hour; the cooled solution was neutralized with 1 *N* hydrochloric acid and evaporated *in vacuo*. The residue was crystallized from water and the product was collected by filtration: yield 384 mg. (74%), m.p. 208–210°. One recrystallization from water gave the analytical sample, which was dried at 100° (0.8 mm.) over phosphorus pentoxide for 48 hours; m.p. 208–210°, $[\alpha]^{26}D$ +8.2 ± 2.7° (0.51% in water); λ_{max} in mμ ($\epsilon \times 10^{-3}$): *p*H 1, 246 (12.8), 306 (4.60); *p*H 7, 233 (15.0), 260 (9.75), 303 (7.05); *p*H 13, 234 (13.4), 259 (9.15), 303 (7.10) $\tilde{\nu}$ in cm.$^{-1}$ (KBr): 3400 and 3250 (OH); 1610 and 1570 (C=N, C=C); 1070, 1050 and 1020 (C–O–).

Anal. Calcd. for $C_{11}H_{14}N_4O_4S$: C, 44.29; H, 4.73; N, 18.78. Found: C, 44.09; H, 4.71; N, 18.62.

2-Dimethylamino-9-β-D-ribofuranosylpurine (IX).—A solution of 500 mg. (1.74 mmoles) of 2-chloro-9-β-D-ribofuranosylpurine (IV) in 17 ml. of a 25% aqueous solution of dimethylamine was diluted with 40 ml. of methanol and heated in a stainless steel bomb at 87° for 15 hours. The resulting dark orange reaction solution was evaporated *in vacuo* to dryness. Crystallization of the residue from water gave the crude product; yield 175 mg. (34%), m.p. 179–185°. The analytical sample was prepared by recrystallization from water and was dried over phosphorus pentoxide at 110° (0.8 mm.) for 72 hours; m.p. 190–191°, $[\alpha]^{32}D$ +9.1 ± 2.9° (0.48% in methanol); λ_{max} in mμ ($\epsilon \times 10^{-3}$): *p*H 1, 232 (32.0); *p*H 7, 226 (22.5), 257 (12.1), 331 (5.65); *p*H 13, 228 (20.8), 257 (11.5), 330 (5.80); $\tilde{\nu}$ in cm.$^{-1}$ (KBr): 3360 (OH); 1610, 1575 and 1550 (C=N, C=C); 1105 and 1050 (C–O–).

Anal. Calcd. for $C_{12}H_{17}N_5O_4$: C, 48.80; H, 5.80; N, 23.72. Found: C, 49.07; H, 5.67; N, 23.34.

2-Benzylthio-9-β-D-ribofuranosylpurine (X).—A solution of 510 mg. (1.78 mmoles) of 2-chloro-9-β-D-ribofuranosylpurine (IV) and 3.56 ml. of 1 *N* sodium benzyl mercaptide[2] in 80 ml. of methanol was heated under reflux for 1.25 hours; the cooled reaction solution was neutralized with 1 *N* hydrochloric acid and evaporated *in vacuo*. The residue was extracted several times with diethyl ether (4 × 75 ml.); concentration of the combined ether extracts gave the crude product. This compound could not be induced to crystallize but was purified by two precipitations from water, and then drying over phosphorus pentoxide at 100° (0.07 mm.) for 24 hours before analysis; m.p. 112–113°, $[\alpha]^{26}D$ +24.2 ± 2.2° (0.63% in methanol); λ_{max} in mμ ($\epsilon \times 10^{-3}$): *p*H 1, 232 (14.6), 253 (11.6), 304 (5.61); *p*H 7, 232 (17.4), 261 (10.3), 303 (7.60); *p*H 13, 259 (9.94), 303 (7.65); $\tilde{\nu}$ in cm.$^{-1}$ (KBr): 3420 (OH); 1605 and 1580 (C=N, C=C); 1105, 1080 and 1045 (C–O–).

Anal. Calcd. for $C_{17}H_{18}N_4O_4S$: C, 54.50; H, 4.87; N, 14.94. Found: C, 54.42; H, 5.09; N, 14.90.

2-Mercapto-9-β-D-ribofuranosylpurine (XI).—To a solution of 570 mg. (1.99 mmoles) of 2-chloro-9-β-D-ribofuranosylpurine (IV) in 100 ml. of methanol was added 10 ml. of 1 *N* methanolic sodium hydrogen sulfide; the solution was heated under reflux for 10 hours during which time a slow stream of hydrogen sulfide was passed through the reaction mixture. The cooled reaction mixture was neutralized with 1 *N* hydrochloric acid and filtered. The filtrate was evaporated *in vacuo* to dryness, and the residue was triturated with chloroform (4 × 50 ml.) to remove free sulfur. The residue was extracted with hot *n*-propyl alcohol (5 × 20 ml.), and the crude product was obtained by concentration of the alcoholic extracts; yield 351 mg. (62%). Several recrystallizations from methanol gave the pure material, which was dried at 110° (0.07 mm.) for 24 hours over phosphorus pentoxide before analysis; m.p. 200° dec.; λ_{max} in mμ ($\epsilon \times 10^{-3}$): *p*H 1, 247 (11.5), 291 (22.1); *p*H 7, 238 (12.6), 281 (12.8); *p*H 13, 238 (14.1), 273 (13.7), 329 (5.73); $\tilde{\nu}$ in cm.$^{-1}$ (KBr): 3400 (broad OH); 2800–2200 (acidic hydrogen); 1645 (unassigned); 1590 and 1520 (C=N, C=C); 1110, 1080 and 1055 (C–O–).

