chloropyrrolidine.[9] This solution was refluxed for 3.5 hr., cooled, and acidified with aqueous hydrochloric acid. The volume of solution was reduced to *ca.* 100 ml. by reduced pressure distillation. The solution was then extracted with three 100-ml. portions of benzene. The benzene extract was washed with three 30-ml. portions of water saturated with sodium chloride. The washings were discarded and the benzene solution dried over sodium sulfate. After the benzene was removed, 15.7 g. (64.0%) of crude solid I was obtained. The solid was dissolved in warm benzene and charcoal was added. This solution was warmed on a steam bath for 10–15 min.; Filter-Cel was added and the solution filtered. After removal of the benzene, the solid was recrystallized from ethyl ether-purified petroleum ether (b.p. 90–100°). The recrystallized white solid was sublimed, m.p. 123–125°.

Anal. Calcd. for $C_{10}H_{13}O_4N$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.92; H, 6.33; N, 6.71.

1-Carboethoxy-2-hydroxy-3-oxopyrrolizidine (IV).—Six grams (0.0285 mole) of sublimed I was dissolved in 50 ml. of 95% ethanol and placed in a hydrogenation bomb, and 3 g. of W-2 Raney nickel was added. At 100° and 2000 p.s.i. the theoretical amount of hydrogen was taken up in 4 hr. The solution was allowed to cool to room temperature and brought to atmospheric pressure. The solution was then filtered. After removal of the solvent the solid was recrystallized from ethyl acetate-purified petroleum ether (b.p. 60–68°) and sublimed, m.p. 128.2–132.1°.

Anal. Calcd. for $C_{10}H_{15}O_4N$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.24; H, 7.01; N, 6.54.

1-Carboethoxy-2-hydroxy-3-oxopyrrolizidine Tosylate (V).—A 0.153-g. (2.31 mmoles) sample of IV was dissolved in 10 ml. of anhydrous pyridine, and 1.11 g. (5.71 mmoles) of recrystallized *p*-toluenesulfonyl chloride was added. The solution was stored at 0° for 17 hr. and then poured onto crushed ice. Within 0.5 hr., a copious white precipitate formed. This was filtered, washed with water, and after being dried, 0.634 g. (67.8%) of V was obtained, recrystallized from ethyl acetate, m.p. 123.1–124.2°.

The infrared spectrum of V in 10% chloroform solution had no absorption bands in the $3.0\text{-}\mu$ region and had peaks at 5.80 and 6.24 μ. The ultraviolet spectrum in 95% ethanol had one peak at 226 mμ (ϵ 12,500).

Anal. Calcd. for $C_{17}H_{21}O_6NS$: C, 55.72; H, 5.50; Found: C, 55.63; H, 5.97.

1-Carboethoxy-3-oxopyrrolizid-1,8-ene (VI).—A 0.529-g. (1.43 mmoles) sample of V was placed in a flask and 50 ml. of anhydrous *t*-butyl alcohol was added. The solution was warmed on a steam bath for 5–10 min., and most of the tosylate dissolved. To this warmed stirred solution, 7.49 ml. of 0.193 *N* (1.43 mmole) of potassium *t*-butoxide in *t*-butyl alcohol was added. The solution became bright red as each drop of base was added, but the color then disappeared and only persisted after *all* the base had been addded. The solution was acidified with dilute hydrochloric acid and then extracted with benzene. The benzene was removed by reduced pressure distillation. The residue was chromatographed on a column packed with Florosil (60/100 mesh, Floridian Co., Tallahassee, Florida). The chromatographed material (over 90%) was sublimed, m.p. 88.9–90.0°.

Anal. Calcd. for $C_{10}H_{13}O_3N$: C, 61.52; H, 6.71; N, 7.18. Found: C, 61.61; H, 6.66; N, 6.55.

Acknowledgment.—This work was supported in part by a grant (RG-3892) from the U.S. Public Health Service. This aid is gratefully acknowledged. The author would like to thank Mr. V. B. Haarstad for the determination and help in the interpretation of the n.m.r. spectrum.

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[9] D. W. Fuhlage and C. A. VanderWerf, *J. Am. Chem. Soc.*, **80**, 6249 (1958).

