Further evidence for the assigned structure is the presence in the infrared spectrum of new bands at 1635 cm.$^{-1}$, presumably due to the exocyclic double bond, and at 985 cm.$^{-1}$ (vinyl group). The -NH region exhibited the characteristic -NH bands[18] at 3485 (unassociated) and 3405 cm.$^{-1}$ (associated, varies with concentration).

Dehydration of 2-pyrrolemethylcarbinol by distillation in the presence of hydroquinone or by flash-distillation from solid potassium hydroxide resulted in the formation of 2-vinylpyrrole in yields of less than 5%. Most of the starting material had been converted to the yellow undistillable resin which the carbinol forms on standing.

2-Propenylpyrrole.—Vapor phase dehydration of 2-pyrroleethylcarbinol in the manner described above formed 2-propenylpyrrole in 52% yield, b.p. 81–82° (9 mm.), n^{26}D 1.5438.

Anal. Calcd. for C_7H_9N: N, 13.07. Found: N, 12.86.

The infrared spectrum of this compound exhibited a fairly strong band at 1655 cm.$^{-1}$ (C═C). The ultraviolet spectrum in 95% ethanol had a maximum at 270 mμ, ε 1130.

β-(2-Pyrrole)-styrene.—A small round-bottom flask containing 10 g. of benzyl-2-pyrrolecarbinol and six pellets of potassium hydroxide was exhausted to 0.2 mm. and heated in an oil-bath to 250–260°. The carbinol melted and started to boil. After ten minutes the apparatus was cooled. The solid which had collected on the flask walls was scraped out and recrystallized from benzene–petroleum ether. The yield of light yellow crystals, m.p. 136–137°, was 22%.

Anal. Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.03; H, 6.47; N, 8.50.

The infrared spectrum contained a new band at 1640 cm.$^{-1}$ (C═C) in addition to the usual phenyl frequencies at 1600 and 1500 cm.$^{-1}$. The ultraviolet absorption spectrum in 95% ethanol had a maximum at 243 mμ, ε 1050.

2-Ethylpyrrole.—A solution of 2 g. of 2-vinylpyrrole in 30 ml. of 95% ethanol was reduced in a low pressure Parr hydrogenator with 10% palladium-on-charcoal catalyst until hydrogen uptake ceased. The product boiled at 67° (19 mm.), n^{24}D 1.4962.

An authentic sample was prepared by refluxing 10.8 g. of 2-acetylpyrrole, 12.8 g. of potassium hydroxide, 5 ml. of hydrazine hydrate and 100 ml. of triethylene glycol at 125° for one hour, distilling until the temperature had reached 205° and continuing to reflux for three hours. The product boiled at 65–68°, n^{24}D 1.4952. The infrared spectra of the two samples were identical.

2-Propylpyrrole.—Catalytic reduction of 2-propenylpyrrole yielded a product of b.p. 67–68° (9 mm.), n^{23}D 1.4980. The authentic sample, prepared by Wolff–Kishner reduction of 2-propionylpyrrole, boiled at 64–65° (9 mm.), n^{25}D 1.4972 (lit.[9] b.p. 70–71° at 17 mm.). The infrared spectra of the two samples were identical.

Benzyl-2-pyrrolemethane.—Catalytic hydrogenation of β-(2-pyrrole)-styrene gave a white solid which was purified by distillation, b.p. 140–147° (7 mm.), and which melted at 46–47° after recrystallization from petroleum ether. A mixed m.p. with a sample prepared by Wolff–Kishner reduction of benzyl 2-pyrrole ketone was not depressed. The infrared spectra of both products were identical.

Anal. Calcd. for $C_{12}H_{13}N$: C, 84.13; H, 7.65. Found: C, 84.36; H, 7.72.

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[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

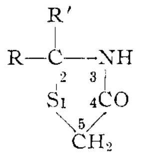
4-Thiazolidones. VI.[1] The Preparation of Some 2-Substituted Derivatives

BY ALEXANDER R. SURREY AND ROYAL A. CUTLER

RECEIVED AUGUST 10, 1953

A general procedure for the preparation of 2-substituted 4-thiazolidones is described. Oxidation of several of the 4-thiazolidones to the corresponding 1-dioxides also is reported.

