Jan Bergman, René Carlsson and Birger Sjöberg

Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm 70, Sweden

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Indole-3-carboxylic acid (as well as indole-3-glyoxylic acid) derivatives are readily prepared from indoles (including oxindoles) and phosgene (oxalyl chloride), respectively. The interaction of these reagents with the indole Grignard reagent afforded several products including the cyclotetramers, **21** and **30**. Indolo-fused heterocycles can be readily prepared from the reaction of phosgene (or oxalyl chloride) with suitable reactants. Thus *e.g.*, phosgene and 2-(2-hydroxyphenyl)-*N*-methylindole readily gave 5,6-dihydro-11-methyl-6-oxobenzo[*a*]pyrano[4,3-*b*]indole (**33**).

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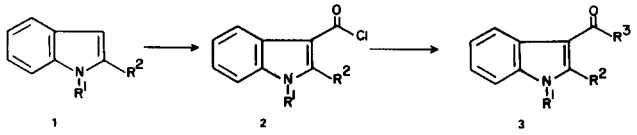
In connection with cyclization studies in the indole series (1) we needed 1,2-dimethylindole-3-carbonyl chloride. The available procedures (2,3) were found to be troublesome. Thus, decarbonylation of 1,2-dimethylindole-3-glyoxylyl chloride gave varying and unsatisfactory yields and the transformation of the carboxylic acid with thionyl chloride to the carbonyl chloride gave several by-products and the desired product only in low yield.

For this reason direct chlorocarbonylation with phosgene was considered. This long-known reaction (As early as 1867, Gräbe and Liebermann (4) chlorocarbonylated anthracene in a sealed tube at 200° and some years later Michler (5) found that *N,N*-dimethylaniline slowly reacted with phosgene at room temperature yielding 4-(*N,N*-dimethylamino)benzoyl chloride.) has only found scattered use (6,7). Some recent examples include azulene (8), benzene (9) (catalyzed by palladium chloride) and a few pyrroles (10). Although the reaction of phosgene with indole Grignard reagents has been studied (11,12), no attempts to chlorocarbonylate indoles have to our knowledge been reported. Addition of phosgene (in toluene)



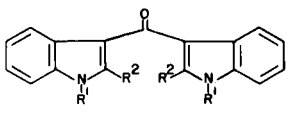
1 2 3

R^3 = OR, NR_2, $NHNR_2$

at 9-11° to a solution of 1,2-dimethylindole in methylene chloride gave the desired product (**2**, $R^1 = R^2 = CH_3$) in high yield. At reflux temperature the symmetrical ketone **4a** was formed. The carbonyl chloride could be directly converted to a wide range of compounds (*cf.* the Table). Heating of the carbonyl chloride (**2**, $R^1 = R^2 = CH_3$) in the presence of pyridine gave, after work-up, the anhydride **5a**, whose structure was proven by an independent synthesis (dehydration of 1,2-dimethylindole-3-carboxylic acid with diisopropylcarbodiimide).

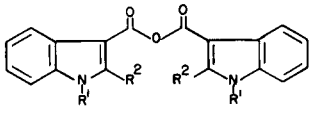
Whereas chlorocarbonylation of other 2-substituted indoles gave similar results, 2-unsubstituted indoles gave complex mixtures containing oligomeric products, unless an equimolecular amount of pyridine was present to capture the hydrogen chloride formed. By this modified procedure *e.g.* 3-carbethoxyindole could be prepared in good yield (*cf.* reference 12a). Reaction of 3-methylindole with phosgene in dioxane in the absence of base gave the dimeric product **6a**, isolated as the *N,N*-dimethylamide derivative **6b**. This same compound could also be prepared by treating the well known (13,14) dimer (**6c**) of 3-methylindole with phosgene followed by *N,N*-dimethylamine. Treatment of 3-methylindole with phosgene in dioxane in the presence of pyridine gave, after work-up, compound **7a**. 3-Phenylindole similarly treated gave **7b**. Interestingly compounds of the pyrrocoline type (15-17) (*e.g.* the known compound **8**) were not formed. Mild hydrolysis of **7a** gave the known (18,19) but unstable 3-methylindole-1-carboxylic acid.

The mass spectra of **7a** and **7b** indicated that carbon dioxide is readily eliminated, presumably with synchronous coupling of the fragments formed. Below the M-44 peak the spectra were almost identical with those of **9a** and **9b**, respectively. The spectra of the anhydrides **5a** and **5b** also showed (but less prominent) M-44 peaks (*cf.* reference 19a).



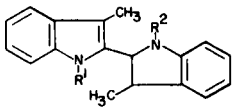
4

a, $R^1 = R^2 = CH_3$
b, $R^1 = H$, $R^2 = C_6H_5$
c, $R^1 = R^2 = H$



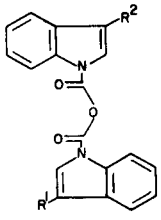
5

a, $R^1 = R^2 = CH_3$
b, $R^1 = C_6H_5$, $R^2 = Cl$



6

a, $R^1 = R^2 = COCl$
b, $R^1 = R^2 = CON(CH_3)_2$
c, $R^1 = R^2 = H$

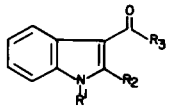


7

a, $R^1 = R^2 = CH_3$
b, $R^1 = R^2 = C_6H_5$

Table

Indole-3-carbonyl Derivatives

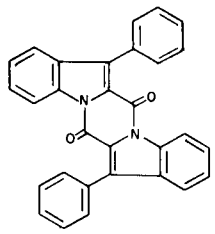


R^1	R^2	R^3	Yield (%)	M.p. (recrystallization solvent)	Lit. m.p.	Elemental Analyses (Calcd.) (Found)	Spectral data ^{1}H Nmr (a)	Mass spectra (b)
CH_3	CH_3	OH	96	202-205° dec. (Water/methanol)	185° dec. (51) 204-205° dec. (52)			(10%, 140): m/e = 190 (27), 189 (M^+, 100), 172 (31), 144 (23), 143 (11)
CH_3	CH_3	$N(CH_3)_2$	90	153-154° (Ethanol)		$C_{13}H_{16}N_2O$: (216.3) C 72.2; 72.1; H 7.5; 7.5; N 13.0. 13.0.	δ = 7.4 (m, $1H_{arom}$), 7.1 (m, $3H_{arom}$), 3.5 (s, 3H, N-CH_3), 3.0 (s, 6H, $N(CH_3)_2$), 2.4 (s, 3H, CH_3)	(5%; 140): m/e = 216 (M^+, 27), 173 (13), 172 (100), 143 (5)
CH_3	CH_3	$NHN(CH_3)_2$	86	178-179° (Methanol)		$C_{13}H_{17}N_3O$: (231.3) C 67.5; 67.3; H 7.4; 7.3; N 18.2. 18.3.	δ = 7.4 (m, $1H_{arom}$), 7.15 (m, $3H_{arom}$), 3.45 (s, 3H, N-CH_3), 2.7 (s, 6H, $N(CH_3)_2$), 2.55 (s, 3H, CH_3)	
CH_3	CH_3	OCH_3	83	142-143° (Methanol)	141-142° (53)			
H	CH_3	OCH_3	73	(Water/methanol)	165° (54)			
H	CH_3	$N(CH_3)_2$	82	225-226° (Methanol)	220° (55)			(5%; 130): m/e = 202 (M^+, 33), 159 (12), 158 (100), 157 (6), 130 (10)
H	CH_3	OH	60	179-180°	180° (56)			
H	C_6H_5	OH	48	187-189° (Washed with cold methanol)	170° (57) 177-181° (58)			(3%; 190): m/e = 237 (M^+, 4), 220 (3), 194 (15), 193 (100), 192 (8), 191 (6), 190 (4)
H	p-BrC_6H_4	OH	62	215-216°		$C_{15}H_{10}BrNO_2$: (316.2) C 57.0; 57.0; H 3.2; 3.1; Br 25.3; 25.1; N 4.4. 4.5.		(5%; 200): m/e = 317 (M^+, 25), 316 (5), 315 (26), 300 (8), 298 (8), 274 (15), 273 (98), 272 (18), 271 (100), 219 (6)

Table (continued)