Formylation of *t*-Butylamine and *t*-Octylamine[1,2]

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Received June 6, 1962

During studies on isocyanides in these laboratories we have had occasion to prepare large quantities of formo-*t*-butylamide. Neither the formylation of *t*-butylamine by formic acid nor the Ritter reaction on isobutylene or *t*-butyl alcohol[3] is appealing as a routine preparation, the former because mixing the very volatile *t*-butylamine with formic acid is a troublesome and tedious procedure, and the latter because of the obvious hazards of working with hydrogen cyanide. We have found that *t*-butylamine can be formylated conveniently by refluxing and then distilling an equimolar mixture of ethyl formate and *t*-butylamine. The high rate of this reaction is in striking contrast with the negligible rate of acetylation of *t*-butylamine by methyl acetate[4] at 25°. Similarly *t*-octylamine (2,4,4-trimethyl-2-pentylamine) is formylated at approximately the same rate.

Experimental[5]

Equimolar quantities of ethyl formate and *t*-butylamine were refluxed in tared flasks, the excess reagents and ethanol were distilled on the water bath, and the residual formo-*t*-butylamide was weighed. The procedure was checked by distilling several batches. Typical yields for 4,16,32, and 48 hr. of reflux were 29.4, 66.8, 79.2, and 84.0%, respectively. Similarly, a mixture of 120 g. (1.0 mole) of *t*-octylamine and 150 g. (2.0 moles) of ethyl formate was refluxed 12 hr. and then distilled. The formo-*t*-octylamide was obtained in a yield of 98 g. (62%), b.p. 245–248°. This material is slightly amber in color and may be better purified by vacuum distillation.

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[1] Abstracted from the M.S. theses of Marvin K. Newton and Gerald J. Papenmeier, University of Kansas City, 1960.

[2] The authors gratefully acknowledge support of this work by the National Science Foundation under Grant No. G10031.

[3] J. J. Ritter and J. Kalish, *J. Am. Chem. Soc.*, **70**, 4048 (1948).

[4] E. McC. Arnett, J. G. Miller, and A. R. Day, *ibid.*, **72**, 5635 (1950).

[5] A gift of *t*-octylamine from the Rohm & Haas Corporation is gratefully acknowledged. The other chemicals were purchased.

Bridged Polycyclic Compounds. XVIII. Addition of Dialkyl Azodicarboxylates to Norbornadiene[1]

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Received November 6, 1961

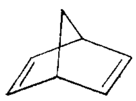
Recent reports have established that norbornadiene (I) exhibits unusual chemical reactivity as compared with ordinary unconjugated dienes.[2] Of particular interest are the observations that I will give 1:1 adducts with dienophiles by a homoconjugate Diels-Alder type addition across the 2,6-position.[2f,g,i,j] In connection with another study, we had occasion to examine the reaction of I with dialkyl azodicarboxylates. Since the latter are well known dienophiles, it was anticipated that analogous 2,6-adducts might be reaction products. This is the case, but in addition, a structurally different 1:1 adduct is also formed.

Methyl azodicarboxylate and norbornadiene (I) were heated at 150–160° for twenty-four hours. Distillation of the reaction mixture, followed by chromatography of the distillate on alumina resulted in separation into two fractions. The first fraction, m.p. 59–60.5°, and the second fraction, m.p. 109.5–110°, were in the ratio of *ca.* 1.8:1, respectively.

Molecular weight determinations and elemental analyses clearly established both products as 1:1 adducts.

Chemically the two fractions behaved differently. Acetone solutions of the 60° product reacted instantly with aqueous potassium permanganate and more slowly with bromine in carbon tetrachloride, while acetone solutions of the 110° product reacted only very slowly with potassium permanganate and not at all with bromine at room temperature. Catalytic hydrogenation of the 60° product with palladium-on-charcoal catalyst in ethanol at room temperature led to rapid absorption of one mole of hydrogen per mole of compound and to the formation of a new product. On the other hand, treatment of the 110° product under identical hydrogenation conditions resulted in recovery of unchanged starting material.

The evidence described above is consistent with structure IIa for the 110° product and either IIIa, IVa, Va, or VIa for the 60.5° isomer.



