dried at 42° (40 μ) to constant weight; 0.146 g. (59%) of III was obtained containing 49% of positive iodine (calcd. for $C_6H_8IN_3$: I, 50.96). Purification attempts did not succeed. Compound III is an amber solid that darkens after few days at room temperature.

Products from different experiments contained between 43 and 49% of positive iodine.

Compound III (60 mg.) was heated in 2 ml. of acetone at 56° for 8 hr. in the dark; removal of the solvent gave a solid which contained only 3% of positive iodine. This material, after washing with sodium sulfite solution and water, was crystallized from alcohol; 30 mg. (50%) of 2-amino-4,6-dimethyl-5-iodopyrimidine (II) was obtained and identified by melting point and mixture melting point and by comparison of the infrared absorption spectra with the sample prepared as indicated in Table I.

2,4-Dimethyl-6-(N-iodo-N-acetylamino)pyrimidine (IV).—The starting material, 2,4-dimethyl-6-acetylaminopyrimidine, was dried at 56° (25 mm.) to constant weight to remove the water of crystallization; reaction as above resulted in 50% yield of IV as an almost white solid that decomposes on standing at room temperature, m.p. 156–158° dec.

Anal. Calcd. for $C_8H_{10}IN_3O$: I, 43.61. Found: positive I, 42.8.

Treatment of 25 mg. of IV with aqueous sodium sulfite solution followed by evaporation and sublimation at 100° (0.1 mm.) provided 14 mg. of 2,4-dimethyl-6-acetylaminopyrimidine which, upon crystallization from water, melted at 181–183° and was identified by mixture melting point and infrared absorption.

By heating IV for 8 hr. in boiling acetone, with or without 1 equiv. of 2,4-dimethyl-6-acetylaminopyrimidine, a very low disappearance of positive iodine occurred. Similar results were obtained in the same manner with stoichiometric amounts of 2,4-dimethyl-6-acetylaminopyrimidine and DIH.

Preparation of α-Iodo Ketones.—The enol acetates, prepared following literature procedures, were iodinated essentially as described[17] using NIS. The positive halogen of α-iodo ketones was analyzed iodometrically in aqueous acetone acidified with sulfuric acid.

3-Iodo-2-heptanone.—To a solution of 0.025 mole of 2-hepten-2-ol acetate in 10 ml. of dioxane 0.023 equiv. of DIH were added; after magnetic stirring for 1 hr. at 90°, the solvent was removed *in vacuo* and the residue was extracted with several portions of carbon tetrachloride.

The insoluble material, m.p. 174–175° (75%), was identified by mixture melting point as 5,5-dimethylhydantoin.

Fractionation of the carbon tetrachloride extract furnished 3-iodo-2-heptanone, 76% yield, b.p. 77–80° (1.7 mm.), lit. b.p. 75° (1.5 mm.).

Anal. Calcd. for $C_7H_{13}IO$: I, 52.86. Found: I, 52.66.

Iodination with NIS afforded the 3-iodo-2-heptanone in 76% yield; reported[17] yield under the same conditions was 58%.

ω-Iodoacetophenone.—A solution of 0.001 mole of 1-phenylethen-1-ol acetate in 0.5 ml. of dioxane and 0.001 equiv. of DIH was magnetically stirred for 3 hr. at 50°; the undissolved DIH disappeared after *ca.* 2.5 hr. The solvent was distilled off under reduced pressure and the residue was extracted with benzene. The 5,5-dimethylhydantoin (87%) that remained undissolved was identified as above.

The benzene extract was heated for 1 hr. at 80° after the addition of 0.5 ml. of pyridine; the crystalline product which separated in the cold, 0.242 g. (88%), gave m.p. 197–199°, raised to 202–204° on recrystallization from water; no depression occurred by mixing with an authentic sample of phenacylpyridinium iodide melting at 202–204°.

Fractionation of the reaction products at low temperature using carbon tetrachloride instead of benzene left an insoluble material which, recrystallized from ethyl acetate, provided 22 mg. (21% yield) of crystals, m.p. 123–127°. The latter, on the basis of infrared spectral comparison, was identical with the monoacetyl derivative of 5,5-dimethylhydantoin preferably described[4a,20] as 2-enol-5,5-dimethylhydantoin acetate.

