[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

THE ADDITION OF BISULFITE TO UNSATURATED ACIDS AND THEIR DERIVATIVES

REMSEN TEN EYCK SCHENCK AND ISIDORE DANISHEFSKY[1]

Received April 12, 1951

The addition of bisulfites to α,β-unsaturated acids is by no means a new reaction: it has, in fact, been known since 1871 (1). These early investigations did not include any effort to establish the mechanism, but were merely observations that the reaction took place. Furthermore, in only one instance was there any attempt to determine the orientation of the resulting sulfoacid (2), and even here, while the structure assigned has been found correct, the evidence on which it was originally based can hardly be considered conclusive. No reports have been located of additions to acids having a double bond more remote from the carboxyl.

A profound difference has been observed between α,β-unsaturated acids and those with the double bond further removed from the carboxyl group, with respect to their behavior with bisulfites. The latter show, qualitatively at least, much the same characteristics as simple olefins, in that they react rather slowly, require more than catalytic quantities of oxidizing agents before addition will occur at all, and are incapable of giving quantitative yields on a basis of bisulfite consumed. While oxidants are necessary, only very small amounts are required: the addition could not be entirely prevented by any attainable means, though evacuation to very low pressures with thorough degassing and addition of an excess of antioxidant did succeed in reducing it to a low value (see Table I). The chain-lengths under such conditions are phenomenal. When the double bond occupies the *omega*-position in the chain, the entering sulfonic acid group becomes attached to the terminal carbon atom, a result consistent with previous observations on the products of free-radical additions.

The results of adding bisulfite to a solution of a salt of an α,β-unsaturated acid are strikingly different. Reaction begins at once, and is rapid, as attested by the rise of temperature. It is complete within a relatively few minutes, with essentially quantitative conversion to the sulfoacid. There is no dependence whatever on oxygen, since the addition is neither speeded up by increasing its availability nor slowed by high vacuum or antioxidants. The air-oxidation of bisulfite can not be completely suppressed, and this appears to be the only factor preventing complete utilization of the bisulfite in sulfoacid formation.

In one respect there is a close parallel between the additions to α,β- and to more-remotely-situated double bonds: in both cases the reacting species is bisulfite ion itself. This has been established for the free-radical mechanism by Kharasch and co-workers (3, 4, 5); the corresponding data for the ionic reaction appear

---

[1] This paper is based upon a part of the thesis submitted by Isidore Danishefsky to the Graduate Faculty of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

in Table II. It will be seen here, that addition is most complete in mixtures made up of equivalent amounts of sodium bisulfite and the sodium carboxylate, and most rapid in the *p*H range where bisulfite ion is at its maximum concentration.

TABLE I

EFFECT OF OXYGEN TENSION ON THE ADDITION OF BISULFITE TO AMMONIUM VINYLACETATE[a]

OXYGEN TENSION, MM. Hg	TIME,[d] HOURS	% BISULFITE DISAPPEARED	% BISULFITE CONVERTED TO SULFONATE
758	24	96	66
154	28	96	80
15	32	94	86
8	48	90	88
1×10^{-4}	72	32	31
2×10^{-5}	48	24	24
1×10^{-5}	96	18	18
1×10^{-4}	72	12	12[b]
6×10^{-3}	48	24	24[c]
1×10^{-5}	96	4	4[c]

[a] The data herein tabulated have been selected from a group of some forty experiments to illustrate the effect of oxidants and antioxidants on the extent to which bisulfite is consumed and the efficiency with which it is converted to the sulfonate.

[b] In the presence of 10 mole-% hydroquinone.

[c] In the presence of 1 mole-% *p-tert*-butylcatechol.

[d] It is not to be assumed that the times indicated are the minimum requisite times for the reaction.

