was identified by conversion to mesitoyldibenzoylmethane, m. p. 193–194° (lit.[6a] 192°) and 3,5-dinitroacetomesitylene, m. p. 138–139.5° (lit.[18] 138–139°).

Fraction 8 (2 ml.) was ozonized at −70° in 15 ml. of dichlorodifluoromethane. A modification of the method of Whitmore and Church[19] was used for the reduction and isolation of the products. Formaldehyde and propionaldehyde were identified as their methone derivatives of m. p. 189–191° and 155–156°, respectively. Acetomesitylene was identified by conversion to *m*-nitrobenzalacetomesitylene, m. p. 98–99° (lit.[20] 98°).

Benzylmagnesium Chloride with Acetomesitylene.—To a solution of benzylmagnesium chloride prepared from 2.4 g. (0.10 gram atom) of magnesium, 9.5 g. (0.075 mole) of freshly distilled benzyl chloride (b. p. 93.5° (50 mm.)) and 100 ml. of ether was added dropwise with stirring 8.0 g. (0.05 mole) of acetomesitylene dissolved in 100 ml. of ether. A brilliant orange-red color developed, which faded to light yellow after all of the ketone had been added. The mixture was poured into iced ammonium chloride solution and the ethereal layer separated and dried. The ether was removed through a column and remainder of the low-boiling material was then distilled into a Dry Ice trap at 50° (5 mm.). Fractionation of this distillate gave 3.7 g. (0.040 mole) of toluene, b. p. 109–110°. The residue (10.3 g.) from the reduced pressure distillation was distilled in a molecular still.

Frac.	Bath temp., °C.	Press., mm.	Wt., g.	$n^{20}D$
1	63–65	3.5×10^{-4}–1.5×10^{-4}	2.7	1.5242
2	65–100	1.5×10^{-4}–3.0×10^{-4}	0.8	1.5520
3	100–110	3.0×10^{-4}	5.9	1.5689
Residue			0.2	

Fraction 1 appeared to be mainly acetomesitylene. Fraction 3 was the addition product. If Fraction 2 is considered to be roughly two-thirds addition product and one-third ketone, the amount of enolization and addition on the basis of the theoretical yields were 38 and 52%, respectively, giving a recovery of 90%. Concordant analyses were not obtained with the addition product. The material apparently absorbed oxygen or water continuously from the air, to judge from the trend of the analytical values.

Anal. Calcd. for $C_{19}H_{18}O$: C, 86.99; H, 6.91. Found: (Fraction 3) C, 85.23, 84.09, 82.97; H, 9.12, 8.67, 8.50.

Fraction 3 (1 g.) was distilled at atmospheric pressure. Water was given off and after the moisture had passed over the product distilled at about 300°. The material was very little discolored in this process and the distillate showed $n^{20}D$ 1.5603.

Fraction 3 (1.51 g.) was oxidized in pyridine[21] solution with potassium permanganate. The acidic products were separated by the procedure of Gilman and Kirby.[22] No phthalic acid was detected. Benzoic acid was isolated and crystallized from a water–alcohol mixture; m. p. and mixed m. p. 117–121°; yield 0.10 g. (32%).

Butenylmagnesium Bromide with Phenylacetylene.—To an ethereal solution of butenylmagnesium bromide (0.094 mole) was added a solution of 11 g. (0.11 mole) of phenylacetylene (b. p. 80.5°, 100 mm.). The resulting butenes were distilled into a Dry Ice trap and purified as previously described.[23]

The butene mixture was analyzed by the infra-red method[17] and found to consists of 1-butene, 93.6%; *cis*-2-butene, 5.4% and *trans*-2-butene, 1.0%.

Summary

Butenylmagnesium bromide was found to add to acetomesitylene to give α-methylallylmesitylmethylcarbinol in 83% yield. Less than 3% of the theoretical quantity of butene was evolved. The addition product was cleaved on heating to give *cis*- and *trans*-2-butene and acetomesitylene.

Benzylmagnesium chloride also added to acetomesitylene to give benzylmesitylmethylcarbinol in 38% yield.

Butenylmagnesium bromide was cleaved by phenylacetylene to give a mixture of butenes, of which at least 93% was 1-butene.

Existing evidence appears to favor the formulation of the butenylmagnesium halides as crotylmagnesium halides.

(18) Fisher, Snyder and Fuson, THIS JOURNAL, **54**, 3665 (1932).

(19) Whitmore and Church, *ibid.*, **54**, 3710 (1932).

