

lization showed features characteristic of both *o*-iodobenzyl alcohol and *o*-iodobenzaldehyde.

**Kinetic Procedure.**—Runs were performed using sealed ampoules surrounded by steam in equilibrium with water at atmospheric pressure. Temperature variation during a run was  $\pm 0.05^\circ$ .

**Nondegassed Runs.**—*o*-Iodosophenylacetic acid (14 mg.) was accurately weighed into each ampoule and the appropriate solution added by pipet. The ampoule was then sealed.

**Degassed Runs.**—The ampoules were filled as described above and the suspension was then frozen in liquid air. The ampoules were evacuated ( $5\text{--}10 \times 10^{-3}$  mm.) and allowed to thaw gradually, and after three of these cycles they were sealed and allowed to stand at room temperature for 10 min. (shielded in case of explosion).

The ampoules were then placed in a steam bath for 2 to 3 min., shaken vigorously to effect solution, and replaced. After 5 or 10 min. the first ampoule was removed for titration, and this was

taken as zero time. At appropriate intervals, ampoules were withdrawn, plunged into ice water, and then frozen in a Dry Ice-acetone bath. The ampoule was then opened and the contents dissolved in water to which 2 *N* sulfuric acid had been added. Solid potassium iodide (0.2 g.) was then added and the liberated iodine titrated against standard 0.01 *N* or 0.02 *N* sodium thiosulfate solution using starch indicator.

**pK<sub>a</sub> Values.**—pK<sub>a</sub> values were obtained by titration of the acids against standard sodium hydroxide solution in an atmosphere of nitrogen. Sodium sulfate was added to the solution to bring the ionic strength to *ca.* 0.1 at half-equivalence. The change in pH was followed using a Beckman model G pH meter and pK<sub>a</sub> values calculated from a number of points on the titration curve using the Henderson equation.

**Acknowledgment.**—The authors are indebted to the National Science Foundation for its support of this work.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON, SEATTLE, WASH.]

## The Syntheses of Cyclopenta[*c*]thiapyran and 2-Phenyl-2-pyridine<sup>1-3</sup>

BY ARTHUR G. ANDERSON, JR., WILLIAM F. HARRISON,<sup>4</sup> AND ROBERT GORDON ANDERSON

RECEIVED JUNE 28, 1963

The syntheses of the compounds in the title, which are iso- $\pi$ -electronic with azulene and the first simple  $\pi$ -excessive<sup>6</sup> heterocyclic analogs of a nonalternant aromatic hydrocarbon, is described. Certain physical properties, *e.g.*, the visible and ultraviolet absorption spectra, of these substances were found to be similar to those of azulene. The n.m.r. and infrared spectra of the new substances are reported.

The demonstration of aromatic character in the azulene molecule<sup>6</sup> led us to the consideration of analogous structures, among which were heterocycles wherein (a) one or more carbons in either the 5- or 7-ring would be replaced by a corresponding number of nitrogens to form molecules related to azulene as pyridine, pyrimidine, etc., are related to benzene<sup>7</sup>; (b) two adjacent carbons in the 7-ring would be replaced by a nitrogen or sulfur to form molecules related to azulene as pyrrole and thiophene are related to benzene.<sup>8</sup> In compounds of the first type there are the same number of  $\pi$ -electrons as ring atoms and the term  $\pi$ -equivalent may be used to describe this condition.<sup>9</sup> Compounds of the second type have more  $\pi$ -electrons than ring

atoms and may be called  $\pi$ -excessive.<sup>9</sup> The first known examples of the latter were methyl nor-harmine and harmine, isolated by Sir Robert Robinson and co-workers more than forty years ago.<sup>10a</sup> A number of related pyridole derivatives are known.<sup>10b</sup> At the inception of the present studies and prior to the preliminary report<sup>3</sup> no mention of the preparation of a simple, unsubstituted  $\pi$ -excessive heteroanalog of azulene was found in the literature,<sup>11</sup> and a comparison of the properties of such compounds with those of azulene seemed of interest. These structures would have a different ring size and shape in addition to the presence of the heteroatom and yet still be nonalternant, and it was the expectation that a comparison of the properties of these molecules with those of azulene would provide data useful in the theoretical interpretation of the role of the heteroatom in  $\pi$ -excessive heteroaromatic compounds in general.

**Syntheses.**—A synthetic route (Fig. 1 and 2) wherein the heteroatom was introduced in the last step prior to the introduction of the unsaturation was chosen because it was direct, uncomplicated, and, more important, permitted the formation of the saturated bicyclic sulfur, nitrogen, and oxygen molecules from the same intermediates. The Dieckmann condensation of diethyl adipate to form **1** (83–89%) was effected with a sodium hydride dispersion and the product was transformed into the cyano ester **2** in *ca.* 70% yield *via* the method of

(1) Supported in part by a contract with the Office of Ordnance Research and a grant from the National Science Foundation.

(2) From the Ph.D. theses of William F. Harrison and Robert G. Anderson.

(3) A portion of this work was reported in preliminary communications: A. G. Anderson, Jr., W. F. Harrison, R. G. Anderson, and A. G. Osborne, *J. Am. Chem. Soc.*, **81**, 1255 (1959); A. G. Anderson, Jr., and W. F. Harrison, *Tetrahedron Letters*, **2**, 11 (1960).

(4) Standard Oil of California Fellow, summer, 1958; National Science Foundation Predoctoral Fellow, 1959–1960.

(5) A. Albert, "Heterocyclic Chemistry. An Introduction," Essential Books, Fair Lawn, N. J., 1959.

(6) A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953). For a general review and discussion see E. Heilbronner, "Non-benzenoid Aromatic Compounds," ed. by D. Ginsburg, Interscience Publishers, Inc., New York, N. Y., 1959, Chapt. V.

(7) The first example of this type, 1-azabenz[*b*]azulene, was prepared in our laboratories: A. G. Anderson, Jr., and J. J. Tazuma, *J. Am. Chem. Soc.*, **74**, 3455 (1952). 1-Aza-, 1,3-diaza-, and 1,2,3-triazazulene were subsequently prepared and studied by T. Nozoe. For reference see T. Nozoe, "Non-Benzenoid Aromatic Compounds," ed. by D. Ginsburg, Interscience Publishers, Inc., New York, N. Y., 1959, Chapt. VII, and W. Keller-Schierlein and E. Heilbronner, *ibid.*, Chapt. VI. K. Hafner and M. Kreuder, *Angew. Chem.*, **73**, 657 (1961), have more recently prepared 5-azazulene.

(8) Structures of this type (including **9** and **12**) were first proposed in our laboratories during a discussion between A. G. A. and Allan G. Osborne and we acknowledge with thanks the contribution of the latter to the initial considerations which resulted in the present work.

