Reaction of Anthranilonitrile and *N*-Methylanthranilonitrile with Phenyl Isocyanate and Phenyl Isothiocyanate[1]

EDWARD C. TAYLOR AND R. V. RAVINDRANATHAN

Frick Chemical Laboratory, Princeton University, Princeton, N. J.

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The condensation of anthranilonitrile with phenyl isothiocyanate is known to give *N*-phenyl-*N'*-(*o*-cyanophenyl)thiourea (*2*). We have found that this compound, upon short boiling in methanol, is converted in quantitative yield to 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*4*) which in turn, upon refluxing in aqueous dimethylformamide, rearranges to 2-thio-4-anilino-1,2-dihydroquinazoline (*5*). *5* is formed directly in quantitative yield from anthranilonitrile and phenyl isothiocyanate under more vigorous conditions. Structures of all products are rigorously established, and the mechanism of the rearrangement is discussed.

Anthranilonitrile condenses similarly with phenyl isocyanate to give either *N*-phenyl-*N'*-(*o*-cyanophenyl)urea (*1*), 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*3*), or 2-oxo-4-anilino-1,2-dihydroquinazoline (*15*) depending upon the reaction conditions. Analogous reactions of *N*-methylanthranilonitrile with both phenyl isothiocyanate and phenyl isocyanate are discussed.

It has been found that 2-methylthio-3-phenyl-4-methylimino-1,2,3,4-tetrahydroquinazoline (*10*) rearranges in high yield to 2-anilino-3-methyl-4-oxo-3,4-dihydroquinazoline (*23*) upon treatment with base. The mechanism of this rearrangement is discussed.

Recent work in this laboratory and elsewhere[2-8] had demonstrated the utility and versatility of *o*-aminonitriles as intermediates for the synthesis of condensed pyrimidine heterocycles. The present paper is concerned with the synthesis and subsequent rearrangement of quinazoline derivatives prepared by the reaction of anthranilonitrile and *N*-methylanthranilonitrile with phenyl isocyanate and phenyl isothiocyanate.

The reaction of anthranilonitrile with phenyl isocyanate and phenyl isothiocyanate to give *N*-phenyl-*N'*-(*o*-cyanophenyl)urea (*1*) and *N*-phenyl-*N'*-(*o*-cyanophenyl)thiourea (*2*), respectively, was described as early as 1896,[9] but the only reported attempt to exploit these intermediates for further synthesis *via* intramolecular cyclization was by Breukink and Verkade,[8] who cyclized *1* to 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*3*) with sodium methoxide in methanol. We have now found that anthranilonitrile reacts readily with phenyl isothiocyanate at 50° in the absence of solvent (rather than over a steam bath in ethanol as previously described)[9] to give *2* in high yield, and that *2* has properties apparently unsuspected by the earlier workers. Upon short boiling in methanol, it was converted in quantitative yield to 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*4*), which in turn, upon refluxing with aqueous dimethylformamide, rearranged to 2-thio-4-anilino-1,2-dihydroquinazoline (*5*). Furthermore, the reaction of anthranilonitrile with phenyl isothiocyanate at elevated temperatures rather than at 50° resulted in a vigorous and exothermic reaction with the formation of *5* in quantitative yield. The sequential formation from anthranilonitrile of *2*, then *4*, and finally *5* is dramatically shown by a determination of the melting point of *2;* it melts, then resolidifies, melts again at the melting point of *4*, resolidifies, and finally melts a third time at the melting point of *5*.

The structures of compounds *4* and *5* have been rigorously confirmed. Thus, 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*4*) on acid hydrolysis gave 2-thio-3-phenyl-4-oxo-1,2,3,4-tetrahydroquinazoline (*6*), identical in every respect with an authentic sample prepared by the reaction of phenyl isothiocyanate with anthranilic acid.[10] Acid hydrolysis of 2-thio-4-anilino-1,2-dihydroquinazoline (*5*) gave 2-thio-4-oxo-1,2,3,4-tetrahydroquinazoline (*7*) which, on desulfurization, gave the well known 4-oxo-3,4-dihydroquinazoline (*8*). Furthermore, direct desulfurization of *5* gave 4-anilinoquinazoline (*9*). These interconversions are illustrated in Fig. 1.

The intramolecular cyclization of *2* to *4* is a further example of the familiar Thorpe-type base-catalyzed condensation of amines with nitriles,[11] the catalyst in this instance being either the thio-

(1) This research was supported by a research grant (CY-2551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service.

(2) E. C. Taylor, A. J. Crovetti, and R. J. Knopf, *J. Am. Chem. Soc.*, **80**, 427 (1958).

(3) E. C. Taylor and K. S. Hartke, *J. Am. Chem. Soc.*, **81**, 2456 (1959).

(4) E. C. Taylor and P. K. Loeffler, *J. Am. Chem. Soc.*, **82**, 3147 (1960).

