3*H*-Indol-3-ols by a Novel Ring Contraction

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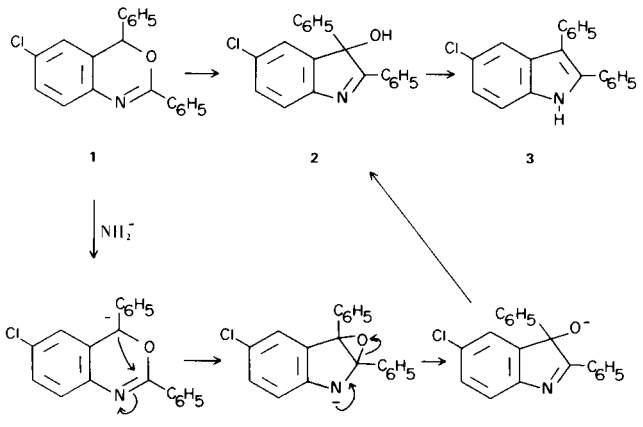
Treatment of α-hydroxy-α-phenyl-*o*-toluidide with phosphorus tribromide afforded a series of 4*H*-3,1-benzoxazines. These last, when reacted with potassium amide in liquid ammonia, ring contracted to 2,3-disubstituted 3*H*-indol-3-ols. The scope of this rearrangement was examined. The indolols on treatment with hot base were found to rearrange to indoxyls. Several of these as well as their *N*-alkylation products are described.

In the course of an investigation of the chemistry of 4*H*-3,1-benzoxazines we had occasion to attempt alkylation of **1** by means of potassium amide in liquid ammonia followed by benzyl chloride. There was obtained on workup a solid product clearly different from starting material. The nmr spectrum of this, while not very informative, did show that this product was not the hoped for benzylated material. Elemental analysis and the mass spectrum showed the unknown to be isomeric with starting material. Treatment with acetic anhydride in pyridine gave a derivative whose ir (max 1750 cm^{-1}) and nmr (singlet at 2.08 δ) spectra indicated an *O*-acetate. Catalytic reduction of the rearrangement product over palladium on charcoal gave 5-chloro-2,3-diphenylindole identical in all respects with an authentic sample (1). These data permit the formulation of the product of the amide reaction as the 3*H*-indol-3-ol, **2**. Though the corresponding 2,3-dialkyl compounds have received considerable attention as products of the air oxidation of indoles (2-6) the diaryl compounds appear not to have been hitherto prepared.

Scheme I



Formation of the indolol can be rationalized as in Scheme I. The reaction is initiated by abstraction of the acidic benzhydryl proton, an assumption borne out by the observation of a transient deep color; the resulting carbanion then adds intramolecularly to the electrophilic imino-ether. "Return" of the electron pair with consequent opening of the oxirane leads to the alkoxide of the observed product; this is neutralized in the course of the workup. With this information at hand, we undertook a study of the scope of this novel rearrangement.

Preparation of Starting Materials.

The requisite 4*H*-3,1-benzoxazines were readily pre-

Scheme II

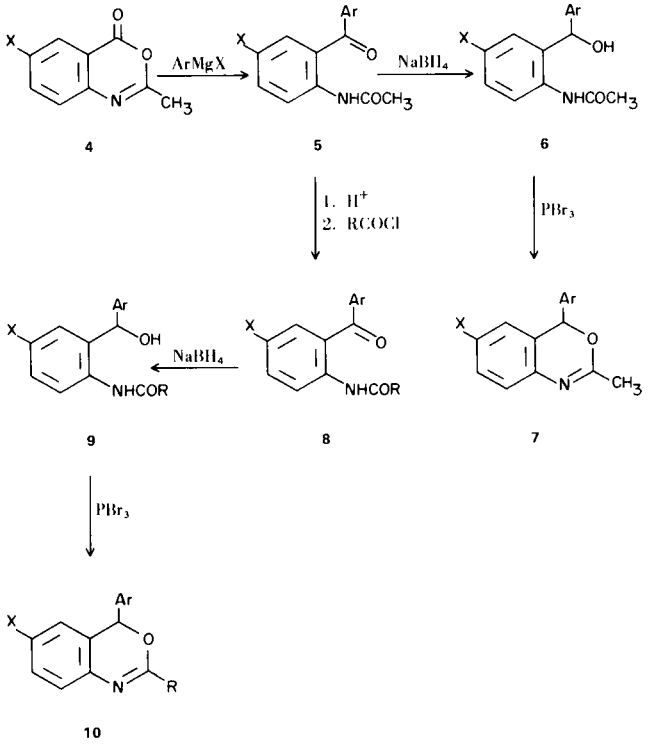
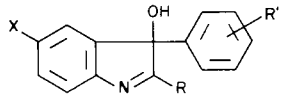