Working in the same fashion, but using NIS, the reaction was not completed, 37% of the halogenating agent (55.3% positive iodine) being recovered. The pyridinium salt (55%), after recrystallization from water, melted at 203–205°.

3-β-Acetoxy-21-iodo-Δ⁵-pregnen-20-one.—The reaction was carried out as described in the literature using NIS.[17] The iodo ketone, purified from methanol–water (56% yield), gave m.p. 139–141° (Kofler micro hot stage) and was identical, according to mixture melting point and infrared absorption, with an authentic specimen obtained in same yield using NIS.

Anal. Calcd. for $C_{23}H_{33}IO_3$: I, 26.19. Found: I, 26.40.

(20) M. R. Salmon and A. Z. Kozlowki, *J. Am. Chem. Soc.*, **67**, 2270 (1945).

The Structures of the Isoisatogens[1,2]

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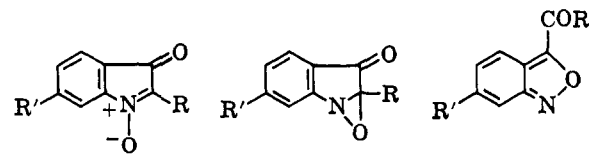
The acid-catalyzed isomerization of isatogens (1) into isoisatogens is shown to give 3-aroylanthranils (3) and not oxaziranes (2) as suggested by Ruggli.

During their extensive studies into the chemistry of nitrogen heterocycles,[5] Ruggli and co-workers investigated the acid-catalyzed isomerization of the bright orange-red isatogens (1) into pale yellow isomers which were called isoisatogens and were formulated as the corresponding oxaziranes (2).[6–12] The reactions were generally carried out in an alcohol solvent at steam-bath temperatures in a pressure vessel employing hydrogen chloride or sulfuric acid as the catalyst. Under



1a-g 2a-e 3a-e

a, R = C_6H_5; R′ = NO_2
b, R = C_6H_5; R′ = $CO_2C_2H_5$
c, R = $C_6H_2NO_2Cl_2$; R′ = H
d, R = C_6H_5; R′ = H
e, R = C_5H_4N; R′ = H
f, R = CO_2CH_3; R′ = H
g, R = $CO_2C_2H_5$; R′ = H

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(2) A portion of this work was reported in a preliminary communication: see J. L. Pinkus, T. Cohen, M. Sundaralingam, and G. A. Jeffrey, *Proc. Chem. Soc.*, 70 (1960).

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(4) To whom inquiries should be addressed.

(5) For a complete listing of P. Ruggli's publications, see H. Rupe, *Helv. Chim. Acta*, **24**, 796 (1946).

(6) P. Ruggli, *Ber.*, **52**, 1 (1919).

(7) P. Ruggli and A. Bolliger, *Helv. Chim. Acta*, **4**, 626 (1921).

(8) P. Ruggli and A. Bolliger, *ibid.*, **4**, 637 (1921).

(9) P. Ruggli, A. Bolliger, and W. Leonhardt, *ibid.*, **6**, 594 (1923).

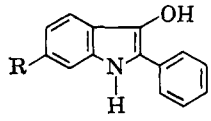
(10) P. Ruggli and H. Zaeslin, *ibid.*, **22**, 134 (1939).

(11) P. Ruggli, E. Caspar, and B. Hegedüs, *ibid.*, **22**, 140 (1939).

(12) P. Ruggli and H. Cuenin, *ibid.*, **27**, 649 (1944).

these experimental conditions 2-phenyl-6-nitroisatogen (**1a**),[6,9] 2-phenyl-6-carbethoxyisatogen (**1b**),[6,11] 2-(2-nitro-3,5-dichlorophenyl)isatogen (**1c**),[10] 2-phenylisatogen (**1d**),[11] and 2-(2-pyridyl)isatogen (**1e**)[12] were converted to the corresponding isoisatogens.