(5) E. C. Taylor, R. J. Knopf, and A. L. Borror, *J. Am. Chem. Soc.*, **82**, 3152 (1960).

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(7) E. C. Taylor and J. A. Zoltewicz, *J. Am. Chem. Soc.*, **83**, 248 (1961).

(8) K. W. Breukink and P. E. Verkade, *Rec. trav. chim.*, **79**, 450 (1960).

(9) J. Pinnow and C. Sämann, *Ber.*, **29**, 623 (1896).

(10) T. N. Ghosh, *J. Indian Chem. Soc.*, **7**, 981 (1930).

(11) V. Migrdichian, *The Chemistry of Organic Cyanogen Compounds*, Reinhold Publishing Corp., New York, 1947, p. 285.

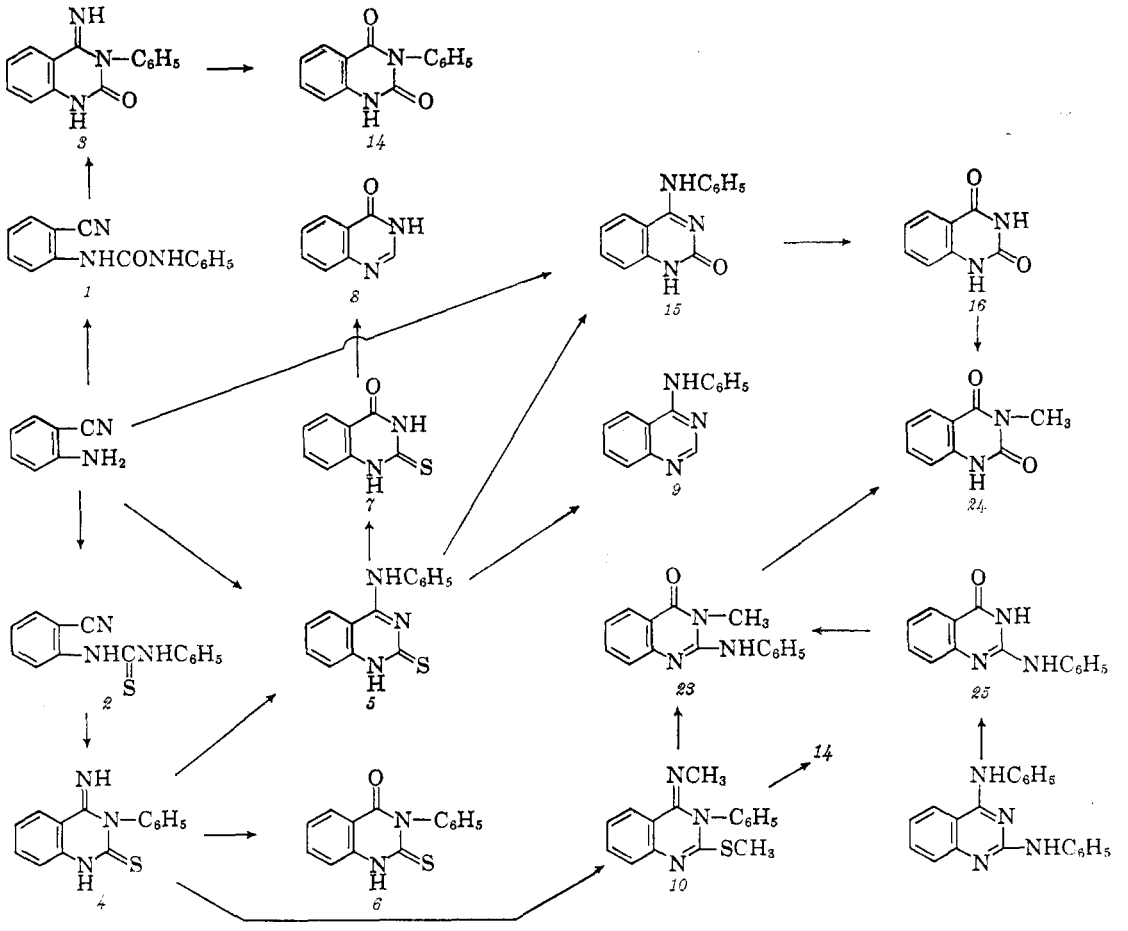

Figure 1

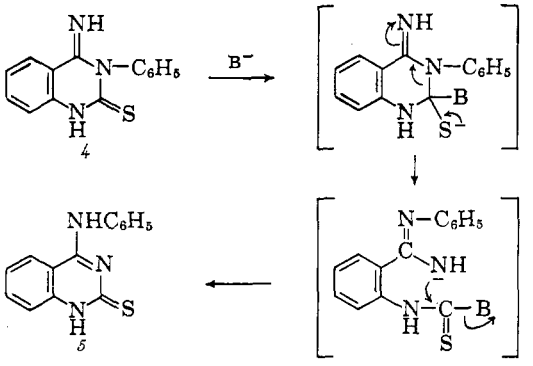

Figure 2

urea (*2*) or the imine (*4*). The conversion of *4* to *5* furnishes an additional example of the 1,3-exo-annular rearrangement, studied in some detail in other systems,[12] and proceeds *via* a ring-opening, ring-closure sequence which requires a basic catalyst (Fig. 2). Here again the basic catalyst in the thermal conversion of *4* to *5* is probably the imine (*4*). An attempt to effect the rearrangement of *4* to *5* with dilute sodium hydroxide resulted only in hydrolysis of the imino group to give 2-thio-3-phenyl-4-oxo-1,2,3,4-tetrahydroquinazoline (*6*).

In order to determine the effect of the presence of the acidic —SH group on the rearrangement reaction, compound *4* was methylated with methyl iodide in the presence of one equivalent of alkali. The product proved to be 2-methylthio-3-phenyl-4-oxo-3,4-dihydroquinazoline rather than the desired 4-imino compound. Methylation with dimethyl sulfate in the presence of an excess of sodium hydroxide gave only 2-methylthio-3-phenyl-4-methylimino-3,4-dihydroquinazoline (*10*). A monomethylated product suitable for rearrangement studies was finally prepared by phosphorus oxychloride–pyridine dehydration of *o*-methylaminobenzamide to *N*-methylanthranilonitrile, followed by reaction with phenyl isothiocyanate at 100° to give 1-methyl-2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*11*) in quantitative yield. The structure of this product was conclusively established by acid hydrolysis to 1-methyl-2-thio-3-phenyl-4-oxo-1,2,3,4-tetrahydroquinazoline (*12*), identical with an authentic sample prepared by the reaction of *N*-methylanthranilic acid with phenyl isothiocyanate.[13] Compound *11* was recovered unchanged

