Anal. Calcd. for C_2H_8NSCl: C, 21.14; H, 7.09; N, 12.32. Found: C, 20.87; H, 7.08; N, 11.98.

The mercuric chloride complex of cysteamine (m.p. 200° dec., yield 15 g.) was also obtained when mercuric chloride was added directly to a solution of XIV (5 g.) in hydrochloric acid and the mixture, containing a gummy precipitate, was heated. After removal of mercuric sulfide, the filtrate was evaporated to dryness *in vacuo* to give 2.7 g. of crystals which were recrystallized— m.p. 69-70° (hygroscopic) alone and on admixture with a sample of XV prepared above.

Acknowledgments.—The authors are indebted to the Service Center of Microanalyses of the Kyushu University and also to the Microanalytical Section of this Institute for the microanalyses.

KATAKASU, FUKUOKA, JAPAN

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, UNIVERSITY OF DELAWARE AND NORTHWESTERN UNIVERSITY]

The Preparation and Properties of 7,12-Dihydro-7-phenylpleiadene[1]

BY PETER T. LANSBURY*

RECEIVED JANUARY 2, 1959

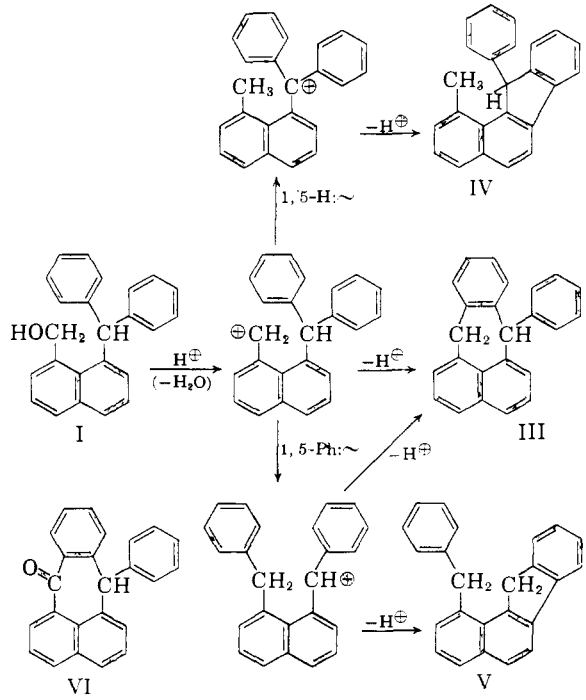
1-(8-Benzhydryl)-naphthylcarbinol (I) undergoes cyclodehydration in acidic media yielding 7,12-dihydro-7-phenylpleiadene (III) quantitatively. The structure of III was elucidated by means of ultraviolet and nuclear magnetic resonance spectroscopy, and by stereochemical considerations of the ring closure; III is a non-planar molecule and a weak donor for molecular complex formation.

In the course of investigating acid-catalyzed rearrangement reactions of *peri*-substituted naphthalenes,[2] the possibility of encountering 1,5-phenyl shifts in the solvolysis of 1-(8-benzhydryl)-naphthylcarbinol (I) seemed quite promising because of the success realized in isomerizing 8-benzhydryl-1-naphthoic acid (II).[2] Other than forming carbonium ions of different geometry, both compounds I and II might be expected to rearrange in acid *via* a 1,5-phenyl group transfer from the proximal *peri*-benzhydryl substituent. This paper reports the preparation of I, its behavior in acidic media, and certain novel stereochemical aspects of the reaction product.

