

of the ethyl ether of 77%, yellow monoclinic prisms, showing a great tendency to form twins and twin clusters. If any condensation product (m. p., 216°) is formed it may be removed by dissolving the ethoxy compound in ether. The pure ether melts at 138°.

The crystals of this ether were examined by Mr. Walter B. Jones of the Geology Department and his report is as follows: photomicrograph $\times 44$; ocular, 2; objective, 3; arc light; exposure 5 seconds through blue glass and through 12 mm. of solution. Triclinic system, tabular habit; basal, macro and brachy pinacoids, usually modified by unit prism, macro and brachy domes. Inclination of angle, $-8^\circ =$.

Subs., 0.5872: AgCl, 0.8015. Calc. for $C_{10}H_{11}O_2N_2Cl_3$: Cl, 33.80. Found: 33.70.

Ethers of the Higher Alcohols.—No ethers could be made with *n*-propyl, *n*-butyl and *iso*-amyl alcohols although both methods of preparation were tried a number of times, and modifications of these methods were resorted to.

Summary.

New ethers are obtained by the action of alcohols upon the addition products of chloral and *meta*- or *para*-nitro-aniline.

The *m*-nitro-aniline product gave ethers with methyl, ethyl, *n*-propyl, *n*-butyl and *iso*-amyl alcohols.

The *p*-nitro-aniline product gave ethers only with methyl and ethyl alcohols. In these cases the amine was made to react with the chloral alcoholate. No ethers of the higher alcohols could be obtained.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE.]

THE PREPARATION OF ESTERS BY DIRECT REPLACEMENT OF ALKOXYL GROUPS.

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In a paper on the action of light on esters of α -cyano-cinnamylideneacetic acid,¹ the preparation of a new unstable ethyl ester of this acid was described. The compound was prepared from the methyl ester by direct replacement of the methoxyl by the ethoxyl group, the procedure being that described by Pfannl² in a paper dealing with this replacement action. The fact that an ester too unstable to be prepared by the usual methods could be formed by replacement of one alkoxy group by another, led to the hope that the method might be found of general application in the preparation of a series of esters of unstable, unsaturated acids. It seemed of interest, therefore, as previously stated¹, to study this reac-

¹ Reimer, *Am. Chem. J.*, **45**, 417 (1911).

² Pfannl, *Monats.*, **31**, 301 (1910).

tion under conditions least apt to bring about isomerization and to test the general applicability of the method under such conditions.

Although many papers dealing with this reaction directly or indirectly, have appeared, there has been, since the time of Pfannl, no investigation of the value of this reaction as a method of ester preparation until the recent one of Emil Fischer¹ on the preparation of esters of glycol and glycerol. Reid² has given a brief summary of the most important investigations since the early work of Claisen³ and of Purdie,⁴ and further study of equilibrium in this reaction has been described in a monograph by Miss Jessie E. Minor.⁵ This paper includes a bibliography.

In our work we have made no attempt to determine equilibria, but have investigated the reaction solely as a method of ester preparation. As the work with esters of unsaturated acids is not yet complete, we give here only the results of preliminary experiments. These have to do with two aspects of the problem: the determination of the best conditions for experimentation, having in mind the applicability of the method to unstable esters; and the study of the types of alcohols and of esters to which the reaction can be applied under these conditions.

In carrying out the replacement reaction it is to be expected that the best yields of any desired ester would be obtained in the presence of a considerable excess of the corresponding alcohol. In case the esters used or formed in the reaction were unstable, the conditions least likely to bring about isomerization to a stable form would be a low temperature, a small amount of catalyst, and a short time in which the catalyst remained in contact with the ester-alcohol mixture. In nearly all the reactions of this kind described in the literature, the reaction mixture has been allowed to stand for several hours or even days, and has been heated, sometimes under pressure to temperatures as high as 200°. Preliminary experiments with methyl benzoate showed that when this ester was shaken for an hour with excess of ethyl alcohol, not only could the replacement be accomplished at room temperature with only 0.05 mole of potassium ethylate as catalyst, but that the best yields of product were obtained under these conditions. This procedure was therefore adopted for subsequent work.

For study of the reaction with primary, secondary, and tertiary alcohols, methyl benzoate was the ester chosen, since the esters of benzoic acid are, for the most part, high-boiling liquids easily separated by distillation, and since a large number of them has been described in the

¹ Fischer, *Ber.*, **53**, 1634 (1920).

² Reid, *Am. Chem. J.*, **45**, 479 (1911).

³ Claisen, *Ber.*, **20**, 646 (1887).

⁴ Purdie, *ibid.*, **20**, 1555 (1887).