Support for the oxazirane structure **2** was inferred from a variety of experimental results,[6-8,13] including the determination of molecular weights[9,11] and reduction of two of the isoisatogens to indoxyls (**4**),[11] one of which was also obtained from the related isatogen **1d**.[14,15]



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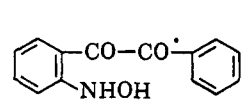
R = H or $CO_2C_2H_5$

That structure **2**[18] is unlikely is suggested by recent studies with authentic oxaziranes which are now known to be less stable than nitrones. Oxaziranes are produced from nitrones by ultraviolet irradiation[20] and can be rearranged to nitrones in acidic media,[21] conditions under which isoisatogens are prepared from nitrones (**1**). Oxaziranes also undergo thermal isomerization to nitrones,[20b,21,22] while 2-arylisoisatogens are converted under similar conditions to 2-aryl-4H-3,1,4-benzoxazones.[23] Whereas oxaziranes are oxidizing agents,[21,22b,c,24] 2-phenylisoisatogen does not liberate iodine from hydriodic acid (see Experimental; *cf.* ref. 11). Furthermore, the carbonyl stretching frequency (1642 cm.$^{-1}$ in Nujol mull) for 2-phenylisoisatogen is about 90 cm.$^{-1}$ too low for the structure **2d**.[25]

Speculations about a reasonable course for the acid-catalyzed rearrangement of isatogens (**1**) suggested that isoisatogens might be 3-aroylanthranils (**3**). For example, acid-catalyzed hydrolysis of the nitrone linkage of **1d** to 2-hydroxylaminobenzil (**5**) might be followed by ring closure to 3-benzoyl-3-hydroxy-2,1-benzisoxazoline (**6**) which could undergo acid-catalyzed 1,4-dehydration to furnish 3-benzoylanthranil (**3d**) (2-phenylisoisatogen).[26]



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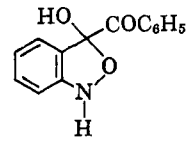

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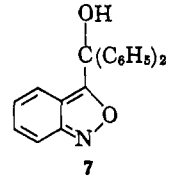
It would be expected that readily obtainable X-ray crystallographic data might easily distinguish between a relatively flat molecule such as **3d** and one containing a tetrahedral carbon atom such as **2d**. The preliminary X-ray crystallographic study by Jeffrey and Sundaralingam[2] did indeed show that structure **2d** is incompatible with the short axis (3.89 Å.) of the crystal unit cell.

That 2-phenylisoisatogen has structure **3d** has now been confirmed by chemical and spectral evidence, and by complete crystal structure analysis.[27] Initial chemical evidence for this structure consisted of the preparation of the same alcohol, assigned the structure 3-anthranilyldiphenylcarbinol (**7**), in yields of 54 and 53%, respectively, from the reaction of phenylmagnesium bromide with both 2-phenylisoisatogen and anthroxanic acid chloride (**8**).[28,29] The carbinol **7** was identified by elemental analysis, and by the presence of hydroxyl absorption and the absence of carbonyl absorption in the infrared spectrum. The ultraviolet spectrum in alcohol is similar to those of other 3-substituted anthranils.[30]



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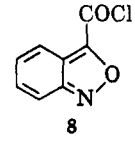

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Rigorous confirmation for structure **3d** was obtained by an alternative synthesis of 3-benzoylanthranil (**3d**) in 40% yield by reaction of anthroxanic acid chloride (**8**) with 1 equiv. of diphenylcadmium.

The position of the carbonyl absorption for **3d** (1642 cm.$^{-1}$ in Nujol and 1650 cm.$^{-1}$ in $CHCl_3$), which is

(13) A. Bolliger, Dissertation, University of Basel, 1921.

(14) P. Ruggli, H. Zaeslin, and R. Grand, *Helv. Chim. Acta*, **21**, 33 (1938).

(15) Early studies on the structures of the isoisatogens, conducted with methyl and ethyl isoisatogenate (prepared from **1f** and **1g**, respectively),[6,7] were shown subsequently by Heller and Boessneck[16] to be misleading, since these supposed isomers were actually the alcohol addition products of the isatogens. When these nitrone addition products[9,16] were heated with acetic acid, with phenyl isocyanate, or in the neat melt, the isatogens (**1f** and **1g**) were regenerated.[7,13] In spite of the correct structural assignments for these addition products (as opposed to an isoisatogen structure), this latter observation[7,13] continues to be quoted periodically[17] as one case or in a general way as an example of the ease of reversibility of the isatogen to isoisatogen rearrangement. The supposed interconvertibility of the isomers would appear to violate thermodynamic principles since such experimental data would suggest a cycle involving two essentially irreversible paths between the two isomers. In two cases, with authentic isoisatogens, reversibility was not demonstrated; 2-phenylisoisatogen remained unaltered when treated with phenyl isocyanate[7] and 2-phenyl-6-nitroisoisatogen did not reconvert (conditions unspecified) to the isatogen.[11]

(16) G. Heller and W. Boessneck, *Ber.*, **55**, 474 (1922).