1-(8-benzhydryl)-naphthylcarbinol was prepared in 90% yield by reduction of ethyl 8-benzhydryl-1-naphthoate[2] with lithium aluminum hydride. Under a variety of acidic solvolysis conditions (see Experimental) compound I was quantitatively converted to a crystalline hydrocarbon, $C_{24}H_{18}$. When the infrared spectrum of this product showed that no oxygen-containing groups were present, it became obvious that a cyclodehydration had occurred at some stage of the solvolysis and, therefore, structures III, IV and V were entertained as possible formulations for $C_{24}H_{18}$.[3]

The dehydration product did not form either a solid picrate or a 1,3,5-trinitrobenzene derivative and reacted only feebly with tetracyanoethylene[4] (TCNE), suggesting a non-planar configuration, which would inhibit molecular complex formation.[5] The greatly reduced ratio of extinction coefficients for the charge transfer spectrum of III with TCNE as compared with naphthalene/TCNE[4] is of the same order of magnitude observed by Merrifield and Phillips[4] in comparing hexamethylbenzene/TCNE with the more hindered hexaethylbenzene complex.

Whereas the infrared spectrum of the dehydration product served mainly to indicate the absence of hydroxyl and ester groups, it seemed that the ultraviolet spectrum would provide some means of



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(1) The name "pleiadene" refers to the tetracyclic ring system currently used in "Chemical Abstracts," as given in "The Ring Index" (A. M. Patterson and L. T. Capell, Reinhold Publishing Corp., New York, N. Y., 1940, p. 385).

(2) P. T. Lansbury and R. L. Letsinger, THIS JOURNAL, **81**, 940 (1959); **78**, 2648 (1956).

(3) Although III is the most obvious structure, and was selected as a working hypothesis, IV and V could readily arise, since aiter a 1,5-hydride or phenyl migration (ref. 2) the resultant carbonium ion would easily lead to a benzfluorene (for examples of acid-catalyzed dehydration of diphenyl-α-naphthylcarbinol and diphenyl-β-naphthylcarbinol to benzfluorenes see F. Ullmann and A. Mourawiew-Winigradoff, *Ber.*, **38**, 2213 (1905); M. Gomberg and W. E. Gordon, THIS JOURNAL, **57**, 119 (1935), and other references cited in "Elsevier's Encyclopedia of Organic Chemistry," Vol. 12B, Elsevier Publishing Co., Inc., New York, N. Y., 1950, pp. 1095-1097).

(4) R. E. Merrifield and W. D. Phillips, *ibid.*, **80**, 2778 (1958).

(5) For some examples of steric effects in molecular complex formation between aromatic compounds and polynitro compounds, see (a) B. R. Brown and D. Ll. Hammick, *J. Chem. Soc.*, 1395 (1948); (b) M. Orchin, *J. Org. Chem.*, **16**, 1165 (1951); and (c) M. S. Newman in "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 472.

distinguishing III, whose chief chromophore is the 1,8-disubstituted naphthalene structure, from IV and V which are substituted 1,2-benzfluorenes. An indication of the correctness of formula III, 7,12-dihydro-7-phenylpleiadene, was the close resemblance of the spectrum of $C_{24}H_{18}$ with that of 1,8-dimethylnaphthalene,[6] and the entirely different absorption curve exhibited by 1,2-benzfluorene,[6] as shown in Fig. 1.

