

Anal. Calcd for $C_{22}H_{23}N_2O_7$: C, 61.10; H, 6.53; N, 6.48. Found: C, 61.04; H, 6.79; N, 6.65.

1,2,5,6-Tetrahydro-12H-12b-phenylpyrrolo[1',2':1,2]azepino[3,4-b]indole (Xb).—A solution of 3.67 g of 1,2,5,6-tetrahydro-3-oxo-12H-12b-phenylpyrrolo[1',2':1,2]azepino[3,4-b]indole in 100 ml of tetrahydrofuran was added dropwise to a slurry of 4.00 g of lithium aluminum hydride in 250 ml of tetrahydrofuran and treated as above. Recrystallization of the residue from absolute ethanol gave 3.13 g of white crystals melting at 105–106°.

Anal. Calcd for $C_{21}H_{22}N_2 \cdot 0.5H_2O$: C, 81.04; H, 7.45; N, 9.00. Found: C, 81.43; H, 7.31; N, 8.38.

The amine has infrared absorptions (Nujol mull) at 3500 (NH and OH) and 760, 741, and 701 cm^{-1} (aromatic); ultraviolet absorptions, λ_{max}^{MeOH} $m\mu$ (log ϵ), 226 (4.51), 283 (3.84), 292 (3.81); λ_{min} $m\mu$ (log ϵ), 255 (3.55).

The picrate was prepared in absolute ethanol and when recrystallized from ethanol gave yellow prisms melting at 205–208° dec.

Anal. Calcd for $C_{27}H_{25}N_5O_7$: C, 61.01; H, 4.74; N, 13.18. Found: C, 61.24; H, 4.92; N, 12.92.

Registry No.—Ia, 14161-47-8; Ib, 14161-48-9; Ic, 14161-49-0; II, 14271-21-7; III, 14161-50-3; IV, 14161-51-4; V, 14161-52-5; VI, 14161-53-6; VII, 14161-54-7; VIIIa, 14161-55-8; VIIIb, 14161-56-9; IXa, 14161-57-0; IXb, 14161-58-1; Xa, 14271-22-8; Xa-picrate, 14161-59-2; Xb, 14161-60-5; Xb-citrate, 14319-48-3.

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Indolothiapyrylium Compounds. III. Pseudoazulenic Thiapyrano[4,3-b]indoles^{1,2}

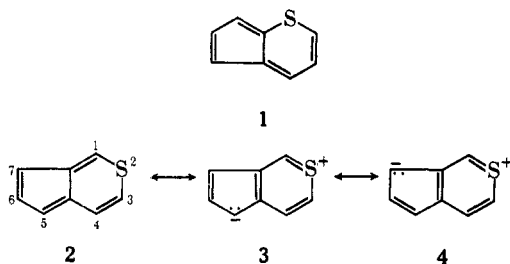
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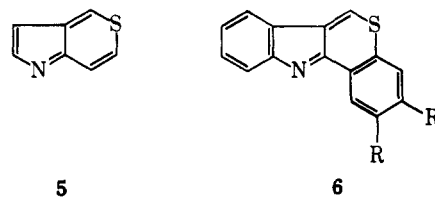
Dehydrogenation of 1,3,4,5-tetrahydrothiapyrano[4,3-b]indoles (**8a–h**) with chloranil or dicyanodichloroquinone gave 2–37% yields of the corresponding yellow-orange thiapyrano[4,3-b]indoles (**9a–h**), which exemplify a new heteroaromatic ring system iso- π -electronic with benz[*a*]azulene. The nmr spectra of these pseudoazulenes (**9**) show two strongly deshielded protons characteristic of H-1 ($\delta = 8.63$ – 8.95 ppm) and H-4 ($\delta = 8.10$ – 8.27 ppm) of the thiapyran ring. HMO calculations on the parent compound (**9a**) clearly show a displacement of electrons from sulfur toward nitrogen, indicating pronounced thiapyrylium character of the sulfur-containing ring.

Although Mayer's⁴ expectation of aromaticity of cyclopenta[*b*]thiapyran (**1**) was not fully realized,⁵ the isomeric cyclopenta[*c*]thiapyran (**2**) has been shown to be a reasonably stable, π -excessive pseudoazulene.^{6,7}



In which dipolar canonical forms such as **3** and **4** contribute significantly to the ground-state structure.⁶ Since Hückel molecular orbital (HMO) calculations⁵ on **2** corroborate the high, and nearly equal, electron densities (*ca.* 1.17) at positions 5 and 7, it seemed to us likely that replacement of the methine carbon at either of these positions by a more electronegative heteroelement, such as nitrogen, would increase the contributions of the dipolar forms in which each ring

tends toward the aromatic sextet condition, and enhance the stability of the resulting π -system. While the parent pyrrolo[3,2-*c*]thiapyran (**5**), formally considered as a 5-aza derivative of cyclopenta[*c*]thiapyran (**2**), is not yet known, we have already reported the synthesis of 1,2,3,4-tetrahydronaphth[2,3-*b*]indolo[2,3-*d*]thiapyran (**6**, R plus R' equals tetramethylene), the first of this new class of pseudoazulenes.² The unsubstituted tetranuclear system (**6**, R and R' are H), several derivatives (**6**, R' = H; R = Cl, Me, MeO), and two higher benzologs have subsequently been described by Buu-Hoi and co-workers.⁸ We now wish to report the synthesis of thiapyrano[4,3-*b*]indole (**9a**) and several substituted derivatives (**9b–h**) along with spectral evidence relevant to π delocalization in this new heteroaromatic system.



