nitrobenzene. Duplicate determinations differed by 5 to 13% but the intensities are assigned an uncertainty of ±20% because of difficulties inherent in the integrations. The spectral slit width at 2280 cm.$^{-1}$ was 8 cm.$^{-1}$.

**Acknowledgment.**—The authors are deeply indebted to the Sloan-Kettering Institute for the mass spectrometric deuterium analyses which were kindly carried out by Mr. Milton Heffler under the supervision of Dr. D. K. Fukushima and Dr. T. F. Gallagher.

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## Reactions of Anisic Acid and Ethyl Anisate in 100% Sulfuric Acid

BY ARTHUR BRADLEY

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Anisic acid (I) has been described as "the first aromatic acid without an *ortho*-substituent which exhibits acylization" in 100% sulfuric acid.[1] This statement was based on (a) the high "*i*" factor observed in this solvent (3.38), and (b) the fact that a solution of I in sulfuric acid gave 15% ethyl anisate on pouring into cold ethanol.

Since in theory an acid undergoing acylization would be expected to have an "*i*" factor of 4.0 and give nearly a quantitative yield of ester in (b) above,[2] Kuhn and Corwin[1] suggested that the acylcarbonium ion was partially removed as the anisyl sulfate, equation 1. This substance would be expected to react with an alcohol to give I, equation 2.

$$CH_3OC_6H_5CO^+ + HSO_4^- \rightleftarrows CH_3OC_6H_5COOSO_3H \quad (1)$$

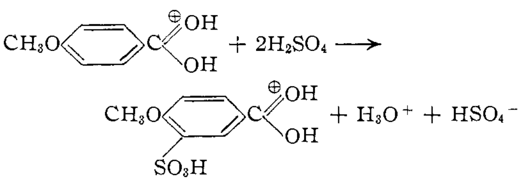
$$CH_3OC_6H_5COOSO_3H + ROH \longrightarrow CH_3OC_6H_5COOH + ROSO_3H \quad (2)$$

It also was implied that the benzoyl and acetyl cations, formed by acylization of certain of their esters, entered similarly into covalent bonds with bisulfate. The predicted "*i*" factor of a completely ionized ester of one of these acids (anisic, benzoic, acetic) would then be 4.0 or above, equation 3. This theory has been incorporated into a treatise on the behavior of organic compounds in sulfuric acid.[3]

$$RO{-}CO{-}R' + 2H_2SO_4 \rightleftarrows ROSO_3H + H_3O^+ + RCO{-}OSO_3H + HSO_4^- \quad (3)$$

It has been shown recently[4] that in sulfuric acid, complete cleavage of acetic and non *ortho*-substituted benzoic esters consistently gave three particles ("*i*" = 3.0). Since this precludes acyl sulfate formation, it was felt that re-evaluation of the experimental observations that led to this theory might be possible. This has been accomplished, and the suggestion that anisate esters yield anisyl sulfate[1] may be considered unwarranted.

Newman and Deno[5] had reported that the "*i*" factor of I increased on standing to 3.8, whereupon it could no longer be recovered by quenching the acid and extracting with ether. They attributed the change of "*i*" factor to slow sulfonation, equation 4.

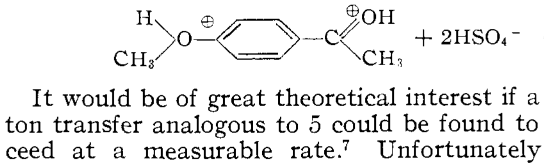


(4)

In repeating this work we found that the "*i*" factor of I as first measured was nearly 3.0, increasing to a fairly stable value of 3.9 after four hours at 50°. Percentage recoveries of I from sulfuric acid solutions at this temperature showed a large drop in the first hour, and then a slow decrease to zero (Table I). Esters of anisic acid have been shown to undergo cleavage to I at a rapid rate.[1,6] In this investigation trichloroethyl anisate gave 80% of I after two minutes. The yields of acid from II showed an early maximum followed by a gradual decline.

