ester	5.41	5.95	7.05	7.84
Wt. of benzanilid	1.74	.10	.54	6.18
Theoretical yield	6.27	6.24	6.27	6.24
% yield	27.8	1.6	8.6	99.1

The darkening of the samples after heating was started was again observed, and in this case it was very much more marked, the solutions being black at the end of the heat. The black material which precipitated on steam distillation made the product somewhat sticky and hard to clean from the flasks.

TEN HOUR HEAT AT 250° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt, of aniline	2.96	2.97	2.97	2.95
Wt. of ester	5.41	5.98	7.10	7.84
Wt. of benzanilid	2.28	.06	.84	6.11
Theoretical yield	6.27	6.29	6.29	6.24
% yield	36.3	.95	13.4	98.0

At this temperature the contents of all four tubes boiled vigorously, while in the previous two trials

no boiling had taken place. Another thing which was noticed was that the samples did not darken during the heating, but were almost as colorless at the end of the heat as at the beginning. Possibly the explanation for this lies in the fact that the reaction tubes were filled with the vapors from the samples, thus allowing no air to come in contact with the aniline and oxidize it. The benzanilid came out clean and white after the steam distillation.

TWENTY HOUR HEAT AT 150° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.96	2.95	2.97	2.94
Wt. of ester	5.42	5.93	7.10	7.81
Wt. of benzanilid	.18	.02	.21	5.31
Theoretical yield	6.27	6.24	6.29	6.22
% yield	2.9	.32	3.34	85.3

TWENTY HOUR HEAT AT 200° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.96	2.96	2.96	2.96
Wt. of ester	5.41	5.96	7.09	7.85
Wt. of benzanilid	4.06	.57	1.17	6.35
Theoretical yield	6.27	6.27	6.27	6.27
% yield	64.7	9.1	18.7	101.

TWENTY HOUR HEAT AT 250° C.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.96	2.96	2.96	2.94
Wt. of ester	5.41	5.96	7.10	7.82
Wt. of benzanilid	4.10	.26	1.50	6.04
Theoretical yield	6.27	6.27	6.27	6.22
% yield	86.2	4.15	23.9	97.1

A strong odor of dimethyl aniline was noticeable in the tube containing the methyl benzoate after completion of the heating, and this side reaction perhaps accounts for the low yield obtained.

TEN HOUR HEAT AT 200° C.

WITH COPPER CATALYZER.

	Methyl	Ethyl	Butyl	Phenyl
Wt. of aniline	2.96	2.96	3.04	2.96
Wt. of ester	5.43	5.96	7.07	7.87
Wt. of benzanilid	1.65	.20	.59	6.20
Theoretical yield	6.27	6.27	6.44	6.27
% yield	26.3	3.2	9.2	98.8

This determination was made in the same way as the others with the exception that a little finely divided copper was added to each of the tubes. It was observed that the darkening of the liquids was very much more marked in this case than in the previous ones,

the alcoholic solutions being very black. The products after steam distillation were jet black and somewhat tarry in nature, and were very hard to remove from the flasks with the exception of the phenyl ester, which was not darkened nearly as much as the others. The copper was removed from the product by filtering the hot alcoholic solution into the flasks by suction.

CONCLUSION.

