1,3,4,5-Tetrahydrobenz[cd]indoles and Related Compounds.   Part II.[1]

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The preparation of 3,4-dihydro-1-(p-tolylsulphonyl)benz[cd]indol-5(1H)-one (2) and its conversion to a wide variety of 5-substituted tetrahydrobenz[cd]indoles are described, thus demonstrating the value of the N-tosyl protecting group in indole chemistry.   Several reactions were also possible with the corresponding 1-acetyl derivative (3).

THE chemistry of 3,4-dihydrobenz[cd]indol-5(1H)-one (1) is dominated by the inherent tendency of the molecule to undergo isomerisation to the more stable naphthalenoid system.[2]   Protection of the indole imino-group as its N-acetyl derivative overcomes this problem only to a

limited extent since the protecting group is labile in alkaline media.   A more promising protecting group should be the tosyl since the stability of N-tosylindole to mild alkali has already been reported by us;[3] removal of the protecting group may be easily achieved in reflux-

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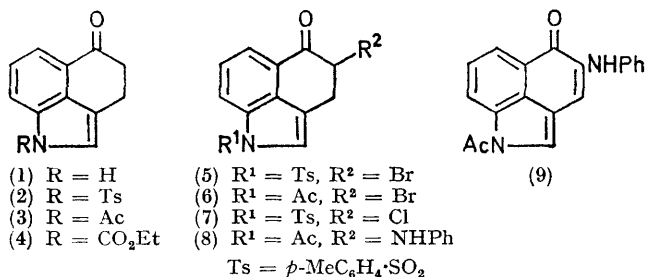
[1] Part I, R. E. Bowman, T. G. Goodburn, and A. A. Reynolds, *J.C.S. Perkin I*, 1972, 1121.

[2] E. C. Kornfeld, E. J. Fornefeld, G. B. Kline, M. J. Mann, D. E. Morrison, R. G. Jones, and R. B. Woodward, *J. Amer. Chem. Soc.*, 1956, **78**, 3087.

[3] R. E. Bowman, D. D. Evans, and P. J. Islip, *Chem. and Ind.*, 1971, 33.

ing alkali. This paper describes the synthesis of 3,4-di-hydro-1-(*p*-tolylsulphonyl)benz[*cd*]indol-5(1*H*)-one (2) and some of its reactions not shown by the parent ketone [4] (1) or the *N*-acetyl derivative [4] (3).

The starting *N*-tosyl ketone (2) was readily prepared by treatment of the ketone (1) with toluene-*p*-sulphonyl chloride in the presence of anhydrous potassium carbonate in ethyl methyl ketone under reflux; the *N*-acetyl and *N*-ethoxycarbonyl derivatives were also prepared similarly with acetic anhydride and ethyl chloroformate respectively. The ease of these reactions is ascribed to


(1) R = H
(2) R = Ts
(3) R = Ac
(4) R = CO$_2$Et

(5) R^1 = Ts, R^2 = Br
(6) R^1 = Ac, R^2 = Br
(7) R^1 = Ts, R^2 = Cl
(8) R^1 = Ac, R^2 = NHPh

Ts = *p*-MeC$_6$H$_4$·SO$_2$

(9)

the electron-attracting properties of the carbonyl group rendering the imino-proton more acidic. This effect has already been reported [3] for appropriately substituted indoles.

The ketones (2) and (3) undergo many of the expected reactions. Ethylene glycol or ethanedithiol in the presence of toluene-*p*-sulphonic acid gave the acetal and thioacetal derivatives. Alkaline hydrolysis of the *N*-acetyl acetal yielded an oil, which had no carbonyl absorption in the i.r. spectrum, and was remarkably sensitive to acid conditions: stirring with aqueous acetic acid for 5 min resulted in complete hydrolysis to the ketone (1) in almost quantitative yield.

Bromination of the ketones (2) and (3) with trimethyl-phenylammonium tribromide takes place α- to the carbonyl group as does chlorination with sulphuryl chloride. Elimination of hydrogen halide from these products occurs readily in the presence of base so that substitution of the halogen atom by amines was possible only with weak bases, *e.g.* aniline. The anilino-derivative (8) was obtained when the reaction was carried out under nitrogen, but in the presence of air the highly coloured unsaturated compound (9) was formed.

The *N*-acetyl ketone (3) underwent the Leuckart reaction to yield the formamido-derivatives (10) and (11); the former was subsequently reduced with lithium aluminium hydride to the dimethylamino-analogue (12). Introduction of a basic group at C-5 was also possible by the following route. Reduction of the *N*-tosyl ketone (2) with lithium aluminium hydride gave the *N*-tosyl alcohol (13), which was converted into the amine (14) *via* the corresponding bromo- and azido-compounds. Reaction of the *N*-tosyl alcohol (13) with thionyl chloride also gave an oily chloro-derivative which could be subsequently reduced to the 5-deoxy-compound.

[4] F. C. Uhle, *J. Amer. Chem. Soc.*, 1949, **71**, 761.

The *N*-tosyl ketone (2) gave a normal Mannich reaction product. A Darzens condensation of the ketone (2) with ethyl chloroacetate gave, in good yield, the glycidic ester which was a convenient starting material for the synthesis [2] of a variety of 5-substituted compounds such
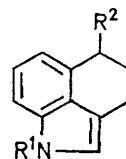
(10) R^1 = Ac, R^2 = NMe·CHO
(11) R^1 = Ac, R^2 = NH·CHO
(12) R^1 = H, R^2 = NMe$_2$
(13) R^1 = Ts, R^2 = OH
(14) R^1 = H, R^2 = NH$_2$
(15) R^1 = Ts, R^2 = CHO
(16) R^1 = Ts, R^2 = CO$_2$H
(17) R^1 = Ts, R^2 = CH:NOH
(18) R^1 = Ts, R^2 = CN
(19) R^1 = Ts, R^2 = CO·NH$_2$
(20) R^1 = Ts, R^2 = CH$_2$·NH$_2$,HCl
(21) R^1 = Ts, R^2 = CH$_2$·NMe$_2$
(22) R^1 = Ts, R^2 = CH$_2$·CO$_2$Et
(23) R^1 = Ts, R^2 = CH$_2$·CO$_2$H
(24) R^1 = H, R^2 = CH$_2$·CO$_2$H

Ts = *p*-MeC$_6$H$_4$·SO$_2$

as the aldehyde (15), the acid (16), the oxime (17), and the nitrile (18); treatment of the latter with hydrogen peroxide gave the corresponding carboxamide (19), and with diborane the 5-aminomethyl derivative (20) was obtained. The corresponding 5-(dimethylamino)methyl derivative (21) was prepared from aldehyde (15) by a Leuckart reaction.