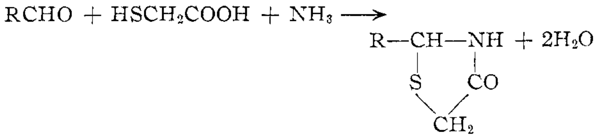
As part of our general investigation of the synthesis of 4-thiazolidones we have prepared a series of compounds unsubstituted in the 3-position (I).



I

The present communication deals mainly with the formation of some 2-(halophenyl) derivatives (I, R = XC_6H_4, $X_2C_6H_3$; R′ = H or CH_3) which were then oxidized to the corresponding 1-dioxides. The latter have been found to possess significant amebacidal activity (*Endamoeba criceti*) when tested in hamsters.[2]

Our general procedure for the synthesis of the 2-substituted 4-thiazolidones consisted of heating a mixture of the appropriate aldehyde or ketone with thioglycolic acid and ammonia or an ammonium salt such as ammonium acetate or carbonate. For the most part the best results were obtained using benzene as the solvent with ammonium carbonate as the source of ammonia, and removing the water as it was formed.



The use of ammonia itself rather than one of its salts, usually gave poorer yields. Usually the reaction mixture was heated until the theoretical amount of water was collected. In most cases the time required ranged from one to eight hours. However, with 4-chlorobenzaldehyde and α-thiobutyric acid the calculated amount of water was collected in 30 minutes and a 76% yield of the 2,5-disubstituted derivative, 2-(4-chlorophenyl)-5-ethyl-4-thiazolidone was obtained. In contrast, in the condensation of the ketone, 4-chloroacetophenone, with thioglycolic acid and ammonium carbonate, the yield of 2-(4-chlorophenyl)-2-methyl-4-thiazolidone was 30% after heating for 56 hours. The use of dioxane as the solvent in the present condensations appears to be most effective with benzaldehydes having electropositive substituents on the ring. For example, with 4-acetamidobenzaldehyde, a 69% yield of the corresponding thiazolidone was obtained after heating the mixture on a steam-bath for 24 hours.

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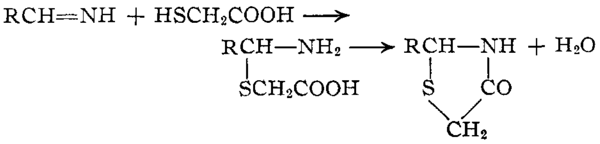
[1] For the previous paper in this series see: A. R. Surrey, THIS JOURNAL, **74**, 3450 (1952).

[2] We are indebted to Dr. D. A. Berberian for the chemotherapeutic testing.

The reaction as represented in the equation above probably involves the initial formation of an aldimine (or ketimine) which then reacts with thioglycolic acid. The formation of thioglycolamide



as the principal intermediate in this sequence is ruled out since it reacts with an aromatic aldehyde under the conditions employed to give only a small yield of the 4-thiazolidone even after prolonged heating. This is not in agreement with the work of Davies, Ramsey and Stove[3] who reported the preparation of 2-phenyl-4-thiazolidone, m.p. 88°, by simply mixing thioglycolamide and benzaldehyde at 52°. When this work was repeated we obtained a product with a similar melting point, which, however, analyzed for a compound formed by the addition of the two reactants with no splitting out of water. Furthermore, when the reaction was carried out by heating in benzene no evidence of a rapid elimination of water was observed. After one hour only a trace of water was collected. After 20 hours of refluxing a 5.5% yield of 2-phenyl-4-thiazolidone was obtained which after recrystallization melted at 126–128°. The same product was obtained in 60% yield after one hour starting with thioglycolic acid and ammonium carbonate according to our general procedure.