(9) A. Albert, *ref. 5*, uses the terms  $\pi$ -deficient and  $\pi$ -excessive for the two types of simple heterocycles derived from benzenoid aromatic compounds to reflect the relative deficiency or excess, respectively, of  $\pi$ -electrons on the ring carbons. As these situations might not obtain in all cases of heterocycles derived from other aromatic systems, we prefer the use of the terms  $\pi$ -equivalent and  $\pi$ -excessive to describe only the relative numbers of  $\pi$ -electrons and ring atoms.

(10) (a) W. H. Perkin, Jr., and R. Robinson, *J. Chem. Soc.*, **115**, 921 (1919); W. O. Kermack, W. H. Perkin, Jr., and R. Robinson, *ibid.*, 1877 (1922); (b) See for example R. H. F. Manske and H. L. Holmes, "The Alkaloids," Vol. 11, Academic Press, Inc., New York, N. Y., 1952, Chapt. 13; E. Gellert, R. Hamet, and E. Schlittler, *Helv. Chim. Acta*, **34**, 642 (1951); R. A. Abramovitch, K. A. H. Adams, and A. D. Notation, *Can. J. Chem.*, **38**, 2152 (1960); L. Paoloni, *ibid.*, **40**, 1717 (1962).

(11) In recent years descriptions of a number of benz-derivatives of such structures have appeared. For leading references see D. Leaver, J. Smolinz, and W. H. Stafford, *J. Chem. Soc.*, 740 (1962); W. Treibs and J. Beger, *Ann.*, **662**, 192, 204, 212 (1962); W. Treibs, W. Schroth, H. Lichtmann, and G. Fischer, *Ann.*, **642**, 97 (1961); M. Los and W. H. Stafford, *J. Chem. Soc.*, 1680 (1959); W. Treibs and G. Kemper, *Ber.*, **92**, 601 (1959); G. V. Boyd, *J. Chem. Soc.*, 55 (1959); G. V. Boyd, *ibid.*, 1978 (1958); M. Los, J. P. Saxema, and W. H. Stafford, *Proc. Chem. Soc.*, 352 (1957).

Subsequent to the completion of our work R. Mayer and J. Franke, *Tetrahedron Letters* **9**, 289 (1961), reported the preparation of the isomeric cyclopenta[*b*]thiapyran.

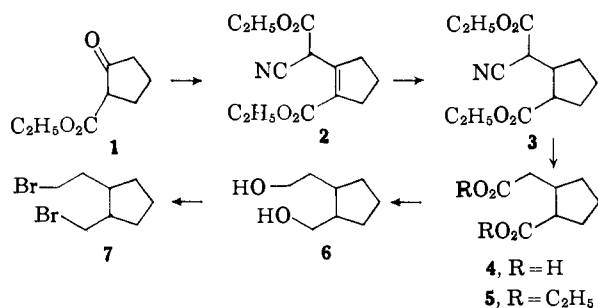


Figure 1.

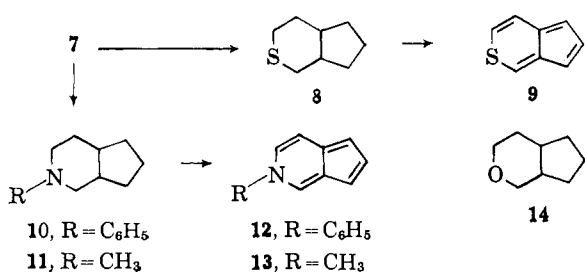


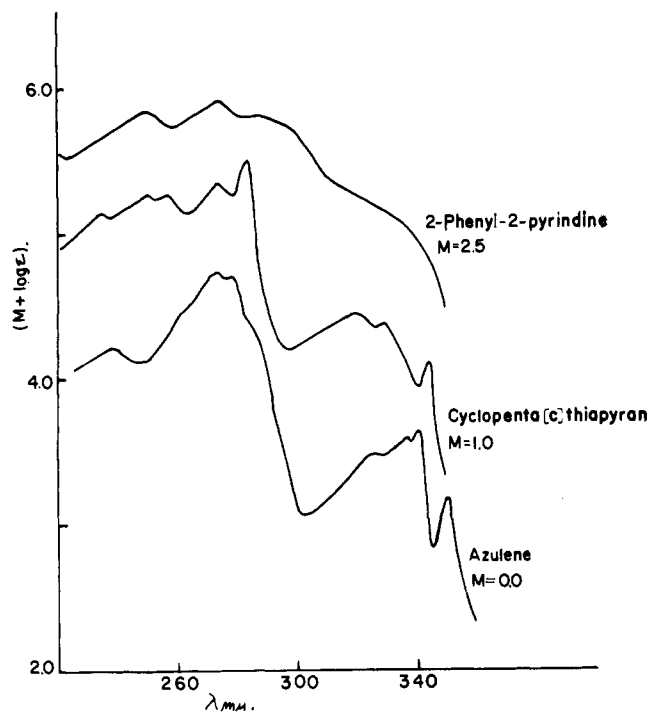
Figure 2.

Kon and Nanji,<sup>12</sup> or alternatively (62%) by the procedure of Cope, *et al.*<sup>13</sup> Reduction of 2 over Adams catalyst gave 3 (84–87%). Hydrolysis and decarboxylation of 3 by heating with concentrated hydrochloric acid<sup>14</sup> gave poor results, but the addition of sufficient acetic acid to form a homogeneous mixture effected the conversion to the diacid 4 in 91% yield. This acid could be reduced with lithium aluminum hydride to the diol 6 in 75% yield, but as the acid was somewhat difficult to purify and reduction of crude material gave quite impure diol, it was found advantageous to convert the crude diacid to the diester 5 which was obtained in 84% yield and was readily purified, and to carry out the reduction to 6 (81%) on the ester. Treatment of 6 with phosphorus tribromide and a small amount of pyridine, or with triphenyl phosphite and bromine,<sup>15</sup> gave variable yields of impure dibromide. When bromine was added slowly as a vapor (carried by dry nitrogen) to a suspension of the diol and phosphorus, however, yields of 56–72% of pure 7 were obtained. The immediate precursors, 6 and 7, of the three saturated heterocyclic molecules were thus at hand.

Reaction of 7 with sodium sulfide afforded octahydrocyclopenta[c]thiapyran (8) in 64% yield. Gas chromatography of the product gave two fractions, the infrared spectra of which were distinctly different in the fingerprint region. As the mixture gave the correct molecular weight and analysis for 8, it is postulated that the fractions represented *cis* and *trans* isomers. If the first fraction is the lower boiling and is, therefore, the *trans* isomer (by analogy to the decalins), the ratio of *trans* to *cis* obtained was *ca.* 2:1. 2-Phenyl- (10) (68%) and 2-methyloctahydro-2-pyridine (11) (72%) were formed from 7 plus aniline and methylamine, respectively. The molecular weights of 10 and 11 were determined spectroscopically on the picrates,<sup>16</sup> and the saturated ring structure of 10 was shown by *p*-nitrosation, cleavage of the nitrosoaniline derivative with base, and comparison of the melting point of the picrate of the perhydropyridine with that reported by

(12) G. R. Kon and H. R. Nanji, *J. Chem. Soc.*, 2429 (1932).(13) A. C. Cope, C. M. Hofmann, and C. W. Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).(14) R. P. Linstead and E. M. Meade, *J. Chem. Soc.*, 935 (1934).(15) D. G. Coe, S. R. Landauer, and H. N. Rydon, *ibid.*, 2281 (1954).