In order to obtain a better understanding of the behavior of I and II in 100% sulfuric acid, many "*i*" factor measurements at short intervals at approximately 10° were made (Fig. 1). At this temperature both sulfonation and cleavage are slow, and it is unlikely that either or both of these reactions could completely account for the observed rapid increase of "*i*" factors. A cryoscopic run on I at 10° was interrupted after 90 minutes ("*i*" = 3.1) and the contents thrown on ice, whereupon 63% of the acid was recovered. Since quantitative recoveries are never obtained,[1] less than 37%, and probably no more than 20% (*i.e.*, "*i*" = 2.4) of the acid had sulfonated. Similarly, the "*i*" factor of II observed after 60 minutes at 10° (3.0) is considerably higher than predicted by 9% cleavage (Table I), even if accompanied by some sulfonation. Evidently another effect contributes to the high "*i*" factor.

The possibility that multiple protonation accounted for the unexpectedly high "*i*" factors in the early stages of the reactions of I and II was considered. It was found that *p*-dimethoxybenzene and *p*-methoxyacetophenone (III) both gave initial values of about 3.0 (Fig. 2). The latter compound (III) was stable indefinitely in 100% sulfuric acid at 10°, and was recovered unchanged in good yield (66%) after one hour at 25°. Since III undoubtedly dissolved as the diprotonated ion (equation 5), it is surprising that both I and II were initially only monoprotonated.



(5)

It would be of great theoretical interest if a proton transfer analogous to 5 could be found to proceed at a measurable rate.[7] Unfortunately the addition of a second proton to anisic acid or ethyl anisate is difficult to establish, and if it occurs is too

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(1) L. P. Kuhn and A. H. Corwin, THIS JOURNAL, **70**, 3370 (1948).

(2) M. S. Newman, *ibid.*, **63**, 2431 (1941).

(3) L. F. Audrieth and J. Kleinberg, "Non-Aqueous Solvents," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 186.

(4) A. Bradley and M. E. Hill, THIS JOURNAL, **77**, 1575 (1955).

(5) M. S. Newman and N. Deno, *ibid.*, **73**, 3644 (1951).

(6) L. P. Kuhn, *ibid.*, **71**, 1575 (1949).

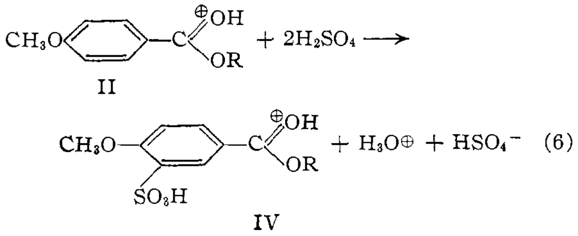
(7) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, New York, 1953, p. 11.

complicated by side reactions to permit a profitable kinetic study.

The quantitative conversion of mesitoic acid to methyl mesitoate by pouring its sulfuric acid solution into cold methanol[2] has been accepted as proof of its complete acylization. However, the preparation of II from I in 15% yield (as in b, first paragraph) does not constitute proof that it existed as the acyl cation to that extent. In this investigation the same experiment carried out with benzoic acid gave as high as 23% ester. Benzoic acid does not undergo significant acylization ("$i$" = 2.0), and it is therefore presumed that under these conditions of high acidity, great excess of alcohol, and intense local heating, any carboxylic acid might be expected to yield some ester.

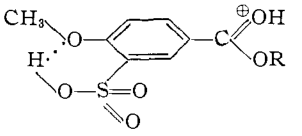
In conclusion, the following interpretation of the behavior of I in 100% sulfuric acid may be advanced: (1) initial protonation of the carboxyl group was very fast; (2) in the first three hours at 10° (and much faster at room temperature) the sulfonation reaction and possibly the addition of a second proton caused a rapid increase in $i$-factor.

The reaction of II was complicated by the fact that sulfonation and cleavage were competing for the monoprotonated ester. The observation that I reached its theoretical limit of four particles (equation 4) rapidly whereas II did not increase above 4.5 in 24 hours indicates that considerable sulfonation of the ester to IV occurred, equation 6.