Pennington, *et al.*,[4] have recently shown that 2-substituted 4-thiazolidones may be prepared (10–50% yields) from thioglycolamide and an aldehyde or ketone in the presence of catalytic amounts of *p*-toluenesulfonic acid. For example, with the methyl ester of pimelaldehydic acid they obtained the antibiotic, 2-(5-carboxypentyl)-4-thiazolidone. These authors have also prepared 2-phenyl-4-thiazolidone, m.p. 127.5–128.5°, by their method and showed that the product melting at 88° is probably a hemimercaptal which is in agreement with our findings.

Several of our 2-substituted thiazolidones were oxidized in acetic acid with potassium permanganate to the corresponding 1-dioxides. The yields of products obtained directly from the reaction mixture, after treatment with sodium bisulfite solution, were generally very satisfactory. In some instances, recrystallization of the 1-dioxides was accompanied by extensive decomposition.

Acknowledgment.—The authors are indebted to Miss M. K. Rukwid for technical assistance and to M. E. Auerbach and K. D. Fleischer and staffs for the corrected melting points and analyses recorded.

Experimental

2-(3,4-Dichlorophenyl)-4-thiazolidone.—A mixture of 35 g. (0.2 mole) of 3,4-dichlorobenzaldehyde, 12 g. (0.125 mole) of ammonium carbonate, 15 ml. (0.216 mole) of thioglycolic acid and 300 ml. of benzene was refluxed for eight hours with a water separator connected to the apparatus. At the end of this time, about 8 ml. of water was collected. The reaction mixture was poured with stirring into 200 ml. of water containing 15 ml. of concentrated ammonium hydroxide. A small amount of alcohol was added to facilitate filtration and the solid was filtered off, stirred in warm water and refiltered; yield 34 g. (72.6%). Recrystallization from alcohol gave 19.5 g. of product melting at 205.8–207° (cor.).

Anal. Calcd. for $C_9H_7Cl_2NOS$: S, 12.92; Cl, 28.58. Found: S, 12.96; Cl, 28.80.

The following compounds were prepared in a similar manner: **2-(4-Bromophenyl)-4-thiazolidone**; yield 39%, m.p. 176.3–177.7° (cor.) after recrystallization from ethylene dichloride. *Anal.* Calcd. for C_9H_8BrNOS: S, 12.42. Found: S, 12.41. **2-(4-Chlorophenyl)-4-thiazolidone**; yield 70%, m.p. 165.4–166.2° (cor.) after recrystallization from ethanol. *Anal.* Calcd. for C_9H_8ClNOS: N, 6.56; S, 15.00. Found: N, 6.50; S, 15.04. **2-Phenyl-4-thiazolidone**; yield 60%, m.p. 128.6–129.8° (cor.) (lit.[4] m.p. 127.5–128.5°) after recrystallization from benzene. *Anal.* Calcd. for C_9H_9NOS: C, 60.30; H, 5.06; N, 7.82; S, 17.89. Found: C, 60.64; H, 5.22; N, 7.67; S, 17.96.

2-(4-Acetamidophenyl)-4-thiazolidone.—To a solution of 20 g. (0.217 mole) of thioglycolic acid in 125 ml. of dioxane was added 6 g. (0.053 mole) of powdered ammonium carbonate and 0.1 mole of 4-acetamidobenzaldehyde. After the mixture was heated with stirring for 24 hours on a steam-bath, the dioxane was removed by distillation under reduced pressure and the residue was shaken thoroughly with a mixture of 25 ml. of ether and 125 ml. of water containing 15 ml. of concentrated ammonium hydroxide. The solid which was obtained was filtered off, washed with water, dried (16.3 g., 69%) and recrystallized from nitromethane, m.p. 219.5–220.9° (cor.) (lit.[4] m.p. 222–223°).

Anal. Calcd. for $C_{11}H_{12}N_2O_2S$: N, 11.86; S, 13.57. Found: N, 11.89; S, 13.79.

2-Furyl-4-thiazolidone.—This compound was prepared in a similar manner as above. After five hours of heating a 28% yield was obtained. Prolonged heating caused extensive decomposition. The product was recrystallized from benzene, m.p. 123–123.8° (cor.) (lit.[4] m.p. 121–123°).

Anal. Calcd. for $C_7H_7NO_2S$: C, 49.69; H, 4.17; N, 8.28; S, 18.95. Found: C, 49.80; H, 4.07; N, 8.23; S, 19.02.

