[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Endocyclic α,β-Unsaturated Ketones. V.[1] Synthesis and Reaction of 3-Bromo-1,1-dimethyl-2-keto-1,2-dihydronaphthalene with Morpholine

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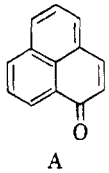
1,1-Dimethyl-2-keto-1,2-dihydronaphthalene (I) was synthesized from 1,1-dimethyl-2-tetralone in good yield and characterized by its physical and chemical properties. The dibromide addition product, III, and the corresponding α-bromo-α,β-unsaturated ketone, IV, were prepared and found to react with morpholine to produce 1,1-dimethyl-2-keto-4-morpholino-1,2-dihydronaphthalene, (V). This product was hydrolyzed to 1,3-diketo-4,4-dimethyltetralin, (VI). Both V and VI were also obtained from 1,1-dimethyl-3,4-epoxy-2-tetralone, which was prepared from the unsaturated ketone, I. 2-Bromo-4,4-dimethyl-1-keto-1,4-dihydronaphthalene reacted with sodium methoxide to give the 2-methoxy product which was hydrolyzed to 1,2-diketo-4,4-dimethyltetralin. The results of these studies are contrasted with those previously reported for the perinaphthenone-7 and 4,4-dimethyl-1-keto-1,2-dihydronaphthalene series.

Endocyclic α,β-unsaturated ketones have been the subject of considerable study in recent years.[1,3-5] Various tetralones are often of interest as intermediates in the synthesis of morphine alkaloids[6,7] and steroids.[8]

Three compounds which are related and yet include a variety of electrical and steric variations are perinaphthenone-7[4] (A), 4,4-dimethyl-1-keto-1,4-dihydronaphthalene,[1,3,5,9] (B), and 1,1-dimethyl-2-keto-1,2-dihydronaphthalene,[10] (I).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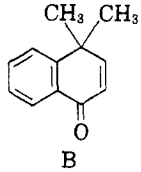
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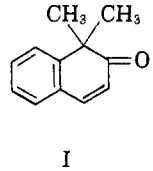
I

The purpose of the present investigation was to study the chemistry of the conjugated unsaturated carbonyl system in the third ketone, I, for comparison with the results previously reported for the first two, A and B. After this investigation was substantially completed Marvell[10] reported a procedure for the preparation of 1,1-dimethyl-2-keto-1,2-dihydronaphthalene (I) which is similar to the one we have used. Marvell did not report the analysis of his product but only of derivatives thereof.

The required β-tetralone was prepared by the reduction of 2-methoxynaphthalene employing pilot plant scale equipment and the procedure previously described starting with 2-ethoxynaphthalene.[11] 1,1-Dimethyl-2-tetralone[7,8] was made in good yield in large runs using sodium hydride as the base.[7] The introduction of the double bond by bromination and dehydrobromination proceeded smoothly to give a good yield of the oily product 1,1-dimethyl-2-keto-1,2-dihydronaphthalene (I), which was purified by efficient fractional distillation. The importance of conjugation in this molecule was indicated by the exaltation (3.06) of the molar refractivity and its aromatic character by the high specific dispersion, 271.5.[12]

When subjected to the usual conditions for the dienone-phenol rearrangement,[9] the unsaturated ketone, I, did not rearrange. Marvell[10] has reported that the rearrangement of the ketone I occurs slowly to give 1,2-dimethyl-4-naphthol. Just as was found to be the case with ketones A[4] and B,[5] morpholine failed to react with ketone I. When treated with *N*-iodobenzylamine, following Southwick's directions for such reactions,[13] the unsaturated ketone I produced only a small amount of material, the analysis and properties (high m.p. and stability to heat) of which seemed to indicate it might be a piperazine, II, a dimer of the expected ethylenimine. Further studies with this reaction are planned.

The dibromide III of the unsaturated ketone I was stable enough to isolate in this series in contrast with those formed with ketones A[4] and B.[5] However, the dibromide III did spontaneously lose hydrogen bromide at room temperature. The practical dehydrobromination of the dibromide was accomplished smoothly with organic or inorganic bases to produce 3-bromo-1,1-dimethyl-2-keto-1,2-

(1) For paper IV in this series, see R. D. Campbell and N. H. Cromwell, *J. Am. Chem. Soc.*, **77**, 5169 (1955).