(16) A. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold, Ltd., London, 1954, p. 290.

Fig. 3.—The ultraviolet absorption spectra of 2-phenyl-2-pyridine, cyclopenta[c]thiapyran, and azulene in *n*-hexane.

Prelog and Metzler.<sup>17</sup> The preparation of octahydrocyclopenta[c]pyran (14) was carried out in 31% yield by the treatment of 6 with *p*-toluenesulfonyl chloride in pyridine.

The first method tried for the dehydrogenation of 8 to form 9 was heating with sulfur at 200°. Neither this nor treatment with chloranil at 80° gave any of the desired substance. A vapor phase process with a Cu–Cr–C catalyst at 300° gave a trace of orange-red material later shown to be 9, but the yield was extremely low. A similar method with a special Pd–C catalyst (described in the Experimental section), however, gave up to 32% of 9 as red plates, m.p. 89–90.5°, plus a small amount of material indicated by its ultraviolet spectrum to be thianaphthene (benzthiophene). The supposition that the latter was formed by thermal rearrangement of 9 in the dehydration furnace was supported by the finding that a 9.5% conversion of 9 to the same substance occurred when 9 was heated alone at 450° for 20 min. It was of interest that the freshly prepared Pd–C catalyst gave appreciably lower yields than catalyst which had been tested several times for the conversion of tetralin, decalin, or hydroazulenes to the corresponding aromatic compounds. The same catalyst and procedure gave a 25% yield of 12 as orange prisms, m.p. 98–110.5°, from 10. That no rearrangement of the molecular skeleton had occurred in this case was shown by the reconversion of 12 into 10 over a Rh–C catalyst with the theoretical uptake of hydrogen. Attempts to prepare 13 from 11 by the same process yielded a yellow-orange crystalline solid, m.p. >20°, which was very unstable to moisture and further purification or other studies were not carried out. The unstable yellow oil obtained from the dehydrogenation of 14 also was not obtained in pure form or studied further.

**Absorption Spectra.**—The absorption spectra of cyclopenta[c]thiapyran (9) showed a marked resemblance to those of azulene. In the ultraviolet region (Fig. 3) the general shapes and intensities of the two curves were very similar with the maxima for 9 shifted

(17) V. Prelog and O. Metzler, *Helv. Chim. Acta*, **29**, 1170 (1946).

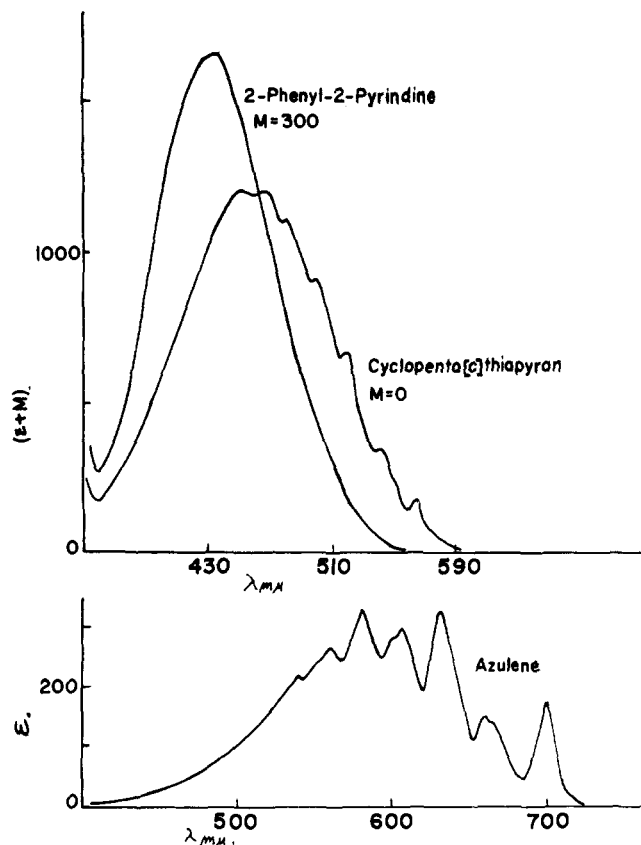


Fig. 4.—The visible absorption spectra of 2-phenyl-2-pyridine, cyclopenta[c]thiapyran, and azulene in *n*-hexane.

approximately  $10\text{ m}\mu$  to shorter wave lengths, and with the intensities for **9** a little lower. The relationship in the visible region was not as close. The spectrum for **9** (Fig. 4) was about four times more intense and at about  $100\text{ m}\mu$  shorter wave length, but displayed the same number (seven) of distinct maxima as the major peaks for azulene. Only a general similarity in the ultraviolet region was found for the absorption of 2-phenyl-2-pyridine (**12**) relative to those of **9** and azulene (Fig. 3), and although the visible spectra of **12** and **9** were alike in intensity, the former occurred at about  $30\text{ m}\mu$  lower wave length and showed only one maximum (Fig. 4).

It had been noted previously with azulene and a number of 1- and 1,3-substitution derivatives that an increase in solvent polarity resulted in a shift of the absorption maxima in the visible region, and to a lesser extent in the ultraviolet, to shorter wave lengths.<sup>18</sup> This property was observed for **9** also in that each of the maxima in the ultraviolet and visible spectra were found at  $0.2$  to  $2.1\text{ m}\mu$  less when recorded in alcohol than when in hexane. These data are evidence that **9** further resembles azulene in that the ground state of **9** is dipolar<sup>19</sup> and that there is a change in the electronic distribution in the molecule in the transition to the excited state<sup>20</sup> since the Franck-Condon principle would apply with respect to the orientation of the more polar solvent molecules (which stabilize the ground state) during photo-excitation. The existence and orientation of a dipolar ground state as shown (Fig. 5) is indicated also by the proton magnetic resonance spectrum

(18) (a) E. J. Cowles, *J. Am. Chem. Soc.*, **79**, 1093 (1957); (b) A. G. Anderson and B. M. Steckler, *ibid.*, **81**, 4941 (1959); (c) E. Heilbronner, "Non-benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 244.

(19) G. W. Wheland and D. E. Mann, *J. Chem. Phys.*, **17**, 264 (1949); reference 18b.

(20) R. Pariser, *ibid.*, **25**, 1112 (1956)

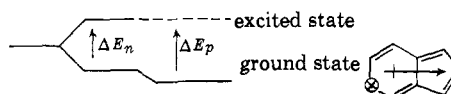


Fig. 5.—Schematic energy level diagram depicting relative excitation energies for cyclopenta[c]thiapyran (**9**) and 2-phenyl-2-pyridine (**12**) in nonpolar ( $\Delta E_n$ ) and polar ( $\Delta E_p$ ) solvents.