TABLE II

EFFECT OF HYDROGEN ION CONCENTRATION ON THE ADDITION TO SODIUM CROTONATE[a]

MOLES SULFITE	MOLES CROTONATE	*p*H		% SULFITE CONVERTED TO SULFONATE
		Initial	Final	
0.0714	0.1116	1.9	2.0	9[b]
.0841	.1011	3.8	9.6	66
.0840	.1204	4.6	9.6	88
.0872	.1204	5.7	9.2	98[c]
.0785	.1302	7.1	11.0	47
.0841	.1020	8.9	11.1	9
.0395	.1012	10.8	11.0	2[d]

[a] Similar results were obtained with sodium acrylate.

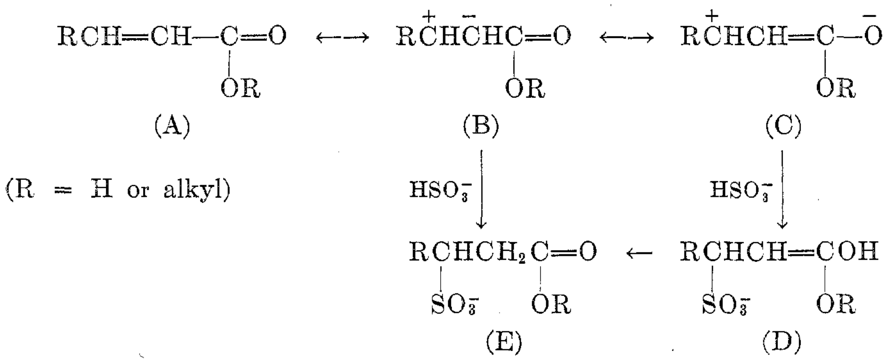
[b] Sodium bisulfite and crotonic acid.

[c] Sodium bisulfite and sodium crotonate.

[d] Sodium sulfite and sodium crotonate.

Only those acids, then, wherein one or more carbon atoms isolate the double bond from the carboxyl group may be classified with simple olefins as substances reacting with bisulfite *via* an oxygen-catalyzed free-radical mechanism. The α,β-

somers add by a more rapid, presumably ionic route, which may be represented schematically as follows:



Similar structures may be written for nitriles. The mechanism may be postulated either in terms of an electron shift induced by the adjacent carboxyl, with the bisulfite adding to the resulting polarized double bond as in structure (B), or as a 1,4-addition to a conjugated system *via* an intermediate of structure (D). The evidence thus far available does not permit a decision between the alternatives, since both the β-orientation of the entering sulfonic acid group and the fact that both esters and nitriles react in the same manner as the salts can be explained equally well by either mechanism.

EXPERIMENTAL[2]

Materials. Crotonic acid was obtained through the courtesy of the Tennessee-Eastman Corporation. It was recrystallized from water before using. Acrylic acid and methyl acrylate were supplied by Rohm and Haas Co. The former was in the form of a 60% aqueous solution stabilized by 1% di-*beta*-naphthol and 0.25% hydroquinone. When the pure acid was desired, the aqueous solution was extracted with ethylene dichloride, the solvent distilled, and the free acid distilled *in vacuo* at 53–56°/24 mm. Methyl acrylate was purified by washing with dilute NaOH to remove the hydroquinone used as a stabilizer, and distilling at 79–80°. Acrylonitrile was obtained through the courtesy of the American Cyanamid Company. Merck's Reagent $NaHSO_3$ and Na_2SO_3 were used. Vinylacetic acid was obtained by hydrolysis of the nitrile (6), which was prepared according to the directions in Organic Syntheses (7) from allyl bromide and cuprous cyanide. S-benzylisothiouronium chloride was prepared from benzyl chloride and thiourea according to the method of Donleavy (8).

General procedure and apparatus. Aqueous solutions of known quantities of the organic compound and sodium bisulfite were shaken together. The reaction vessel, filled with an atmosphere of the desired oxygen concentration, was connected to an oxygen reservoir with the gas slightly above atmospheric pressure, and allowed to stand until oxygen consumption ceased completely or was extremely slow. This insured the maintenance of a constant oxygen-concentration throughout the entire period of the reaction. By following this procedure, it was possible to mark the end of the reaction, and to determine the amount of sulfite which was oxidized to sulfate.

