TABLE III

12-Methylpyrido[2,1-b]benzo[f]1,3-thiazepinium Perchlorates (V)

V, R =	Yield, %	M.P.[c]	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
H	35[a]	163–164[d]	$C_{14}H_{12}ClNO_4S$	51.61	51.48	3.71	3.70	4.30	4.51
4-CH_3	61	252–255[e]	$C_{15}H_{14}ClNO_4S$	53.02	53.34	4.15	4.50	4.12	4.39
3-CH_3	54	133–135[f]	$C_{15}H_{14}ClNO_4S$	53.02	53.04	4.15	4.11	4.12	4.40
3-OCH_3	12[b]	241.5–242.5[g]	$C_{15}H_{14}ClNO_5S$	50.63	50.56	3.97	4.08	3.94	4.20

[a] A cyclization attempt carried out in refluxing 48% hydrobromic acid (5 days) yielded only starting material (recovered as the perchlorate). [b] Over-all yield from *m*-methoxybenzenethiol. The procedure was the same as in the other cases, except that cyclization was carried out by heating for 24 hr. in concentrated hydrochloric acid. [c] All analytical samples were recrystallized from methanol. [d] Long colorless needles, λ_{max} 316 mμ, log ε 4.86. [e] Light brown needles, λ_{max} mμ (log ε) 275 (3.71), 322 (3.73). [f] Nearly colorless microcrystalline powder, λ_{max} 323 mμ, log ε 3.92. [g] Bright yellow needles, λ_{max} mμ (log ε) 235 (4.36), 327 (3.82).

polyphosphoric acid[9] and the mixture heated and stirred for 12 hr. in a Wood's metal bath at 150–160°. The mixture was diluted by the cautious addition of about 200 g. of ice in small portions. After the mixture had cooled to room temperature, 35% perchloric acid was added until no further cloudiness was observed. The mixture was allowed to stand in the refrigerator for 4 days, after which the solid material was collected and recrystallized from methanol (Norit) and ethyl acetate. The results are summarized in Table III.

Durham, N.C.

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[9] We are indebted to the Victor Chemical Co. for a generous gift of polyphosphoric acid.

[Contribution from the Department of Chemistry, Hope College]

Synthesis of *N*-Substituted Aminothianaphthenes by Condensation of Amines with Hydroxythianaphthenes by Reduction of *N*-Substituted Aminothianaphthene 1,1-Dioxides

GERRIT VAN ZYL, DON C. DE JONGH, VICTOR L. HEASLEY, and JOHN W. VAN DYKE

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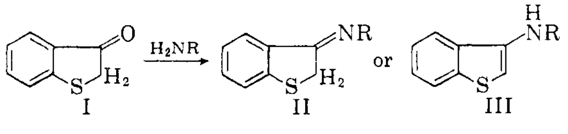
By condensing primary aliphatic amines and secondary aromatic amines with 3-hydroxythianaphthene, the corresponding 3-thianaphthenylamines have been synthesized. By the reaction of aliphatic secondary amines with 3-bromothianaphthene 1,1-dioxide and the reduction of the resulting aminothianaphthene 1,1-dioxides with lithium aluminum hydride, the corresponding thianaphthenylamines were formed. A method for the preparation of 2-hydroxythianaphthene in good yields has been found. Its condensation with amines has been explored.

The first attempt at synthesis, which involved the reduction of the substituted 3-amino-2-nitrothianaphthenes, proved unsuccessful. Also 3-hydroxythianaphthene was condensed with nitrosoamines to give anils.[1] Subsequent reduction with lithium aluminum hydroxide yielded only tarry materials.

Prior to this work, the only *N*-substituted aminothianaphthene which had been reported is 2-(1-piperidinyl)thianaphthene.[2] It was prepared by heating 2-bromothianaphthene in an autoclave with piperidine.

The condensation of aniline with 3-hydroxythianaphthene[3] has been reported by Fries and Bartholomaus,[4] who state that 3-keto-2,3-dihydrothianaphthene (II) is formed. No evidence for this structure was given. Although it is known that 3-hydroxythianaphthene exists almost entirely in the keto form,[5,6] it was considered possible that the effect of heat might cause a tautomeric shift to form III. The infrared spectrum of the compound prepared in our laboratory shows a sharp N-H stretching band at 3400 cm.$^{-1}$ and no band at 1600–1700 cm.$^{-1}$, where the band for the Schiff's base should appear. The same N—H stretching band at 3400 cm.$^{-1}$, with no band at 1600–1700 cm.$^{-1}$, was observed in the spectrum of the compound made from benzylamine and 3-hydroxythianaphthene.



