[CONTRIBUTION FROM THE AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

THE ESTERIFICATION OF CERTAIN NITROPHENOLS WITH METHANESULFONYL CHLORIDE

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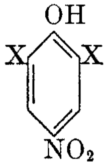
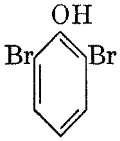
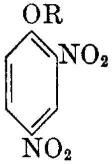
The esterification of phenolic compounds with methanesulfonyl chloride in pyridine solution apparently was first investigated by Helferich and Papalambrous (1), although *p*-toluenesulfonic esters have been prepared from phenols in this manner for several years (2–7). The present work comprises a study of the methanesulfonation of certain mononitrophenols, 2,4-dinitrophenol, and picric acid in pyridine medium. Very short reaction periods were employed in studying the esterification of the latter two substances.



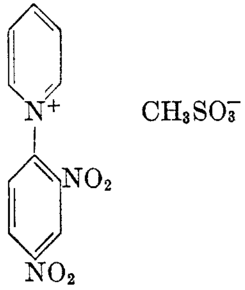
I, X = H   IV, X = I
II, X = CH_3 V, X = Cl
III, X = Br   X, X = NO_2



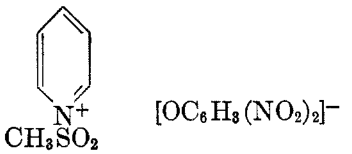
VI



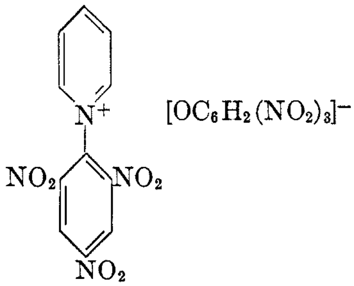
VII, R = H
VIIa, R = SO_2CH_3



VIII



IX



XI

Methanesulfonation of the mononitrophenols (I, II, III, IV) in 0.25 *molar* pyridine solution for 48 hours at approximately 5° gives virtually quantitative yields of the crude methanesulfonates. The sulfonic esters thus obtained are readily purified, colorless, well-defined crystalline solids, which are suggested as suitable derivatives for identifying the phenols in question, especially since methanesulfonyl chloride is now commercially available. *p*-Nitrophenyl methanesulfonate has been previously prepared in aqueous alkali, although the yield was not reported (8). The yield of ester from the methanesulfonation of 2,6-dichloro-4-nitrophenol (V) was lowered by the formation of a black solid, insoluble in pyridine, upon initial admixture of the reactants. 2,6-Diiodo-4-nitrophenol (IV) has very recently been reported as difficult to methylate (9), indicating that in at least one instance methanesulfonation is more facile than methylation. The activation of the nitro group *para* to the phenolic hydroxyl is not essential to the success of the reaction, since 2,6-dibromophenyl methanesulfonate is obtained in 92% yield from 2,6-dibromophenol (VI).

Attempts to extend the procedure employed with mononitrophenols to 2,4-dinitrophenol (VII) gave no yield of ester. Failure to isolate the starting phenol, or any compound soluble in organic solvents, however, indicated the possibility of ionic side reactions. Reduction of the reaction period to either three or five minutes has resulted in the isolation of yields of ester slightly in excess of 50%. This apparently is the first isolation of a 2,4-dinitrophenyl sulfonic ester from a pyridine reaction medium. No ester was isolable under the conditions employed if the reaction proceeded for one hour. The yields obtained at intermediate time intervals are listed in the Experimental. Melting points, yield data and analyses for all sulfonic esters prepared are reported in Table I.

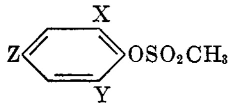
2,4-Dinitrophenyl methanesulfonate (VIIa) reacts with dry pyridine at 5° to give a pale yellow, crystalline solid which separates from the basic solution. On the basis of analysis, hygroscopic character, solubility in water, elevated melting point, and solubility in hydrochloric acid without regeneration of the water-insoluble ester over a period of several weeks, this reaction product is probably either 2,4-dinitrophenylpyridinium methanesulfonate (VIII) or methanesulfonylpyridinium 2,4-dinitrophenoxide (IX). In the author's opinion, the latter (IX) would be at least partially decomposed by strong acid to give the sparingly soluble 2,4-dinitrophenol. Since there was no evidence of the formation of 2,4-dinitrophenol when the acid solution was evaporated slowly to a small volume, 2,4-dinitrophenylpyridinium methanesulfonate (VIII) is considered the more reasonable. Regardless of the structure of the reaction product (VIII or IX), quaternization of the ester is strongly indicated as the most important side reaction resulting in no yield of ester if conventional reaction periods (12–48 hours) are employed.

The methanesulfonic esters of both *p*-nitrophenol and 2,4-dinitrophenol are readily hydrolyzed by dilute sodium hydroxide at room temperature. Neither ester is appreciably hydrolyzed at the boiling point by aqueous or alcoholic hydrochloric acid.