The solution was diluted to a definite volume and an aliquot was analyzed iodometrically for sulfite. (It was demonstrated that none of the unsaturated compounds used react with iodine or affect the titration between iodine and sodium bisulfite.) The bisulfite consumed

---

[2] New compounds are indicated by asterisks.

was thus ascertained, while from the volume of oxygen absorbed it was possible to calculate the amount of sulfite which was oxidized to sulfate. In many experiments, the quantity of unsaturated substance was determined by bromide-bromate titration. The amount of addition product isolated was always in good agreement with both the olefinic acid consumed and the bisulfite utilized (corrected for oxygen uptake).

Additions at low pressure were conducted in a device consisting of two cylindrical bulbs, each of about 40-cc. volume, sealed to a common yoke, which was in turn sealed to a high-vacuum line through a stopcock. A preformed constriction between yoke and stopcock facilitated sealing off the evacuated assembly.

Solutions of the two reactants were placed in the two bulbs, frozen in Dry Ice-acetone, and evacuated. After degassing, the yoke was sealed off at the constriction and the reaction instituted by tilting the apparatus so that all the liquid collected in one bulb.

After the mixture had stood for the requisite length of time, it was worked up by one of three methods. The elaborate manipulations were required in order to eliminate the possibility of reaction during analysis and isolation of the sulfonate.

Method I. With the entire solution contained in one of the bulbs of the evacuated assembly, the water was distilled over into the other arm until only a dry residue was left. The container was then opened and the water analyzed for SO_2. The solid residue was extracted with alcohol to remove any unreacted organic substance, and the alcohol-insoluble fraction dissolved in water and titrated for sulfite. The sum gave the amount of bisulfite which did not react. The product was then isolated in the manner described for the reactions conducted at atmospheric pressure.

Method II. The vessel was opened and the contents were poured immediately into excess cold NaOH solution. The base was used in order to convert all the unreacted bisulfite to sulfite; the latter is not capable of addition to the organic reagent during the analyses and isolations. An aliquot of the resulting solution was analyzed for sulfite by iodine titration. Analysis of another aliquot with standard bromide-bromate reagent gave a measure of the sulfite remaining plus the unreacted olefinic acid; by subtracting the value for the former determined iodometrically, the latter was indirectly calculated.

Method III. Small amounts of reactants were used (.001 mole), and when the vessel was opened, the contents were poured immediately into a measured excess of standard iodine solution. Back titration with standard thiosulfate gave the amount of unreacted sulfite.

Results by all methods were in good agreement.

When the organic reactant was methyl acrylate or acrylonitrile the procedure was modified slightly. After evacuation and degassing, the organic compound was distilled, not poured, over into the bulb containing the bisulfite solution. The bulb containing the mixture was then sealed off, instead of the entire yoke. After this had been shaken and allowed to stand for the desired length of time, it was opened and the contents were poured into cold aqueous NaOH. Unreacted ester or nitrile was extracted with ether and the aqueous layer analyzed for unreacted sulfite.

The effect of antioxidants was studied by adding 10 mole per cent of hydroquinone or one mole per cent of *p-tert.*-butylcatechol to the sulfite or bisulfite solution.

Addition of sodium bisulfite to sodium acrylate. A solution of 9.4 g. (0.10 mole) of sodium acrylate in 25 cc. of water was added to 25 cc. of 3.3040 M (0.0826 mole) $NaHSO_3$. The reaction vessel, filled with air at atmospheric pressure, was connected to oxygen as indicated in the "general procedure." In 5 minutes, the temperature had risen 12°. At the end of 24 hours, 26 cc. of oxygen (converted to N.T.P.) (0.0012 mole) had been consumed. Titration of an aliquot of the reaction mixture established that the solution contained 0.0035 mole of unreacted sulfite. This indicated that 94% of the bisulfite was converted to the sulfonate.