(12) J. A. Zoltewicz, Ph.D. thesis, Princeton University, 1960.

(13) J. E. McCarty, E. L. Haines, and C. A. Vanderwerf, *J. Am. Chem. Soc.*, **82**, 965 (1960).

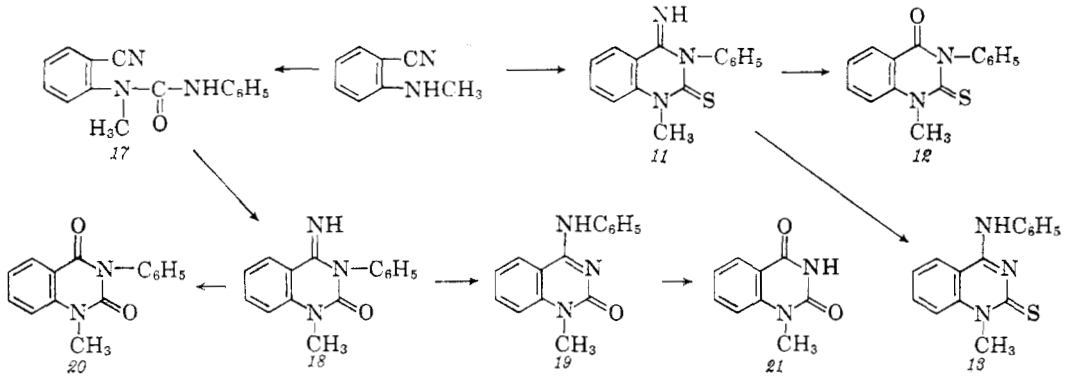

Figure 3

from refluxing aqueous dimethylformamide and was hydrolyzed to *12* with 0.05 *N* sodium hydroxide, but underwent partial rearrangement to 1-methyl-2-thio-4-anilino-1,2-dihydroquinazoline (*13*) upon refluxing with 0.05 *N* methanolic sodium methoxide in methanol (Fig. 3).

Related studies have also been carried out with phenyl isocyanate (Fig. 1). Reaction of anthranilonitrile with phenyl isocyanate gave 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*3*), but all attempts to rearrange this material to 2-oxo-4-anilino-1,2-dihydroquinazoline (*15*) were unsuccessful. Thus, *3* was recovered unchanged from refluxing aqueous dimethylformamide and from numerous other basic solvent systems, and underwent hydrolysis to 3-phenyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*14*) on heating with 1 *N* sodium hydroxide. However, when anthranilonitrile and one equivalent of phenyl isocyanate were heated together at a higher temperature (135°), the rearranged product, 2-oxo-4-anilino-1,2-dihydroquinazoline (*15*) was formed in a vigorously exothermic reaction in 52% yield. The structure of *15* was conclusively established by acid hydrolysis to 2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*16*) and by an independent synthesis from 2-thio-4-anilino-1,2-dihydroquinazoline (*5*) and alkaline hydrogen peroxide. Although it seems clear that the conversion of anthranilonitrile to *15* must proceed through 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*3*), heating the latter compound with phenyl isocyanate failed to bring about rearrangement, apparently because of decomposition under the reaction conditions employed.