Anal. Calcd. for $C_{10}H_{12}N_4O_4S$: C, 42.23; H, 4.26; N, 19.72. Found: C, 42.01; H, 4.25; N, 19.89.

BIRMINGHAM 5, ALA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

A Novel Conversion of Derivatives of Oxindoles to Indoles[1]

BY ERNEST WENKERT, BRUCE S. BERNSTEIN AND JOHN H. UDELHOFEN

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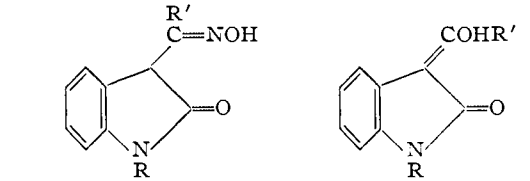
Catalytic hydrogenation of 3-acyloxindole oximes leads to 3-(α-aminoalkylidene)-oxindoles and 2-alkylindoles. Acetate treatment of the oximes also leads to indoles. The mechanisms of the reactions and their influence on the interpretation of intramolecular reaction processes in the oxindole field are discussed.

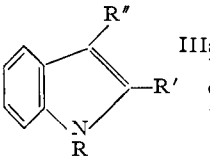
As part of continuing studies in the chemistry of oxindole[2] we have investigated the reported conversion of 3-phenylacetyloxindole oxime (Ia) into 3-(β-phenylethyl)-indole (IIIa).[2c] In order to ascertain the generality of such a transformation, several 3-acyloxindole oximes were exposed to hydrogenation with platinum in acetic acid. The starting materials were obtained by standard oximination of 3-(α-hydroxyalkylidene)-oxindoles (II) which, in turn, had been produced by base-catalyzed condensation of oxindole or N-methyloxindole with ethyl phenylacetate or ethyl acetate.

Whereas the catalytic hydrogenation of the oximes proceeded readily, it initially yielded exclusively 3-(α-aminoalkylidene)-oxindoles (IV). Even though this was not necessarily an unexpected result, being interpretable on the basis of hydrogenolysis of the N–O single bond followed by tautomeric change of the resulting imine, the uptake



Ia, R = H, R′ = $CH_2C_6H_5$
b, R = H, R′ = CH_3
c, R = CH_3, R′ = $CH_2C_6H_5$
d, R = CH_3, R′ = CH_3

II



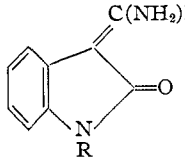
IIIa, R = R′ = H, R″ = $CH_2CH_2C_6H_5$
b, R = H, R′ = $CH_2C_6H_5$, R″ = CH_3
c, R = R″ = H, R′ = $CH_2C_6H_5$
d, R = R″ = H, R′ = CH_3
e, R = CH_3, R′ = $CH_2C_6H_5$, R″ = H

of more than one mole of hydrogen, later erratic yields of products and the general dependence of

(1) Presented before the 133rd Meeting of the American Chemical Society, San Francisco, Calif., April 13–18, 1958.

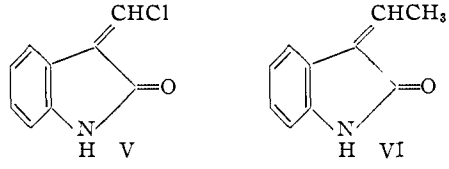
(2) (a) E. Wenkert, A. K. Bose and T. L. Reid, THIS JOURNAL, **75**, 5514 (1953); (b) E. Wenkert and T. L. Reid, *Chemistry and Industry*, 1390 (1953); (c) E. Wenkert and T. L. Reid, *Experientia*, **10**, 417 (1954); (d) E. Wenkert, N. K. Bhattacharyya, T. L. Reid and T. S. Stevens, THIS JOURNAL, **78**, 797 (1956).

the reaction on the nature of the catalyst suggested, as in a previous case of irreproducibility,[2a] a need for change of reaction conditions. When the hydrogenation was carried out with palladium–charcoal in ethanol, consistent results were obtained. The N-unsubstituted oxindoles Ia and b led to mixtures of indoles and enamines IVa and b, respectively. The N-methyl compounds Ic and d, however, yielded only enamines IVc and d, respectively.[3]



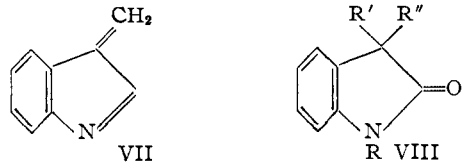
IVa, R = H, R′ = $CH_2C_6H_5$
b, R = H, R′ = CH_3
c, R = CH_3, R′ = $CH_2C_6H_5$
d, R = CH_3, R′ = CH_3