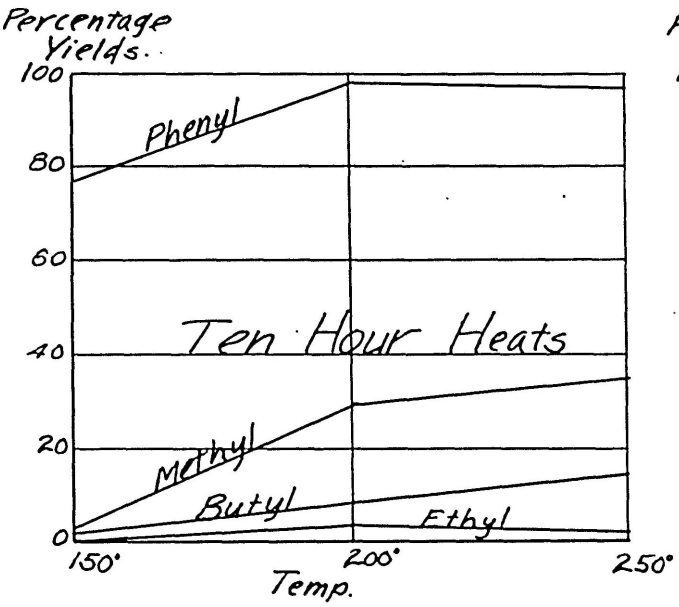
Study of the table of results on page 22 and the graphs reveals several interesting things. In the first place it shows that aniline does react with esters of benzoic acid with the formation of benzanilid and an alcohol. Of the four esters used, the phenyl ester is by far the most reactive, the methyl ester much less so, the butyl ester only slightly reactive, and the ethyl ester almost unreactive under the conditions used. It appears also that in general a greater increase in reaction takes place between 150° and 200° than between 200° and 250°. The phenyl ester is the only one which gives much of a reaction at 150°, the yield of benzanilid from the other three being almost negligible. All of the esters except the phenyl give much more of a reaction in the second ten hours than they do in the first, which would seem to indicate that autocatalysis occurs. The phenyl ester is almost completely hydrolyzed in the first ten hours and it is therefore not possible to say if such a speeding up of the reaction occurs in this case. The reaction is not speeded up by the presence of finely divided metallic copper, but a side reaction in which

a black tarry substance is formed seems to be increased. It would not be possible from these results to state a general rule as to the comparative reactivity of esters of benzoic acid with aniline.

TABLES OF RESULTS.