Reaction of *N*-methylanthranilonitrile with phenyl isocyanate yielded *N*-phenyl-*N'*-methyl-*N'*-(*o*-cyanophenyl)urea (*17*) in high yield (Fig. 3). Heating with 0.05 *N* sodium methoxide in methanol gave a mixture of 1-methyl-2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*18*) and its rearrangement product, 1-methyl-2-oxo-4-anilino-1,2-dihydroquinazoline (*19*). The structures of these products were established by acid hydrolysis to 1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinazoline (*20*) and 1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*21*), respectively. Attempts to rearrange *18* to *19* with dilute sodium hydroxide resulted only in hydrolysis to *20*, but partial and slow rearrangement could be effected by prolonged heating with 0.05 *N* sodium methoxide in methanol.

It was mentioned above that treatment of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*4*) with dimethyl sulfate and an excess of sodium hydroxide gave a dimethylated product, to which the structure 2-methylthio-3-phenyl-4-methylimino-3,4-dihydroquinazoline (*10*) was assigned. This structural assignment was based on analysis and the observation that acid hydrolysis gave 3-phenyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*14*). An unusual and facile rearrangement took place upon warming *10* with weak aqueous methanolic sodium hydroxide. Methyl mercaptan was evolved and a product formed in high yield which was shown to be 2-anilino-3-methyl-4-oxo-3,4-dihydroquinazoline (*23*). Thus, although attempted hydrolysis of *23* with hydrochloric acid yielded only the hydrochloride salt of *23*, refluxing with 1 *N* sodium hydroxide gave 3-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*24*), which was identical with an authentic sample prepared by methylation of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline (*16*). Furthermore, compound *23* was prepared independently from 2,4-dianilinoquinazoline by hydrolysis with dilute hydrochloric acid to give 2-anilino-4-oxo-3,4-dihydroquinazoline (*25*), followed by methylation with dimethyl sulfate and alkali. We suggest that this hydrolytic rearrangement proceeds *via* the ring-opening, ring-closure sequence pictured in Fig. 4, which is formally similar to that suggested by Cheng and Robins[14] for the related conversion of 1-methyl-4-amino-6-chloropyrazolo[3,4-*d*]pyrimidine to 1-methyl-4-hydroxy-6-aminopyrazolo[3,4-*d*]-pyrimidine upon treatment with alkali.

(14) C. C. Cheng and R. K. Robins, *J. Org. Chem.*, **24**, 1570 (1959).

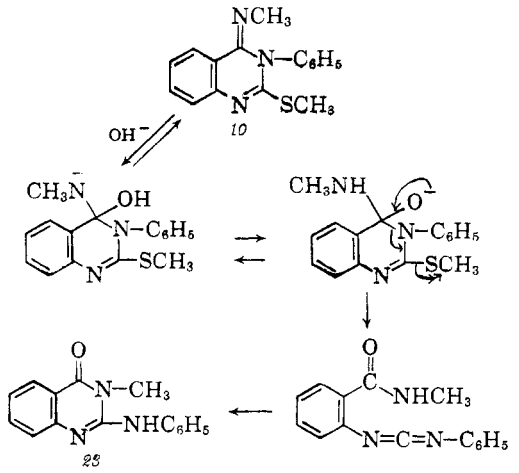

Figure 4

Experimental[15]

N-Phenyl-N'-(o-cyanophenyl)urea (*1*) was prepared by the method of Breukink and Verkade,[8] but melted at 186–188° rather than at 168° as previously reported. The infrared spectrum showed a strong nitrile band at 2225 cm.$^{-1}$

Anal. Calcd. for $C_{14}H_{11}N_3O$: C, 70.9; H, 4.6; N, 17.7. Found: C, 70.2; H, 4.6; N, 17.7.

N-Phenyl-N'-(o-cyanophenyl)thiourea (*2*). A mixture of 1.1 g. of anthranilonitrile[16] and 1.5 g. of phenyl isothiocyanate in a test tube was heated at 50 ± 2° for 20 hr. with occasional stirring. The cooled mixture was then removed from the tube, powdered, and extracted three times with 15-ml. portions of ether. The residue (2.0 g., 85%) melted at 165–168°, but upon resolidification remelted at 195–198°. This material was previously reported not to melt below 300°.[9]

2-Thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*4*). Method A. A solution of 2.3 g. of anthranilonitrile and 2.7 g. of phenyl isothiocyanate in 10 ml. of benzene was heated under reflux for 20 hr., cooled, and the precipitated solid was collected by filtration to give 2.6 g. (53%), m.p. 195–198°. Recrystallization from methanol gave glistening pale yellow crystals.