(*vide infra*). The data do not show whether the dipole in the excited state becomes very small (or zero), or is reversed (as in azulene) and the direction of the solvent effect on the excited state is therefore not known. A similar effect of solvent polarity on the ultraviolet and visible spectra of **12** was observed, and in this case the shifts of the maxima in comparing hexane and ethanol solutions ranged from  $0.3$  to  $8\text{ m}\mu$ .

The infrared spectrum of **9** was similar to that of thianaphthene in that the relative positions of the C-C bands for these compounds were  $6.39$  and  $6.34\text{ }\mu$ , and of the C-H bands were  $3.3$  and  $3.26\text{ }\mu$ , respectively. Also, the spectrum of **9** showed nine strong absorptions in the region  $6.25$ – $14\text{ }\mu$  and six of these occurred within  $20\text{ cm.}^{-1}$  of peaks of corresponding intensities in the infrared spectrum of azulene. Thus it seems that the change of mass (by six units) and of ring geometry represented by **9** as compared to azulene did not greatly alter the ring vibrations. The infrared spectrum of **12** showed C-C bands at  $6.20$  and  $6.26\text{ }\mu$  and C-H bands at  $3.32$  and  $3.38\text{ }\mu$ , and the remainder of the spectrum did not closely resemble those of **9** or azulene, as would be expected because of the presence of the phenyl ring.

**N.m.r. Spectra.**—The proton magnetic resonance spectrum of **9** (Fig. 6) was found to be consistent with

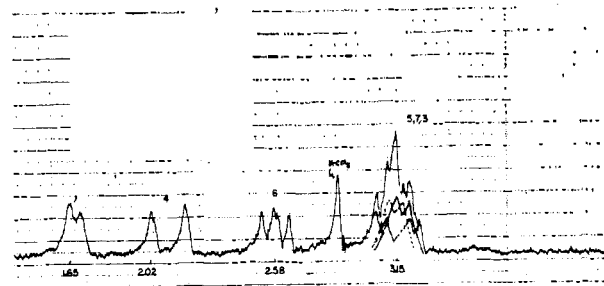


Fig. 6.—The n.m.r. spectrum of cyclopenta[c]thiapyran relative to tetramethylsilane (internal).

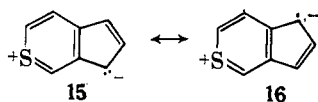
the structure given. The doublet of unit intensity near  $1.65\text{ }\tau$  was assigned to the 1-proton and the spin-spin splitting ( $J \approx 2.9\text{ c.p.s.}$ ) of this was attributed to interaction with the 3-proton.<sup>21</sup> The next two peaks upfield (one at  $2.02\text{ }\tau$ ) have a total area corresponding to one hydrogen. This doublet ( $J \approx 9.2\text{ c.p.s.}$ ) is assigned to the 4-hydrogen.<sup>22</sup> Discernible in each of the peaks for the 1- and 4-hydrogens was a very small secondary splitting corresponding to  $J \approx 0.6\text{ c.p.s.}$  which possibly represents the coupling between these two hydrogens. The group of unity intensity near  $2.58\text{ }\tau$  was attributed to the 6-hydrogen, the only one which can couple with two hydrogens on adjacent carbons. This portion corresponds to that for an  $AB_2$  system wherein the central two peaks of the quartet for A are partially superimposed.<sup>23</sup> The absorption centered at

(21) H. M. McConnell, *J. Mol. Spectry.*, **1**, 11 (1957); P. L. Corio and I. Weinberg, *J. Chem. Phys.*, **31**, 569 (1959).

(22) The 1- and 4-hydrogens in **9** occupy positions corresponding to those of the analogous 4- and 8-positions in azulene, and the resonance absorption peaks assigned to the latter are the ones at lowest field ( $1.84\text{ }\tau$ ); cf. S. S. Danyluk and W. G. Schneider, *J. Am. Chem. Soc.*, **82**, 997 (1960); W. G. Schneider, H. J. Bernstein, and J. A. Pople, *ibid.*, **80**, 3497 (1958); L. L. Replogle, Ph.D. Thesis, University of Washington, 1960.

(23) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp. 127–128.

*ca.* 3.15  $\tau$  had a relative intensity which accounted for the remaining 3-, 5-, and 7-hydrogens. Through the use of the  $J_{13}$  and  $J_{14}$  values, and with the assumption that the screening of the 5- and 7-hydrogens would differ slightly because of the nonidentity of these positions, it was possible to construct appropriate curves representing the absorptions of the individual hydrogens such that the sum of their intensities closely approximated the observed spectrum. These curves are illustrated in Fig. 6. The relative chemical shifts for the hydrogens in cyclopenta[c]thiapyran, and their similarity to the corresponding hydrogens in azulene suggest that there is a charge displacement in the ground state of the molecule with a dipole vector in the direction of the five-membered ring. This interpretation is consistent with the observed absorption shift in the ultraviolet and visible regions with a change in solvent polarity discussed earlier. The fact that absorptions for the 5-, 6-, and 7-hydrogens of the thiapyran are found further upfield than those of the 1-, 2-, and 3-hydrogens of azulene provides an indication that charge separated structures (*e.g.*, 15 and 16) contribute relatively more to the ground state of thiapyran than for azulene.



The proton magnetic resonance spectrum of 2-phenyl-2-pyrindine (Fig. 7) was complicated by absorptions of the phenyl hydrogens. The singlet at 1.83  $\tau$  most probably arises from the 1-hydrogen. It is of interest that, in contrast with the observation for 9, no significant splitting of this (with the 3-hydrogen) occurred. In that the absorptions expected for the 4- and 6-hydrogens, and apparently in part for others as well, were obscured by the chloroform and the large phenyl peaks, no further assignments were made. The location of the absorption for the 1-hydrogen at higher field than found for 9 (which would be the case even if the proposed assignment were incorrect) again points to an enhanced contribution of charge separated structures (analogous to 15 and 16) of the phenylpyrindine to the ground state.

Subsequent to the completion of these studies Hafner<sup>24</sup> reported (but gave no experimental data) a synthesis of 9, 12, and 13, which appears to be superior in that no dehydrogenation step is involved and the aromatic structures are formed directly in good yield.

### Experimental<sup>25</sup>

**Ethyl Cyclopentanone-2-carboxylate (1).** **Method A.**—Diethyl adipate<sup>26a</sup> was treated as described by Pinkney<sup>26b</sup> and yielded 194 g. (75%) of the desired product, b.p. 108–111° at 15 mm. (lit.<sup>26b</sup> b.p. 108–111° at 15 mm.).

