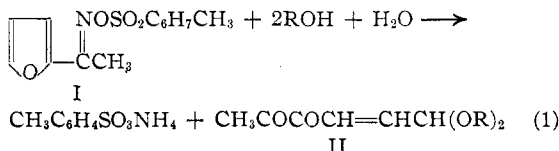


[CONTRIBUTION FROM THE ORGANIC CHEMICAL INSTITUTE OF THE HUNGARIAN UNIVERSITY, "BOLYAI" OF RUMANIA]

Studies on Furan Compounds. IV. Reactions of the *p*-Toluenesulfonyl Derivatives of Several Furylketoximes with Alcohols

BY L. VARGHA AND F. GÖNCZY

It was demonstrated by previous work¹ that the action of methanol and ethanol, respectively, upon the *p*-toluenesulfonyl ester of 2-acetylfuranoxime (I) results in the production of ammonium *p*-toluenesulfonate and the acetal of 4,5-diketo-2-hexenal (II).

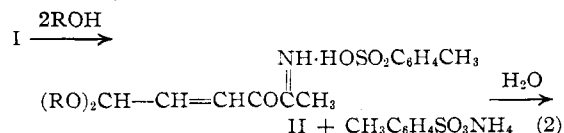


It was further shown² that the *p*-toluenesulfonyl ester of 2-acetylbenzofuranoxime reacts in the first phase in a similar way; the resulting unstable *o*-quinonoid acetal, however, undergoes hydrolysis and rearrangement to yield 3-hydroxy-2-methylchromone.

Since the conversions mentioned above seemed to be interesting from the preparative as well as the theoretical point of view, we carried out analogous experiments with other furan derivatives. Though our expectations, from the preparative point of view, could not be realized because of the unforeseen course of the reactions, the results might afford a basis for theoretical considerations.

We first studied the influence of the ester groups on the reaction represented by scheme 1. Since, according to our experiments, 2-acetylfuran and its oxime are stable toward alcohols, the reaction was made possible by the presence of the *p*-toluenesulfonyl group. The corresponding benzoyl and trichloroacetyl derivatives of 2-acetylfuranoxime did not react even in boiling alcohol, though trichloroacetic acid is a stronger acid than *p*-toluenesulfonic acid. In another experiment we tried to establish whether I was attacked primarily by water or by alcohol. While the substance proved to be quite stable toward water, the reaction took place even in absolute alcohol. It was not possible to isolate an intermediate.

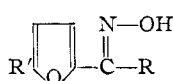
These facts make it seem probable that the primary attack is effected by the alcohol, perhaps according to scheme 2.



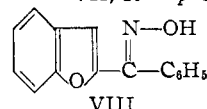
At present, however, we are unable to explain the origin of the water, necessary in a stoichiometrical

proportion, when the conversion is carried out in absolute alcohol.

In the course of our further work the toluenesulfonyl derivatives of the following furyl ketoximes were examined: 2-propionyl- (III), 2-hydroxyacetyl- (IV), 5-methyl-2-acetyl- (V), 2-benzoyl- (VI), 2-*p*-methoxybenzoylfuranoxime (VII) and 2-benzoylbenzofuranoxime (VIII).



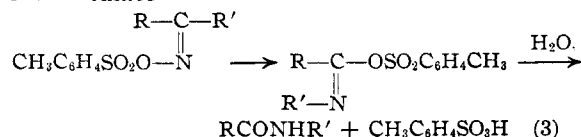
III, R = C₂H₅, R' = H
IV, R = CH₂OH, R' = H
V, R = CH₃, R' = CH₃
VI, R = C₆H₅, R' = H
VII, R = *p*-CH₃OC₆H₄, R' = H



The corresponding ketones have been described previously in the literature, the oximes and esters being new. The *p*-toluenesulfonyl esters of the two furfuraloximes (*syn* and *anti*) could not be obtained. When treated with *p*-toluenesulfonyl chloride in pyridine, or in aqueous alkaline solution, these oximes yielded furonitrile and *p*-toluenesulfonic acid.