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[1] R. Pummerer, *Ber.*, **43**, 1370 (1910).

[2] K. H. Brower and E. D. Amstutz, *J. Org. Chem.*, 19, 411 (1954).

[3] C. Hansch and H. G. Lindwall, *J. Org. Chem.*, **10**, 381 (1945).

[4] K. Fries and E. Bartholomaus, *Ann.* **405**, 373 (1914).

[5] K. V. Auwers, *Ber.*, **B53**, 2285 (1920).

[6] S. J. Holt, A. E. Kellie, D. G. O'Sullivan, and P. W. Sadler, *J. Chem. Soc.*, 1217 (1958).

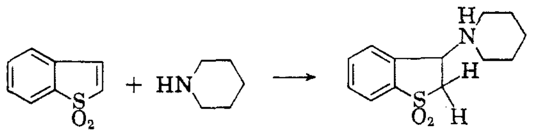
Secondary aromatic amines also were made with 3-hydroxythianaphthene, *e.g.*, *N*-methylaniline.

As the condensation between secondary aliphatic amines proceeded either in poor yields or not at all, the tertiary amines were prepared by lithium aluminum hydride reduction of 3-*N*-substituted aminothianaphthene 1,1-dioxides.[7]

3-(1-Piperidinyl)thianaphthene 1,1-dioxide was prepared by the method of Bordwell[7] and Albisetti, Jr. This sulfone was then reduced with lithium aluminum hydride to yield a solid, m.p. 63–64°. Its hydrochloride melted at 163–165°. The analysis of both of these compounds agreed with the calculated values for the unsaturated compound. 3-(1-Piperidinyl)thianaphthene was prepared also by the condensation of 3-hydroxythianaphthene and piperidine. A mixed melting point showed no depression.

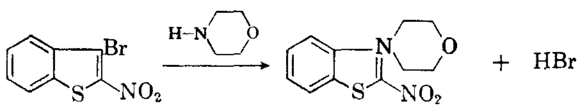
Bordwell and McKellin have found that thianaphthene 1,1-dioxide can be reduced to 2,3-dihydrothianaphthene in 33% yield with lithium aluminum hydride.[8] Rao has reduced thianaphthene 1,1-dioxides with alkyl groups in the 2- and 3-positions with lithium aluminum hydride.[9] He found that the sulfone group was always completely reduced, but that the 2,3-double bond was reduced to varying extents. Upon reducing the *N*-substituted aminothianaphthene 1,1-dioxides in this laboratory, it was found that the 2,3-double bond was not reduced.

To prove that the 2,3-dihydro product was not being obtained, 3-(1-piperidinyl)-2,3-dihydrothianaphthene 1,1-dioxide (IV), was prepared according to the method used by Bordwell and McKellin.[10] Upon lithium aluminum hydride reduction of IV, a viscous liquid, having the correct analysis for 3-(1-piperidinyl)-2,3-dihydrothianaphthene, was isolated. Its salt with hydrogen chloride gas melted at 201–203°; the analysis was found to agree with the calculated value.



IV

3-(1-Morpholinyl)thianaphthene, prepared by the reduction of the sulfone, was nitrated. The product was 3-(1-morpholinyl)-2-nitrothianaphthene. This nitro compound was identical with that obtained from the following reaction:



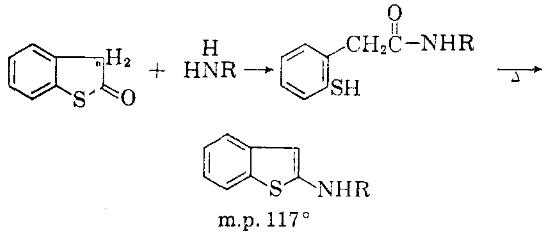
A mixed melting point showed no depression.

3-Thianaphthenylbenzylamine prepared by the reduction of the sulfone gave the same phenylisothiocyanate derivative as was obtained from the condensation product of benzylamine with 3-hydroxythianaphthene.

Since all types of 3-thianaphthenylamines had been synthesized successfully, it was decided to attempt the synthesis of the isomeric 2-thianaphthenylamines by condensing 2-hydroxythianaphthene with amines.