The structures of the enamine products (IV) became apparent from their elemental analysis, from the absence of any carbonyl absorption below 6 μ in their infrared spectra and from their characteristic ultraviolet absorption maxima at 272–277 mμ. For reference the ultraviolet spectrum of 3-(α-aminoethylidene)-oxindole (IVb) was compared with the spectra of 3-(α-hydroxyethylidene)-oxindole (IIb), 3-chloromethyleneoxindole[4] (V) and 3-ethylideneoxindole[5] (VI), prepared by hydrogenation of Ib with palladium–charcoal in ethanol followed by acid treatment[6] (*cf.* Fig. 1).



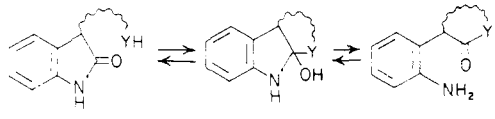
The structure of the indolic product from the hydrogenation of oxime Ia, originally assumed to be IIIa,[2a] was investigated next. While its ultraviolet and infrared spectra were characteristic of an indole, its melting point differed from that reported for IIIa.[7] However, since the latter's previous synthesis, an interaction of gramine methiodide with benzylmagnesium chloride, could have led to either 2-benzyl-3-methylindole (IIIb) or 3-(β-phenylethyl)-indole (IIIa) by way of 1,2- or 1,4-addition to the intermediate methyleneindolenine (VII), an unambiguous synthesis of IIIa was required. Hydrogenation of IIa over platinum-in-acetic acid yielded 3-(β-phenylethyl)-oxindole (VIII), which was reduced to the indole IIIa by sodium and butanol. The physical properties of this substance were identical with those reported by Snyder[7] but different from the product of reduction of the oxime.

The first indication that the latter was perhaps a 2-alkylindole was the observation that its alcohol was quite unstable in air in contrast to a solution of IIIa. This fact as well as a mechanistic interpretation of the reaction path (see below) led to the suspicion that the product was 2-benzylindole (IIIc). A comparison of the compound with an authentic sample[8] verified this supposition. The indolic product of the hydrogenation of Ib was also shown to be 2-methylindole (IIId) by comparison with an authentic specimen.

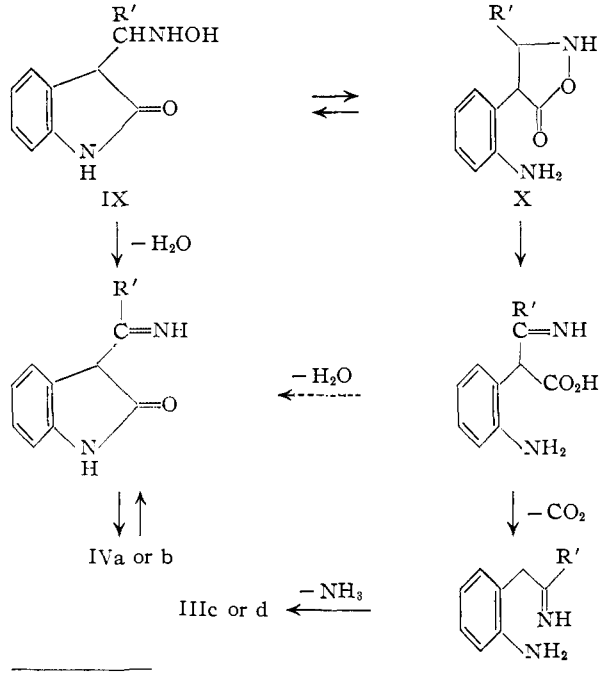


a, R = R′ = H, R″ = $CH_2CH_2C_6H_5$
b, R = R′ = H, R″ = Et
c, R = R′ = R″ = H
d, R = H, R′ = R″ = CH_2CN
e, R = R′ = H, R″ = CH_2CN
f, R = $COCH_2C_6H_5$, R′ = H, R″ = CH_2CN
g, R = $COCH_3$, R′ = R″ = H

The formation of the indoles, involving obviously an extraordinary rearrangement, appeared to be another example of previously described[2c] intramolecular oxindole ring openings. 3-Substituted oxindoles, containing a hetero atom Y on their sidechain located a suitable number of atoms away from the oxindole carbonyl group, are susceptible to ready ring cleavage. This prerequisite for



intramolecular interaction was satisfied in the primary reduction products (IX) of the oximes Ia and b, if not in the oximes themselves. Thus, the formation of the dihydroisoöxazolone X and its subsequent predictable breakdown[9] represent a reasonable mechanistic rationale of the rearrange-



(3) An analogous study has been made of the oximes of 3-hydroxymethyleneoxindole and its N-methyl derivative. Their slightly different behavior will be described in a future communication.

(4) H. Behringer and H. Weissauer, *Chem. Ber.*, **85**, 743 (1952).