Anal. Calcd. for $C_{14}H_{11}N_3S$: C, 66.4; H, 4.35; N, 16.6. Found: C, 66.3; H, 4.4; N, 16.4

Method B. A solution of 0.100 g. of *N*-phenyl-*N'*-(*o*-cyanophenyl)thiourea in 20 ml. of methanol was heated under reflux for 10 minutes and then evaporated to dryness under reduced pressure to give 0.095 g. (95%), identical with the product obtained by Method A.

2-Thio-4-anilino-1,2-dihydroquinazoline (*5*). Method A. An intimate mixture of 23.6 g. of anthranilonitrile and 27.0 g. of phenyl isothiocyanate in a 150-ml. Erlenmeyer flask was heated at 100°, whereupon a vigorous exothermic reaction took place within the first few minutes and the clear melt partially solidified to an orange-red jelly. The mixture was maintained at 100° for 12 hr. and the resulting yellow solid was removed from the flask, powdered, and extracted several times with ether to remove unreacted starting material; yield, 49.3 g. (97%), m.p. 238–241°. Recrystallization from methanol raised the melting point to 240–242°.

Anal. Calcd. for $C_{14}H_{11}N_3S$: C, 66.4; H, 4.35; N, 16.6; S, 12.6. Found: C, 66.4; H, 4.6; N, 16.5; S, 12.5.

Method B. A solution of 0.45 g. of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in a mixture of 15 ml. of dimethylformamide and 30 ml. of water was heated under reflux for 1 hr. and then evaporated to a small volume under reduced pressure. Addition of water to the residue resulted in the separation of 0.41 g. (91%) of a light yellow solid, m.p. 238–240°, identical in every respect with the product obtained by Method A above.

2-Thio-3-phenyl-4-oxo-1,2,3,4-tetrahydroquinazoline (*6*). A solution of 0.40 g. of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 50 ml. of 10% hydrochloric acid was heated under reflux for 1 hr., allowed to stand at room temperature for 4 hr. and then filtered. The collected solid was washed thoroughly with cold water and dried to give 0.31 g. (78%) of slightly yellow crude product, m.p. 285–295°. Extraction with boiling water removed the color and raised the melting point to 305–306°. This compound has been reported to melt above 300°.[10]

Anal. Calcd. for $C_{14}H_{10}N_2OS$: C, 66.1; H, 3.9; N, 11.0. Found: C, 65.7; H, 4.0; N, 11.2.

2-Thio-4-oxo-1,2,3,4-tetrahydroquinazoline (*7*). Heating a solution of 6.0 g. of 2-thio-4-anilino-1,2-dihydroquinazoline in 500 ml. of 10% hydrochloric acid for 2.5 hr., cooling, and filtering gave 3.6 g. (86%) of pale yellow crystals, m.p. 311–313°. Recrystallization from methanol raised the melting point to 313–314°.

Anal. Calcd. for $C_8H_6N_2OS$: C, 53.9; H, 3.3; N, 15.7; S, 18.0. Found: C, 54.4; H, 3.5; N, 15.7; S, 17.6.

4-Oxo-3,4-dihydroquinazoline (*8*). A mixture of 3.60 g. of 2-thio-4-oxo-1,2,3,4-tetrahydroquinazoline, 18 g. of freshly prepared W7 Raney nickel, and 500 ml. of methanol was heated under reflux for 6 hr., filtered to remove the Raney nickel, and the filtrate evaporated to dryness under reduced pressure to give 2.03 g. of a pale green solid, m.p. 195–206°, which evidently still contained nickel. It was boiled with 150 ml. of water, filtered, and the filtrate concentrated and cooled to give 1.28 g. (39%) of colorless crystals, m.p. 217–218°, identical with an authentic sample.

4-Anilinoquinazoline (*9*). Desulfurization of 0.50 g. of 2-thio-4-anilino-1,2-dihydroquinazoline by the procedure described above gave 0.27 g. (62%) of crude product, m.p. 209–216°. Recrystallization from methanol yielded glistening colorless platelets, m.p. 220–221°. This compound is reported to melt at 216–217°[17] and at 221–222°.[18]

Anal. Calcd. for $C_{14}H_{11}N_3$: C, 76.0; H, 5.0; N, 19.0. Found: C, 76.3; H, 5.3; N, 18.8.

2-Methylthio-3-phenyl-4-oxo-3,4-dihydroquinazoline. A mixture of 5.06 g. of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline, 3 g. of methyl iodide and 0.8 g. of sodium hydroxide in 100 ml. of water was heated under reflux for 3 hr. The yellow oil which separated solidified on cooling of the reaction mixture at 0° overnight, and was separated by filtration; yield, 4.80 g. (90%), m.p. 95–112°. Recrystallization from ethanol gave colorless needles, m.p. 125°. This compound has been reported to melt at 130–130.5°.[18]

Anal. Calcd. for $C_{15}H_{12}N_2SO$: C, 67.2; H, 4.5; N, 10.45; S, 11.9. Found: C, 67.1; H, 4.5; N, 10.5; S, 11.9.