Two cc. of 1.8 M H_2SO_4 was added to the mixture and the solution was heated on a water bath for 15 min. The solution was then made basic to phenolphthalein, by adding aqueous NaOH, and evaporated to dryness under reduced pressure. The solid residue was extracted twice with boiling 95% alcohol to remove unreacted sodium acrylate. The remaining solid was extracted in a Soxhlet for 24 hrs. with 80% alcohol. The extract was evaporated to dryness, yielding 14.0 g. of the disodium salt of β-sulfopropionic acid. This represents a 91% recovery of the amount of sulfonate expected on the basis of the titration and the amount of oxygen consumed. Twelve grams of the sodium salt was dissolved in 300 cc. of boiling water, and 16 g. of $BaCl_2 \cdot 2H_2O$ was added to the solution. The solution was filtered while hot and allowed to cool to room temperature. The crystals were collected and the mother liquor was then concentrated to 80 cc. and a second crop was taken; yield 22.4 g.

Anal. Calc'd for $Ba(C_3H_4O_5S) \cdot 5H_2O$: H_2O, 23.73; Ba, 36.21.
Found: H_2O, 23.90; Ba, 36.38.

A solution of 2 g. of the sodium salt in 5 cc. of water was added to 4 g. of S-benzylisothiouronium chloride dissolved in 8 cc. of 10% aqueous alcohol. A white solid crystallized on cooling. This, recrystallized twice from 10% alcohol and dried over H_2SO_4 in a vacuum, melted at 152.3–152.5°.

Anal. Calc'd for $C_{19}H_{26}N_4O_5S_3$; N, 11.51. Found: N, 11.55.

Authentic α-sulfopropionic acid was synthesized from propionic acid and SO_3 according to the method of Backer and Dubsky (9). The S-benzylisothiourionium derivative*, prepared from the sodium salt, melted at 149.2–150.2°.

Anal. Calc'd for $C_{19}H_{26}N_4O_5S_3$; N, 11.51. Found: N, 11.62.

Authentic β-sulfopropionic acid. The cyclic anhydride of β-sulfopropionic acid was obtained by the method of Kharasch and Brown (10). This was converted into the disodium salt by treating with two moles of aqueous NaOH and evaporating to dryness. The S-benzylisothiouronium compound* derived from the sodium salt melted at 152.2–153.0°.

Anal. Calc'd for $C_{19}H_{26}N_4O_5S_3$; N, 11.51. Found: N, 11.39.

Identification of the acrylate addition product. The melting point of a mixture of the S-benzylisothiouronium salt of the addition product with that of the β-sulfoacid gave no depression, while a mixture of the former with the derivative of the α-isomer showed a marked depression.

Addition of bisulfite to sodium crotonate. The reaction was conducted and the product was isolated in the same manner as with sodium acrylate. The yield was 94% based on the bisulfite consumed, corrected for oxygen uptake. The salt was dried for 3 hrs. at 115° and analyzed for sodium.

Anal. Calc'd for $C_4H_6NaO_5S$: Na, 21.68. Found: Na, 21.57.

The S-benzylisothiouronium salt was prepared by the procedure previously indicated; m.p. 153.5–154.0°.

Anal. Calc'd for $C_{20}H_{28}N_4O_5S_3$: N, 11.19. Found: N, 11.08.

Authentic α-sulfobutyric acid was prepared by the method of Backer and de Boer (11). Its S-benzylisothiouronium salt* melted at 167.5–168.0°.

Anal. Calc'd for $C_{20}H_{28}N_4O_5S_3$: N, 11.19. Found: N, 11.07.

β-sulfobutyric acid was prepared according to Levene and Mileska (12). The S-benzylisothiouronium derivative* had the melting point 153.2–153.4°.

