in color from bright yellow to bright red and in some instances separated as a pasty mass or an oil without interference in the subsequent reaction with hydrazoic acid.

1-Phenyltetrazole was also prepared from phenyl isocyanide and hydrazoic acid[4] in benzene solution and by Dimroth's method from benzene diazonium chloride and diformyl hydrazide. In both instances the yields were poor but the products were identical with the material prepared from formanilide.

1-Isobutyltetrazole was prepared by interaction of 17.9 g. (0.18 mole) of *N*-isobutylformamide in 100 ml. of toluene with 37 g. (0.18 mole) of phosphorus pentachloride followed by treatment with 100 ml. of a 16% solution of hydrazoic acid in toluene. After addition of the hydrazoic acid solution the reaction mixture was stirred for 1 hr. at room temperature and then for 3 hr. under reflux on a steam bath. The mixture was poured onto ice and made alkaline with sodium hydroxide. After separation of the toluene layer the aqueous layer was shaken once with toluene and then discarded. The combined toluene solutions were dried and the residue left after removal of the solvent was fractionated. 1-Isobutyltetrazole was collected at 121–123° at 1 mm., n_D^{20} 1.4590, yield 4.0 g. (18%). This product and the material prepared from isobutyl isocyanide gave identical infrared spectra.

Ultraviolet absorption spectra were determined with $1 \times 10^{-4}M$ solutions in 95% ethanol using a Beckman Model DU spectrophotometer. Readings were made with 1-cm. cells with 95% ethanol as the blank. The region 210–300 mμ was scanned at 5-mμ intervals and near the maxima readings were taken at 1-mμ intervals. Tetrazole and the 1-alkyltetrazoles showed only little absorption and no maxima in the region examined although in these cases concentrations as high as $1 \times 10^{-2}M$ were used. All the 1-aryltetrazoles exhibited a broad absorption band; maxima and extinction coefficients are recorded in Table II.

TABLE II

ULTRAVIOLET ABSORPTION MAXIMA OF SOME 1- AND 5-ARYLTETRAZOLES

Aryl	1-Aryltetrazoles Max. (mμ)	ε	5-Aryltetrazoles Max. (mμ)	ε
Phenyl	236	9,300	241[a]	15,900
m-Tolyl	239	8,700	243	13,600
p-Tolyl	243	10,100	246	16,700
o-Chlorophenyl	(215)[b]	(10,400)	234[a]	9,600
m-Chlorophenyl	239	8,800	242[a]	14,000
p-Chlorophenyl	242	14,000	247[a]	20,400
o-Methoxyphenyl	235	5,800	246[a]	11,600
	282	3,800	294	4,900
p-Methoxyphenyl	255	10,900	259[a]	16,900

[a] Ref. 12. [b] Shoulder.

EAST LANSING, MICH.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POMONA COLLEGE]

Catalytic Synthesis of Heterocycles. IX.[1] Dehydrocyclization of 2-Methyl-5-ethyl-4-pyridinethiol to 6-Methyl-5-azathianaphthene

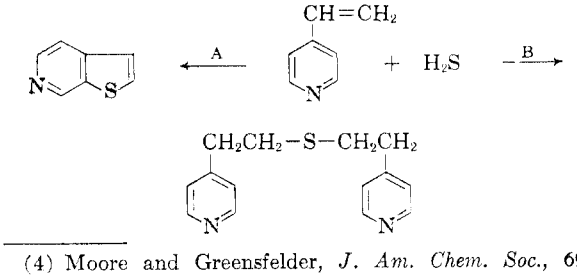
CORWIN HANSCH AND WAYNE CARPENTER

Received February 25, 1957

A procedure for the synthesis of 2-methyl-5-ethyl-4-pyridinethiol from 2-methyl-5-ethylpyridine has been developed. The dehydrogenation of this *o*-ethylthiol to 6-methyl-5-azathianaphthene is discussed.

After considering suitable systems in which to extend the use of the dehydrocyclization reaction it was decided that the pyridine ring offered a highly stable and interesting structure for such a study. In particular this ring system offers an approach to the synthesis of heterocycles containing two hetero atoms. The fact that ethylpyridines are available commercially and that improved methods have been worked out for the introduction of substituents into the pyridine ring[2,3] indicated that the necessary starting materials should be relatively easy to prepare. Formation of the thiophene ring was chosen for the first of these experiments because previous work[1] had shown that the dehydrocyclization reaction is particularly useful in its formation.