(17) (a) C. Hollins, "The Synthesis of Nitrogen Ring Compounds," Ernest Benn Ltd., London, 1924, p. 125; (b) L. I. Smith, *Chem. Rev.*, **23**, 193 (1938); (c) A. A. Morton, "The Chemistry of Heterocyclic Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1946, p. 140; (d) W. C. Sumpter and F. M. Miller, "The Chemistry of Heterocyclic Compounds," Vol. 8, Interscience Publishers, Inc., New York, N. Y., 1954, Chapter 5, p. 159; (e) D. A. Jones, Dissertation, University of Minnesota, 1961, p. 27.

(18) A dimeric structure resulting from ring closure of two nitrone functions[19] is ruled out for 2-phenylisoisatogen by a cryoscopic molecular weight determination.[11] This molecular weight was confirmed in the present work (see Experimental).

(19) (a) J. Thesing and H. Mayer, *Ber.*, **89**, 2159 (1956); (b) J. Thesing and H. Mayer, *Ann.*, **609**, 46 (1957).

(20) (a) M. L. Scheinbaum, *J. Org. Chem.*, **29**, 2200 (1964); (b) W. Metlesics, G. Silverman, and L. H. Sternbach, *ibid.*, **28**, 2459 (1963); (c) H. Shindo and B. Umezawa, *Chem. Pharm. Bull.* (Tokyo), **10**, 492 (1962); (d) J. S. Splitter and M. Calvin, *J. Org. Chem.*, **23**, 651 (1958); (e) M. J. Kamlet and L. A. Kaplan, *ibid.*, **22**, 576 (1957); (f) F. Kröhnke, *Ann.*, **604**, 203 (1957).

(21) W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 5739 (1957).

(22) (a) M. F. Hawthorne and R. D. Strahm, *J. Org. Chem.*, **22**, 1263 (1957); (b) L. Horner and E. Jürgens, *Ber.*, **90**, 2184 (1957); (c) H. Krimm, *ibid.*, **91**, 1057 (1958).

(23) J. L. Pinkus, R. J. O'Brien, Jr., G. Pinkus, and T. Cohen, unpublished observations.

(24) E. Schmitz, R. Ohme, and D. Murawski, *Angew. Chem.*, **73**, 708 (1961).

(25) W. M. Schubert and W. A. Sweeney, *J. Am. Chem. Soc.*, **77**, 4172 (1955).

(26) An alternative name (IUPAC) is 3-benzoyl-2,1-benzisoxazole.

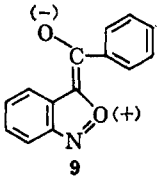
(27) The crystal structure analysis has been presented elsewhere: see M. Sundaralingam and G. A. Jeffrey, *Acta Cryst.*, **15**, 1035 (1962).

(28) F. Arndt, L. Ergener, and O. Kutlu, *Ber.*, **86**, 957 (1953).

(29) The reaction of 2-phenylisoisatogen or **8** with a large excess of diphenylcadmium was reported to furnish the carbinol **7**.[2] The possibility that the carbinol arose in both cases from reaction of unconverted phenylmagnesium bromide with 2-phenylisoisatogen was not rigorously excluded. Recent investigations indicate that this is probably the case (see Experimental).