(20) Barnes and Spriggs, *ibid.*, **67**, 134 (1945). In our first experiments this material was isolated in an unstable form as pale yellow prisms, m. p. 82–83°. A solution of the compound seeded with a crystal of the stable form kindly furnished by Dr. Barnes gave the bright lemon-yellow crystals of the stable form, m. p. 98–99°.

(21) (a) Bucher, *ibid.*, **32**, 374 (1910); (b) Smith and Spoehr, *J. Biol. Chem.*, **86**, 87 (1930).

(22) Gilman and Kirby, THIS JOURNAL, **54**, 345 (1932).

(23) Young and Roberts, *ibid.*, **67**, 1040 (1945).

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[CONTRIBUTION FROM THE WESTERN REGIONAL RESEARCH LABORATORY[1]]

Esterification of Galacturonic Acid and Polyuronides with Methanol–Hydrogen Chloride

BY EUGENE F. JANSEN AND ROSIE JANG

A simple method for the preparation of the methyl ester of α-D-galacturonic acid became desirable in our investigations of the specificity of pectinesterase. Furthermore the ester, as opposed to the free acid, has been shown to inhibit the growth of many dysentery bacteria *in vitro*.[2] Esterification in acidic methanol would be expected to lead to partial or complete formation of the methyl glycoside as well as the methyl ester. For this reason the methyl ester of α-D-galacturonic acid has been prepared by the laborious and somewhat hazardous diazomethane method.[3] Fraenkel-Conrat and Olcott[4] found, in the course of studies of esterification of carboxyl groups of proteins and model substances, including acetic, lactic, benzoic and galacturonic acids, that galacturonic acid is readily esterified at room temperature in methanol containing 0.02 to 0.1 *N* mineral acid. This observation raised

(1) Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

(2) Steinhaus and Georgi, *J. Infectious Diseases*, **69**, 1 (1941).

(3) Morell and Link, *J. Biol. Chem.*, **108**, 763 (1935).

(4) Fraenkel-Conrat and Olcott, *ibid.*, **161**, 259 (1945).

the question whether appreciable quantities of the methyl glycoside would be formed under these mild conditions before the esterification was essentially complete. The data reported in this paper are concerned with relative rates of glycoside formation and esterification at 0° and at 24–25° of galacturonic acid in absolute methanol containing various concentrations of dry hydrogen chloride. The percentage conversions in both reactions, as functions of catalyst concentration, time, and temperature, are reported in Table I. The esterification reaction was first

TABLE I

ESTERIFICATION AND GLYCOSIDE FORMATION OF GALACTURONIC ACID[a] IN VARIOUS NORMALITIES OF METHANOLIC HYDROGEN CHLORIDE

Time, hr.	Esterification, % 0.10 N	0.02 N	0.01 N	0.005 N	Glycoside formation, % 0.10 N	0.02 N	0.01 N	0.005 N
			0°					
2	42	14	5.3	1.7	..	..	..	..
4	62	24	11	4.4	..	..	..	..
6	74	34	17	5.9	1	..	..	..
24	95	77	51	23	12	3	..	..
48	96	92	72	37	23	5	..	..
72	..	96	85	50	28	..	..	..
96	..	..	90	58	35	..	..	..
168	..	..	97	77	61	19	7	1
			24–25°					
1	85	43	25	7.5	10	..	..	..
2	93	65	40	15	22	4	..	..
3	95	78	52	22	33	5	..	..
4	96	85	62	27	42	7	..	..
5	97	88	69	31	49	13	9	..
24	98	98	95	75	76	40	27	3
48	..	..	98	89	80	59	33	10
72	..	..	..	96	..	65	49	15

[a] 2.5 g. of galacturonic acid monohydrate was dissolved in absolute methanol and the appropriate amount of stock solution of dry hydrogen chloride–methanol added to give the desired normality in a final volume of 77.5 ml.

order until more than half of the carboxyl groups had been esterified. The rate of glycoside formation at 24–25° was first order. This was true until more than 50% of the reaction had occurred in the instances where it was allowed to continue to that extent. At 0° the rate of glycoside formation departed from first order after ninety-six hours. The first order reaction constants k in Table II show that: (a) except at lowest concentration, the rates were approximately proportional to the catalyst concentration; (b) the esterification rates were nearly 10 times faster at 25° than at 0°; and (c) esterification was at least 25 times greater than glycoside formation at 25° and at least 55 times greater at 0°. The energy of activation, calculated from the Arrhenius equation for the temperature range studied, is 14,000 ± 700 cal.[5] for the esterification reaction and 21,000 ± 1,000 cal. for the glycoside formation reaction. Such a difference in temperature coefficient signifies that the lower the temperature the less will be the glycoside formation for a given amount of ester formation.