2-Methylthio-3-phenyl-4-methylimino-3,4-dihydroquinazoline (*10*). To a solution of 15.0 g. of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 200 ml. of 1 *N* sodium hydroxide was added 20 g. of dimethyl sulfate, and the mixture was stirred at room temperature for 15 min. and then allowed to stand for 24 hr. The precipitated solid was collected by filtration, washed, and dried to give 14.8 g. (89%) of crude product, m.p. 128–132°. Recrystallization from methanol raised the melting point to 135–136°.

Anal. Calcd. for $C_{16}H_{15}N_3S$: C, 68.3; H, 5.3; N, 14.9; S, 11.4. Found: C, 68.1; H, 5.6; N, 14.75; S, 11.2.

N-Methylanthranilonitrile. To a stirred solution of 45 g. of

(15) All melting points are uncorrected. We are indebted for the microanalyses to Dr. George Robertson, Florham Park, N. J.

(16) G. R. Bedford and M. W. Partridge, *J. Chem. Soc.*, 1633 (1959).

(17) N. J. Leonard and D. Y. Curtin, *J. Org. Chem.*, 11, 349 (1946).

(18) N. A. Lange and F. E. Sheibley, *J. Am. Chem. Soc.*, 53, 3867 (1931).

dry *o*-methylaminobenzamide[19] in 50 ml. of dry pyridine immersed in an ice bath was added dropwise over a period of 20 min. 46 g. of phosphorus oxychloride. The reaction mixture was stirred at 0° for an additional 40 min. and then poured into 1200 ml. of ice water. The precipitated solid was collected by filtration, washed well with water and dried to give 15 g. of crude product, m.p. 72–74°. An additional 15 g. of product, m.p. 73–74° (total yield, 76%), separated from the filtrate upon standing at room temperature for 48 hr. Recrystallization from petroleum ether (b.p. 30–60°) gave colorless leaflets, m.p. 73–74°. This compound has previously been prepared in very poor yield by methylation of anthranilonitrile and was reported to melt at 64–68°[20] and at 70°.[21]

1-Methyl-2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*11*). A mixture of 1.32 g. of *N*-methylanthranilonitrile, 1.35 g. of phenyl isothiocyanate, and 15 ml. of dry pyridine was heated with stirring at 100° for 2 hr. and then poured into 250 ml. of ice water. The mixture was stirred for 15 min. and then filtered to give 2.31 g. (87%) of crude product, m.p. 208–215°. Recrystallization from methanol yielded cream-colored needles melting at 215–217°.

Anal. Calcd. for $C_{15}H_{13}N_3S$: C, 67.4; H, 4.9; N, 15.7; S, 12.0. Found: C, 67.3; H, 4.8; N, 15.9; S, 11.9.

1-Methyl-2-thio-3-phenyl-4-oxo-1,2,3,4-tetrahydroquinazoline (*12*). A solution of 0.50 g. of 1-methyl-2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 100 ml. of 10% hydrochloric acid was heated under reflux for 6 hr. and then filtered to give 0.41 g. (82%) of pale yellow crystals, m.p. 298–302°. Recrystallization from a mixture of benzene and ethanol gave white needles, m.p. 302–303°, identical in every respect with an authentic sample prepared from *N*-methylanthranilic acid and phenyl isothiocyanate.[13]

Anal. Calcd. for $C_{15}H_{12}N_2OS$: C, 67.2; H, 4.5; N, 10.45; S, 12.0. Found: C, 67.2; H, 4.5; N, 10.3; S, 11.9.

1-Methyl-2-thio-4-anilino-1,2-dihydroquinazoline (*13*). A solution of 5.0 g. of 1-methyl-2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 500 ml. of 0.05 *N* sodium methoxide in methanol was heated under reflux for 30 hr., then cooled and neutralized with dilute acetic acid. Evaporation to dryness followed by fractional crystallization of the residue from methanol yielded, as the less soluble component, 2.1 g. (41%) of yellow crystals, m.p. 184–186°.

Anal. Calcd. for $C_{15}H_{13}N_3S$: C, 67.4; H, 4.9; N, 15.7; S, 12.0. Found: C, 66.9; H, 4.8; N, 15.3; S, 11.9.

The more soluble, higher melting (214–216°) fraction proved to be unchanged starting material.