(30) J. L. Pinkus and R. M. Gerkin, unpublished data.

unusually low even for a diaryl ketone,[31] can now be attributed to resonance interaction with the anthranil ring. A canonical structure such as **9**, in which the



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quinoid ring has taken on benzenoid character, would be expected to be an important contributor to the hybrid.[32] This would shift the absorption to lower frequency than, say, benzophenone ($\lambda_{max}^{C=O}$ 1670 cm.$^{-1}$ in CCl_4[33a] and 1668 cm.$^{-1}$ in $CHCl_2CHCl_2$[33b]). In accord with this explanation, the oxygen–nitrogen bond order[27] is increased relative to that of anthranil.[34,35]

The ultraviolet spectrum of **3d** in ethanol is in accord with an anthranil structure. The longest wave-length band occurs at 352 mμ (log ε 4.03) which is bathochromically displaced *ca.* 37 mμ relative to the longest wave-length band found for a number of 3-alkylanthranils.[30]

The structure **3d** for 2-phenylisoisatogen and by analogy structure **3** for other isoisatogens are in accord with the known reactions and properties of the isoisatogens.[2,6–12] Reasonable routes[36] can now be written for the reductive cleavage[37] (catalytic or with zinc and acetic acid) of the isoxazole ring of the 3-aroylanthranil and subsequent cyclization to an indole derivative.[11]

Experimental[38–41]

General.—All phenylmagnesium bromide solutions were filtered and standardized[42]; reactions were conducted under a dry nitrogen atmosphere.

(31) (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y. 1958, p. 132; (b) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p. 42.

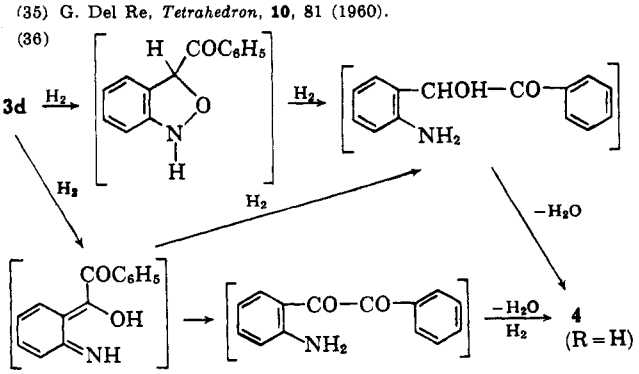
(32) The analogous resonance structure for anthroxanic acid (3-carboxyanthranil) has not been considered important: see R. A. Abramovitch, *Proc. Chem. Soc.*, 8 (1957).

(33) (a) E. Briner and S. Fliszár, *Helv. Chim. Acta*, **43**, 1113 (1960); (b) R. S. Becker, *J. Mol. Spectry.*, **3**, 1 (1959).

(34) M. Sundaralingam, Dissertation, University of Pittsburgh, 1961, p. 126.

(35) G. Del Re, *Tetrahedron*, **10**, 81 (1960).

(36)



(37) (a) G. N. Walker, *J. Org. Chem.*, **27**, 1929 (1962); (b) J. C. E. Simpson and O. Stephenson, *J. Chem. Soc.*, 353 (1942); (c) Th. Zincke and K. Siebert, *Ber.*, **39**, 1930 (1906); (d) P. Friedlander, *ibid.*, **15**, 2572 (1882).

(38) (a) Melting points were taken in a capillary tube and are uncorrected. (b) Microanalysis or ultraviolet spectral determinations was performed in the Microanalytical Department, State University, Groningen, under the supervision of Mr. W. M. Hazenberg. (c) Microanalysis was performed by the Elek Microanalytical Laboratories, Torrance, Calif. (d) Microanalysis was performed by the Microanalytical Laboratory, Mellon Institute, Pittsburgh, Pa.