It was first expected that azathianaphthenes could be obtained by the reaction of hydrogen sulfide with vinyl pyridines. It is known[4] that styrene and hydrogen sulfide react at 600° to give thianaphthene. A number of runs were made using the catalyst of Moore and Greensfelder,[4] as well as with the catalyst used in the dehydrocyclization of *o*-ethylthiophenol.[1] The products from the reaction of 4-vinylpyridine and hydrogen sulfide at 600° were separated into two fractions: one was a red, tarry material soluble in water, but insoluble in ether, and the other was a yellow oil which was soluble in ether and insoluble in water. Of two possible paths which the reaction might take, A or B, a work-up of the ether soluble fraction indicated that this material was formed *via* path B as follows:



(1) For the previous paper in this series see *J. Org. Chem.*, 21, 265 (1956).

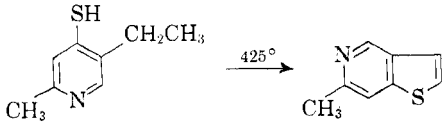
(2) Den Hertog and Combe, *Rec. trav. chim.*, 70, 581 (1951).

(3) Ochiai, *J. Org. Chem.*, 18, 534 (1953).

(4) Moore and Greensfelder, *J. Am. Chem. Soc.*, 69, 2008 (1947).

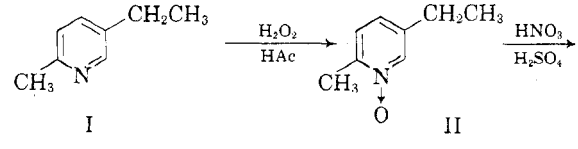
The ether soluble fraction was subjected to chromatographic analysis in an attempt to determine its composition and discover any azathianaphthene which might have formed. No azathianaphthene was isolated. A yellow oil which gave analytical data corresponding to that expected for the addition of two molecules of pyridine to one of hydrogen sulfide was the only pure substance which could be isolated from the ether soluble fraction.

Another approach to the synthesis of the azathianaphthenes is the possible dehydrogenation of an *ortho* ethylarylthiol. Previous work[1] has shown that this procedure worked well with benzenethiols and therefore we decided to apply this approach to a pyridinethiol according to the following equation:

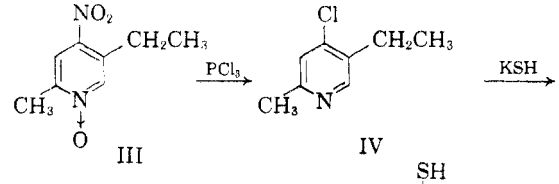


VI

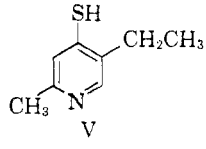
2-Methyl-5-ethyl-4-pyridinethiol was used as a model compound since it is relatively easily made from 2-methyl-5-ethylpyridine, an inexpensive commercial product.[5] The following procedure was used for its synthesis:



I II



III IV



V

The 4-pyridinethiol was chosen partly because of its relative ease of synthesis, and partly because it was of interest to determine whether a 4-pyridinethiol which would be in equilibrium with thione would undergo the dehydrocyclization reaction as well as a benzenethiol. It was expected that the thione might not give as good results, and indeed, this was found to be true.

In the synthesis of the 2-methyl-5-ethyl-4-pyridinethiol commercial grade 2-methyl-5-ethylpyridine was oxidized to the oxide by the procedure of Ochiai[3] in yields of better than 95%. The nitration of the oxide to the nitro compound III did not give high yields. Experiments were carried out using various strengths of nitric acid and various reaction times and temperatures; however, yields of 40 to 45% were the best obtained. The main cause for the low yields was the oxidation of the molecule which occurs much more readily with an ethylpyridine than with a methylpyridine. Preliminary work on the nitration of 3-ethylpyridine oxide indicates that this molecule is also very easily oxidized by a mixture of nitric and sulfuric acid. Compound III was smoothly converted to IV in yields of 70–75% by refluxing with PCl_3 in chloroform. The conversion of IV to the thiol V proceeded poorly. Refluxing IV in ethylene glycol with potassium hydrogen sulfide gave about 50% of crude V, which could be purified with some difficulty by recrystallization from either acetone or ethanol-benzene.