⁵ Minor, "A Study of the Equilibrium in the Alcoholysis of Esters." Dissertation, Bryn Mawr College, 1917.

literature. The primary alcohols used were ethyl, propyl, butyl, *iso*-butyl, *iso*-amyl, and benzyl. In each case a reaction took place, the ester of benzoic acid corresponding to the alcohol used being formed in yields varying from 72 to 97%. The reaction was rapid and the products pure. The secondary alcohols used were *iso*-propyl, *sec.*-butyl, and menthol. A trace of reaction product was isolated in the case of *sec.*-butyl alcohol. The others did not react. The method, under these conditions, is, therefore, not available for esters of secondary alcohols. In view of these results and of the difficulty usually experienced in preparation of esters of tertiary alcohols, it was not to be expected that the latter could be prepared by this method. This was found to be the case: *tert.*-butyl alcohol and ethyldiphenyl-carbinol gave no reaction with methyl benzoate.

Since there was found to be such marked hindrance when secondary and tertiary alcohols were used, it seemed advisable to investigate esters of substituted benzoic acids with a view to determining the effect of the relative positions of the substituting groups. The methyl esters of salicylic, *o*-bromo- and *o*-nitrobenzoic acids were treated with ethyl alcohol and potassium ethylate under the conditions already described. There was no reaction. The experiments were then repeated with the corresponding *para* substituted esters. From methyl and ethyl *p*-nitrobenzoate, and methyl and ethyl *p*-bromobenzoates very nearly quantitative yields of reaction products were obtained. Methyl and ethyl *p*-hydroxyl-benzoates, however, gave but small quantities of the reaction products. As these esters hydrolyze with great ease, the poor yield of product may have been due to partial neutralization of the catalyst by free acid. Repetition of the reaction with increased proportions of the catalyst, however, did not increase the yield.

Experiments with dibasic acids were carried out with two objects in view: to test the effect of the space relations of the carboxyl groups on the replacement reactions; and to find a method for the preparation of certain esters not readily obtained otherwise in the pure condition, notably those of malonic and substituted malonic acids. This reaction with various dibasic acids has been studied by other investigators but not under comparable conditions. When special precautions against saponification of these esters were taken, yields ranging from 58 to 86% were obtained, except in the case of methyl and ethyl *o*-phthalate which, like the other *ortho* substituted esters studied, did not give any appreciable yields of reaction products.

Experimental.

The alcohols used were Kahlbaum products with the exception of methyl and ethyl alcohols. They were carefully dried and redistilled until boiling at constant temperature. Carefully calibrated Anschutz

thermometers were used for determining boiling points, and the stem of the thermometer was completely surrounded by the vapor of the boiling liquid during distillation.

Preliminary experiments for determining the best conditions for the reaction were carried out as follows. A solution of methyl benzoate in at least 10 times the calculated amount of ethyl alcohol was shaken on an electric shaking machine, at room temperature, for different lengths of time, with amounts of potassium ethylate varying from one mole to 0.05 mole. Dil. sulfuric acid was then added to the reaction mixture in quantity just sufficient to neutralize the alkali, and then enough water to dissolve the potassium sulfate formed. The solution was extracted with ether, the ethereal extract washed first with a dilute solution of sodium carbonate to dissolve any benzoic acid present as a result of hydrolysis, and then twice with distilled water. The extract was dried over fused sodium sulfate and fractionated. The weight of ester corresponding to the benzoic acid recovered from the sodium carbonate solution was subtracted from the weight of methyl benzoate used. The results are given in the following table. 100 cc. of alcohol was used in each experiment.

Amount of potassium.		Weight of ester used. G.	Weight of acid by hydrolysis. G.	Time in minutes.	Yield of ester. %.	Average yield. %.
G.	Moles.					
5.55	1	19.87	0	10	73.92	...
5.84	1	19.98	0.33	10	71.90	72.91
0.6	0.1	19.89	0.40	10	80.10	...
0.6	0.1	20.06	0.40	10	87.32	83.71
0.3	0.05	19.28	0.30	10	64.73	...
0.3	0.05	19.16	0.28	10	79.64	72.08
0.3	0.05	19.72	0.30	30	89.23	...
0.3	0.05	19.96	0.16	30	88.65	88.94
0.3	0.05	20.24	0.17	60	93.80	...
0.3	0.05	20.00	0.17	60	96.79	95.29

On the basis of these results, in all subsequent experiments, 0.05 mole of potassium alcoholate was used for each mole of ester, and the shaking continued for one hour.

Esters of Benzoic Acid.

