2-Methylthio-5-methylbenzo-1,3-dithiolium Perchlorate (17b).—Six grams of toluene-3,4-dithiol (Eastern Chemical Corp., Newark, N. J.) was dissolved in 15 ml. of methyl chlorothioformate,[16] and 6 ml. of 70% perchloric acid was added dropwise (caution!)[1c] to the rapidly stirring solution. After *ca.* 3 ml. of the acid had been added, evolution of hydrogen chloride was observed, and a strong exothermic reaction ensued. After stirring an additional 15 min., the cooled solution was diluted with 100 ml. of ethyl acetate. The yellow solid which separated was collected and washed with additional ethyl acetate; purification of a portion of the material was effected by precipitation from 70% perchloric acid by the addition of ethyl acetate. The yellow plates, obtained in 33% yield, had m.p. 149–151° (lit.[6a] m.p. 140–142°); τ_{CF_3COOH} 1.78–2.42 m (3), 6.72 (3), 7.35 (3).[17]

Anal. Calcd. for $C_9H_9ClO_4S_3$: C, 34.55; H, 2.90; S, 30.75. Found: C, 34.79; H, 3.02; S, 30.62.

An attempt was made to prepare 2-methylthiobenzo-1,3-dithiolium perchlorate (**17a**) in the preceeding manner. However, insolubility of the reagents gave rise to a heterogeneous mixture, and no reaction occurred upon addition of the acid. A homogenous solution resulted when ethyl acetate was added, and subsequent heating of the mixture at 100° caused a copious evolution of hydrogen chloride. After 1 hr., the solution was cooled and diluted with additional ethyl acetate. A red solid, m.p. 130–140°, obtained in 37% yield, had an infrared spectrum nearly identical with pure **17a**; however, due to the low yield and impurity of product by this procedure, the method of Wizinger and Dürr[6c] was employed. In this manner, **17a** was obtained in an over-all 94% yield starting from benzene-1,2-dithiol.[16]

Phenacyl N-Methyl-N-phenyldithiocarbamate (13a).—The method outlined by Seman[18] was used. In a 300-ml., round-bottom, three-necked flask equipped with reflux condenser, dropping funnel, and magnetic stirrer was suspensed 2.5 g. of 90% practical grade sodium amide in 50 ml. of benzene. Methylaniline (6.3 g., 0.059 mole) in 50 ml. of benzene was added and the mixture was stirred overnight at room temperature. Carbon disulfide (5.4 g., an excess) in 50 ml. of benzene was added, and finally 8.3 g. (0.054 mole) of phenacyl chloride in 50 ml. of benzene was dropped slowly into the stirring mixture. After 15 min., the mixture was refluxed gently for 1 hr., cooled, and poured into 500 ml. of water. The organic layer was separated, washed with water, dried ($MgSO_4$), and evaporated to yield 13.4 g. (83%) of product, which, after recrystallization from 95% ethanol, melted at 157–158°.

Anal. Calcd. for $C_{16}H_{15}NOS_2$: C, 63.75; H, 5.0; S, 21.28. Found: C, 63.84; H, 5.10; S, 21.36.

Phenacyl N,N-Diphenyldithiocarbamate (13b).—**13b** was prepared in the same manner. Thus, 10 g. of diphenylamine yielded 15.5 g. (79%) of product, m.p. 166–167° (95% ethanol).

Anal. Calcd. for $C_{21}H_{17}NOS_2$: C, 69.39; H, 4.72; S, 17.64. Found: C, 69.79; H, 4.93; S, 17.71.

N-Methyl-N-phenyl-2-amino-4-phenyl-1,3-dithiolium Perchlorate (14a).—One gram of **13a** was warmed at 100° in 2 ml. of 70% perchloric acid for 5 min. The solution was then cooled and diluted with *ca.* 200 ml. of ethyl acetate; the colorless solid which separated was collected, dried, and recrystallized from glacial acetic acid. The product, 1.05 g. (83%), melted at 214–215°. A mixture melting point of this material with the methylaniline adduct of **5** was undepressed, and the spectral properties of these compounds were identical: τ_{CF_3COOH} 2.15–2.75 m (11), 6.00, 6.05 (3)[17]; $\lambda_{max}^{95\%\ EtOH}$ 234 mμ (log ε 4.13), 330 (4.03).

2-Diphenylamino-4-phenyl-1,3-dithiolium Perchlorate (14b).—The β-keto dithiocarbamate **13b** (0.6 g.) was warmed at 100° with 5 ml. of 70% perchloric acid for 20 min. The solution was cooled and diluted with ethyl acetate, giving a gray-blue solid (0.64 g., 87%). Recrystallization (Norit) twice from 95% alcohol gave colorless needles: m.p. 277–278°; τ_{CF_3COOH} 2.30 (10), 2.53 (5), 2.63 (1)[17]; $\lambda_{max}^{95\%\ EtOH}$ 238 mμ (log ε 4.21), 343 (3.97).

Anal. Calcd. for $C_{21}H_{16}ClNO_4S_2$: C, 56.56; H, 3.62; S, 14.38. Found: C, 56.46; H, 3.67; S, 14.63.

3-Methylthio-5-phenyl-1,2-dithiolium Perchlorate (8).—Ten grams of 5-phenyl-1,2-dithiole-3-thione[10] was heated in 30 ml. of dimethyl sulfate to 160° for 15 min., and allowed to cool to room temperature. Then 70 ml. of glacial acetic acid was added, followed by 8 ml. of 70% perchloric acid. After stirring thoroughly, 200 ml. of ether was added; the yellow solid (12 g., 78%) which separated was collected and washed with additional quantities of ether and ethyl acetate, and melted at 165–170°. This material was used in the reactions with secondary amines. A portion of the material was recrystallized from 70% perchloric acid by the addition of ethyl acetate, and had m.p. 174–175°; τ_{CF_3COOH} 1.72 (1), 1.98–2.43 m (5), 6.90 (3).[17]

Anal. Calcd. for $C_{10}H_9ClO_4S_3$: C, 36.97; H, 2.79; S, 29.62. Found: C, 36.96; H, 2.72; S, 29.49.

(16) We wish to express our gratitude to Dr. Walter Reifschneider of the Dow Chemical Co., Midland, Mich., for a sample of benzene-1,2-dithiol, and to the Stauffer Chemical Co. for a sample of methyl chlorothioformate.

(17) N.m.r. is reported in τ-units (number of protons).

(18) W. L. Seman, U. S. Patent 2,046,884; *Chem. Abstr.*, **30**, P5592[5,6] (1936).

