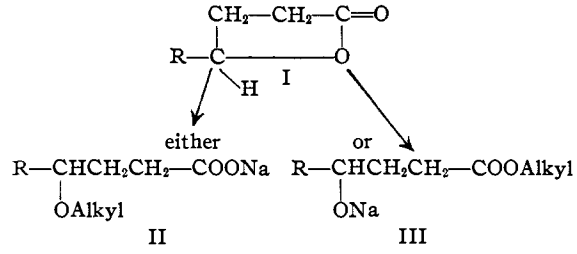
[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

The Action of Sodium Alkoxides on Lactones

BY E. Y. SPENCER AND GEORGE F. WRIGHT

An investigation into the chemical properties of yellow birch lignin, prepared by extraction of the wood with acetic acid, has shown that this isolated lignin reacts as if it contained lactonized carbonyl groups.[1] One of these reactions involved the action of sodium alkoxides on the suspected lactone linkage. The product contained the elements of the sodium alkoxide which was used. According to the existing literature it was impossible to determine from the data whether the lactone linkage was aliphatic or aromatic in character, *i. e.*, γ-butyrolactone or coumarin type. Thus, coumarin was known to react with sodium alkoxides to yield the sodium salt of the alkyl *o*-hydroxycinnamate.[2] On the other hand, butyrolactone was reported by Fittig and Strom[3] to be alcoholized in the opposite manner to give sodium 4-alkoxybutanoate, II (R = H). Both sodium salts would be stable in water, as was the sodium salt obtained when the lignin was treated with sodium methoxide. If butyrolactone alcoholized in the same manner as coumarin, then the lignin might be considered as a coumarin type since the sodium salt of a compound like the alkyl 4-hydroxybutanoate, III (R = H) would not have been stable in water. It therefore became of interest to us that Allen and co-workers[4] have questioned Fittig's formulation and consider his compound to have been III rather than II. These authors have kindly relinquished this study to us.



Fittig's work may be questioned in several respects. It has been pointed out[4] that his so-called 4-ethoxybutanoic acid (which was a minor product in the preparation of dibutolactone, VII (R = H)) boiled at the same temperature as the "γ-hydroxybutanoic acid" which he obtained from it by a very questionable series of reactions. He also encountered some difficulty in analyzing the supposed 4-ethoxybutanoic acid. Although he obtained none of the analogous product from valerolactone, we have re-investigated the action of sodium alkoxides on both of these lactones and find that homologous compounds are formed.

Fittig heated his reactions, but since we wished to simulate the conditions used in the lignin research our first experiments were carried out at room temperature. When one equivalent of sodium methoxide in methanol was treated with valerolactone for either two or four days and the solvent subsequently evaporated *in vacuo*, the products reported by Fittig were obtained: divalolactone, VII (R = CH_3), and valerolactone. The latter product was contaminated with a methoxyl-containing substance. We found however, that the formation of the condensation product could be avoided if, subsequent to the reaction period, the solution was saturated with carbon dioxide. Under these conditions, using either sodium methoxide or ethoxide, only valerolactone and a *non-acidic* alkoxyl-containing substance were obtained. While these two compounds were not completely separable through bicarbonate extraction of an ether solution, since valerolactone distributes itself between the two phases, that portion of the valerolactone which could be regenerated by acidification of the bicarbonate layer contained no methoxylated impurity. An alkoxybutanoic acid would have been detected at this point.

The non-acidic fraction which contained valerolactone as well as a methoxylated compound (the mixture analyzed for about 10% OCH_3) could not be separated by direct fractional distillation, owing to loss of alkoxyl.[5] The mixtures were therefore acetylated with pyridine and acetic anhydride. After having been stabilized in this manner, the mixtures were fractionally distilled to yield valerolactone and either ethyl or methyl 4-acetoxypentanoate, identified by elementary

(1) Unpublished results by Bell, Wright and Hibbert, completed at McGill University in August, 1937.

(2) Fries and Klostermann, *Ann.*, **362**, 11 (1908).