(5) (a) L. Horner, *Ann.*, **548**, 117 (1941); (b) H. Kondo, T. Nozoye and M. Tobita, *Ann. Reports Itsuu Lab.*, **1**, 32 (1950).

(6) *Cf.* P. L. Julian and H. C. Printy, THIS JOURNAL, **75**, 5301 (1953).

(7) H. R. Snyder, E. L. Eliel and R. E. Carnahan, *ibid.*, **73**, 970 (1951).

(8) G. R. Clemo and J. C. Seaton, *J. Chem. Soc.*, 2582 (1954).

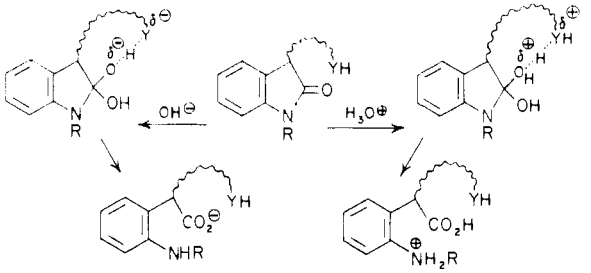
(9) For previous examples of this process *cf.* G. Shaw, *ibid.*, 1019 (1951), and references cited therein.

ment. The lack of indole production in the N-methyloxindole cases (Ic and d) can be ascribed to a slower rate of conversion of IX into X, due to the greater steric requirements of the carbonyl addition intermediate and, hence, a more favorable competitive removal of IX toward IV.

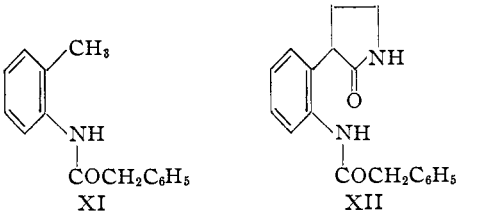
In an attempt to synthesize IX for a more precise study of the mechanism of the reaction, 3-ethylideneoxindole (VI) was treated with hydroxylamine at various *p*H's, but the product in every case was 3-ethyloxindole (VIIIb). Although the synthesis thus failed, *this reaction appears to represent the first instance of the reduction of an α,β-unsaturated carbonyl system by hydroxylamine.*

The ease of the above rearrangement under reducing conditions suggested that the oximes I could be converted to indoles also under hydrolytic conditions, able to remove the rigidity of the oxime multiple bond. This prediction was validated when it was shown that refluxing the oximes Ia, b and c with potassium acetate solution transformed them into indoles IIIc, d and e. Since this treatment was similar to the reaction conditions employed in the initial production of the oximes I from their 3-acyloxindole (II) precursors, it was of interest to ascertain whether indoles were side-products of the oximination process. Indeed, careful work-up of the reaction involving the conversion of IIb to Ib led to a small amount of IIId. To ensure that the indole was a hydrolysis product of the oxime and not of the 3-acyloxindole, the latter (IIb) was exposed to 5% hydrochloric acid hydrolysis as well as 5% sodium hydroxide hydrolysis. The former led merely to a recovery of starting material, while the alkaline hydrolysis gave the *retro*-Claisen product, oxindole (VIIIc).

While the hydrolytic conversions of oxindoles to indoles bear a formal resemblance to the reductive transformations, their mechanistic pathways need not be the same. Although the ease of opening of the oxindole nucleus must still be due to the participation of the sidechain hetero atom in the hydrolytic process, its initial action need not be an addition to the lactam carbonyl group. An alternative role for the hetero atom in its great enhancement of the rate of hydrolysis of the oxindole ring[2c] would appear to be its facility to solvate internally the hydration intermediates and hence lower the activation energy of the reaction; *e. g.*



In connection with other oxindole studies another intramolecular ring opening was encountered which is worth mentioning at this time.[10] When an acetone solution of 3-phenylacetyloxindole enol (IIa), anhydrous potassium carbonate and excess chloroacetonitrile was refluxed for 48 hours, 3,3-dicyanomethyloxindole (VIIId) was obtained. A similar treatment with an equimolar quantity of the halide for 17 hours led to 3-cyanomethyloxindole (VIIIe).[11] Finally, reaction of the same starting materials for six hours resulted in the formation of 1-phenylacetyl-3-cyanomethyloxindole (VIIIf). The structure of the last product became evident from a comparison of its spectra with those of 1-acetyloxindole (VIIIg).[12] Catalytic hydrogenation of VIIIf gave a neutral product whose infrared spectrum indicated a structure other than an N-acyloxindole. Its elemental analysis and the similarity of its ultraviolet spectrum to that of phenylacetyl-*o*-toluide (XI) proved it to be XII. Thus the aminoethyl group, produced by reduction of the cyano function, had interacted with the oxindole carbonyl linkage, ruptured the oxindole nucleus and formed a pyrrolidone.