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(3) N. H. Cromwell, H. H. Eby, and D. B. Capps, *J. Am. Chem. Soc.* **73**, 1224 (1951).

(4) N. H. Cromwell, D. B. Capps, and S. E. Palmer, *J. Am. Chem. Soc.*, **73**, 1226 (1951).

(5) N. H. Cromwell, H. H. Eby, and D. B. Capps, *J. Am. Chem. Soc.*, **73**, 1230 (1951).

(6) G. Stork and H. Conroy, *J. Am. Chem. Soc.*, **73**, 4743 (1951).

(7) M. D. Soffer *et al.*, *J. Am. Chem. Soc.*, **72**, 3704 (1950).

(8) R. M. Dodson and W. P. Webb, *J. Am. Chem. Soc.*, **73**, 2767 (1951).

(9) R. T. Arnold, J. S. Buckley, and J. Richter, *J. Am. Chem. Soc.*, **69**, 2322 (1947).

(10) E. N. Marvell and J. L. Stephenson, *J. Am. Chem. Soc.*, **77**, 5177 (1955).

(11) M. D. Soffer *et al.*, *Org. Syntheses*, **32**, 97 (1952).

(12) A. V. Grosse and R. C. Wackher, *Ind. Eng. Chem., Anal. Ed.*, **11**, 614 (1939).

(13) P. L. Southwick and D. R. Christman, *J. Am. Chem. Soc.*, **74**, 1886 (1952).

TABLE I

Ketone	No.	Ultraviolet Max.[a] λ, mμ	Ultraviolet Max.[a] ε × 10⁻³	Infrared Bands[b] Band	Infrared Bands[b] Cm.⁻¹/% Abs.
1,1-Dimethyl-2-keto-1,2-dihydronaphthalene	(I)	230	15.4	C=O	1662/95
		236	15.8	C=C	1624/53
		294	10.2		
		300	10.1		
3-Bromo	(IV)	210	10.4	C=O	1678/92
		235	11.7	C=C	1610/42
		242	12.6		
		316	13.2		
4-Morpholino	(V)	220	9.1	C=O	1670/92
		245	15.0	C=C	1610/63
		353	8.8		
4-Hydroxy	(VIA)	222	7.1	O—H	3450/64
		243	12.8	C=O	1663/88
		251	14.5		1646/91
		335	9.4		

[a] Ultraviolet spectra were determined at about 25° employing 1 × 10^{-4} molar concentration of 2,2,4-trimethylpentane solutions using a Cary recording spectrophotometer and 1 cm. fused silica cells. [b] Infrared spectra determinations were made with a Perkin-Elmer recording instrument Model 21 using 12 mg./ml. of carbon tetrachloride solutions in matched 1.0 mm. sodium chloride cells.

dihydronaphthalene, (IV). That this product IV was the α-bromo derivative was indicated by analogy with the results obtained in the related ketone A[4] and B[5] series and by spectral studies[14]; see Table I. The dibromide III reacted with excess benzylamine in benzene solution to give only the α-bromo-α,β-unsaturated ketone, IV. Previous investigations with other cyclic α-bromo-α,β-unsaturated ketones have shown them to be relatively inert to primary or secondary amines in benzene, ether, or alcohol solution at room temperatures.[4,5]

The dibromide III and the unsaturated bromide IV both reacted on warming with an excess of morpholine to give a good yield of 1,1-dimethyl-2-keto-4-morpholino-1,2-dihydronaphthalene, (V). Acid hydrolysis in the usual manner[4,5] of the amino ketone V produced the corresponding diketone VI. This diketone did not condense with *o*-phenylenediamine, nor did it give the color change expected for 1,2-diketones with titanous chloride.[15]