TABLE I

3*H*-Indol-3-ols

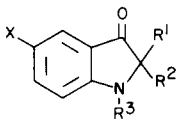


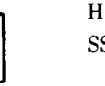
X	R	R′	Chromat. (a) Solv.	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
Cl	CH_3	H	5% Me_2CO	C_6H_{12}	166-176.5	31	$C_{15}H_{12}ClNO$	69.90	4.70	69.83	4.82
Cl	C_6H_5	H	---	EtOAc-C_6H_{12}	223-223.5	58	$C_{20}H_{14}ClNO$	75.11	4.41	74.91	5.07
H	CH_3	H	5,10% Me_2CO	EtOAc	189-191	59	$C_{15}H_{13}NO$	80.69	5.87	80.66	5.89
H	C_6H_5	H	---	MeOH-H_2O	197-199	56	$C_{20}H_{15}NO$	84.18	5.30	84.10	5.18
H	*p*-$CH_3OC_6H_4$	H	---	CH_3CN	225-227	71	$C_{21}H_{17}NO_2$	79.98	5.43	80.01	5.25
H	*p*-$CH_3OC_6H_4$	*p*-OCH_3	---	MeOH	197-198	49	$C_{22}H_{19}NO_3$	76.50	5.55	76.37	5.51
H	$C(CH_3)_3$	H	---	SSB (b)	160-162	38	$C_{18}H_{19}NO$	81.47	7.22	81.19	7.04
H	CH_3	*m*-CF_3	5,10% Me_2CO	Me_2CO:SSB	148-149	23	$C_{16}H_{12}F_3NO$	65.97	4.15	65.83	4.33
H	C_6H_5	*m*-CF_3	---	Me_2CO:SSB	206-208	10 (c)	$C_{21}H_{14}F_3NO$	71.38	3.99	71.08	3.88
H	C_6H_5	*p*-CH_3	---	MeOH	208-212	--	$C_{21}H_{17}NO$	84.25	5.72	83.95	5.66

(a) Chromatography solvent, percentage acetone of an acetone:Skellysolve B mixture. (b) Skellysolve B; a petroleum fraction of b.p. 60-70° marketed by the Skelly Oil Co. (c) Based on amidoalcohol.

TABLE II

Indoxyls

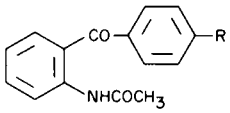


X	R′	R^2	R^3	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
H	C_6H_5	C_6H_5	H	Me_2CO:SSB	177-178 (a,b)	79	$C_{20}H_{15}NO$	84.18	5.30	84.29	6.36
Cl	CH_3	C_6H_5	H	H_2O-MeOH	154-155.5 (c)	76	$C_{15}H_{12}ClNO$	69.90	4.70	69.85	5.11
H	C_6H_5	C_6H_5	CH_2CH_2N 	SSB	132-134	79	$C_{26}H_{26}N_2O$	8a.64	6.85	81.67	6.90
H	C_6H_5	C_6H_5	$(CH_2)_3N(CH_3)_2$	SSB	101-105	35	$C_{25}H_{26}N_2O$	81.04	7.07	81.20	7.09
Cl	CH_3	C_6H_5	$(CH_2)_3N(CH_3)_2$	CH_2Cl_2:EtOAc	143-146	85	$C_{20}H_{24}ClIN_2O$ (d)	51.02	5.14	51.23	4.94

(a) Lit. (10) m.p. 185-186. (b) λ max 237 (31,300), 404 (3600). (c) λ max 235 (31,500), 409 (3650). (d) Isolated as the hydroiodide.

TABLE III

o-Aroylacetanilides



R-	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
m-CF_3	SSB	89-91	25	$C_{16}H_{12}F_3NO_2$	62.54	3.94	62.85	3.89
p-F	SSB	85.5-87.5	29	$C_{15}H_{12}FNO_2$	70.03	4.70	69.95	4.90
p-CH_3	Et_2O:SSB	113-115.5 (a)	48 (a)	$C_{16}H_{15}NO_2$	75.87	5.97	75.76	5.77

(a) Lit. m.p. 114-116°; J. Moszew and A. Inasinski, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, 9, 303 (1961).