With the exception of the nitro compound (**8h**), the precursor 1,3,4,5-tetrahydrothiapyrano[4,3-*b*]indoles (**8a–g**) were all obtained directly in yields of 10–63% by condensation of tetrahydro-1,4-thiapyrone (**7**)⁹ with the appropriately substituted phenylhydrazine in

(1) Abstracted in part from the Ph.D. thesis of C. J. Ohnmacht, Lehigh University, 1966.

(2) Part II: T. E. Young and P. H. Scott, *J. Org. Chem.*, **31**, 343 (1966).

(3) Warner-Lambert Research Fellow, 1965–1966.

(4) R. Mayer, *Angew. Chem.*, **69**, 481 (1957).

(5) R. Mayer, J. Franke, V. Horák, I. Hanker, and R. Zahradník, *Tetrahedron Letters*, 289 (1961).

(6) 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., W. F. Harrison, and R. G. Anderson, *ibid.*, **85**, 3448 (1963).

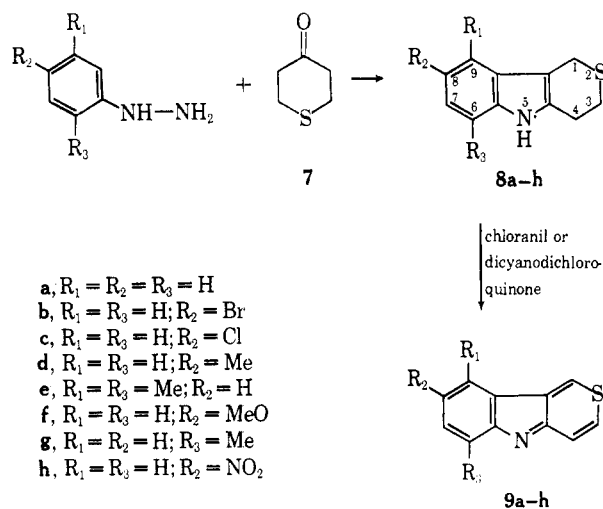
(7) A. G. Anderson, Jr., and W. F. Harrison, *Tetrahedron Letters*, 11 (1960); A. G. Anderson, Jr., and W. F. Harrison, *J. Am. Chem. Soc.*, **86**, 708 (1964).

(8) N. P. Buu-Hoi, A. Croisy, A. Ricci, P. Jacquinet, and F. Perin, *Chem. Commun.*, 269 (1966); N. P. Buu-Hoi, A. Martani, A. Croisy, P. Jacquinet, and F. Perin, *J. Chem. Soc., C*, 1787 (1966).

(9) E. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **70**, 1813 (1948).

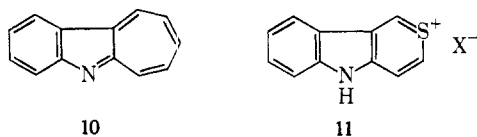
boiling glacial acetic acid without isolation of the intermediate phenylhydrazones. Analogous attempts to condense *p*-nitrophenylhydrazine with **7** yielded only tetrahydro-1,4-thiapyrone *p*-nitrophenylhydrazone, which, however, underwent Fischer indolization to **8h** in 91% yield when heated with concentrated hydrochloric acid, a procedure found effective in the formation of other nitroindoles.¹⁰

Dehydrogenation of these tetrahydro compounds (**8**) with chloranil (for **8a-d**) or dicyanodichloroquinone (for **8e** and **h**) in refluxing xylene or toluene afforded modest yields (15–37%) of the corresponding thiapyrano[4,3-*b*]indoles (**9a-e, h**), while similar reactions of **8f** and **8g** afforded tarry crude products from which the thiapyranindoles **9f** and **9g** could be iso-



lated in yields of only 2 and 3%, respectively. Attempts to dehydrogenate **8a** and **8f** with 10% palladium on charcoal in refluxing decalin gave only recovered starting materials.

The thiapyrano[4,3-*b*]indoles (**9a-h**) were yellow to orange crystalline compounds, stable to prolonged storage under normal ambient conditions. They showed no N-H stretching frequencies in their infrared spectra, which were otherwise not revealing except as fingerprints and exhibited electronic spectra of which the visible regions were characterized by broad bands having maxima in the 400–426-m μ region. The electronic spectrum of the parent compound (**9a**) is illustrated in Figure 1, along with the comparable ultraviolet spectrum¹¹ of the iso- π -electronic benz[*b*]-1-azaazulene (**10**),^{11,12} which also exhibits a visible maximum (not shown) at 500 m μ .¹¹



Although attempts to convert several of the compounds (**9**) to the corresponding thiapyrylium chlorides (*e.g.*, **11**, X⁻ = Cl⁻) by reaction with anhydrous hydrogen chloride gave tars which were difficult to

