TABLE I

CARBONYL STRETCHING FREQUENCIES AND ACID STRENGTHS OF A SERIES OF NITRATOCARBOXYLIC ACIDS AND THE CORRESPONDINGLY SUBSTITUTED BROMOACIDS

Acid	*p*K	ν (C=O), cm^{-1}
Acetic	4.74	1711
α-Bromoacetic	2.87	1720
α-Nitratoacetic	2.26	1740
Propionic	4.88	1712
α-Bromopropionic	2.98	1721
α-Nitratopropionic	2.39	1736
β-Bromopropionic	4.02	1717
β-Nitratopropionic	3.97	1720
Butyric	4.82	1709
α-Bromobutyric	2.99	1720
α-Nitratobutyric	2.39	1731

TABLE II

PREPARATION OF NITRATOACIDS

Acid	B.p. °C.	mm.	Neutral Equivalent Calc'd	Found	Yield, %
Nitratoacetic[a]	45[d]	1.0	121.0	121.0	27
α-Nitratopropionic[b]	68	0.3	135.1	135.0	25
β-Nitratopropionic[c]	90[e]	0.7	135.1	135.0	64
α-Nitratobutyric[b]	85	0.3	149.1	149.3	35

[a] Duval, *Bull. soc. chim.*, [3], **29**, 601 (1903). [b] Duval, *Compt. rend.*, **137**, 1263 (1903). [c] *Anal.* Calc'd for $C_3H_5NO_5$: C, 26.67; H, 3.70; N, 10.37. Found: C, 26.60; H, 3.82; N, 10.63. [d] Sublimed, m.p. 55° after recrystallization from carbon tetrachloride. [e] M.p. 48–50° after recrystallization from carbon tetrachloride.

sion in the undissociated acid between the very electronegative nitrato group and the ionizable proton; hence less work is required to remove the proton from the nitratoacid than from the bromoacid.[6] It is interesting to note, however, that the carbonyl frequencies of the nitrato acids are considerably higher even than those of the bromoacids. This simply reflects the tightening up of the carbon-oxygen bond of the carbonyl group caused by the strong electrostatic repulsion between the carbonyl and nitrate dipoles (with its formally charged atoms).[7] This repulsion in the undissociated nitrato acid has the effect of markedly increasing its energy content relative to either the bromoacid or unsubstituted acid. The free energy contents of each of the corresponding anions, however, may well be much closer to one another since the resonance energy of the carboxylate function and solvation energies and entropies will tend to mask differences in free energy arising from dipole interactions. On this basis it would also appear reasonable to assign the higher acid strength of nitratoacids as compared with bromoacids to the difference in free energy content of the undissociated acids rather than of the carboxylate anions.

Acknowledgment. We are indebted to Dr. M. F. Hawthorne for helpful discussion of this problem.

EXPERIMENTAL

The nitratoacids with the exception of β-nitratopropionic acid were all prepared from the corresponding bromides. The latter compound was obtained from β-iodopropionic acid and silver nitrate. The physical properties and yields of pure acids are summarized in Table II, and as a typical example the preparation of α-nitratopropionic acid is described below.

α-Nitratopropionic acid. To a solution of 25.5 g. (0.15 mole) of silver nitrate in 100 ml. of dry acetonitrile was added 15.3 g. (0.1 mole) of α-bromopropionic acid in 50 ml. of the same solvent. The resulting solution was heated with stirring under reflux for 25 minutes. At this point oxides of nitrogen were evolved so the solution was cooled to room temperature and allowed to stand overnight. The silver bromide (18.1 g. 96%) was collected on a filter and the acetonitrile was removed at reduced pressure. At this point some silver salts precipitated so 50 ml. of methylene chloride was added and the solution was filtered. The solvent then was evaporated, and the residue was distilled. After 2.0 g. of forerun, b.p. 65–68° (0.3 mm), had been obtained, a center cut was collected b.p. 68–70° (0.3 mm), yield 3.8 g. (25%). This sample was redistilled just before its *p*K was determined.