Quinazolines. I. Formation of a Guanidinoquinazoline during the Three-Component Synthesis of a 4,6-Diamino-1-aryl-1,2-dihydro-s-triazine[1]

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The structure of a high-melting companion product, $C_{14}H_{13}N_5 \cdot HCl$, isolated during the three-component synthesis of 4,6-diamino-2,2-dimethyl-1-(2-naphthyl)-1,2-dihydro-*s*-triazine hydrochloride (I·HCl) from 2-naphthylamine hydrochloride, dicyandiamide, and acetone has been investigated. On the basis of a combination of degradative and synthetic evidence, this by-product has been formulated as the hitherto unreported compound 3-guanidino-1-methylbenzo[*f*]quinazoline hydrochloride (XVII·HCl).

Biologically active 4,6-diamino-1-aryl-1,2-dihydro-*s*-triazines have been synthesized in large numbers since 1951, both in this laboratory[2–4] and elsewhere,[5–9] by either of two general routes (eq. 1). The chemistry of these dihydrotriazines has been surveyed in a recent review,[10] and they have been shown to exhibit a wide variety of significant biological properties, including

(1) This work was supported in part by a research grant (C6516) from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(2) E. J. Modest, G. E. Foley, M. M. Pechet, and S. Farber, *J. Am. Chem. Soc.*, **74**, 855 (1952).

(3) E. J. Modest, *J. Org. Chem.*, **21**, 1 (1956).

(4) E. J. Modest and P. Levine, *ibid.*, **21**, 14 (1956).

(5) H. C. Carrington, A. F. Crowther, D. G. Davey, A. A. Levi, and F. L. Rose, *Nature*, **168**, 1080 (1951).

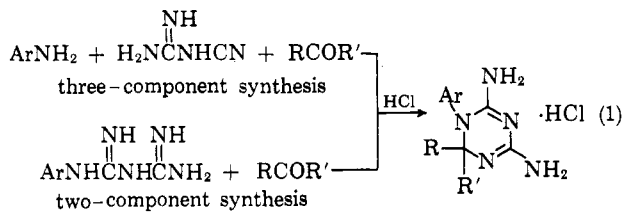
(6) H. C. Carrington, A. F. Crowther, and G. J. Stacey, *J. Chem. Soc.*, 1017 (1954).

(7) U. P. Basu and A. K. Sen, *J. Sci. Ind. Research (India)*, **11B**, 312 (1952).

(8) T. L. Loo, *J. Am. Chem. Soc.*, **76**, 5096 (1954).

(9) H. L. Bami, *J. Sci. Ind. Research (India)*, **14C**, 231 (1955).

(10) E. J. Modest in "Heterocyclic Compounds," Vol. 7, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 697.



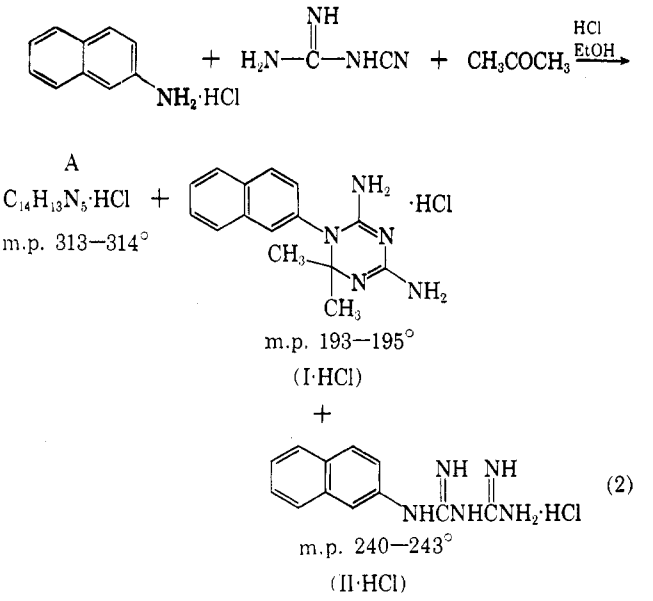
inhibitory activity against certain experimental tumors.[11,12]

The isolation of a biologically active high-melting by-product from the condensation of 2-naphthylamine hydrochloride, dicyandiamide, and acetone has been reported in a preliminary communication.[13] Although it was possible, on the basis of information then available, to propose two possible isomeric structures, an unequivocal assignment could not be made. We now wish to present evidence that this anomalous companion product is the hydrochloride salt of 3-guanidino-1-methylbenzo[*f*]quinazoline (XVII), rather than that of the linear isomer 2-guanidino-4-methylbenzo[*g*]-quinazoline (XVI).

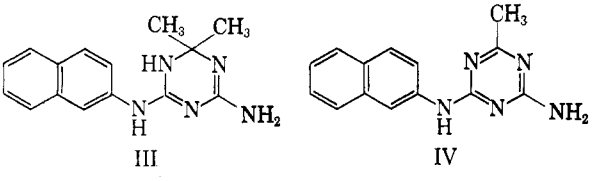
Refluxing 2-naphthylamine hydrochloride, dicyandiamide, and acetone in ethanol for 6 hr. furnished a 17% yield of a substance A (m.p. 313–314° dec.) with the empirical formula, $C_{14}H_{13}N_5 \cdot HCl$. Work-up of the mother liquor afforded a 41% yield of the normal three-component synthesis product, the hydrochloride salt of 4,6-diamino-2,2-dimethyl-1-(2-naphthyl)-1,2-dihydro-*s*-triazine (I·HCl, m.p. 193–195°). In a modified run, from which compound A was isolated in 15% yield, careful work-up of the mother liquor afforded a 27% yield of the normal product (I·HCl) and, in addition, a 21% yield of the hydrochloride salt of N^1-(2-naphthyl)biguanide (II·HCl, m.p. 240–243°). Identification of the latter was made on the basis of a positive biguanide test (pink precipitate with alkaline copper ammonium sulfate),[3,4] and comparison with an authentic sample prepared from 2-naphthylamine hydrochloride and dicyandiamide by the method of King and Tonkin.[14]

The generation of high-melting companion product A during the three-component synthesis of I·HCl appears to be a fairly rapid process. This may be due, in part at least, to the sparing solubility of compound A in the reaction medium. The isolation and identification of N^1-(2-naphthyl)biguanide hydrochloride (II·HCl) in the mother liquor after removal of the normal product I·HCl lends support to the view that a biguanide may be, as has been postulated,[3,10] the intermediate involved in the three-component synthesis of dihydrotriazines.

Neutralization of an aqueous solution of compound A with dilute alkali furnished a free base, $C_{14}H_{13}N_5$ (m.p. 244–245°), from which compound A could be regenerated by acidification of an alcoholic solution with dilute hydrochloric acid. Addition of alkaline copper ammonium sulfate to an aqueous methanolic solution of compound A gave a dense pale greenish solid[15] instead of the pink precipitate characteristic of biguanide II and many other N^1-substituted biguanides.[3] Quantitative ultraviolet absorption maxima for compound A, as well as for a number of degradation products and related substances, are summarized in Table I (p. 2885).