R^1	R^2	R^3	Yield (%)	M.p. (recrystallization solvent)	Lit. m.p.	Elemental Analyses (Calcd.) (Found)	Spectral data ^{1}H Nmr (a)	Mass spectra (b)
H	C_6H_5	OCH_3	57	149-151° (Ether-*n*-hexane)	148-151° (58) (c)			
CH_3	Cl	OH	72	228-230° dec. (Water/ethanol)	218° dec. (63)			
H	C_6H_5	OC_2H_5	62	154-156° (Ether-*n*-hexane)	153-155° (58) (c) 160° (57)			
H	C_6H_5	NH_2	62	179-180° (acetonitrile)	180-181° (59)			
H	H	OC_2H_5	56	124-125°	126-124° (27) 126-127° (60)			
H	H	NH_2	84	199-200° (Acetonitrile)	196-197° (3)			
H	H	$N(CH_3)_2$	55	233-236° (Ethanol)	236° (61)			(10%; 100): m/e = 188 (M^+, 39), 145 (11), 144 (100), 116 (15).
H	H	$NHNH_2$	60	224-226° (Methanol)	224-226° (3)			
H	H	OH	50	219-222° dec.	220-224° dec. (3) 245-247° (62)			
CH_3	Cl	$N(CH_3)_2$	88	109-110°		$C_{12}H_{13}ClN_2O$: (236.7) C 60.9; 61.1; H 5.5; 5.5; Cl 15.0; 15.0; N 11.8; 11.9	δ = 7.6 (m, 1H$_{arom}$), 7.2 (m, 3H$_{arom}$), 3.6 (s, 3H, N-CH_3), 3.05 (s, 6H, (N-CH_3)$_2$).	(10%; 100): m/e = 238 (M^+, 11), 236 (M^+, 30), 194 (35), 193 (11), 192 (100).
CH_3	Cl	OCH_3	73			$C_{11}H_{10}ClNO_2$: (223.7) C 59.1; 58.9; H 4.5; 4.7; Cl 15.9; 15.7; N 6.3; 6.2	δ = 8.1 (m, 1H$_{arom}$), 7.15 (m, 3H$_{arom}$), 3.9 (s, 3H, N-CH_3), 3.4 (s, 3H, OCH_3)	

(a) Deuteriochloroform was used as solvent. The chemical shifts are given relative to TMS. (b) Only peaks stronger than X% of the base peak and m/e greater than Y are listed; indicated as (X%, Y). (c) A sample kindly provided by Professor Neuenschwander was identical with our product.



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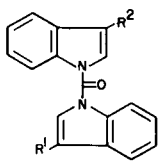


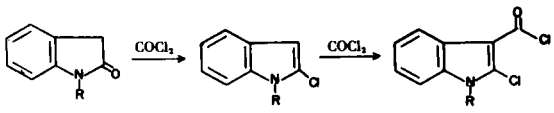
9

a, $R^1 = R^2 = CH_3$
b, $R^1 = R^2 = C_6H_5$
c, $R^1 = R^2 = H$

Chlorocarbonylation of 2-arylindoles required higher temperature (25-30°) and addition of pyridine in order to give good yields. Without pyridine considerable amounts of *e.g.* the symmetrical ketone **4b** was formed. The preferred pyridine/phosgene ratio was 1:1. The indole used as reactant could, as expected (*cf.* reference 20 for the corresponding conversion of *N*-methylpyrrolidone to 2-chloro-4,5-dihydro-1-methylpyrrole-3-carbonyl chloride in 26% yield), also be generated *in situ* from oxindoles as outlined in the Scheme. The intermediates, 2-chloroindole (**11a**) and 2-chloro-*N*-methylindole (**11b**), respectively, could be isolated. We feel that the final product **12** (yield > 67%) in this reaction should be of interest for the preparation of fused indole derivatives *e.g.* diazacarbazoles and indolodiazepines. Related derivatives of these ring-systems have recently been prepared by Stoess, *et al.* (21, 22) starting form 2-chloro-1-methylindole-3-carboxaldehyde.

Oxalyl chloride and oxindole similarly gave 2-chloro-

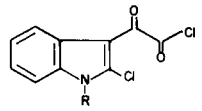
Scheme 1



10 11 12

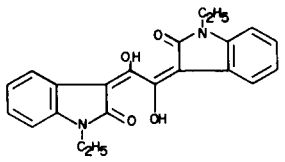
a, R = H
b, R = CH_3
c, R = C_2H_5

3-indolylglyoxylyl chloride (**13a**) which on heating (125-145°) underwent decarbonylation giving **12a** (22a). *N*-Methyloxindole similarly gave **13b**, whereas *N*-ethyloxindole under the same conditions gave a mixture of **13c** and two compounds assigned the structures **14a** and **14b**. Interestingly **12b** gave **15** when treated with excess dimethylamine at 25°, whereas **13b** under the same conditions yielded **16**, showing that the chlorine atom on the heterocyclic ring is, as expected, more readily substituted in the intermediate *N*,*N*-dimethylglyoxamide than in the amide **15**. Treatment of pure **12b** or **15** with excess dimethylamine in dimethyl formamide at 110° for 2 hours gave a mixture containing 2-chloro-*N*-methylindole (*cf.* reference 23) and **17** (24) but no 2-dimethylamino-*N*-

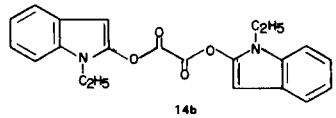


13

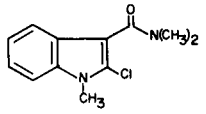
a, R = H
b, R = CH_3
c, R = C_2H_5



14a



14b



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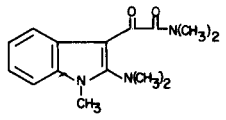

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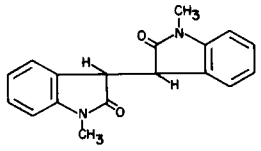
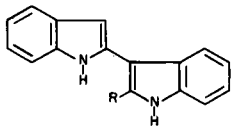
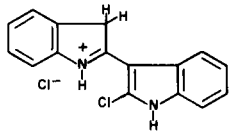


17





18 a, R = H
b, R = Cl

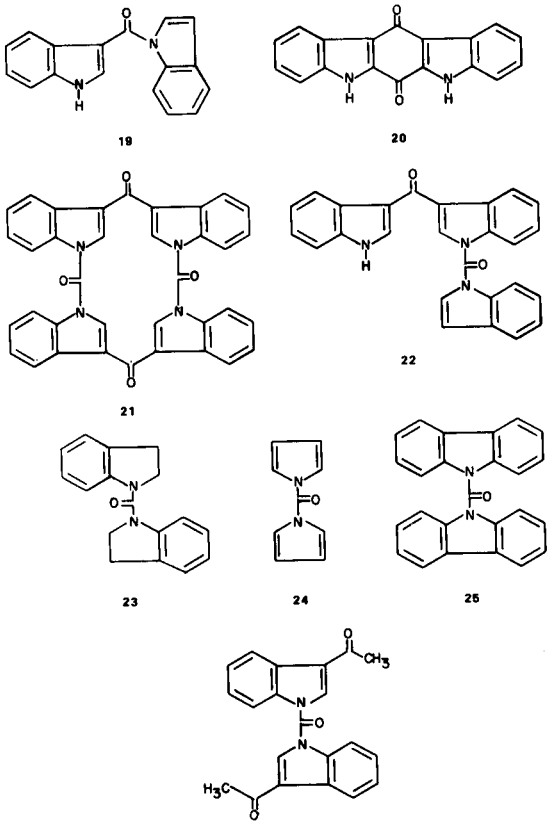
18c

methylindole-3-*N*,*N*-dimethylcarboxamide (*cf.* reference 25).

Interaction of oxindole (**10**, R = H) with phosgene in toluene at a slightly higher temperature (45°) gave considerable amounts of the resonance-stabilized hydrochloride **18c** of the dimeric indole **18b**, which on treatment with magnesium in dry tetrahydrofurane gave the parent compound **18a**.

The Reaction of Phosgene with the Indole Grignard Reagent.