In order to ascertain whether the above alkylation of a 3-acyloxindole could be a general synthesis of 3-alkyloxindoles, 3-acetyloxindole enol (IIb) was treated with various halides. The results, however, were not too encouraging.[13,14]

Acknowledgment.—The authors express their sincere thanks to the Upjohn Co. and the National Institutes of Health, Department of Health, Education and Welfare (M-1301), for generous financial support and to the Institute for Atomic Research, Ames, Iowa, for the use of a Baird infrared spectrophotometer.

Experimental

3-(α-Hydroxyalkylidene)-oxindoles (II).—A slurry of the oxindole and ethyl ester was added to a warm sodium ethoxide solution, prepared from sodium and absolute ethanol. The mixture was refluxed for two hours, cooled and neutralized with dilute hydrochloric acid. The resulting precipitate was filtered, washed with cold ethanol and water, dried and crystallized from dilute ethanol.

From 5.0 g. (38 mmoles) of oxindole, 8.0 g. (49 mmoles) of ethyl phenylacetate and a solution made from 1.1 g. (49 mmoles) of sodium in 13 ml. of absolute ethanol there were obtained 8.5 g. (90%) of 3-(α-hydroxyphenylethylidene)-oxindole (IIa), m.p. 195–197°. Crystallization from dilute ethanol gave white, fluffy needles, m.p. 207°; spectra:

(10) The major phase of the continuing discussion pertains to work carried out by E. W. at Harvard University (*cf.* E. Wenkert, Ph.D. dissertation Harvard, 1951). The authors are most grateful to Professor Woodward for permitting the inclusion of the results of this investigation, and E. W. wishes to express his sincere appreciation to Professor Woodward for his generous guidance of the progress of the work.

(11) J. W. Cornforth, R. H. Cornforth, C. E. Dagliesh and A Neuberger, *Biochem. J.*, **48**, 591 (1951).

(12) W. Suida, *Ber.*, **12**, 1326 (1879).

(13) For details inspect the Experimental section.

(14) Reduction of 3-cyanomethyloxindole (XId) could lead to oxytryptamine. However, no such studies were pursued beacuse of similar investigations in other laboratories (J. Harley-Mason, private communication; J. B. Hendrickson, Ph.D. dissertation, Harvard, 1954). Since the completion of this manuscript there appeared a paper by K. Freter, H. Weissbach, B. Redfield, S. Udenfriend and B. Witkop [THIS JOURNAL, **80**, 983 (1958)] which illustrates further examples of the processes described above.

ultraviolet (95% ethanol), λ_{max} 267 mμ (log ε 4.20) and 310 mμ (log ε 3.92); infrared (Nujol), C=O 6.02(s) μ.

Anal. Calcd. for $C_{16}H_{13}O_2N$: C, 76.5; H, 5.22; N, 5.58. Found: C, 76.24; H, 5.12; N, 5.26.

Horner's procedure,[5a] modified by the use of continuous stirring of the reaction mixture, gave a 72% yield of 3-(α-hydroxyethylidene)-oxindole (IIb), m.p. 205° (lit.[5a] m.p. 203°).

Phenylacetylation of 4.0 g. of 1-methyloxindole gave 5.4 g. (75%) of 1-methyl-3-(α-hydroxyphenylethylidene)-oxindole (IIc), m.p. 147°; spectra: ultraviolet (95% ethanol), λ_{max} 269 mμ (log ε 4.34) and 305 mμ (log ε 4.01); infrared (Nujol), C=O 6.07(s) μ.

Anal. Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70; N, 5.29. Found: C, 77.00; H, 5.43; N, 5.1.

Julian's method[15] led to a 77% yield of 1-methyl-3-(α-hydroxyethylidene)-oxindole (IId), m.p. 113–114° (lit.[15] m.p. 109°).

3-Acyloxindole Oximes (I).—An absolute ethanol solution of a 1:1.1 mixture of 3-(α-hydroxyalkylidene)-oxindole and hydroxylamine, prepared from hydroxylamine hydrochloride and sodium acetate, was refluxed for two hours. After removal of the inorganic salts by filtration, vacuum concentration of the filtrate and addition of a small quantity of water to the latter, the product was filtered, washed with water and recrystallized from dilute ethanol.

Compound IIa (2.5 g.) was converted to 2.2 g. (83%) of colorless 3-phenylacetyloxindole oxime (Ia), m.p. 180°; spectra: ultraviolet (95% alcohol), λ_{max} 254 mμ (log ε 3.89); infrared (Nujol), C=O 5.87(s) μ.

Anal. Calcd. for $C_{16}H_{14}O_2N_2$: C, 72.2; H, 5.30; N, 10.53. Found: C, 72.24; H, 5.47; N, 10.28.

Oximination of 1.0 g. of IIb gave 0.82 g. (76%) of crystalline 3-acetyloxindole oxime (Ib), m.p. 180–181°.

Anal. Calcd. for $C_{10}H_{10}O_2N_2$: C, 63.14; H, 5.30; N, 14.7. Found: C, 63.27; H, 5.48; N, 14.4.

Conversion of 3.2 g. of IIc to its oxime led to 2.9 g. (76%) of 1-methyl-3-phenylacetyloxindole oxime (Ic), m.p. 156°.