2-Oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*3*). To a cooled solution of 0.20 g. of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline and 0.1 g. of sodium hydroxide in 5 ml. of water and 65 ml. of ethanol was added dropwise and with stirring 0.6 g. of 30% hydrogen peroxide. After 4 hr. at room temperature, the mixture had completely decolorized, and it was then evaporated to a small volume under reduced pressure, neutralized with dilute acetic acid and filtered; yield, 0.15 g. (80%), m.p. 215–218°. Recrystallization from methanol gave colorless crystals melting at 222–223°. The product was identical with an authentic sample of 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline prepared by cyclization of *N*-phenyl-*N'*-(*o*-cyanophenyl)urea with sodium methoxide in methanol.[8] Hydrolysis with 10% hydrochloric acid gave 2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinazoline, m.p. 278–281°, identical in every respect with an authentic sample prepared from anthranilic acid and phenyl isocyanate.[8]

2-Oxo-4-anilino-1,2-dihydroquinazoline (*15*). Method A. A mixture of 1.18 g. of finely powdered anthranilonitrile and 1.10 g. of phenyl isocyanate contained in a test tube was immersed in an oil bath preheated to 130°. Within a few minutes a vigorous exothermic reaction took place, and the reaction mixture solidified to an orange-red solid. Heating was continued at 130° overnight, and then the solid material was removed from the tube, powdered and extracted with 300 ml. of hot 1*N* sodium hydroxide. Acidification of the filtrate caused the separation of 1.24 g. (52%) of a pale yellow solid, m.p. 252–260°. Recrystallization from absolute methanol gave glistening yellow platelets melting at 265–266°.

Anal. Calcd. for $C_{14}H_{11}N_3O$: $\frac{1}{2}$ CH_3OH: C, 68.8; H, 5.1; N, 16.6. Found: C, 68.8; H, 5.05; N, 16.5.

Method B. Hydrolytic desulfurization of 2-thio-4-anilino-1,2-dihydroquinazoline with hydrogen peroxide and alkali, as described above for the conversion of 2-thio-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline to 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline, afforded 2-oxo-4-anilino-1,2-dihydroquinazoline in 82% yield. The product obtained in this way was identical in every respect with the product obtained by Method A above.

Hydrolysis of (15) with hydrochloric acid yielded 2,4-dioxo-1,2,3,4-tetrahydroquinazoline, m.p. 353–354°,[22] in good yield.

N-Phenyl-N'-methyl-N'-(o-cyanophenyl)urea (*17*). A mixture of 13.2 g. of *N*-methylanthranilonitrile, 12 g. of phenyl isocyanate, and 50 ml. of benzene was heated under reflux overnight, cooled, and filtered to give 18.2 g. of glistening white crystals, m.p. 214–216°. Concentration of the filtrate afforded an additional 4.1 g. of product for a total yield of 89%. Recrystallization from ethanol–benzene (1:1) raised the melting point to 217–218°. This compound was previously reported to melt at 186°.[23]

Anal. Calcd. for $C_{15}H_{13}N_3O$: C, 71.7; H, 5.2; N, 16.7. Found: C, 71.5; H, 5.3; N, 16.6.

1-Methyl-2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline (*18*). Method A. A solution of 12.6 g. of *N*-phenyl-*N'*-methyl-*N'*-(*o*-cyanophenyl)urea in 500 ml. of 0.05 *N* sodium methoxide in methanol was heated under reflux for 18 hr., neutralized with dilute acetic acid, and evaporated to dryness. Fractional recrystallization of the residue (12.3 g., m.p. 146–154°, then 230–240°) afforded, as the more soluble fraction, 7.3 g. (58%) of stout colorless needles, m.p. 158–159°.

Anal. Calcd. for $C_{15}H_{13}N_3O$: C, 71.7; H, 5.2; N, 16.7. Found: C, 71.6; H, 5.3; N, 16.6.

Hydrolysis of this material with 10% hydrochloric acid gave 1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinazoline, m.p. 224°, identical in every respect with an authentic sample prepared from *N*-methylanthranilic acid and phenyl isocyanate (reported m.p. 233°).[24]

Method B. A solution of 2.4 g. of 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 100 ml. of cold 1*N* sodium hydroxide was treated with 3 g. of dimethyl sulfate and stirred overnight. Filtration yielded 2.1 g. of colorless crystals which were recrystallized from methanol. The product, m.p. 158–159°, was identical in every respect with the product obtained by Method A above.

1-Methyl-2-oxo-4-anilino-1,2-dihydroquinazoline (*19*) Method A. The less soluble fraction from Method A above weighed 3.1 g. (25%) and melted at 248–251°. Further recrystallization from methanol raised the melting point to 252° and gave fine glistening colorless crystals.

Anal. Calcd. for $C_{15}H_{13}N_3O$: C, 71.7; H, 5.2; N, 16.7. Found: C, 71.5; H, 5.35; N, 16.6.

Hydrolysis of this material with 10% hydrochloric acid gave 1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline, m.p. 273–274°, identical with an authentic sample prepared from

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N-methylanthranilic acid and potassium cyanate. This compound is reported to melt at 265°.[25]

Method B. A solution of 1.50 g. of 1-methyl-2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline in 250 ml. of 0.05*N* sodium methoxide in methanol was heated under reflux for 30 hr. The solution was then neutralized with dilute acetic acid, evaporated to a small volume, and cooled to give 0.77 g. (51%) of colorless crystals, m.p. 251–252°, identical in every respect with the material prepared by Method A above.