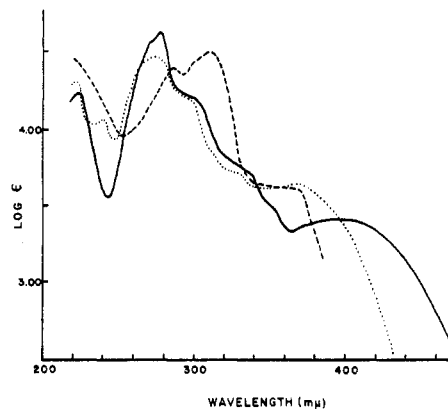


Figure 1.—Electronic absorption spectra of thiapyrano[4,3-*b*]indole (**9a**; in 95% ethanol) (—); the conjugate acid (**11**, X⁻ = Cl⁻; apparent molar absorption curve for a ratio of **11**:**9a** of 13:1 in 95% ethanol) (.....); and benz[*b*]-1-azaazulene (**10**; in cyclohexane; from ref 11) (-----).

purify,¹³ the parent thiapyranindole **9a** at 10⁻⁴ M concentration in 95% ethanol reacted with ethanolic hydrogen chloride solution to give the conjugate cation **11**¹⁴ whose spectrum is also shown in Figure 1.

A spectrophotometric titration of **9a** under these conditions (using the absorbance at 450 m μ for the determination) revealed well-defined isobestic points at 226.5, 232, 267, 340, and 394 m μ , indicative of simple equilibrium protonation, and gave an apparent pK_a = 5.2 at 25° for cation **11** in 95% ethanol.

The hypsochromic shift of the long-wavelength-absorption band in going from the free base (subscript B for **9a**; λ_B 400 m μ) to the conjugate acid (subscript BH⁺ for cation **11**; λ_{BH^+} 366 m μ) is in accord with HMO calculations of the energy changes (Δm , in β units) corresponding to the first $\pi \rightarrow \pi^*$ transition frequencies ($\bar{\nu}$) for species **9a** and **11**. That is, according to simple theory,¹⁵ $\bar{\nu} \propto \Delta m$, hence the ratio $\bar{\nu}_{BH^+}/\bar{\nu}_B$ should approximately equal $\Delta m_{BH^+}/\Delta m_B$. Based on HMO theory, the calculated¹⁶⁻¹⁹ ratio $\Delta m_{BH^+}/\Delta m_B$ is 1.1545/0.9877 = 1.17, while the observed frequency ratio is $\bar{\nu}_{BH^+}/\bar{\nu}_B = \lambda_B/\lambda_{BH^+} = 400/366 = 1.09$. Although exact agreement would be fortuitous due to, *inter alia*, some arbitrariness in selection of parameters¹⁶⁻¹⁹ (especially for nitrogen), the qualitative agreement alone is satisfactorily convincing that the long-wavelength absorption represents the first $\pi \rightarrow \pi^*$ transitions of delocalized π -electron systems.

(13) Contrast the well-defined salt formation of compounds **6** with HCl as reported in ref 2 and 8.

(14) We have subsequently isolated indolo[3,2-*c*]thiapyrylium perchlorate (**11**, X⁻ = ClO₄⁻) via an alternative route and found its electronic spectrum to be virtually identical with that of the conjugate acid shown in Figure 1. Detailed characterization of this perchlorate will be presented in a later article.

(15) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961.

(16) HMO calculations were performed in the usual way¹⁵ using a G. E. 225 computer and a standard eigenvalue-eigenvector program for a symmetrical matrix. For the free base **9a** the parameters, $\alpha_N = \alpha + 0.5\beta$ and $\beta_{CN} = \beta$, for pyridine-like nitrogen were used, and for the conjugate acid **11**, $\alpha_N = \alpha + 2\beta$ and $\beta_{CN} = \beta$, parameters for pyridinium-like nitrogen were chosen.¹⁷ Although we later reported slightly refined parameters for σ -bivalent sulfur,¹⁸ the present calculations for both **9a** and **11** employed Zahradnik's model B2,¹⁹ for which $\alpha = \alpha + \beta$ and $\beta_{CS} = 0.6\beta$. This parameter discrepancy is slight compared with the arbitrariness in selection of the nitrogen parameters.

(17) R. Zahradnik and J. Koutecký, *Advan. Heterocyclic Chem.*, **5**, 72 (1965), and references cited therein.

(18) T. E. Young and C. J. Ohnmacht, *J. Org. Chem.*, **32**, 444 (1967).

(19) R. Zahradnik, *Advan. Heterocyclic Chem.*, **5**, 1 (1965).

(10) D. Deorha and S. Jashi, *J. Org. Chem.*, **26**, 3527 (1961).

(11) C. W. Muth, D. O. Steiniger, and Z. B. Papanastassiou, *J. Am. Chem. Soc.*, **77**, 1006 (1955).

(12) A. G. Anderson, Jr., and J. Tazuma, *ibid.*, **74**, 3455 (1952).