The loss of the elements of methane relative to 4,6-diamino-2,2-dimethyl-1-(2-naphthyl)-1,2-dihydro-*s*-triazine (I) led to the initial consideration of N^2-(2-naphthyl)acetoguanamine (IV) as a possible structure for the free base of compound A. This product could conceivably arise by demethylation and concomitant aromatization of 4-amino-2,2-dimethyl-6-(2-naphthylamino)-1,2-dihydro-*s*-triazine (III), which could in turn be formed from I according to a rearrangement characteristic of compounds of this type.[2–6] Although rearrangement of I to III would not normally be expected under acid conditions, the relief of the steric crowding of neighboring 2-naphthyl and *gem*-dimethyl substituents in I, followed by the ultimate formation of planar structure IV, might favor such a process. Unambiguous synthesis of IV from II and ethyl acetate according to the conventional method[16] disposed of this possibility, however, since the authentic specimen in no way resembled companion substance A.



Several chemical transformations, summarized in Chart I, were then undertaken in an effort to assign a structure to compound A. Although compound A

(11) (a) S. Farber, I. Diamond, G. Foley, and E. J. Modest, *Am. J. Pathol.*, **28**, 559 (1952); (b) S. Farber, G. Foley, V. Downing, R. Appleton, and J. King, Proceedings of the American Association for Cancer Research, Vol. 1, 1953, p. 15.

(12) S. Farber, E. J. Modest, A. H. Handler, and C. L. Maddock, *ibid.*, **4**, 19 (1963).

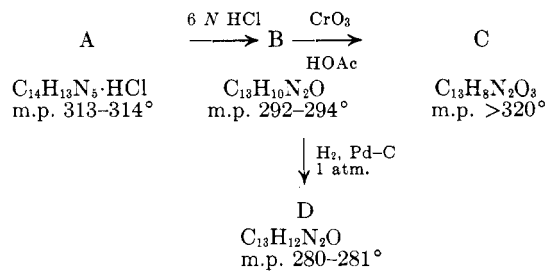
(13) (a) A. Rosowsky, H. Kangur, and E. J. Modest, Abstracts of Papers, 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April, 1963, p. 35-L. (b) Microbiological studies in the *Streptococcus faecalis* 8043–folic acid assay system, kindly performed by Dr. George E. Foley and co-workers, showed compound A to have a 50% growth-inhibiting dose (ID_{50}) of 3.5 γ/ml. at a folic acid level of 0.001 γ/ml. Against KB cells (human epidermoid carcinoma) in mammalian cell culture systems, the ID_{50} value was 1.0 γ/ml.

(14) H. King and I. M. Tonkin, *J. Chem. Soc.*, 1063 (1946).

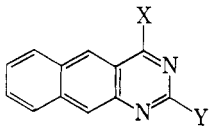
(15) We have observed that a number of condensed pyrimidines substituted at C-2 by a guanidine function form grayish green precipitates with alkaline copper ammonium sulfate. This color reaction appears to be characteristic for such compounds.

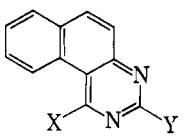
(16) U. S. Patents 2,309,663 and 2,344 784 (1943), and similar patents.

CHART I



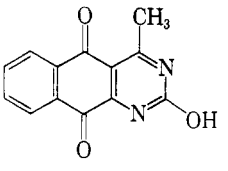
exhibited surprising stability toward both acid and alkaline hydrolysis, vigorous treatment with 6 *N* hydrochloric acid converted it into an amphoteric substance B (m.p. 292–294°) with the empirical formula, $C_{13}H_{10}N_2O$. The loss of the elements of guanidine during acid hydrolysis suggested that a guanidino function was present in A, an assumption which was confirmed by the observation of a positive Sakaguchi test.[17] On the basis of the elemental analysis and ultraviolet absorption spectrum and the finding that it was amphoteric, acid hydrolysis product B was suspected to be a condensed pyrimidine system containing methyl and hydroxyl groups on the pyrimidine ring. The four possible candidates considered in this connection were 4-hydroxy-2-methylbenzo[*g*]quinazoline (V),[18] 1-hydroxy-3-methylbenzo[*f*]quinazoline (VI),[19] 2-hydroxy-4-methylbenzo[*g*]quinazoline (VII), and 3-hydroxy-1-methylbenzo[*f*]quinazoline (VIII). Of these, compounds V and VI were eliminated by comparison of acid hydrolysis product B with authentic specimens prepared according to literature methods. Unfortunately, however, neither of the remaining two isomers, VII and VIII, had been reported prior to this investigation.



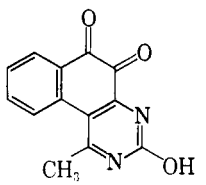


V, X = OH; Y = CH_3 VI, X = OH; Y = CH_3
VII, X = CH_3; Y = OH VIII, X = CH_3; Y = OH
XIV, X = Y = OH XV, X = Y = OH

Oxidation of acid hydrolysis product B with chromic acid in acetic acid afforded a pale yellow quinone (no melting point below 320°) with the empirical formula, $C_{13}H_8N_2O_3$. This substance resisted attempts to form a derivative with *o*-phenylenediamine, failed to undergo further oxidation with neutral potassium permanganate, and was recovered unchanged on treatment with hot aqueous base. On the basis of literature analogy,[20,21] these reactions might have been expected to convert X into a quinoxaline derivative, a dicarboxylic acid cleavage product, and a benzilic acid type rearrangement product, respectively. Although 5,6-quinones derived from 1,7-diazaphenanthrene and 1,10-diazaphenanthrene are known to undergo such transformations readily,[20,21] these compounds do not necessarily constitute adequate models from which to predict the behavior of a quinone like X, in which the presence of an additional hydroxyl group capable of tautomerizing with one of the carbonyl functions might reduce the amount of *ortho*-quinonoid character in the system. Although suggestive of linear structure IX for quinone C, the above observations by themselves could not be regarded as conclusive.

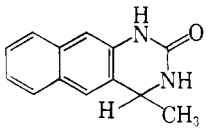


IX

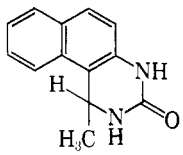


X

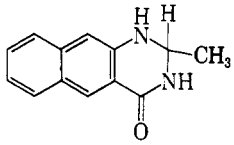
Catalytic reduction of the acid hydrolysis product at atmospheric pressure over 10% palladium on carbon furnished a crystalline dihydro derivative D ($C_{13}H_{12}N_2O$, m.p. 280–281°, XI or XII). A similar transformation has been reported by Etienne and Legrand,[18] who obtained dihydro compound XIII on reduction of 4-hydroxy-2-methylbenzo[*g*]quinazoline (V) with lithium aluminum hydride. The preparation of compound D provided additional support for the two proposed hydroxypyrimidine structures, VII and VIII, but once again did not permit a choice to be made between them.