Percentage Yields From Ten Hour Heats

Temp.	Methyl	Ethyl	Butyl	Phenyl
150°	1.6	---	.95	76.8
200°	27.8	1.6	8.6	99.1
250°	36.3	.95	13.4	98.0
	Copper Catalyzed			
200°	26.3	3.2	9.2	98.8
	Twenty Hour Heats			
150°	2.9	.32	3.34	85.3
200°	64.7	9.1	18.7	101.
250°	86.2	4.15	23.9	97.1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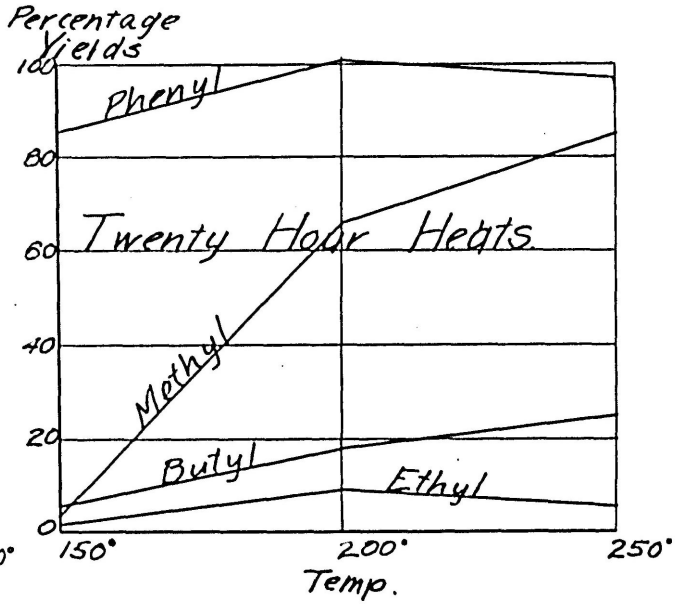
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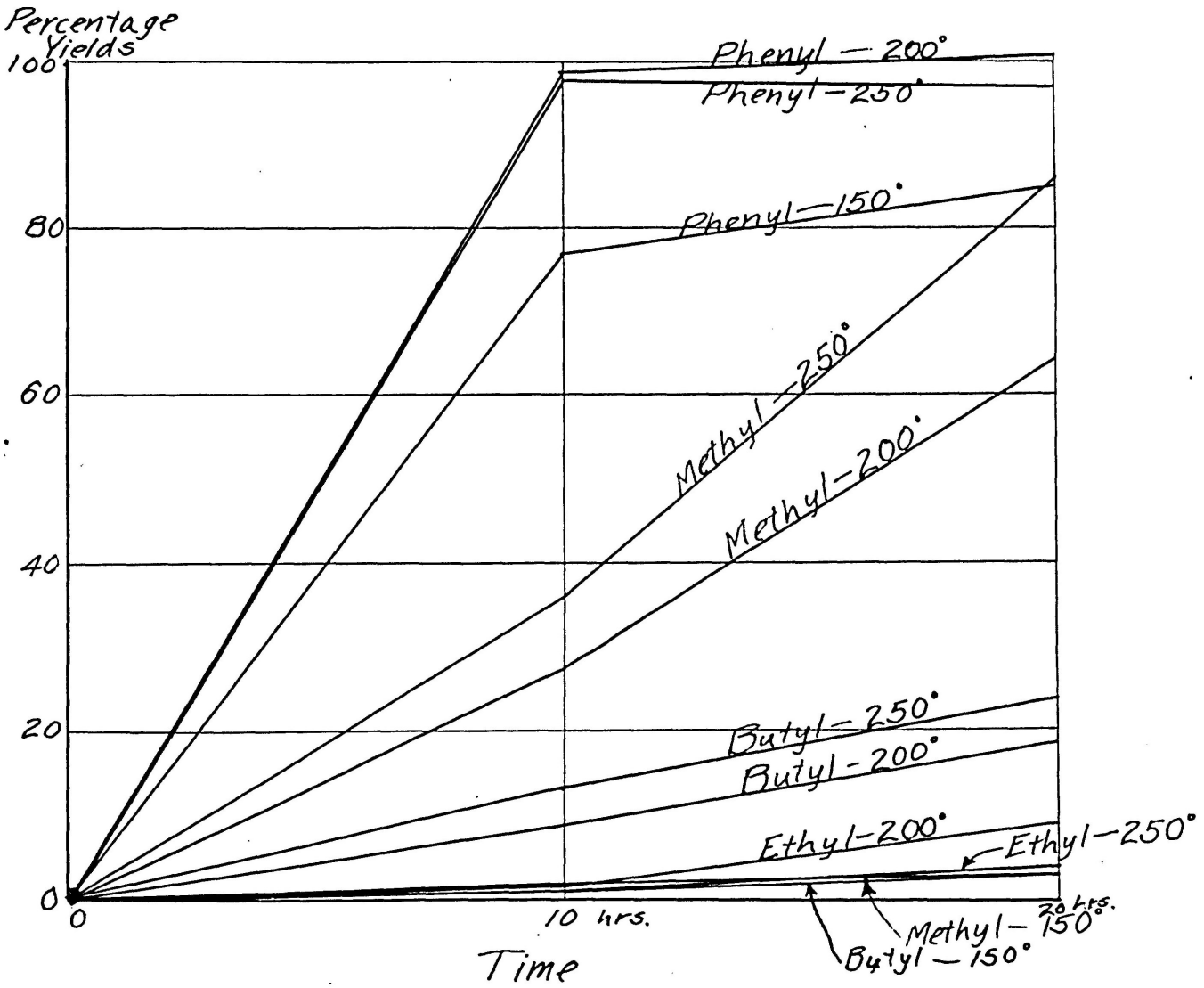
Percentage Yields
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80
60
40
20
0
Phenyl — 200°
Phenyl — 250°
Phenyl — 150°
Methyl — 250°
Methyl — 200°
Butyl — 250°
Butyl — 200°
Ethyl — 200°
Ethyl — 250°
0
10 hrs.
20 hrs.
Methyl — 150°
Butyl — 150°
Time