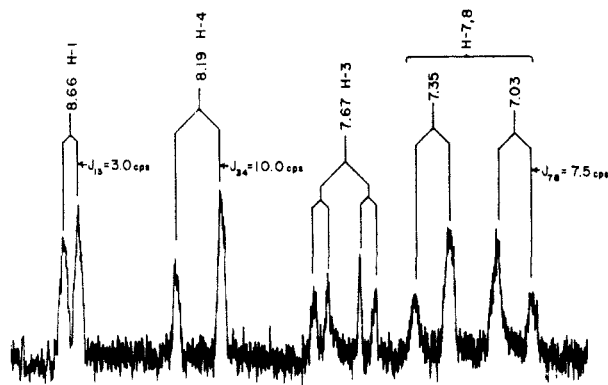
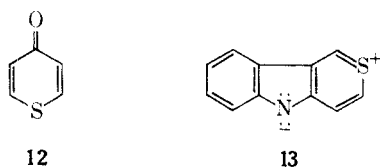
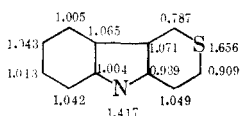


Figure 2.—Nmr spectrum of 6,9-dimethylthiapyranol[4,3-b]indole (9e) in deuteriochloroform; aromatic region only. Values of δ are in parts per million with respect to tetramethylsilane. The two methyl groups appeared as singlets of δ 2.79 and 2.67.

Further evidence for the electronic character of the thiapyranindoles (9) was provided by their nmr spectra (in deuteriochloroform), of which that of the 6,9-dimethylthiapyranol[4,3-b]indole (9e), illustrated in Figure 2, was especially revealing since each proton stands clearly isolated from the rest. The two lowest field protons, H-1 ($\delta = 8.66$ ppm) and H-4 ($\delta = 8.19$ ppm), appeared consistently in the spectra of the remaining compounds 9 with $J_{13} = 3.0$ cps and $J_{34} = 10.0$ cps.²⁰ The extent of the deshielding of H-1 and H-4 in compounds 9 is greater than that observed for 1,4-thiapyrone (12),²¹ and is comparable with, though less extensive than, that observed ($\delta = 10.69$ – 9.42 ppm) for a number of thiapyrylium ions, which have low electron densities on the sulfur-containing ring.²² This evidence suggests that, from a simple resonance point of view, polar canonical forms, such as 13, do indeed contribute significantly to the structure of the thiapyranol[4,3-b]indoles (9).



More explicitly, HMO calculations¹⁶ on the base 9a yield an electron density pattern (summarized on 14) clearly showing the displacement of charge (-0.417 on nitrogen, $+0.344$ on sulfur) and indicating appreciable thiapyrylium character of the sulfur-containing ring. Furthermore, as in the case of the thiapyrylium salts



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(20) In some of these spectra the low-field doublets showed additional fine splitting consistent with $J_{14} = 0.9$ cps, which is about the same magnitude as *para*-proton coupling in benzenoid aromatic rings; cf. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p 85.

(21) J. Jonás, W. Derbyshire, and H. S. Gutowsky [*J. Phys. Chem.*, **69**, 1 (1965)] have presented a rigorous analysis of the A₂B₂ spectrum of 1,4-thiapyrone (12), which exhibits (in CDCl₂) multiplets at δ 7.83 (H-2) and 6.93 (H-3) with $J_{23} = 10.74$, $J_{25} = 4.12$, $J_{35} = 2.00$, and $J_{26} = 0.44$ cps.

(22) T. E. Young and C. J. Ohnmacht, *J. Org. Chem.*, **32**, 1558 (1967).

previously reported,²² the lowest field protons in the nmr spectra of 9 are associated with the thiapyrylium-like ring²³ and again show pronounced α, α' -coupling ($J_{1,3} = 3.0$ cps) *via* conjugation through the thionium sulfur.

Experimental Section²⁴

1,3,4,5-Tetrahydrothiapyranol[4,3-b]indole (8a).—The following procedure is an improved modification of the method of Bennet and Waddington,²⁵ who isolated the intermediate phenylhydrazone.

A solution of 13.00 g (0.120 mole) of phenylhydrazine and 13.00 g (0.112 mole) of tetrahydro-1,4-thiapyrone⁹ (7) in 50 ml of glacial acetic acid was refluxed for 3 hr and the resulting deep red solution then was allowed to cool to room temperature. The crystals which formed were collected by filtration, washed three times with glacial acetic acid, then with petroleum ether (bp 30–40°), and oven dried at 110° for 2 hr. The yield of the white crystalline solid, mp 158–159.5°, was 10.66 g (50%). Sublimation at 132° (0.05 mm) gave a sample having mp 159.5–161°; lit.²⁵ mp 157°.

6,9-Dimethyl-1,3,4,5-tetrahydrothiapyranol[4,3-b]indole (8e).—In a similar manner 18.0 g (0.129 mole) of 2,5-dimethylphenylhydrazine,²⁶ and 15.0 g (0.129 mole) of 7 in 100 ml of acetic acid, heated on the steam bath 0.5 hr, gave on cooling, 9.50 g (34%), mp 159–161°, and on concentration a second crop (tan), 1.10 g (4%), mp 158–160°. Sublimation at 130° (0.1 mm) gave pure 8e, as white crystals, mp 159.5–161.5°.

Anal. Calcd for C₁₃H₁₅NS: C, 71.84; H, 6.96; S, 14.75. Found: C, 71.55; H, 7.07; S, 14.80.

8-Methoxy-1,3,4,5-tetrahydrothiapyranol[4,3-b]indole (8f).—*p*-Methoxyphenylhydrazine²⁷ (7.00 g, 0.052 mole) and 7 (5.00 g, 0.043 mole) in 100 ml of acetic acid reacted exothermically at 70° and crystals of product began to separate within 5 min. After standing overnight, the solid was collected and dried *in vacuo* to give 6.04 g (63%) of crude product, mp 166–168°. Recrystallization from methanol and sublimation at 155° (0.05 mm) gave pure 8f, mp 167–168.5°.

Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; S, 14.62. Found: C, 66.01; H, 6.22; S, 14.55.

8-Methyl-1,3,4,5-tetrahydrothiapyranol[4,3-b]indole (8d).—A mixture of 9.45 g (0.0596 mole) of *p*-tolylhydrazine hydrochloride, 6.90 g (0.0596 mole) of 7, and 8.10 g (0.0596 mole) of sodium acetate trihydrate in 100 ml of glacial acetic acid was refluxed for 2.25 hr. The resulting mixture was filtered hot to remove a little insoluble solid and the filtrate was allowed to cool to room temperature. The crystals which formed were collected by filtration, washed three times with acetic acid, then with petroleum ether (bp 30–40°), air dried 1 hr, then dried *in vacuo* over potassium hydroxide. The crude product weighed 8.61 g and melted mainly at 173–176° but contained a residue which remained unfused up to 350°. This crude solid was washed thoroughly by stirring it with water for 0.5 hr (the aqueous extract gave a strong positive test for chloride ion) then redried at 110° for 1 hr, and finally sublimed at 163° (0.06 mm) to give 6.75 g (55.8% yield) of product, mp 174–6°. One recrystallization from glacial acetic acid followed by sublimation at 163° (0.06 mm) gave analytically pure material as white crystals, mp 175–177°.

Anal. Calcd for C₁₂H₁₃NS: C, 70.89; H, 6.45; N, 6.89; S, 15.77. Found: C, 71.00; H, 6.71; N, 6.89; S, 15.82.

8-Bromo-1,3,4,5-tetrahydrothiapyranol[4,3-b]indole (8b).—Following the procedure for 8d, 10.00 g (0.045 mole) of *p*-bromophenylhydrazine hydrochloride, 5.22 g (0.045 mole) of 7, and

(23) In the present series of compounds 9, the lowest field proton again corresponds to the position of lowest electron density (C-1). However, as indicated in a previous article,²² electron densities above the range of 0.7 to 0.8 are not a reliable index of deshielding because of other heteroatom-anisotropic effects.

(24) Melting points were determined in capillary tubes using a Mel-Temp apparatus (Laboratory Devices, Cambridge, Mass.) and are corrected. Ultraviolet-visible spectra were recorded on a Beckman DK-2A spectrophotometer. Nmr spectra were determined on a Varian A-60 instrument in deuteriochloroform using tetramethylsilane as internal standard.

(25) G. M. Bennet and W. B. Waddington, *J. Chem. Soc.*, 2829 (1929).

(26) R. Carlin and D. Carlson, *J. Am. Chem. Soc.*, **81**, 4673 (1959).

(27) K. G. Blake and W. H. Perkin, *J. Chem. Soc.*, 125, 313 (1924).

6.12 g (0.045 mole) of sodium acetate trihydrate in 100 ml of acetic acid gave, after 22 hr of reflux, 6.38 g (53%) of **8b**, mp 165.5–166.5° (lit.²⁵ mp 162°). This compound decomposed extensively on attempted sublimation at 160° (0.05 mm).

8-Chloro-1,3,4,5-tetrahydrothiapyrano[4,3-*b*]indole (8c).—In a similar manner, 7.70 g (0.043 mole) of *p*-chlorophenylhydrazine hydrochloride, 5.00 g (0.043 mole) of **7**, and 3.53 g (0.043 mole) of sodium acetate trihydrate in 100 ml of acetic acid was refluxed 30 hr and poured into water; the crude solid was recrystallized from benzene-cyclohexane to give 5.40 g (56%) of yellowish crystals, mp 138–142° with shrinking at 130°. Recrystallization from petroleum ether (bp 60–70°) and sublimation at 125° (0.1 mm) gave white crystals of **8c**, mp 142–144°.

Anal. Calcd for C₁₁H₁₀ClNS: C, 59.06; H, 4.51; S, 14.33. Found: C, 59.30; H, 4.69; S, 14.28.

6-Methyl-1,3,4,5-tetrahydrothiapyrano[4,3-*b*]indole (8g).—Similarly, 31.7 g (0.22 mole) of *o*-tolylhydrazine hydrochloride, 23.2 g (0.20 mole) of **7**, and 16.4 g of anhydrous sodium acetate in 50 ml of acetic acid was refluxed 12 hr, and the solution was poured into water to give an oil, which was extracted into benzene. The benzene solution, after being dried (K₂CO₃) and evaporated, again yielded an oil which was crystallized from ethyl acetate-petroleum ether (bp 60–70°) to give 6.0 g of crude product, mp 135–148°. Further recrystallization from aqueous ethanol and final sublimation at 130° (0.04 mm) afforded 3.7 g of pure **8g** as white crystals, mp 154–158°.

Anal. Calcd for C₁₂H₁₃NS: C, 70.89; H, 6.45; N, 6.89; S, 15.77. Found: C, 70.98; H, 6.22; N, 7.07; S, 15.80.

8-Nitro-1,3,4,5-tetrahydrothiapyrano[4,3-*b*]indole (8h).—The following procedure was adapted from that of Deorha and Jashi¹⁰ for the preparation of nitroindoles.