**Method B.**—The procedure of method A was followed except that the "molecular sodium" was replaced by 104 g. (2.13 moles) of a 48% dispersion of sodium hydride in mineral oil for the cyclization of 303 g. (1.5 moles) of diethyl adipate. The

(24) K. Hafner, K. H. Hafner, C. König, M. Kreider, G. Ploss, E. Sturm, and K. H. Vögel, *Angew. Chem.*, **75**, 35 (1963).

(25) Melting points are corrected and boiling points are uncorrected unless otherwise indicated. Infrared spectra were recorded with a Perkin-Elmer Model 21 spectrophotometer with a sodium chloride or calcium fluoride prism. Ultraviolet and visible spectra were taken on a Cary Model 11S or Model 14 spectrophotometer. Nuclear magnetic resonance spectra were recorded by Mr. B. J. Nist on a 60-cycle Varian Associates n.m.r. spectrophotometer, Model V-K3507. Mass spectra were taken by Mr. B. J. Nist on a Type 21-103 Consolidated Engineering Corp. mass spectrometer. Vapor phase chromatograms were run on an Aerograph Model A-90-C instrument. Microanalyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford, England; Dr. Alfred Bernhardt, Max Planck Institute, Mulheim, Germany; or by B. J. Nist, L. Ho, A. Kuo, and C. H. Ludwig.

(26) (a) P. S. Pinkney, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 116; (b) P. S. Pinkney, *ibid.*, p. 119.

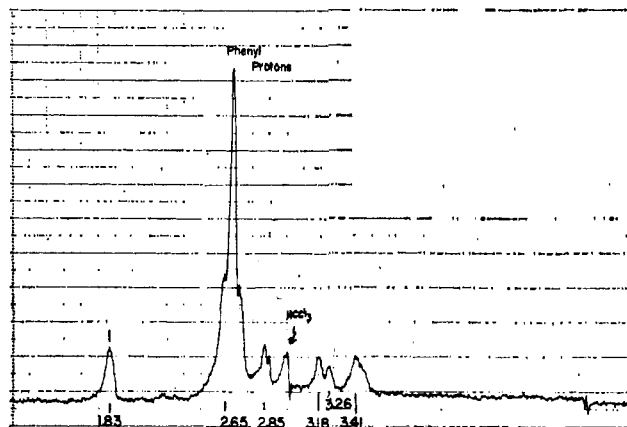


Fig. 7.—The n.m.r. spectrum of 2-phenyl-2-pyrindine relative to tetramethylsilane (internal).

reaction was quite vigorous and moderation by cooling in an ice bath was necessary. The yield was 207 g. (89%) of material which distilled at 106–110° (15 mm.).<sup>26b</sup>

**Ethyl 2-Carboethoxycyclopenten-1-ylcyanoacetate (2).** **Method A.**—The condensation of ethyl cyclopentanone-2-carboxylate (168 g., 0.99 mole) with ethyl cyanoacetate (114 g., 0.99 mole) was carried out under a nitrogen atmosphere by the method of Kon and Nanji.<sup>12</sup> The yield of product boiling at 149–150° at 1.2 mm.,  $n_D^{20}$  1.4825 (lit.<sup>12</sup> b.p. 188° at 16 mm.,  $n_D^{20}$  1.4838), was 182.8 g. (72%).

**Method B.**—In accordance with the general procedure described by Cope, *et al.*,<sup>13</sup> a solution of ethyl cyanoacetate (56.5 g., 0.5 mole), ethyl cyclopentanone-2-carboxylate (85.8 g., 0.55 mole), and ammonium acetate (3.85 g., 0.05 mole) in 6 ml. of acetic acid and 50 ml. of benzene was heated under reflux in a modified Dean-Stark phase separator apparatus until separation of an aqueous phase ceased (3 days). The cooled reaction mixture was extracted with several portions of water and the aqueous extracts were washed with benzene. The combined benzene extracts and original organic layer were dried over magnesium sulfate and the solvent was then removed under pressure. Distillation of the red residual material gave 78.3 g. (62.4%) of product, b.p. 150–154° at 1 mm.<sup>12</sup>

**Ethyl 2-Carboethoxycyclopentanylcyanacetate (3).**—A solution of ethyl 2-carboethoxycyclopenten-1-ylcyanoacetate (50.2 g., 0.2 mole) in 250 ml. of absolute ethanol was treated with hydrogen at *ca.* 3 atm. pressure over a platinum oxide catalyst in a Parr apparatus until 3–5% more than the theoretical amount of hydrogen was absorbed. The catalyst was separated, the filtrate was concentrated under reduced pressure, and the residue was distilled. The product (43.7 g., 86.5%) was collected as the fraction boiling at 154–158° (3.3–3.5 mm.).  $n_D^{20}$  1.4580 (lit.<sup>14</sup> b.p. 158–163° at 5 mm.).

**Cyclopentane-1-carboxy-2-acetic Acid (4).**—A solution of ethyl 2-carboethoxycyclopentanylcyanacetate (9.7 g., 0.038 mole) in 29 ml. of concentrated hydrochloric acid and enough glacial acetic acid (*ca.* 20 ml.) to form a homogeneous solution was heated under reflux for 30 hr. A small amount of insoluble material was removed by filtration, the filtrate was evaporated to dryness under reduced pressure, and the organic acid portion of the residue was separated from the ammonium chloride by extraction with ether. The solvent was removed under reduced pressure from the dried (magnesium sulfate) ethereal solution, the viscous brown residue was dissolved in the minimum amount of water, and the aqueous solution thus formed was saturated with hydrogen chloride. After a period of 24 hr. at refrigerator temperature, the product which had precipitated was collected. The yield of acid, m.p. 87–89° (reported<sup>14</sup> 89°), was 6 g. (91%). The infrared spectrum of a Nujol mull was recorded.

**$\beta$ -(2-Hydroxymethylcyclopentanyl)-ethyl Alcohol (6).** **Method A.**—A solution of ethyl 2-carboethoxycyclopentanylcyanacetate (375 g., 1.48 moles) in 1121 ml. of hydrochloric acid and 774 ml. of acetic acid was heated under reflux for 36 hr. The mixture was then evaporated to dryness (reduced pressure), the residue extracted with ether, and the solvent was then removed (reduced pressure) from the dried (magnesium sulfate) ethereal solution. A solution of the viscous brown residue in 1100 ml. of ethanol, 950 ml. of benzene, and 20 ml. of sulfuric acid was heated under reflux for 24 hr. After the addition of 500 ml. of benzene, the cooled reaction mixture was washed successively with water, 10% aqueous sodium bicarbonate, and then water. The residue from the dried (sodium sulfate) organic solution was distilled and afforded 283.4 g. (84%) of product collected at 98–100° (1.1 mm.)  $n_D^{20}$  1.4469, which was presumed to be ethyl 2-carboethoxycyclopentanylcyanacetate (5). The infrared spectrum (neat) was consistent with this structure.