XI



XII



XIII

Efforts to oxidize compound B with sodium hypobromite to either of the known compounds, 2,4-dihydroxybenzo[*g*]quinazoline (XVI) or 1,3-dihydroxybenzo[*f*]quinazoline (XV), following a reaction previously used successfully by Siegle and Christensen[22] to convert 2,4-dimethylquinazoline into 4-hydroxy-2-methylquinazoline, met with failure, unchanged starting material being recovered.

A strong clue to the structure of compound A and to its origin in the three-component synthesis was provided by a brief paper by Brown.[23] This investigator described the conversion of Knoevenagel's aniline "acetone anil" (2,2,4-trimethyl-1,2-dihydroquinoline,[24] to 2-guanidino-4-methylquinazoline and isobutylene on treatment with dicyandiamide and hydrochloric acid. Since several "acetone anils" of arylamines have been described in the literature,[25–28] it seemed perfectly

(17) R. J. Block, E. T. Durrum, and G. Zweig, "Manual of Paper Chromatography and Paper Electrophoresis," Academic Press, Inc., New York, N. Y., 1955, p. 92.

(18) A. Etienne and M. Legrand, *Compt. rend.*, **229**, 220 (1949).

(19) T. Bhattacharyya, P. K. Boss, and J. N. Ray, *J. Indian Chem. Soc.*, **6**, 279 (1929).

(20) P. Karrer, A. Platscher, and W. Manz, *Helv. Chim. Acta*, **30**, 1146 (1947).

(21) J. Druey and P. Schmidt, *ibid.*, **33**, 1080 (1950).

(22) J. Siegle and B. E. Christensen, *J. Am. Chem. Soc.*, **73**, 5777 (1951).

(23) J. P. Brown, *Chem. Ind.* (London), 233 (1960).

(24) (a) I. W. Elliott, Jr., and P. Yates, *J. Org. Chem.*, **26**, 1287 (1961), including discussion of the structure of aniline "acetone anil" and references to previous work. (b) Additional aspects of the chemistry of this substance have been presented recently in the following papers: C. C. Tung, *Tetrahedron*, **19**, 1685 (1963); E. J. Zobian, W. S. Kelley, and H. C. Dunathan, *J. Org. Chem.*, **29**, 584 (1964).

(25) E. Knoevenagel, *Ber.*, **54**, 1722 (1921).

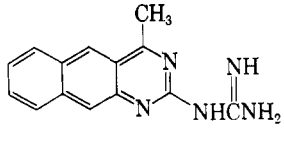
(26) G. Reddelien and A. Thurm, *ibid.*, **65**, 1511 (1932).

(27) J. T. Murray, W. F. Short, and R. Stansfield, *J. Am. Chem. Soc.*, **55**, 2805 (1933).

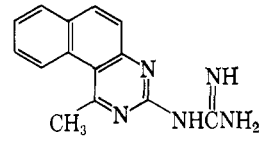
(28) W. H. Cliffe, *J. Chem. Soc.*, 1327 (1933).

reasonable to suppose that 2-naphthylamine is likewise capable of forming an adduct with 2 moles of acetone.[29] If such an "acetone anil" intermediate were being generated competitively with N^1-(2-naphthyl)-biguanide (II) during the three-component synthesis, it would give rise to a guanidino compound analogous to that obtained by Brown.[23] The structure of this guanidino compound could be either 2-guanidino-4-methylbenzo[*g*]quinazoline (XVI) or 3-guanidino-1-methylbenzo[*f*]quinazoline (XVII), depending on whether the hypothetical 2-naphthylamine "acetone anil" has the linear structure, 2,2,4-trimethyl-1,2-dihydrobenzo[*g*]quinoline (XVIII), or the angular structure, 1,3,3-trimethyl-3,4-dihydrobenzo[*f*]quinoline (XIX).

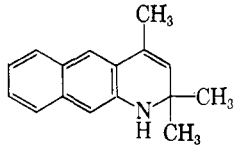
An "acetone anil" of 2-naphthylamine was prepared according to the directions given by Knoevenagel for aniline and related arylamines.[25] The same adduct could be formed equally well, it was found, if acetone was replaced by mesityl oxide. The reaction yielded a dark amber-colored viscous oil, which could not be crystallized and was therefore used without further purification in most cases. Evidence that the expected adduct was formed was obtained on examination of the n.m.r. spectrum of the crude oily product. In addition to a complex aromatic pattern, there were present four bands with τ-values[30] of 8.76 (singlet), 7.60 (doublet), 6.29 (broad), and 4.62 (broad). These peaks have been assigned to *gem*-dimethyl, single methyl, amine, and vinyl protons, respectively, and are in reasonable agreement with the values published recently by Elliott and Yates[24] for aniline "acetone anil."



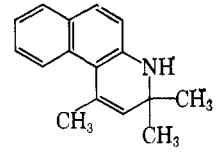
XVI



XVII



XVIII

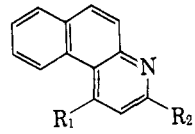


XIX

Treatment of the crude "acetone anil" of 2-naphthylamine with dicyandiamide and hydrochloric acid in aqueous ethanol produced vigorous gas evolution (presumably isobutylene, by analogy with the work of Brown[23]). A high-melting white hydrochloride salt was isolated in about 65% yield, and found to be identical with compound A in every respect.

In order to assign a structure to compound A, it remained only to establish whether the "acetone anil" of 2-naphthylamine was being formed by linear or angular cyclization.[31] For this purpose, palladium-catalyzed demethylation and aromatization to a benzoquinoline derivative was carried out. Heating partly purified 2-naphthylamine "acetone anil" with 10% palladium on carbon at 280°[32] gave a high yield of a product which proved to be identical with an authentic sample of 1,3-dimethylbenzo[*f*]quinoline (XX), prepared according to the procedure of Johnson and co-workers[34] by condensation of 2,4-pentanedione with 2-naphthylamine and cyclization of the resulting adduct in the presence of zinc chloride and 2-naphthylamine hydrochloride. The angular character of XX was assigned by Johnson and co-workers on the basis of ultraviolet spectral and chemical properties.[34] The identity of the two samples was established by comparison of the properties of the free bases, hydrochlorides, and picrates, including their infrared, ultraviolet, and n.m.r. spectra. No evidence for the existence of any linear isomer was found in the present work.