The only study published of the reaction of phosgene with the indole Grignard reagent is that (11) of Oddo and Mingoia in 1927. The Italian workers claimed the isolation of compounds **4c**, **9c** and **19**. In addition they discussed the possible formation of the 2,2-, 1,2- and 2,3-isomers of the compounds isolated as well as compound **20**. The reaction was performed as described by Oddo and Mingoia (*i.e.* addition of phosgene to the indole Grignard reagent in ether). The ether-insoluble product obtained after work-



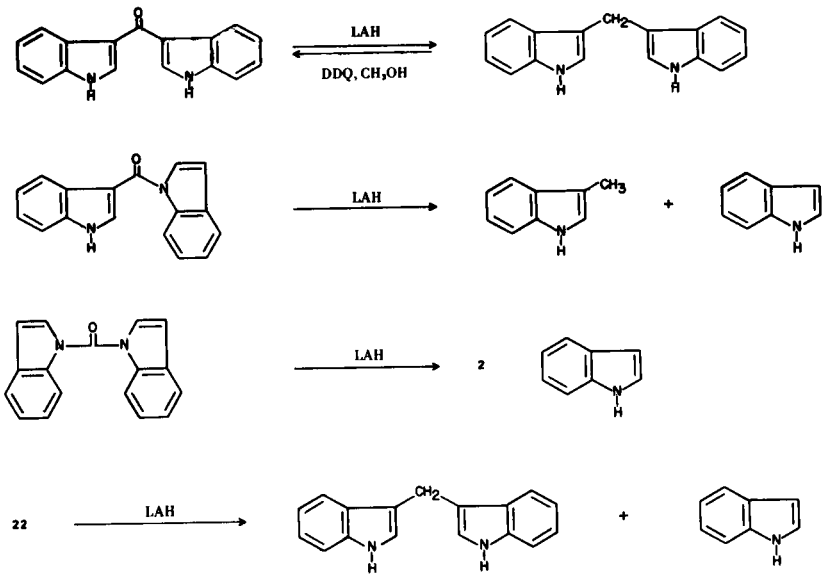
up was found to be a mixture of **4c** and **21**, which could be readily separated. The fact that compounds **4c** and **21** have approximately the same melting points makes it difficult to decide which compound Oddo and Mingoia actually isolated. Column chromatography of the ether soluble reaction products gave the following compounds (in order of eluation) **9c**, **19**, **4c** and **22** (26). In agreement with Heacock's and Kaŝpárek's (27) observation in their study of the reaction of indole magnesium iodide with ethyl chloroformate it was found that high reaction temperatures (refluxing ether) favored the formation of the 1,3-disubstituted product (*i.e.* in the present case compound **21**). Low temperature (0°) favored the formation of **9c**.

As our melting point data differed strikingly from the literature data, *e.g.* **9c**, 100-101° (lit. (11) 245°), we decided to prove the structure of all the $C_{17}H_{12}N_2O$ isomers. Oxidation of 3,3'-diindolylmethane with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in methanol gave, *via* 3-indolidene-3*H*-indole, 3,3'-diindolyl ketone (**4c**) (*cf.* references 28-30). The results from reductions with lithium aluminium hydride (LAH) are summarized in Scheme 2. Furthermore compound **9c** could, in excellent yield, be independently synthesized from indole and *N,N'*-carbonylimidazole in dimethyl sulfoxide (2 hours/125°) as well as by dehydrogenation of **23** with DDQ (*cf.* reference 28). Compounds **9a**, **9b**, **24** and **25** could also be prepared *via* carbonyltransfer. Carbonylation of **4c** with phosgene in the presence of triethylamine gave **21** in good yield. This reaction is general for 3-acylindoles. Thus *e.g.* 3-acetylindole similarly gave **26**. Photolysis of **9c** gave a mixture of **19**, **4c** and indole, but apparently not any 2-substituted isomers (*cf.* reference 30a). Hydrolysis of **22** gave **4c** and indole.

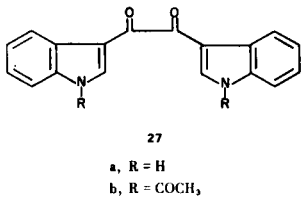
The Reaction of Oxalyl Chloride with the Indole Grignard Reagent.

The results discussed in the preceding section prompted a reinvestigation (for earlier studies, see reference 12) of

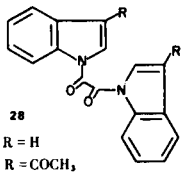
Scheme 2



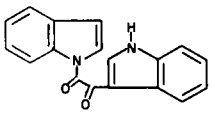
the reaction of oxalyl chloride with the indole Grignard reagent. The predominant product in all experiments was **27a**, but small amounts of **28a**, **29** and a new high-melting compound assigned structure **30** could also be isolated from certain experiments. All the minor products could be sufficiently prepared by other methods. Thus, addition of oxalyl chloride to a solution of indole and triethylamine in dioxane gave a good yield of **28a**. Compound **30** could be similarly synthesized starting with **27a**. This acylation method appears to be general as **27a** and triethylamine-acetyl chloride similarly gave **27b**. The assignment of structure **30** to the high-melting compound is based on elemental analysis, infrared spectroscopy (which indicated no NH and C=O absorptions at 1702 and 1656 cm^{-1}) and hydrolysis studies which gave **27a**. On the other hand no parent ion peak, nor fragmentation peaks above m/e 288, could be detected in the mass spectrum. This appearance may be explained by low volatility and ready fragmentation between the adjacent carbonyl groups, a pattern prevalent in the spectrum of **27a** too. In contrast to the ready cleavage of **30** the related cyclotetrameric compound **21** did give rise to a strong parent ion peak.



27
a, R = H
b, R = $COCH_3$



28
a, R = H
b, R = $COCH_3$



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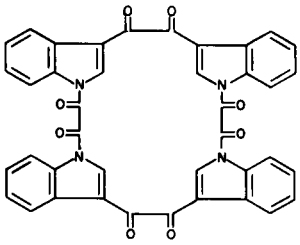
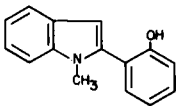
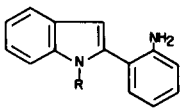


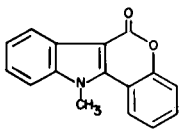
30



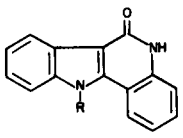
31



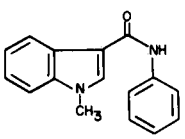
32 a, R = H
b, R = CH_3



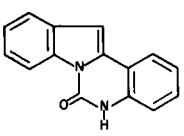
33



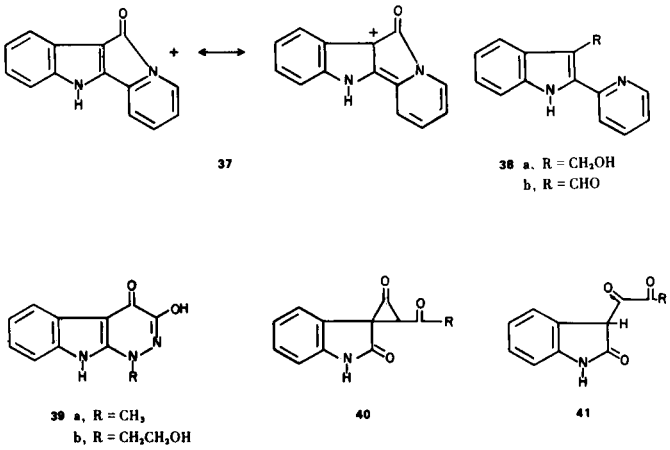
34 a, R = H
b, R = CH_3



35



36



37

38 a, R = CH_2OH
b, R = CHO

39 a, R = CH_3
b, R = CH_2CH_2OH

40

41

Synthesis of Indolo-fused Heterocycles *via* Cyclization with Phosgene.

The reaction of phosgene (or oxalyl chloride) with suitably substituted 2-arylindoles should be expected to give indolo-fused heterocycles. Thus **31** and **32b** readily gave **33** and **34b**, respectively, in high yields. Compound **33** has recently (31) been prepared in a 5-step synthesis starting with **31**. Compound **34b** could also be prepared by photochemical cyclization of **35** (*cf.* references 32-34). Cyclization of **32a** with phosgene gave **36** and not **34a**. Reaction of 2-(2-pyridyl)-indole with phosgene in dioxane yielded a dark-green (at first violet-red) solution, presumably due to the formation of the resonance stabilized cation **37** (only two canonical forms shown). Treatment of this mixture with sodium borohydride afforded the alcohol **38a**, which also could be prepared by reduction of **38b** with sodium borohydride. Treatment of **13a** with *e.g.* methylhydrazine readily gave **39**. Related compounds (prepared *via* **40** and **41**) have recently been reported by Hill (35).

EXPERIMENTAL

Melting points were determined on a micro hot stage melting point apparatus and are uncorrected. Elemental analyses were carried out by A Bernhardt, Elbach über Engelskirchen, West Germany, or Centrala Analyslaboratoriet, Uppsala, Sweden. Ir spectra were recorded with a Perkin Elmer 421 infrared spectrophotometer, the spectra of solids being determined as potassium bromide discs. ^1H Nmr spectra were recorded with a Varian A60 instrument or a JEOL JNM-NH-100 instrument. Mass spectra were recorded with a LKB 9000 instrument.

1,2-Dimethylindole-3-carbonyl Chloride.

Phosgene in toluene (75 ml., 12.5%) was added dropwise during 15 minutes to a well stirred solution of 1,2-dimethylindole (14.5 0.1 mole) in methylene chloride (120 ml.) at 9-11°. The slurry obtained was stirred for 3 hours at 9-11°, whereupon the precipitate of 1,2-dimethylindole-3-carbonyl chloride (13.5 g.) was collected. The mother-liquor was concentrated using reduced pressure to give a second crop (4.1 g.). Total yield, 17.6 g. (85%), m.p. 105-115° dec. (elimination of HCl).