2-(4-Chlorophenyl)-5-ethyl-4-thiazolidone.—A mixture of 14.05 g. (0.1 mole) of 4-chlorobenzaldehyde, 12.5 g. (0.104 mole) of α-thiobutyric acid, 6 g. (0.16 mole) of powdered ammonium carbonate and 125 ml. of benzene was refluxed for 30 minutes with a water separator connected to the apparatus. At the end of this time the theoretical amount of water had separated. The benzene solution was extracted with water containing 10 ml. of concentrated ammonium hydroxide. After drying, the benzene was distilled off *in vacuo* to give a light yellow solid, 15.7 g. (65%) m.p. 120–125°. After recrystallization from Skellysolve C the product (10 g.) melted at 123.5–124.2° (cor.).

Anal. Calcd. for $C_{11}H_{12}ClNOS$: N, 5.80; S, 13.26. Found: N, 5.96; S, 13.28.

2-(4-Chlorophenyl)-2-methyl-4-thiazolidone.—A mixture of 31 g. (0.2 mole) of 4-chloroacetophenone, 15 ml. (0.216 mole) of thioglycolic acid, 12 g. (0.125 mole) of powdered ammonium carbonate and 300 ml. of benzene was refluxed for 56 hours with a water separator connected to the apparatus. The benzene solution was washed with dilute ammonium hydroxide solution and then with water. Removal of the benzene *in vacuo* gave an oil which was dissolved in warm Skellysolve C. Upon cooling and scratching the product crystallized out; 14 g. (30.6%), m.p. 99–105°. Two recrystallizations from Skellysolve C raised the melting point to 110.2–111.2° (cor.).

Anal. Calcd. for $C_{10}H_{10}ClNOS$: Cl, 15.57; S, 14.08. Found: Cl, 15.48; S, 14.08.

Reaction of Thioglycolamide with Benzaldehyde.—A mixture of 9 g. (0.1 mole) of thioglycolamide and 10.6 g. (0.1 mole) of benzaldehyde in 100 ml. of benzene was stirred at 52° for a few minutes and then cooled to 20°. The product was filtered off, triturated with chloroform and dried, 10.5 g. (53%); m.p. 84–86°. A sample was recrystallized from benzene, m.p. 86.1–87.4° (cor.).

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Anal. Calcd. for $C_9H_{11}NO_2S$: N, 7.39; S, 16.54. Found: N, 7.10; S, 16.26.

2-(3,4-Dichlorophenyl)-4-thiazolidone-1-dioxide.—To a solution of 8 g. (0.0322 mole) of 2-(3,4-dichlorophenyl)-4-thiazolidone in 200 ml. of acetic acid was added with stirring 7.5 g. (0.0475 mole) of potassium permanganate in 75 ml. of water. The temperature was kept below 30° by external cooling. After the addition was complete, sodium bisulfite solution was added to the reaction mixture to dissolve the manganese dioxide. The mixture was diluted with an equal volume of water and the colorless product was filtered off, washed thoroughly with water and dried. The yield of product melting at 192.4–193.4° (cor.) was 7.5 g. (83%).

Anal. Calcd. for $C_9H_7Cl_2NO_3S$: Cl, 25.31; S, 11.45. Found: Cl, 25.30; S, 11.49.

The following 1-dioxides were prepared in a similar manner: **2-(4-Bromophenyl)-4-thiazolidone-1-dioxide** (crude yield 70%) was recrystallized by dissolving it in a large volume of hot nitromethane and cooling quickly, m.p. 196.2–196.6° (cor.). *Anal.* Calcd. for $C_9H_8BrNO_3S$: Br, 27.55; S, 11.05. Found: Br, 27.10; S, 11.08. **2-(4-Chlorophenyl)-4-thiazolidone-1-dioxide** (90% yield), m.p. 172–173.5° dec. *Anal.* Calcd. for $C_9H_8ClNO_3S$: N, 5.70; S, 13.05. Found: N, 5.86; S, 13.08. **2-(4-Chlorophenyl)-2-methyl-4-thiazolidone-1-dioxide** (crude yield 75%) was recrystallized from methanol, m.p. 145.7–146.8° (cor.). *Anal.* Calcd. for $C_{10}H_{10}ClNO_3S$: Cl, 13.65; S, 12.35. Found: Cl, 13.62; S, 12.42.