The dehydrocyclization of V to 6-methyl-5-azathianaphthene gave yields of 20–25% on runs of 10 g. On larger runs it is likely that the yields would be lower since the activity of the catalyst decreases with use. One of the most important causes of the low yield is the hydrogenolysis of the thiol to give hydrogen sulfide. Analysis of the H_2S evolved indicated that 35–40% of compound V underwent hydrogenolysis. About 10–15% of the thiol was recovered leaving about 20–35% of the starting material unaccounted for. A certain amount of charring in the catalyst tube and dark material in the product indicated that some of the starting material was lost by thermal decomposition.

The identity of the 6-methyl-5-azathianaphthene was confirmed by carbon and hydrogen analysis, and by the fact that the methiodide con-

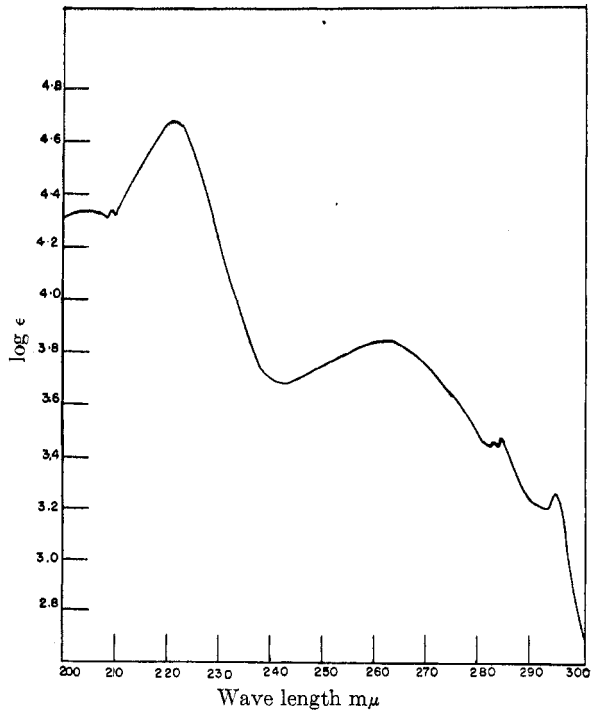


FIG. 1. ULTRAVIOLET SPECTRUM OF 6-METHYL-5-AZATHIANAPHTHENE.

(5) Purchased from Union Carbide Chemicals Co., South Charleston, W. Va.

densed readily with benzaldehyde indicating an active methyl group. Its ultraviolet absorption spectrum (Fig. 1) is similar to that obtained for 5-azathianaphthene by Herz and Tsai.[6]

EXPERIMENTAL[7]

Reaction of 4-vinylpyridine with hydrogen sulfide. After 10 ml. of iron oxide on alumina catalyst was reduced according to the procedure of Moore and Greensfelder[4] hydrogen sulfide was started over it at the rate of 1000 ml./ml. catalyst/hour, the temperature being held at 600°. Then 30 g. of 4-vinylpyridine was processed over the catalyst in the hydrogen sulfide stream during the course of 135 min. A liquid condensate was removed from the effluent gas stream by means of an ice trap, after which the hydrogen sulfide was removed by passing the gases through two dry ice traps. The red condensate from the ice cooled receiver was extracted with ether. Evaporation of the ether gave 10.8 g. of yellow oil. The red oil not soluble in ether amounted to 8.2 g. Of the ether soluble material 8.7 g. was chromatographed over 200 g. of alumina. The effluent solvents from the elution of the column were collected in 27 100-ml. fractions. The column was first eluted with benzene (7 fractions), then ether (16 fractions), and finally methanol (4 fractions). The oil obtained from the evaporation of the eleventh ether fraction yielded a picrate of m.p. 185–186°. Ether fractions 6 through 12 were combined and evaporated to give 6.9 g. of light yellow oil. This material was converted to the picrate which after five recrystallizations from 1:1 water-methanol gave a product which melted at 180–182°. Decomposition of the picrate gave 1.2 g. of oil, a small sample of which was distilled under high vacuum prior to analysis.