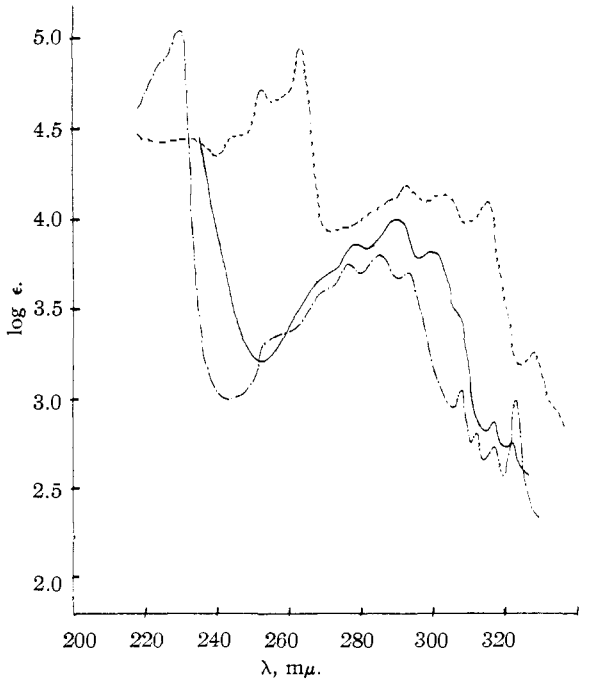


Fig. 1.—Ultraviolet spectra of 7,12-dihydro-7-phenylpleiadene (III) and model compounds: ———, III in ethanol; – – – –, 1,2-benzfluorene in 95% ethanol (ref. 6); – · – · –, 1,8-dimethylnaphthalene in isoöctane (ref. 6).

Final confirmation of structure III as the dehydration product was achieved by examining the nuclear magnetic resonance (n.m.r.) spectrum of this material.[7] If one examines the above three possible structures, the following ratios of aliphatic protons is present: III, 2 to 1; IV, 3 to 1; V, 2 to 2 (all diarylmethane-type). Therefore, in addition to the large major peak to be expected from the aryl-bound protons (relative peak area, 14 or 15), the peak area ratios of the aliphatic proton resonance peaks should allow for a choice among structures III, IV or V. The spectrum obtained from 7,12-dihydro-7-phenylpleiadene (shown in Fig. 2) has a single band attributable to the C_7-proton (δ = +0.7 p.p.m.), and two doublets (δ = −0.4 and −1.3 p.p.m.) which were thought to arise from the non-equivalent C_{12} protons (*vide infra*), the spin–spin splitting (J = 15 c.p.s.) being due to interaction of these hydrogens with each other. It is interesting that each of the four latter peaks is half as intense as the triarylmethyl

(6) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, spectra numbers 205 and 415.

(7) A Varian Associates high resolution, dual purpose spectrometer was used. Spectra were measured at 40 mc. frequency with water as external annulus.

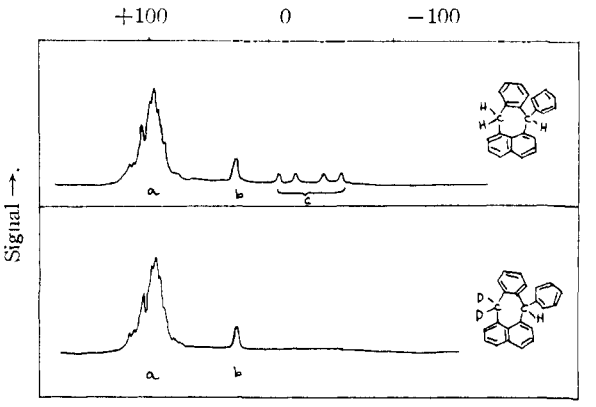
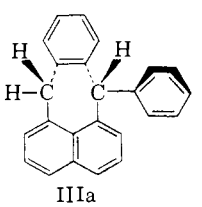


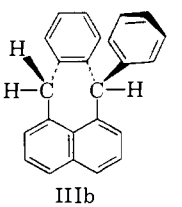
Fig. 2.—Proton nuclear magnetic resonance spectra at 40 mc., with resonance assignments: upper curve, $C_{24}H_{18}$ in CCl_4 (a, nuclear protons; *b*, C_7-proton; c, C_{12}-protons—non-equivalent, with spin–spin splitting); lower curve, $C_{24}H_{16}D_2$ in CCl_4 (a and b as above).

proton peak, thus producing the over-all 2:1 peak area ratio predicted for III. In order to confirm that the assignment of the two doublets to the resonance of the C_{12}-protons was a correct conclusion, 7,12-dihydro-7-phenylpleiadene-12,12-d_2 was prepared by reducing ethyl 1-(8-benzhydryl)-naphthoate with lithium aluminum deuteride and then cyclodehydrating the alcohol with acetic acid–sulfuric acid to give $C_{24}H_{16}D_2$. In harmony with our expectations, the n.m.r. spectrum of this material (δ = +2.4 and +0.7 p.p.m.) was identical with $C_{24}H_{18}$, except that the two doublets assigned to the non-equivalent protons on C_{12} in III have disappeared entirely. Hence, further evidence is obtained which favors III and eliminates IV and V as suitable structures for the dehydration product of I.