Reaction of the ketone (2) with ethoxyethynylmag-nesium bromide yielded the ethoxyethynyl alcohol, which with dilute acid was converted into the unsatu-rated ester (25). Hydrogenation then gave the sub-stituted acetate (22), which, on hydrolysis with dilute alkali, gave the acid (23), and with 3N-aqueous alcoholic potassium hydroxide yielded the indolic acid (24).
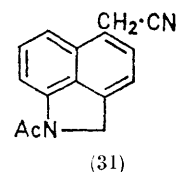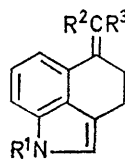

(25) R^1 = Ts, R^2 = H, R^3 = CO$_2$Et
(26) R^1 = Ts, R^2 = CN, R^3 = CN
(27) R^1 = Ts, R^2 = CN, R^3 = CO$_2$Et
(28) R^1 = Ac, R^2 = CN, R^3 = CO$_2$Et
(29) R^1 = Ac, R^2 = CN, R^3 = CO$_2$H
(30) R^1 = Ac, R^2 = CN, R^3 = H

(31)

In the Cope–Knoevenagel reaction both ketones (2) and (3) were converted into the expected products (26)—(29). Decarboxylation of the cyano-acid (29) in boiling dimethylacetamide gave initially (after 1 min) the nitrile (30) ($\nu_{max.}$ 1690 cm^{-1}), whereas after 1 h the main product was the indolinyl-nitrile (31) ($\nu_{max.}$ 1660 cm^{-1}). Reduction of the malononitrile (26) and the cyano-ester (28) proceeded readily to give the correspond-ing saturated compounds (32) and (33); reaction
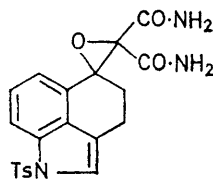
of the malononitrile (26) with hydrogen peroxide [5] afforded the epoxy-diamide (34) in good yield.
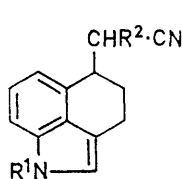
(32) R^1 = Ts, R^2 = CN
(33) R^1 = Ac, R^2 = CO_2Et

(34)

The oximes derived from the two ketones (2) and (3) were found to undergo Beckmann rearrangement with thionyl chloride, with consequent ring expansion to the azepinones (35) and (36). Subsequent mild alkaline hydrolysis of the latter yielded the azepinone (37) which was converted into the dimethyl analogue (38) with methyl iodide in dimethylformamide in the presence of sodium hydride. This compound (38) was also isolated in low yield after methylation of the N-acetylazepinone (36) under the same conditions, this displacement of the indole N-acetyl group under anhydrous methylation conditions was unexpected, and a further example will also be reported in a subsequent paper. Reduction with lithium aluminium hydride of the azepinone (37) gave a crystalline base having a pK_a of 7·95, indicative of a benzylamino-, rather than an anilino-system, in accordance with the azepine structure (40); the corresponding 1,5-dimethyl (41) and 5-methyl (42) compounds were similarly prepared from the lactam (38) and the urethane (43) respectively.
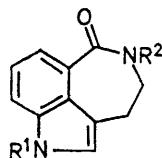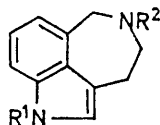

(35) R^1 = Ts, R^2 = H
(36) R^1 = Ac, R^2 = H
(37) R^1 = R^2 = H
(38) R^1 = R^2 = Me
(39) R^1 = H, R^2 = Me

(40) R^1 = R^2 = H
(41) R^1 = R^2 = Me
(42) R^1 = H, R^2 = Me
(43) R^1 = H, R^2 = CO_2Me

EXPERIMENTAL

M.p.s were determined on a Kofler block. U.v. spectra were determined for ethanolic solutions and i.r. spectra for Nujol mulls, unless otherwise specified. Potentiometric titrations were determined in aqueous ethanol (1 : 1 v/v).

3,4-Dihydro-1-(p-tolylsulphonyl)benz[cd]indol-5(1H)-one (2).—A stirred mixture of 3,4-dihydrobenz[cd]indol-5(1H)-one (6·3 g), anhydrous potassium carbonate (21 g), toluene-p-sulphonyl chloride (15 g), and ethyl methyl ketone (120 ml) was heated under reflux for 4 h, filtered, and the filtrate was evaporated to dryness in vacuo. A solution of the residue in toluene was evaporated to dryness in vacuo to leave a solid. Trituration of the solid with ether (200 ml) yielded the p-tolylsulphonyl ketone (9·55 g), m.p. 137—142 and 154—157°. The ethereal mother liquor was evaporated to dryness, and the residual oil, after chromatography, gave a second crop (1·48 g) of the p-tolylsulphonyl ketone, m.p. 142—144 and 156—158° (yield 92%). An

analytical sample obtained by recrystallisation from ethanol had m.p. 143—144 and 157—158° (Found: C, 66·6; H, 4·7; N, 3·9. $C_{18}H_{15}NO_3S$ requires C, 66·4; H, 4·65; N, 4·3%).