Reactions with Secondary and Tertiary Alcohols.—Experiments were conducted in the same way as with the primary alcohols. 20.14 g. of methyl benzoate, 0.3 g. of potassium, and 111 cc. of *iso*-propyl alcohol were used. The product was distilled under diminished pressure. The only high boiling distillate obtained was methyl benzoate. A repetition of the experiment gave the same result.

17.55 g. of methyl benzoate, 0.25 g. of potassium and 104 g. of *sec.*-butyl alcohol were treated in the other cases. 60% of the methyl benzoate was regained. The remainder boiled between 200° and 230°. This may have contained some *sec.*-butyl benzoate, but no constant boiling fraction could be obtained.

ESTERS FORMED.

	Reagents.			Benzoic acid recovered.	Yield.		B. p.	
	Potas- sium. G.	alco- hol. Cc.	Methyl ester. G.		G.	%	Found. C.	Recorded. C.
Benzoate.								
Ethyl.....	0.3	100	20.42	0.17 I	20.88	93.8	209-11.6	211.2
				II		91.79		
Propyl.....	0.3	111	20.92	.. I	20.42	80.7	228-30	229.5
				II		84.2		
<i>n</i> -Butyl.....	0.25	100	17.84	..	16.01	71.9	246-50	248
<i>iso</i> -Butyl.....	0.25	130	17.55	.. I	18.94	78.0	237-40	237
				II		78.0		
<i>iso</i> -Amyl.....	0.3	160	20.03	0.5	23.06	83.85	256-60	260.7
Benzyl.....	0.1	50 g.	7.0	..	8.4	77.0	192.5 (20 mm.)	
Methyl.....	0.33	60	21.1 ^a	.. I	17.18	89.76	199-200	199.2
				II		88.18		
Ethyl <i>p</i> -Nitro.....	0.25	100	20	..	quant.		57 (m. p.)	...
Methyl <i>p</i> -Nitro....	0.25	100	20 ^a	..	quant.		96 (m. p.)	...
Ethyl <i>p</i> -Bromo....	0.21	175 g.	11.23 (80°)	..	9.95	82	262	...
Methyl <i>p</i> -Bromo....	0.15	100	6.9 ^a	..	5.9	93	74 (m. p.)	116
Ethyl <i>p</i> -Hydroxy...	0.15	200	10	..	3.0 ^b	..	115-20	...
Methyl <i>p</i> -Hydroxy..	none

^a The corresponding ethyl esters were used in these experiments.

^b A mixture of ethyl and methyl esters obtained. This was extracted repeatedly with cold alcohol in which the methyl ester is slightly more soluble than the methyl.

4.98 g. of methyl benzoate, 0.1 g. potassium, and 95 g. of menthol were brought together in enough dry ether to dissolve the menthol. From this, after the usual procedure, the methyl ester and the menthol were recovered unchanged, by fractional distillation under diminished pressure. In order to calculate any possible effect of the ether in this reaction, the experiment with methyl benzoate and ethyl alcohol was repeated, a volume of ether equal to that of the ethyl alcohol, being added. A 76% yield of ethyl benzoate was obtained. The presence of a volume of ether sufficient to bring the menthol into solution might, therefore, decrease the yield of the product, but would not be expected to inhibit the reaction entirely. In the preparation of esters of glycol and glycerol already referred to, Fischer has used ether and even chloroform and pyridine, as solvents, with good results.

No reaction products were obtained from methyl benzoate with tertiary butyl alcohol, nor was there reaction with ethyl diphenyl carbonol, nor with triphenyl carbinol in ethereal solution.

 Esters of Dibasic Acids.¹

Because of the extraordinary ease of hydrolysis of oxalic and malonic esters, a different method of procedure was used with these substances, water being carefully excluded not only from the reaction mixture, but during the separation and purification of the product. After the alcoholic solution of ester and catalyst had been shaken for an hour, the quantity of hydrogen chloride necessary for neutralization of the catalyst was added in absolute alcohol solution. The potassium chloride was

¹ For the results with esters of oxalic and malonic acids we wish to gratefully acknowledge our indebtedness to Miss Elizabeth LaBoyteaux.

removed, the alcohol distilled off, and the residue fractionally distilled or allowed to crystallize. In this way the ester did not come into contact with moisture during the process and hydrolysis was avoided. The low yields of esters of oxalic acid noted by Pfannl¹ and by Gomberg and Buchler² may be, at least in part, accounted for by the fact that water was not excluded from the reaction.

Esters of Oxalic Acid.—These experiments were repeated many times before the best conditions were found. By taking all possible precautions against moisture during the whole procedure, the yield of diethyl oxalate, boiling at 182°, obtained from the crystalline dimethyl oxalate, was raised from 0 to 64%.