Anal. Calcd. for $C_{14}H_{16}N_2S$: C, 68.81; H, 6.60. Found: C, 68.47; H, 7.02.

The picrate appeared to contain two molecules of picric acid.

Anal. Calcd. for $C_{26}H_{22}N_8O_{14}S$: C, 44.45; H, 3.16. Found: C, 44.70; H, 3.36.

The benzene fractions contained 0.8 g. of material which may have contained some azathionaphthene, but attempts to isolate it were unsuccessful. The methanol fractions contained 0.36 g. of crude material.

2-Methyl-5-ethylpyridine oxide (II). 2-Methyl-5-ethylpyridine (240 g.) was dissolved in 1200 ml. of glacial acetic acid and to this solution was added 160 ml. of 30% hydrogen peroxide. After heating the mixture on a water bath for 4 hr. at 60–70°, 160 ml. more hydrogen peroxide was added and the heating continued for 5 hr. The reaction mixture was then evaporated as far as possible by means of an aspirator and a steam bath; 300 ml. of water was added and the process was repeated. Excess anhydrous potassium carbonate was added to remove small amounts of acetic acid still present, and the product was separated from the carbonate with chloroform. Evaporating the chloroform and distillating the resulting oil gave 252.5 g. of oxide, b.p. 102°/0.7 mm., n_D^{25} 1.5591.

Anal. Calcd. for $C_8H_{11}NO$: C, 70.04; H, 8.08. Found: C, 69.69; H, 8.41.

2-Methyl-5-ethyl-4-nitropyridine oxide (III). Compound II (120 g.) was added with cooling to 100 ml. of concd. sulfuric acid. This solution was added slowly from a dropping funnel to a mixture of 200 ml. of concd. sulfuric acid and 130 ml. of nitric acid (sp. gr. 1.49) held at 105–110°. About 1.5 hr. were required for the addition, after which the mixture was heated at 130° for 2.5 hr. Then the solution was poured onto crushed ice, neutralized with ammonium hydroxide, cooled, and extracted four times with chloroform. The chloroform solution was evaporated to a small volume and poured into ether where, upon cooling, 74 g. of crystals of m.p. 74–78° separated. Recrystallization from ether gave 61.9 g., m.p. 78–79°.

Anal. Calcd. for $C_8H_{10}N_2O_3$: C, 52.74; H, 5.53. Found: C, 52.97; H, 5.83.

2-Methyl-5-ethyl-4-chloropyridine (IV). Compound III (23 g.) was dissolved in 300 ml. of chloroform and 40 ml. of phosphorus trichloride was added slowly with cooling. After the initial exothermic reaction had subsided the solution was refluxed for 5 hr. Then it was poured onto crushed ice, neutralized with ammonium hydroxide, and the product extracted with chloroform. The chloroform was evaporated from the extracts and the residue was distilled to give 16 g. of yellow oil of b.p. 70–71°/5 mm., n_D^{25} 1.5170.

Anal. Calcd. for $C_8H_{10}ClN$: C, 61.74; H, 6.48. Found: C, 61.99; H, 6.69.

Preparation of the picrate gave a substance which melted at 129.5–132.5° after recrystallization from ethanol.

Anal. Calcd. for $C_{14}H_{13}ClN_4O_7$: C, 43.70; H, 3.40. Found: C, 44.24; H, 3.63.

If insufficient phosphorus trichloride was used, or if the reflux time was too short, a second substance was obtained in the distillation of the 2-methyl-5-ethyl-4-chloropyridine. This material boiled at 95–100°/5 mm. and on treatment with phosphorus trichloride in chloroform was converted into 2-methyl-5-ethyl-4-chloropyridine. A picrate was made which, after recrystallization from ethanol, melted at 116–118°. The nitrogen analysis of the picrate would indicate that this higher boiling material is 2-methyl-5-ethyl-4-chloropyridine oxide.

Anal. Calcd. for $C_{14}H_{13}ClN_4O_8$: N, 13.98. Found: N, 13.99.