Anal. Calcd. for $C_{11}H_{10}ClNO$: C, 63.6; H, 4.9; Cl, 17.1; N, 6.7. Found: C, 63.9; H, 4.8; Cl, 16.9; N, 6.8.

1,2-Dimethylindole-3-carboxylic Acid.

1,2-Dimethylindole-3-carbonyl chloride (208 mg., 1 mmole) was added to water (25°, 25 ml.) under stirring. After 10 minutes the acid formed was collected, washed with water and dried.

2-Methylindole-3-carbonyl Chloride.

Phosgene in toluene (75 ml., 12.5%) was added dropwise during 30 minutes to a well stirred solution of 2-methylindole (13.1 g., 0.1 mole) in methylene chloride (75 ml.) at 9-11°. The solution obtained was stirred at 9-11° for 2 hours, whereupon the solution was concentrated to *ca* 75 ml. using reduced pressure. The free chloride was not isolated but converted directly to derivatives by using 15 ml. samples.

2-Methyl-3-carbomethoxyindole.

Methanol (5 ml.) was added to 2-methylindole-3-carbonyl chloride in toluene (15 ml.). The solvents were evaporated and the residue recrystallized from methanol (with final cooling to -20°).

2-Phenylindole-3-carbonyl Chloride.

Phosgene in toluene (75 ml., 12.5%) was added to a well stirred solution of 2-phenylindole (9.65 g., 0.05 mole) and pyridine (3.95 g., 0.05 mole) in toluene (75 ml.) at 25°. The mixture was stirred for 3 hours at 25°. The free chloride was not isolated but converted directly to derivatives.

3-Carboethoxyindole.

Indole was reacted with phosgene in the presence of pyridine as described for 2-phenylindole-3-carbonyl chloride. The reaction mixture was treated with ethanol, the solvents evaporated and the residue crystallized from methanol.

Indole-3-carboxamide. Method A.

Indole-3-carbonyl chloride obtained as described above was treated with a stream of ammonia. The solvents were evaporated and the residue recrystallized from acetonitrile, yield, 84%, m.p. 199-200° (lit. (3) 196-197°).

Indole-3-carboxamide. Method B.

Indole-3-(*N*-chlorosulfonyl)carboxamide (25.9 g., 0.1 mole), prepared (36) from indole and chlorosulfonyl isocyanate, was heated with water (500 ml.) until (*ca* 10 minutes) a clear solution was obtained. On cooling crystals of indole-3-carboxamide, identical with those obtained by method A were formed, yield, 82%, m.p. 199-200°.

Di-(2-phenyl-3-indolyl)ketone (**4b**).

A solution of 2-phenylindole (1.93 g., 0.01 mole) was heated in toluene (40 ml. containing 6% phosgene) at 40° for 4 hours. The crude product was recrystallized from methanol to give di-(2-phenyl-3-indolyl)ketone, yield, 1.68 g. (80%), m.p. 333-335°; ms m/e (% relative intensity): 413 (36), 412 (100), 411 (27), 396 (14), 395 (54), 335 (31), 307 (14), 306 (12), 260 (13), 220 (29), 206 (22), 192 (30), 177 (13), 165 (25) and 153 (12). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{29}H_{20}N_2O$: C, 84.4; H, 4.9; N, 6.8. Found: C, 84.2; H, 4.9; N, 6.8.

2-Chloro-1-methylindole-3-glyoxylyl Chloride (**13b**).

1-Methyloxindole (37) (14.7 g., 0.1 mole) was added to a stirred solution of oxalyl chloride (25.4 g., 0.2 mole) in ether (100 ml.) at 20°. The solid reactant dissolved, carbon dioxide and carbon monoxide evolved. After 24 hours at 20° the mixture was cooled to -10° and the crystals of **13b** collected, yield, 17.5 g. (68%), m.p. 123-125° (dec., decarbonylation).

Anal. Calcd. for $C_{11}H_7Cl_2NO_2$: C, 51.6; H, 2.8; Cl, 27.7; N, 5.5. Found: C, 52.0; H, 2.6; Cl, 27.3; N, 5.6.

2-*N*,*N*-Dimethylamino-1-methylindole-3-glyoxylyl-*N*,*N*-dimethylamide (**16**).

This compound had m.p. 109-110°, (yield, 85%); ms m/e (% relative intensity): 273 (17), 202 (14), 201 (100), 186 (7) and 158 (8). Only peaks stronger than 5% of the base peak and above m/e 100 are listed; ^1H nmr (deuteriochloroform): δ = 7.7-7.4 (m, 1 H, arom), 7.2-7.0 (3 H, arom), 3.5 (s, 3 H, NCH_3), 3.0 and 2.85 (two s, 6 H, $CON(CH_3)_2$) and 2.95 (s, 6 H, $N(CH_3)_2$).

Anal. Calcd. for $C_{15}H_{19}N_3O_2$: C, 65.9; H, 7.0; N, 15.4. Found: C, 65.6; H, 7.0; N, 15.6.

2-Chloroindole-3-glyoxylyl Chloride.

Oxindole (2.62 g., 20 mmoles) was added in portions to a stirred solution of oxalyl chloride (5.08 g., 40 mmoles) in methylene chloride (30 ml.) at 25°. Every addition caused vigorous evolution of gas (carbon monoxide and carbon dioxide). After 2.5 hours at 25° the solid was collected and dried in an exsiccator over potassium hydroxide, yield, 4.35 g. (92%), m.p. 140-145° (dec. decarbonylation).

Anal. Calcd. for $C_{10}H_5Cl_2NO_2$: C, 53.11; H, 2.23; N, 6.19; Cl, 31.36. Found: C, 53.35; H, 2.28; N, 6.22; Cl, 30.92.

As a derivative of the chloride the methyl ester was prepared: m.p. 201-202°; ms m/e (% relative intensity): 237 (10), 180 (34), 179 (11), 150 (13) and 123 (14). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{11}H_8ClNO_3$: C, 55.13; H, 4.21; Cl, 14.79; N, 5.84. Found: C, 55.36; H, 4.15; Cl, 14.57; N, 5.72.

Methyl 2-Bromo-*N*-methylindole-3-glyoxylate.

This ester was analogously prepared from *N*-methyloxindole and oxalyl bromide, yield, (74%), m.p. 167-168°; ms m/e (% relative intensity): 297 (9), 295 (8), 278 (28), 276 (26), 248 (33), 246 (34), 147 (88) and 118 (100). Only peaks stronger than 5% of the base peak and above m/e 100 are listed.

Anal. Calcd. for $C_{12}H_{10}BrNO_3$: C, 48.67; H, 3.40; N, 4.73; Br, 26.98. Found: C, 48.53; H, 3.28; N, 4.90; Br, 27.21.

Reaction of 1-Ethyloxindole with Oxalyl Chloride.

1-Ethyloxindole (1.61 g., 10 mmoles) was added to a stirred solution of oxalyl chloride (2.54 g., 20 mmoles) in ether (100 ml.) at 20°. After 24 hours at 20° the solid formed was washed with methanol, dried and chromatographed on silica gel using dichloromethane as eluent giving **14b**, yield, 151 mg. (8%), m.p. 200-205° dec.; ir cm^{-1}: 1724 (C=O); ms m/e (% relative intensity): 374 (5), 330 (6), 188 (15), 187 (100), 173 (10), 172 (75), 159 (17), 158 (5), 144 (16), 131 (8) and 130 (22). Only peaks above m/e 130 and stronger than 5% of the base peak are listed.

Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.44; H, 5.50; N, 7.17.

Continued elution of the column using dichloromethane containing increasing amounts of methanol gave the isomer **14c**, yield, 11 mg. (0.6%), m.p. 250-252°; ms m/e (% relative intensity): 374 (2), 188 (15), 187 (100), 173 (10), 172 (75), 159 (72), 158 (37), 144 (29), 131 (12) and 130 (42). Only peaks above m/e 130 and stronger than 5% of the base peak are listed.

Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.43; H, 5.40; N, 7.38.

Methanol (10 ml.) was added to the ether solution obtained above. After evaporation the residue was recrystallized from acetonitrile giving methyl 2-chloro-1-ethylindole-3-glyoxylate,

yield, 1.55 g. (59%), m.p. 96-97°; ir cm^{-1}: 1744, 1625 (C=O); ^1H nmr (deuteriochloroform): δ = 8.4-8.1 (m, 1 H, arom), 7.35-7.15 (3 H, arom), 4.2 (q, 2 H, CH_2), 3.9 (s, 3 H, OCH_3) and 1.3 (t, 3 H, CH_3); ms m/e (% relative intensity): 267 (5), 265 (15), 208 (32), 207 (12), 206 (100) and 178 (26). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; Cl, 13.34; N, 5.27. Found: C, 58.63; H, 4.72; Cl, 13.13; N, 5.20.