Similarly obtained was the N-acetyl ketone (3), m.p. 145—147° (lit.,[4] 148—149°) and ethyl 3,4-dihydro-5-oxo-1H-benz[cd]indole-1-carboxylate (4) (obtained by stirring the reactants for 60 h at room temperature), m.p. 110—112° (Found: C, 69·2; H, 5·7; N, 5·9. $C_{14}H_{13}NO_3$ requires C, 69·1; H, 5·4; N, 5·8%).

1-Acetyl-1,3,4,5-tetrahydrobenz[cd]indole-5-spiro-2'-(1,3-dioxolan).—A stirred mixture of 1-acetyl-3,4-dihydrobenz[cd]indol-5(1H)-one (5·3 g), ethylene glycol (2·5 ml), toluene-p-sulphonic acid (125 mg), and benzene (125 ml) was heated under reflux for 90 min, cooled, and the supernatant liquor was decanted from a black insoluble tar. The solution was washed with saturated sodium hydrogen carbonate solution, with water until neutral, dried (MgSO$_4$), filtered, and evaporated to dryness in vacuo. Crystallisation of the residual solid (6·1 g) from methanol gave the acetal (4·62 g), m.p. 120—123°. An analytical sample had m.p. 121—124° (from methanol) (Found: C, 70·3; H, 5·9; N, 5·4. $C_{15}H_{15}NO_3$ requires C, 70·0; H, 5·9; N, 5·4%), $\nu_{max.}$ 1700 cm^{-1}.

A similar method gave the corresponding p-tolylsulphonyl acetal, m.p. 69—79° (Found: C, 64·6; H, 5·9; N, 3·3%. $C_{20}H_{19}NO_4S$ requires C, 65·0; H, 5·2; N, 3·8%), and substitution of ethanedithiol for ethylene glycol gave the thioacetal of the N-acetyl ketone, m.p. 142—143°, $\lambda_{max.}$ 246, 267sh, 279, and 310 nm (ε, 20,300, 10,410, 9900, 7000, and 7120) (Found: C, 62·2; H, 5·1; N, 5·0. $C_{15}H_{15}NOS_2$ requires C, 62·25; H, 5·2; N, 4·8%).

Hydrolysis of the Acetyl Ketone Acetal.—A 5% methanolic potassium hydroxide solution (2 ml) was added to a hot stirred solution of the N-acetyl acetal (1·0 g) in methanol (12 ml) and stirring was continued for 10 min while the mixture cooled to room temperature, and a further 20 min in an ice-bath. Dilution of the clear solution with water gave an oil, which failed to crystallise. The methanol was evaporated in vacuo, and the oil was extracted into ether–dichloromethane. Evaporation of the washed and dried extract gave an oil (990 mg) which had no carbonyl absorption in the i.r. spectrum, but strong absorption at $\nu_{max.}$ 3450 cm^{-1}. The oil was stirred with glacial acetic acid (0·5 ml) for 5 min and the solution was diluted with water (0·5 ml). Trituration of the oily suspension gave a mustard-coloured solid, which was washed thoroughly with water and dried to give 3,4-dihydrobenz[cd]indol-5(1H)-one (606 mg, 91%), m.p. 161—163° (lit.,[4] 165—166°) with an identical i.r. spectrum to an authentic sample (Found: C, 76·6; H, 5·6; N, 8·0. Calc. for $C_{11}H_9NO$: C, 77·2; H, 5·3; N, 8·2%).

4-Bromo-3,4-dihydro-1-(p-tolylsulphonyl)benz[cd]indol-5-(1H)-one (5).—A solution of trimethylphenylammonium tribromide (11·2 g) in tetrahydrofuran (60 ml) was added to an ice-cooled solution of 3,4-dihydro-1-(p-tolylsulphonyl)benz[cd]indol-5(1H)-one (2) (9·74 g) in tetrahydrofuran (200 ml) Stirring was continued at 0° for 10 min, the mixture was filtered, and the red filtrate was evaporated to dryness in vacuo. Trituration of the residual red oil yielded the bromo-ketone (11·8 g), m.p. 163—164° (from acetonitrile) (Found: C, 53·9; H, 3·9; N, 3·6. $C_{18}H_{14}BrNO_3S$ requires C, 53·5; H, 3·5; N, 3·5%), $\nu_{max.}$ 1680, 1175, and 1185 cm^{-1}

[5] G. B. Payne, J. Org. Chem., 1961, 26, 663.

A similar method gave 1-acetyl-4-bromo-3,4-dihydrobenz[cd]indol-5-(1H)-one [4] (6), m.p. 162—165° (from acetonitrile) (Found: C, 53·9; H, 3·45; N, 4·6; Br, 27·1. Calc. for $C_{13}H_{10}BrNO_2$: C, 53·25; H, 3·45; N, 4·8; Br, 27·3%).

4-*Chloro*-3,4-*dihydro*-1-(p-*tolylsulphonyl*)benz[cd]indol-5(1H)-one (7).—Sulphuryl chloride (0·5 ml) was added to a solution of the ketone (2) (2·0 g) in chloroform (10 ml) and after 30 min the *chloro-ketone* was filtered off as a light brown solid (1·0 g), m.p. 188—190° (from benzene) (Found: C, 60·25; H, 3·9; N, 3·75. $C_{18}H_{14}ClNO_3S$ requires C, 60·1; H, 3·9; N, 3·9%). Work-up of the mother liquors gave a second crop (0·5 g) of the chloro-ketone.

1-*Acetyl*-4-*anilinobenz*[cd]*indol*-5(1H)-*one* (9).—A solution of 1-acetyl-4-bromo-3,4-dihydrobenz[cd]indol-5(1H)-one (6) (0·5 g) and aniline (1·37 ml) in benzene (13·7 ml) was heated under reflux until a quantitative yield of aniline hydrobromide was obtained. The aniline hydrobromide was filtered off and the filtrate, after evaporation to dryness, gave a brown oil, which was washed with light petroleum (b.p. 40—60°) and then triturated with ether. The solid (0·2 g), m.p. 160—163°, obtained was crystallised from ethanol and gave the dark red *anilino-compound*, m.p. 162—164°, $\nu_{max.}$ 1610, 1670, 1700, and 3330 cm^{-1} (Found: C, 75·3; H, 5·0; N, 9·2. $C_{19}H_{14}N_2O_2$ requires C, 75·5; H, 4·7; N, 9·3%).