Infrared spectra. The spectra of the acids were obtained from 0.02 *M* solutions in carbon tetrachloride in cells of 0.5 mm. light path using a Perkin-Elmer Model 21 spectrophotometer with a sodium chloride prism.

Acid dissociation constants. Samples of from 0.2–0.3 g. of each acid were dissolved in 100 ml. of distilled water and titrated with carbonate-free 0.1 *N* sodium hydroxide. The *p*H of the solution was read from a Beckman Model G *p*H meter previously standardized against the Beckman *p*H-7 buffer. At least 20 readings were taken after successive additions of sodium hydroxide. The *p*K was calculated from the *p*H at each point, correcting for hydrolysis and repression of the ionization of the acid.[8] These values then were averaged to obtain the tabulated values. The difference from the *p*H at half neutralization was significant due to the strength of the acids.

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[6] Wheland, *Advanced Organic Chemistry*, John Wiley and Sons, New York, N. Y., 1949, pp. 440–450.

[7] This electrostatic repulsion is actually the vectorial sum of two terms, *i.e.*, an inductive effect operating through polarization of the carbon σ-bonds and a dipole-dipole field effect operating through space.

[8] Bennett, Brooks, and Glasstone, *J. Chem. Soc.*, 1821 (1935).

The Preparation of 2,6-Dimethoxybenzoic Acid

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2,6-Dimethoxybenzoic acid is the key intermediate in the preparation of *gamma*-resorcylic acid which has been described as having activity against rheumatic fever.[1] The demethylation of 2,6-dimethoxybenzoic acid with aluminum chloride

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[1] Reid, Watson, Cochran, and Sproull, *Brit. Med. J.*, **2**, 321 (1951).

is described by Cartwright, *et al.*,[2] and will not be discussed here.

To obtain an adequate quantity of *gamma*-resorcylic acid[2a] for further clinical evaluation a synthesis has been developed utilizing 2-methylresorcinol which is available commercially.[3] The conversion of 2-methylresorcinol to 2,6-dimethoxytoluene was carried out in a methanol-dimethyl sulfate solution using sodium methoxide and gave a 75% yield.

The oxidation of 2,6-dimethoxytoluene was carried out using aqueous pyridine and potassium permanganate and gave a pure product in 55% yield. Neither step can be considered conventional or straightforward.

Cartwright, *et al.*,[2] discuss briefly a similar approach in which the reactions are carried out in aqueous media. These conditions are not adequate. For example, a repetition of their aqueous methylation step gave no better than a 20% conversion to 2,6-dimethoxytoluene. The difficulty of completely methylating 2-methylresorcinol is shown by the fact that even in methanol with the theoretical quantity of dimethyl sulfate (1 mole:2 moles) a maximum yield of only 38% was obtained. A large excess of dimethyl sulfate is required.

A repetition of the Cartwright, *et al.*,[2] procedure for the aqueous potassium permanganate oxidation of 2,6-dimethoxytoluene gave at best a 14% conversion to 2,6-dimethoxybenzoic acid. The use of pyridine is necessary to obtain good yields in this oxidation.

Acknowledgment. The author would like to express his appreciation to Dr. Robert E. Mosher of Providence Hospital, Detroit, Michigan for his helpful suggestions. This work was supported in part by the Michigan Heart Association.

EXPERIMENTAL[4]

2,6-Dimethoxytoluene. A solution of 74.4 g. (0.6 mole) of 2-methylresorcinol (m.p. 115–120°, as received; m.p. 119–120°),[5] 302.4 g. (2.4 moles) of dimethyl sulfate, and 200 ml. of methanol was treated dropwise over a period of two hours with a solution of 129.6 g. (2.4 moles) of sodium methoxide in 600 ml. of methanol, keeping the temperature at 25–30°.