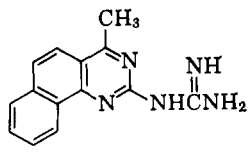
That cyclization of 2-naphthylamine with 2 equiv. of acetone (or with mesityl oxide) furnishes an angular isomer is consistent with the fact that 2-naphthylamine is known to undergo the Doebner–Miller reaction with 2 equiv. of acetaldehyde, affording the angular compound 1-methylbenzo[*f*]quinoline (XXI).[35] In the same manner, 2-naphthylamine has been reported to condense with an equimolar mixture of acetone and acetaldehyde to give the angular compound, 1,3-dimethylbenzo[*f*]quinoline (XX).[36a]



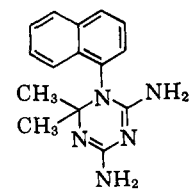
XX, $R_1=R_2=CH_3$
XXI, $R_1=H$; $R_2=CH_3$

The isolation and identification of 3-guanidino-1-methylbenzo[*f*]quinazoline (XVII) as a companion product formed in appreciable quantity during the three-component synthesis of 4,6-diamino-2,2-dimethyl-

(29) Although the existence of an analogous "acetone anil" of 1-naphthylamine that could presumably give rise to 2-guanidino-4-methylbenzo[*h*]-quinazoline (i) was considered, careful search revealed no high-melting companion product when 4,6-diamino-2,2-dimethyl-1-(1-naphthyl)-1,2-dihydro-*s*-triazine (ii) was prepared by the three-component synthesis (see Experimental). The absence of a by-product is consistent with Knoevenagel's observation [*Ber.*, **55**, 2309, 2319 (1922)] that 1-naphthylamine reacts with only 1 equiv. of acetone under the usual conditions of "acetone anil" formation, giving a simple Schiff's base.



i



ii

(30) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(31) For a discussion of numerous reactions involving 2-naphthylamine in an angular cyclization, see J. A. VanAllan in "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1958, Chapter III; or L. P. Walls in "Heterocyclic Compounds," Vol. 4, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, Chapter 5.

(32) Although aniline "acetone anil" has been reported[33] to undergo smooth conversion to 2,4-dimethylquinoline on heating with sodium anilide, a benzoquinoline could not be obtained from 2-naphthylamine "acetone anil" by this method.

(33) W. R. Vaughan, *Org. Syn.*, **28**, 49 (1948).

(34) W. S. Johnson, E. Woroch, and F. J. Mathews, *J. Am. Chem. Soc.*, **69**, 566 (1947).

(35) O. Doebner and W. von Miller, *Ber.*, **17**, 1698 (1884).

(36) (a) J. H. Reed, *J. prakt. Chem.*, [2]**35**, 299 (1887). (b) Following the completion of this work it was learned that Mamalis and co-workers (private communication) arrived at similar conclusions regarding the structure of XVII.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA

Compd.	pH 1 λ_{max}, mμ	pH 1 ε × 10⁻³	pH 10 λ_{max}, mμ	pH 10 ε × 10⁻³	95% ethanol λ_{max}, mμ	95% ethanol ε × 10⁻³
V	249[a]	29.60	240	39.30	235	37.66
	266	46.05	253[a]	39.14	252[a]	41.32
	274	43.74	260	44.24	260	52.32
	311	3.31	269	45.22	296	4.15
	352	3.14	299	3.54	308	4.90
			311	3.96	322	3.88
			324	2.99	345[a]	2.46
			360	3.62	357	3.75
			372[a]	2.96	373	2.76
VI	240[a]	11.19	262	41.08	261[b]	42.69
	270	31.05	290	7.31	270	38.46
	324	4.68	316	3.17	298	8.02
	340	2.90	331	3.69	316	4.06
			346	3.82	331	4.63
					340	2.91
					346	5.01
VIII	232	52.16	235	37.97	235[b]	52.86
(compd. B)	257	16.92	248	27.71	250	24.87
	277	6.32	258	29.50	259	20.76
	288	7.90	264	29.83	284	8.27
	360	9.43	282	12.28	318	7.15
			305[a]	4.94	358	5.30
			356	4.30	371	5.24
			367	4.17		
X	224	25.17	252	43.98	225[a]	28.26
(compd. C)	231	27.17	259[a]	40.66	245	42.82
	240[a]	30.74	281[a]	8.95	252	44.97
	246[a]	34.85	288[a]	7.16	262	22.74
	251	36.60	300–303[c]	5.15	284[a]	4.10
	297[a]	5.52	338	3.98	295	5.48
	307	6.39	351	5.08	307	6.46
	336	4.25	371	3.33	325[a]	2.87
	350	3.95			338	4.33
					352	4.22
XII	243	46.20	243	45.15	244[b]	48.35
(compd. D)	248	45.51	248	44.64	249	50.24
	275	4.28	276	4.22	276	4.45
	286	5.29	287	5.22	286	5.52
	297	4.09	298	4.06	297	4.22
	324	1.51	325	1.49	326	1.64
	336	1.53	337	1.50	338	1.67
XVII	233	29.94	233	18.03	233	29.92
(compd. A)	269	48.75	280	48.33	269	52.73
	304–310[c]	5.85	352	2.88	305[a]	6.70
	335	3.24			336	3.14
	351	2.88			352	3.15

[a] Inflection. [b] 50% ethanol. [c] Plateau.

1-(2-naphthyl)-1,2-dihydro-*s*-triazine (I) has prompted a search for other examples of this type.[36b] Further exploration of the scope of such an abnormal three-component synthesis is currently in progress and will be reported at a later date.

Experimental

The ultraviolet absorption spectra reported here were measured with a Cary Model 11 recording spectrophotometer. Spectra at pH 1 were taken in 0.1 *N* hydrochloric acid and at pH 10 in 0.05 *M* sodium carbonate–sodium borate buffer. Infrared spectra were taken in potassium bromide disks with a Perkin-Elmer Model 137B double-beam recording spectrophotometer (sodium chloride prism). N.m.r. spectra were determined in deuteriochloroform with a Varian A-60 spectrometer, tetramethylsilane being used as the internal reference.

Unless otherwise stated, analytical samples were dried at 70–100° for 17 hr. *in vacuo* over phosphorus pentoxide. Melting points were determined in sealed Pyrex capillary tubes in a modified Wagner–Meyer melting point apparatus,[37] and are corrected wherever possible. The temperatures at which compounds are reported to melt are generally decomposition points, and have been found to depend to a significant degree on whether the capillary tube is sealed or open, on the age and state of subdivision of the sample, on the rate of heating, and on the immersion temperature. Corrected melting points were taken under uniform conditions at a heating rate of 2°/min.

Microanalyses were performed by Scandinavian Microanalytical Laboratory, Herlev, Denmark, and by Galbraith Laboratories, Knoxville, Tenn.

Condensation of 2-Naphthylamine, Dicyandiamide, and Acetone (Three-Component Synthesis). A. Standard Conditions.—A mixture of 2-naphthylamine hydrochloride (18.0 g., 0.1 mole) and dicyandiamide (9.0 g., 0.11 mole) in 30 ml. of acetone and 40 ml. of absolute ethanol was stirred under reflux for 6 hr. A clear amber solution was obtained at reflux, but a colorless solid began to appear after 20 min. The reaction mixture was kept at room temperature overnight, and the solid was collected, washed with acetone, and dried at 70°. The pale yellow prismatic needles, yield 5.0 g. (17%), melted at 313–315° dec. Two crystallizations from water, in 88% recovery, afforded analytically pure colorless prismatic needles of **3-guanidino-1-methylbenzo[*f*]quinazoline hydrochloride (XVII·HCl)**, m.p. 313–314° dec. This material gave a greenish white precipitate with alkaline copper ammonium sulfate (negative biguanide test),[3,4] and a deep red color with alkaline 1-naphthol–sodium hypobromite (positive Sakaguchi guanidine test). The infrared spectrum of XVII·HCl contained a strong, sharp peak at 5.93 μ, which was absent in the free base.