2-Chloro-1-methylindole (**11b**).

1-Methyloxindole (147 mg., 1 mmole) and pyridine (79 mg., 1 mmole) was added to a stirred solution of phosgene in toluene (6.25%, 15 ml.) at 25°. After 1 hour the solvent was evaporated using reduced pressure. The residue chromatographed on silica gel using methylene chloride gave 2-chloro-1-methylindole, yield, 96 mg. (58%), m.p. 64-65°; ms m/e (% relative intensity): 167 (32), 166 (20), 165 (100), 164 (33), 150 (13), 130 (6), 128 (11), 123 (6), 102 (5), 101 (7), 90 (20), 89 (14) and 82.5 (6). Only peaks stronger than 5% of the base peak are listed.

Anal. Calcd. for C_9H_8ClN: C, 65.23; H, 4.86; N, 8.51. Found: C, 65.55; H, 4.97; N, 8.72.

2-Chloroindole (**11a**).

The method described above was used, yield (79%), m.p. 73-76° (lit. (38) 72-76°).

Di-(1,2-dimethyl-3-indolyl)ketone (**4a**).

This compound was prepared analogously with **4b**, yield, (82%), m.p. 253-254°; ir cm^{-1}: 1600-1500 (C=O, broad) (no absorption in the region 1800-1600, *cf.* reference 39); ms m/e (% relative intensity): 316 (31), 302 (20), 301 (100), 172 (13), 171 (21), 144 (14) and 143 (21). Only peaks stronger than 15% of the base peak are listed.

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.7; H, 6.4; N, 8.9. Found: C, 79.9; H, 6.5; N, 8.7.

1,2-Dimethylindole-3-carboxylic Anhydride (**5a**). Method A.

A reaction mixture from 1,2-dimethylindole and phosgene in methylene chloride (see above) was treated with pyridine (12 ml.). After stirring for 15 minutes at 25°, water (100 ml.) was added and the solid formed was collected and recrystallized from dimethyl sulfoxide, yield (85%), m.p. 214-216°; ir cm^{-1}: 1726, 1678 (C=O); ms m/e (% relative intensity): 360 (12), 189 (8), 173 (13), 172 (100), 171 (23), 144 (8), 143 (8) and 115 (5). Only peaks stronger than 5% of the base peak are listed.

Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.31; H, 5.59; N, 7.77. Found: C, 73.06; H, 5.42; N, 7.60.

1,2-Dimethylindole-3-carboxylic Anhydride (**5a**). Method B.

A solution of 1,2-dimethylindole-3-carboxylic acid (189 mg., 1 mmole) and diisopropylcarbodiimide (63 mg., 0.5 mmole) in dimethyl sulfoxide (12 ml.) was heated (100°) for 4 hours. The solid formed on cooling was recrystallized from dimethyl sulfoxide giving **5a**, yield, 110 mg. (61%), m.p. 214-216°.

2-Chloro-1-ethylindole-3-carboxylic Anhydride (**5b**).

Method A above was used starting with 1-ethyloxindole (1.61 g., 10 mmoles). The crude product was recrystallized from methyl acetate/benzene, yield (55%), m.p. 163-164°; ir cm^{-1}: 1739, 1708 (C=O); ms m/e (% relative intensity): 430 (2), 428 (3), 222 (5), 208 (5), 207 (38), 206 (12), 205 (100), 179 (5), 177 (15) and 149 (6). Only peaks stronger than 5% of the base peak are listed.

3-Methylindole-1-carboxylic Anhydride (**7a**).

3-Methylindole (262 mg., 2 mmoles) in dioxane (10 ml.) was added to a mixture of phosgene in dioxane (4.0 ml., 6.25%) and pyridine (2.7 ml.). After 6 hours at 25° the mixture was poured into water (250 ml.). The thick oil obtained was washed with water and dissolved in acetonitrile. After *ca* 10 minutes, crystals separated, yield, 165 mg. (48%), m.p. 195-196°; ir cm^{-1}: 1805, 1734 (C=O), no absorption above 3150; ms m/e (% relative intensity): 332 (12), 288 (15), 273 (12), 158 (52), 130 (100), 103 (14) and 77 (15). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43. Found: C, 72.10; H, 4.82; N, 8.55.

The following compound was similarly prepared from 3-phenylindole (40).

3-Phenylindole-1-carboxylic Anhydride (**7b**).

This compound had m.p. 171-172°, yield, (42%); ir cm^{-1}: 1789, 1728 (C=O); ms m/e (% relative intensity): 456 (1), 413 (22), 412 (72), 220 (15), 193 (22), 192 (100) and 165 (28); m 143.1 (192 → 165). Only peaks stronger than 15% of the base peak are listed (except the M^+ peak).

Anal. Calcd. for $C_{30}H_{20}N_2O_3$: C, 78.93; H, 4.42; N, 6.14. Found: C, 78.95; H, 4.48; N, 6.08.

3-Methylindole-1-carboxylic Acid.

3-Methylindole-1-carboxylic anhydride (100 mg.) was added to a stirred mixture of ethanol (20 ml.), water (5 ml.) and potassium hydroxide (250 mg.). The resulting suspension was stirred for 6 hours at 25°. Acidification, of the now clear solution, with diluted hydrochloric acid gave 3-methylindole-1-carboxylic acid, yield, 89 mg. (89%), m.p. 115-118° (lit. (19) 128°); ir cm^{-1}: 1700 (C=O).

2,2'-(1-*N*,*N*-Dimethylcarboxamido-3-methylindolyl)-3-methylindoline-1-*N*,*N*-dimethylaminocarboxamide (**6b**).

3-Methylindole or its dimer **6c** (2.62 g.) was dissolved in phosgene in toluene (12.5%, 50 ml.). After 24 hours at 25°, a precipitate (0.7 g.) of the hydrochloride of the 3-methylindole dimer was removed. Gaseous dimethylamine was introduced to the filtrate, which was then evaporated and treated with methanol. The solid formed was washed with water and then recrystallized from methoxyethanol, yield, 1.3 g. (32%), m.p. 243-246°; ir cm^{-1}: 1645 (C=O); ms m/e (% relative intensity): 404 (12), 333 (25), 332 (71), 331 (19), 288 (27), 287 (100), 286 (23), 274 (18), 259 (17) and 144 (13). Only peaks stronger than 10% of the base peak and above m/e 100 are listed.

Anal. Calcd. for $C_{24}H_{28}N_4O_2$: C, 70.56; H, 6.91; N, 6.86. Found: C, 70.32; H, 7.11; N, 6.53.

1,1'-Carbonylindole (**9c**). Method A.

A solution of indole (5.85 g., 0.05 mole) and 1,1'-carbonylimidazole (4.50 g., 0.02 mole) in dry dimethyl sulfoxide (50 ml.) was heated at 125° for 2 hours. After cooling the reaction solution was poured into water (500 ml.) and the solid formed collected and recrystallized form methanol or ethanol, yield, 5.9 g. (91%), m.p. 100-101° (lit. (11) 245°); ir cm^{-1}: 1708 (C=O); ms m/e (% relative intensity): 261 (17), 260 (100), 259 (35), 145 (67), 117 (11), 116.5 (12) and 116 (87); m* 182.8 (260 → 218). Only peaks stronger than 10% of the base peak and above m/e 100 are listed.

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.49; H, 4.69; N, 10.62.

1,1'-Carbonylindole (**9c**). Method B.

A solution of 1,1'-carbonylindoline (264 mg., 1 mmole) and 2,3-dichloro-4,5-dicyanoquinone (454 mg., 2 mmoles) in dioxane (20 ml.) was heated (75°) for 3 hours. After cooling and filtration the solvent was evaporated and the residue extracted with methylene chloride (2 x 30 ml.) and sodium hydrogen carbonate

(aqueous, 5%, 30 ml.). The methylene chloride extract filtered through a short column of silica gel, evaporated and recrystallized from ethanol gave 1,1'-carbonylindole, yield, 195 mg. (75%).

The following compounds were similarly prepared (using method A):

1,1'-Carbonyl-3-methylindole (**9a**).

This compound had m.p. 123-124°, yield, (93%); ir cm^{-1}: 1706 (C=O); ms m/e (% relative intensity): 289 (17), 288 (90), 273 (43), 158 (67), 130 (100) and 103 (15); m* 258.8 (288 → 273). Only peaks stronger than 15% of the base peak and above m/e 100 are listed.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.88; H, 5.31; N, 9.59.