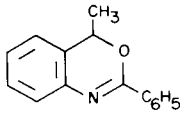
pared by the general route depicted in Scheme II. Reaction of the benzoxazinones **4** with the appropriate aryl Grignard reagents (7) gave the *o*-aroylacetanilides **5**. Reduction of these compounds to the α-hydroxy-α-aryltoluidides was effected smoothly by means of sodium borohydride.

Hydrolysis of the acetanilides **5** followed by re-acylation gave the amides represented by **8**. These too, were reduced by means of sodium borohydride.

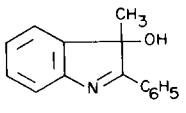
Cyclization of the α-hydroxy-α-aryl-σ-toluidide **9** (Ar = R = C_6H_5, X = H) by means of hydrogen bromide has been reported (8). We found the same transformation to be effected in good yield by means of phosphorus tribromide in chloroform in the cold. In general, the arylanilides **9** gave good yields of the benzoxazines; in contrast to this, the acetanilides **6** as a rule gave low yields of the often non-crystalline benzoxazines. When the products failed to crystallize they were used in the rearrangement reaction directly as obtained from chromatographic purification; in a few cases, the total crude cyclized product was subjected to rearrangement conditions.

Rearrangement Reaction.

After some preliminary experiments the standard procedure for effecting the rearrangement was adopted. This consisted in adding a solution of the benzoxazine in tetrahydrofuran to a solution of one equivalent of freshly prepared potassium amide in liquid ammonia. Following ten minutes' reaction time, the mixture was neutralized with ammonium chloride. In those cases where R was an aryl group (**10**, R = aryl) the product could be isolated by direct crystallization. The yields from the rearrangement of the methylated benzoxazines **7** tended to be lower; in these cases chromatography had to be employed in the isolation of the product. We consider it not unlikely that ionization of the methyl protons competes with that of the benzhydryl proton, to lead to side reactions. Results of these experiments are summarized in Table I.



11



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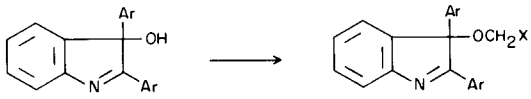
When the lability of the benzylic proton is reduced by replacement of the phenyl by methyl as in compound **11** (9) the rearrangement still proceeds albeit very slowly; at the end of three hours' reaction time only 5% of product was obtained along with large amounts of starting material.

Chemistry of the 3*H*-Indol-3-ols.

Treatment of the indolol **13** or **14** with an equivalent of sodium hydride followed by either benzyl bromide or ethyl bromoacetate (followed by hydrolysis) led in each case to the straightforward product of *O*-alkylation.



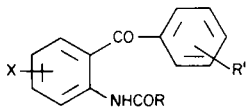
13 Ar = C_6H_5
14 Ar = *p*-$CH_3OC_6H_4$

15 Ar = C_6H_5; X = CO_2H
16 Ar = C_6H_5; X = C_6H_5
17 Ar = *p*-$CH_3OC_6H_4$; X = CO_2H

In marked contrast to this, alkylation of the anion of **13** with *N*-(β-chloroethyl)pyrrolidine afforded a bright yellow product characterized by a strong u.v. absorption band at 404 mμ. It was subsequently found that treatment of **13** at reflux in the presence of methanolic sodium hydroxide leads to the indoxyl **18**. Alkylation of this last

TABLE IV

2-Aroylanilides

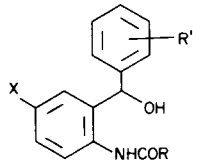


X	R	R'	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
Cl	C_6H_5	H	Et_2O	104-106 (a)	72	$C_{20}H_{14}ClNO_2$	---	---	---	---
H	C_6H_5	H	MeOH	85-88 (b)	92	$C_{20}H_{15}NO_2$	---	---	---	---
H	p-$C_6H_4OCH_3$	p-OCH_3	CH_2Cl_2:MeOH	134-136	77	$C_{22}H_{19}NO_4$	73.11	5.30	73.31	5.74
H	$C(CH_3)_3$	H	SSB	81.5-83.5	81	$C_{18}H_{19}NO_2$	76.84	6.81	76.93	7.01
H	p-$C_6H_4OCH_3$	p-OCH_3	MeOH	94-98	86	$C_{21}H_{17}NO_3$	---	---	---	---
H	C_6H_5	m-CF_3	MeOH	145-147	91	$C_{21}H_{14}F_3NO_2$	68.29	3.82	68.32	4.08
H	C_6H_5	p-CH_3	MeOH	85-87	80	$C_{21}H_{17}NO_2$	79.98	5.43	79.38	5.67