Anal. Calc'd for $C_{20}H_{28}N_4O_5S_3$: N, 11.19. Found: N, 11.26.

Identification of the crotonate addition product. The melting point of a mixture of the S-benzylisothiouronium salt of the β-sulfoacid with that of the addition product gave no depression, whereas a mixture of the latter with the derivative of the α-isomer showed a definite depression.

Addition of bisulfite to methyl acrylate. Nine grams (0.1 mole) of methyl acrylate was added to 25 cc. of 0.8600 *M* (0.0205 mole) Na_2SO_3 and 25 cc. of 2.2820 *M* (0.0570 mole) $NaHSO_3$ solutions. The reaction flask, filled with air and connected to an oxygen reservoir with the gas at slight pressure, was shaken mechanically. After 24 hrs. 66 cc. (corrected to N.T.P.) (0.0030 mole) of oxygen had been absorbed. Iodometric titration of an aliquot showed that there was 0.0210 mole of sulfite left. This indicates that out of the 0.0565 mole of sulfite which disappeared, 0.0505 mole or 90% reacted with methyl acrylate.

The solution was extracted twice with 50 cc. of ether and evaporated to dryness under reduced pressure. The solid residue was exhaustively extracted in a Soxhlet with 150 cc.

of methanol. The alcoholic extract was evaporated to dryness and the residual salt recrystallized from methanol. A yield of 12.7 g. or 90% of sulfonate was obtained. The product was dried for one hour at 110°.

Anal. Calc'd for $C_4H_7NaO_5S$: Na, 12.01. Found: Na, 11.86.

Two grams of the sodium salt was converted to the S-benzylthiouronium salt*, using 2 g. of the reagent in aqueous solution. The product melted at 129.5–130.2°.

Anal. Calc'd for $C_{12}H_{18}N_2O_5S_2$: N, 8.38. Found: N, 8.44.

Identification of the methyl acrylate addition product. A solution of 3.8 g. (0.02 mole) of the sodium salt of the sulfo ester and 0.8 g. (0.02 mole) of NaOH in 50 cc. of water was refluxed for 3 hrs. The clear solution was evaporated to dryness and the solid residue washed with alcohol. The disodium salt thus formed was converted to the S-benzylisothiouronium compound by the procedure which was followed in the preparation of the derivative of β-sulfopropionic acid. The resulting Donleavy salt had the melting point 153.0–153.8°.

Anal. Calc'd for $C_{19}H_{26}N_4O_5S_3$: N, 11.51. Found: N, 11.42.

Mixed melting point determinations of this derivative with that of authentic β-sulfopropionic acid gave no depression whereas with the derivative of α-sulfopropionic acid there was a large depression and melting over a wide range.

Addition of sodium bisulfite to acrylonitrile. Ten grams (0.19 mole) of acrylonitrile was added to 50 cc. of 3.6811 *M* (0.1841 mole) of sodium bisulfite solution. The reaction was carried out by the same procedure as that with methyl acrylate. Analysis showed that 99% of the $NaHSO_3$ had disappeared and 96% had been converted to the sulfonate. The basic solution was neutralized with H_2SO_4 and evaporated to dryness *in vacuo*. The solid residue was extracted with boiling 80% alcohol and the alcoholic solution was evaporated to dryness. The residual solid was recrystallized from 80% alcohol, giving 24.90 g. of the pure sulfonate. This corresponds to an 89% recovery.

Anal. Calc'd for $C_3H_4NaO_3S$: Na, 14.66. Found: Na, 14.48.

The S-benzylisothiouronium salt* was prepared from a water solution. It melted at 113.2–114.6°.

Anal. Calc'd for $C_{11}H_{15}N_3O_3S_2$: N, 13.94. Found: N, 13.76.

Identification of the acrylonitrile addition product. Three grams (0.01 mole) of the acrylonitrile addition product was refluxed with 100 cc. of 0.1 *M* (0.01 mole) of NaOH for 3 hrs. The solution was evaporated to dryness and the solid residue was washed with alcohol. The disodium salt was converted to the S-benzylisothiouronium derivative, which melted at 153.0–153.6°.