The value of $i$ = 4.5 lies between that for rapid sulfonation (4.0) and complete cleavage (5.0, including sulfonation of I produced), and it may be estimated therefore that these reactions took place at comparable rates. Like other negatively substituted esters,[4] IV would be cleaved only with great difficulty.

Neither the sulfonated acid or ester are considered susceptible to multiple protonation. This is reasonable considering that an $o$-sulfonic acid group is in excellent position to form an intramolecular hydrogen bond in either case.



R = H, $C_2H_5$

Isopropyl benzoate has been found to undergo rapid cleavage to benzoic acid, presumably by an initial protonation followed by alkyl–oxygen fission.[4,6] The first step in this sequence now has been verified by extrapolating the freezing point data at 10° (Fig. 2) back to zero time, where "$i$" = 2.0.

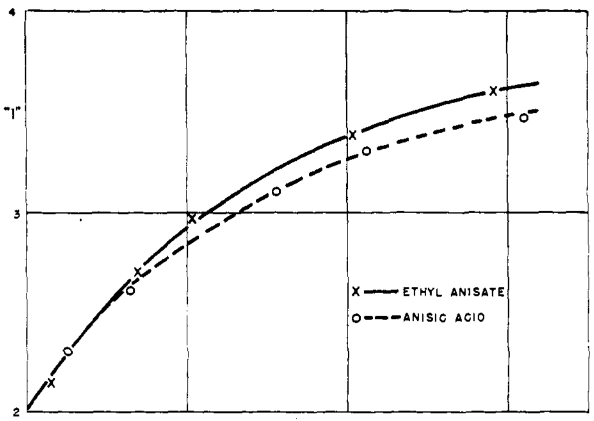


FIG. 1.

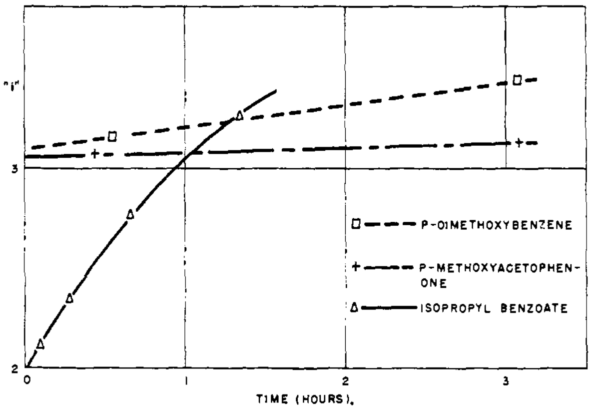


Fig. 2.

TABLE I

PERCENTAGE RECOVERY OF ORGANIC ACID FROM 100% SULFURIC ACID SOLUTION

| Temp., °C. | | Time intervals 2 min. | 15 min. | 1 hr. | 3 hr. | 7 hr. |
|---|---|---|---|---|---|---|
| 25 | Anisic acid (I) | 85[1] | 67 | 23 | 10 | 1 |
| | Ethyl anisate (II) | 6 | 10[a] | 19 | 8 | 1 |
| | Trichloroethyl anisate | 80 | 79 | | | |
| 10 | Anisic acid (I) | | | 70 | 37 | 15 |
| | Ethyl anisate (II) | | | 9 | 15 | 11 |
| | Isopropyl benzoate | | 14 | 50 | | |

[a] After 30 minutes at 25°, 16% anisic acid was obtained.

## Experimental

**Materials.**—Trichloroethyl anisate, m.p. 46°,[8] was kindly supplied by Mr. M. E. Hill, of this Laboratory. Ethyl anisate, anisic acid, $p$-methoxyacetophenone (recrystallized from ether–petroleum ether), $p$-dimethoxybenzene and isopropyl benzoate were carefully dried commercial C.P. reagents. The solvent for both hydrolysis experiments and freezing point determinations was 100% sulfuric acid prepared by the method previously described.[9]

**Freezing Point Measurements.**—The cryoscopic method and equations have been discussed elsewhere.[4,9] It was possible to take freezing point measurements in five to ten minutes by cooling the apparatus to just below the freezing point in an ice-bath before placing it in the air jacket, connecting the stirrer, and seeding with Dry Ice. After each measurement the vessel was again removed from the air jacket and the contents thawed by rapid manual stirring. When the last crystal had disappeared (and the tempera-

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(8) M. E. Hill, THIS JOURNAL, **76**, 2329 (1954).