(a) Lit. m.p. 108°; K. Dziewonski and L. Sternbach, *Bull. Intern. Acad. Polonaise, Classe Sci. Math. Nat.*, A, 333 (1935). (b) Lit. m.p. 118-119°; C. Mentzer, D. Molho and Y. Berguer, *Bull. Soc. Chim. France*, 55 (1950).

TABLE V

α-Hydroxy-α-aryl-*o*-toluidides

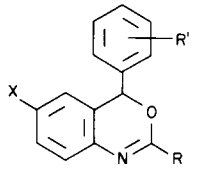


X	R	R'	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
Cl	CH_3	H	EtOAc·C_6H_{12}	134-135.5	88	$C_{15}H_{14}ClNO_2$	---	---	---	---
Cl	C_6H_5	H	EtOAc·C_6H_{12}	153.5-154	90	$C_{20}H_{16}ClNO_2$	71.11	4.78	70.96	4.92
H	C_6H_5	H	Me_2CO:SSB	117-118 (a)	90	$C_{20}H_{17}NO_2$	---	---	---	---
H	CH_3	H	CH_2Cl_2·C_6H_{12}	117-120	79	$C_{15}H_{15}NO_2$	---	---	---	---
H	CH_3	p-OCH_3	MeOH	136-138	85	$C_{16}H_{17}NO_3$	70.83	6.32	70.78	6.22
H	p-$C_6H_4OCH_3$	p-OCH_3	MeOH	144-147	85	$C_{22}H_{21}NO_4$	72.71	5.82	71.94	5.99
H	$C(CH_3)_3$	H	C_6H_{12}	124-125.5	89	$C_{18}H_{21}NO_2$	76.29	7.47	76.35	7.52
H	CH_3	m-CF_3	EtOAc·C_6H_{12}	120.5-122.5	86	$C_{16}H_{14}F_3NO_2$	62.13	4.56	62.02	4.70
H	C_6H_5	m-CF_3	EtOAc·C_6H_{12}	177-179	87	$C_{21}H_{16}F_3NO_2$	67.92	4.34	67.98	4.05
H	CH_3	p-F	Et_2O·SSB	102-105	87	$C_{15}H_{14}FNO_2$	69.48	5.44	69.64	5.44
H	C_6H_5	p-CH_3	Et_2O·SSB	127.5-130.5	93	$C_{21}H_{19}NO_2$	79.47	6.03	79.62	5.98

(a) Lit. m.p. 118-119° (8).