The reluctance of III to form molecular complexes, and also the non-equivalence of the C_{12}-hydrogens, as observed in the n.m.r. spectrum, were now reconsidered. The construction of a Catalin model of III showed that two non-interconvertible conformations are possible, both of which have non-equivalent protons on position 12. Structure IIIa is favored for two reasons: (1) it places the 7-phenyl group in the least crowded,



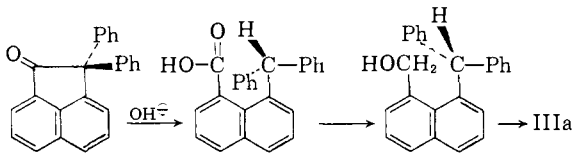
IIIa



IIIb

or sterically favored, position; and (2) this conformation is the expected one, assuming that in I the carbinol group hinders rotation of the 8-benzhydryl group to the extent that only its hydrogen atom can rotate past the *peri* group, resulting in the flanking of the carbinol group (and the carbonium ion derived from it) by the hydrogen and one phenyl group. This also applies to the acid precursor II, which has a similar favored con-

formation, based on its mode of formation from 2,2-diphenylacenaphthenone.[8] Hence, intramolecular



alkylation of I from either the front or back side of the planar benzylic carbonium ion will result in IIIa. The fact that 8-benzhydryl-1-naphthoic acid (II) rearranged in acid[2] may be a consequence of the different geometry of the acylonium ion, in which the empty π-orbital is not directed toward the *o*-position of the proximal phenyl group (as is the case in the benzylic carbonium ion derived from I), thereby favoring rearrangement over alkylation.

The chemical behavior of compound III was briefly investigated. In accord with the pleiadene structure, chromic acid oxidation yielded 12-phenyl-7(12*H*)-pleiadenone (VI), the infrared spectrum of which exhibited a strong, sharp carbonyl band at 6.03 mμ, as expected for a diaryl ketone,[9] and no hydroxyl bands. The observed reluctance of the C_7-carbon–hydrogen bond to undergo oxidation to hydroxy, whereas 8-benzhydryl-1-naphthoic acid is oxidized with CrO_3 to diphenyl-1,8-naphthalide,[10] may be due to the rigid disposition of the carbon–carbon bonds at C_7, which prevents hydride abstraction (a planar carbonium ion would be required). Similarly, Bartlett and co-workers[11] found that triptycene did not undergo bridgehead hydroxylation with chromic acid. The oxidation of the less-restricted C_{12}-methylene group to carbonyl finds analogy with the oxidation of 7,12-dihydropleiadene[12] to 1,8-diphthaloylnaphthalene. Attempts to prepare a hydrazone and a 2,4-dinitrophenylhydrazone of VI met with failure. Several efforts to metalate III with organolithium compounds[13] failed to provide a carboxylic acid after carbonation of the reaction mixture.

Acknowledgment.—We are grateful for a stimulating discussion about the n.m.r. spectra with Dr. E. G. Brame, Polychemicals Department, du Pont Experimental Station. Financial assistance for this work was provided by the University of Delaware Research Foundation.

Experimental[14]

Preparation of 1-(8-Benzhydryl)-naphthylcarbinol (I). A. From II.—A solution of 0.10 g. (2.6 mmoles) of lithium aluminum hydride and 0.34 g. (1.0 mmole) of II[8] in 50 ml. of absolute ether was refluxed overnight and then hydrolyzed with saturated sodium carbonate solution. Separation and evaporation of the ether layer yielded a solid which, after recrystallization from 80% ethanol, gave 0.25 g. (76%) of the alcohol, m.p. 168.5–169°, whose infrared spectrum (in chloroform) exhibited the following strong peaks: 2.76 (sharp), 2.90 (broad), 10.09, 12.38, 14.10 and 14.31 μ; there was no absorption at 5.6–6.0 μ.