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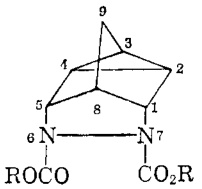

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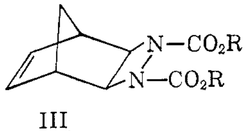

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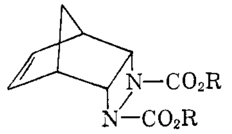

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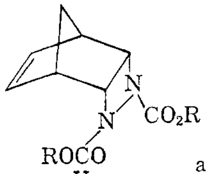
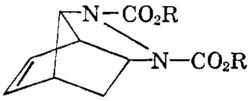


V



VI

a. R=CH_3
b. R=C_2H_5

Spectra and Structure.—The infrared spectra of the 60° and 110° products show over-all similarity, but there are some significant differences. The 110° isomer has split carbonyl absorptions of nearly equal intensity at 5.72 and 5.80 μ while the 60° compound has a sharp, single absorption at 5.95 μ. No absorption peak was noted in the 12.3-μ region for the 60° product, a region presumed to be characteristic of the nortricyclene system.[2c,3] An absorption peak was apparent at 12.25 μ for the 110° product. Further evidence that a three-membered ring is present in the latter compound is revealed by the spectral features of the carbon–hydrogen stretching region. This material has a peak at 3.27 μ, a value diagnostic of hydrogen atoms attached to three-membered rings.[3b,4] A similar absorption band at 3.25 μ for the other isomer may be ascribed to the ethylenic hydrogen.

An examination of the proton n.m.r. spectra of the two adducts is of value. The observed resonance frequencies and relative peak intensities are summarized in Table I.

TABLE I

N.M.R. SPECTRAL DATA[a]

60° Product		110° Product	
τ	Relative peak areas	τ	Relative peak areas
8.29	2	8.49	3
6.89	2	8.21	2
6.26[b]	7	7.97	1
5.65[c]	1	6.26	6
3.72[d]	2	5.57	2

[a] All values are p.p.m. referred to tetramethylsilane (internal standard) as 10.00 [see G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)]; only multiplet centers are indicated. Spectra were obtained from *ca.* 7% solutions in carbon tetrachloride at room temperature. [b] This number refers to the value of the singlet band for the six methoxyl protons. Somewhat upfield there is another proton which is partially concealed by the methoxyl proton signal. [c] This number refers to the center of a doublet. [d] This number refers to the center of an eight-line spectrum of two non-equivalent vinyl protons.

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(1) Previous papers in series: S. J. Cristol, J. R. Douglas, W. C. Firth, Jr., and R. E. Krall, *J. Org. Chem.*, **27**, 2711 (1962).

(2) (a) H. Bluestone, S. B. Soloway, J. Hyman, and R. E. Lidov, U.S. Patent 2,730,548 (January 10, 1956); U.S. Patent 2,738,356 (March 13, 1956); U.S. Patent 2,782,238 (February 19, 1957); (b) S. Winstein and M. Shatavsky, *J. Am. Chem. Soc.*, **78**, 592 (1956); (c) L. Schmerling, J. P. Luvisi, and R. W. Welch, *ibid.*, **78**, 2819 (1956); (d) S. J. Cristol, R. P. Arganbright, G. D. Brindell, and R. M. Heitz, *ibid.*, **79**, 6035 (1957); (e) S. J. Cristol, G. D. Brindell, and J. A. Reeder, *ibid.*, **80**, 635 (1958); (f) E. F. Ullman, *Chem. Ind.* (London), 1173 (1958); (g) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, **81**, 667 (1959); (h) F. Joy and M. F. Lappert, *Proc. Chem. Soc.*, 353 (1960); (i) H. K. Hall, Jr., *J. Org. Chem.*, **25**, 42 (1960); (j) C. J. Krespan, B. C. McKusick, and T. L. Cairns, *J. Am. Chem. Soc.*, **83**, 3428 (1961).

(3) (a) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950); (b) E. R. Lippincott, *ibid.*, **73**, 2001 (1951); (c) A. Winston and P. Wilder, Jr., *ibid.*, **76**, 3045 (1954).

(4) S. J. Cristol and R. L. Snell, *ibid.*, **80**, 1950 (1958).

