(b.p. 60–70°) gave white crystals melting at 65–73° (reported[13] m.p. 73–74°).

A second fraction collected at 75–85°/0.5 mm. did not absorb in the carbonyl region. Analysis indicated the diketal, 1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 60.13; H, 7.96.

Treatment of an ether solution containing 0.07 mole of phenyllithium with 7.0 g. of 1,4-dioxaspiro[4.5]-8-decanone (0.045 mole) and subsequent work-up as described in I gave an oily residue. This was distilled and 3.90 g. of 8-phenyl-1,4-dioxaspiro[4.5]-8-decanol (37%) was collected at 150–155°/1 mm. The product solidified and was recrystallized from ether-heptane, m.p. 94–96°.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.96; H, 7.57.

Department of Pharmaceutical Chemistry
University of Kansas
Lawrence, Kan.

(13) P. D. Gardner, G. R. Haynes, and R. L Brandon, *J. Org. Chem.*, 22, 1206 (1957).

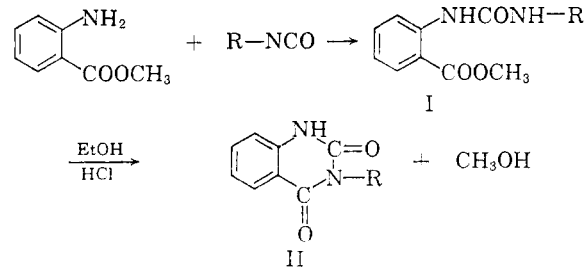
3-Substituted 2,4-Quinazolinediones

Bernard Taub and John B. Hino

Received July 3, 1961

The known methods for the preparation of 3-substituted 2,4-quinazolinediones are complicated and result in relatively low yields. For example, 3-methyl and 3-ethyl-2,4-quinazolinedione are prepared by treating *N*-methyl and *N*-ethyl phthalamide with potassium hypobromite[1] in yields of 48% and 53%, respectively. Another method of synthesizing 3-substituted quinazolinediones involves heating aromatic isocyanates or their dimers with a molten mixture of aluminum chloride and sodium chloride.[2] Yields by this procedure are in the order of 49–64%. It has been reported also[3] that 3-phenyl-2,4-quinazolinedione is obtained when 1,3-diphenylurea is heated with potassium carbonate at 260° under 50 atm. of carbon dioxide pressure. Staiger and Wagner[4] report a synthesis of quinazolinediones by treating isatoic anhydride with primary amines followed by ring closure of the resulting ω-substituted uramidobenzoic acids with dilute sulfuric acid. The latter method has two major drawbacks: the formation of varying amounts of substituted anthranilamides and the failure of some of the uramidobenzoic acids to ring-close.

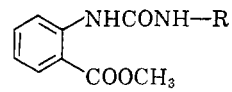
We have now found that a convenient method, and one that produces 3-substituted 2,4-quinazolinediones (II) in excellent yields, involves treating methyl anthranilate with an isocyanate to yield the corresponding ω-substituted methyl uramidobenzoate (I) which in turn is cyclized by treatment with a solution of hydrochloric acid in ethanol. The following equation illustrates the course of the reaction.



The preparation of the ω-substituted methyl uramidobenzoates (I) is most conveniently carried out by treating methyl anthranilate with an isocyanate in the presence of a solvent; *e.g.*, petroleum ether, toluene, diethyl ether, *etc.* Triethylamine is added to facilitate the reaction. Table I lists several ω-substituted methyl uramidobenzoates prepared by this procedure.

TABLE I

ω-Substituted Methyl Uramidobenzoates



R	Yield, %	M.P.[a]	Nitrogen, % Calcd.	Nitrogen, % Found
n-Propyl	91	97–99	11.86	11.44
n-Butyl	88	79–80	11.19	11.00
Cyclohexyl	94	163–164	10.14	9.97
Phenyl	93	144–145	10.36	10.14
p-Tolyl	78	151–152	9.85	9.70
α-Naphthyl	90	190–191	8.75	8.87

[a] Melting points are uncorrected.

The cyclization of the ω-substituted methyl uramidobenzoates listed in Table I was accomplished by refluxing the disubstituted urea esters with an ethanol–hydrochloric acid solution (1:1 by volume). Dilute sulfuric acid, of 10% or 20% concentration, gave varied results; the propyl and butyl derivatives cyclized readily, while the other urea esters were recovered unchanged even after prolonged heating at elevated temperatures. However, by increasing the acid concentration to 37% sulfuric acid, the formation of the quinazoline derivative could be accomplished.

Table II lists the 3-substituted 2,4-quinazolinediones prepared by the cyclization of the ω-substituted methyl uramidobenzoates with ethanolic hydrochloric acid.

(1) F. S. Spring and J. C. Woods, *J. Chem. Soc.*, 625–28 (1945).

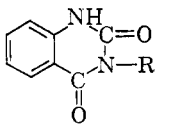
(2) N. S. Dokunikhin and L. A. Gaera, *Zhur. Obshcheĭ Khim.*, 23, 606–10 (1953).

(3) A. I. Kizber and A. S. Glagoleva, *Doklady Akad. Nauk S.S.S.R.*, 83, 89–92 (1952).

(4) R. P. Staiger and E. C. Wagner, *J. Org. Chem.*, 18, 1427–39 (1953).

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.

ALLIED CHEMICAL CORP.
NATIONAL ANILINE DIVISION
BUFFALO 5, N. Y.

(5) F. Zetzsche, E. Luscher, and H. E. Meyer, *Ber.*, **71B**, 1088–93 (1938).
(6) G. Jacini, *Gazz. chim. ital.*, **73**, 85–8 (1943).

Di(2-thenoyl)furoxan[1]

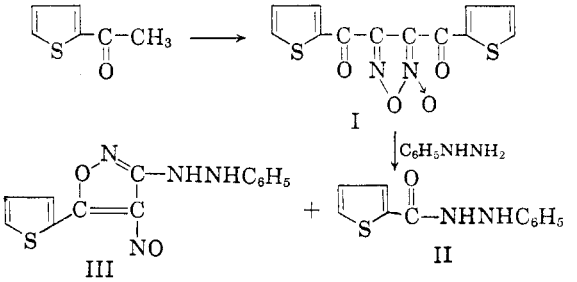
M. S. CHANG AND A. J. MATUSZKO

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.
(2) A. F. Holleman, *Ber.*, **20**, 3359 (1887).
(3) N. E. Boyer, G. M. Czerniak, H. S. Gutowsky, and H. R. Snyder, *J. Am. Chem. Soc.*, **77**, 4238 (1955).
(4) J. H. Boyer and M. S. Chang, *J. Am. Chem. Soc.*, **82**, 2220 (1960).
(5) D. A. Shirley, B. H. Gross, and M. J. Danzig, *J. Org. Chem.*, **23**, 1024 (1958).
(6) A. Peter, *Ber.*, **17**, 2646 (1884).
(7) W. Quist, *Acta Acad. Aboensis, Math. et Phys.*, **5**, 16 (1928); *Chem. Zentr.*, **100** (I), 892 (1929).
(8) J. H. Boyer, U. Toggweiler, and G. A. Stoner, *J. Am. Chem. Soc.*, **79**, 1748 (1957).