The esters mentioned above, except IV, showed a diminished reactivity toward alcohols. They underwent change only at elevated temperature, even V being recovered almost quantitatively after forty-eight hours of boiling. The reactions took place in two different ways. Compound III yielded ammonium *p*-toluenesulfonate and some 2-propionylfuran after twenty hours of boiling in 95% alcohol. The expected unsaturated acetal (CH₃CH₂COCOCH=CHCH(OR)₂), probably owing to its sensitivity, could not be obtained. In spite of this fact the formation of ammonium *p*-toluenesulfonate indicates that the reaction took place according to scheme 2. Compound IV reacted in the same way as III, also at room temperature; to our surprise, however, we obtained, in addition to *p*-toluenesulfonate, II instead of the hydroxyl derivative of II (HOCH₂COCOCH=CHCH(OR)₂). We cannot explain at present the substitution of a hydroxyl group by hydrogen under the conditions in which the reaction was carried out.

Compounds VI, VII and VIII reacted with alcohol in a different way, involving a Beckmann rearrangement and subsequent hydrolysis of the intermediate



(1) Vargha, Ramonczai and Bite, *THIS JOURNAL*, **70**, 371 (1948).

(2) Vargha, Ramonczai and Báthory, *ibid.*, **71**, 2652 (1949).

Thus VI yielded furanilide,³ VII *p*-methoxyfuranilide (previously unknown) and VIII benzfuranilide.⁴ The formation of these anilides indicates, according to Meisenheimer's rule,⁵ the *syn* configuration of the oximes with respect to the furan ring.

In conclusion we may say that the reactions of the *p*-toluenesulfonyl derivatives of the aliphatic furyl ketoximes with alcohols seem to take place according to scheme 1, those of the aromatic furyl ketoximes according to scheme 3. The preparative exploitation of the reactions, represented by scheme 1, failed because of the sensitivity of the resulting substances and the difficulties encountered in preparing other furan compounds suitable for similar conversions.

Experimental

Action of Water and Alcohol on *p*-Toluenesulfonyl-2-acetylfuranoxime (I).¹—(1) Two grams of I, dissolved in 20 cc. of pure ether, was shaken with 10 cc. of water for fifty hours at room temperature. After the ethereal layer had been separated, dried and evaporated, the solid residue was recrystallized from benzene by adding petroleum ether (b. p., 50–60°); yield, 1.6 g.; melting point and mixed melting point with I, 80°.

(2) Into a tube, constricted in the middle and containing 1 g. of I, 5 cc. of absolute ethanol was distilled from sodium metal with careful exclusion of air moisture, and the tube immediately sealed. After seven days the crystals were collected on a filter and washed with absolute ethanol. They proved to be ammonium *p*-toluenesulfonate. The filtrate was evaporated *in vacuo*, and an aqueous solution of hydroxylamine hydrochloride was added to the oily residue. The oxime soon precipitated from the solution and was recrystallized from water; melting point and mixed melting point with an authentic sample of 4,5-diketo-2-hexenaldoxime,¹ 235°.

Trichloroacetyl-2-acetylfuranoxime.—A solution of trichloroacetyl chloride (9 g.) in 10 cc. of pyridine was gradually added, with stirring, to a solution of 2-acetylfuranoxime¹ (6.25 g.) in a mixture of chloroform (25 cc.) and pyridine (5 cc.) at –10°. After being allowed to stand at room temperature for thirty minutes, the reaction mixture was poured into ice water. The chloroform layer was washed with water and dried with anhydrous sodium sulfate. The substance, obtained after evaporation of the chloroform *in vacuo*, was recrystallized from benzene; m. p., 98°; yield, 54%.

Anal. Calcd. for C₇H₅O₃NCl₃: N, 5.17; Cl, 39.32. Found: N, 5.16; Cl, 39.45.

The substance (2 g.) did not change after fourteen days of standing in 95% alcohol (20 cc.) at 35°. Also benzoyl-2-acetylfuranoxime⁶ (5 g.) remained unchanged in 95% alcohol (25 cc.) after being boiled for seven hours.