2-Methyl-5-ethyl-4-pyridinethiol (V). The procedure used in the preparation of this compound is a modification of that described by Thirtle.[8] Potassium hydroxide (198 g.) was dissolved in 600 ml. of ethylene glycol and then hydrogen sulfide was bubbled into the solution until a gain in weight of 102 g. was obtained. This mixture was then distilled until the temperature of the material distilling reached 190° to remove the water. To this solution was added 136 g. of compound IV after which the mixture was refluxed for 8 hr. Then it was cooled, diluted with ethanol, and the potassium chloride which separated was removed by filtration. The ethylene glycol and ethanol were then distilled under vacuum. The semi-solid residue which resulted was dissolved in water and carefully neutralized with acetic acid. The solid product which separated was crystallized from acetone to give 71 g. of product, m.p. 141–149°. Recrystallization from acetone gave 53 g., m.p. 154–158°. The pure substance obtained by another crystallization melted at 159–161°.

Anal. Calcd. for $C_8H_{11}NS$: C, 62.70; H, 7.24. Found: C, 62.83; H, 7.38.

6-Methyl-5-azathianaphthene (VI). In the dehydrogenation of V to VI 10 ml. of the previously described[1] catalyst was used. Compound V (10 g.) was dissolved in 35 ml. of pyridine. In several experiments phenol was substituted for pyridine; the yields, however, were 10–20% lower using this solvent. This solution was then processed over the catalyst at 425° during the course of 100 min. The liquid condensate was collected in an ice bath and the effluent gases were passed through an Ascarite tube. The gain in weight of this tube was considered to be hydrogen sulfide formed from the hydrogenolysis of the thiol group. Hydrogenolysis calculated this way amounted to 30–35% of the starting material. The liquid condensate was transferred to an efficient distilling column and all but traces of the pyridine removed by fractionation. Petroleum ether was added to the residue in the distilling pot whereupon some of the starting thiol separated. Washing the petroleum ether solution with dilute sodium hydroxide solution extracted a small additional amount to give in all 1–1.5 g. of crude V.

(6) Herz and Tsai, *J. Am. Chem. Soc.*, **75**, 5122 (1953).

(7) Microanalyses by C. F. Geiger, Chaffey College, Ontario, Calif.

(8) Thirtle, *J. Am. Chem. Soc.*, **68**, 342 (1946).

The petroleum ether solution was then poured over a column of activated alumina (30 g.) and the azathianaphthene eluted with a solution of 25% ether-petroleum ether. This treatment removed tarry material which was difficult to remove by crystallization. The solvent was then evaporated and the residue vacuum sublimed at 60°/0.1 mm. to give 2.2 g. of product of m.p. 71.5–72.5°.

Anal. Calcd. for C_8H_7NS: C, 64.39; H, 4.73. Found: C, 64.58; H, 5.11.

The picrate was prepared and crystallized from ethanol to give a product which melted at 222–224°.

Anal. Calcd. for $C_{14}H_{10}N_4O_7S$: C, 44.45; H, 2.66. Found: C, 44.85; H, 2.96.

6-Methyl-5-azathianaphthene methiodide (VII). Compound VI was refluxed for a few minutes with excess methyl iodide and the mixture then was diluted with ether. The solid product which separated was removed by filtration and recrystallized from methanol to give a substance of m.p. 240–242°.

Anal. Calcd. for $C_9H_{10}INS$: C, 37.09; H, 3.46. Found: C, 37.18; H, 3.77.

1-Phenyl-2-[6-(5-azathianaphthenyl)]ethene methiodide (VIII). Compound VII (1.5 g.), 2 ml. of benzaldehyde, and 1 ml. of piperidine were placed in 20 ml. of methanol and refluxed for 12 hr. Cooling the mixture caused 1.03 g. of yellow solid m.p. 290–292° (decomp.) to separate. The filtrate from which the yellow solid separated was refluxed for 12 hr. more and then cooled, whereupon 0.27 g. more of the product crystallized. Recrystallization of these two fractions did not raise the melting point.

Anal. Calcd. for $C_{16}H_{14}INS$: C, 50.28; H, 3.69. Found: C, 50.97; H, 3.98.

1-Phenyl-2-[6-(5-azathianaphthenyl)]ethene (IX). Compound VIII (526 mg.) was heated at 280°/0.25 mm. which caused it to decompose and sublime. The 318 mg. of product melted at 118–120°. After recrystallization from ligroin it melted at 126–127°.