1,1'-Carbonyl-3-phenylindole (**9b**).

This compound had m.p. 96-97°, yield, (88%); ir cm^{-1}: 1724 (C=O); ms m/e (% relative intensity): 413 (29), 412 (90), 411 (11), 220 (20), 193 (23), 192 (100) and 165 (29). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{29}H_{20}N_2O$: C, 84.44; H, 4.89; N, 6.79. Found: C, 84.69; H, 4.64; N, 6.73.

1,1'-Carbonylpyrrole (**24**).

This compound had m.p. 61-62° (lit. (41) 61°), yield, (76%).

1,1'-Carbonylcarbazole (**25**).

This compound had m.p. 247-248°, yield, (94%).

Anal. Calcd. for $C_{25}H_{16}N_2O$: C, 83.31; H, 4.48; N, 7.77. Found: C, 83.60; H, 4.22; N, 7.93.

1,1'-Carbonylindoline (**23**).

This compound had m.p. 178-179°, yield, (95%); ir cm^{-1}: 1668 (C=O); ms m/e (% relative intensity): 264 (42), 147 (11), 146 (100), 128 (39), 117 (24) and 103 (45); m* 111.5 (146 → 128). Only peaks stronger than 10% of the base peak and above m/e 100 are listed.

Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.43; H, 6.01; N, 10.54.

1,1'-Carbonyl-3-acetylindole (**26**).

3-Acetylindole (1.59 g.) was dissolved in phosgene in toluene (40 ml., 3%), whereupon triethylamine (1.5 g.) was slowly added to the stirred solution. After 2 hours at 25° the reaction mixture was poured into water (250 ml.). The solid formed was crystallized from acetonitrile, yield, 1.41 g. (82%), m.p. 236-237°; ir cm^{-1}: 1730, 1665 (C=O); ms m/e (% relative intensity): 344 (25), 329 (13), 302 (13), 301 (46), 259 (17), 187 (21), 157 (11), 144 (16), 130 (21) and 43 (100); m* 223.0 (301 → 259) and 263.8 (329 → 301). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.14. Found: C, 73.33; H, 4.66; N, 8.02.

Reaction of 2-Chloro-1-methylindole-3-*N*,*N*-dimethylcarboxamide (**15**) with Dimethylamine at 110°.

A stream of dimethylamine was introduced to a solution of **15** (2.37 g.) in dimethyl formamide (40 ml.) at 110° for 2 hours. The reaction mixture was concentrated and treated with methanol. The solid formed was recrystallized from pyridine/ethanol to give **17** (24), yield, (38%), m.p. 255-257° dec.; ms m/e (% relative intensity): 292 (3), 291 (10), 162 (10), 161 (33), 148 (10), 147 (100), 133 (16) and 132 (13). Only peaks stronger than 10% of the base peak and m/e above 120 are listed.

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.98; H, 5.52; N, 9.59. Found: C, 74.11; H, 5.70; N, 9.51.

The methanol/dimethylformamide mother liquor was evaporated and chromatographed on silica gel with methylene chloride gave *N*-methyl-2-chloroindole.

Reaction of Phosgene with Indolylmagnesium Bromide in Refluxing Ether.

A solution of phosgene in toluene (40 ml., 12.5%) was added dropwise to a well stirred mixture of indolylmagnesium bromide (from 5.85 g. of indole) in ether (450 ml.) at reflux temperature. After completed addition the mixture was refluxed for 4 hours and then treated with cold water (250 ml.) followed by a saturated solution of ammonium chloride (150 ml.). After 45 minutes, the solid formed was collected, washed with water, dried and treated with hot methoxyethanol. The remaining solid recrystallized from 1,2-diacetoxyethane gave **21**, yield, 1.5 g. (21%), m.p. 300-302°; ir cm^{-1}: 1736, 1644 (C=O); ms m/e (% relative intensity): 572 (8), 181 (8) and 131 (26). Only peaks above m/e 100 are listed.

Anal. Calcd. for $C_{36}H_{20}N_4O_4$: C, 75.51; H, 3.52; N, 9.79. Found: C, 75.32; H, 3.44; N, 9.74.

The methoxyethanol mother liquor obtained above was evaporated, and the solid formed recrystallized from acetone gave di-(3-indolyl)ketone, yield, 2.6 g. (39%), m.p. 301-302°; ir cm^{-1}: 3170 (NH, broad), 1600-1500 (C=O, broad); ms m/e (% relative intensity): 261 (10), 260 (54), 259 (38), 246 (45), 245 (64), 243 (22), 206 (11), 144 (25), 130 (14), 118 (10) and 117 (100). Only peaks stronger than 10% of the base peak are listed.

The ether/water mixture obtained from the Grignard reaction above, was separated and the ether phase dried and evaporated. The residue was dissolved in methylene chloride and chromatographed on silica gel. The following compounds were isolated (in order of eluation): 1. 1,1'-Carbonyl indole, yield, 7%, m.p. 100-101°; 2. Indole, yield, 15%; 3. 1,3'-Carbonyl indole, yield, 4%, m.p. 227-229°; 4. Di(3-indolyl)ketone, yield, 9%, m.p. 301-302°; 5. A fraction containing two yellow compounds (not yet identified); 6. Compound **22**, yield, 0.5%, m.p. 279-280°.

1,3'-Carbonylindole.

This compound gave the following spectra and analytical data; ir cm^{-1}: 3235 (NH), 1633 (C=O); ms m/e (% relative intensity): 260 (31), 145 (11), 144 (100), 117 (94) and 116 (37). Only peaks above m/e 100 are listed.

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.71; H, 4.54; N, 10.89.

Compound **22**.

This compound gave the following spectra and analytical data; ir cm^{-1}: 1722, 1642 (C=O).

Anal. Calcd. for $C_{26}H_{17}N_3O_2$: C, 77.40; H, 4.25; N, 10.42. Found: C, 77.12; H, 4.29; N, 10.15.

Reaction of Phosgene with Indole Magnesium Bromide in Ether at 0°.

The experiment just described was repeated at 0°. The yields (%) in the two experiments are compared in the following table.

	0°	35°
21	0.5	11
9c	22	7
19	7	4
4c	30	48
22	–	0.5

Photolysis of 1,1'-Carbonylindole.

1,1'-Carbonylindole (2.60 g.) in ether was irradiated (250 nm)

under nitrogen in a Rayonet RPR-100 photoreactor for 48 hours at 25°. The reaction mixture was evaporated and chromatographed as described above giving: 1,1'-Carbonylindole, 0.93 g. (36%); Indole, 0.23 g. (10%); 1,3'-Carbonylindole, 0.87 g. (33%); 3,3'-Diindolyl ketone, 0.18 g. (7%).

3,3'-Diindolylmethane.

3,3'-Diindolyl ketone (260 mg.) was added to a mixture of lithium aluminium hydride (0.1 g.) in tetrahydrofurane (50 ml.). After a reflux period (6 hours) the reaction mixture after usual work-up yielded 3,3'-diindolylmethane, yield, 180 mg. (73%), m.p. 167-168° (lit. (42) 168°).

Reductive Cleavage of 1,3'-Diindolyl Ketone.

1,3'-Diindolyl ketone was treated with lithium aluminium hydride as described above. Preparative tlc (silica gel, hexane/methylene chloride) of the reaction mixture gave indole (yield 95%) and 3-methylindole (yield 92%).

Reductive Cleavage of **22**.

The same procedure was used giving 3,3'-diindolylmethane and indole (yield 94%).

Reductive Cleavage of 1,1'-Carbonylindole.

The same procedure was used giving indole (yield 96%).

Oxidation of 3,3'-Diindolylmethane with DDQ.

DDQ (454 mg., 2 mmoles) in dioxane (5 ml.) was added to 3,3'-diindolylmethane (246 mg., 1 mmole) in methanol (10 ml.) and water (1 ml.). After 2 hours at 50° sodium hydroxide (100 mg.) in water (10 ml.) was added and the solid collected, washed with sodium hydroxide (aqueous 1%), water, ethanol and dried, yield, 195 mg. (75%), m.p. 301-302°.

5,6-Dihydro-11-methyl-6-oxo-indolo[3,2-*c*]quinoline (**34b**). Method A.

A solution of phosgene in dioxane (20 ml., 12.5%) was added to a stirred solution of 2-(2-aminophenyl)-1-methylindole (43) (4.44 g., 10 mmoles) in dioxane (50 ml.) at 30°. Five minutes after completed addition, pyridine (2 ml.) was added and the mixture was stirred for 1 hour. The solid formed on addition to water (300 ml.) was recrystallized from methoxyethanol, yield, 4.15 g. (83%), m.p. 323-326°; ir cm^{-1}: 1650 (C=O); ms m/e (% relative intensity): 249 (18), 248 (100), 247 (11), 219 (12), 205 (10) and 110 (10). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.06; H, 4.52; N, 11.33.