The n.m.r. data are entirely consistent with the assignment of structure methyl 6,7-diazaquadricyclo[3.2.1.1^{3,8}.0^{2,4}]nonane 6,7-dicarboxylate (IIa) to the 110° product. The fact that no resonance signals occur below $\tau = 5.57$ rules out the presence of any vinyl protons.[5] The six protons observed at $\tau = 6.26$ are at the proper position for the two methoxyl groups.[5c] The additional bands at $\tau = 8.49, 8.21, 7.97$, and 5.57 may correspond to protons at ring positions 3 and 9, 2 and 4, 8, and 1 and 5, respectively, based on the relative peak areas and the chemical shifts.[6] Another possible assignment is $\tau = 8.49$ (2, 3, and 4) and $\tau = 8.2$ (9).

The n.m.r. spectrum of the 60° isomer shows more complexity. Two vinyl protons are observed at $\tau = 3.72$, the proper chemical shift for the bicyclo[2.2.1]heptyl system.[5] These appear as two bands which are essentially identical unsymmetrical quartets with underlying fine multiplet structure. It is interesting to note that each quartet represents a proton and that these two protons are non-equivalent. This latter point was shown clearly by determination of the spectrum at field strengths of 40 and 60 Mc., the separation of the two four-line patterns being *ca.* 14 and 20 c.p.s., respectively. The separation of the lines within each quartet remains constant at *ca.* 3 c.p.s. with change of field strength. The doublet at $\tau \sim 5.65$ corresponds to one proton ($J \sim 7$ c.p.s.). At $\tau \sim 6.4$ there appears to be another proton multiplet (probably a doublet with $J \sim 7$ c.p.s.) partially hidden by the six methoxyl protons at $\tau = 6.26$. The broad unresolved peak at $\tau = 6.89$ and the single peak at $\tau = 8.29$ each correspond to two protons. Especially pertinent to the assignment of structure is the occurrence of two non-equivalent vinyl protons. This fact apparently rules out structures like III and IV since in such structures the two vinyl protons see identical proton environments and consequently they would have the same chemical shift. Presumably either the conformation V or the structure VI would furnish the molecular asymmetry necessary for non-equivalent vinyl protons.

Treatment of I with ethyl azodicarboxylate also gave two materials separable by column chromatography. The first fraction, b.p. 128–131° (0.4 mm.), and the second fraction, b.p. 126–127° (0.1 mm.), were in the ratio of *ca.* 1.6:1, respectively. On the basis of the order of elution and on chemical tests for unsaturation, the structures of the first and second fractions correspond to the structures of the 60° and 110° products, respectively.

Experimental[7]

Dimethyl and diethyl azodicarboxylate were obtained by the procedure of Rabjohn.[8] These were purified by repeated washing with cold 3% aqueous sodium carbonate as directed by Wright and co-workers.[9]

Reaction of Norbornadiene (I) with Methyl Azodicarboxylate.—A solution of 43 g. (0.29 mole) of methyl azodicarboxylate, 54 g. (0.59 mole) of freshly distilled I (Shell Chemical Co.), and 0.1 g. of *p-t*-butylcatechol was heated in a sealed, thick-walled Pyrex glass tube for 24 hr. at 150–160°. The cooled reaction mixture was flash-distilled under reduced pressure to give a recovery of 24 g. (0.26 mole) of (I) (*ca.* 90% of theoretical excess). The remaining very viscous residue was dissolved in ether, washed with cold 5% sodium hydroxide solution, and finally dried with anhydrous magnesium sulfate. Removal of the solvent followed by simple vacuum distillation of the concentrate yielded 21 g. (30%) of a viscous liquid, b.p. 120–135° (*ca.* 0.1 mm.). Elution chromatography of the distillate on Merck aluminum oxide (reagent grade, no. 71707) resulted in a clean separation into two different fractions. The first fraction, which was eluted with petroleum ether (b.p. 35–60°)–benzene solvent mixtures amounted to 12.5 g. Recrystallization of this residue from petroleum ether, b.p. 35–60°, afforded pure product, m.p. 59.0–60.5°. The second fraction was readily eluted with ether and amounted to 6.9 g. Pure product was obtained by recrystallization of the latter concentrate from petroleum ether, b.p. 60–70°, m.p. 109.5–110.0°.

Anal. Calcd. for $C_{11}H_{14}O_4N_2$: C, 55.45; H, 5.92; N, 11.76; mol. wt., 238. Found for the 60° fraction: C, 55.35; H, 5.74; N, 11.72; mol. wt., 232. Found for the 110° fraction: C, 55.24; H, 5.99; mol. wt., 228.