A similar procedure but under nitrogen gave yellow 1-*acetyl*-4-*anilino*-3,4-*dihydrobenz*[cd]*indol*-5(1H)-*one* (8), m.p. 195—200°, $\nu_{max.}$ 1665 and 3330 cm^{-1} (Found: C, 75·1; H, 5·2; N, 9·1. $C_{19}H_{16}N_2O_2$ requires C, 75·0; H, 5·3; N, 9·0%).

N-(1-*Acetyl*-1,3,4,5-*tetrahydrobenz*[cd]*indol*-5-*yl*)-N-*methylformamide* (10).—A solution of 1-acetyl-3,4-dihydrobenz[cd]indol-5(1H)-one (430 mg) in N-methylformamide (1 ml) and formic acid (1 ml) was heated gently under reflux under nitrogen for 3·5 h before being poured onto ice. An excess of sodium hydrogen carbonate solution was added and the product extracted with dichloromethane. Evaporation of the washed and dried (MgSO$_4$) extract gave an oil (462 mg), which was dissolved in hot ethanol. Cooling gave the *formamide* (220 mg), m.p. 137—141°. Two recrystallisations gave an analytical sample, m.p. 141—142° (Found: C, 70·1; H, 6·3; N, 10·9. $C_{15}H_{16}N_2O_2$ requires C, 70·3; H, 6·3; N, 10·9%).

A similar reaction with formamide and heating for 5 h gave N-(1-*acetyl*-1,3,4,5-*tetrahydrobenz*[cd]-*indol*-5-*yl*)*formamide* (11), m.p. 167—170° (Found: C, 69·7; H, 5·9; N, 11·4. $C_{14}H_{14}N_2O_2$ requires C, 69·4; H, 5·8; N, 11·6%).

5-*Dimethylamino*-1,3,4,5-*tetrahydrobenz*[cd]*indole* (12).—A stirred mixture of N-(1-acetyl-1,3,4,5-tetrahydrobenz[cd]-indol-5-yl)-N-methylformamide (510 mg) and lithium aluminium hydride (250 mg) in tetrahydrofuran (30 ml) was heated under reflux for 8 h, cooled, and treated successively with water (0·25 ml), 4N-sodium hydroxide (0·25 ml), and water (0·75 ml). The inorganic material was filtered off, and the filtrate, evaporated to dryness in vacuo, gave a solid (416 mg), m.p. 142—148°. Two recrystallisations from ethanol yielded 5-*dimethylamino*-1,3,4,5-*tetrahydrobenz*[cd]*indole*, m.p. 151°, pK$_a$ 8·51 (Found: C, 77·15; H, 8·9; N, 14·1%; equiv., 202. $C_{13}H_{16}N_2$ requires C, 78·0; H, 8·0; N, 14·0%; equiv., 200).

1,3,4,5-*Tetrahydro*-1-(p-*tolylsulphonyl*)benz[cd]*indol*-5-*ol* (13).—A solution of 3,4-dihydro-1-(p-tolylsulphonyl)benz-[cd]indol-5(1H)-one (5 g) in tetrahydrofuran (100 ml) was added to a stirred suspension of lithium aluminium hydride (1 g) in tetrahydrofuran (150 ml) and stirring continued for a

further 20 min. Work-up as in the previous experiment yielded an oil (4·8 g), which after trituration with ether, gave a solvated solid (3·6 g), m.p. 124—126°. A sample crystallised from acetone–n-hexane yielded the *alcohol*, m.p. 145—147° (Found: C, 66·05; H, 5·3; N, 4·2. $C_{18}H_{17}$-NO$_3$S requires C, 66·05; H, 5·2; N, 4·3%).

5-*Amino*-1,3,4,5-*tetrahydrobenz*[cd]*indole* (14).—Anhydrous hydrogen bromide was bubbled through a cooled (10°) solution of the alcohol (13) (2·0 g) in benzene (200 ml) for 45 min and for a further 2 h at room temperature. The solution was washed successively with water, saturated sodium hydrogen carbonate solution, and sodium chloride solution until neutral; evaporation of the dried extract gave an oil (2·53 g). To a solution of the oil in acetonitrile (70 ml), was added a solution of sodium azide (1·12 g) in water (14 ml) and the mixture was stirred at room temperature overnight. The acetonitrile was evaporated in vacuo, and the residue was partitioned between ether and water. The ethereal extract was washed with water, dried (MgSO$_4$), filtered, and evaporated to dryness in vacuo to give an oil (2·02 g), $\nu_{max.}$ 2100 cm^{-1} (azide). A solution of the oil (1·01 g) in tetrahydrofuran (80 ml) was added to a stirred suspension of lithium aluminium hydride (1·0 g) in tetrahydrofuran (40 ml), the mixture was heated under reflux overnight, and worked-up as before to give an oil (0·6 g), which on trituration with ether yielded a white solid (160 mg), m.p. 138—144°. Two recrystallisations from aqueous ethanol gave the *amine*, m.p. 144—148° (Found: C, 76·1; H, 7·1; N, 16·0. $C_{11}H_{12}N_2$ requires C, 76·7; H, 7·0; N, 16·3%).

1,3,4,5-*Tetrahydro*-1-(p-*tolylsulphonyl*)benz[cd]*indole*.—Thionyl chloride (1·0 ml) was added to a stirred suspension of p-tolylsulphonyl alcohol (13) (645 mg) in benzene (30 ml) and the mixture stirred for 40 min before being evaporated to dryness in vacuo. The residual oil (720 mg) was hydrogenated in ethyl acetate (50 ml) in the presence of 10% palladised charcoal and sodium hydrogen carbonate (1·0 g) to give 1,3,4,5-*tetrahydro*-1-(p-*tolylsulphonyl*)benz[cd]*indole* (570 mg), m.p. 153—155° (Found: C, 68·9; H, 5·1; N, 4·5. $C_{18}H_{17}NO_2S$ requires C, 69·4; H, 5·5; N, 4·5%).