(3) Fittig and Strom, *ibid.*, **267**, 191 (1891).

(4) Allen, Massey and Nicholls, THIS JOURNAL, **59**, 679 (1937).

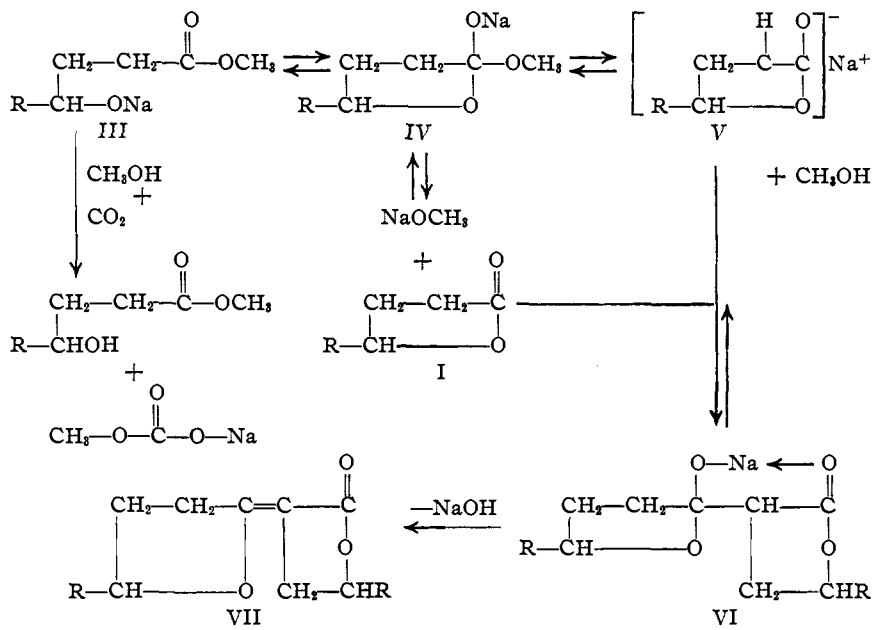
(5) (a) Thomas, Schuette and Cowley, *ibid.*, **53**, 3861 (1931); (b) Neugebauer, *Ann.*, **227**, 101 (1885); (c) Lease and McElvain, THIS JOURNAL, **55**, 806 (1933).

analysis and saponification equivalent. This designates the product of the reaction as the hydroxy ester corresponding to III (R = CH_3) in contradiction to Fittig.

We then applied this technique, involving neutralization with carbon dioxide and acetylation before distillation, to butyrolactone since this was the specific compound from which Fittig claimed to have isolated the ethoxy acid II (R = H). We thus avoided the formation of the dibutolactone VII (R = H) and obtained instead a mixture of butyrolactone and ethyl 4-acetoxybutanoate, but none of the ethoxy acid II. It therefore seems clear that Fittig was misled concerning his product and that the alcoholysis of a saturated lactone proceeds in the direction I ⟶ III as does the coumarin type.

The elimination of the condensation reaction by carbon dioxide suggested existence of a reaction series such as has been outlined by Hauser and co-workers[6] for carbonyl condensations. It therefore seemed of interest to find the optimum conditions for preparation of divalolactone. A series of such reactions were carried out wherein the equivalence of alkali and the concentration of reactants were varied. The per cent. yields are significant only as they relate to each other since the analytical method necessarily involves some loss of material. Table I summarizes these experiments, which show that yields markedly decrease as the alkali equivalence exceeds one, and that high concentrations of both reactants in methanol give better yields than low concentrations.