TABLE VI

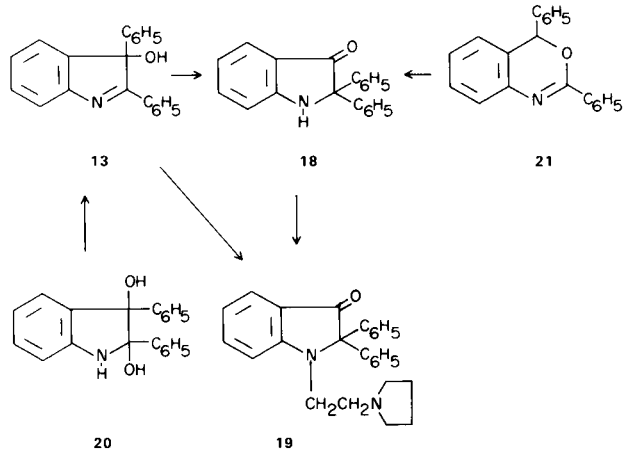
4*H*-3,1-Benzoxazines



X	R	R′	Chromat. (a) Solv.	Rxtal. Solv.	M.p. °C	Yield %	Formula	Anal. Calcd. C	Calcd. H	Found C	Found H
Cl	CH_3	H	3% Me_2CO	Et_2O:SSB	84-87	50	$C_{15}H_{12}ClNO$	69.90	4.66	70.00	4.88
Cl	C_6H_5	H	---	SSB	111-115	72	$C_{20}H_{14}ClNO$	75.11	4.41	74.84	4.37
H	CH_3	H	3% Me_2CO	--- (c)	---	41	$C_{15}H_{13}NO$	---	---	---	---
H	C_6H_5	H	---	SSB	110-113 (b)	83	$C_{20}H_{15}NO$	---	---	---	---
H	*p*-$CH_3OC_6H_4$	H	---	SSB	115-116	91	$C_{21}H_{17}NO_2$	79.98	5.43	80.10	4.99
H	*p*-$CH_3OC_6H_4$	*p*-OCH_3	---	Me_2CO:SSB	96-99	89	$C_{22}H_{19}NO_3$	76.50	5.55	76.25	5.72
H	$C(CH_3)_3$	H	---	SSB	93.5-96	81	$C_{18}H_{19}NO$	81.47	7.22	81.15	6.50
H	CH_3	*m*-CF_3	5% Me_2CO	--- (c)	---	37	$C_{16}H_{12}F_3NO$	---	---	---	---
H	C_6H_5	*m*-CF_3	--(d)	---	---	----	---	---	---	--	---
H	C_6H_5	*p*-CH_3	---	SSB	77-78.5	84	$C_{21}H_{17}NO$	84.25	5.72	84.21	5.72

(a) Only % Me_2CO in Me_2CO:SSB mixture is specified. (b) Lit. m.p. 114-115°. (c) Product non-crystalline. (d) Product used as obtained in next step.

material with *N*-(β-chloroethyl)pyrrolidine by means of sodium hydride affords a product identical in all respects to that obtained by the one step process above. It is thus likely that formation of **19** in fact proceeds *via* **18**. It is of note in this connection that the first reported preparation of **18** (10) was by treatment of the glycol **20** with hot base; the authors in fact proposed **13** as an intermediate in this process.



We further found that it was possible by means of potassium *t*-butoxide in refluxing *t*-butyl alcohol to proceed directly from the benzoxazine **21** to the indoxyl **18**. It would thus seem that the anion of the indolol is relatively stable at room temperature and below; when heated, this anion undergoes a benzilic acid type rearrangement to an indoxyl. Table II lists the characteristics of some of the indoxyl prepared and their *N*-alkylation products.

EXPERIMENTAL (11)

o-Aroylacetanilides (Table III).

In a typical experiment a solution of 0.20 mole of the appropriate Grignard reagent in 200 ml. of THF (tetrahydrofuran) was added over 2.25 hours to an ice cooled solution of 32.34 g. (0.20 mole) of the benzoxazinone in 200 ml. of ether and 400 ml. of benzene. The mixture was then stirred for 1.5 hours in the cold and 1.5 hours at room temperature. The mixture was then cooled in ice and 2.5 *N* hydrochloric acid (200 ml.) added at such a rate as to keep the temperature below 4°. Following an additional 15 minutes stirring the organic layer was separated, washed in turn with water, 5% sodium hydroxide, water and brine and taken to dryness. The residue was then chromatographed over Florisil (12) (elution with 5% acetone in Skellysolve B).

o-Aroylanilines.

Typically, a mixture of 0.274 mole of the amide and 37 ml. each of concentrated hydrochloric acid and water in 70 ml. of ethanol was heated at reflux for 18 hours. The bulk of the solvent was removed in vacuum and the residue extracted with methylene chloride. The organic layer was taken to dryness and the residue recrystallized.

o-Aroylanilides (Table IV).

To an ice cold solution of 0.18 mole of the aroylaniline in 110 ml. of pyridine, there was added 22.3 ml. of benzoyl chloride. Following 3.5 hours standing at room temperature the mixture was poured into 1300 ml. of water. The precipitated solid was collected on a filter, dried and recrystallized.

α-Hydroxy-α-aryl-*o*-toluidides (Table V).

Sodium borohydride (5.0 g.) was added in small portions to a well stirred mixture of 0.093 moles of the aroylanilide and 500 ml. of ethanol. Following 2 hours stirring at room temperature, the bulk of the solvent was removed in vacuum. The residue was treated with water and the precipitated solid collected on a filter. The solid was then dried and recrystallized.

4*H*-3,1-Benzoxazines (Table VI).