4-[(*Dimethylamino*)*methyl*]-3,4-*dihydro*-1-(p-*tolylsulphonyl*)benz[cd]*indol*-5(1H)-*one Hydrochloride*.—A stirred mixture of 3,4-dihydro-1-(p-tolylsulphonyl)benz[cd]indol-5(1H)-one (3·9 g, 12 mmol), paraformaldehyde (1·08 g, 12 mmol), dimethylamine hydrochloride (1·46 g, 15 mmol), ethanol (39 ml), and concentrated hydrochloric acid (0·39 ml) was heated under reflux for 4 h, additional paraformaldehyde (1·08 g) added, and the heating continued for a further 2 h. The cooled solution gave a cream-coloured solid (3·03 g), which was dissolved in hot ethanol (30 ml), the solution cooled to 35°, and diluted with ether (30 ml) to give the *hydrochloride* (2·27 g), m.p. 113—116° (Found: C, 57·4; H, 5·6; N, 6·2. $C_{21}H_{23}ClN_2O_3S,H_2O$ requires C, 57·7; H, 5·8; N, 6·4%).

Ethyl 1,3,4,5-*Tetrahydro*-1-(p-*tolylsulphonyl*)benz[cd]*indole*-5-*spiro*-2'-*oxiran*-3'-*carboxylate*.—A stirred solution of the ketone (2) (972 mg, 3 mmol) and ethyl chloroacetate (0·51 ml) in benzene (10 ml) under nitrogen was cooled in an ice-bath and a solution of potassium t-butoxide [from potassium (537 mg)] was added over 15 min. The mixture was stirred for a further 30 min and finally warmed at 75° for 1 h before being evaporated to dryness in vacuo. A solution of the residue in ethyl acetate was washed successively with dilute sulphuric acid, sodium hydrogen carbonate solution, and water. Evaporation of the dried solution yielded the *ester* (1·24 g), m.p. 129—134° (from methanol), $\nu_{max.}$

1725 cm^{-1} (Found: C, 63·9; H, 5·3; N, 3·4. C$_{22}$H$_{21}$NO$_3$S requires C, 64·2; H, 5·15; N, 3·4%).

Subsequent experiments showed that this reaction could be carried out equally well at room temperature for 2·5 h.

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole-5-carboxylic Acid (16).—A suspension of the foregoing ester (1·63 g) in ethanol (16 ml) and 10N-sodium hydroxide (0·8 ml) was warmed at 75° for 5 min, cooled, and refrigerated overnight, and the sodium salt of the spiro-oxiran acid (1·5 g) was filtered off and dried. The crude salt was dissolved in water (10 ml), sodium metabisulphate (5 g) was added, and the mixture was shaken at room temperature for 30 min. During this time the solid which had precipitated on addition of the sodium metabisulphate redissolved. The solution was cooled in an ice-bath for 10 min and the gelatinous precipitate separated by centrifuging. The damp solid was dissolved in water (10 ml) and concentrated hydrochloric acid–acetic acid (5 ml; 1 : 1 v/v) was added; the gum which separated slowly solidified on trituration and after 20 h at room temperature the amorphous aldehyde (965 mg), $\nu_{max.}$ 1715 cm^{-1}, was filtered off and washed with water.

A solution of the crude aldehyde (15) (500 mg) in acetone (50 ml) was cooled in an ice-bath and treated with Jones chromic acid (0·3 ml) during 2 min. Stirring was continued for a further 3 min before methanol (1 ml) was added and the solvents evaporated *in vacuo*. The residue was partitioned between water and ethyl acetate, and the organic phase separated. The acidic product was extracted with sodium hydrogen carbonate solution, which was subsequently acidified and extracted with ether to give a solid (220 mg), m.p. 193—197°. Recrystallisation from nitromethane gave the *acid* (16), m.p. 197—199°, $\nu_{max.}$ 1185 and 1700 cm^{-1} (Found: C, 63·8; H, 5·0; N, 4·4. C$_{19}$H$_{17}$NO$_4$S requires C, 64·2; H, 4·8; N, 3·95%).

Hydrolysis of the acid (16) with 15% aqueous ethanolic (1 : 9) potassium hydroxide for 2·5 h under nitrogen gave *1,3,4,5-tetrahydrobenz[cd]indole-5-carboxylic acid*, m.p. 149—151° (from nitromethane), $\nu_{max.}$ 1700 and 3500 cm^{-1} (Found: C, 71·6; H, 5·7; N, 6·8. C$_{12}$H$_{11}$NO$_2$ requires C, 71·6; H, 5·5; N, 7·0%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole-5-carboxaldehyde Oxime (17).—A suspension of the spiro-oxiran ester (17 g) in ethanol (170 ml), water (34 ml), and 10N-sodium hydroxide (5 ml) was warmed to 50—60° and the clear brown solution set aside at room temperature. Hydroxylamine hydrochloride (20·5 g), sodium acetate (20·5 g), water (68 ml), and ethanol (120 ml) were added, and the whole was then heated under reflux for 2·5 h. Hot water (300 ml) was added, the solution was left to cool and after the initial formation of an oil there separated a cream-coloured solid (6·64 g), m.p. 155—162°. Further dilution with water gave a second crop (5·42 g). Recrystallisation of the first crop from ethanol gave the *oxime* (17), m.p. 158—166° (Found: C, 63·0; H, 5·1; N, 7·3. C$_{19}$H$_{18}$N$_2$O$_3$S,EtOH requires C, 63·0; H, 5·1; N, 7·9%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole-5-carbonitrile (18).—Thionyl chloride (25 ml) was added to a solution of the oxime (17) (12·67 g) in benzene (325 ml) over a period of 15 min; the temperature was kept <10°. The solution was stirred for a further 45 min at 5° before being evaporated *in vacuo* at <25°. A solution of the residual amber-coloured oil in ether (100 ml) gave crystals (9·63 g, 80%), m.p. 108—114°. The residue, chromatographed on alumina (23 g) with benzene, gave a pale yellow