The 60° product in acetone solution instantly decolorized 2% aqueous potassium permanganate. A solution of the product in ethyl acetate decolorized a solution of bromine in carbon tetrachloride quite rapidly. When 346 mg. of the product in 40 ml. of absolute ethanol was subjected to hydrogenation over 33 mg. of 10% palladium-on-charcoal catalyst at one atmosphere pressure, one mole of hydrogen per mole of compound was absorbed in *ca.* 10 min. No more hydrogen was adsorbed during another 7 hr. Catalyst and solvent removal gave saturated product, m.p. 70–72°.

Anal. Calcd. for $C_{11}H_{16}O_4N_2$: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.75; H, 6.81; N, 11.62.

The 110° product in acetone solution did not appreciably decolorize 2% aqueous potassium permanganate. Treatment of an ethyl acetate solution of this material with bromine in carbon tetrachloride showed little decolorization, even after standing for a long period of time. When the product was subjected to the hydrogenation conditions described in the preceding paragraph, only unchanged starting material was recovered; mixed m.p. 109.5–110.0°; identical infrared spectrum.

Reaction of Norbornadiene (I) with Ethyl Azodicarboxylate.—This reaction was carried out exactly as described for the reaction with methyl azodicarboxylate, except that the

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(5) Signals for vinyl protons in the norbornene system occur in the range of *ca.* 3.3 to 4.4τ. (a) H. E. Simmons, *J. Am. Chem. Soc.*, **83**, 1657 (1961); (b) K. B. Wiberg and B. J. Nist, *ibid.*, **83**, 1227 (1961); (c) "NMR Summary," G. V. D. Tiers, Minnesota Mining and Manufacturing Co., St. Paul, Minn., private communication.

(6) E. F. Ullman,[2f] reports a very similar n.m.r. spectrum for the adduct formed from I and maleic anhydride.

(7) Elemental analyses and molecular weight measurements (Rast procedure) were performed by Galbraith Microanalytical Laboratories, Knoxville, Tennessee. All melting points were taken on a Fisher-Johns melting point apparatus and are corrected. Boiling points are uncorrected. Infrared spectra were determined on a Beckman IR-5 double-beam spectrophotometer equipped with sodium chloride optics. Spectra were obtained in potassium bromide disks except that the 3-μ region data were taken in tetrachloroethylene solution. The proton n.m.r. spectra were obtained using a Varian high-resolution n.m.r. spectrometer and electromagnet at a frequency of 60 Mc. Relative proton intensities were obtained by means of a voltage integrator.

(8) N. Rabjohn in E. C. Horning, Organic Syntheses, Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p. 375.

(9) J. C. J. MacKenzie, A. Rodgman, and G. F. Wright, *J. Org. Chem.* **17**, 1666 (1952).

temperature was 165–169°. Vacuum distillation of the reaction residue resulted in collection of a 31% yield of a viscous liquid, b.p. 122–140° (*ca.* 0.2 mm.). Elution chromatography on Merck aluminum oxide gave a separation into two fractions. The first fraction was eluted with benzene and benzene–ether mixtures and the second fraction was eluted with methanol. The ratio of first to second fraction was *ca.* 1.6:1. Both fractions were further purified by vacuum distillation: first fraction, b.p. 128–131° (0.4 mm.), n^{25}_{D} 1.5036; second fraction, b.p. 126–127° (0.1 mm.), n^{25}_{D} 1.4966. Neither product could be made to crystallize. The analytical results show both products to be somewhat impure. However, it is clear that they are 1:1 adducts.

Anal. Calcd. for $C_{13}H_{18}O_4N_2$: C, 58.63; H, 6.81; N, 10.52; mol. wt., 266. Found for the first fraction: C, 59.27; H, 7.35; N, 10.38; mol. wt., 271. Found for the second fraction: C, 58.96; H, 7.34; N, 10.40; mol. wt. 270.

A solution of the first fraction product in carbon tetrachloride rapidly decolorized a solution of bromine in carbon tetrachloride. The second fraction product decolorized bromine much more slowly.

Acknowledgment.—E. L. A. is indebted to the National Science Foundation for a post-doctoral fellowship under which this research was initiated. D. L. W. was a recipient of a National Science Foundation grant for teacher training through research participation. The n.m.r. spectra were kindly determined by Mr. Bernard J. Nist of the University of Washington.