An attempt to esterify picric acid (X) with methanesulfonyl chloride in pyridine using a one-minute reaction period has not led to the ester. Instead, there was obtained a bright yellow solid, m.p. approximately 168°, which was not isolated in a pure state. However, upon repeated crystallization it gave a different crystalline yellow solid, m.p. 221° (dec.), for which analysis indicated the empirical formula $C_{17}H_9N_7O_{13}$. The assignment of the structure of picrylpyridinium picrate (XI) to the latter product appears reasonable in light of the previous description of the formation of this compound under a wide variety of conditions (10, 11), and especially in view of Bell's demonstration that picric acid reacts with *p*-toluenesulfonyl chloride in pyridine over a twelve-hour period to give picrylpyridinium *p*-toluenesulfonate, which upon repeated crystallization yields XI (12).

TABLE I

METHANESULFONIC ESTERS



X	Y	Z	M.P., °C.[b]	YIELD, %	FORMULA	ANALYSIS[a]			
						Calc'd		Found	
						C	H	C	H
H	H	NO_2	92–93	89	$C_7H_7NO_5S$	—	—	—	—
CH_3	CH_3	NO_2	129.5–130	95	$C_9H_{11}NO_5S$	44.07	4.52	44.21	4.44
Br	Br	NO_2	136.5–137.5	93	$C_7H_5Br_2NO_5S$	22.42	1.34	22.73	1.41
I	I	NO_2	177–178.5	96	$C_7H_5I_2NO_5S$	17.92	1.07	17.78	1.02
Cl	Cl	NO_2	90–91	34	$C_7H_5Cl_2NO_5S$	29.39	1.76	29.63	1.39
Br	Br	H	92–93	92	$C_7H_6Br_2O_3S$	25.47	1.83	25.73	1.70
H	NO_2	NO_2	83–84	54	$C_7H_6N_2O_7S$	32.06	2.31	32.13	2.07

[a] Presence of sulfur in all derivatives demonstrated qualitatively.

[b] Recrystallization from methanol, except for 2,6-diiodo-4-nitrophenyl methanesulfonate, which was recrystallized from ethyl acetate.

EXPERIMENTAL

All melting points reported are uncorrected. All analyses listed in this paper are by the Clark Microanalytical Laboratory. Methanesulfonyl chloride and phenolic compounds, except those for which methods of preparation are given in the sequel, are available from the Eastman Kodak Co.

2,6-Dimethyl-4-nitrophenol. This compound was prepared by the method of Auwers and Markovits (13).

2,6-Diiodo-4-nitrophenol. Use of the general procedure of Lal Datta and Prosad (14) necessitated considerable modification and elaboration, since these workers give very little detailed information about their procedure. *p*-Nitrophenol (20 g.) was dissolved in 200 ml. of an ammonium hydroxide solution (prepared by adding one part of water to one part of 28% conc'd aqueous ammonia) by heating on a water-bath. A solution of iodine in potassium iodide (made by dissolving 70 g. of iodine in a solution previously prepared by dissolving 50 g. of potassium iodide in 150 ml. of water) was added portionwise (10–15 ml. for each addition), with very vigorous shaking of the stoppered reaction vessel after each addition, over a period of 90 minutes. The temperature of the reaction mixture was maintained at approximately 50° during the addition of the iodine solution, and at 100° for roughly 20 minutes after the addition was completed. The reaction mixture was permitted to stand at room temperature overnight. The orange-yellow product present was collected, washed with 50 ml. of 10% potassium iodide solution, then with water until the color of the washings changed from red to yellow, and then was dried in the air overnight; yield of bright yellow material, 45 g. This product was probably the ammonium salt of 2,6-diiodo-4-nitrophenol. Recrystallization of the yellow product from 360 ml. of boiling glacial acetic acid containing 10 ml. of water gave 31 g. of cream-colored 2,6-diiodo-4-nitrophenol, m.p. 155° (dec.) [lit. (14), m.p. 157° (dec.)]. The phenol showed a marked tendency to turn yellow on the surface of the filter cake, and, after being dried at 65°, was stored in a dark container. Additional material (2.1 g.) was obtained by diluting the acetic acid mother liquor with water, giving a total yield of 33.1 g. (60%). The above conditions are not optimum conditions.

Preparation of mononitrophenyl methanesulfonates. To a solution of the nitrophenol (0.01 mole) in reagent pyridine (39 ml.), previously cooled in ice to approximately 5°, was added all at once a solution of methanesulfonyl chloride (0.02 mole; weighed quantity) in 3–4 ml. of pyridine. The reaction mixture was permitted to stand under refrigeration for 48 hours and then was poured into 400 ml. of water. The precipitated crude ester was collected, washed with water until free of a pyridine odor, and air-dried at least 48 hours. Yields, m.p.'s, solvents for recrystallization, and analyses are given in Table I.