oil (2·1 g), which yielded, after trituration with ether, a solid (1·72 g), m.p. 108—115°. The first crop of solid crystallised from methanol in two forms simultaneously; needles, m.p. 109—120°, and rhombs, 120—126°. Mixed m.p. of these two crystalline forms was 111—126°. Recrystallisation of the mixed crystals from methanol gave a sample, m.p. 113—126°, which was recrystallised twice to give rhombs, m.p. 123—131°. Recrystallisation from methanol again, however, gave the *nitrile* (18) as long, broad needles, m.p. 110—120° (Found: C, 66·4; H, 4·9; N, 8·2. C$_{19}$H$_{16}$N$_2$O$_2$S,-0·5MeOH requires C, 66·5; H, 5·15; N, 7·95%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole-5-carboxamide (19).—Aqueous hydrogen peroxide (30%) (40 ml) was added to a mixture of sodium phosphate dodecahydrate (4·0 g), and the nitrile (18) (12·0 g) in acetone (120 ml) and water (40 ml) and the stirred mixture brought to reflux in an oil-bath pre-heated to 80°. Additional aqueous hydrogen peroxide (30%, 40 ml), was added to the clear boiling mixture and a cream-coloured solid was precipitated. The stirred mixture was cooled in an ice-bath, the solid was filtered off, washed twice with aqueous acetone (1 : 1, 50 ml), and finally water. Crystallisation from ethyl acetate gave the *amide* (10·3 g), m.p. 220—223°, $\nu_{max.}$ 1170, 1650, 3250, and 3450 cm^{-1} (Found: C, 64·5; H, 5·3; N, 7·8. C$_{19}$H$_{18}$-N$_2$O$_3$S requires C, 64·4; H, 5·1; N, 7·9%).

5-Aminomethyl-1,3,4,5-tetrahydro-1-(p-tolylsulphonyl)benz-[cd]indole Hydrochloride (20).—A solution of the nitrile (18) (672 mg, 2 mmol) and diborane (2 mmol) in tetrahydrofuran (20 ml) was stirred at room temperature under nitrogen for 3 h. Ethanol was added to the cooled solution, the solution was evaporated to dryness, and the residue was extracted with aqueous citric acid. The aqueous acid solution was made basic and extracted with ether. Addition of ethereal hydrogen chloride to the washed and dried extract gave the *amine hydrochloride*, m.p. 245—250° (from methanol), pK_a 8·65 (Found: C, 60·85; H, 5·7; N, 7·2%; equiv., 376. C$_{19}$H$_{21}$ClN$_2$O$_2$S requires C, 60·6; H, 5·6; N, 7·45%; equiv., 377).

5-[(Dimethylamino)methyl]-1,3,4,5-tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole (21).—A mixture of the aldehyde (15) (339 mg), 100% formic acid (2 ml), and dimethylformamide (1 ml) was stirred at 150—160° under nitrogen for 4 h. The cooled mixture was poured onto ice, and made basic with sodium hydrogen carbonate solution. The product was extracted with ethyl acetate, the extract was washed with water, and extracted with aqueous citric acid solution. The acid extract was washed with ethyl acetate, made alkaline with 5N-sodium hydroxide, and the product extracted with ethyl acetate. Evaporation of the washed and dried extract gave the *dimethylaminomethyl derivative* (328 mg), m.p. 123—125° (twice from ethanol) (Found: C, 68·7; H, 6·8; N, 7·6. C$_{21}$H$_{24}$N$_2$O$_2$S requires C, 68·4; H, 6·6; N, 7·6%).

Ethyl 1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indol-5-ylideneacetate (25).—A solution of ethoxyethynylmagnesium bromide [from ethoxyacetylene (3 mmol) and ethylmagnesium bromide] in tetrahydrofuran (2 ml) was added to a solution of the ketone (2) (325 mg, 1 mmol) in anhydrous tetrahydrofuran and the mixture stirred at 40° for 2 h. Ammonium chloride solution was added, the product was extracted with benzene, and the washed and dried extract was evaporated *in vacuo* to an oil (340 mg), $\nu_{max.}$ 2270 cm^{-1} (C≡C). The oil was dissolved in ethanol, 2N-sulphuric acid (0·5 ml) added, and the solution was set aside for 2 min. The pale yellow *ethyl ester* was filtered off, m.p. 156—159°

(from ethanol), $\nu_{max.}$ 1700 and 1625 cm^{-1} (Found: C, 66·9; H, 5·6. $C_{22}H_{21}NO_4S$ requires C, 66·9; H, 5·6%).

Ethyl 1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indol-5-ylacetate (22).—The unsaturated ester (25) (500 mg) was hydrogenated in ethanol (35 ml) over 10% palladised strontium carbonate (0·5 g) to give the saturated *ethyl ester*, m.p. 74—76° (from methanol) (Found: C, 67·1; H, 6·1; N, 3·6. $C_{22}H_{23}NO_4S$ requires C, 66·5; H, 5·8; N, 3·5%).

Hydrolysis of the ester (22) in ethanol with 2N-sodium hydroxide at room temperature for 20 h gave the free *acid* (23), m.p. 162—164°, $\nu_{max.}$ 1100, 1160, 1170, 1185, and 1700 cm^{-1}, pK_a 5·76 (Found: C, 65·15; H, 5·4; N, 3·7%; equiv., 368. $C_{20}H_{19}NO_4S$ requires C, 65·0; H, 5·2; N, 3·8%; equiv., 369).