A solution of the product (128 g., 0.56 mole) in 250 ml. of anhydrous ether was added dropwise with stirring to a suspension of lithium aluminum hydride (28 g., 0.74 mole) in 700 ml. of anhydrous ether. The mixture was then heated under reflux for 5 hr., the excess lithium aluminum hydride was destroyed by the cautious addition of ethyl acetate, and the salts formed were hydrolyzed with water. The remaining solid was triturated with 400 ml. of ether and then dissolved in 10% sulfuric acid. The acidic solution was extracted with two 250 ml. portions of ether. The combined extracts were washed successively with water, 10% aqueous sodium bicarbonate, and water and then dried (magnesium sulfate) and concentrated under reduced pressure. Distillation of the residue gave 60 g. (81%) of **6**, b.p. 125–129° at 0.6–0.8 mm.,  $n_D^{25}$  1.4846. The infrared spectrum was recorded.

The product was analyzed as the diurethan which crystallized from carbon tetrachloride as colorless plates, m.p. 106–107°.

*Anal.* Calcd. for  $C_{22}H_{28}N_2O_4$ : C, 69.08; H, 6.85. Found: C, 69.36; H, 6.67.

**Method B.**—To a cold (0°) suspension of lithium aluminum hydride (2 g., 53 mmoles) in 50 ml. of anhydrous ether was added dropwise with stirring a solution of 4 g. (23 mmoles) of cyclopentane-1-carboxy-2-acetic acid in 80 ml. of anhydrous ether. The reaction mixture was allowed to come to room temperature, then cooled to 0° and the excess lithium aluminum hydride destroyed by the cautious addition of water. The metallo-organic complex was decomposed with sulfuric acid (10%) and the aqueous solution was extracted with ether. The ether extracts were washed with water and dilute sodium bicarbonate solution, dried over magnesium sulfate, and the solvent was then removed under reduced pressure. Distillation of the colorless residue gave 2.4 g. (75%) of product, b.p. 125–130° at 0.2 mm., which was identical (infrared spectrum) with that obtained in A.

**Method C.**—A solution of 5.5 g. (32 mmoles) of cyclopentane-1-carboxy-2-acetic acid in 35 ml. of ethanol, 25 ml. of benzene, and 0.5 ml. of sulfuric acid was heated with sulfur in a Dean-Stark phase separator until no more aqueous phase separated (12 hr.). After the addition of 25 ml. of benzene, the cooled reaction mixture was washed successively with water, sodium bicarbonate (10%), and a saturated solution of sodium chloride. The solvent was removed from the dried (magnesium sulfate) organic layer under reduced pressure, and distillation of the residue yielded 6.3 g. (86%) of product, b.p. 88–89° at 0.2 mm.,  $n_D^{25}$  1.4477, identical (infrared spectrum) with the intermediate obtained in method A and presumed to be ethyl 2-carbethoxycyclopentylacetate (**5**). A solution of this material in 63 ml. of anhydrous ether was treated with 2.1 g. (56 mmoles) of lithium aluminum hydride as described for the reduction of cyclopentane-1-carboxy-2-acetic acid in method B. Distillation of the crude product afforded 3.3 g. (85%) of the diol **6**, b.p. 125–130° at 0.2 mm., identical (infrared spectrum) with the products from methods A and B.

**$\beta$ -(2-Bromomethylcyclopentanyl)-ethyl Bromide (7).**—A slow stream of dry nitrogen was passed over the surface of 36 g. (0.23 mole) of boiling bromine and the bromine-nitrogen vapor was conducted through a glass tube into a suspension of 2.86 g. (23.3 mmoles) of phosphorus and 30 g. (0.21 mole) of  $\beta$ -(2-hydroxymethylcyclopentanyl)-ethyl alcohol heated to 110°. When the addition of bromine was completed (2.5 hr.) the mixture was heated at 125° for 45 min. Water and *n*-hexane were added to the cooled black, gelatinous slurry and the whole was filtered with suction through sintered glass. The separated hexane layer was then extracted with water until the aqueous extracts were neutral to litmus, and the solvent was removed from the dried (sodium sulfate) solution under reduced pressure. Distillation of the residue gave 36.5 g. (63%) of the desired product (**7**), b.p. 85–89° at 0.4–0.6 mm.,  $n_D^{25}$  1.5290. The infrared spectrum was recorded. The yields in a number of runs ranged from 56–72%.

*Anal.* Calcd. for  $C_8H_{14}Br_2$ : C, 35.58; H, 5.23; Br, 59.19. Found: C, 35.76; H, 5.24; Br, 58.71.

**Octahydrocyclopenta[c]thiapyran (8).**—A solution of 50 g. (0.185 mole) of  $\beta$ -(2-bromomethylcyclopentanyl)-ethyl bromide in 74 ml. of absolute ethanol, and a solution of 44.4 g. (0.19 mole) of sodium sulfide monohydrate in 74 ml. of absolute ethanol and 37 ml. of water were added concurrently dropwise to 19 ml. of stirred, refluxing 95% ethanol. After one-half of each solution had been added (1 hr.) the mixture was stirred and heated under reflux for 5 hr. The addition of reactants was then resumed and completed in 1 hr. The mixture was again heated under reflux with stirring for 3 hr. and then distilled. The first 100 ml. of distillate was collected, diluted with 4 volumes of water, and the whole was extracted with *n*-hexane. The remaining reaction mixture was diluted with water and steam distilled until no oily droplets were present in the distillate (which amounted to ca. 1 l.). The distillate was extracted with *n*-hexane, these extracts were combined with those from the first distillate, and the solvent was removed from the dried (potassium hydroxide) solution by

flash distillation. The residue was dissolved in 3 volumes of *n*-pentane and the solution was allowed to stand over sodium wire for 6 hr. Removal of the solvent (reduced pressure) from the separated solution and distillation of the residue gave 16.9 g. (64%) of product **8** as a colorless liquid, b.p. 107–108° at 31 mm.;  $n_D^{25}$  1.5210. The infrared spectrum was recorded. A mass spectrometric determination of the molecular weight (scan of 28–180 *m/e* at 70 v.) gave a value of 142 (calcd. for  $C_8H_{14}S$ : 142).

*Anal.* Calcd. for  $C_8H_{14}S$ : C, 67.54; H, 9.92. Found: C, 67.74; H, 9.68.

**2-Phenylcyclooctahydro-2-pyridine (10).**—A slurry of 16 g. (59 mmoles) of  $\beta$ -(2-bromomethylcyclopentanyl)-ethyl bromide, 6.24 g. (69 mmoles) of aniline, and 10.05 g. (95 mmoles) of sodium carbonate was heated (oil bath) under a nitrogen atmosphere until a vigorous evolution of carbon dioxide began (ca. 135°). The bath was removed, and then replaced after the gas evolution had subsided and the mixture was maintained at 130° for an additional 30 min. Then 0.9 g. of aniline was added and the heating was continued for 2 hr. Benzene was added to the cooled mixture and the solution was filtered. The salts on the filter were washed with benzene until they were colorless. The filtrate was concentrated by flash distillation (reduced pressure) and distillation of the residue gave 8.96 g. (68%) of **10** as a colorless liquid, b.p. 125–127° at 1.3–1.4 mm.,  $n_D^{25}$  1.5655. The infrared spectrum was recorded.