Anal. Calcd. for $C_{17}H_{16}O_2N_2$: C, 72.83; H, 5.75; N, 10.0. Found: C, 72.59; H, 5.64; N, 9.9.

Oximination of 3.85 g. of IId yielded 3.0 g. (73%) of 1-methyl-3-acetyloxindole oxime (Id), colorless crystals, m.p. 167°.

Anal. Calcd. for $C_{11}H_{12}O_2N_2$: C, 64.69; H, 5.93; N, 13.7. Found: C, 64.94; H, 6.04; N, 14.0.

Catalytic Hydrogenation of the Oximes.—An ethanol solution of the oxime (1.00 g. in 50 ml.) was hydrogenated over palladium–charcoal (10%, by weight, of the oxime) at atmospheric pressure. When hydrogen uptake had ceased, the catalyst was filtered, the solvent evaporated at a low temperature and the residue chromatographed on alumina.

Reduction of 1.00 g. of Ia led to 200 mg. (26%) of 2-benzylindole (IIIc), m.p. 84° (eluted with petroleum ether), identical in m.p., mixed m.p., ultraviolet and infrared spectra with an authentic sample,[8] and to 375 mg. (40%) of 3-(α-amino-β-phenylethylidene)-oxindole (IVa), m.p. 181–182° (eluted with chloroform). Crystallization of the latter from dilute ethanol gave colorless crystals, m.p. 195°; spectra: ultraviolet (95% ethanol), λ_{max} 274 mμ (log ε 4.24) and 338 mμ (log ε 4.10); infrared ($CHCl_3$), NH 2.92(m) μ, C=O 6.04(s) μ.

Anal. Calcd. for $C_{16}H_{14}ON_2$: C, 76.80; H, 5.60; N, 11.20. Found: C, 76.91; H, 5.33; N, 11.09.

Hydrogenation of 100 mg. of Ib yielded 15 mg. (21%) of 2-methylindole (IIId), m.p. 61° (eluted with petroleum ether), identical in m.p., mixed m.p., ultraviolet and infrared spectra with an authentic specimen[8]; and 60 mg. (66%) of 3-(α-aminoethylidene)-oxindole (IVb), m.p. 225° (eluted with chloroform); spectra: ultravioet (95% ethanol), λ_{max} 272 mμ (log ε 4.23) and 330 mμ (log ε 4.03); infrared ($CHCl_3$), NH 2.92(m) μ, C=O 6.03(s) μ.

Anal. Calcd. for $C_{10}H_{10}O_2N$: C, 68.94; H, 5.79; N, 16.08. Found: C, 68.89; H, 5.80; N, 15.9.

Reduction of 500 mg. of Ic gave 450 mg. (96%) of colorless 1-methyl-3-(α-amino-β-phenylethylidene)-oxindole (IVc) which on crystallization from dilute ethanol melted at 176°; spectra: ultraviolet (95% ethanol), λ_{max} 277 mμ (log ε 4.31) and 318 mμ (log ε 4.15); infrared ($CHCl_3$), NH 2.92 (m) μ, C=O, 6.10(s) μ.

Anal. Calcd. for $C_{17}H_{16}ON_2$: C, 77.24; H, 6.12; N, 10.6. Found: C, 77.49; H, 6.24; N, 10.3.

Hydrogenation of 50 mg. of Id resulted in 40 mg. (90%) of colorless 1-methyl-3-(α-aminoethylidene)-oxindole (IVd) whose m.p. after crystallization from dilute ethanol was 205°; spectra: ultraviolet (95% ethanol), λ_{max} 275 mμ (log ε 4.38) and 320 mμ (log ε 4.17); infrared ($CHCl_3$), NH 2.85(m) μ, C=O 6.10(s) μ.

Anal. Calcd. for $C_{11}H_{12}ON_2$: C, 70.26; H, 6.39; N, 14.89. Found: C, 70.54; H, 6.3; N, 14.9.

3-(β-Phenylethyl)-indole (IIIa).—Two grams of 3-phenylacetyloxindole enol (IIa) in 100 ml. of glacial acetic acid was hydrogenated over 150 mg. of platinum oxide. When the reduction had stopped after a 250-ml. uptake of hydrogen, the catalyst was filtered, the filtrate neutralized with 10% sodium bicarbonate solution, extracted three times with chloroform and the extracts dried over anhydrous sodium sulfate. Removal of the solvent left a semi-solid residue, which gave a positive ferric chloride test, and whose benzene washings were concentrated and chromatographed on alumina. Elution with 1:1 benzene–ether gave a clear oil whose 252 mμ ultraviolet absorption maximum agreed well with the one expected for 3-(β-phenylethyl)-oxindole (VIIIa).