(5) This value for the energy of activation for esterification is considerably higher than that found by Smith, THIS JOURNAL, **61**, 254 (1939), for the esterification of normal aliphatic acids in methanol.

TABLE II

FIRST ORDER REACTION CONSTANTS, k[a]

HCl concn., N	Esterification 0°	25°	Glycoside formation 0°	25°	Relative rate[b] 0°	25°
0.005	0.0046	0.034	~0.00008[c]	0.00096	60	35
.01	.013	.099	~ .0002[c]	.0038	60	26
.02	.029	.204	.00049	.0077	59	26
.10	.11	..[d]	.0020	.061	55	..

[a] k is expressed in hr.$^{-1}$ log to the base 10. The values of k are for the first portion (50%) of the reaction course. [b] These values are the quotient of k for esterification divided by k for glycoside formation. [c] Rates were too slow for an accurate determination of k. [d] Rate was too fast for an accurate determination of k.

It can be estimated from Table I that the maximum yield of the simple ester at 25° will occur at about 90% of total esterification and will be of the order of 80% of the total galacturonic acid. If the esterification is permitted to proceed much beyond 90%, the yield of simple ester will decrease as a result of formation of methyl glycoside of the ester. At 0° it appears that an 85 to 90% conversion to the simple ester can be obtained by permitting esterification to proceed to about 95%. The desired conversion at 25° requires about six hours with 0.02 N hydrochloric acid; at 0° it requires about twenty hours with 0.1 N hydrochloric acid. Lower temperatures and higher acid concentrations might be used with correspondingly different reaction times.

Alginic acid suspended in dry 0.025 N hydrogen chloride–methanol at room temperature was esterified to the extent of 21, 37, 51 and 60% in 1, 2, 5 and 13 days, respectively. However, pectic acid under the same conditions was esterified only 1, 3, 9 and 12%.

Experimental

The rate of esterification was followed by the removal of aliquots at the desired times, dilution with water, and titration with 0.02 N sodium hydroxide and the per cent. esterification was calculated from the decrease in acidity. Glycoside formation was followed by determining the reducing value of aliquots by a modified Willstätter–Schudel hypoiodite method as previously described.[6]

Isolation of Methyl-α-D-galacturonate.—To 1550 ml. of 0.02 N hydrogen chloride in absolute methanol at 0° was added 50 g. of galacturonic acid monohydrate. After the reaction mixture was allowed to stand at 0° for sixty-six hours, 98% esterification and 8% glycoside formation had occurred. The mixture was neutralized with 1 N potassium hydroxide in methanol and the precipitate (unesterified material) filtered off. The methanol was distilled off under reduced pressure at 40° to a volume of 100 ml. after which 900 ml. of ether was added. The resulting sirup slowly crystallized and 45 g. of the crude ester was obtained. One recrystallization from a warm mixture of 2 volumes of dioxane to 1 volume of methanol yielded 27 g. of the pure ester. The product was recrystallized twice more from dioxane–methanol and dried for analysis. An

(6) Jansen and MacDonnell, *Arch. Biochem.*, **8**, 97 (1945).

initial value of $[\alpha]^{25}D$ 94° (c, 1.86 in absolute methanol) and an equilibrium value of 34° was obtained.[7]

Anal. Calcd. for $C_5H_9O_5COOCH_3$: OCH_3 14.9, mol. wt., 208. Found: OCH_3 14.9; mol. wt. 202 (by reducing value), 210 (by saponification).

The ester was also isolated from a reaction mixture which had been allowed to proceed at 25° for seventeen hours in the presence of 0.01 N hydrochloric acid after which 93% esterification and 20% glycoside formation had occurred. The yield of pure ester was lower.

Esterification of Alginic and Pectic Acids.—Several 1-g. samples of finely ground alginic acid and orange pectinesterase-prepared citrus pectic acid were suspended in 31 ml. of anhydrous 0.025 N hydrogen chloride–methanol. After the desired time the solid was centrifuged off, washed with methanol, and dried for four hours at 100°. Solutions of 0.2-g. samples in water were titrated with 0.1 N alkali, and the per cent. esterification was calculated. This procedure appeared to give a good approximation, since a sample of alginic acid which had been 78% esterified according to this method of determination actually contained 11.7% methoxyl (72% of theoretical) after humidifying to remove retained alcohol[8] and redrying.

