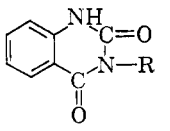
TABLE II

3-SUBSTITUTED 2,4-QUINAZOLINEDIONES



R	Yield, %	M.P.[a]	Literature Value	Nitrogen, % Calcd.	Found
n-Propyl	93	187–188	186–187[4]		
n-Butyl	90	156–157	156[4]	12.84	12.80
Cyclohexyl	57	270–271	270–271[4]		
Phenyl	91	280–282	280[2]		
p-Tolyl	88	265–266	270[5]	11.11	11.20
α-Naphthyl	91	273–274	268[6]	9.72	10.10

[a] Melting points are uncorrected.

EXPERIMENTAL

ω-Substituted methyl uramidobenzoates (I). Into a flask equipped with an agitator, thermometer, and reflux condenser was placed a solution of 0.2 mole of methyl anthranilate in 100 ml. of petroleum ether (b.p. 90–100°). Then, while agitating, 0.2 mole of an isocyanate was added all at once. After several minutes, 2 ml. of triethylamine was added, after which the reaction mixture was refluxed for 18 hr. Upon cooling, the ω-substituted methyl uramidobenzoates crystallized from solution. The yields obtained and the physical constants of the various compounds are listed in Table I.

N-Substituted 2,4-quinazolinediones (II). Into a flask equipped with an agitator, thermometer, and reflux condenser was placed 0.02 mole of an ω-substituted methyl uramidobenzoate. A solution of 50 ml. of concd. hydrochloric acid in 50 ml. of ethanol was added, after which the reaction mixture was refluxed for 3 hr. After cooling to room temperature, the 3-substituted 2,4-quinazolinedione was filtered, washed free of acid, and dried. The yields and physical constants of the compounds are listed in Table II.

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Di(2-thenoyl)furoxan[1]

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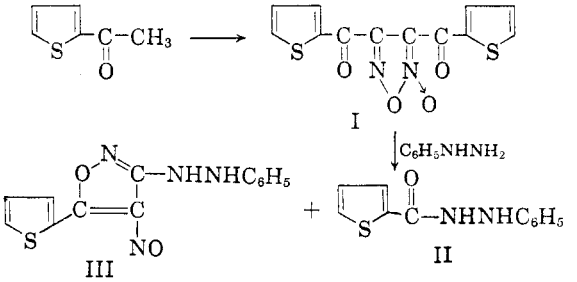
Received July 7, 1961

The reaction of acetophenone and nitric acid has been known since 1887.[2] The formation of dibenzoylfuroxan as the main product by dimerization of benzoylnitrile *N*-oxide has been proposed[3] and recently a minor product in this reaction was assigned the structure of the dibenzoate ester of bis(benzoylformaldoximino)furoxan.[4] Shirley[5] and his co-workers assigned the bis(3-thianaphthenoyl)furoxan structure to the product formed by the action of nitric acid on 3-acetylthianaphthene. Since no by-product was reported it is not certain whether a second product was formed in this reaction.

Our efforts have been directed toward a study of the reaction of 2-acetylthiophene and nitric acid in the hope of obtaining two products similar to the ones obtained in the acetophenone–nitric acid reaction. The reaction of 2-acetylthiophene and nitric acid gave only di(2-thenoyl)furoxan (I), as white crystalline needles, m.p. 114–115°. This product was obviously not a nitro derivative of the 2-acetylthiophene since 5-nitro-2-acetylthiophene (m.p. 86°) was reported by Peter[6] from nitration of 2-acetylthiophene with fuming nitric acid at −8°. Attempts at the isolation of a by-product were unsuccessful. This inability to obtain a second product in the reaction may be due to the greater ease of dimerization of 2-thenoylnitrile *N*-oxide to form I than is the case with benzoylnitrile *N*-oxide to form dibenzoylfuroxan.

Alkaline hydrolysis of compound I resulted in nearly quantitative transformation of one mole of di(2-thenoyl)furoxan to two moles of 2-thiophenecarboxylic acid. The reaction of phenylhydrazine with I gave two products, 1-thenoyl-2-phenylhydrazine (II), and 3-(β-phenylhydrazino)-4-nitroso-5-thienylisoxazole (III); similar derivatives were obtained from the reaction of phenylhydrazine and dibenzoylfuroxan.[7] Infrared and ultraviolet spectra for I gave absorption bands characteristic of furoxan.[3,8] The evidence cited together with elemental analyses and molecular weight determinations led to the assignment of structure I.



(1) Published with the permission of the Bureau of Naval Weapons, Navy Department. The opinions and conclusions are those of the authors.
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EXPERIMENTAL[9]

To 12.6 g. (0.1 mole) of 2-acetylthiophene in 10 ml. of acetic acid at 90–100°, 13 ml. of 69% nitric acid (*d*, 1.42) in 10 ml. of glacial acetic acid was added in one portion with stirring. Immediately a small amount of sodium nitrate was added. Stirring was continued for several minutes until the exothermic reaction subsided. Dilution with 200 ml. of water caused separation of a yellow oil which solidified. The solid was washed with aqueous sodium carbonate and dried in a vacuum desiccator, wt. 12.3 g. (0.04 mole, 80%). The solid was recrystallized from methanol, m.p. 114–115°. Infrared absorption ($cm.^{-1}$) for di(2-thenoyl)furoxan was obtained from a potassium bromide pellet, 1635S, 1605S 1510M, 1475M, 1410S, 1335M, 1250M, 1050M, 1020W, 890W, 835M, 775M, 755M, 675M. Ultraviolet absorption in ethanol was 282 mμ.