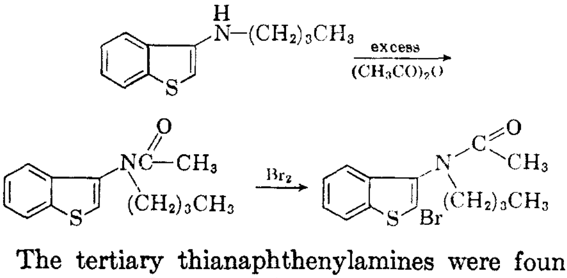
2-Hydroxythianaphthene was prepared by the oxidation of 2-thianaphthenyllthium in the presence of an alkyl Grignard reagent in much better yields than previously obtained by other methods.[11,12] Contrary to previous reports[11] 2-hydroxythianaphthene was found to be extremely stable in air.

The reactivity of 2-hydroxythianaphthene toward amines differs markedly from that of 3-hydroxythianaphthene. In most cases (*n*-buthylamine, *n*-methylaniline, piperidine, di-*n*-butylamine) there was no reaction, and when reaction did occur (aniline and benzylamine) an intermediate amide was formed which only in the case of aniline proceeded to the desired amine.



It was found that all of the secondary thianaphthenylamines would react with acetyl chloride or benzoyl chloride to yield viscous oils.

Acylation of 3-thianaphthenyl-*n*-butylamine in excess acetic anhydride, followed by bromination, yielded a white crystalline compound which had the correct analysis for *N*-(1-butyl)-*N*-3-(2-bromothianaphthenyl)acetamide.



The tertiary thianaphthenylamines were found to react both with picric acid and hydrogen chloride gas to give crystalline derivatives.

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[7] F. G. Bordwell and C. G. Albisetti, Jr., *J. Am. Chem. Soc.*, **70**, 1558 (1948).

[8] F. G. Bordwell and W. H. Mc Kellin, *J. Am. Chem. Soc.*, **73**, 2251 (1951).

[9] D. S. Rao, Abstracts of Papers, 137th Meeting, American Chemical Society, p. 26, and private communication.

[10] F. G. Bordwell and W. H. McKellin, *J. Am. Chem. Soc.*, **72**, 1985 (1950).

[11] C. Marshalk, *Ber.*, **45**, 1481 (1912).

[12] C. Marshalk, *J. Prakt. Chem.*, **88**, 246 (1913).

TABLE I[a]

N-Substituted Thianaphthenylamines by Condensation of 3-Hydroxythianaphthene with Amines
Method A

Amine	Formula		C, %	H, %	N, %	S, %	M.P.	B.P.	Yield, %
Phenyl	$C_{14}H_{11}NS$	Calcd.	74.63	4.92	6.22	14.24			
		Found	74.84	4.81	6.26	14.04	88		90
Phenylisothio-cyanate	$C_{21}H_{16}N_2S_2$	Calcd.	69.99	4.45	7.77	17.79			
		Found	70.09	4.76	7.72	18.02	223–224		
n-Butyl	$C_{12}H_{15}NS$	Calcd.	70.19	7.36	6.82	15.62			
		Found	69.93	7.57	6.63	15.51		117–120	75
Benzyl	$C_{15}H_{13}NS$	Calcd.	75.27	5.48	5.90	13.40			
		Found	75.50	5.62	5.70	13.09		165–170/1 mm.	87
Phenylisothio-cyanate	$C_{22}H_{18}N_2S_2$	Calcd.	70.55	4.84	7.48	17.15			
		Found	70.75	4.67	7.65	16.98	146		
Methylphenyl	$C_{15}H_{13}NS$	Calcd.	75.26	5.48	5.86	13.38		134–136/0.1 mm.	38
		Found	75.58	5.55	5.81	13.45			
Piperininyl	See Table II						60–63	105–110/0.1 mm.	7

[a] All melting points and boiling points are uncorrected. All analyses were performed by Schwarzkoff Microanalytical Laboratory.

TABLE II[a]

N-Substituted Thianaphthenylamines by Reduction of 1,1-Dioxides with Lithium Aluminum Hydride