One gram of sodium was added in several small portions to a 1-butanol solution (25 ml.) of 275 mg. of VIIIa. After dissolution of all sodium, the mixture was cooled, water added, the butanol removed under vacuum and the aqueous residue extracted with ether. Removal of the solvent, after drying of the ether extracts over sodium sulfate, gave 100 mg. (39%) of residue which crystallized on standing, m.p. 116–118°. Recrystallization from dilute ethanol produced pure 3-(β-phenylethyl)-indole (IIIa), m.p. 119–120°, identical in m.p., mixed m.p., infrared and ultraviolet spectra with an authentic sample prepared in 86% yield by the Snyder method.[7]

3-Ethyloxindole (VIIIb).—Two grams of 3-acetyloxindole enol (IIb) in 50 ml. of absolute ethanol was hydrogenated over 1 g. of 5% palladium–charcoal. After cessation of hydrogen uptake, filtration of the catalyst and concentration of the filtrate *in vacuo* the oily residue was chromatographed on alumina. Benzene elution gave 1.5 g. (82%) of a yellow solid, m.p. 130–132°. Recrystallization from benzene gave 3-ethylideneoxindole (VI), m.p. 142° (lit.[5a] m.p. 140°); spectra: ultraviolet, *cf.* Fig. 1; infrared (CCl_4), C=O 5.88(s) μ, C=C 6.09(m) μ.

A solution of 100 mg. of VI, 40 mg. of hydroxylamine hydrochloride and 88 mg. of potassium acetate in 25 ml. of absolute ethanol was refluxed for three hours. After filtration of the inorganic salts the solvent was removed *in vacuo* and the residue chromatographed on alumina. Elution with ether gave 40 mg. of crystals. Crystallization from benzene–petroleum ether yielded 3-ethyloxindole (VIIIb), m.p. 104° (lit. value[5a] m.p. 104°); infrared spectrum ($CHCl_3$), C=O 5.82(s) μ.

Similar runs, however, with adjustment of the *p*H to approximately 10 by the addition of solid sodium hydroxide or by acidification by the addition of acetic acid and a trace of *p*-toluenesulfonic acid, led to similar results.

Oxime Hydrolyses.—A solution of 500 mg. of 3-phenylacetyloxindole oxime (Ia) and 500 mg. of potassium acetate in 35 ml. of ethanol was refluxed for six hours. After filtration of the inorganic salts the solution was concentrated and the brown gummy residue chromatographed on alumina. Elution with petroleum ether yielded 100 mg. (25%) of 2-benzylindole (IIIc), m.p. 84°, identical in m.p., mixed m.p. and spectra with a sample above.

A similar procedure with 1-methyl-3-phenylacetyloxindole oxime (Ic) led to a 14% yield of 1-methyl-2-benzylindole (IIIe), m.p. 60° (lit.[16] m.p. 60°); picrate, m.p. 97° (lit.[16] m.p. 97°).

A solution of 6.0 g. of 3-acetyloxindole enol (IIb), 3.0 g. of hydroxylamine hydrochloride and 6.0 g. of potassium acetate in 100 ml. of ethanol was refluxed for 15 hours. After the usual work-up of an oximination reaction the brown oily product was chromatographed on alumina, leading in the petroleum ether eluate to 1.5 g. (34%) of 2-methylindole (IIId), m.p. 60°, identical in all respects with the sample above.

(15) P. Julian, J. Pikl and F. Wantz, THIS JOURNAL, **57**, 2026 (1935).

(16) P. L. Julian and J. Pikl, *ibid.*, **55**, 2105 (1933).

Hydrolyses of 3-(α-Hydroxyethylidene)-oxindole (IIb).—A mixture of 1 g. of IIb and 15 ml. of 5% HCl solution was refluxed for two hours. After cooling of the reaction mixture the entire starting material could be recovered.

A solution of 1 g. of IIb in 15 ml. of 5% aqueous sodium hydroxide was refluxed for two hours. Cooling of the solution and neutralization with dilute HCl gave 700 mg. (92%) of oxindole, m.p. 126°.

Alkylations of IIa.—A mixture of 2.88 g. of IIa, 2–3 g. of chloroacetonitrile, 5 g. of fused sodium iodide and 5 g. of anhydrous potassium carbonate was refluxed for 48 hours. The mixture was concentrated under vacuum to a quarter its volume, water added, the solution extracted with ether and the extracts dried over sodium sulfate. Evaporation of the solvent gave a white, crystalline solid, m.p. 206–208°, which after two crystallizations amounted to 1.9 g. (37%) of 3,3-dicyanomethyloxindole (VIIId), m.p. 209–210°; spectra: ultraviolet (95% ethanol), λ_{max} 251 mμ (log ε 4.04) and 286 mμ (log ε 3.87); infrared ($CHCl_3$), C≡N 4.48(w) μ, C=O 5.82(s) μ.

Anal. Calcd. for $C_{12}H_9ON$: C, 68.3; H, 4.29. Found: C, 68.14; H, 4.39.