Anal. Calcd. for $C_{14}H_{13}N_5 \cdot HCl$: C, 58.33; H, 4.55; N, 24.44. Found: C, 58.37; H, 4.95; N, 24.78.

For the preparation of XVII free base, a 1-g. portion of the hydrochloride salt was dissolved in 100 ml. of hot water and the resulting solution was adjusted to approximately pH 11 with 5 *N* sodium hydroxide. The precipitate was collected, washed with cold water, and crystallized directly from 95% ethanol with the aid of Darco.[38] The yield of analytically pure pale yellow prismatic rods was 0.56 g. (64%), m.p. 244–245° dec. (Addition of a few drops of 6 *N* hydrochloric acid to a solution of free base XVII in *n*-propyl alcohol, and brief refrigeration, regenerated hyrochloride XVII·HCl in excellent yield.)

Anal. Calcd. for $C_{14}H_{13}N_5$: C, 66.91; H, 5.21; N, 28.01. Found: C, 66.53; H, 5.47; N, 27.77.

The aqueous ethanol mother liquor and acetone washes were combined, treated with Darco, and concentrated under reduced pressure. Trituration of the resulting sirupy residue with acetone afforded a crystalline solid, which was collected and dried at 70°, yielding 12.3 g. (41%) of small off-white prisms, m.p. 206–209° (uncor.). A 5.2-g. portion of this product was crystallized from 12 ml. of 20% ethanol after treatment with Darco (30% recovery), recrystallized from water, and dried for 72 hr. *in vacuo* at 50°. The analytically pure colorless prisms of **4,6-diamino-2,2-dimethyl-1-(2-naphthyl)-1,2-dihydro-*s*-triazine hydrochloride (I·HCl)** melted at 193–195°[39] (lit.[40] 211–212°).

Anal. Calcd. for $C_{15}H_{17}N_5 \cdot HCl \cdot 0.5H_2O$: C, 57.59; H. 6.12; N, 22.39. Found: C, 57.89; H, 6.38; N, 22.42.

The above product formed no precipitate with alkaline copper ammonium sulfate and gave a negative Sakaguchi test.

B. Interrupted Synthesis.—In a separate experiment, the reaction was interrupted after 30 min. and cooled. The white solid that had formed in the amber-colored solution was collected, washed with hot ethanol until colorless, and dried *in vacuo* at 45° for 1 hr. to give 2.87 g. (10%) of XVII·HCl, m.p. 306–310° dec. Refluxing of the combined mother liquor and wash solutions for an additional 16 hr. furnished a second crop of insoluble products, which was purified and dried as above to bring the total yield of XVII·HCl in this experiment to 4.34 g. (15%).

The mother liquor was concentrated to dryness under reduced pressure. Repeated trituration of the resulting viscous residue

(37) E. C. Wagner and J. F. Meyer, *Ind. Eng. Chem., Anal. Ed.*, **10**, 584 (1938).

(38) Darco G-60 activated carbon, Atlas Chemical Industries, Inc., Wilmington, Del.

(39) The melting point of carefully purified I·HCl was lower than that of the crude material, presumably because the latter was contaminated with small quantities of higher melting impurities, such as XVII·HCl or II·HCl.

(40) P. Mamalis, J. Green, D. J. Outred, and M. Rix, *J. Chem. Soc.*, 3915 (1962).

with acetone, and cooling, furnished a solid which was collected and purified by crystallization from aqueous ethanol, yielding 8.20 g. (27%) of I·HCl, m.p. 206–207° (uncor.).

Refrigeration of the acetone triturate for several days afforded an additional 5.62 g. (21%) of white solid which gave a pink precipitate with alkaline copper ammonium sulfate (positive biguanide test).[3,4] Examination of the infrared absorption spectrum and comparison with an authentic specimen, m.p. 240–243°, prepared according to King and Tonkin,[14] indicated this fraction to consist chiefly of **N¹-(2-naphthyl)biguanide hydrochloride**.

1,3,3-Trimethyl-3,4-dihydrobenzo[*f*]quinoline (2-Naphthylamine "Acetone Anil," XIX).—A solution of 2-naphthylamine (1.43 g., 0.01 mole), mesityl oxide (1.2 ml., 0.01 mole), and iodine (0.07 g.) in 15 ml. of absolute ethanol was stirred under reflux for 21 hr. The dark amber solution (λ_{max}^{EtOH} 238 and 258 mμ, λ_{min}^{EtOH} 249 mμ) was diluted to 50 ml. with water, and the product was extracted into two 50-ml. portions of ether. The combined ether extracts were shaken with 5% sodium thiosulfate, rinsed with water, dried over anhydrous sodium sulfate, and concentrated to dryness under reduced pressure. The viscous amber residue (1.94 g., 87% of theoretical) began to solidify after a few hours at room temperature, but did not crystallize completely even after prolonged refrigeration. The same product could be obtained equally well from 2-naphthylamine and acetone in the presence of iodine (see next experiment). This compound was therefore used in subsequent reactions without further purification.

Condensation of 2-Naphthylamine "Acetone Anil" with Dicyandiamide.—A solution of 2-naphthylamine (11.5 g., 0.08 mole) and iodine (1 g.) in anhydrous acetone (50 ml.) was refluxed for 24 hr.[25] and concentrated to dryness under reduced pressure. The dark oily residue was dissolved in 200 ml. of benzene and the solution was extracted with several portions of 10% aqueous sodium thiosulfate (300-ml. total), rinsed thoroughly with distilled water, dried over anhydrous sodium sulfate, and concentrated to dryness *in vacuo*. To the resulting dark viscous oil (crude XIX) was added a solution of dicyandiamide (6.8 g., 0.081 mole) and concentrated hydrochloric acid (10 ml., 50% excess) in 50% ethanol (100 ml.), and the mixture was stirred under reflux for 2 hr. The dense precipitate that formed upon cooling in an ice bath was collected, washed thoroughly with water and acetone, and air-dried. The yield of pale yellow prismatic crystals was 13.8 g. (60%). Upon concentration of the combined mother liquor and washes an additional 4.2 g. (18%) of tan crystalline solid was obtained. The total yield of crude XVII·HCl was 18.0 g. (78%). Crystallization of 3.75 g. of the above solid from 20 ml. of water after treatment with Darco afforded 3.13 g. (84% recovery) of small colorless prismatic needles, m.p. 313–314° dec. The infrared spectrum of this material was identical with that of XVII·HCl obtained from the three-component synthesis.