Hydrolysis of the ester (22) with 3N-aqueous ethanolic (1 : 8) potassium hydroxide for 1 h gave the *acid* (24), m.p. 156—159°, $\nu_{max.}$ 1195, 1690, and 3400 cm^{-1}, pK_a 5·89 (Found: C, 72·0; H, 6·1; N, 6·2%; equiv., 219. $C_{13}H_{13}$-NO_2 requires C, 72·5; H, 6·1; N, 6·5%; equiv., 215).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indol-5-ylidenemalononitrile (26).—A mixture of the ketone (2) (487 mg), malononitrile (1·0 g), 20% solution of ammonium acetate in acetic acid (0·2 ml), and toluene (10 ml) was heated under reflux for 45 min, and more of the ammonium acetate solution (0·2 ml) was added. Heating was continued for a further 45 min, and the supernatant liquor, after decanting from a viscous oil, gave crystals of the *malononitrile* (380 mg), m.p. 219—221° (from acetonitrile), $\nu_{max.}$ 2250 and 1550 cm^{-1} (Found: C, 67·3; H, 4·25; N, 11·8. $C_{21}H_{15}N_3O_2S$ requires C, 67·55; H, 4·05; N, 11·3%). Work-up of the viscous oil and mother liquors gave a second batch of material (115 mg), m.p. 215—218°.

Similarly the following cyano-(1,3,4,5-tetrahydrobenz-[cd]indol-5-ylidene)acetates were prepared: the *ethyl 1-(p-tolylsulphonyl) ester* (27), m.p. 168—169°, $\nu_{max.}$ 1130, 1185, 1575, 1725, and 2240 cm^{-1} (Found: C, 65·8; H, 5·0; N, 5·9. $C_{23}H_{20}N_2O_4S$ requires C, 65·7; H, 5·8; N, 6·7%); the *ethyl 1-acetyl ester* (28), m.p. 150—151°, $\nu_{max.}$ 1550, 1710, 1720sh, and 2240 cm^{-1} (Found: C, 70·2; H, 5·4; N, 9·2. $C_{18}H_{16}$-N_2O_3 requires C, 70·1; H, 5·2; N, 9·1%); and the *1-acetyl acid* (29), m.p. 206—207°, $\nu_{max.}$ 1565, 1655, 1710, and 2230 cm^{-1} (Found: C, 67·5; H, 4·4; N, 9·7. $C_{16}H_{12}N_2O_3$,-$0·25H_2O$ requires C, 67·5; H, 4·4; N, 9·8%).

Decarboxylation of (1-Acetyl-1,3,4,5-tetrahydrobenz[cd]-indol-5-ylidene)cyanoacetic Acid.—A solution of the cyanoacetic acid (29) (750 mg) in dimethyl acetamide (5 ml) was boiled for (a) 1 min, rapidly quenched, and diluted with sodium hydrogen carbonate solution. The precipitated solid (500 mg) was filtered off, dried, and crystallised from ethanol (35 ml) to give the *indolylideneacetonitrile* (30) as yellow needles, m.p. 130—135°, $\nu_{max.}$ 1690 and 2280 cm^{-1} (Found: C, 76·1; H, 5·2; N, 11·9. $C_{15}H_{12}N_2O$ requires C, 76·25; H, 5·1; N, 11·9%). The alkaline filtrate gave, on acidification, the unchanged cyano-acid (200 mg), m.p. 196—198°.

(b) Heating for 1 h and work-up as in (a) gave the *1-acetyl-1,2-dihydrobenz[cd]indol-5-ylacetonitrile* (31) (600 mg), m.p. 151—153° (from benzene), $\nu_{max.}$ 1660 and 2280 cm^{-1} (Found: C, 77·55; H, 5·2; N, 11·0. $C_{15}H_{12}N_2O$,-$0·33C_6H_6$ requires C, 77·8; H, 5·4; N, 10·7%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indol-5-yl-malononitrile (32).—Potassium borohydride (500 mg) was added to a stirred suspension of the malononitrile (26) (500 mg) in methanol (20 ml) and within 30 min the suspension had cleared. Aqueous acetic acid was added to bring the

pH to 4—5, followed by water (40 ml). The precipitate (470 mg) obtained was recrystallised from methanol and gave the *malononitrile*, m.p. 133—138° (Found: C, 67·3; H, 4·45; N, 11·0. $C_{21}H_{17}N_3O_2S$ requires C, 67·2; H, 4·6; N, 11·2%).

Reduction of the ethyl 1-acetyl cyano-ester (28) by a similar method gave *ethyl (1-acetyl-1,3,4,5-tetrahydrobenz[cd]-indol-5-yl)cyanoacetate* (33), m.p. 150—154°, $\nu_{max.}$ 1685 and 1735 cm^{-1} (Found: C, 69·6; H, 5·8; N, 9·15. $C_{18}H_{18}N_3O_2$ requires C, 69·7; H, 5·85; N, 9·0%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)benz[cd]indole-5-spiro-2'-oxiran-3',3'-dicarboxamide (34).—A stirred mixture of the indolylidene-malononitrile (26) (930 mg, 2·5 mmol), sodium phosphate dodecahydrate (250 mg), 30% aqueous hydrogen peroxide solution (0·55 ml, 5 mmol), and ethanol (25 ml) was heated at 60° for 10 min, cooled, diluted with water, and the ethanol was evaporated *in vacuo*. The aqueous mixture was extracted with ethyl acetate, and the washed and dried extract was evaporated to dryness *in vacuo*. The residual oil was dissolved in ethyl acetate, and the solution, when diluted slowly with ether, gave the *dicarboxamide*, m.p. 195—197°, $\nu_{max.}$ 3470, 3360, and 1670 cm^{-1} (Found: C, 59·1; H, 4·2; N, 10·0. $C_{21}H_{19}N_3O_5S$ requires C, 59·3; H, 4·5; N, 9·9%).