A similar reaction carried out with a 1:1 molar ratio of IIa and chloroacetonitrile for 17 hours yielded an oil which on high vacuum sublimation, followed by benzene trituration was converted to a solid, m.p. 159–162°. Crystallization from benzene gave a 17% yield of 3-cyanomethyloxindole (VIIIe), m.p. 163–164° (lit. m.p. 162–165°); spectra: ultraviolet (95% ethanol), λ_{max} 252 mμ (log ε 3.92) and 285 mμ (log ε 3.12); infrared ($CHCl_3$), C≡N 4.51(w) μ, C=O 5.80(s) μ.

A six-hour run of the last reaction led to crystals which on repeated crystallizations from benzene gave a 43% yield of 1-phenylacetyl-3-cyanomethyloxindole (VIIIf), m.p. 154–155°; spectra: ultraviolet (95% ethanol), λ_{max} 229 mμ (log ε 4.20); infrared ($CHCl_3$), C=O 5.65(s) μ, 5.85(s) μ.

Anal. Calcd. for $C_{18}H_{14}O_2N_2$: C, 74.4; H, 4.86; N, 9.66. Found: C, 74.9; H, 4.91; N, 9.93.

A mixture of 63 mg. of platinum oxide and 1.05 g. of VIIIf in 20 ml. of glacial acetic acid and 2 ml. of ethanol was hydrogenated at atmospheric pressure. Filtration of the catalyst and vacuum removal of the solvent led to a gummy residue which was sublimed. Trituration of the sublimate with benzene yielded a solid product. Crystallization from benzene gave 270 mg. (25% yield) of crystalline 3-(β-phenylacetamidophenyl)-2-pyrrolidone (XII), m.p. 162–163°; spectra: ultraviolet (95% ethanol), $\lambda_{shoulder}$ 240–250 mμ (log ε 3.90–3.85); infrared ($CHCl_3$), C=O 5.95(s) μ.

Anal. Calcd. for $C_{18}H_{18}O_2N_2$: C, 73.4; H, 6.18; N, 9.52. Found: C, 73.41; H, 6.28; N, 9.41.

Alkylations of IIb.—A mixture of 5.0 g. of IIb, 10 g. of dry potassium carbonate and 2 ml. of methyl iodide in 100 ml. of dry acetone was refluxed for four hours. Water was added to the cooled mixture, acetone removed under vacuum, the aqueous residue extracted with ether and the organic extracts dried over anhydrous magnesium sulfate. Evaporation of the solvent left a red oil which on ether elution from an alumina chromatogram gave 2.0 g. (48%) of a solid, m.p. 115–120°. Crystallization from ether–petroleum ether yielded crystalline 3-methyloxindole, m.p. 124° (lit.[5a] 123°). Chloroform elution led to 100 mg. of a solid, m.p. 135–145°, which on crystallization from ethyl acetate resulted in 3,3-dimethyloxindole, m.p. 150° (lit.[17] 152–153°).

A 30-hour run with isopropyl iodide led to recovery of two-thirds of IIb and a 50% yield (based on recovered IIb) of 3-isopropyloxindole, m.p. 110°.[2d]

A six-hour run with chloroacetonitrile gave a 50% yield of 3-cyanomethyloxindole (VIIIe), m.p. 163° (*vide infra*).[18]

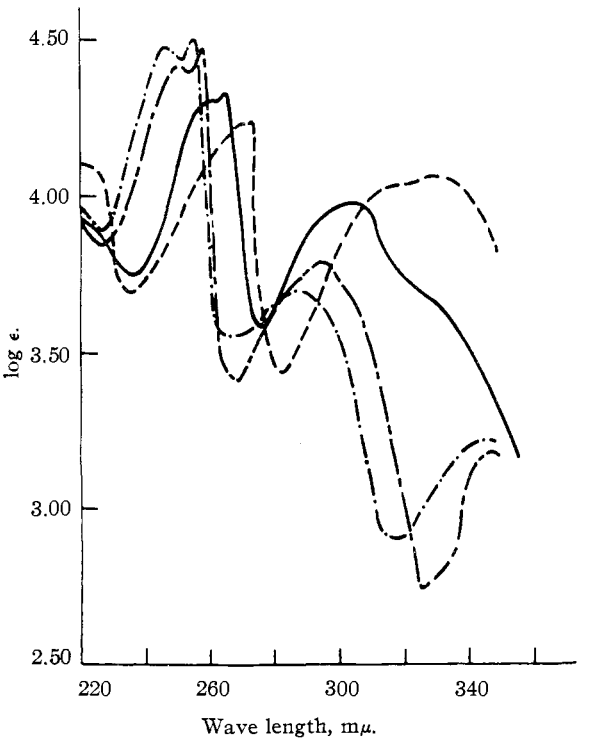


Fig. 1.—Ultraviolet spectra of: ———, 3-(α-hydroxyethylidene)-oxindole; - - - -, 3-(α-aminoethylidene)-oxindole; — — —, 3-chloromethyleneoxindole; —·—·—, 3-ethylideneoxindole. These spectra were run on 95% alcohol solutions on a Beckman DU spectrophotometer.

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(17) K. Brunner, *Monatsh.*, **18**, 98 (1897).

(18) This reaction was worked out initially by Dr. N. K. Bhattacharyya in this Laboratory.