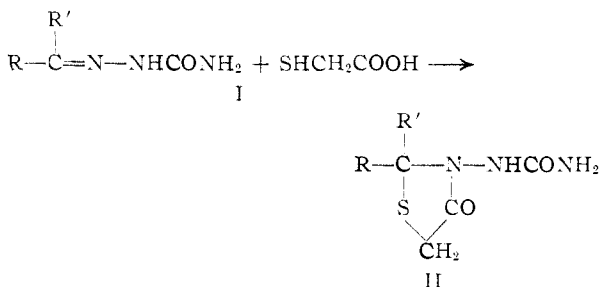


#### 4-Thiazolidones. V. The Reaction of Some Semicarbazones with Thioglycolic Acid

BY ALEXANDER R. SURREY

RECEIVED JANUARY 16, 1952

The present communication deals with the preparation of several 3-ureido-4-thiazolidones, II, (Table I) by the reaction of thioglycolic acid with semicarbazones, I.



For the most part, the procedure employed is similar to that described for the reaction of thioglycolic acid with Schiff bases.<sup>1</sup> A mixture of the reactants and benzene was heated under reflux with a water separator connected to the apparatus, until no further evidence of water elimination was observed. In no instance was the theoretical amount of water collected even in those cases where a large excess of thioglycolic acid was employed. The reaction times were considerably longer than those used for the Schiff bases especially those derived from aliphatic amines. This is probably due partly to the insolubility of the semicarbazones. However, if the mechanism of the addition of thioglycolic acid to the C=N linkage involves a nucleophilic attack of the sulfur atom on the carbon atom,

crystalline compounds. Two of the compounds, the 4-chlorophenyl- and 2,2-dimethyl-3-ureido-4-thiazolidones were oxidized in acetic acid with potassium permanganate to the corresponding 1-dioxides.

#### Experimental<sup>2</sup>

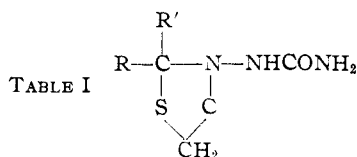
Examples of the different procedures employed in the preparation of the compounds listed in Table I are given below.

**2-(4-Chlorophenyl)-3-ureido-4-thiazolidone.**—A mixture of 25 g. of 4-chlorobenzaldehyde semicarbazone, 25 g. of thioglycolic acid and 150 ml. of benzene was refluxed with stirring for 18 hours with a continuous water separator connected to the apparatus. An additional 25 g. of thioglycolic acid was added after three hours. The reaction mixture was cooled in ice and the solid which separated was collected by filtration, 14 g. It proved to be unreacted 4-chlorobenzaldehyde semicarbazone. Ether was added to the benzene filtrate to give 15 g. of product which was washed with acetone and then recrystallized from alcohol.

When 18 g. of 4-chlorobenzaldehyde semicarbazone, 40 g. of thioglycolic acid, 2 g. of *p*-toluenesulfonic acid and 200 ml. of benzene was refluxed as above for 23 hours 9 g. of product melting at 201–202° (uncor.) was obtained after recrystallization from alcohol.

**2-*n*-Propyl-3-ureido-4-thiazolidone.**—A mixture of 12 g. of *n*-butyraldehyde semicarbazone, 20 g. of thioglycolic acid and 10 ml. of benzene was refluxed with stirring for 18 hours; 2 ml. of water was collected. After cooling, a small amount of solid was removed by filtration. The filtrate was stirred in an excess of 10% sodium carbonate solution and cooled in ice. The solid which separated was collected and recrystallized twice from water.

**2-(4-Nitrophenyl)-3-ureido-4-thiazolidone.**—A mixture of 7 g. of 4-nitrobenzaldehyde semicarbazone and 50 ml. of thioglycolic acid was heated on the steam-bath for 20 hours. The clear solution was poured into an excess of 10% sodium carbonate solution and a small amount of solid was removed by filtration. On standing for three days at room temperature some solid (5 g.) separated from the filtrate, m.p. 182–185° dec. (uncor.). A mixed melting point determination with a sample of the starting semicarbazone was depressed. After recrystallization from absolute alcohol the product melted at 186.5–187.5° (uncor.).



R	R'	Yield, %	M.p., °C. <sup>a</sup>	Formula	Nitrogen, %		Sulfur, %	
					Calcd.	Found	Calcd.	Found
C <sub>6</sub> H <sub>5</sub>	H	10 <sup>b</sup>	195.5–197.5	C <sub>10</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S	17.72	17.97	13.50	13.51
4-ClC <sub>6</sub> H <sub>4</sub>	H	50 <sup>b</sup>	212–213.5	C <sub>10</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub> S	15.47	15.21	11.79	11.98
4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	24	192–193	C <sub>11</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S	15.72	15.81	11.99	11.81
4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	40	190–191.8	C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub> S	19.86	20.11	11.36	11.56
4-OH-3-OCH <sub>3</sub> C <sub>6</sub> H <sub>3</sub>	H	43 <sup>b</sup>	188.8–190	C <sub>11</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S	14.84	14.84	11.31	11.47
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	25	159.1–160.3	C <sub>7</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	20.68	20.57	15.77	15.68
CH <sub>3</sub>	CH <sub>3</sub>	26	187.6–189.2	C <sub>6</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S	22.22	22.05	16.95	16.99

<sup>a</sup> Corrected melting points. <sup>b</sup> Based on recovered semicarbazone.

these differences in reactivity can be explained. One would expect that the more basic the nitrogen atom the faster the reaction. The presence of catalytic amounts of *p*-toluenesulfonic acid in the reaction with 4-chlorobenzaldehyde semicarbazone appeared to have some advantage. However, this was not observed in other cases. The use of a large excess of thioglycolic acid as the solvent may have some value. This procedure has not been investigated thoroughly.