These data may be explained by the mechanism



According to this scheme an appreciable amount of the addition product IV is formed when the lactone I is treated with sodium methoxide at room temperature. The stability of this addition product in the solvent methanol either precludes formation of the ion V or so completely removes free lactone from the solution that such an ion finds no carbonyl with which to condense. Under these conditions of stability for IV at room temperature the addition of carbon dioxide, a stronger acid in the solvent methanol than the enol V, will force the equilibrium through III into the methyl 4-hydroxyalkanoate. If, however, the temperature of the system is increased without carbon dioxide addition, the complex IV decomposes according to its several equilibria. A certain amount of the ion V, thus formed, combines with regenerated lactone I to give the addition product VI from which, by subsequent acidification of the reaction mixture, dibuto- (R = H) or divalolactone (R = CH_3) is obtained. The chelated structure of VI explains the fact that the white

TABLE I

PREPARATION OF DIVALONIC ACID FROM 0.005 MOLE OF VALEROLACTONE

Expt.	NaOMe, mole	Vol., ml.	Concn. NaOMe, mole per l.	Concn. lactone, mole per l.	Divalonic acid, G.	Divalonic acid, %
1	0.0025	7.0	0.36	0.71	0.15	30
2	.0037	10.0	.37	.50	.07	14
3	.0050	13.0	.38	.38	.05	10
4	.0050	10.5	.48	.48	.11	22
5	.0050	9.3	.54	.54	.15	30
6	.0050	5.5	.91	.91	.10	20[a]
7	.0075	20.0	.37	.25	.04	8
8	.0100	6.0	1.67	.84	.06	12
9	.0100	16.5	0.61	.30	.03	6

[a] Solvent evaporated *in vacuo* on hot water-bath.

(6) Hauser and Renfrow, THIS JOURNAL, **59**, 1823 (1937); Hauser and Breslow, *ibid.*, **61**, 793 (1939).

TABLE II

PREPARATION OF DIBUTOLACTONE FROM 0.01 MOLE OF BUTYROLACTONE

Expt.	NaOMe, mole	Vol., ml.	Concn. NaOMe, mole/l.	Concn. lactone, mole/l.	Temp. of react. mixt., °C.	Crude prod. M. p., °C.	Crude prod. Wt., g.	Dibutolactone M. p., °C.	Dibutolactone Wt., g.	%
10	0.005	2.7	1.85	3.70	83	Oil	0.31	84–86	0.09	12
11	.005	4.8	1.04	2.08	67	...	.58	86	.32	41
12	.005	6.8	0.73	1.47	67	...	.58	85	.30	39
13	.005	9.8	.51	1.02	68	74–75	.33	82–83	.15	20
14	.01	4.8	2.08	2.08	79	...	.31	87	.20	26
15	.01	8.8	1.14	1.14	69	72	.32	86–87	.25	33
16	.01	16.0	0.63	0.63		...	..	85	.10	13[a]
17	.01	29.8	.34	.34		84–85	.20	86–87	.12	16
18	.02	8.8	2.28	1.14	76	...	.25	85–86	.12	16

[a] Reaction period 6.5 hours instead of three hours.

residue left after methanol evaporation from the reaction mixture does not yield an ether soluble compound when dissolved in water, until hydrochloric acid is added subsequently. It must therefore have a stabilized structure similar to those of β-diketone and acetoacetic ester salts.

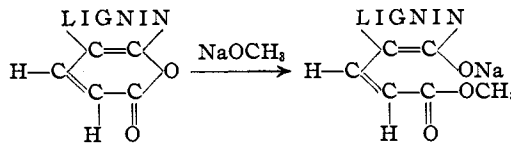
Under these conditions, increased dilution would favor the unimolecular decompositions IV ⟶ III and IV ⟶ I over the bimolecular condensation I + V ⟶ VI and hence the lowered yields with increased dilution shown in Table I would be expected. Likewise one might expect that an excess of sodium methoxide would reduce the available amount of reacting lactone, I, by forcing the equilibrium I ⇄ IV in the direction of the addition product, IV. Inspection of Table I shows that the optimum amount of methoxide is one-half to one equivalent, and that larger amounts tend to reduce the yield (compare Expts. 1, 5 and 8).