The separation of pure dimethyl oxalate from the reverse reaction presented certain difficulties as it was not possible to free it completely from traces of diethyl oxalate by fractional distillation. The procedure finally used was as follows: 20 g. of diethyl oxalate, 200 g. of methyl alcohol, and 0.27 g. of potassium were shaken for one hour, methyl alcohol saturated with hydrogen chloride added, the mixture filtered, and about 4/5 of the alcohol distilled off. From the residue, cooled in a freezing mixture, the dimethyl oxalate separated in glistening plates. These were rapidly filtered out, the filtrate evaporated, again cooled, and so on, until only about 5 cc. of the filtrate remained. In this way good yields of dimethyl oxalate were obtained. Since this ester is not only readily soluble in alcohol at room temperature, but is also volatile, it is necessary to separate and dry it carefully and rapidly. The increase in yield following increased care in preparation, is shown by the following results.

Expt.	Diethyl oxalate used. G.	Dimethyl oxalate obtained. G.	Yield. %
1 ^a	29.7	7.2	30
2	20	9.5	59
3	20	10.0	62
4	20	10.8	67
5	40	25	77

^a Pfannl, *loc. cit.*

Esters of Malonic Acid.—Because of the ease of saponification of these esters, the same precautions were taken as with the oxalates. This method was also adopted for the other dibasic acid esters.

Dimethyl malonate, boiling sharply at 181.5°, was obtained in yield of 79% by fractional distillation of the product from the reaction of potassium methylate in methyl alcohol on ethyl malonate. The reverse reaction gave a much poorer yield:

Expt.	Dimethyl malonate used. G.	Diethyl malonate obtained. G.	Yield. %
1	15	10.5	57.7
2	20	13.1	54
3	60	40	55

This difference in the amount of replacement according to whether methyl or ethyl alcohols are used, is marked in several cases. It is due in part to difference in ease of separation of one ester or the other from the reaction mixture, there being considerable loss in manipulation. There seems to be, however, a real difference in ease of replacement, in some esters the methoxyl, in others the ethoxyl group being more readily replaced.³

¹ *Loc. cit.*

² Gomberg and Buchler, *THIS JOURNAL*, **42**, 2059 (1920).

³ Cf. Hessler and Lamb, *ibid.*, **43**, 205 (1921).

Reactions with substituted malonic acids are still in progress.

Esters of Succinic Acid.—Twenty-five g. of dimethyl succinate, boiling at 196.9°, was treated with 0.4 g. of potassium in 250 g. of ethyl alcohol. 21.6 g. of diethyl ester, boiling chiefly at 216.4 to 216.6°, was obtained, a yield of 74%.

From 25.48 g. of diethyl succinate, 12.8 g. of dimethyl ester boiling at 196° to 200° was obtained, a yield of 61%.

Esters of Phthalic Acid.—Neither dimethyl nor diethyl phthalate entered into reaction to an appreciable extent under the conditions used. This is in harmony with the results obtained with other *ortho* substituted esters.

Esters of Terephthalic Acid.—Ten g. of dimethyl terephthalate, 0.4 g. of potassium, and 130 g. of ethyl alcohol were used. 9.1 g. of diethyl terephthalate was obtained, a yield of 83%.

10 g. of diethyl terephthalate subjected to similar treatment, gave 7.5 g. of dimethyl ester, an 86.2% yield.

Summary.

As a result of these experiments the conclusion may be drawn that the direct replacement of one alkoxyl group by another may be carried out at room temperature, with a very small amount of alkaline reagent. This is of importance for ester preparation in general, but especially for that of unstable esters which cannot be prepared at high temperatures, or under the influence of acid reagents.

Under the conditions here described, the reaction is restricted to primary alcohols. The change from methyl esters to those of higher primary alcohols, and of ethyl esters to methyl, can be brought about in good yields with esters of all the acids studied with the exception of those which usually show "hindrance" to ester formation.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE IDAHO STATE EXPERIMENT STATION.]

THE APPLICATION OF THE VAN SLYKE METHOD TO HYDROLYZED PROTEIN EXTRACTS OF SILAGE CROPS.¹

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Newer knowledge of the rôle that amino acids play in nutrition has led investigators to attempt to analyze the protein molecule of feeding stuffs to learn of its composition, especially the percentage of amino acids. Since the introduction of Van Slyke's² method for determining the amino acids in pure proteins, investigators have studied the composition of feeding stuffs by means of applying the Van Slyke method directly to a hydrolyzed extract of the original material. Chief among

¹ Published with the permission of the Director of the Idaho State Experiment Station.

² D. D. Van Slyke, *ibid.*, 10, 15 (1911-12).