Anal. Calcd. for $C_{15}H_{11}NS$: C, 75.91; H, 4.67. Found: C, 76.08; H, 5.13.

CLAREMONT, CALIF.

[CONTRIBUTION NO. 1007 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Synthesis of Nitrogen-Containing Ketones. VII. A Study of the Acylation of 4-Picoline[1,2]

CARL OSUCH[3] AND ROBERT LEVINE

Received March 11, 1957

The lateral metalation of 4-picoline cannot be effected by means of phenylmagnesium bromide, methylmagnesium iodide, or ethylmagnesium bromide. However, its reaction with phenyllithium by either the Standard Addition method (S.A.) or the Reverse Addition method (R.A.) followed by the addition of an acylating ester gives mixtures of the desired 4-picolyl ketone and the azomethine addition products, 2-phenyl-4-methylpyridine and 2,6-diphenyl-4-methylpyridine. Although the reaction of 4-picoline, *n*-butyllithium, and methyl benzoate by the S.A. method gives a mixture of 2-*n*-butyl-4-methylpyridine, A, (36%) and 4,4′-dimethyl-2,2′-dipyridyl and none of the desired 4-phenacylpyridine, B, repeating this reaction by the R.A. method gave a 15.5% yield of A and a 39.8% yield of B. Furthermore, 4-picoline may be acylated with esters in acceptable yields by using both methyllithium and sodium amide as the condensing agents.

The previous papers in this series have been concerned with the synthesis of ketones containing pyridine and quinoline rings by the side-chain acylation of 2-picoline,[4,5] 3-picoline,[6] quinaldine,[5] and certain related compounds.[2,5,7] The present report deals with the acylation of 4-picoline and certain of its derivatives.

A survey of the literature indicated that a general method for the synthesis of ketones of the type, $4\text{-}C_5H_4NCH_2COR$ (I), has apparently not been devised. In the aromatic series (I, R = aryl) the following results have been reported. Chichibabin[8] obtained 4-phenacylpyridine, II (I, R = C_6H_5), in unreported yield by the reaction of sodium amide, 4-picoline, and benzonitrile followed by hydrolysis of the resulting ketimine. Although only a low yield of this ketone was also obtained by Smith *et al.*[9] from the reaction of 4-picoline, phenyllithium, and benzonitrile, these workers obtained fair to good yields of II and related ketones by applying, in the 4-picoline series, the multi-stage method developed by Scheuing and Winterhalder[10] for the synthesis of aryl 2-picolyl ketones. This route involves the following steps: $4\text{-}C_5H_4NCH_3 + ArCHO \rightarrow 4\text{-}C_5H_4NCH{=}CHAr \rightarrow 4\text{-}C_5H_4NCHBrCHBrAr \rightarrow 4\text{-}C_5H_4NC{\equiv}CAr \rightarrow 4\text{-}C_5H_4NCH_2COAr$

(1) This work was performed under Contract No. AT(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

(2) For paper VI in this series, see C. Osuch and R. Levine, *J. Org. Chem.*, **21**, 1099 (1956).

(3) This paper is based on part of the thesis presented by Carl Osuch to the Graduate Faculty of the University of Pittsburgh in partial fulfillment of the requirements for the Ph.D. degree; present address: Monsanto Chemical Co., St. Louis, Mo.

(4) N. N. Goldberg, L. B. Barkley, and R. Levine, *J. Am. Chem. Soc.*, **73**, 4301 (1951).

(5) N. N. Goldberg and R. Levine, *J. Am. Chem. Soc.*, **74**, 5217 (1952).

(6) A. D. Miller, C. Osuch, N. N. Goldberg, and R. Levine, *J. Am. Chem. Soc.*, **78**, 674 (1956).

(7) N. N. Goldberg and R. Levine, *J. Am. Chem. Soc.*, **77**, 3647 (1955).

(8) A. E. Chichibabin, *Rec. trav. chim.*, **57**, 582 (1938).

(9) J. M. Smith, H. W. Stewart, B. Roth, and E. H. Northey, *J. Am. Chem. Soc.*, **70**, 3997 (1948).

(10) G. Scheuing and L. Winterhalder, *Ann.*, **473**, 126 (1929); German Patent **594,849**, March 22, 1934 [*Chem. Abstr.*, **28**, 4542 (1934)].