4-Hydroxy-2-methylbenzo[*g*]quinazoline (V), m.p. 319–320° dec. (lit.[18] 320°), was prepared from 2-amino-3-naphthoic acid and acetamide by the method of Etienne and Legrand.[18]

1-Hydroxy-3-methylbenzo[*f*]quinazoline (VI), m.p. 290–292° dec. (lit.[19] 295°), was prepared according to the procedure of Bhattacharyya and co-workers,[19] by condensation of 2-naphthylamine with N-acetylurethane, and cyclization of the resulting N-(2-naphthyl)-N′-acetylurea in the presence of phosphorus pentoxide.

3-Hydroxy-1-methylbenzo[*f*]quinazoline (VIII).—A mixture of 10.0 g. (0.0348 mole) of 3-guanidino-1-methylbenzo[*f*]quinazoline hydrochloride (XVII·HCl) and 300 ml. of concentrated hydrochloric acid was refluxed for 18 hr. and the resulting greenish yellow solution was refrigerated. The solid that had formed was collected, washed with acetone and ether, and air-dried, yielding 7.67 g. of shiny yellow prismatic plates. This solid was dissolved in 2 l. of 95% ethanol to which sufficient ammonium hydroxide had been added to bring the pH to approximately 8, and the volume of the resulting pinkish amber solution was reduced to 900 ml. After refrigeration for 2 hr. the solid was collected, washed with acetone and ether, and dried for 17 hr. at 52° *in vacuo*, yielding 4.85 g. (66%) of slightly colored long prismatic needles. One further crystallization from 95% ethanol afforded analytically pure, nearly colorless, long prismatic needles, m.p. 292–294° dec. after being dried for 64 hr. at 70° over phosphorus pentoxide *in vacuo*.

Anal. Calcd. for $C_{13}H_{10}N_2O$: C, 74.26; H, 4.81. Found: C, 73.94; H, 4.82.

3-Hydroxy-1-methylbenzo[*f*]quinazoline-5,6-dione (X).—3-Hydroxy-1-methylbenzo[*f*]quinazoline (VIII, 1.35 g., 0.006 mole) in 100 ml. of warm glacial acetic acid was oxidized with 3.2 g. (0.032 mole) of chromium trioxide in 30 ml. of water. The solution was heated on a steam bath for 30 min., diluted to 500 ml. with water, and cooled briefly. The solid that formed was collected, washed thoroughly with water, and dried at 60° *in vacuo*, yielding 1.0 g. (70%) of salmon-colored needles, m.p. >320° with loss of color above 200°. One crystallization from nitrobenzene afforded analytically pure pale yellow needles.

Anal. Calcd. for $C_{13}H_8N_2O_3$: C, 65.01; H, 3.36; N, 11.66. Found: C, 65.01, 64.94; H, 3.32, 3.55; N, 11.92.

1-Methyl-1,2-dihydrobenzo[*f*]quinazolin-3(4H)-one (XII).

A.—3-Hydroxy-1-methylbenzo[*f*]quinazoline (VIII, 20.7 mg., 0.0985 mmole) in 15 ml. of 10% 2-(2-ethoxyethoxy)ethanol in absolute methanol was reduced with 10.2 mg. of 10% palladium on carbon in a microhydrogenation apparatus at atmospheric pressure. The reaction was terminated after 22 hr., during which time approximately 1 equiv. of hydrogen was absorbed. Removal of the catalyst and evaporation of the solvent under reduced pressure afforded a colorless crystalline residue, yield 11.8 mg. (56%). For analysis this solid was crystallized from a minimal volume of absolute methanol, yielding 10.4 mg. (88% recovery) of colorless flat prismatic rods, m.p. 280–281° dec.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.80; H, 5.74; N, 13.02.

B.—In another large-scale preparation, 1.26 g. (0.006 mole) of VIII was reduced for 3–4 hr. (in six separate portions on account of the low solubility of VIII) in a Parr hydrogenation apparatus at 48 lb. initial hydrogen pressure, and the reaction mixture was treated exactly as above. The crude crystalline residue, yield 1.09 g. (85%), was dissolved in 350 ml. of absolute methanol, treated with Darco, and the volume was concentrated to approximately 75 ml. After overnight refrigeration, the solid was collected, washed with ether, and dried for 17 hr. at 52° *in vacuo*. The pale yellow diamond-shaped prismatic plates (yield 0.794 g., 73% recovery) melted at 280–281° dec.

1,3-Dimethylbenzo[*f*]quinoline (XX). **A.**—An authentic specimen of this substance, m.p. 127–128° (lit.[34] 126–127.5°), after repeated recrystallization from aqueous ethanol, was prepared from 2-naphthylamine and acetylacetone according to the method of Johnson and co-workers.[34] The picrate was prepared and purified by recrystallization from absolute methanol, yielding bright yellow needles, m.p. 233.5° dec. (lit.[36] 215° dec.).

Anal. Calcd. for $C_{21}H_{16}N_4O_7$: C, 57.79; H, 3.70; N, 12.84. Found: C, 57.66; H, 3.90; N, 12.81.

The hydrochloride salt XX·HCl was prepared as follows. To a suspension of 0.31 g. of XX·picrate in 100 ml. of 2 *N* hydrochloric acid was added 150 ml. of ether, and the mixture was stirred with a magnetic stirrer. The yellow ether layer was withdrawn periodically with a pipet and replaced with fresh ether, a total of 600 ml. being used before essentially colorless ether layers were obtained. The aqueous phase was chilled and the very pale yellow solid was collected, washed thoroughly with ether, and dried to give 0.14 g. (82%) of crude XX·HCl. This solid was dissolved in 5 ml. of boiling water, and the pale yellow solution was treated with Darco. Addition of a few drops of concentrated hydrochloric acid and refrigeration afforded 0.12 g. (86% recovery) of nearly colorless, analytically pure needles, m.p. 285° dec.

Anal. Calcd. for $C_{15}H_{13}N·HCl$: C, 73.90; H, 5.80; N, 5.75. Found: C, 73.57; H, 5.91; N, 5.36.

The free base of XX was regenerated by neutralization of an aqueous solution of XX·HCl and extraction with ether. Alternatively, the free base could be prepared directly from the picrate by treatment with excess dilute aqueous ammonia or sodium carbonate in the presence of ether or benzene and evaporation of the organic solvent to dryness. Analytically pure material was obtained by vacuum sublimation at 105° (0.4 mm.), yielding small white crystals, m.p. 124–126°.

Anal. Calcd. for $C_{15}H_{13}N$: C, 86.91; H, 6.33; N, 6.76. Found: C, 86.52; H, 6.35; N, 6.63.