The diketone VI was shown to be the new 1,3-diketone, 4,4-dimethyl-1,3-diketotetralin by its reaction with alkaline hypochlorite, which cleaves cyclic 1,3-diketones to the corresponding dibasic acid and chloroform.[16] The diketone VI produced α,α-dimethylhomophthalic acid, (VII), shown to be identical with an authentic sample.[17] This diketone VI seemed to be nearly completely enolic in character and probably has essentially the structure VIA instead of VI;[14] see Table I. It gave a characteristic purple-brown color with ferric chloride and failed to react with periodic acid. It was readily soluble in dilute sodium hydroxide. This diketone failed to condense with morpholine on heating, possibly because of the formation of a stable morpholine salt of the enol VIA.[18]

The above described experiments established the structure of the amino ketone V as a β-amino-α,β-unsaturated ketone. On the basis of previous studies[4,5,18] α-bromo-α,β-unsaturated ketones can be expected to react with morpholine to give either α-amino or β-amino-α,β-unsaturated ketones. The mechanism[4] of reaction must involve as a first step the 1,4-addition of the amine to produce the α-bromo-β-aminoketone, D. The last step involves the loss of hydrogen bromide. The fact that no α-morpholino isomer could be isolated in these experiments may indicate that an ethylenimmonium bromide intermediate is not involved in this loss of hydrogen bromide.

A basic solution of hydrogen peroxide reacted with the unsaturated ketone I to give 1,1-dimethyl-3,4-epoxy-2-tetralone, (VIII), in more than 50% yield which was not isolated but used in solution. Attempts to crystallize VIII from aqueous ethanol rearranged it to the 1,3-diketone VI. Acid catalysis also accomplished this rearrangement. Treatment of the epoxide solution with morpholine produced the aminoketone, V. It is interesting that in the perinaphthenone-7 series the epoxide undergoes similar reactions to give the α-isomers in good yields.[4,19]

Another attempted synthesis of the diketone VI from 2-bromo-4,4-dimethyl-1-keto-1,4-dihydronaphthalene, (E),[9] led to the formation of 4,4-dimethyl-1-keto-2-methoxy-1,4-dihydronaphthalene, (IX). It had been hoped that the 3-methoxy isomer would be formed, which then could be hydrolyzed

(14) In a forthcoming publication a comprehensive comparison and discussion of the ultraviolet and infrared spectra of compounds in these three related series of ketones A, B, and I will be given.

(15) F. Weygand and E. Csendes, *Ber.*, **85**, 45 (1952).

(16) R. C. Fuson and B. A. Bull, *Chem. Revs.*, **15**, 275 (1934).

(17) S. Gabriel, *Ber.*, **20**, 1198 (1887).

(18) N. H. Cromwell *Chem. Revs.*, **38**, 83 (1946).

(19) L. F. Fieser and L. W. Newton, *J. Am. Chem. Soc.*, **64**, 917 (1942).

to VI. Hydrolysis of IX gave the known 1,2-diketone X, establishing the location of the methoxy group in the α-position.

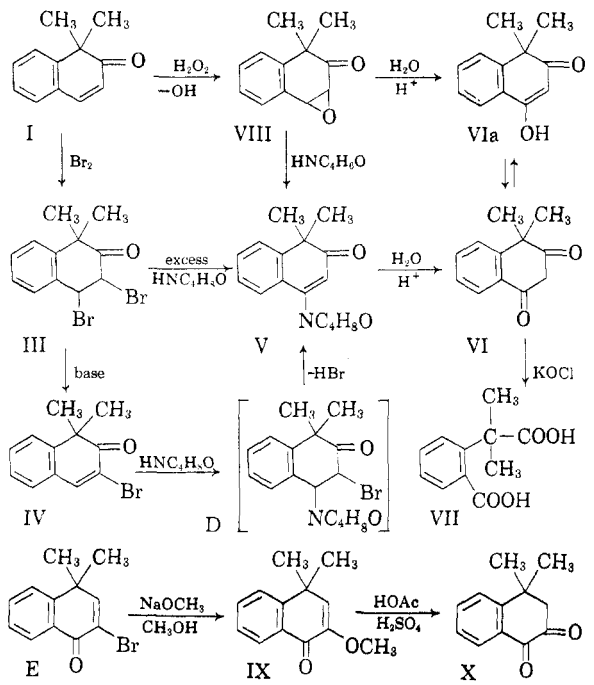

CHART 1. REACTIONS OF ENDOCYCLIC KETONES

EXPERIMENTAL

β-Tetralone. The procedure[11] described for the reduction of 2-ethoxynaphthalene was applied to 2-methoxynaphthalene and the reaction carried out in a 40 l. kettle. A continuous liquid-liquid extractor was used in extracting the hydrolysis mixture, and also in extracting the β-tetralone bisulfite addition product decomposition mixture. The reported[11] yields were duplicated in runs involving four times the described[11] quantities.