(9) M. S. Newman, H. G. Kuivila and A. B. Garrett, *ibid.*, **67**, 704 (1945).

ture began to rise above 10°) the cycle could be repeated. In this way the values plotted in Figs. 1 and 2 were obtained.

In one experiment 0.556 g. of anisic acid in 50.0 ml. of 99.9% sulfuric acid (a typical freezing point solution) was poured onto ice after 90 minutes at approximately 10°. The precipitated anisic acid was filtered, washed with water and dried under vacuum. It weighed 0.349 g. (63% recovery).

**Hydrolysis of Ethyl Anisate.**—In a typical experiment, 0.761 g. (0.00458 mole) of II was added to 10.0 ml. of 100% sulfuric acid at 10°. The solution warmed rapidly on stirring, and was poured onto ice after 15 minutes at 25°. The precipitate was recrystallized from ether-petroleum ether, and identified as anisic acid, m.p. 181–183°. It weighed 0.070 g. (0.00046 mole, 10%).

**Recovery of *p*-Methoxyacetophenone (III) from Sulfuric Acid.**—A solution of 0.643 g. of III in 100% sulfuric acid was maintained at 25° for one hour and poured onto ice. The solid material, after recrystallization from ether-petroleum ether, had a m.p. and mixed m.p. with III of 37–38°. It weighed 0.423 g. (66% recovery). The same experiment carried out with *p*-dimethoxybenzene failed to yield any water-insoluble material.

**Esterification of Benzoic Acid.**—A solution of 2.23 g. (0.0183 mole) of benzoic acid in 10.0 ml. of 100% sulfuric acid was allowed to stand at room temperature for one hour and then poured into 50 cc. of cold (−5°) methanol. Water (100 cc.) was added and the mixture extracted with 100 cc. of ether, which was washed with dilute base and water, and evaporated to 1 cc. The remaining solvent was removed under vacuum, leaving 0.58 g. of methyl benzoate, $n^{30}\text{D}$ 1.5126. The yield was 0.0043 mole, or 23%. An authentic sample of methyl benzoate gave $n^{30}\text{D}$ 1.5129.

TABLE II

FREEZING POINT DATA

| Time, 25° | Molality | F.p., °C. | $\Delta\theta$ | $i$ |
|---|---|---|---|---|
| | Anisic acid (I) | | | |
| | None | 9.904 | | |
| [a] | 0.1931 (1.430 g.) | 8.156 | 1.738 | 2.83 |
| 4 hr. | | 7.514 | 2.390 | 3.91 |
| 24 hr. | | 7.474 | 2.430 | 3.99 |
| | Ethyl anisate (II) | | | |
| | None | 9.735 | | |
| [a] | 0.0628 (0.950 g.) | 8.734 | 1.001 | 2.69 |
| 1 hr. | | 8.565 | 1.170 | 3.15 |
| 3 hr. | | 8.263 | 1.472 | 3.96 |
| 24 hr. | | 8.092 | 1.643 | 4.43 |

[a] Approximately 30 minutes at 10–15°.

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# Fate of the Carboxyl Group in the Conversion of Furoic Acid to Mucobromic Acid

BY WALTER J. GENSLER, ELLI SMAKULA AND AARON L. BLUHM

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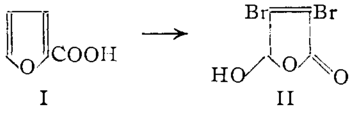
Bromine water oxidizes furoic acid (I) to mucobromic acid (II) and carbon dioxide.[1,2] *A priori*, the carbon dioxide could come either from the carboxyl group or from the 5-position of the furoic acid. Wasserman and his co-workers,[3] in their study of the conversion of 4-chlorofuroic acid to mucochlorobromic acid, showed that the carbon dioxide originates in the carboxyl group. We wish to report direct evidence corroborating this finding.