Studies in Thiazinoquinazolines

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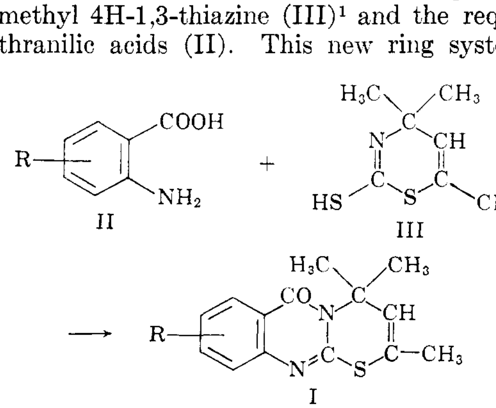
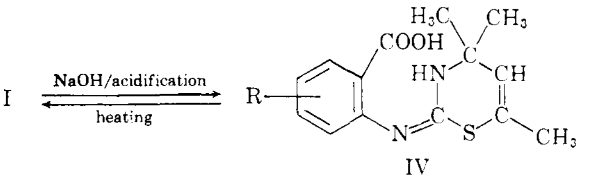
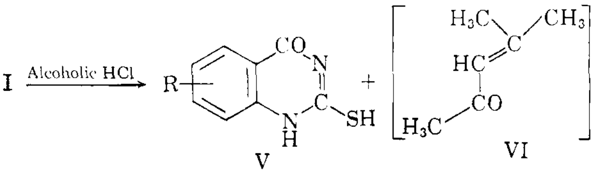
Department of Chemistry, Panjab University, Candigarh, India

Received January 31, 1961

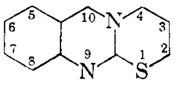
Thiazinoquinazolines (I), a new heterocyclic system which incorporates the physiologically active rings as thiazine and quinazoline present in febrifugine and methylene blue, respectively, have been prepared by a very simple method, which involves a condensation between 2-mercapto-4,4,6-trimethyl 4H-1,3-thiazine (III)[1] and the requisite anthranilic acids (II). This new ring system is quite stable towards cold alkali and remains unaffected for a number of days in 5% sodium hydroxide. The quinazoline ring opens to furnish IV on prolonged heating with 5% sodium hydroxide at 60–70°. The acid (IV) is transformed back to I on either heating in the dry state or refluxing in alcohol.







These thiazino-quinazolines are also insoluble in aqueous hydrochloric acid and undergo a degradation to V and VI on refluxing in alcoholic hydrochloric acid.



VII

The parent ring system (VII) can be named 1,3-thiazino[2,3-b]quinazoline and thus I will be 2,4,4-trimethyl-4H,10H-1,3-thiazino[2,3-b]quinazoline-10-one.

Antibacterial Results.—On preliminary testing the compounds no. 1, 2, 3, 4, 5 (Table I) have proved bacteriosidal to the strains of proteus vulgaris at a dilution of 1:5000.

Experimental

1. **1,3-Thiazino[2,3-b]quinazolines (Table I).**—An equimolar mixture of 2-mercapto-4,4,6-trimethyl-4H-1,3-thiazine and the requisite anthranilic acid was heated in an oil bath at 120–125° for 4 hr.; the completion of the reaction is indicated when hydrogen sulfide no longer evolves. The slurry was cooled, neutralized with sodium carbonate, filtered, and the residue thoroughly washed with water. In all cases it could be crystallized from dilute ethanol or acetic acid.

2. **Treatment of I with Alkali and Isolation of IV.**—Thiazinoquinazoline (I) (R = H) was taken in 5% sodium hydroxide and heated at 60–70° for 5 hr. The solution was acidified with acetic acid and the resulting precipitate purified by dissolving in sodium hydroxide and reprecipitation and finally crystallization from dilute ethanol. The product melted at 290°.

Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 64.61; H, 6.1; N, 10.77. Found: C, 64.23; H, 5.9; N, 10.90.

3. **Treatment of I with Alcoholic Hydrochloric Acid; Isolation of 2-Thio-4-keto-tetrahydroquinazoline (V).**—I (R = H) was dissolved in ethanol and saturated with dry hydrochloric acid. The solution then refluxed over a steam bath for 8 hr. The solvent was removed by dis-

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(1) J. E. Jansen and R. A. Mathes, *J. Am. Chem. Soc.*, **77**, 5431 (1955)