In order to check this mechanism the condensation of butyrolactone to dibutolactone (I to VII, R = H) was carried out essentially as was outlined by Fittig except that methanol and sodium methoxide were used instead of ethanol and the ethoxide. Because of this latter variation we cannot say conclusively that Fittig's supposed "ethoxybutanoic acid" was owing to impurities in his butyrolactone, but it seems probable since we obtained no discoloration of the reaction mixture which he mentions during the three-hour reflux period. Subsequent to this reaction period we altered his procedure by removing the solvent under reduced pressure in order to provide a contrast to the conditions we employed for formation of divalolactone; thus, formation of divalolactone involved reaction at room temperature and solvent removal on the steam-bath, whereas dibutolactone formation involved reaction at *ca.* 67° and solvent removal below room temperature. Owing to its higher melting point the dibutolactone could be isolated directly in a state of purity, and hence more reliably than the divalolactone, which had to be isolated as divalonic acid.

Inspection of Table II shows that these variations have introduced no contradictions to the proposed mechanism. Thus an increase of sodium methoxide from 0.5 to 2 equivalents decreases the yield to about one-half (compare Expts. 11, 14, 18). Likewise increased dilution tends to lower the yield (Expts. 15 *vs.* 17 and 11 *vs.* 13), and this is thought not to be due to incomplete reaction at the greater dilution, since a longer reaction time at an intermediate dilution did not increase the yield, but actually decreased it (Expt. 16), probably owing to side reactions. Indeed a consideration of the conditions imposed on the several lactones shows that attainment of equilibria must be fairly rapid. A further, not unexpected, factor which is apparent in the data included in Table II, shows that the equilibrium is affected by temperature as is indicated by a comparison of Expts. 10 and 11, 12, 13.

The reversibility of the reaction was demonstrated by treatment of dibutolactone with sodium methoxide in methanol. Although excess aqueous alkali will convert dibutolactone to oxetonecarboxylic acid, a complete scission occurs when excess sodium methoxide is used. When the lactone is treated with one equivalent of methoxide, 60% of the dibutolactone is recovered. If reversion to the addition product IV had occurred, a 50% recovery might have been expected. The reversibility of this reaction is being investigated further in order to identify the scission products.

Correlation of the data included in this paper with the action of sodium methoxide on acetic acid birch lignin is not unequivocal. The sodium derivative thus obtained from the lignin was stable in water. This was shown by the fact that the sodium methoxide addition product, which was soluble in chloroform, retained the sodium atom when shaken in water and lost it only when shaken in dilute hydrochloric acid. If the reaction involved were simply addition to lactone carbonyl with subsequent scission as shown in the formulation I ⟶ III, then the lactone linkage in lignin would appear to be coumarin-like in type, since the sodium salt would then be phenolic and hence stable in water, whereas the sodium salt of the alcohol would be hydrolyzed by water. If, however, condensation had occurred, then the sodium salt might be as stable as the white residue formulated as structure VI was found to be, since dibutolactone could not be extracted from an aqueous solution of the white residue until hydrochloric acid was added. There would, then, be no way of deciding on the basis of stability in water whether the sodium derivative from the lignin was a sodium phenoxide or the sodium derivative of a dibutolactone-like condensation product. A decision in favor of the coumarin type of lactone linkage is afforded by the analytical data, which show an increase in methoxyl content of the lignin following treatment with sodium methoxide. This methoxyl increase would not occur because of condensation but would be expected from the methanolysis of a coumarin type.