3-Anthranilyldiphenylcarbinol (7). A. From 8 and Phenylmagnesium Bromide.—To a stirred ether solution (40 ml.) of phenylmagnesium bromide (16.8 mmoles) was added gradually during several minutes a solution of 1.25 g. (6.88 mmoles) of anthroxanic acid chloride (**8**)[28] in 10 ml. of ether. After the initial vigorous reaction had subsided, the mixture was maintained at reflux temperature for 1.5 hr. The cooled reaction mixture was treated with 150 ml. of 20% ammonium chloride solution. Additional ether (110 ml.) was added and the red organic layer was separated. The aqueous layer was extracted with three 25-ml. portions of ether. The ether extracts were combined and washed with four 25-ml. portions of water, three 25-ml. portions of saturated sodium bicarbonate solution, and three 25-ml. portions of water. After two treatments with activated charcoal and filtration, the reddish ether solution was subjected to steam distillation for 10 min. to remove biphenyl and the pot residue was extracted with 90 ml. of ether. The dried (Drierite) ether solution was evaporated under reduced pressure to yield 1.73 g. of a light orange oil which slowly crystallized. After 2 days some of the oil remained unsolidified. The crude product was dissolved in petroleum ether (b.p. 64–69°)–benzene, diluted with petroleum ether (b.p. 35–40°), and stored at 2° overnight. Filtration afforded 1.10 g. (53.0%) of faintly yellow crystals, m.p. 118–119°. Recrystallization from a mixture of methanol, ethanol, and water furnished 0.99 g. (90% recovery) of 3-anthranilyldiphenylcarbinol (**7**) as stout colorless needles, m.p. 119.5–120.0°. The analytical sample (from ethanol–water) had m.p. 121–122°.

Anal.[38c] Calcd. for $C_{20}H_{15}NO_2$: C, 79.73; H, 5.02; N, 4.65. Found: C, 79.97; H, 5.30; N, 5.03.

A previous preparation of the analytical sample, carried out in a similar manner, had m.p. 122.5–124.5°.[2] After drying *in vacuo* with phosphorus pentoxide at room temperature for 15 hr., the melting point was 121.5–123.0°.

Anal.[38d] Calcd. for $C_{20}H_{15}NO_2$: C, 79.73; H, 5.02; N, 4.65. Found: C, 79.50, 79.73; H, 5.00, 5.15; N, 4.99.

The carbinol **7** dissolved in concentrated sulfuric acid to give a burgundy solution whose color was quenched when poured into several volumes of water. The infrared spectrum[39a] of **7** (KBr disk) showed absorption maxima at 3247 (s, br) (O–H), 1642 (m), 1603 (vw), 1522 (w), 1495 (m), 1456 (s), 1431 (vw), 1361 (w, br), 1319 (vw), 1271 (vw), 1203 (m), 1171 (m), 1156 (m), 1143 (w), 1098 (w), 1072 (w), 1055 (m), doublet at 1033 (w) and 1029 (w), 1002 (vw), 986 (vw), 955 (vw), 942 (vw), doublet at 910 (m) and 901 (m), 876 (m), 849 (vw), 837 (vw), 773 (m), 765 (s), 755 (s), doublet at 746 (s) and 742 (s), 700 (s), and 685 cm.$^{-1}$ (vw). The ultraviolet spectrum[40b] (determined by Gerkin[30]) in ethanol had λ_{max} (log ε) at 283 (3.31) (sh) and 316 mμ (3.78) with a series of lesser bands between 252 and 270 mμ.

B. From 3-Benzoylanthranil (3d).—To a stirred ether solution (40 ml.) containing 1.58 g. (7.08 mmoles) of **3d** was added a solution of phenylmagnesium bromide (9.20 mmoles) in 20 ml. of ether during 15 min. A yellow slush was observed after a few minutes. The reaction mixture was maintained at reflux temperature for an additional 30 min., allowed to cool to room temperature, diluted with 50 ml. of ether, and treated with 100 ml. of 20% ammonium chloride solution. The layers were separated and the aqueous solution was extracted with two 20-ml. portions of ether. The combined ether extracts were washed with 15 ml. of water, two 15-ml. portions of saturated sodium bicarbonate solution, and three 15-ml. portions of water. The ether solution was subjected to steam distillation for 15 min., and the pot residue was extracted with three 15-ml. portions of carbon tetrachloride. The dried (Drierite) extract was evaporated under reduced pressure, the residue was dissolved in 20 ml. of dry benzene, and the solution, at reflux temperature, was

(39) Infrared spectra were determined using (a) a Beckman Model IR-8 spectrophotometer, (b) a Perkin-Elmer Model 21 spectrophotometer equipped with sodium chloride optics, or (c) a Leitz recording spectrophotometer.

(40) Ultraviolet spectra were determined using (a) a Beckman DE-2 spectrophotometer or (b) a Bausch and Lomb Spectronic 505 recording spectrophotometer.