Amine	Formula		C, %	H, %	N, %	S, %	M.P.	B.P.	Yield, %
Piperidinyl	$C_{13}H_{15}NS$	Calcd.	71.84	6.96	6.45	14.75			
		Found	72.05	7.02	6.31	14.91	64–65	105–107/0.1 mm.	55
Picrate	$C_{19}H_{18}N_4O_7S$	Calcd.	51.12	4.06	12.55	7.18	131–132		
		Found	51.18	3.92	12.43	7.04			
HCl salt							163–165		
1-Morpholinyl							50–51	120–140/0.4 mm.	30
Diethyl	$C_{16}H_{15}NS$	Calcd.	70.19	7.36	6.82	15.62		100–105/0.1 mm.	64
		Found	69.92	7.35	6.64	15.80			
Picrate	$C_{18}H_{18}N_4O_7S$	Calcd.	49.76	4.18	12.90	7.36	174–175		
		Found	50.09	4.20	12.81	7.27			
Di-*n*-butyl								110–120/0.4 mm.	27
Picrate	$C_{22}H_{26}N_4O_7S$	Calcd.	53.86	5.34	11.22	6.54	146–146.5		
		Found	54.25	5.47	11.47	6.66			
Benzyl	$C_{15}H_{13}NS$	Calcd.	75.28	5.47	5.85	13.40			
		Found	75.44	5.74	6.02	13.28		160–167/1.0 mm.	66

EXPERIMENTAL.

3-Thianaphthenylamines. Method A (Table I). 3-Thianaphthenyl-n-butylamine. Five and one-half grams of 3-hydroxythianaphthene was refluxed with an excess of *n*-butylamine for 9 hr. Upon distillation of the reaction mixture, 4.7. g. of viscous yellow liquid was obtained, b.p. 117–120°, 75%.

3-Thianaphthenylamines. Method B. Table II. 3-(1-Piperidinyl)thianaphthene. Eleven grams of 3-(1-piperidinyl)thianaphthene 1,1-dioxide was added to 6 g. of lithium aluminum hydride in 300 ml. of anhydrous diethyl ether. The flask was placed in a Dry Ice-acetone bath, and the mixture was stirred and was allowed to come to room temperature. At the end of 4 hr., the excess hydride was destroyed with ethyl acetate. Five and one-half grams of product was obtained on distillation, b.p. 105–107°/0.1 mm., m.p. 64–65°, 60%.

N-(n-Butyl)-N-3-(2-bromothianaphthenyl)acetamide. Five grams of 3-thianaphthenyl-1-*n*-butylamine was dissolved in 25 ml. of acetic anhydride. To this was added a slight excess of bromine (3.9 g.). The mixture was stirred for several minutes and poured into a 25% sodium hydroxide solution at 0°. The dark liquid soon crystallized. After several recrystallizations from 50% dioxane–50% water solution a quantitative yield was obtained, m.p. 110–111°.

Anal. Calcd. for $C_{14}H_{16}NOSBr$: C, 51.54; H, 4.94; N, 4.29; S, 9.83; Br, 24.49. Found: 51.66; H, 5.10; N, 4.15; S, 9.59; Br, 24.26.

3-(Morpholinyl)-2-nitrothianaphthene. In a Dry Ice–acetone bath, a two-fold excess of fuming nitric acid was added to an acetic anhydride solution of 3-(morpholinyl)thianaphthene. After the nitration mixture was stirred for 3 min., it was added to water and neutralized with sodium hydroxide. The red solid obtained was recrystallized from ethanol, m.p. 165–166.5°. The same compound was prepared from 3-bromo-2-nitrothianaphthene and morpholine in benzene, m.p. 165–167°. The mixed melting point was 165–167°. The sample used for analysis melted at 168–169°.

Anal. Calcd. for $C_{12}H_{12}N_2O_3S$: C, 54.52; H, 4.58:, N, 12.13; S, 10.60. Found: C, 54.58; H, 4.80; N, 12.12; S, 10.88.

2-Hydroxythianaphthene. A 2-l. flask containing 0.5 mole of thianaphthenyllithium was placed in a pan of methanol which contained sufficient Dry Ice to keep the temperature at about −20°. One-half mole of alkyl Grignard (butylmagnesium bromide) was added. Oxygen, which was purified by passing it through a tower containing potassium hydroxide and calcium chloride, was bubbled through the solution for 2 hr. Next, 0.25 mole of alkyl Grignard was added, and the temperature was allowed to rise to 0° with continued stirring and oxidation for 2 hr. Then the remaining 0.25 mole of alkyl Grignard reagent was added, and stirring and oxidation were continued for 1 hr. in an ice bath. The solution was then stirred and oxidized for 2 hr. at room temperature. After the salts had been dissolved with dilute hydrochloric acid, the solution was extracted with ether. After drying over anhydrous sodium sulfate, the ether was removed under vacuum. Thirty grams of 2-hydroxythianaphthene distilled at 60–90°/0.1 mm. Recrystallization from petroleum ether (b.p. 00–00°) low boiling gave the keto form, m.p. 32–35°, 40%.