General Procedure for the Preparation of the Oximes.—A mixture of ketone (0.1 mole), hydroxylamine hydrochloride (0.1 mole + 20% excess), sodium acetate (0.1 mole + 20% excess) and 80 cc. of 95% alcohol was refluxed for five hours. The hot solution was filtered from precipitated sodium chloride, and the filtrate evaporated *in vacuo*. The residual oximes soon crystallized after addition of cold water.

5-Methyl-2-acetylfuranoxime.—Prepared from 5-methyl-2-acetylfuran⁷; white plates from petroleum ether (b. p., 50–60°); m. p. 78–79°; yield, 80%.

Anal. Calcd. for C₇H₉O₃N: C, 60.40; H, 6.52; N, 10.07. Found: C, 60.41; H, 6.55; N, 10.14.

2-Propionylfuranoxime.—Prepared from 2-propionylfuran⁸; white needles from water, m. p., 77°, yield, 82%.

Anal. Calcd. for C₇H₉O₃N: C, 60.40; H, 6.52; N, 10.07. Found: C, 60.52; H, 6.59; N, 9.85.

2-Hydroxyacetylfuranoxime.—Prepared from 2-hydroxyacetylfuran⁹; recrystallized from water; m. p., 132–134°; yield, 78%.

Anal. Calcd. for C₆H₇O₃N: C, 51.42; H, 5.03; N, 9.99. Found: C, 51.76; H, 5.50; N, 10.15.

2-*p*-Methoxybenzoylfuranoxime.—Prepared from 2-*p*-methoxybenzoylfuran¹⁰; recrystallized from 50% ethanol; m. p., 135–137°; yield, 75%.

Anal. Calcd. for C₁₂H₁₁O₃N: C, 66.34; H, 5.10; N, 6.45. Found: C, 66.46; H, 5.26; N, 6.65.

General Procedure for the Preparation of the *p*-Toluenesulfonyl Derivatives of the Oximes.—To a solution of the oxime (0.1 mole) in 50 cc. of pyridine was added gradually at –10°, with stirring, 0.1 mole of powdered *p*-toluenesulfonyl chloride. After being allowed to stand at 0° for two hours, the reaction mixture was poured into ice water. The precipitated esters crystallized on standing at 0°. They were collected on a filter, washed carefully with cold water and dried *in vacuo*.

***p*-Toluenesulfonyl-5-methyl-2-acetylfuranoxime.**—White needles from benzene and petroleum ether (b. p., 50–60°); m. p. with decomposition, 111°; yield, 85%.

Anal. Calcd. for C₁₄H₁₅O₄NS: C, 57.32; H, 5.15; N, 4.77. Found: C, 57.32; H, 5.19; N, 4.71.

The substance (2 g.) remained unchanged after refluxing with 20 cc. of 95% alcohol for forty-eight hours.

***p*-Toluenesulfonyl-2-propionylfuranoxime.**—White needles from petroleum ether (b. p., 50–60°); m. p., 68°; yield, 83%.

Anal. Calcd. for C₁₄H₁₅O₄NS: C, 57.32; H, 5.15; N, 4.77. Found: C, 57.58; H, 5.18; N, 4.85.

***p*-Toluenesulfonyl-2-hydroxyacetylfuranoxime.**—White crystals from benzene and petroleum ether (b. p., 50–60°); m. p. 86–87°, with decomposition, yield, 80%.

Anal. Calcd. for C₁₂H₁₃O₅NS: C, 52.82; H, 4.43. Found: C, 52.95; H, 4.78.

***p*-Toluenesulfonyl-2-benzoylfuranoxime.**—Prepared from 2-benzoylfuranoxime¹¹; recrystallized cautiously from ethanol; m. p., 118° with decomposition; yield 50%.

Anal. Calcd. for C₁₈H₁₅O₄NS: C, 63.34; H, 4.43; N, 4.10. Found: C, 63.65; H, 4.48; N, 4.29.

***p*-Toluenesulfonyl-2-*p*-methoxybenzoylfuranoxime.**—White plates from benzene and petroleum ether, m. p. 119–120°, yield 72%.

Anal. Calcd. for C₁₉H₁₇O₅NS: C, 61.44; H, 4.61; N, 3.77. Found: C, 61.50; H, 4.85; N, 3.87.