Experimental

Methyl 4-Acetoxypentanoate.—To a solution of 22 g. (0.96 atom) of sodium in 250 cc. of absolute methanol was added 47.8 g. (0.478 mole) of γ-valerolactone (prepared by catalytic reduction of levulinic acid[7]), b. p. 82–83° (10 mm.), $n^{23.5}D$ 1.4320. After two days at room temperature an excess of dry-ice was added to the solution. The solvent was then removed at 55° (15 mm.). The residue, dissolved in water, was extracted with ether to yield, upon evaporation of this solvent, 27 g. of material. The aqueous solution was then acidified and extracted once with ether. This extraction removed 3.3 g. (6% of original) of valerolactone, b. p. 88–90° (13 mm.), $n^{24}D$ 1.4314, and no trace of methoxyl-containing compound was present. If any 4-methoxypentanoic acid had been present it would have appeared in this partial extraction of residual valerolactone. A micro-Zeisel determination showed no methoxyl content. The bicarbonate-insoluble ether extract was contaminated with valerolactone, as was shown by its methoxy content of about 10%. It was treated with 40.5 g. (0.40 mole) of acetic anhydride and 54.5 cc. (0.68 mole) of anhydrous pyridine at 1° for one day, then poured into iced 18% hydrochloric acid and extracted six times with 5-cc. portions of ether. This extract, washed with sodium bicarbonate and dried with magnesium sulfate, was fractionated at 12 mm.: Fraction 1, b. p. 80–88°, 5.2 g., $n^{15}D$ 1.4290; fraction 2, b. p. 88–92°, 4.1 g., $n^{15}D$ 1.4280; fraction 3, b. p. 92–96°, 1.1 g., $n^{15}D$ 1.4260. The over-all yield (Fractions 2 and 3) was 5% of theoretical. Fraction 3 was analyzed.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.2; H, 8.11; sapon. equiv., 87. Found: C, 54.5; H, 8.15; sapon. equiv., 85.

Ethyl 4-Acetoxypentanoate.—To a solution of 0.7 g. (0.03 atom) of sodium in 15 cc. of absolute ethanol was added 3 g. (0.03 mole) of valerolactone. After subsequent processing as outlined above, no ethoxy-containing acidic fraction was obtained, although 0.4 g. of non-acidic fraction was obtained which gave 0.05 g. (1% of theoretical) of product b. p. 118–125° (16 mm.) after repeated distillation.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.4; H, 8.51; sapon. equiv., 94. Found: C, 57.2; H, 8.65; sapon. equiv., 90.

Ethyl 4-Acetoxybutanoate.—To a solution of 2.94 g. (0.128 atom) of sodium in 65 cc. of absolute ethanol was added 11.0 g. (0.128 mole) of butyrolactone (b. p. 86–87° (16 mm.) $n^{21}D$ 1.4365). An initial failure to obtain a pure product was traced to the butyrolactone prepared from trimethylene glycol through the chlorobromide and chloronitrile.[8] We were unable by this method to obtain an odorless butyrolactone which gave correct analyses, but were successful when the lactone was prepared from diethyl malonate and ethylene oxide[9] via carbethoxybutyrolactone.[10] This butyrolactone was odorless, gave correct elementary analyses and saponification equivalent, and when treated with sodium ethoxide and subsequently processed as outlined above gave no 4-ethoxybutanoic acid, but 5.2 g. (23% of theoretical) of ethyl 4-ethoxybutanoate, b. p. 105–108° (16 mm.). This was redistilled, b. p. 102.5° (13 mm.), $n^{20}D$ 1.4226.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.1; H, 8.16; C_2H_5O, 25.9; sapon. equiv., 82. Found: C, 55.0; H, 8.01; C_2H_5O, 26.0; sapon. equiv., 84.

Divalolactone.—To a solution of 8.6 g. (0.375 atom) of sodium in 200 cc. of absolute methanol was added 37.5 g. (0.375 mole) of valerolactone. After four days the methanol was evaporated at 55° (15 mm.). The residue was dissolved in iced water and shaken out three times with ether to remove a mixture of valerolactone and methyl 4-hydroxyvalerate, weight 2.26 g., $n^{24}D$ 1.4286. The remaining aqueous solution was acidified to *p*H 7 and extracted seven times with ether. The combined extracts, dried with magnesium sulfate and evaporated, were distilled to give valerolactone, b. p. 63–65° (2 mm.), and sub-

(7) Schuette and Thomas, THIS JOURNAL, **52**, 3010 (1930).

(8) Henry, *Bull. soc. chim.*, [2] **45**, 341 (1886).

(9) Traube and Lehmann, *Ber.*, **34**, 1977 (1901).

(10) Michael and Weiner, THIS JOURNAL, **58**, 1002 (1936).

sequently 15.8 g. of divalolactone, b. p. 163–166° (2 mm.), $n^{26}D$ 1.5068, or 46% of theoretical.