1,1-Dimethyl-2-tetralone. The procedure of Soffer *et al.*[7] was employed. Large runs using up to 87 g. of β-tetralone gave yields from 83 to 87%. A larger run using 120 g. of β-tetralone produced a 77% yield. The oil product was rectified in a spinning band column[20] at 14.5 mm. Constant refractive index was obtained with four consecutive fractions at n_D^{27}, 1.5395.[7] Compensator prism reading 23.1°. Specific dispersion, 147.

1,1-Dimethyl-2-keto-1,2-dihydronaphthalene (I). A solution of 55.4 g. of bromine in 200 ml. of carbon tetrachloride was added dropwise to a stirred solution of 53.3 g. of 1,1-dimethyl-2-tetralone in 300 ml. of the same solvent. The solvent and excess bromine were removed under vacuum with warming. The residual oil was mixed with 200 ml. of collidine and warmed on the steam bath for 1 hr. and then heated under reflux for an additional hour. The reaction mixture was cooled, diluted with ether, and the collidine hydrobromide removed by filtration, 58.4 g. (0.94 molar equiv.). The ether solution was well washed with 10% hydrochloric acid and then water and dried over anhyd. $MgSO_4$. Distillation at 18 mm. gave 33.2 g. (62.8% yield) of oil, b.p. 146–150°, n_D^{23}, 1.5915. Redistillation at 120 microns of 28 g. of the crude product using a Nester spinning band column[20] gave 17 g. in nine consecutive fractions with identical refractive indices, n_D^{27}, 1.5889, compensator prism reading 34.1°, $d^{28.2}$ 1.066; abs. molar refractivity, 54.40, calc. from partials,[21] 51.34, exaltation, +3.06, specific dispersion, 271.5 (naphthalene 270[12]).

Anal. Calcd. for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.54; H, 6.99.

2,4-Dinitrophenylhydrazone of I, orange needles, m.p. 225–228° dec. (lit.,[10] 225.5°).

Anal. Calcd. for $C_{18}H_{16}N_4O_4$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.79; H, 4.52; N, 15.68.

Semicarbazone of I, recrystallized from aq. ethanol, m.p. 198–200° (lit.,[10] 188°).

Anal. Calcd. for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 68.09; H, 6.48; N, 18.05.

Stability of I to acid. Under the conditions for the dienone-phenol rearrangement[9] after 40 hr. at room temperature, 86% of the starting ketone was recovered as the 2,4-dinitrophenylhydrazone derivative. A small amount of an unidentified tan solid, m.p. 215–222° was also obtained.

Stability of I to amines. A solution of 10 ml. of morpholine and 1.98 g. of the unsaturated ketone, I, in 100 ml. of petroleum ether (b.p. 30–40°) stood at room temperature for 5 days, and in the refrigerator for 1 month. No product formed. When the solution was refluxed for several hours only the starting materials were obtained from the cooled solution.

Reaction of I with iodine and benzylamine. A solution of 4.09 g. of ketone I in 20 ml. of benzene was added all at once to a solution of 3.97 g. of iodine and 13 g. of benzylamine in 80 ml. of benzene. The red color slowly disappeared. After standing over night the reaction solution was colorless. The benzylamine hydroiodide was removed by filtration and the solution washed with water. Evaporation of the benzene and recrystallization of the residue from methanol gave 0.22 g., m.p. 224°, of colorless needles, product II.

Anal. Calcd. for $C_{19}H_{19}NO$ or dimer: C, 82.26; H, 6.91; N, 5.05. Found: C, 82.41; H, 7.03; N, 4.76.