Anal. Calc'd for $C_{19}H_{26}N_4O_5S_3$: N, 11.51. Found: N, 11.42.

Mixed melting point determinations of this derivative with that of authentic β-sulfopropionic acid gave no depression, while with the derivative of the α-isomer there was a definite depression.

Addition of bisulfite to ammonium vinylacetate. The reaction was carried out in the same manner as the addition to sodium acrylate. After the reaction was completed, the ammonium ion was replaced by sodium, by heating with sodium hydroxide. The isolation of the product was then carried out in the manner described for the other salts. The amount of sulfonate recovered was 76%. Analysis of the product for sodium was made after it had been dried for 5 hrs. at 120°.

Anal. Calc'd for $C_4H_6NaO_5S$: Na, 21.68. Found: Na, 21.50.

The S-benzylisothiouronium salt was prepared in the same manner as that of β-sulfobutyric acid. The recrystallized product melted at 160.6–161.4°.

Anal. Calc'd for $C_{20}H_{28}N_4O_5S_3$: N, 11.19. Found: N, 11.25.

Authentic γ-sulfobutyric acid was synthesized according to the method described by Backer and Benninga (13). The S-benzylisothiouronium compound* prepared from the sodium salt melted at 160.4–161.2°.

Anal. Calc'd for $C_{20}H_{28}N_4O_5S_3$: N, 11.19. Found: N, 11.26.

Identification of the Vinylacetate Addition Product. The melting point of a mixture of the S-benzylisothiouronium salt of γ-sulfobutyric acid with that of the addition product gave no depression, while a mixture of the latter with the derivatives of the α- or β-sulfoacids showed a marked depression.

SUMMARY

The product of the addition of sodium bisulfite to salts and derivatives of α,β-unsaturated acids (specifically, salts of acrylic and crotonic acids, methyl acrylate and acrylonitrile) has been demonstrated to be the *beta*-sulfonate. The reactions have been found to be independent of oxygen concentration and antioxidants, and it is therefore believed that they proceed by an ionic mechanism.

Salts of β,γ-unsaturated acids (for example, vinylacetic acid) have been shown to react with bisulfite to yield the *gamma*-sulfonate through a free radical mechanism.

A number of new S-benzylisothiouronium salts have been prepared and characterized.

NEW YORK 3, N. Y.

REFERENCES

(1) MESSEL, *Ann.*, **157**, 15 (1871).
(2) ROSENTHAL, *Ann.*, **233**, 33 (1886).
(3) KHARASCH, MAY AND MAYO, *Chem. and Ind.*, **57**, 774 (1938).
(4) KHARASCH, MAY AND MAYO, *J. Org. Chem.*, **3**, 175 (1938).
(5) KHARASCH, SCHENCK AND MAYO, *J. Am. Chem. Soc.*, **61**, 3092 (1939).
(6) DRAKE (editor), *Organic Syntheses, Vol. XXIV*, p. 96, John Wiley and Sons, Inc., New York (1944).
(7) GILMAN AND BLATT (editors), *Organic Syntheses, Coll. Vol. I* (2nd ed.), p. 46, John Wiley and Sons, Inc., New York (1941).
(8) DONLEAVY, *J. Am. Chem. Soc.*, **58**, 1004 (1936).
(9) BACKER AND DUBSKY, *Rec. trav. chim.*, **39**, 964 (1920).
(10) KHARASCH AND BROWN, *J. Am. Chem. Soc.*, **62**, 925 (1940).
(11) BACKER AND DE BOER, *Rec. trav. chim.*, **43**, 297 (1924).
(12) LEVENE AND MILESKA, *J. Biol. Chem.*, **70**, 373, (1926).
(13) BACKER AND BENNINGA, *Rec. trav. chim.*, **55**, 605 (1936).