***p*-Toluenesulfonyl-2-benzoylbenzofuranoxime.**—Prepared from 2-benzoylbenzofuranoxime¹²; recrystallized from ethanol, m. p., 118° with decomposition, yield 50%.

Anal. Calcd. for C₂₂H₁₇O₄NS: C, 67.50; H, 4.37; N, 3.57. Found: C, 67.74; H, 4.41; N, 3.52.

Acetal of 4,5-Diketo-2-hexenal¹ (II) from *p*-Toluenesulfonyl-2-hydroxyacetylfuranoxime.—The solution of the oxime (10 g.) in 50 cc. of 95% alcohol was kept at 30° for twenty-four hours. Then the reaction mixture was treated as described previously.¹ The resulting solid was found to be ammonium *p*-toluenesulfonate; the liquid showed the same boiling point (71–73°, 2 mm.) and properties as II; and the oxime, prepared from it, proved to be the aldoxime of 4,5-diketo-2-hexenal,¹ according to its melting point (235°) and mixed melting point with an authentic sample.

(3) Baum, *Ber.*, **37**, 2954 (1904).

(4) Störmer and Calov, *ibid.*, **34**, 773 (1901).

(5) Meisenheimer, *Ann.*, **446**, 205 (1926).

(6) Bouveault, *Ber.*, **34**, 1073 (1901).

(7) Reichstein, *Helv. Chim. Acta*, **13**, 356 (1930).

(8) Ramonczai and Vargha, *This Journal*, **72**, 2737 (1950).

(9) Kipnis, Soloway and Ornfeldt, *ibid.*, **70**, 142 (1948).

(10) Borsche and Leditschke, *Ann.*, **529**, 112 (1937).

(11) Marquis, *Compt. rend.*, **129**, 111 (1899).

(12) Rap, *Gazz. chim. ital.*, **25**, II, 288 (1895).

Furanilide from *p*-Toluenesulfonyl-2-benzoylfuranoxime.—A suspension of 10 g. of the oxime in 50 cc. of 95% alcohol was kept at 30° for ten days with occasional shaking. During this time the oxime dissolved gradually. Then the solvent was removed *in vacuo* and the residue dissolved in 25 cc. of ether and 25 cc. of water. The acidic aqueous layer was neutralized with ammonia, and after treatment with charcoal evaporated to dryness. The residue, which could be recrystallized from absolute ethanol, was found to be ammonium *p*-toluenesulfonate. The ether layer was then evaporated and the residue recrystallized from ethanol with charcoal. The substance proved to be furanilide according to its melting point (124°), and mixed melting point with an authentic sample and analysis.

Anal. Calcd. for $C_{11}H_9O_2N$: C, 70.57; H, 4.84; N, 7.48. Found: C, 70.82; H, 5.12; N, 7.57.

***p*-Methoxyfuranilide.**—A solution of *p*-toluenesulfonyl-2-*p*-methoxybenzoylfuranoxime in 15 cc. of 95% ethanol was refluxed for five hours. The residue, obtained after evaporation of the reaction mixture, was dissolved in ether and water. After being neutralized with ammonia the aqueous solution yielded ammonium *p*-toluenesulfonate. The ether solution was evaporated and the residue recrystallized from water. The product formed white needles melting at 105–106°; yield, 60%. The substance yielded 2-furoic acid (m. p. 132–133°) and *p*-methoxyaniline (m. p., 54–55°) on hydrolysis with 2 *N* sulfuric acid. This fact established its identity as *p*-methoxyfuranilide. Its structure was confirmed by synthesis. For this purpose a solution of furyl chloride (2.6 g.) in 10 cc. of benzene was added to the solution of *p*-methoxyfuranilide (5 g.) in 20 cc. of benzene and the mixture was kept at room temperature for one day. The precipitate was collected on a filter, washed with ethanol and water, and recrystallized from water; melting point and mixed melting point with the substance mentioned above, 105–106°.

Anal. Calcd. for $C_{12}H_{11}O_3N$: C, 66.34; H, 5.10; N, 6.45. Found: C, 66.59; H, 5.17; N, 6.53.