RENSSELAER, NEW YORK

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF KANSAS]

Formation of N,N'-Dibenzoylurea from Nitromethane and Benzoyl Chloride in Pyridine Solution

BY ROBERT H. TERSS[1] AND WILLIAM E. MCEWEN

RECEIVED JULY 20, 1953

The reaction of nitromethane and benzoyl chloride in pyridine solution afforded N,N'-dibenzoylurea (III) together with small amounts of 3,5-diphenyl-1,2,4-oxadiazole (IV), benzamide, benzonitrile and a compound of formula $C_{15}H_{10}N_2O_2$, which has tentatively been assigned the structure 2,6-diphenyl-4-keto-1,3,5-oxadiazine (V). Carbon dioxide was evolved during the course of the reaction. Evidence is presented which indicates that fulminic acid (VII) and benzoyl isocyanate (VIII) are intermediates in the formation of N,N'-dibenzoylurea (III). The reaction of phenylnitromethane with benzoyl chloride in pyridine solution gave dibenzhydroxamic acid (XI) as the main isolable organic product.

The chemistry of acylpyridinium salts, particularly acylpyridinium chlorides I, has been investigated fairly extensively during the past half century. Attention has been directed to: (1) the preparation of crystalline acylpyridinium salts,[2] (2) the acylating properties of these salts (or, what amounts to the same thing, solutions of the acid chlorides in pyridine) toward water, hydrogen sulfide, alcohols, phenols, enols, primary and secondary amines and amides and other compounds containing active hydrogen[2a,3] (3) their use in the cleavage of ethers[2b]; (4) the condensation of these salts with a variety of nucleophilic reagents to form either 4-substituted pyridines or 4-substituted-1-acyl-1,4-dihydropyridines[4]; and (5) the self condensation reactions of the various acylpyridinium cations in the presence of reducing agents to give, at least initially, N,N'-diacyltetrahydro-4,4'-bipyridyls.[5] Many analogous reactions of acyl-quinolinium salts are also known, the condensation reactions with nucleophilic reagents to form 2-substituted-1-acyl-1,2-dihydroquinolines[4b,6] being of particular interest with respect to our work. The addition of bases to the 2- and 4-positions of alkylpyridinium and alkylquinolinium cations are also well known reactions.[7]

In all of the condensation reactions involving external bases and acylpyridinium or acylquinolinium salts in which the structures of the products have been firmly established the results have indicated

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[1] Pan-American Oil Refining Corporation Fellow, 1952–1953.

[2] (a) H. Adkins and Q. E. Thompson, THIS JOURNAL, **71**, 2242 (1949); (b) V. Prey, *Ber.*, **75**, 537 (1942); (c) W. M. Dehn, THIS JOURNAL, **34**, 1399 (1912); (d) W. M. Dehn and A. A. Ball, *ibid.*, **36**, 2091 (1914); (e) G. L. Schwartz and W. M. Dehn, *ibid.*, **39**, 2444 (1917); (f) S. I. Lur'e, *J. Gen. Chem.* (*U. S. S. R.*), **18**, 1517 (1948); (g) K. Freudenberg and D. Peters, *Ber.*, **52**, 1463 (1919); (h) M. Dennstedt and J. Zimmermann, *ibid.*, **19**, 75 (1886); (i) G. Minunni, *Gazz. chim. ital.*, [II], **22**, 213 (1892); (j) H. Staudinger and H. Stockmann, *Ber.*, **42**, 3485 (1909); (k) H. O. Jones and H. Tasker, *Proc. Chem. Soc.*, **24**, 271 (1908); (l) E. Gebauer-Fulnegg and F. Riesenfeld, *Monatsh.*, **47**, 185 (1926); (m) H. E. Baumgarten, THIS JOURNAL, **75**, 1239 (1953).

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