(7) This value is lower than that of 38° reported by Morell and Link. However, we found that three days were necessary before equilibrium was reached either with this sample or with one prepared by the diazomethane method.

Summary

The esterification of galacturonic acid in methanol containing small concentrations of hydrogen chloride (0.005 to 0.1 N) proceeded at a rate at least 25 times more rapid at 25° and 55 times more rapid at 0° than did glycoside formation. Both reactions were first order to at least 50% conversion and the energies of activation for the esterification and glycoside formation reactions were 14,000 ± 700 and 21,000 ± 1,000 cal., respectively.

Methyl α-D-galacturonate was isolated in good yields from such reaction mixtures.

Alginic acid was partially esterified by a similar procedure. However, pectic acid under the same conditions was only very slowly esterified.

(8) Jansen, Waisbrot and Rietz, *Ind. Eng. Chem., Anal. Ed.*, **16**, 523 (1944).

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[CONTRIBUTION FROM KOPPERS CO., INC., MULTIPLE FELLOWSHIP ON TAR SYNTHETICS, MELLON INSTITUTE]

Alkylation of Thiophene by Olefins and Alcohols

BY WALTER M. KUTZ AND B. B. CORSON

This paper describes for the first time the direct alkylation of thiophene by olefins and alcohols. The alumina–silica type of catalyst was found suitable for this reaction. Thiophene was alkylated by propylene, butylene-1, isobutylene, amylene, cyclohexene, isopropyl alcohol, and tertiary butyl alcohol. Suitable conditions were not found for the ethylation of thiophene.

In general, the catalysts and conditions employed for the alkylation of aromatics are not suitable for the alkylation of thiophene. For example, we were unable to find any set of conditions under which sulfuric acid or the chlorides of aluminum, iron, or tin catalyzed the isopropylation of thiophene. Strong sulfuric acid sulfonated the thiophene; dilute sulfuric acid allowed the thiophene to survive but did not catalyze the alkylation reaction. Sulfuric acid concentrations ranging from 96 to 50% were tested, the reaction temperature being 0–5°. Only very small yields of material boiling above thiophene were obtained. However, thiophene was alkylated at 60° by isobutylene with 100% phosphoric acid as catalyst. Aluminum chloride and ferric chlorides were tested at 0–5° and at 25°, respectively. Negligible yields of liquid product boiling above thiophene were obtained. When stannic chloride was employed according to the directions of Johnson and May[1] for the acetylation of thiophene, practically all the thiophene was recovered unchanged. Boron trifluoride–dimethyl ether complex and hydrogen fluoride yielded resinous products.

The structure of isopropylthiophene, obtained by the alkylation of thiophene by propylene and also by isopropyl alcohol, was established as the 2-isomer by specific color tests and by converting it into the known oxime and *p*-nitrophenylhydrazone of its 5-acetyl derivative.[2] Numerous unsuccessful attempts were initially made to oxidize isopropylthiophene to the corresponding thenoyl formic or thiophenic acid. The structures of the other alkyl thiophenes were not determined, but it is likely that they are also 2-isomers.

Experimental

Materials.—Thiophene, obtained from the Socony-Vacuum Oil Co., was used without further purification.[3] Ethylene and propylene were of 99.5 and 75% purity, respectively, the contaminant of the propylene being propane. Butylene-1 (99% pure) and isobutylene (95% pure) were products of the Phillips Petroleum Co. Amylene, obtained from the Sharples Solvents Co., consisted of a mixture of methylethylethylene and trimethylethylene. Filtrol catalyst (X-143) was supplied by the Filtrol Corp., anhydrous hydrogen fluoride by the Harshaw Chemical Co., and boron trifluoride–dimethyl ether complex by the General Chemical Co.

Apparatus and Procedure.—The superatmospheric pressure alkylation experiments with Filtrol, hydrogen fluoride, and boron trifluoride–dimethyl ether complex were made in a 3500-cc. stainless steel, rotating autoclave of the Ipatieff type, gaseous catalysts and olefins (except ethylene) being condensed in metal or glass traps which

(1) Johnson and May, "Organic Syntheses," Coll. Vol. II, p. 8 (1944).

(2) Scheibler and Schmidt, *Ber.*, **54**, 139 (1921).

(3) Fawcett and Rasmussen, THIS JOURNAL, **67**, 1705 (1945).