Anal. Calcd. for $C_{24}H_{20}O$: C, 88.86; H, 6.17. Found[15]: C, 89.21; H, 6.09.

Preparation of the *p*-toluenesulfonate by the procedure of Tipson[16] yielded a product, m.p. 225–227° (from ether–ethanol), which could not be obtained analytically pure.

Anal. Calcd. for $C_{31}H_{26}SO_3$: C, 77.79; H, 5.43. Found[15]: C, 78.91; H, 5.44.

B. **From Ethyl 1-(8-Benzhydryl)-naphthoate.**[2]—A solution of the ester (0.75 g., 2 mmoles) and lithium aluminum hydride (0.12 g., 3 mmoles) in 50 ml. of ether was refluxed for four hours and then worked up as in part A, giving 0.60 g. (90%) of I, m.p. 167–168°, which was pure enough for further use (recrystallization from 80% ethanol raised the m.p. to 168.5°).

Dehydration of I.—When 0.28 g. of the carbinol I was dissolved in 5 ml. of warm acetic acid and a drop of sulfuric acid added, a blue-green color was produced. This solution was warmed for an hour on a steam-bath, during which it became yellow and finally colorless. On cooling, the product separated as fine needles; these were removed by filtration, washed with ethanol, and recrystallized from ethanol–acetone, yielding 0.26 g. (100%) of 7,12-dihydro-7-phenylpleiadene, m.p. 179–179.5°. The infrared spectrum showed strong bands at 12.18, 12.60, 12.90, 13.18, 13.60 and 14.33 μ, and no absorption in the hydroxyl or carbonyl regions. The ultraviolet spectrum was recorded, using 1-cm. quartz cells: λ_{max}^{EtOH} (log ϵ): 278 (3.86), 289 (3.99) and 300 mμ (3.82).

Anal. Calcd. for $C_{24}H_{18}$: C, 94.04, H, 5.96. Found[15]: C, 94.44; H, 6.02.

A solution of III in ethanol with excess picric acid gave no solid product after heating for 30 minutes and then standing for a week. Likewise no solid *sym*-trinitrobenzene derivative could be obtained after refluxing III and excess nitro compound in ethanol for 15 minutes and subsequent standing for several days, although a pale yellow color had been generated from the two reactants.

A few drops of a chloroform solution of tetracyanoethylene was added to III, dissolved in chloroform. A pale aqua color developed, whereas a comparative test with naphthalene gave an intense wine-red color. Measurement of the TCNE/III visible spectrum using 5-cm. cells gave $\lambda_{max}^{CH_2Cl_2}$ (ϵ): 610 (10), 417 mμ (14) for a 1.5×10^{-1} *M* solution.

The dehydration of I to III was also accomplished in excellent yield (>90%) by heating in 98% formic acid, acetic anhydride containing a trace of sulfuric acid, or 90% acetic acid containing *p*-toluenesulfonic acid. In all cases, pure III was obtained by addition of a small amount of water to the acid solution and cooling.

Preparation of 1-(8-Benzhydryl)-naphthylcarbinol-α,α-d_2.—A solution of ethyl 1-(8-benzhydryl)-naphthoate (0.75 g., 2 mmoles) and lithium aluminum deuteride (Metal Hydrides, Inc., 98% pure) (0.18 g., 4.3 mmoles) in 50 ml. of ether was refluxed for five hours and then worked up as above giving 0.55 g. (75%) of the deuterated carbinol, m.p. 167–167.5°, which was recrystallized from dilute ethanol: m.p. 168°, and mixed m.p. with I, 167.5–168°. This product had strong bands in the infrared at 2.75, 9.45, 10.52, 11.89, 12.41, 12.85, 13.49, 14.05 and 14.20 μ; there was no carbonyl absorption and only weak absorption at 4.5–4.8 μ (C–D stretching).