The mixture was refluxed for 30 minutes and 650 ml. of solvent was removed by distillation. The cooled residue was treated with 600 ml. of water. The oily product was collected by filtration, washed with 500 ml. of water, dried and distilled; yield 79.7 g. (87.4%), b.p. 219–220°/731 mm., m.p. 37.5–40° (Previous b.p. 220–222°, m.p. 35°;[6] m.p. 39°.[7] The crystals had a slight oily quality which was removed by recrystallization from 7.5:1 methanol-water; yield 68.4 g. (75%), m.p. 39–40.5°.

The distillate can be used in the oxidation without recrystallization. In the example below the purified material was used.

2,6-Dimethoxybenzoic acid. A vigorously stirred mixture of 50.6 g. (0.33 mole) of 2,6-dimethoxytoluene, 125 ml. (1.55 moles) of pyridine, and 400 ml. of water was treated with 158 g. (1 mole) of potassium permanganate in small portions over a period of one hour while keeping the mixture at 45–50°. Stirring was continued for an additional two hours at the same temperature. The mixture was allowed to stand overnight, filtered, and the manganese dioxide was washed with 150 ml. of water. The combined filtrate was distilled under reduced pressure until a total of 300 g. of solvent had been removed.

The cooled, aqueous residue was extracted twice with 100 ml. of ether. The ether was added to the manganese dioxide. The aqueous portion was treated with 100 g. of 40% sulfuric acid (by wt.). The colorless product was collected, washed with 100 ml. of water, and dried at 60°; yield 35.8 g. (65.5%), m.p. 183–186.5°. The product was recrystallized from ethylene dichloride; yield 30.5 g. (55.8%), m.p. 187.5–188.5°; Literature m.p. 186–187°.[2]

A total of 4.5 g. of 2,6-dimethoxytoluene was recovered from the manganese dioxide by ether extraction. The yield of acid is based on the starting material actually consumed.

Anal. Calc'd for $C_9H_{10}O_4$: Neut. equiv., 182.2. Found: 183.4.

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(2) Cartwright, Jones, and Marmion, *J. Chem. Soc.*, 3499 (1952).

(2a) While reading proof, it came to our attention that γ-resorcylic acid was now available in this country (Aldrich Chemical Co., Milwaukee, Wis.)

(3) Sold by Coalite and Chemical Products, Ltd., Bolsover, near Chesterfield, England.

(4) Melting points and boiling points are uncorrected.

(5) Bauer-Benedikt and Punzengruber, *Monatsh.*, **81**, 772 (1950).

(6) Mitter and Biswas, *J. Indian Chem. Soc.*, **7**, 839 (1930).

(7) Shibata, *J. Pharm. Soc. Japan*, **59**, 111 (1939).

Chain Scission in the Oxidation of Hevea. III. Effect of Temperature[1]

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When molecular oxygen reacts with raw hevea rubber in latex at 90°, two molecules of carbon dioxide and two of "volatile acid" (one each of acetic and formic) are produced for each apparent scission of the hydrocarbon chain, estimated from solution viscosity changes. This corresponds to the complete destruction of one isoprene unit, and if the severed hydrocarbon end-groups are oxidized, requires a minimum of six molecules of oxygen per scission.[2] Estimates of oxygen requirements for scission during accelerated oxidation of vulcanized hevea much lower than this have been made.[3] It has been suggested the apparent high efficiency of scission in vulcanized rubber is the result of the predominance of scission at crosslinks over random cutting of the hydrocarbon chain.[4,2] To investigate the less likely

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(1) Contribution No. 150 from this Laboratory.

(2) Bevilacqua, *J. Am. Chem. Soc.*, **77**, 5396 (1955).

(3) Tobolsky, Metz, and Mesrobian, *J. Am. Chem. Soc.*, **72**, 1942 (1950); *cf.* also Baxter, Potts, and Vodden, *Ind. Eng. Chem.*, **47**, 1481 (1955).

(4) Bueche, *J. Chem. Physics*, **21**, 614 (1953); Berry and Watson, *J. Polymer Sci.*, **18**, 201 (1955).