Benzfuranilide from *p*-Toluenesulfonyl-2-benzoylbenzofuranoxime.—A solution of the oxime (5 g.) in 40 cc. of ethanol was refluxed for four hours. After evaporation of the solvent the residue was dissolved in ether and water. The water solution yielded ammonium *p*-toluenesulfonate after neutralization with ammonia, and evaporation. The ethereal solution was evaporated and the residue recrystallized from 40% ethanol; melting point and mixed melting point with benzfuranilide⁴ prepared in another way 158°, yield 84%.

Anal. Calcd. for $C_{15}H_{11}O_3N$: C, 75.95; H, 4.67; N, 5.90. Found: C, 76.25; H, 4.40; N, 6.05.

Summary

The reactions with methanol and ethanol of the *p*-toluenesulfonyl derivatives of several aliphatic and aromatic furyl ketoximes have been studied: 2-propionyl-, 2-hydroxyacetyl-, 2-benzoyl-, 2-(*p*-methoxybenzoyl)-furanoxime and 2-benzoylbenzofuranoxime (III–VIII).

It has been found that the aliphatic *p*-toluenesulfonyl furylketoximes react with alcohols according to scheme 1, illustrated by *p*-toluenesulfonyl-2-acetofuranoxime, and the aromatic ones with a Beckmann rearrangement according to scheme 3.

The experimental results make it seem probable that the mechanism of the reaction represented by scheme 1 consists in the opening of the furan ring with acetal formation and subsequent substitution of the imino group by oxygen according to scheme 2.

SZEGED, HUNGARY

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Sulfonation of Ketones and Aldehydes

BY WILLIAM E. TRUCE AND C. C. ALFIERI¹

This paper reports on the reaction of dioxane sulfotrioxide with ketones and aldehydes leading to the formation of ketone- α -sulfonic acids and aldehyde- α -sulfonic acids, respectively. Analogous reactions have been observed in a few isolated cases previously. Acetophenone- ω -sulfonic acid has been obtained by treating a solution of acetophenone in acetic anhydride and ether with 15% oleum at 0°. The action of chlorosulfonic acid on acetophenone has produced the 2, ω -disulfonyl chloride while acetophenone-4-sulfonic acid with chlorosulfonic acid has probably formed the 4, ω -disulfonyl chloride.³ The sulfonation of acetophenone with 45% oleum at temperatures which do not cause cleavage (to acetic acid and benzenesulfonic acid⁴) has yielded a mixture of ortho and meta acetophenonesulfonic acids.

(1) This paper is taken from the Ph.D. thesis of C. C. Alfieri. A portion of this work was presented before the Division of Organic Chemistry at the 116th Meeting of the American Chemical Society, Atlantic City, September, 1949.

(2) Doering and Beringer, *This Journal*, **71**, 2221 (1949).

(3) Weston and Suter, *ibid.*, **61**, 389 (1938).

(4) Kreckeler, *Ber.*, **19**, 676, 2627 (1886).

Acetophenone, 2-acetothienone and acetomesitylene were converted to the corresponding sodium ω -ketonesulfonates in approximately 70% yields (recrystallized) by treatment with dioxane sulfotrioxide followed by neutralization. β -Acetonaphthone yielded a mixture of products. One of these products was shown to be the expected sodium β -acetonaphthone- ω -sulfonate, while another product was a disulfonate. Presumably, the second sulfonic acid group entered the non-substituted ring.

Pinacolone, propiophenone and isobutyrophe none were converted in approximately 70% yields to the corresponding sodium ketonesulfonates, i.e., $(CH_3)_3CCOCH_2SO_3Na$, $C_6H_5COCH(CH_3)SO_3Na$, and $C_6H_5COC(CH_3)_2SO_3Na$, respectively. Similar results were obtained with acetone and cyclohexanone; however, it was more difficult to obtain a pure product in these cases.

The direct sulfonation of an aliphatic aldehyde has not been previously reported. Dioxane sulfotrioxide was found to react with phenylacetaldehyde, heptaldehyde and isobutyraldehyde to form