Method B.

1-Methylindole-3-carboxanilide (44) was cyclized photochemically using the procedure given by Kanaoka (33) for the cyclization of indole-2-carboxanilide, yield (62%).

The following compounds were similarly prepared using method A:

5,6-Dihydro-11-methyl-6-oxobenzo[*a*]pyrano[4,3-*b*]indole (**33**).

This compound had m.p. 247-248° (lit. (31) 248°), yield, (84%); ir cm^{-1}: 1725 (C=O); ms m/e (% relative intensity): 250 (18), 249 (100), 248 (30) and 220 (19). Only peaks stronger than 10% of the base peak and above m/e 100 are listed.

11,12-Dihydro-11-oxo-indolo[1,2-*c*]quinazoline (**36**).

This compound had m.p. 300°, yield, (67%); ms m/e (% relative intensity): 235 (18), 234 (100), 206 (14), 205 (15) and 117 (10); m* 182.0 (234 → 206). Only peaks stronger than 10% of the base peak are listed.

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 77.06; H, 4.11; N, 12.07.

1,1'-Diindolylethanedione (**28a**).

Oxalyl chloride (0.84 ml.) was added slowly to a stirred solution of indole (2.34 g., 20 mmoles) and triethylamine (2.0 ml.) in dioxane (60 ml.) at 30°. After completed addition the mixture was stirred for 3 hours at 30° and then poured into water. The solid formed was collected, washed with water and recrystallized from ethanol, yield, 2.3 g. (77%), m.p. 157-158° (lit. (47) 155-156°); ir cm^{-1}: 1682 (C=O); ms m/e (% relative intensity): 289 (13), 288 (64), 260 (14), 259 (21), 144 (62), 117 (18) and 116 (100); m* 235.1 (288 → 259). Only peaks stronger than 10% of the base peak are listed.

1,3-Diindolylethanedione (**29**).

The procedure above was used, replacing oxalyl chloride with indolyl-3-glyoxylyl chloride (46) (2.07 g., 10 mmoles). The amount of indole was reduced to 10 mmoles, yield, 62%, m.p. 224-225° (lit. (45,47) 224-225°, 224-226°).

1,1-(Di-3-acetylindolyl)ethanedione (**28b**).

The procedure given above was used using 3-acetylindole (3.18 g.) as substrate, yield, 3.5 g. (94%), m.p. 190-191°; ir cm^{-1}: 1695, 1670 (C=O); ms m/e (% relative intensity): 373 (20), 329 (29), 301 (18), 259 (10), 186 (28), 171 (17), 144 (18), 130 (19), 115 (10) and 43 (100); m* 291.0 (301 → 259). Only peaks stronger than 10% of the base peak are listed. The analytical sample was recrystallized from 1,2-diacetoxyethane.

Anal. Calcd. for $C_{22}H_{16}N_2O_4$: C, 70.96; H, 4.33; N, 7.52. Found: C, 71.12; H, 4.38; N, 7.47.

1,1-(Di-3-methylindolyl)ethanedione.

The procedure given above was used, yield, (78%), m.p. 180-182° (lit. (39) 183.6-184.2°); ir cm^{-1}: 1683 (C=O); ms m/e (% relative intensity): 317 (15), 316 (69), 274 (27), 158 (70), 131 (15) and 130 (100); m* 259.8 (289 → 274). Only peaks stronger than 10% of the base peak and above m/e 120 are listed.

The Cyclotetramer **30**.

Compound **27a** (288 mg., 1 mmole) was dissolved in hot dioxane (40 ml.) containing triethylamine (1 ml.). Oxalyl chloride (0.4 ml.) was then added at 45° to the stirred solution. After completed addition the stirring was continued for 4 hours at 45° and then poured into water. The solid formed was washed repeatedly with water and ethanol and then recrystallized from 1,2-diacetoxyethane to give **30**, yield, 184 mg. (53%), m.p. >360°; ir cm^{-1}: 1702, 1656 (C=O).

Anal. Calcd. for $C_{40}H_{20}N_4O_8$: C, 71.00; H, 2.98; N, 16.56. Found: C, 70.59; H, 3.23; N, 16.71.

Reaction of Oxalyl Chloride with Indole Magnesium Bromide.

A solution of oxalyl chloride (12.7 g., 0.1 mole) in ether (25 ml.) was added dropwise to a well stirred mixture of indole magnesium bromide (0.1 mole from 11.7 g. of indole) and ether (500 ml.) at reflux temperature. After completed addition the mixture was stirred overnight. Water (200 ml.) followed by aqueous ammonium chloride (200 ml., saturated) was then added. After 90 minutes, the solid formed was collected, washed with water and ethanol, dried and treated with hot methoxyethanol. The remaining solid recrystallized from 1,2-diacetoxyethane gave **30**, yield, 0.52 (3%), m.p. >360°.

The organic phases obtained above, evaporated and chromatographed on silica gel gave the following compounds (in order of evaluation): 1. 1,1-Diindolylethanedione, 4% (157-158°); 2. Indole, 22%; 3. 1,3-Diindolylethanedione, 5% (224-226°); 4. 3,3-

Diindolylethanedione, 38% (267-269°).

3-Hydroxy-1-methyl-4*H*-pyridazino[3,4-*b*]indol-4-one (**39a**).

2-Chloroindole-3-glyoxylyl chloride (**13a**) (2.42 g., 10 mmoles) was added to a stirred solution of methylhydrazine (10 ml.) in water (50 ml.) at 25°. After 5 minutes methanol (25 ml.) was added, whereupon the mixture was boiled for 2 minutes and allowed to cool. The crystals formed were collected after 8 hours, washed with water and dried, yield, 1.77 g. (82%), m.p. 340-343° dec.; ms m/e (% relative intensity): 216 (26), 215 (100), 187 (18), 172 (26), 159 (13), 158 (16), 157 (40), 144 (43) and 143 (17). Only peaks stronger than 15% of the base peak and above m/e 120 are listed.

Anal. Calcd. for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.03; H, 4.02; N, 19.66.

3-Hydroxy-1-(2-hydroxyethyl)-4*H*-pyridazino[3,4-*b*]indol-4-one (**39b**).

The procedure given above was used, yield, (75%), m.p. 310-313°; ms m/e (% relative intensity): 246 (15), 245 (100), 214 (37), 201 (69), 171 (48) and 158 (15). Only peaks stronger than 15% of the base peak and above m/e 120 are listed.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found: C, 63.04; H, 4.99; N, 18.09.

2-Hydroxymethyl-2-(2-pyridyl)indole. Method A.

2-(2-Pyridyl)indole (1.94 g., 10 mmoles) was added to a stirred solution of phosgene in dioxane (3%, 50 ml.) at 30° to give a violet-red solution, which turned dark-green after *ca* 3 hours. After 24 hours at 30° solid sodium borohydride (500 mg.) was added followed 2 hours later by methanol (20 ml.). After 2 hours at 45° the mixture was poured into water. The brownish solid formed was dried and chromatographed on silica gel using methylene chloride containing increasing amounts of methanol as eluent gave 2-(2-pyridyl)indole (602 mg., 31% recovery) and finally 3-hydroxymethyl-2-(2-pyridyl)indole, yield, 1.1 g. (49%), m.p. 290-293° dec.; ir cm^{-1}: 3450 (OH), 3240 (NH).

Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.99; H, 5.38; N, 12.49. Found: C, 74.73; H, 5.54; N, 12.46.

Method B.

2-(2-Pyridyl)indole-3-carboxaldehyde (47) (1.11 g., 5 mmoles) was added in portions to sodium borohydride (0.5 g.) in methanol (50 ml.). The mixture was stirred at 40° for 4 hours, whereupon water (150 ml.) was added. The crude product was recrystallized from ethanol/water, yield, 0.93 g. (84%).

2′-Chloro-2,3′-biindolyl (**18b**).

Oxindole (1.31 g., 10 mmoles) in methylene chloride (15 ml.) was added to a stirred solution of phosgene in toluene (12.5%, 40 ml.) at 45°. After 3 hours at this temperature the solid formed was collected, washed with aqueous sodium carbonate, water and toluene, dried and recrystallized from benzene/methyl acetate, yield, 0.61 g. (44%), m.p. 146-147°; ms m/e (% relative intensity): 268 (33), 267 (20), 266 (100), 232 (41), 230 (15) and 133 (18). Only peaks stronger than 15% of the base peak and above m/e 120 are listed.