Anal. Calcd. for $C_{12}H_6N_2O_4S_2$ (mol. wt. 306): C, 47.05; H, 1.96; N, 9.15; S, 20.91. Found: C, 47.15; H, 2.24; N, 8.87; S, 21.23; Mol. wt., 319.

Alkaline hydrolysis. A suspension of 0.5 g. (0.0016 mole) of di(2-thenoyl)furoxan in 10 ml. of 10% sodium hydroxide was heated to boiling for 10 min. and then allowed to cool. On acidification with acid and extraction with ether, 0.4 g. (0.0031 mole, 96% based on 1 mole of furoxan to 2 moles of acid) of 2-thiophenecarboxylic acid, m.p. 128°, was obtained.

Anal. Calcd. for $C_5H_4SO_2$: C, 46.87; H, 3.12; S, 25.00. Found: C, 47.15; H, 3.31; S, 25.22.

Reaction of di(2-thenoyl)furoxan with phenylhydrazine. One gram (0.0209 mole) of the furoxan was suspended in 5 ml. of phenylhydrazine in a small flask and shaken until an exothermic reaction began. This was noted by the evolution of a gas. The flask was allowed to cool slowly to room temperature. The reaction mixture was then poured into a large volume of water. After decanting the water layer, the residue was fractionally crystallized from ethanol to yield two fractions, 0.50 g. (0.001 mole, 81%) which melted at 175–176° and 0.3 g. (0.0013 mole, 62%) which melted at 180–181°.

The material melting at 175–176° was yellow and appeared to be 3-(β-phenylhydrazino-4-nitroso-5-thienylisoxazole (III) which would be analogous to the product obtained by Quist[7] from the reaction of dibenzoylfuroxan with phenylhydrazine.

Anal. Calcd. for $C_{13}H_{10}N_4O_2S$: C, 54.54; H, 3.49; N, 19.58; S, 11.18. Found: C, 54.78; H, 3.09; N, 19.29; S, 11.19.

The material melting at 180–181° was white and appeared to be 1-thenoyl-2-phenylhydrazine (II) which would be analogous to a second product Quist[7] isolated from the reaction of dibenzoylfuroxan with phenylhydrazine.

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.55; H, 4.58; N, 12.84; S, 14.67. Found: C, 60.65; H, 4.58; N, 12.76.

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(9) Melting points are uncorrected.

Nucleophilic Substitution of 9α-Bromo-11-ketoprogesterone

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Received July 7, 1961

The recent publication by Cox[1] on the nucleophilic substitution of 9α-bromo-11-keto steroids in the 5α- and 5β-pregnane series prompts us to report our results with a similar reaction on 9α-bromo-11-ketoprogesterone[2] (I). Reaction of I with sodium methoxide in methanol under the conditions of the Favorskii rearrangement[3] furnished a product II in 30% yield which was bromine-free, gave correct analyses for $C_{22}H_{30}O_4$ and contained one methoxyl group. In order to differentiate between the expected Favorskii rearrangement product—*i.e.*, a 9α- or 11α-carbomethoxylated C-nor compound and an unrearranged methoxy derivative formed by displacement of bromine by methoxyl II was reduced with lithium aluminum hydride. Acetylation of the product afforded a crystalline product III which gave an analysis corresponding to $C_{26}H_{40}O_6$, and which had retained the methoxyl group. Thus, displacement of the bromine by methoxyl must have occurred. From the results of Cox[1] it would seem likely that the methoxyl occupied the 12α-position. Indeed, comparison of the proton magnetic resonance spectra[4] of I and 11-ketoprogesterone provided convincing support for this assumption. The peaks which are ascribed[5] to the two protons at position 12 in 11-ketoprogesterone (τ = 7.41 and 7.45) had disappeared in the spectrum of I and been replaced by two new bands, one (area three protons) at 6.65 τ corresponding to the three protons of the methoxyl group and one (area one proton) at 6.56 τ representing the 12β-proton, which had been shifted to lower field because of its attachment to C-12 carrying a methoxyl, as well as being α to the C-11 carbonyl.

In order to confirm that I was 12α-methoxy-11-ketoprogesterone, 11β,12β-oxidoprogesterone[6] (IV) was treated with methanol and perchloric acid[7] to give 12α-methoxy-11β-hydroxyprogesterone[8] (V), which was oxidized with chromic acid[9] to give

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(4) The proton magnetic resonance spectra were taken in deuterochloroform with tetramethylsilane as an internal standard using a Varian Model A-60 instrument.

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