A stirred slurry of 5.95 g of tetrahydro-1,4-thiapyrone *p*-nitrophenylhydrazone (mp 155–156.5°, lit.²⁵ mp 156°) in 59.5 ml of concentrated hydrochloric acid was heated cautiously (foaming initially) for 4 hr at 85–95°. After 0.5 hr the phenylhydrazone had dissolved to give a red solution, which subsequently became cloudy as the nitroindole began to precipitate. At the end of the 4-hr period the mixture was cooled; the solid was collected by filtration and dried. This crude product (4.5 g, 91% yield, mp 206–213°) was recrystallized from acetonitrile, sublimed at 185° (0.1 mm), and again recrystallized from acetic acid to give orange needles of **8h**, mp 221–223°.

Anal. Calcd for C₁₁H₁₀N₂O₂S: C, 56.40; H, 4.30; S, 13.69. Found: C, 56.60; H, 4.50; S, 13.63.

Thiapyrano[4,3-*b*]indole (9a).—Into a 1-l. three-neck flask equipped with stirrer and condenser were introduced 13.4 g (0.0545 mole) of chloranil, 5.10 g (0.0270 mole) of **8a**, and 300 ml of xylene. A deeply colored partial solution resulted. The mixture was then stirred at reflux for 5 hr, and filtered while hot. The brown, xylene-insoluble precipitate was washed with petroleum ether (bp 30–40°), air dried, then stirred with 50 ml of 10% sodium hydroxide until it was converted to a yellow powder (ca. 4 hr). The alkali-insoluble residue was collected by centrifugation, washed thoroughly with water, and air dried to give 2.00 g of ochre yellow powder, which was sublimed at 140° (0.07 mm) to yield 1.14 g (23%) of yellow crystals, mp 168–171° dec. Two recrystallizations from 1:1 benzene-cyclohexane afforded golden yellow needles, mp 178–179.5°, which were again sublimed to yield pure product, mp 178–180.5° (clear amber melt).

Anal. Calcd for C₁₁H₇NS: C, 71.32; H, 3.81; N, 7.56; S, 17.31. Found: C, 71.37; H, 3.72; N, 7.51; S, 17.07.

Ultraviolet-visible spectrum showed $\lambda_{\text{max}}^{95\% \text{EtOH}}$ 224 m μ (log ϵ 4.24), 274 (4.58) sh, 279 (4.63), 296 (4.23) sh, 352 (3.51) sh, 400 (3.43).

The nmr spectrum showed H-1 at δ 8.65 (doublet, $J_{13} = 3.0$ cps), H-4 at δ 8.11 (doublet, $J_{34} = 10.0$ cps), and the remaining five protons as an unresolved multiplet from δ 7.97 to 7.21.

8-Bromothiapyrano[4,3-*b*]indole (9b).—A mixture of 1.26 g (0.0047 mole) of **8b**, 2.32 g (0.0094 mole) of chloranil, and 50 ml of xylene was refluxed for 4 hr, then filtered while hot. The crude xylene-insoluble residue was air dried, then stirred with 10% sodium hydroxide until it was reduced to a yellow powder (ca. 4 hr). This material was collected by centrifugation, washed with water and air dried; weight 0.97 g, mp 199–201° dec. Recrystallization from cyclohexane followed by sublimation at 162° (0.07 mm) gave 0.29 g (22% yield) of pure product as yellow crystals, mp 207–209° dec.

Anal. Calcd for C₁₁H₆BrNS: C, 50.01; H, 2.29; N, 5.30; S, 12.14. Found: C, 50.22; H, 2.44; N, 5.37; S, 11.95.

Ultraviolet-visible spectrum showed $\lambda_{\text{max}}^{95\% \text{EtOH}}$ 227 m μ (log ϵ 4.32), 277 (4.46) sh, 283 (4.58), 301 (4.37) sh, 354 (3.57), 407 (3.43).

The nmr spectrum of this product again showed H-1 at δ 8.95 (doublet, $J = 3.0$ cps), and additional multiplets at 8.27 and from 8.07 to 7.80; however, because of the low solubility of this material in CDCl₃ neither an accurate integration nor clear resolution of the H-4 absorption were possible.

8-Chlorothiapyrano[4,3-*b*]indole (9c).—In a similar manner 2.24 g of **8c** and 4.92 g of chloranil in 150 ml of xylene yielded, after alkaline decomposition of the brown complex, 0.60 g (27.2%) of **9c**, mp 192–196° dec, which after two sublimations, the last at 130° (0.1 mm), afforded yellow-orange crystals of pure product, mp 194–196.5° dec.

Anal. Calcd for C₁₁H₆ClNS: C, 60.13; H, 2.75; Cl, 16.14; N, 6.38; S, 14.60. Found: C, 60.16; H, 2.77; Cl, 16.34; N, 6.35; S, 14.55.

Ultraviolet-visible spectrum showed $\lambda_{\text{max}}^{95\% \text{EtOH}}$ 229 m μ (log ϵ 4.41), 278 (4.49), 284 (4.61), 303 (4.40), 356 (3.59), 410 (3.44).

The nmr spectrum showed H-1 at δ 8.80 (doublet, $J_{13} = 3.0$ cps), H-4 at δ 8.18 (doublet, $J_{34} = 10.0$ cps), and a multiplet at 8.00–7.50 integrating for four protons (H-3, -6, -7, and -9).