Anal. Calcd. for $C_{16}H_{11}ClN$: C, 76.04; H, 4.37; Cl, 14.03; N, 5.54. Found: C, 75.60; H, 4.53; Cl, 14.41; N, 5.51.

Reduction of 2′-Chloro-2,3′-biindolyl.

2′-Chloro-2,3′-biindolyl (134 mg.) and activated magnesium (35 mg.) in dry tetrahydrofurane (10 ml.) was refluxed under nitrogen for 4 hours, whereupon the reaction mixture was treated with water (100 ml.) and chloroform (50 ml.). The organic phase was washed with water, dried and evaporated. The residue recrystallized from toluene gave 2,3-biindolyl, yield, 78 mg. (67%); m.p. 203-205° (lit. (49,50) 203-205°, 190-191°).

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REFERENCES AND NOTES

(1) J. Bergman and J.-E. Bäckvall, *Tetrahedron*, 31, 2063 (1975).

(2) P. E. Peterson, J. P. Wolf III and C. Nieman, *J. Org. Chem.*, 23, 303 (1958).

(3) F. P. Doyle, W. Ferrier, D. O. Holland, M. D. Mehta and J. H. C. Nayler, *J. Chem. Soc.*, 2853 (1956).

(4) C. Gräbe and C. Liebermann, *Ber.*, 2, 678 (1867).

(5) W. Michler, *ibid.*, 9, 400 (1867).

(6) H. Babad and A. G. Zeiler, *Chem. Rev.*, 73, 75 (1973).

(7) G. M. Dyson, *ibid.*, 4, 109 (1927).

(8) W. Treibs, H.-J. Neupert and J. Hiebsch, *Chem. Ber.*, 92, 1216 (1959).

(9) Great Britain Patent 987,516 (to ICI).

(10) A. Gossauer, "Die Chemie der Pyrrole", Springer-Verlag, Berlin, Heidelberg, New York, N. Y., 1974, pp. 307, 314 and 315.

(11) B. Oddo and Q. Mingoia, *Gazz. Chim. Ital.*, 57, 473 (1927).

(12) R. A. Heacock and S. Kašpárek, *Adv. Heterocyclic Chem.*, 10, 43 (1969).

(12a) B. Stanovnik, M. Tisler and J. T. Carlock, *Synthesis*, 754 (1976).

(13) G. F. Smith and A. E. Walters, *J. Chem. Soc.*, 940 (1961).

(14) G. F. Smith, *Adv. Heterocyclic Chem.*, 2, 287 (1963).

(15) W. Borsche and A. Klein, *Ann. Chem.*, 548, 64 (1941).

(16) S. Inaba, K. Ishizumi and H. Yamamoto, *Chem. Pharm. Bull.*, 19, 263 (1971).

(17) R. J. Boatman and H. W. Whitlock, *J. Org. Chem.*, 41, 3050 (1976).

(18) D. P. Landucci, M. S. Thesis, Univ. of Minnesota, Minneapolis (1969).

(19) C. W. Whittle and R. N. Castle, *J. Pharm. Sci.*, 52, 646 (1963).

(19a) N. Garcia-Martinez, *Diss. Abstr. B*, 30, 4560 (1970).

(20) R. Buyle and H. G. Viehe, *Tetrahedron*, 24, 4217 (1968).

(21) U. Stoess, *Diss. Münster*, (1967).

(22) K. E. Schulte, J. Reisch and U. Stoess, *Arch. Pharm.*, 305, 523 (1972).

(22a) Oxalyl bromide reacted similarly. Thus, *e.g.*, methyl 2-bromo-*N*-methylindole-3-glyoxylate could readily be prepared (see Experimental).

(23) J. Powers, *Tetrahedron Letters*, 655 (1965).

(24a) This procedure gives a high-melting (255-257°, dec.) form of **17**, presumably the mesoform, (*cf.* references 24b and 24c). The low-melting (194-196°) form reported by Hino (24c) might be the racemate.

(24b) J. Harley-Mason and R. F. J. Ingleby, *J. Chem. Soc.*, 4782 (1958).

(24c) T. Hino, *Chem. Pharm. Bull.*, 9, 979 (1961).

(25) A. Deberley, D. Abenhaim and J. Bourdais, *J. Heterocyclic Chem.*, 12, 1087 (1975).

(26) In addition small amounts of two, so far undetermined, yellow compounds were isolated.

(27) R. Kašpárek and R. A. Heacock, *Can. J. Chem.*, 44, 2805 (1966).

(28) J. Bergman, R. Carlsson and S. Misztal, *Acta Chem. Scand.*, 30B, 853 (1976).

(29) K. Yamane, *Bull. Chem. Soc. Japan*, 49, 1101 (1976).
(30) Y. Oikawa and O. Yonemitsu, *Heterocycles*, 4, 1859 (1976).
(30a) J. M. Patterson and D. M. Bruser, *Tetrahedron Letters*, 2959 (1973).
(31) J. Bourdais and A. Lorre, *J. Heterocyclic Chem.*, 12, 1111 (1975).
(32) E. Winterfeldt and H. J. Altmann, *Angew. Chem.*, 80, 486 (1968).
(33) Y. Kanaoka and K. Itoh, *Synthesis*, 36 (1972).
(34) Y. Kanaoka, S. Nakao and Y. Hatanaka, *Heterocycles*, 5, 261 (1976).
(35) J. H. M. Hill, 172nd National ACS Meeting, San Francisco, Aug. 30-Sept. 3 (1976).
(36) H. Vorbrüggen, *Tetrahedron Letters*, 1631 (1968).
(37) M. Makosza and M. Fedorynski, *Rocz. Chem.*, 45, 1861 (1971).
(38) J. Powers, *J. Org. Chem.*, 31, 2627 (1966).
(39) F. Millich and E. I. Becker, *ibid.*, 23, 1096 (1958).
(40) J. Bergman, *Acta Chem. Scand.*, 25, 1277 (1971).
(41) W. Tschelinzeff and B. Maxoroff, *Ber.*, 60, 194 (1927).
(42) J. Thesing, *Chem. Ber.*, 87, 692 (1954).
(43) A. K. Kiang, F. G. Mann, A. F. Prior and A. Topham, *J. Chem. Soc.*, 1319 (1956).
(44) J. M. Weinmann, Ph.D. Thesis, Minneapolis (1964).
(45) R. Majima and T. Shigematsu, *Ber.*, 57, 1449 (1924).
(46) M. E. Speeter and W. C. Anthony, *J. Am. Chem. Soc.*, 76, 6208 (1954).
(47) S. Hichida, *Nippon Kagaku Zasshi*, 72, 312 (1951).
(48) G. Buchmann and H. Tischer, *Wiss. Z. Tech. Hochsch. Chem. "Carl Schorlemmer" Leuna-Merseburg*, 8, 26 (1966).
(49) J. Bergman, *J. Heterocyclic Chem.*, 10, 121 (1973).
(50a) S. Al-Azawe and G. Y. Sarkis, *J. Chem. Eng. Data*, 18, 109 (1973).
(50b) We have repeated the synthesis of 2,3-biindolyl (from 3-acetylindole and phenylhydrazine) claimed by Al-Azawe, *et al.*, (50a) several times but always get the starting material, 3-acetylindole (m.p. 191-192°!) back. Unfortunately, the Iraqian workers failed to compare the data of their product with data from the literature.
(51) J. Degen, *Ann. Chem.*, 236, 157 (1886).
(52) V. I. Shvedov, A. V. Bocharnikova and A. N. Grinev, *Khim. Geterosikl, Soedin.*, 137 (1968).
(53) J. Hillard, K. V. Reddy, K. C. Majumdar and B. S. Thyagarajan, *J. Heterocyclic Chem.*, 11, 369 (1974).
(54) W. B. Whalley, *J. Chem. Soc.*, 3229 (1951).
(55) J. Bourdais, French Demande 2,121,394.
(56) G. Hart and K. T. Potts, *J. Org. Chem.*, 27, 2940 (1962).
(57) V. Sprio and P. Madonia, *Gazz. Chim. Ital.*, 87, 454 (1957).
(58) U. Stauss, H. P. Harter, M. Neuenschwander and O. Schindler, *Helv. Chim. Acta*, 55, 771 (1972).
(59) T. Nishiwaki, *J. Chem. Soc., Perkin Trans. I*, 1867 (1974).
(60) W. E. Noland and R. D. Rieke, *J. Org. Chem.*, 27, 2250 (1962).
(61) J. Bourdais and C. Germain, *J. Heterocyclic Chem.*, 13, 1209 (1976).
(62) S. Kašpárek and R. A Heacock, *Can. J. Chem.*, 45, 771 (1967).
(63) L. Marchetti and A. Andreani, *Ann. Chim.*, 53, 681 (1973).