(41) Some of the work reported was carried out in the Laboratory for Organic Chemistry, State University, Groningen, The Netherlands, during the tenure of a Fulbright grant held by J. L. P., who would like to express his appreciation to Professor J. F. Arens for many stimulating discussions and for making available the laboratory facilities.

(42) H. Gilman, E. A. Zoellner, and J. B. Dickey, *J. Am. Chem. Soc.*, **51**, 1576 (1929); (b) C. Blomberg, A. D. Vreugdenhil, and P. Vink, *Rec. trav. chim.*, **83**, 662 (1964).

treated with activated charcoal. After filtration, the solvent was removed under reduced pressure and the slowly solidifying residue was recrystallized once from benzene–petroleum ether (b.p. 64–69°) and once from benzene–petroleum ether mixture (b.p. 64–69° and b.p. 35–40°) to furnish 1.15 g. (53.8%) of sturdy colorless needles, m.p. 118.5–120°. Recrystallization from ethanol–water gave needles, m.p. 119.5–120.5°. Mixture melting point with a sample prepared according to procedure A showed no depression. The infrared spectra (KBr disk) of the two samples were identical.

3-Benzoylanthranil (3d). A. From 2-Phenylisatogen (1d).—The anthranil **3d** was prepared by isomerization of **1d**[43] in methanol–sulfuric acid at *ca.* 100°[11,44] or in refluxing ethanol–sulfuric acid as described by Jones.[45] Purification and separation from unchanged **1d** was most readily achieved by chromatography on alumina (100 g./g. of crude **3d**; elution with 2:1 and 4:1 benzene–petroleum ether, b.p. 64–69°) as described by Jones.[45] Recrystallization from petroleum ether (b.p. 64–69°, 25 ml./g.) or methanol–water gave long colorless needles, m.p. 95.5–96.0°, lit.[11] m.p. 94°. An infrared spectrum[39a] of **3d** (KBr disk) showed absorption maxima at 1647 (s, C=O), 1623 (m), 1597 (m), 1575 (m), 1553 (m), 1451 (s), 1427 (m), 1399 (w), 1346 (w), 1323 (m), 1311 (w), 1289 (s), 1236 (s, br), 1189 (m), 1182 (m), 1161 (m), 1142 (w), 1074 (vw, br), 1028 (vw), 1002 (vw), 977 (vw), 934 (m), 907 (vw), 889 (s), 795 (vw, br), 769 (m), 763 (m), 752 (s), 712 (m), 694 (s), and 682 cm.$^{-1}$ (m). In a Nujol mull and in chloroform solution the carbonyl band was at 1642[39b] and 1650[39c] cm.$^{-1}$, respectively. The ultraviolet spectrum[38b,40a] in ethanol showed λ_{max} (log ϵ) at 258 (4.07) (sh) and 352 mμ (4.03).[46] The spectrum was unchanged in acidified or basified ethanol solution (apparent pH ~1 and ~11, respectively). A solution of **3d** in ethanol–water did not liberate iodine from a potassium iodide aqueous alcohol solution acidified with sulfuric acid. A similar result was obtained with the solvent system described by Horner and Jürgens.[22b] The colorless needles of **3d** acquired a greenish tint when left in the air and light. A similar color change was most pronounced when a KBr disk of **3d** was irradiated with a 100-w. mercury-vapor lamp for 5 hr.; however, no change in the infrared spectrum was detected. The anthranil may be stored in a tightly stoppered container in the dark without apparent decomposition. In fact, a *ca.* 19-year-old sample of **3d** (slightly contaminated with **1d**) prepared by Dr. E. Caspar[47] had the m.p. 91–94° while an analytical sample of the isoisatogen,[11] prepared by repeated recrystallization from methanol, had the m.p. 95°.

Anal.[38b] Calcd. for $C_{14}H_9NO_2$: C, 75.33; H, 4.07; N, 6.27; mol. wt., 223. Found: C, 75.42, 75.32; H, 4.11, 4.23; N, 6.36, 6.25; mol. wt., 237 (Rast, camphor).