N-o-Mercaptophenyl-N-phenylacetamide. The addition of 2-hydroxythianaphthene to aniline resulted in an instantaneous formation of the amide, which after recrystallization from ethylene glycol dimethyl ether, melted at 212.5°.

Anal. Calcd. for $C_{14}H_{13}NOS$: C, 69.11; H, 5.38; N, 5.76; S, 13.18. Found: C, 69.04; H, 5.14; N, 5.99; S, 13.18.

2-Thianaphthenylphenylamine. Five grams of 2-hydroxythianaphthene was added to 12.5 g. of aniline. Three drops of hydrochloric acid was added as a catalyst. The reaction mixture was refluxed for 24 hr. Upon vacuum distillation a compound melting at 117–118° was obtained. Both analysis and the infrared spectrum substantiate the amine structure.

Anal. Calcd. for $C_{14}H_{11}NS$: C, 74.63; H, 4.96; N, 622; S, 14.23; Found: C, 74.49; H, 4.70; N, 6.28; S, 14.49.

Acknowledgment. This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of said fund.

HOLLAND, MICH.

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, DEPAUW UNIVERSITY]

Bromination Studies of Alkyl-Substituted 2-Pyridones and 2-Quinolones[1]

D. J. COOK, RONALD E. BOWEN, PETER SORTER, AND EDWARD DANIELS[2]

Received June 12, 1961

A number of brominated 2-pyridines and 2-quinolones have been prepared and identified. The usefulness of *N*-bromosuccinimide for side chain bromination on *N*-methyl-3- and 5-methyl-2-pyridones has been demonstrated as well as the bromination of side chains in the homocyclic ring of the 2-quinolones. If the active 3- position of the carbostyrils is substituted by a methyl group, *N*-bromosuccinimide will introduce a bromine atom into this group. If the 3- position is open and no methyl groups appear in the homocyclic ring of the carbostyril, the ring is brominated in the 3- position. Some evidence is given which indicates that *N*-bromosuccinimide bromination proceeds by two different mechanisms. The action of *N*-bromosuccinimide on the substituted carbostyrils appears to be similar to the action of *N*-bromosuccinimide on coumarins.

Since the early 1940's the Wohl-Ziegler reaction has been extended to include a large number of allylic systems. The purpose of this work was to undertake a study of how *N*-bromosuccinimide acts upon the methyl-substituted 2-pyridones and 2-quinolones. The latter compounds are commonly called carbostyrils.

Adams and Schrecker[3] have used *N*-bromosuccinimide in an attempt to prepare 6-bromomethyl-2-pyridone from 6-methyl-2-pyridone. They obtained 3,5-dibromo-6-methyl-2-pyridone. Similar results were obtained by Mariella and Belcher[4] when they treated 4,6-dimethyl-2-pyridone with *N*-bromosuccinimide and obtained 3,5-dibromo-4,6-dimethyl-2-pyridone. Under drastic free radical conditions with *N*-bromosuccinimide the compound 3,5-dibromo-4,6-dibromomethyl-2-pyridone was obtained. Although elementary bromine has been used to brominate 1,4-dimethylcarbostyril[5] and 4-methylcarbostyril[6] to produce a 3-bromo-substituted carbostyril in each case, *N*-bromosuccinimide has not been previously used as a reagent for the bromination of methyl-substituted carbostyrils.

Hasegawa[7] has been able to prepare 4-bromomethylcarbostyril by the bromination of acetoacetanilide with bromine in chloroform and subsequent ring closure of the ω-bromoacetoacetanilide to the brominated carbostyril.

Since the use of *N*-bromosuccinimide on 2-pyridones easily substituted the 3- and 5-ring positions with bromine,[3,4] it was of interest to see the results of *N*-bromosuccinimide with benzoyl peroxide as a catalyst on 3-methyl-, 5-methyl-, 1,3-dimethyl-, and 1,5-dimethyl-2-pyridone. In the reaction of the dimethyl-2-pyridones, reactive monobromo derivatives were obtained which are believed to be 3-bromomethyl-1-methyl-2-pyridone (I) and 5-bromomethyl-1-methyl-2-pyridone (II), respectively. The monomethyl 2-pyridones gave oils which decomposed upon distillation.

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[1] Presented in part before the Division of Organic Chemistry at the 138th Meeting of the American Chemical Society, New York, N. Y., Sept. 16, 1960.

[2] Portions of this article are taken from the theses of R.E.B. (1960) and P.S. (1958) which were presented to the Chemistry Department of DePauw University in partial fulfillment of the M.A. degrees.

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