The 3-ureido-4-thiazolidones are stable, colorless,

(1) (a) A. R. Surrey, *THIS JOURNAL*, **69**, 2911 (1947); (b) **70**, 4262 (1948).

**2-(4-Chlorophenyl)-3-ureido-4-thiazolidone-1-dioxide.**—To 9 g. of 2-(4-chlorophenyl)-3-ureido-4-thiazolidone in 100 ml. of acetic acid was added with stirring a solution of 10.3 g. of potassium permanganate in 150 ml. of water. The temperature was maintained at 30–40°. After the addition was complete the reaction mixture was treated with sodium bisulfite solution to remove the manganese dioxide. A brown product separated which after recrystallization from a large volume of water gave 5 g. melting at 220–221°.

*Anal.* Calcd. for C<sub>10</sub>H<sub>10</sub>ClN<sub>3</sub>O<sub>4</sub>S: N, 13.84; S, 10.52. Found: N, 13.71; S, 10.65.

**2,2-Dimethyl-3-ureido-4-thiazolidone-1-dioxide.**—The

(2) The corrected melting points and analyses recorded were obtained by the analytical staff of these laboratories under the direction of M. E. Auerbach and K. D. Fleischer.

product prepared as above melted at 202–202.7° after two recrystallizations from water.

Anal. Calcd. for  $C_8H_{11}N_3O_4S$ ; N, 19.00; S, 14.50. Found: N, 19.10; S, 14.62.

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RENSSELAER, NEW YORK

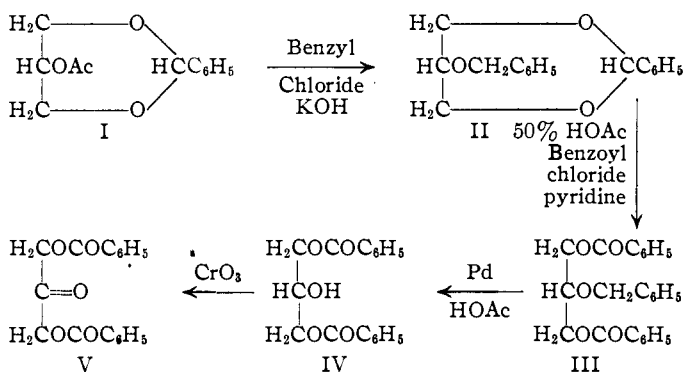
## Some New Glycerol Derivatives

BY HOWARD L. WHITE<sup>1</sup>

RECEIVED FEBRUARY 18, 1952

As part of a projected synthesis of the interesting sugar streptose, which envisioned as one of the critical steps the oxidation of 2,4-dibenzoyl-5-desoxy-L-arabinose dimethyl acetal to the 3-ketone, it became desirable to study as a model the oxidation of 1,3-dibenzoylglycerol to the corresponding dihydroxyacetone derivative. The unduly cumbersome procedure employed in the synthesis of the required 1,3-dibenzoylglycerol was chosen to parallel in some of the essential steps the projected preparation of the above desoxyarabinose derivative from monoacetone-5-desoxy-L-arabinose.<sup>2</sup>

The reaction scheme employed, which is shown in formulas I–IV, follows essentially the procedure of Sowden and Fischer<sup>3</sup> for the preparation of 1,2-diacylglycerols from 1,2-monoacetoneglycerol. It consists first in the benzylation of 2-acetyl-1,3-benzylideneglycerol (I)<sup>4</sup> with benzyl chloride and powdered potassium hydroxide (a procedure used previously by Zemplén<sup>5</sup> for the benzylation of triacetyllevoglucosan). The benzylidene group was eliminated by hydrolysis with 50% acetic acid, and the dried residue benzoyleated in pyridine solution. Finally, removal of the benzyl group was achieved by catalytic reduction with palladium-in-glacial acetic acid.



The desired oxidation of IV to the corresponding dihydroxyacetone derivative V previously prepared by Fischer<sup>6</sup> was readily effected with chromium trioxide in glacial acetic acid. An attempt to use the Oppenauer procedure for the oxidation, using cyclohexanone in boiling toluene as the hydrogen acceptor, failed to yield ketonic material.

(1) Armour and Company, Research Division, Chicago 9, Illinois.

(2) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 189 (1936).

(3) J. C. Sowden and H. O. L. Fischer, *THIS JOURNAL*, **63**, 3244 (1941).