Dehydration of the Deuterated Carbinol.—A drop of sulfuric acid was added to a solution of 0.30 g. of the alcohol in 6 ml. of warm acetic acid. After 1.5 hr. on the steam-bath, the initially blue-green solution had become colorless. Dilution to turbidity with hot water and subsequent cooling gave 7,12-dihydro-7-phenylpleiadene-12,12-d_2, which was removed by filtration and dried, m.p. 177.5–179°, weight 0.25 g. (88%). Recrystallization from acetone–ethanol sharpened the melting point to 178–178.5°; mixed m.p. with III (m.p. 179°) was 178.5–179°. The infrared spectrum, devoid of carbonyl and hydroxyl absorption, showed

(8) W. E. Bachmann and E. Chu, THIS JOURNAL, **58**, 1118 (1936).

(9) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 114.

(10) M. Zsuffa, *Ber.*, **43**, 2915 (1910).

(11) P. D. Bartlett, M. J. Ryan and S. G. Cohen, THIS JOURNAL, **64**, 2649 (1942).

(12) A. Rieche, H. Sauthoff and O. Muller, *Ber.*, **65**, 1371 (1932).

(13) For the successful metalation of 1-naphthylphenylmethane, see H. Gilman and R. L. Bebb, THIS JOURNAL, **61**, 109 (1939).

(14) Infrared spectra were recorded with a Baird double beam spectrometer equipped with NaCl optics, using potassium bromide disks unless otherwise noted. Ultraviolet and visible spectra were obtained with a Perkin-Elmer model 4000 spectracord. Melting points were taken on a Fisher-Johns block and are uncorrected.

(15) Microanalysis by Miss H. Beck, Northwestern University.

(16) R. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

strong bands at 11.90, 12.16, 12.93, 13.15, 13.62 and 14.31 μ.

Oxidation of 7,12-Dihydro-7-phenylpleiadene.—A solution of 0.35 g. (3.5 mmoles) of chromium trioxide in 1.5 ml. of water and 10 ml. of acetic acid was gradually added to a solution of III (0.52 g., 1.7 mmoles) in 15 ml. of warm acetic acid. After one hour on the steam-bath, the dark green solution was poured into excess ice-water and the mixture extracted once with ether and then with benzene. The extracts were combined, washed with water, 5% sodium carbonate (no solid acid obtained on acidification), water again, and then dried over sodium sulfate. After the orange solution had been concentrated to *ca.* 5 ml. it was chromatographed over alumina (20 × 1 cm. column), using benzene as eluent; 0.10 g. of III was first eluted from the column (19% recovery), this being followed by 0.35 g. (65%) of a colorless, crystalline product (VI), m.p. 198–198.5° (from ethanol–acetone). No additional products were obtained although several colored bands remained on the column.

Compound VI was characterized by infrared as a diaryl ketone,[9] showing strong bands at 6.03, 10.95, 11.99, 12.60, 13.15, 13.48, 13.78 and 14.30 mμ, and no absorption in the hydroxyl region.

Anal. Calcd. for $C_{24}H_{16}O$: C, 89.97; H, 5.04. Found[17]: C, 90.16; H, 5.10.

Unsuccessful attempts were made to prepare a 2,4-DNPH using ethanolic 2,4-dinitrophenylhydrazine hydrochloride, and a hydrazone, by refluxing VI in excess ethanolic hydrazine hydrate.

(17) Microanalysis by Dr. Alfred Bernhardt, Mulheim, Germany.

Newark, Dela.

[Contribution No. 24 from the L. G. Ryan Research Laboratories of Monsanto Canada Ltd. and Research Laboratories of Ayerst, McKenna and Harrison Ltd.]