*Anal.* Calcd. for  $C_{14}H_{19}N$ : C, 83.53; H, 9.51; N, 6.96. Found: C, 83.51; H, 9.63; N, 7.27.

A picrate was crystallized from 95% ethanol and after two recrystallizations melted at 158.5–161.5°. A spectroscopic determination of the molecular weight<sup>16</sup> gave a value of 444 (calcd. for  $C_{20}H_{22}N_4O_7$ : 430).

**2-H-Octahydro-2-pyridine.**—A solution of 0.37 g. (5.4 mmoles) of sodium nitrite in 2 ml. of water was added slowly to a stirred mixture of 1 g. (5.2 mmoles) of 2-phenylcyclooctahydro-2-pyridine, 2.5 ml. of 12 *N* hydrochloric acid, and 2 g. of ice. The solution was maintained at 0° for 1 hr. and then warmed to room temperature (30 min.). Most of the acid was removed under reduced pressure and the residue was neutralized with sodium carbonate. A green oil phase was formed and a portion (0.8 g., ca. 3.4 mmoles) of this crude material (presumed to be largely the *p*-nitroso product) was added to a solution of 3.12 g. (30 mmoles) of sodium bisulfite in 26 ml. of water. The mixture was stirred at room temperature for 1 hr. and then heated for 30 min. on a steam bath. After the addition of 2 g. (50 mmoles) of sodium hydroxide and 10 ml. of water, the cooled solution was stirred for an additional hour. The mixture was then extracted with ether. The ether layer was dried, the solvent was removed under reduced pressure, and the residue was fractionated in a molecular still. The fraction collected at a bath temperature of 83–89° at 25 mm. (lit.<sup>17</sup> 80° at 11 mm.) amounted to 69 mg. (20%) of product which showed a strong N–H absorption at 3200  $cm^{-1}$ .

A picrate was obtained from 95% ethanol and after two recrystallizations melted at 142.5–143.3° (lit.<sup>17</sup> 143–144° for picrate of *cis*-2H-octahydro-2-pyridine). A spectroscopic determination of the molecular weight<sup>16</sup> gave a value of 362 (calcd. for  $C_{14}H_{18}N_4O_7$ : 354).

**2-Methylcyclooctahydro-2-pyridine (11).**—A solution of 30 g. (0.11 mole) of  $\beta$ -(2-bromomethylcyclopentanyl)-ethyl bromide, 33 ml. of 40% aqueous methylamine (0.13 mole), and 180 ml. of methanol was shaken on a Parr apparatus for 3 days. A second 10-ml. portion of 40% aqueous methylamine was added and the mixture was again shaken for 2 days. Most of the methanol and methylamine were removed by distillation and the residue was diluted with aqueous sodium hydroxide and then extracted with ether. The solvent was removed from the dried (sodium sulfate) organic layer under reduced pressure and distillation of the residue gave 10.1 g. (72%) of product **11** as a colorless liquid, b.p. 166–172° at 760 mm.,  $n_D^{25}$  1.4708. The infrared spectrum was recorded.

*Anal.* Calcd. for  $C_9H_{17}N$ : C, 77.63; H, 12.31; N, 10.06. Found: C, 77.43; H, 12.23; N, 9.87.

A picrate was obtained from 95% ethanol and after two recrystallizations melted at 212.5–213.5°. A spectroscopic molecular weight determination<sup>16</sup> gave a value of 375 (calcd. for  $C_{15}H_{20}N_4O_7$ : 368).

**Octahydrocyclopenta[c]pyran (14).**—A solution of 7.15 g. (38 mmoles) of *p*-toluenesulfonyl chloride in 20 ml. of pyridine was slowly added (1 hr.) to a refluxing solution of 0.5 g. (3.5 mmoles) of  $\beta$ -(2-hydroxymethylcyclopentanyl)-ethyl alcohol in 20 ml. of pyridine. After 3 hr. under reflux the solution was cooled, diluted with water, and extracted with *n*-hexane. The combined hexane extracts were washed with 0.5 *N* hydrochloric acid, then with water, and then were dried over sodium sulfate. Most of the solvent was removed by flash distillation and then sodium wire was added. Distillation of the decantate from the sodium and sodium alcoholate gave 1.33 g. (31%) of product **14** as a colorless liquid, b.p. 167–169° at 760 mm.,  $n_D^{25}$  1.4680. The infrared spectrum was recorded.

*Anal.* Calcd. for  $C_8H_{14}O$ : C, 76.14; H, 11.18. Found: C, 76.39; H, 11.14.

**Dehydrogenation Catalyst.**—The procedure used was a modification of that of Kovats, Plattner, and Gunthard.<sup>27</sup> Bone charcoal (40 g. of *ca.* 10 mesh) was purified by warming with 10% nitric acid, washing with distilled water until the washings were neutral, and then drying under reduced pressure. The charcoal was then placed in a 300-ml. round-bottomed flask and degassed by continuous pumping at 0.1 mm. for 24 hr. Hydrogen was admitted to the flask and, in such a manner as to avoid the entry of air, a solution of 3 g. of palladium chloride in 4 ml. of concentrated hydrochloric acid and 100 ml. of cool but freshly boiled distilled water was added. The reaction of the charcoal with the solution was somewhat exothermic. After a period of 10 min. the solution was carefully decanted into a clean flask which was stoppered and set aside. The flask containing the charcoal was then evacuated until the charcoal was dry (or nearly so) and then hydrogen was again admitted. The treatment with the acidic palladium solution, decantation, evacuation, and admission of hydrogen were repeated once more, and then a third time through the decantation step. Freshly boiled distilled water (*ca.* 100 ml.) was added to the Pd-C (air excluded), and air-free steam generated from distilled water was passed into the mixture in the manner of a steam distillation for 18 hr. The water was then decanted and the catalyst was treated with 90 ml. of 1 *N* ammonium hydroxide (prepared from boiled distilled water and reagent grade concentrated ammonium hydroxide) for 20 min. This solution was then decanted and the catalyst was washed continuously with occasional *gentle* stirring (a stirring blade tended to pulverize the catalyst) for not less than 8 hr. with a flow of not less than 20 l. of air-free distilled water. The washed catalyst was collected by filtration (but not sucked dry), dried in a flask at 100° *ca.* 10 mm., and then at 0.1 mm. for 24 hr. Oxygen-free nitrogen was admitted to relieve the vacuum and the catalyst was stored in this atmosphere and never exposed to oxygen until spent.