3,4-Dibromo-1,1-dimethyl-2-tetralone (III). A solution of 7.27 g. of the unsaturated ketone, I, in 50 ml. of carbon disulfide was stirred rapidly at 0° as bromine in carbon disulfide was added. Addition was discontinued when the bromine color persisted. The solvent and excess bromine were removed under vacuum with gentle warming. The residue was recrystallized from petroleum ether, b.p. 60–70°, to give 10.85 g. (73% yield) of large colorless crystals, m.p. 102–104°.

Anal. Calcd. for $C_{12}H_{12}OBr_2$: C, 43.25; H, 3.63. Found: C, 43.38; H, 3.56. On standing at room temperature the dibromoketone III spontaneously lost hydrogen bromide.

3-Bromo-1,1-dimethyl-2-keto-1,2-dihydronaphthalene (IV). (*a*) *Reaction of III with benzylamine.* A solution of 5.66 g. of the dibromoketone III and 5.16 g. of benzylamine in dry benzene was allowed to stand at room temperature for two days. Filtration gave 3.27 g. (1.1 molar equiv.) of benzylamine hydrobromide. The filtrate was well washed with water, dried, and evaporated. The residue was crystallized from ether and petroleum ether to produce colorless plates, m.p. 36–37°, 1.9 g.

Anal. Calcd. for $C_{12}H_{11}OBr$: C, 57.39; H, 4.42. Found: C, 57.62; H, 4.40.

(*b*) *Reaction of III with sodium carbonate.* A 22 g. of sample of the crude dibromoketone was dissolved in ethanol and a 10% excess of sodium carbonate added. The mixture was shaken occasionally and allowed to stand for 24 hr. The inorganic material was removed by filtration and the filtrate distilled to give 14.0 g. (81% yield) of fairly pure monobromoketone, IV, b.p. 110–130°/12 mm., which partially solidified on standing.

1,1-Dimethyl-2-keto-4-morpholino-1,2-dihydronaphthalene (V). (*a*) *From dibromoketone, III.* A 5.9 g. sample of the di-

(20) The column used in this work generously has been made available to the University of Nebraska by E. I. du Pont de Nemours and Co., Wilmington, Del. See, R. G. Nester, U. S. Pat, **2,712,520**, *Chem. Abstr.*, **49**, 12,890 (1955).

(21) R. L. Shriner and R. C. Fuson *The Systematic Identification of Organic Compounds* 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 44.

bromoketone was mixed with 40 ml. of morpholine and warmed to 65° for 24 hr. and then allowed to stand at room temperature for the same length of time. Ether was added and 8.5 g. of morpholine hydrobromide removed by filtration. The filtrate was washed with water, dried and evaporated to give a solid residue which was recrystallized from aqueous methanol; wt. 2.9 g. (67% yield); yellow needles, m.p. 102–103°.

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.46; N, 5.44. Found: C, 75.00; H, 7.20; N, 5.46.

(*b*) *From the α-bromoketone, IV.* Using conditions similar to those described under (a), 2.0 g. of the bromoketone IV produced 1.2 g. of the aminoketone, V.

1,3-Diketo-4,4-dimethyl-tetralin, VI. A 5.0 g. sample of the aminoketone, V, was dissolved in 20 ml. of 20% sulfuric acid, and heated for 2 hr. on the steam bath. The precipitated material was crystallized from aqueous methanol to give 3.5 g. (95% yield) of colorless crystals, m.p. 101–102.° The compound sublimes readily above 80° at 1 mm pressure.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.59; H, 6.54.

The 1,3-diketone, VI, gave a deep purple-brown color with ferric chloride in ethanol, and a very pale yellow color with titanous chloride (no color change) in methanol. The diketone dissolved in 5% sodium hydroxide to give a yellow solution. No reaction was obtained on refluxing the diketone with morpholine in the presence of a drop of concentrated hydrochloric acid. This 1,3-diketone was uneffected by periodic acid in a glacial acetic acid solution after 72 hr. at room temperature. No reaction of the 1,3-diketone took place with *o*-phenylenediamine or its hydrochloride in ethanol on heating on the steam bath for several hours.