Furoic acid carrying C-14 in the carboxyl group[4] was treated with bromine and water to form mucobromic acid. It was found that this mucobromic acid showed no activity, whereas the carbon dioxide evolved (and collected as barium carbonate) did show activity. It follows, accordingly, that all four carbon atoms of mucobromic acid—and presumably of the other mucohalic acids—must come from the ring carbons of furoic acid, while the carbon dioxide comes from the carboxyl group.



I II

## Experimental

The preparation of mucobromic acid was based on published directions[1] modified, after considerable experimentation, to fit our needs. The procedure of Johnson[5] offered but little advantage. Carboxyl-labeled furoic acid,[4] m.p. 133° (cor.), assaying at 0.245 millicurie of C-14 per mole, was used as the starting material. The acid was prepared by carbonating furyllithium with radioactive carbon dioxide.[4]

Into a 25-ml. round-bottomed flask was placed 61.8 mg. of the labeled furoic acid, and then 0.62 ml. of water followed by 0.13 ml. of bromine. The flask under a water-cooled condenser and containing a small boiling chip (carborundum) was placed in an oil-bath at 80°. The temperature was raised rapidly to 110° and held at this point until bubbles no longer formed on the boiling chip (*ca.* four minutes). The condenser was removed, a fresh chip was added to the reaction mixture, and the temperature of the bath was brought to 125°. Evaporation was allowed to continue for ten minutes at this temperature and for another ten minutes as the bath temperature dropped to 95°. Cooling and seeding at this point gave a mass of white crystals. After adding 0.6 ml. of water, the crystals were dissolved by warming the mixture on the steam-bath. The hot yellow solution was suction filtered through a preheated funnel (glass nail type), and the funnel and flask were rinsed with approximately 0.4 ml. of hot water. The combined filtrates were cooled to ice-bath temperature and the crystals collected by filtration. The white product was washed with 0.5 ml. of ice-water, sucked on the funnel for one-half hour, and finally dried *in vacuo* at 80° for two hours. White crystalline mucobromic acid (a small amount of discolored crystals was discarded), weighing 79.3 mg. (63%) and melting at 121.4–121.8°, was obtained.

A sample of mucobromic acid, m.p. 120.8–121.3°, prepared in an analogous manner from unlabeled furoic acid, was analyzed.

*Anal.* Calcd. for $C_4H_2O_3Br_2$: C, 18.6; H, 0.8; Br, 62.2. Found[6]: C, 18.7; H, 0.9; Br, 62.2.

Activity measurements were made with a Tracerlab flow counter. No increase in the background count was observed when a sample of the mucobromic acid from the radioactive furoic acid was bound on a small shallow dish with a minimal amount of lacquer and was placed in the counter. Further check was obtained by burning the compound in a standard combustion train. After removing water vapor in an absorption tube, the carbon dioxide was precipitated and collected as barium carbonate.[7] The barium carbonate again gave no counts over background.

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[1] *Cf.* O. R. Jackson and H. B. Hill, *Ber.*, **11**, 1671 (1878); *Am. Chem. J.*, **3**, 33 (1881).

[2] A complete summary of the literature is given in "The Furans," by A. P. Dunlop and F. N. Peters, Am. Chem. Soc. Monograph Series No. 119, Reinhold Publishing Corp., New York, N. Y., 1953.

[3] H. H. Wasserman, F. M. Precopio and Tien-Chuan Liu, THIS JOURNAL, **75**, 2527 (1953).

[4] *Cf.* W. J. Gensler and G. L. McLeod, Abstracts Am. Chem. Soc. Meeting, Sept., 1954, p. 88-0.

[5] J. R. Johnson, "Preparation of Nitro Compounds," Report to Division B, National Defense Research Committee of Office of Scientific Research and Development, Serial No. 98, September 15, 1941.

[6] Analysis by Carol K. Fitz, Ph.D., 115 Lexington Avenue, Needham Heights 94, Mass.

[7] The weights of water and barium carbonate from the mucobromic acid corresponded to a hydrogen content of 0.7% and a carbon content of 19.4%.