2-Anilino-4-oxo-3,4-dihyroquinazoline (25). A solution of 3.50 g. of 2,4-dianilinoquinazoline[19] in 500 ml. of 10% hydrochloric acid was heated under reflux for 4 hr., cooled, filtered and neutralized with sodium hydroxide. Filtration then gave 1.81 g. (68%) of colorless crystals, m.p. 258–260°. Recrystallization from ethanol raised the melting point to 261°. The product was identical with an authentic sample of 2-anilino-4-oxo-3,4-dihydroquinazoline prepared by the method of Grout and Partridge.[26]

2-Anilino 3-methyl-4-oxo-3,4-dihydroquinazoline (23). Method A. A mixture of 0.50 g. of 2-methylthio-3-phenyl-4-methylimino-3,4-dihydroquinazoline, 40 ml. of methanol, 20 ml. of water, and 2 ml. of 1*N* sodium hydroxide was heated under reflux for 3 hr. (in the hood). The light yellow reaction mixture was cooled and neutralized with dilute acetic acid, and then concentrated under reduced pressure to approximately 15 ml. Cooling gave 0.42 g. (94%) or colorless plates, m.p. 202–205°. Recrystallization from methanol raised the melting point to 206–207°.

Anal. Calcd. for $C_{15}H_{13}N_3O$: C, 71.7; H, 5.2; N, 16.7. Found: C, 71.6; H, 5.0; N, 16.7.

Method B. To a solution of 0.50 g. of 2-anilino-4-oxo-3,4-dihydroquinazoline in 25 ml. of cold 1*N* sodium hydroxide was added 1 ml. of dimethyl sulfate, and the mixture was stirred at room temperature for 15 min. Filtration then gave 0.43 g. (81%) of crude product, m.p. 198–202°. Recrystallization from methanol raised the melting point to 206–207°. The product was identical in every respect with the product obtained by Method A above.

3-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline (24). A solution of 1.00 g. of 2-anilino-3-methyl-4-oxo-3,4-dihydroquinazoline in 150 ml. of 1*N* sodium hydroxide was heated under reflux for 8 hr. with stirring. The clear, pale yellow solution was cooled, neutralized wih acetic acid, and chilled overnight. Filtration then gave 0.47 g. (68%) of a colorless solid, m.p. 241–243°. The melting point was raised to 244–245° by recrystallization from methanol. This compound was previously reported to melt at 230–233°.[27] Comparison of the reaction product with an authentic sample of 3-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline showed them to be identical.

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Formation of 1-Methylcyclopentene in the Thermal Decomposition of *N,N,N*-Trimethylcyclopentylmethylammonium Hydroxide[1]

ARTHUR C. COPE, JOSEPH LAZAR,[2] NORMAN A. LEBEL,[3] AND DANIEL L. ROSS

Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Massachusetts

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It has been shown that the 1-methylcyclopentene formed as a by-product in the thermal decomposition of *N,N,N*-trimethylcyclopentylmethylammonium hydroxide is produced from the initial product formed by β-elimination, methylenecyclopentane, by base-catalyzed isomerization. This conclusion was reached by study of the decomposition of deuterium-labeled quaternary bases and by decomposition of *N,N*-dimethylcyclopentylmethylamine oxide in the presence of potassium hydroxide.

The thermal decomposition of *N,N,N*-trimethylcyclopentylmethylammonium hydroxide produces varying amounts of 1-methylcyclopentene in addition to the expected methylenecyclopentane.[4] It appeared that the formation of the abnormal olefin could be explained by the operation of one or more of three mechanisms. Two of these would involve direct formation of the compound by bimolecular eliminations accompanied by hydride shifts, while the third is the seemingly obvious possibility that the initially formed methylenecyclopentane isomerizes during the pyrolysis in the strongly basic reaction medium.

Methylenecyclopentane, however, failed to isomerize when heated at 150° for forty-eight hours in a sealed tube in the presence of 40% aqueous tetramethylammonium hydroxide. Attempts to minimize the contact of methylenecyclopentane with base and thereby decrease the amount of 1-methylcyclopentene produced the opposite result. Thus, when a concentrated solution of the quaternary base was added dropwise to a heated evacuated flask, it was found that the olefins were formed in good yield and that the ratio of the *endo* to the *exo* isomer was much higher than that found when the pyrolysis was carried out in the usual manner. In addition, it was shown that, when the pyrolysis was carried out at 0.05 and 0.01 mm. pressure rather than at 12 mm. (the pressure usually employed), the highest yields of olefins as well as the highest proportion of the abnormal product were obtained (see Table I).

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