1,3,4,5-Tetrahydro-1-(p-tolylsulphonyl)-6H-azepino[5,4,3-cd]indol-6-one (35).—A mixture of 3,4-dihydro-1-(p-tolyl-sulphonyl)benz[cd]indol-5(1H)-one oxime (680 mg) and thionyl chloride (0·8 ml) was warmed to give a solution, which was stood at room temperature for 2 h before being poured onto ice. Trituration of the precipitated oil gave a green solid, which was dissolved in acetonitrile, treated with charcoal, filtered, and the filtrate was evaporated to dryness *in vacuo*. The residual solid was washed with ether and gave the pale brown *lactam* (437 mg), m.p. 192—194° (twice from acetone–ether) (Found, after drying at 110°, C, 63·7; H, 5·15; N, 8·15. $C_{18}H_{16}N_2O_3S$ requires C, 63·5; H, 4·7; N, 8·2%).

A similar procedure gave *1-acetyl-1,3,4,5-tetrahydro-6H-azepino[5,4,3-cd]indol-6-one* (36), m.p. 264—265° (from acetonitrile), $\nu_{max.}$ 1650, 1705, and 3230 cm^{-1} (Found: C, 68·5; H, 5·3; N, 12·3. $C_{13}H_{12}N_2O_2$ requires C, 68·4; H, 5·3; N, 12·3%).

1,3,4,5-Tetrahydro-6H-azepino[5,4,3-cd]indol-6-one (37).—A mixture of the lactam (36) (228 mg), 2N-sodium carbonate solution (4 ml), and ethanol (10 ml) was stirred at room temperature for 2 h, and then filtered. Evaporation of the filtrate gave the white *lactam* (200 mg), m.p. 237—239° (from aqueous methanol) (Found: C, 70·9; H, 5·4; N, 14·8. $C_{11}H_{10}N_2O$ requires C, 70·95; H, 5·4; N, 15·05%).

1,3,4,5-Tetrahydro-1,5-dimethyl-6H-azepino[5,4,3-cd]indol-6-one (38).—The azepinoindolone (37) (558 mg, 3 mmol) was added to a solution of sodium hydride (40% oil dispersion; 540 mg, 9 mmol) in a mixture of dimethylform-amide and benzene (obtained by concentrating 25 ml of 1 : 1 mixture to 16 ml) and the mixture was stirred for 15 min. Methyl iodide (1·1 ml) was added portion-wise, and the solution stirred at 80° for 2·5 h. Acetic acid was added to the solution, which was then evaporated to dryness *in vacuo*, and the residue was extracted with ethyl acetate. Evaporation of the washed and dried extract gave a solid, which after washing successively with light petroleum, and ether yielded a solid (335 mg), m.p. 119—121°. Crystallisation from benzene–light petroleum gave the *dimethyl compound* (38), m.p. 129—132°, $\nu_{max.}$ 1620 cm^{-1} (Found: C, 72·6; H, 6·7; N, 13·1. $C_{13}H_{14}N_2O$ requires C, 72·9; H,

6·6; N, 13·1%). The same compound, m.p. 125—128°, and identical i.r. spectrum was obtained, under these conditions, from the N-acetylazepinoindolone (36).

3,4,5,6-*Tetrahydro*-1H-*azepino*[5,4,3-cd]*indole* (40).—A suspension of the lactam (37) (228 mg) in tetrahydrofuran (10 ml) was added to a stirred suspension of lithium aluminium hydride (228 mg) in tetrahydrofuran (10 ml) and the mixture was heated under reflux for 4 h. The cooled mixture was poured into Rochelle salt solution, and the product extracted with ethyl acetate. The basic material was extracted with aqueous citric acid, the acidic extract was made alkaline with 2N-sodium hydroxide and the base was extracted with ethyl acetate. Evaporation of the washed and dried extract gave the white *azepinoindole* (140 mg), m.p. 226—228° (from acetonitrile), $\nu_{max.}$ 3330 cm^{-1} (Found: C, 76·8; H, 7·3; N, 16·5. $C_{11}H_{12}N_2$ requires C, 76·7; H, 7·0; N, 16·3%). A subsequent experiment gave a sample of the azepinoindole with m.p. 231—233°. Reduction of the N-acetylazepinoindolone (36) yielded the same compound. *Methyl* 3,4,5,6-*tetrahydro*-1H-*azepino*[5,4,3-cd]*indole*-5-*carboxylate* (43), m.p. 210—212° (from aqueous ethanol), $\nu_{max.}$

1260, 1675, and 3350 cm^{-1} (Found: C, 68·2; H, 6·3; N, 12·2. $C_{13}H_{14}N_2O_2$ requires C, 67·8; H, 6·1; N, 12·2%), on reduction with lithium aluminium hydride in tetrahydrofuran under reflux overnight gave 3,4,5,6-*tetrahydro*-5-*methyl*-1H-*azepino*[5,4,3-cd]*indole* (42), m.p. 195—197°, pK_a 7·92 (Found: C, 77·6; H, 7·88; N, 15·05%; equiv., 187. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·6; N, 15·0%; equiv., 186); *hydrochloride*, m.p. 252—257°, pK_a 8·12 (Found: equiv., 223. $C_{12}H_{15}ClN_2$ requires equiv., 223).

3,4,5,6-*Tetrahydro*-1,5-*dimethyl*-1H-*azepino*[5,4,3-cd]*indole* (41).—Reduction of the 1,5-dimethylazepinoindolone (38) (3·75 g) with lithium aluminium hydride (3·75 g) in tetrahydrofuran (450 ml) under reflux, as described in the preceding experiment, gave the crude 1,5-*dimethylazepine* (41), m.p. 45—50°, pK_a 7·82 (Found: C, 78·8; H, 8·3; N, 13·6%; equiv., 203. $C_{13}H_{16}N_2$ requires C, 78·0; H, 8·05; N, 14·0%; equiv., 200); *hydrochloride*, m.p. 250—252°, pK_a 7·84 (Found: C, 65·6; H, 7·1; N, 11·85%; equiv., 236. $C_{13}H_{17}ClN_2$ requires C, 65·9; H, 7·2; N, 11·85%; equiv., 237).