B. From Anthroxanic Acid Chloride (8).—To a stirred solution of phenylmagnesium bromide (5.80 mmoles) in 25 ml. of ether was added 0.570 g. (3.11 mmoles) of anhydrous cadmium chloride. After 25 min. a Michler ketone test[48] for the presence of Grignard reagent was negative. A solution of 0.997 g. (5.49 mmoles) of anthroxanic acid chloride (**8**)[28] in 20 ml. of ether was added during 5 min. After the solution had been stirred at room temperature for 30 min., the ether was replaced during distillation by 30 ml. of anhydrous benzene, and the reaction mixture was maintained at reflux temperature for 1 hr. After the solution had cooled to room temperature, 75 ml. of ether was added, and the reaction mixture was treated with 150 ml. of 20% ammonium chloride solution. The separated aqueous layer was extracted with three 50-ml. portions of ether. The combined ether extracts were subjected to steam distillation for 10 min., and the pot residue was extracted with three 25-ml portions of ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and with water. The dried (Drierite) ether solution was evaporated under reduced pressure and the residue was recrystallized from methanol–water to furnish 0.385 g. (31.4%) of 3-benzoylanthranil (**3d**) as light yellow needles, m.p. 91–93°. The methanol–water filtrate was worked up to afford an oil which, after chromatography on alumina, gave an additional 0.111 g. (9.1%) of **3d**. Recrystallization from methanol–water furnished nearly colorless needles, m.p. 94–95°, undepressed on admixture with an authentic sample of **3d** prepared from **1d**. The infrared spectrum (KBr disk) was identical with that of the authentic sample.

Attempted Reaction of 3-Benzoylanthranil (3d) with Diphenylcadmium.—With 1 equiv. of diphenylcadmium, **3d** was recovered (85%) after 95 min. in benzene at reflux temperature. Reaction did occur when 11 equiv. of diphenylcadmium were used with a reaction time of 1 hr. in benzene at reflux temperature. However, neither **3d** nor **7** could be isolated from the oily reaction product. A small amount of a solid, m.p. 132–133°, was isolated but not identified.

(43) (a) F. Kröhnke and M. Meyer-Delius, *Ber.*, **84**, 932 (1951); (b) F. Kröhnke and I. Vogt, *ibid.*, **85**, 376 (1952).

(44) B. Hegedüs, Dissertation, University of Basel, 1939, p. 30. We thank Dr. Hegedüs for kindly providing a copy of his dissertation.

(45) See ref. 17e, p. 114.

(46) A subsequent determination[30] of the ultraviolet spectrum[40b] showed $\lambda_{max}^{C_2H_5OH}$ (log ϵ) at 218 (3.85) (sh), 261 (3.95), 293 (3.78) (sh), 308 (3.69) (sh), and 354 mμ (4.00).

(47) A number of original samples of nitrogen heterocycles prepared by Professor P. Ruggli and co-workers at the University of Basel were kindly furnished by Professors T. Reichstein and H. Dahn.

(48) A. I. Vogel, "Practical Organic Chemistry," 3rd Ed., Longmans, Green and Co., London, 1957, p. 241.

Indole Alkaloids. III.[1] Oxidation of Secondary Alcohols to Ketones

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Oxidation of yohimbine, methyl reserpate, 16α-methylyohimban-17α-ol, and α-yohimbine with N,N'-dicyclohexylcarbodiimide, orthophosphoric acid, and dimethyl sulfoxide gives the corresponding ketones in 60–80% yields. β-Yohimbine O-*p*-toluenesulfonate is oxidized with dimethyl sulfoxide and tripropylamine to give 25% of yohimban-17-one, but yohimbine O-*p*-toluenesulfonate yields apoyohimbine. Acid hydrolysis of yohimbinone affords yohimban-17-one, whereas base hydrolysis cleaves the E ring with formation of diacid **4**.

Methods for oxidation of a secondary hydroxyl group in indole alkaloids to a ketone are severely limited owing to the sensitivity of the indole moiety to oxidation. The various oxidizing agents involving chromium trioxide, so successful in other fields, are of limited value. The only consistently successful method for oxidation of a hydroxyl group in an indole alkaloid is the modified Oppenauer oxidation.[2] Many variations in the conditions of the Oppenauer oxidation as applied to alkaloids have been developed[3,4]; however, in many

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(4) M.-M. Janot, R. Goutarel, E. W. Warnhoff, and A. Le Hir, *Bull. soc. chim. France*, 637 (1961).