In a typical experiment 2.6 ml. (7.4 g., 0.0275 mole) of phosphorus tribromide was added to a well stirred, ice cooled solution of 0.0275 mole of the α-hydroxy-α-phenyl-*o*-toluidide in 200 ml. of chloroform. Following 4 hours standing in the cold, the mixture was poured into ice water. The organic layer was separated, washed in turn with ice-cold saturated sodium bicarbonate, water and brine and taken to dryness. The residue, if crystalline, was then recrystallized. In the event the residue was a gum, this was chromatographed over Florisil. In several cases (see Table VI) the total crude product was used as such in the next step.

3*H*-Indol-3-ols (Table I).

To a solution of potassium amide prepared from 0.80 g. (0.02 mole) of potassium in 200 ml. of redistilled liquid ammonia there was added 0.0195 mole of the benzoxazine in 60 ml. of THF. The mixture was stirred for 10 minutes and then 5 g. of ammonium chloride was added. The solvent was then evaporated with a stream of nitrogen. The residue was dissolved in ether:methylene chloride and water. The organic layer was separated, washed with water and brine and taken to dryness. The residue was recrystallized and if non-crystalline, chromatographed on Florisil.

2-Phenyl-3-methyl-3*H*-indol-3-ol.

A solution of 4.46 g. of the benzoxazine (**11**) in 80 ml. of THF was added to a solution of 0.02 mole of potassium amide in 200 ml. of liquid ammonia. The mixture was stirred under a dry ice condenser for 3 hours and then "neutralized" with 4 g. of ammonium chloride. The solvent was evaporated with a stream of nitrogen and the residue dissolved in ether and water. The organic layer was washed in turn with water and brine and taken to dryness. The residue was chromatographed on Florisil. Elution with 1% acetone in Skellysolve B afforded 3.25 g. of recovered starting material, m.p. 37-39°. The crystalline fractions obtained on elution with 5% acetone were combined and recrystallized from acetone-Skellysolve B. There was obtained 0.21 g. (5%; 15% based on starting material consumed) of product, m.p. 144-145°.

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87. Found: C, 80.70; H, 6.30.

3-Acetoxy-5-chloro-2,3-diphenyl-3*H*-indole.

A mixture of 2.0 g. of the indolol **2**, 4 ml. of acetic anhydride and 12 ml. of pyridine was allowed to stand at room temperature for 16 days. The solid, which was obtained when the mixture was poured into water, was recrystallized twice from methanol. There was obtained 1.28 g. of the acetate, m.p. 158-160°.

The analytical sample from an earlier run melted at 156.5-160°; ν max 1750 cm^{-1}; NMR, singlet (3*H*) at 2.08 δ.

Anal. Calcd. for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46. Found: C, 73.33; H, 4.71.

3-Acetoxy-2,3-diphenyl-3*H*-indole.

A solution of 2.30 g. of 2,3-diphenyl-3*H*-indol-3-ol and 5 ml. of acetic anhydride in 15 ml. of pyridine was allowed to stand at room temperature for one week. The mixture was then poured into ice and water. The precipitated solid was collected on a filter and recrystallized several times from acetone-cyclohexane. There was obtained 1.51 g. (58%) of the acetate, m.p. 167-170°.

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23. Found: C, 80.76; H, 5.63.

Catalytic Reduction of 5-Chloro-2,3-diphenyl-3*H*-indol-3-ol.

A mixture of 0.80 g. of the indolol and 0.10 g. of 10% palladium on charcoal in 200 ml. of ethyl acetate was shaken under hydrogen for 20 hours. The catalyst was removed by filtration and the filtrate taken to dryness. The residue was chromatographed on two 25 g. preparative silica gel tlc plates (development with methylene chloride). The solid which was obtained on elution of the main fraction was recrystallized twice from Skellysolve B to afford 0.40 g. (50%) of product, m.p. 128.5-130°, m.m.p. with authentic 5-chloro-2,3-diphenylindole, 129-130°.

[(2,3-Diphenyl-3*H*-indol-3-yl)oxy]acetic Acid.

To a solution of 2.85 g. of 2,3-diphenyl-3*H*-indol-3-ol in 15 ml. of DMF and 80 ml. of benzene there was added 0.43 g. of sodium hydride (56% in mineral oil). After 5 minutes, 1.1 ml. (1.67 g.) of ethyl bromoacetate was added and the mixture brought to reflux. At the end of 6 hours the mixture was allowed to cool, washed with water and brine and taken to dryness.