Bacteriostats. II.[1] The Chemical and Bacteriostatic Properties of Isothiocyanates and their Derivatives

By A. F. McKay,[2] D. L. Garmaise,[2] R. Gaudry,[3] H. A. Baker,[3] G. Y. Paris,[2] R. W. Kay,[2] G. E. Just[2] and R. Schwartz[2]

Received February 18, 1959

A number of cyanoalkyl isothiocyanates, substituted benzyl isothiocyanates, substituted benzyl benzyldithiocarbamates and substituted benzyl thioureas were prepared for evaluation as bacteriostats. The preparations and relative bacteriostatic properties of these compounds are described.

A number of substituted amines were converted to the corresponding isothiocyanates which were evaluated as bacteriostats. Some of the amines were prepared by the Gabriel synthesis and the new phthalimide derivatives, which were isolated as intermediates, are described in Table I. One of the amines, (±)-3-aminobutyronitrile, was resolved into its enantiomorphs. The amines were converted into isothiocyanates by a modification of the Kaluza[4–6] procedure. The properties of these isothiocyanates are described in Table II. These isothiocyanates were further characterized by their use in the formation of substituted thioureas. The thioureas together with their physical constants are listed in Table III. When the ω-cyanoalkyl isothiocyanates were added to aliphatic diamines in an anhydrous medium, a number of N,N′-di-(substitutedthiocarbamyl)-polymethylenediamines (Table IV) were obtained. The corresponding N,N′-di-(substituted carbamyl)-hexamethylenediamines (Table V) were prepared by the addition of hexamethylene diisocyanate to two equivalents of the amine in an inert solvent.

Some of the substituted amines were converted into the corresponding urethan derivatives (Table VI) by reaction with ethyl chloroformate. 4-(2-Cyanoethyl)- and 4-(10-cyanodecyl)-thiosemicarbazides also were prepared.

A series of substituted benzyl benzyldithiocarbamates were prepared by the condensation of substituted benzyl chlorides with the triethylamine salts of substituted benzyldithiocarbamic acids. The products are described in Table VII.

Bacteriostatic Activities.—A large number of isothiocyanates have been isolated[7] from seeds of plants belonging to the Cruciferae family. They exist in plants in the combined form as glycosides. Several plants containing isothiocyanates have antibiotic properties and have been used in home remedies for a number of ailments. Allyl isothiocyanate, which is present in horse-radish, has been found[8] to have antibacterial properties. More recently Das, Kurup and Rao[9] have identified benzyl isothiocyanate as a component of the antibiotic, Pterygospermin, which was isolated from the Indian Drumstick tree (*Moringa pterygosperma*). They found that benzyl isothiocyanate possessed strong bacteriostatic properties. It proved to be more effective than either phenylethyl or phenyl isothiocyanates. In view of these observations, it is of interest to compare the bacteriostatic activities of alkyl and benzyl isothiocyanates with the new isothiocyanates described in Table II.

Table VIII lists the bacteriostatic activities of the isothiocyanates against several gram-positive and gram-negative organisms. The cyanoalkyl isothiocyanates having a two-carbon chain between the cyano and isothiocyanate groups are more effective against gram negative organisms than the

(1) Paper I: M. E. Kreling and A. F. McKay, *Can. J. Chem.*, **36**, 775 (1958).

(2) Monsanto Canada, Ltd., Ville LaSalle, Que.

(3) Ayerst, McKenna and Harrison, Ltd., Montreal, Que.

(4) (a) L. Kaluza, *Monatsh.*, **30**, 717 (1909); (b) **33**, 364 (1912).

(5) J. E. Hodgkins and M. G. Ettlinger, *J. Org. Chem.*, **21**, 404 (1956).

(6) D. L. Garmaise, R. Schwartz and A. F. McKay, This Journal, **80**, 3332 (1958).

(7) C. M. Suter, "Medicinal Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 245.

(8) M. J. Foter, *J. Bact.*, **38**, 353 (1939).

(9) B. R. Das, P. A. Kurup and P. L. N. Rao, *Naturwissenschaften*, **41**, 95 (1954).