It was found that yields of dehydrogenation products varied appreciably with the batch and the history of the catalyst. In general the fresh catalyst was excellent for the dehydrogenation of decalin or tetralin but fair to poor for the heterocyclic azulene analogs. The ability to dehydrogenate the latter improved markedly with use, however, and after this was discovered several runs totaling about 6 g. of decalin, tetralin, or, better, a hydroazulene, were made on each new batch of catalyst before exposure to any of the heterocyclic compounds.

**Dehydrogenation Apparatus.**—A Vycor tube 44 cm. long and 13 mm. i.d. having 19/38 standard taper joints at each end (male at bottom, female at top) and a few indentations above the bottom joint was wrapped with asbestos paper, then nichrome wire, then asbestos gauze. A thermocouple was placed between the asbestos paper and the tube and midway between turns of the nichrome wire at approximately the midpoint of the catalyst bed (about 14 cm. from the top of the bottom joint). The lower 8 cm. of the tube was filled with Pyrex glass wool and this supported a 12 cm. layer of the Pd-C catalyst (described above) which was kept under an inert nitrogen atmosphere at all times. A short inlet tube which was connected by standard taper joints to the top of the furnace tube and to a small flask which contained the material to be dehydrogenated was also wrapped with asbestos and nichrome wire. The sample flask was constructed such that a controlled stream of carrier gas could be admitted through a small tube and directed against the surface of the sample, and the mixture of nitrogen and sample vapor conducted directly into the inlet tube of the furnace. The lower end of the furnace tube was connected to two traps (in series) which were cooled by Dry Ice-acetone baths. The nichrome heating wires were connected to a Variac. It was ascertained that the temperature measured by the thermocouple corresponded to within 20° to the temperature in the catalyst bed over the range of nitrogen flow rates that were actually used.

**General Dehydrogenation Procedure.**—The carrier gas was nitrogen which was purified by passage through a series of cold

(Dry Ice-acetone) traps, then a series of Drierite and barium oxide columns, and finally through a 3 × 50 cm. column of copper wire (generated by the reduction with hydrogen of *ca.* 1 × 5 mm. lengths of pure copper oxide) heated at *ca.* 500°. The rate of evaporation of the sample was controlled by the rate of nitrogen flow and warming (or cooling) the sample flask in an appropriate bath. The furnace and catalyst were preheated under pure nitrogen to 350–360° before any sample was introduced.

**Cyclopenta[c]thiapyran (9).**—By means of the procedure described above 4 g. (28 mmoles) of octahydrocyclopenta[c]thiapyran was passed over the Pd-C catalyst (see above). The flow rate of nitrogen was 200–225 ml./min., the column was maintained at 340–360°, the sample flask was kept at room temperature (water bath), and the sample was evaporated into the nitrogen stream over a period of 75 hr. A dense concentration of red crystalline material (m.p. *ca.* 25°) formed at the top of the first cold trap and below this a lower melting fraction solidified. Chromatography of the latter fraction on alumina with *n*-pentane as the eluent afforded a small amount of a substance which was indicated to be thianaphthene by its ultraviolet spectrum.<sup>28,29</sup> Both red chromatograph fractions were sensitive to chromatography on alumina, Florisil, or silica gel. Purification of the higher melting fraction was accomplished by two recrystallizations from *n*-pentane and gave 1.2 g. (32%) of product 9 as red plates, m.p. 89–90.5°, which sublimed readily at 70° and 60 mm. A *n*-hexane solution showed  $\lambda_{max}$  in  $m\mu$  (log  $\epsilon$ ) at 234 (4.15), 249 (4.28), 257 (4.28), 273 (4.34), 283 (4.52), 321 (3.45), 329 (3.38), 344 (3.11), 465 (3.08), 483 (3.04), 500 (2.97), 520 (2.54), 542 (2.54), and 565 (2.26). The infrared spectrum (carbon tetrachloride) showed  $\lambda_{max}$  in  $\mu$  at 3.33(w), 6.40(s), 6.73(w), 7.02-(m), 7.30(s), 8.06(w), 8.24(s), 8.92(s), 9.40(s), 11.45(s), 11.85-(s), and 13.88(s). A mass spectrometer scan of 98–150 *m/e* at 70 v. gave a molecular weight value of 134 (calcd. for  $C_8H_8S$ : 134). It was found that the major portion of unconverted starting material could be recovered from the liquid portion of the products and the filtrates.

*Anal.* Calcd. for  $C_8H_8S$ : C, 71.60; H, 4.51. Found: C, 71.89; H, 4.45.

**2-Phenyl-2-pyridine (12).**—In the manner described for the preparation of cyclopenta[c]thiapyran except that the nitrogen flow rate was 250–260 ml./min., the column was maintained at 355–365°, and the sample flask was kept at 126–148°, a total of 2.5 g. (12 mmoles) of 2-phenyloctahydro-2-pyridine was introduced into the column over a period of 41 hr. The crude dehydrogenation product was a mixture of an orange oil and an orange solid (which decomposed quite rapidly on alumina or silica gel to give a number of highly colored substances which were not studied). Dissolution of the crude material in *n*-hexane, crystallization, and then recrystallization from this solvent gave 0.7 g. (29%) of product 12 as yellow-orange prisms, m.p. 98.5–100.5°, which sublimed at 90° and 0.5 mm. A *n*-hexane solution showed  $\lambda_{max}$  in  $m\mu$  (log  $\epsilon$ ) at 251 (4.34), 274 (4.38), 286 (4.30), and 432 (3.30). The infrared spectrum (chloroform) showed  $\lambda_{max}$  in  $\mu$  at 3.39(w), 6.20(s), 6.26(s), 6.70(s), 7.24(s), 7.45(s), 7.65(s), 7.99(m), 8.79(s), 9.44(m), 9.67(m), 9.85(w), 9.98(m), 11.28(m), 11.70(w), and 14.40(m).

*Anal.* Calcd. for  $C_{14}H_{11}N$ : C, 87.01; H, 5.74; N, 7.25. Found: C, 86.92; H, 5.82; N, 7.13.

Hydrogenation of a solution of 8.4 mg. (0.044 mmole) of 12 in 10 ml. of ethanol in the presence of 36 mg. of a 5% Rh-C catalyst gave a rapid uptake of 3.89 ml. (0.17 mmole, 97% of theory) of hydrogen and yielded 2-phenyloctahydro-2-pyridine (10), identical (ultraviolet and infrared spectra) with an authentic sample.

(28) M. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951.

(29) When a thick-walled tube containing 16.2 mg. of cyclopenta[c]thiapyran was evacuated to a pressure of 1 mm. and heated for 40 min. at *ca.* 500° there was obtained (by chromatography of the concentrate of *n*-hexane extracts over alumina) a substance having an ultraviolet spectrum identical with that reported (ref. 28) for thianaphthene. The yield, based on the reported  $\epsilon$  for thianaphthene, was 9.5%.

(27) E. Kovats, Pl. A. Plattner, and Hs. H. Gunthard, *Helv. Chim. Acta*, **37**, 983 (1954).