Oxidation of VI with potassium hypochlorite. A 0.47 g. sample of VI was dissolved in a solution of 1.4 g. of potassium hydroxide in 10 ml. of water and chlorine passed in slowly for 1 hr. during which time the temperature of the reaction mixture rose to 40–50°. After standing for 24 hr. the mixture was filtered and acidified to give a solid, which was redissolved in aqueous alkali. This solution was decolorized with charcoal, saturated with carbon dioxide, and filtered. The filtrate was acidified to give colorless needles, m.p. 109–115°; recrystallized from aqueous ethanol, m.p. 123°. This product was found to be identical with an authentic sample of α,α-dimethylhomophthalic acid, VII.[17]

Epoxidation of 1,1-Dimethyl-2-keto-1,2-dihydronaphthalene, I. A solution of 3.7 g. of the unsaturated ketone I in 40 ml. of ethanol was warmed and 4 ml. of 30% hydrogen peroxide and 20 ml. of 4% sodium carbonate added. When the evolution of gas ceased, the mixture was worked up for the ether soluble portion. The epoxide VIII was not isolated and the ether solution containing it was divided into two equal portions for the following reactions.

(*a*) *With morpholine.* The ether was evaporated from one half of the above epoxide solution and the residue heated with 10 ml. of morpholine on the steam bath for 30 min. From this reaction was obtained 0.42 g. (22% based on ketone I) of pale yellow needles, m.p. 101–102°; mixed m.p. with V, 101–103°.

(*b*) *With sulfuric acid.* The second half of the ethereal epoxide solution was evaporated and the residue dissolved in concentrated sulfuric acid to give a red-brown homogeneous solution. This was cooled and crushed ice added to give a gummy solid which was recrystallized from methanol to give 0.45 g. (25% yield based on ketone I) of colorless crystals, m.p. 100–103°, identical with the 1,3-diketone, VI.

On attempting to isolate the pure epoxide in another experiment it was found that even an ethanol and water mixture at 80° for 30 min. converted the epoxide to the 1,3-diketone, VI.

4,4-Dimethyl-1-keto-2-methoxy-1,4-dihydronaphthalene, IX. A 7.1 g. sample of 2-bromo-4,4-dimethyl-1-keto-1,4-dihydronaphthalene[5,9] in methanol was heated with an excess of sodium methoxide on the steam bath for 12 hr. Acidification with hydrochloric acid produced 5.03 g. (88% yield) of crude IX, m.p. 108–116°; recrystallized from aqueous ethanol, m.p. 116–117°. The compound sublimed rapidly above 90°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.90; H, 6.77.

Hydrolysis of the methoxyketone, IX. A solution of 0.5 g. of IX in 0.5 g. of sulfuric acid and 4.5 ml. of glacial acetic acid was heated to boiling and then immediately poured into cold water. The precipitated oil was taken up in ether and this solution washed with water and extracted with 10% aqueous sodium hydroxide. The ether raffinate contained 0.396 g. (80%) of the starting methoxyketone, IX. Acidification of the sodium hydroxide extract gave 0.05 g. (10%) of 4,4-dimethyl-1,2-diketotetralin,[5] m.p. 65°.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Synthesis of Some Dibenzothiophene Derivatives

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Several dibenzothiophene derivatives have been synthesized by the use of a halogen-metal interconversion reaction on the corresponding bromo compound followed by a reaction with the desired precursor. The oxidation of dibenzothiophene compounds using 30% hydrogen peroxide in glacial acetic acid has been shown to be a convenient method for the synthesis of various sulfones. Several series of monosubstituted dibenzothiophene derivatives have been made complete by the synthesis of various sulfones and other hitherto rather inaccessible compounds.

During the course of a study of the chemical and physical properties of dibenzothiophene derivatives, it was found desirable to include the preparation of a number of the more fundamental type monosubstituted isomers. The 1- position of dibenzothiophene has been rather inaccessible because of the indirect route that had to be taken for the preparation of those derivatives. It has been shown that the action of hydrobromic acid in ethanol on 1-nitro-2-acetamidodibenzothiophene gives 1-bromodibenzothiophene.[1] This compound may

(1) H. Gilman and G. R. Wilder, *J. Am. Chem. Soc.*, **76**, 2906 (1954).