8-Methylthiapyrano[4,3-*b*]indole (9d).—Analogously with the foregoing procedure, 2.03 g of **8d**, 4.92 g of chloranil, and 100 ml of xylene gave, after the alkali treatment, 1.34 g of crude yellow solid, mp 144–153°. Recrystallization from 1:1 benzene-cyclohexane afforded 0.30 g (15% yield) of **9d**, mp 160–166°. Sublimation at 150° (0.07 mm) gave pure product as yellow-orange crystals, mp 171–172° dec.

Anal. Calcd for C₁₂H₉NS: C, 72.32; H, 4.55; N, 7.03; S, 16.09. Found: C, 72.42; H, 4.49; N, 7.15; S, 15.88.

Ultraviolet-visible spectrum gave $\lambda_{\text{max}}^{95\% \text{EtOH}}$ 226 m μ (log ϵ 4.26), 238 (3.90) sh, 277 (4.55) sh, 282 (4.62), 299 (4.29) sh, 358 (3.48) sh, 408 (3.36).

The nmr spectrum showed H-1 at δ 8.63 (doublet, $J_{13} = 3.0$ cps, with fine splitting $J_{14} = 0.9$ cps), H-4 at δ 8.10 (essential doublet, $J_{34} = 10.0$ cps with fine splitting $J_{14} = 0.9$ cps), H-3, -6, -7, and -9 as an unresolved multiplet at δ 7.90–7.35, and CH₃ at δ 2.52 (singlet integrating for three protons).

6,9-Dimethylthiapyrano[4,3-*b*]indole (9e).—A mixture of 2.17 g (0.010 mole) of **8e**, 4.54 g (0.020 mole) of dicyanodichloroquinone, and 50 ml of dry toluene was refluxed for 30 min, the initially red solution and precipitate turning to a chocolate brown after the first 5 min. The hot mixture was filtered and the resulting insoluble complex was collected by filtration, washed with ether, and air dried. This material was then stirred with 10% sodium hydroxide solution for 2 hr and the crystals collected by suction filtration. After drying *in vacuo* at 80° for a few hours the yield of ochre crystals was 1.81 g, mp 129–134° with shrinking at 120°. The crude product was then extracted in a Soxhlet apparatus with cyclohexane. On cooling and filtration 0.80 g (37%) of orange crystals, mp 142–145°, was obtained. Recrystallization once more from cyclohexane gave analytical material of melting point 145–147°.

Anal. Calcd for C₁₃H₁₁NS: C, 73.20; H, 5.20; S, 15.03. Found: C, 72.97; H, 5.39; S, 14.91.

Ultraviolet-visible spectrum gave $\lambda_{\text{max}}^{\text{cyclohexane}}$ 233 m μ (log ϵ 4.06), 275.5 (4.66), 309 (3.99) sh, 332 (3.96) sh, 366 (3.43), 420 (3.44).

The nmr spectrum and its analysis are shown in Figure 2.

8-Methoxythiapyrano[4,3-*b*]indole (9f).—In a similar manner, 2.17 g of **8f** and 4.56 g of dicyanodichloroquinone in 150 ml of xylene was refluxed 5 hr, and the resulting brown complex was collected by filtration. This solid was stirred overnight with 200 ml of 10% sodium hydroxide to give a gummy solid, which was dried *in vacuo* over KOH then sublimed at 142° (0.08 mm) to yield 0.040 g (2%) of red-orange crystals, mp 135–136°, and resolidified and remelted at 148–149°.

Anal. Calcd for C₁₂H₉NOS: C, 66.95; H, 4.21; N, 6.51; S, 14.90. Found: C, 66.92; H, 4.09; N, 6.42; S, 14.77.

Ultraviolet-visible spectrum showed $\lambda_{\text{max}}^{95\% \text{EtOH}}$ 226 m μ (log ϵ 4.28), 286 (4.60), 295 (4.55) sh, 367 (3.51) sh, 426 (3.24).

The nmr spectrum showed H-1 at δ 8.75 (doublet, $J_{13} = 3.0$ cps), H-4 at δ 8.15 (doublet, $J_{34} = 9.5$ cps), H-3, -6, -7, and -9 as a multiplet from δ 7.96 to 7.16, and CH₃ at δ 3.93 (singlet integrating for three protons).

6-Methylthiapyrano[4,3-*b*]indole (9g).—An analogous reaction of 2.03 g of **8g** with 4.92 g of chloranil in 150 ml of xylene gave a crude product, which was sublimed at 160° (0.09 mm) to yield 0.060 g (3%) of **9g** as yellow crystals, mp 162.5–165°.

Anal. Calcd for $C_{12}H_9NS$: C, 72.32; H, 4.55; N, 7.03; S, 16.09. Found: C, 72.25; H, 4.53; N, 7.19; S, 16.03.

Ultraviolet-visible spectrum gave $\lambda_{\max}^{95\%EtOH}$ 228 $m\mu$ ($\log \epsilon$ 4.23), 275 (4.59), 300 (4.14), 359 (3.47) sh, 413 (3.48).

The nmr spectrum showed H-1 at δ 8.76 (doublet, $J_{14} = 3.0$ cps), H-4 at δ 8.27 (doublet, $J_{34} = 9.5$ cps), H-3, -7, -8, and -9 as a multiplet from δ 8.00 to 7.20, and the CH_3 at δ 2.82.