Divalonic Acid.—This compound is obtained ordinarily by dissolving divalolactone in hot alkali, cooling to 0° and acidifying the solution. Its isolation was used to evaluate optimum conditions in the condensations recorded in Table I, where the following procedure was standardized to give reproducible relative yields rather than the highest obtainable. The solution of sodium methoxide and valerolactone in absolute methanol was let stand for three hours. The solvent was then evaporated on the steam-bath (with the exception of Expt. 6) until no more methanol distilled (one-half hour); the remainder was removed under 12 mm. pressure. The residue was taken up in water, cooled to 3° and acidified with 12% hydrochloric acid. After three hours the precipitated oil was taken up in ether. The ether solution was washed with 1% sodium hydroxide solution to remove valerolactone, then evaporated, and the residue in 2 cc. of water was heated on the steam-bath with 0.5 cc. of 10% sodium hydroxide until the solution was homogeneous. After cooling to 3° the solution was acidified with 12% hydrochloric acid. When the precipitated oil solidified it was filtered off, m. p. 136–138° cor. Re-solution of the compound in alkali, followed by acidification as before raised this melting point to 138–139° cor. with a loss of 0.03 g. of divalonic acid per 2 cc. of solution. This correction owing to solubility was added to each of the yields shown in Table I.

Preparation of Dibutolactone.—When a solution of pure butyrolactone ($n^{21}D$ 1.4365) and sodium methoxide in dry methanol (trace of precipitate with aluminum isopropoxide) was heated for three hours (or for six and one-half hours in the case of Expt. 16), the solution did not change in color, nor did the residue obtained after vacuum distillation of the solvent contain any material soluble in dry ether. All preparations were refluxed except nos. 11 and 12. When the white residue was taken up in water and extracted with ether, no dibutolactone was found in the ether phase. The aqueous solution of the white residue was chilled to 0° while 12% hydrochloric acid was added until red to congo paper, and then was exhaustively extracted with ether (7 to 20 times). The combined extracts were dried with potassium carbonate and then evaporated under 12 mm. to give a crude product which was dissolved in 6 cc. of 2% aqueous sodium hydroxide solution. Seven to ten extractions of this solution removed the dibutolactone which was isolated by vacuum evaporation of the ether extracts dried with magnesium sulfate. The error in the yield determination is about 5%. The absence of unchanged butyrolactone in the white residue resulting from vacuum evaporation of the solvent can be explained by the observation that 0.25 g. of butyrolactone was completely volatilized by vacuum evaporation of 2 cc. of methanol in which it was dissolved.

Reactions of Dibutolactone.—A repetition of Fittig's saponification of dibutolactone with hot alkali yielded oxetonecarboxylic acid; this could be accomplished quite as successfully by twelve hours' contact of an ether solution of dibutolactone with aqueous sodium hydroxide. The product, oxetonecarboxylic acid, melted at 160–161° cor. as contrasted to Fittig's melting point of 156°. When dibutolactone was treated in methanol solution with an excess of sodium methoxide or aqueous sodium hydroxide, no dibutolactone or oxetonecarboxylic acid could be found. When dibutolactone was treated with exactly one equivalent of sodium methoxide in methanol, 19/32 of the dibutolactone was recovered by continuous ether-extraction of the water solution. When this water solution was subsequently acidified and continuously ether-extracted no oxetonecarboxylic acid was found in the ether, although a faint odor of oxetone was present in the oily residue resulting from evaporation of the ether.

Summary

1. It has been shown that, contrary to the report of Fittig, the action of sodium alkoxides on γ-lactones results in alkyl esters of γ-hydroxy acids rather than γ-alkoxy acids.

2. Either the alcoholysis of butyrolactone and valerolactone or the condensation of each to the so-called dilactones can be increased at the expense of the other reaction. A mechanism is proposed to account for this.

3. The behavior of these saturated lactones toward sodium alkoxides indicates that the lactone linkage suspected in lignins is of coumarin type.

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