(4) M. Bergmann and N. M. Carter, *Z. physiol. Chem.*, **191**, 211 (1930).

(5) G. Zemplén, Z. Csuros and S. Angyal, *Ber.*, **70**, 1848 (1937).

(6) H. O. L. Fischer, C. Taube and E. Baer, *ibid.*, **60**, 479 (1927).

## Experimental

**1,3-Benzylideneglycerol.**—The procedure of Hibbert and Carter<sup>7</sup> as modified by Bergmann and Carter<sup>4</sup> was used. The best yield obtained after one recrystallization from ether was 15% of material, m.p. 82–83°.

**2-Acetyl-1,3-benzylideneglycerol (I).**—A mixture of 2.5 g. of 1,3-benzylidene glycerol, 10 ml. of acetic anhydride and 10 ml. of pyridine was allowed to stand overnight at room temperature and was then poured into excess ice-water. The product was recrystallized once from ether; wt. 2.5 g., m.p. 100–102°.

**2-Benzyl-1,3-benzylideneglycerol (II).**—A mixture of 1.1 g. (5 millimoles) of 2-acetyl-1,3-benzylideneglycerol, 2.8 ml. (24 millimoles) of benzyl chloride and 25 ml. of xylene was stirred vigorously on the steam-bath for 4 hours with 13 g. (232 millimoles) of powdered potassium hydroxide. The mixture was cooled, ice was added and the xylene layer washed with water until neutral. It was then dried over calcium chloride and concentrated to dryness. The product was recrystallized once from ether; wt. 900 mg., m.p. 77–78°.

Anal. Calcd. for  $C_{17}H_{18}O_3$ : C, 75.53; H, 6.71. Found: C, 75.9, 76.1; H, 6.75, 6.70.

**2-Benzyl-1,3-Dibenzoylglycerol (III).**—A mixture of 9 g. of 2-benzyl-1,3-benzylideneglycerol and 100 ml. of 50% acetic acid was refluxed for 2 hours. Then 100 ml. of water was added and the solution concentrated *in vacuo*. The residue, dried by azeotropic distillation with alcohol followed by benzene, was dissolved in 80 ml. of dry pyridine and the solution cooled to 0°. To this was added a solution of 7.7 g. of benzoyl chloride (freshly distilled), in 80 ml. of dry pyridine. This mixture was allowed to stand at 4° for 40 hours. A few pieces of ice were added, the mixture allowed to stand a half hour, and then poured into a large excess of water. The ether extract of the resulting suspension was washed with ice-cold potassium bisulfate and sodium bicarbonate solution, dried over calcium chloride and concentrated to dryness. The residue after one recrystallization from ether weighed 3.3 g., m.p. 71.5–72.5°.

Anal. Calcd. for  $C_{24}H_{22}O_5$ : C, 73.84; H, 5.68. Found: C, 73.96; H, 5.65.

**1,3-Dibenzoylglycerol (IV).**—A solution of 3 g. (8 millimoles) of 2-benzyl-1,3-dibenzoylglycerol in 25 cc. of acetic acid was shaken with a previously reduced suspension of 250 mg. of palladium black (J. T. Baker) in 50 ml. of acetic acid under one atmosphere of hydrogen. After 10 millimoles of hydrogen was absorbed, the filtered solution was freeze dried. The oily residue (2.5 g., 8 millimoles) crystallized in the ice-box overnight and was used without further purification for the oxidation described below. For recrystallization the product was dissolved in ether and hexane was added to incipient turbidity. On cooling, preferably in a Dry Ice-bath, crystallization occurred, m.p. 51.5–54°.

Anal. Calcd. for  $C_{17}H_{16}O_5$ : C, 68.00; H, 5.37;  $2C_6H_5CO$ , 70.0. Found: C, 68.03; H, 5.34;  $C_6H_5CO$ ,<sup>8</sup> 70.9.

**Dibenzoyldihydroxyacetone (V).**—A solution of 300 mg. (1 millimole) of 1,3-dibenzoylglycerol in 30 ml. of glacial acetic acid was mixed with a solution of 66 mg. (0.65 millimole, equivalent amount) of chromium trioxide in 30 ml. of glacial acetic acid. After one hour, a little ethanol was added and the mixture was concentrated to dryness *in vacuo*. The residue was dissolved in ether and the solution was washed with water, 10% sodium bicarbonate and again with water, dried over calcium chloride and concentrated to dryness *in vacuo*. The product crystallized from ether as long needles; wt. 96 mg., m.p. 118–119°.

Anal. Calcd. for  $C_{17}H_{14}O_5$ : C, 68.45; H, 4.73. Found: C, 68.65; H, 4.61.

Dibenzoyldihydroxyacetone was prepared by benzylation of authentic dihydroxyacetone (purchased from Nutritional Biochemicals, Inc., Cleveland, Ohio) according to Fischer.<sup>6</sup> After two recrystallizations from ether, a 50%

(7) H. Hibbert and N. M. Carter, *THIS JOURNAL*, **51**, 1601 (1929).

(8) Pregl-Roth, "Die Quantitative organische Microanalyse," Julius Springer, Berlin, 1935, p. 235.