B.—Crude 2-naphthylamine "acetone anil" (XIX, 3.4 g., 0.015 mole) was heated for 10 min. in a sublimation apparatus immersed in a molten metal bath preheated to 270°, while a gentle stream of nitrogen was passed through the system. There was isolated a small quantity of sublimate, whose infrared and ultraviolet absorption spectra resembled those of 2-naphthylamine (presumably the unreacted portion of the 2-naphthylamine used in the formation of the "acetone anil"). An intimate mix-

ture of the resulting partly purified 2-naphthylamine "acetone anil" and 0.8 g. of 10% palladium on carbon was heated at 270–285° (bath temperature) in the same apparatus for 2 hr. The reaction mixture was cooled, taken up in a minimum quantity of ether, filtered free of the catalyst, and transferred to a clean sublimation tube. After removal of the solvent under a gentle stream of nitrogen, the gummy residue was sublimed at 100–110° (0.01 mm.) over a period of 48 hr. Large sticky yellow crystals formed in the cool zone and were removed periodically. A total of 3.1 g. (91% based on crude 2-naphthylamine "acetone anil" used) was collected in this manner, but still appeared severely contaminated with 2-naphthylamine on the basis of its ultraviolet absorption spectrum. Efforts to purify the crude dehydrogenation product by resublimation or repeated recrystallization from aqueous ethanol were only partly successful, and were therefore abandoned in favor of the picrate–hydrochloride–free base route used in procedure A.

The picrate was prepared and found to melt sharply with decomposition at 231.5° after one recrystallization from absolute methanol. A mixture melting point with the picrate of authentic 1,3-dimethylbenzo[*f*]quinoline was undepressed.

Anal. Calcd. for $C_{21}H_{16}N_4O_7$: C, 57.79; H, 3.70; N, 12.84. Found: C, 57.38; H, 3.95; N, 12.63.

The hydrochloride was prepared in excellent yield from the picrate by metathetiel exchange, as in procedure A, and was found to decompose at approximately 285°, after recrystallization from dilute hydrochloric acid. The infrared spectrum of this hydrochloride was completely superimposable on that of authentic 1,3-dimethylbenzo[*f*]quinoline hydrochloride.

Anal. Calcd. for $C_{15}H_{13}N\cdot HCl$: C, 73.90; H, 5.80; N, 5.75. Found: C, 73.46; H, 6.27; N, 5.25.

Neutralization of an aqueous solution of the hydrochloride liberated the free base. Extraction into ether, drying, removal of solvent, and finally sublimation at 105° (0.4 mm.) furnished small white crystals, m.p. 125–126°. Infrared, ultraviolet, and n.m.r. spectra of the free bases prepared by procedures A and B were completely superimposable, and a mixture melting point was undepressed.

Anal. Calcd. for $C_{15}H_{13}N$: C, 86.91; H, 6.33; N, 6.76. Found: C, 86.79; H, 6.55; N, 6.69.

4,6-Diamino-2,2-dimethyl-1-(1-naphthyl)-1,2-dihydro-*s*-triazine Hydrochloride.—A mixture of 1-naphthylamine (43 g., 0.3 mole), dicyandiamide (27 g., 0.32 mole), and 25 ml. of concentrated hydrochloric acid in 40 ml. of acetone and 150 ml. of 95% ethanol was stirred under reflux for 16 hr. Nearly complete solution was achieved in 30 min., but solid began to deposit gradually. The reaction mixture was cooled in an ice bath and the product was collected, washed with acetone, and dried at 70°, yielding 49 g. (54%) of small colorless prisms, m.p. 231–239°. A 3-g. portion of this solid was crystallized from 25 ml. of water in 87% recovery. Two further crystallizations from water afforded analytically pure colorless prismatic rods, m.p. 220–222° (lit.[40] 226–228°). No high-melting material could be found under these conditions.

Anal. Calcd. for $C_{15}H_{17}N_5\cdot HCl$: C, 59.30; H, 5.97; N, 22.77. Found: C, 59.21; H, 6.06; N, 23.06.

N^2-(2-Naphthyl)acetoguanamine (IV).—A mixture of N^1-(2-naphthyl)biguanide (4.54 g., 0.02 mole), ethyl acetate (2.35 g., 0.0256 mole), and potassium hydroxide (0.37 g., 0.0066 mole) in 11.5 ml. of absolute methanol was stirred under reflux for 18 hr. and cooled to room temperature. The product was collected, washed with water and small portions of absolute methanol, and air-dried. The white, finely powdered solid weighed 1.75 g. (50%, allowing for 1.35 g. of starting material recovered from the mother liquor on dilution with water and further cooling) and melted at 195–200°. Purification by repeated crystallization from 50% aqueous ethanol gave product melting at 200–201°.

Anal. Calcd. for $C_{14}H_{13}N_5$: C, 66.91; H, 5.21. Found: C, 66.31; H, 5.40.

For the preparation of the hydrochloride salt of IV a solution of 72 mg. of free base in 5 ml. of *n*-propyl alcohol was saturated with dry hydrogen chloride gas and refrigerated briefly. The white solid that had formed was collected, washed with acetone, and crystallized from aqueous *n*-propyl alcohol, yielding colorless crystals, m.p. 232–238°.

Anal. Calcd. for $C_{14}H_{13}N_5\cdot HCl\cdot 0.5H_2O$: C, 56.57; H, 5.05; N, 23.74. Found: C, 56.12; H, 5.30; N, 23.62.

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Investigations in Heterocycles. XVIII. The Synthesis of 1,2-Disubstituted 5,6,7,8-Tetrahydro-4-quinazolinethiones[1]

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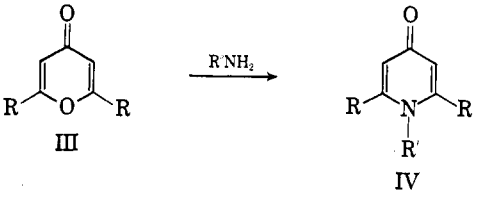
Two methods for the synthesis of 1,2-disubstituted 5,6,7,8-tetrahydro-4-quinazolinethiones are described: (a) the reaction of 5,6,7,8-tetrahydro-2-phenyl-4-benzoxazinethione with various primary amines and (b) the condensation of a N-monosubstituted enamine with an acylisothiocyanate. Some chemical transformations of this heterocyclic system are discussed.

Because of the continuing interest in our laboratories[2–4] in the synthesis of various heterocyclic systems for biological evaluation, our attention was recently drawn to the work of Hünig and Hübner who reported the formation of 5,6,7,8-tetrahydro-2-phenyl-4-benzoxazinethione (II) in 50% yield from the interaction of morpholinocyclohexene (I) with benzoylisothiocyanate (Scheme I, p. 2888).

Since 1,3-oxazine-4-ones can be considered to bear a formal resemblance to 1,4-pyrones with regard to the disposition of the double bonds, and, inasmuch as 1,4-pyrones (III) upon heating with primary amines can readily be transformed to 4-pyridones[6] (IV), it was of interest to us to explore the reactivity of II towards such amines.



III IV

(1) Presented in part before the Organic Chemistry Division at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, Abstracts, p. 59Q.

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