8-Nitrothiapyrano[4,3-b]indole (9h).—Dehydrogenation of 2.35 g of **8h** with 4.56 g of dicyanodichloroquinone in 200 ml of refluxing xylene for 3 hr similarly gave a dark, insoluble complex which was decomposed by stirring for 24 hr with 10% sodium hydroxide solution. The yellow-brown alkali-insoluble product (0.5 g) was sublimed at 220° (0.6 mm) to give 0.35 g (15%) of pure **9h** as yellow crystals, mp $272-273^\circ$.

Anal. Calcd for $C_{11}H_8N_2O_2S$: C, 57.38; H, 2.63; N, 12.17; S, 13.93. Found: C, 57.52; H, 2.74; N, 11.82; S, 13.72.

Ultraviolet-visible spectrum showed $\lambda_{\max}^{95\%EtOH}$ 273 $m\mu$ ($\log \epsilon$ 4.48), 320 (3.89), 398 (3.55).

Because of the low solubility of this compound its nmr spec-

trum could not be measured in $CDCl_3$ for direct comparison with the other members of the series.

Registry No.—**8a**, 7076-17-7; **8c**, 14120-24-2; **8d**, 14120-25-3; **8e**, 14120-26-4; **8f**, 14120-27-5; **8g**, 14120-28-6; **8h**, 14120-29-7; **9a**, 244-75-7; **9b**, 14120-30-0; **9c**, 14120-31-1; **9d**, 14120-32-2; **9e**, 14120-33-3; **9f**, 14120-34-4; **9g**, 14120-35-5; **9h**, 14120-36-6; **11** (X = Cl^{11}), 14120-37-7.

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Structure and Stereochemistry of the Benzilic Acid Rearrangement Product of $3\alpha,17\beta$ -Diacetoxy-11-hydroxy- 5β -androst-9(11)-en-12-one¹

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The formation of $3\alpha,11\alpha,17\beta$ -trihydroxy- 13α -C-nor- 5β -androstane-11 β -carboxylic acid **11a**, 17 -lactone from $3\alpha,17\beta$ -diacetoxy-11-hydroxy- 5β -androst-9(11)-en-12-one in a benzilic acid rearrangement required that the latter be preceded by a retro-aldol condensation leading to epimerization at C_{13} of the starting diketone. The stereochemical formulation of the lactone was based on spectral, thermodynamic, and mechanistic considerations. The stepwise degradation of the lactone to $3\alpha,17\beta$ -dihydroxy- 13α -C-nor- 5β -androstan-11-one furnished chemical proof for its structure.

As a part of a continuing effort² to study the structural alteration of natural steroids, this report deals with an attempt to alter ring C in the 5β -androstane series.

A mixture of the known 11α - and 11β -bromo- $3\alpha,17\beta$ -diacetoxy- 5β -androstan-12-one (**2a** and **2b**), obtained from $3\alpha,17\beta$ -diacetoxy- 5β -androstan-12-one (**1**) by bromination,³ was treated with sodium hydroxide in aqueous methanol to afford the new $3\alpha,12\beta,17\beta$ -trihydroxy- 5β -androstan-11-one (**3a**) as the main product of the reaction. Oxidation of this triolone with bismuth trioxide in acetic acid solution⁴ yielded $3\alpha,17\beta$ -diacetoxy-11-hydroxy- 5β -androst-9(11)-en-12-one (**5a**). The new enolic diketone absorbed in the ultraviolet at 282 nm (ϵ 9600),⁵ and in its nmr spectrum the expected C_{10} methyl proton absorption at 73 cps⁶ was observed. Two by-products from this oxidation mixture were demonstrated to be the triacetate **3b**, identical with that obtained by acetylation of **3a**, and the diacetate **3c** which upon acetylation furnished **3b**. The nmr spectrum of the strongly hydrogen bonded 12-equatorial monohydroxy compound **3c** was of interest since the hydroxyl proton and the 12-axial proton formed an isolated AB system giving rise to an AB quartet with the OH doublet and the 12α -H dou-

blet appearing at 212 and 238 cps, respectively ($J_{AB} = 4.5$ cps).⁷ After the addition of deuterium oxide, the axial proton at C_{12} absorbed as a singlet at 239 cps. This observation confirmed the 12-hydroxy-11-oxo structure; the C_{11} proton of an 11-hydroxy-12-oxo compound would be coupled with the proton at C_9 and a more complex nmr pattern could be expected.

Since the triolone **3a** was obtained by alkali treatment of a mixture of the 11α - and 11β -bromo 12-ketones **2a** and **2b**, the possibility of epimerization at C_{13} by a retro-aldol condensation, similar to that postulated below, had to be considered. For that reason it was necessary to investigate the stereochemistry of this intermediate. Its triacetate **3b** was reduced with calcium in liquid ammonia⁸ and the resulting product was acetylated to yield the known⁹ $3\alpha,17\beta$ -diacetoxy- 5β -androstan-11-one (**4**). This finding allows the assignment of the stereochemistry of the natural steroids at C_{13} to the triacetate **3b**, the diacetate **3c**, the triolone **3a**, the oxidation product **5a**, and its derived acetate **5b**.

The attempted reduction of the 12-acetoxy group of **3b** with zinc dust in acetic acid¹⁰ was shown to lead to the almost quantitative recovery of the starting material. This finding supported the assignment of the

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