A solution of the above residue and 2 ml. of 50% sodium hydroxide in 40 ml. of methanol was heated at reflux for 6 hours. The bulk of the solvent was then removed in vacuum and the residue dissolved in ether and water. The aqueous layer was acidified to afford the crude acid. Two recrystallizations from aqueous methanol gave 1.46 g. (43%) of colorless product, m.p. 200-201.5°.

Anal. Calcd. for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.95. Found: C, 75.88; H, 5.06.

[(2,3-Di)*p*-methoxyphenyl)-3*H*-indol-3-yl)oxy]acetic Acid.

Proceeding exactly as above, 2.0 g. of 2,3-di(*p*-methoxyphenyl)-3*H*-indol-3-ol was alkylated by means of 0.25 g. of sodium hydride (56%) and 0.97 g. of ethyl bromoacetate. The crude ether was hydrolyzed with 3 ml. of 50% sodium hydroxide in 100 ml. of methanol. This last reaction was worked up as above and the acidic product recrystallized twice from aqueous methanol to give 1.23 g. (52%) of acid, m.p. 191-192°.

Anal. Calcd. for $C_{24}H_{21}NO_5$: C, 71.45; H, 5.25. Found: C, 71.50; H, 5.19.

3-(Benzyloxy)-2,3-diphenyl-3*H*-indole.

To a solution of 1.43 g. of 2,3-diphenyl-3*H*-indol-3-ol in 8 ml. of DMF and 40 ml. of benzene there was added 0.24 g. of sodium hydride and after 15 minutes 0.90 g. of benzyl chloride. Following 3 hours heating at reflux the mixture was allowed to cool, washed in turn with water and brine and taken to dryness. The residue was chromatographed in turn over Florisil (elution with 5% acetone in Skellysolve B) and silica gel (same eluent). The crystalline fractions obtained from this last column were combined and recrystallized twice from a small volume of methanol. There was obtained 1.16 g. (62%) of colorless product, m.p. 107-110°.

Anal. Calcd. for $C_{27}H_{21}NO$: C, 86.37; H, 5.64. Found: C, 85.41; H, 5.77.

2,2-Disubstituted-3-indolinones (Table II).

In a typical experiment a solution of 7.10 g. of the indolol and 7 ml. of 50% aqueous sodium hydroxide in 120 ml. of methanol was heated at reflux for 6 hours. The bulk of the solvent was removed in vacuum and the residue suspended in water. The intensely yellow solid was collected on a filter, dried and recrystallized.

N-Alkylated-2,2-disubstituted-3-indolinones (Table II).

A solution of 0.007 mole of the appropriate indoxyl in 10 ml. of DMF and 50 ml. of benzene was heated with 0.3 g. of sodium hydride (56% in mineral oil). At the end of 10 minutes 0.007 mole of the appropriate amine was added to the dark red mixture. Following 17 hours heating at reflux the now yellow solution was diluted with benzene and washed with water and brine. The organic layer was taken to dryness, and the residue dissolved in ether. To this solution there was added slightly over an equivalent of 3.7 *N* hydrogen chloride in ether. The precipitated solid was collected on a filter. The product was in several cases purified as this hydrochloride. Alternately, the salt was converted to the free base and this recrystallized.

2,2-Diphenyl-1-[2-(1-pyrrolidinyl)ethyl]-3-indolinone from 2,3-Diphenyl-3*H*-indol-3-ol.

A solution of 2.85 g. (0.01 mole) of the indolol in 15 ml. of DMF and 80 ml. of benzene was treated with 0.43 g. of sodium hydride (56% in mineral oil) and 5 minutes later 2.70 g. of a 1:1 mixture of β-chloroethylpyrrolidine and toluene. As the mixture was brought to reflux an intense red color developed. Following 18 hours heating at reflux the now light yellow mixture was worked up as above. The free base was recrystallized twice from Skellysolve B to afford 2.10 g. of product, m.p. 132-134°; λ max 328 (31,000), 422 (4,550).

The mixed m.p. of this with product obtained by direct alkylation of the indoxyl was 132-134°.

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(11) All melting points are uncorrected and recorded as obtained on a Thomas-Hoover melting point apparatus. N.M.R. spectra were determined on a Varian A-60A Spectrometer in deuteriochloroform. The authors are indebted to the Department of Physical and Analytical Chemistry of The Upjohn Co. for elemental and spectral determinations.

(12) Florisil is a synthetic magnesia-silica gel absorbent manufactured by the Floridin Co., Warren, Pa.

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