2,4-Dinitrophenyl methanesulfonate. 2,4-Dinitrophenol (4.60 g., 0.025 mole), completely dissolved in 98 ml. of reagent pyridine by vigorous shaking and agitation of the mixture, was cooled to approximately 5° in ice. A weighed quantity of 5.75 g. of methanesulfonyl chloride (0.05 mole), dissolved in 6 ml. of pyridine just prior to the addition, was added all at once. The reaction mixture was maintained at 5° for the duration of the reaction, which was varied irregularly from 3 to 60 minutes. The reaction was stopped by pouring the reaction mixture into 800 ml. of water. The precipitated crude ester was collected immediately, washed with water, and dried in the air for 48 hours. The precipitation was quantitative, since no ester could be recovered from the aqueous mother liquor upon acidification and extraction with ethyl acetate. The yields (in %) obtained at 3, 5, 10, 15, 30, 45, and 60 minutes were 54, 53, 39, 28, 23, 4, and 0 respectively. Two crystallizations from methanol (decolorizing charcoal) gave the colorless ester (Table I).

It must be stressed that the formation of methanesulfonic ester from 2,4-dinitrophenol is very sensitive to reaction conditions. Application of the procedure immediately above to 9.2 g. of the phenol in 80 ml. of pyridine using 11.5 g. of methanesulfonyl chloride in 12 ml. of pyridine over two hours gave a 14% yield of ester, which was very difficult to purify.

Quaternization of 2,4-dinitrophenyl methanesulfonate. Pure 2,4-dinitrophenyl methanesulfonate (1 g.), m.p. 83–84°, was dissolved in 16 ml. of dry pyridine, previously cooled to 5°. A yellow color developed immediately, which changed to dark red upon standing under refrigeration for 48 hours. The pale yellow, crystalline material then present was collected and transferred immediately to a vacuum desiccator; yield after drying 6 hours, 0.97 g. After drying for seven weeks in a vacuum, there was obtained a crystalline solid, m.p. 165–166.5°. Recrystallization did not prove possible.

Anal. Calc'd for $C_{12}H_{11}N_3O_7S$: C, 42.23; H, 3.25; N, 12.32; S, 9.39.

Found: C, 42.48; H, 3.16; N, 11.85; S. 9.59.

The quaternary compound was extremely hygroscopic, very soluble in water, and dissolved completely in dilute hydrochloric acid. The acid solution stood at room temperature for about three months without separation of any solid material.

Hydrolysis experiments. Solution of 1 g. of *p*-nitrophenyl methanesulfonate or 0.5 g. of 2,4-dinitrophenyl methanesulfonate in 25 ml. of 5% aqueous sodium hydroxide for 24 hours, followed by acidification and refrigeration, gave the phenol. Solution of 0.5 g. of either ester in 25 ml. of either 6 *N* aqueous or 6 *N* alcoholic hydrochloric acid for 24 hours, followed by two hours at the boiling point, gave only unchanged ester.

Isolation of picrylpyridinium picrate from attempted methanesulfonation of picric acid. To a solution of dry picric acid (5.73 g., 0.025 mole) in 98 ml. of reagent pyridine at a temperature of approximately 5° was added a weighed quantity (5.75 g., 0.05 mole) of methanesulfonyl chloride in 6 ml. of pyridine. The reaction mixture developed a deep red color and after exactly one minute was poured into 800 ml. of water. The aqueous solution remained clear for a few minutes, but upon vigorous stirring deposited a bright yellow, crystalline product; yield 3.41 g., m.p. approximately 168°. Washing with 600 ml. of water at room temperature, then with 100 ml. of boiling water, then with 100 ml. of anhydrous ethyl acetate gave a product melting over 200°. This product dissolved slowly in boiling acetone with a red coloration, and was treated with decolorizing charcoal. Addition of water with refrigeration of the resulting solution caused the crystallization of bright yellow plates, which upon recrystallization gave pure picrylpyridinium picrate, m.p., in bath preheated to 190°, 221° (dec.) [lit. m.p.'s, 223° (10), 226° (11), 222° (12)].

Anal. Calc'd for $C_{17}H_9N_7O_{13}$: C, 39.32; H, 1.75; N, 18.88.
Found: C, 39.93; H, 1.83; N, 18.67.

SUMMARY

1. The preparation of *p*-nitrophenyl methanesulfonate and certain 2,6-disubstituted-4-nitrophenyl methanesulfonates in pyridine is described.
2. The isolation of 2,4-dinitrophenyl methanesulfonate by interaction of methanesulfonyl chloride and 2,4-dinitrophenol in pyridine is possible only when a very short reaction period is employed.
3. 2,4-Dinitrophenyl methanesulfonate undergoes quaternization in dry pyridine to give a crystalline quaternary compound, probably 2,4-dinitrophenylpyridinium methanesulfonate.
4. The attempted esterification of picric acid in pyridine has led only to the isolation of picrylpyridinium picrate.

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