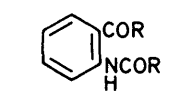
Oxidation of 2,3-Disubstituted Indoles with *m*-Chloroperbenzoic Acid. Formation of *o*-Aminophenol Derivatives and a Dimeric Product

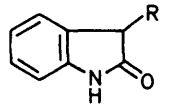
Tohru Hino,* Hitoshi Yamaguchi, Kenji Matsuki, Kumiko Nakano, Mikiko Sodeoka, and Masako Nakagawa
Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho, Chiba-shi, 260 Japan

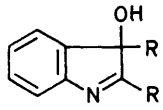
Oxidation of tetrahydrocarbazole (5) with *m*-chloroperbenzoic acid in methylene dichloride at −60 °C gave the *N*-benzoyl-*o*-aminophenol (11) together with the hydroxy-3*H*-indole (7) and the indol-3(2*H*)-one (9). The *N*-benzoyl-*o*-aminophenol (11) was found to be derived from the hydroxy-4a*H*-carbazole (7) *via* an unstable tertiary amine intermediate (17) by further oxidation. The *N*-benzoyl-*o*-aminophenol (11) was also obtained by the oxidation of the other hydroxy-3*H*-indoles (18), (19), and (24). On the other hand, similar oxidation of *N*-methyl-tetrahydrocarbazole (6) gave the hydroxyenamine (28) and its dimer (27), and of 2,3-diphenylindole (31) and the *N*-methyl derivative (30) gave the hydroxy-3*H*-indole (19) and the ketoamide (33), while the 1,4-benzoxazine derivatives (34) and (35) were obtained in the case of the *N*-acetyl derivative (32).

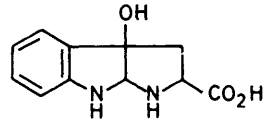
Oxidation of 3-substituted and 2,3-disubstituted indoles with peracids is known to give 2,3-bond-cleaved products (1),[1] oxoindoles (2),[2] hydroxy-3*H*-indoles (3),[3] and other products.[4] Recently a hydroxypyrrolo-indole derivative (4) was obtained by the oxidation of tryptophan with peracetic acid.[5] The pyrrolo-indole (4) was converted into 2-hydroxytryptophan on treatment with acid. We now report that *o*-aminophenol derivatives and a dimeric product which have not been reported previously were obtained by the oxidation of tetrahydrocarbazoles and 2,3-diphenylindoles with *m*-chloroperbenzoic acid (*m*-CPBA).

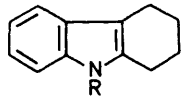
Oxidation of tetrahydrocarbazole (5) with hydrogen peroxide in ether has been reported to give a small amount of 4a-hydroxytetrahydro-4a*H*-carbazole (7) and carbazole,[6] while the hydroxyindolenine (7) is known to be oxidized to the ketoamide (8) by perbenzoic acid [7] in chloroform in good yield. We carried out the oxidation of compound (5) with one equivalent of *m*-CPBA in methylene dichloride at −60 °C. The reaction mixture was separated on a silica-gel column to give the hydroxy-4a*H*-carbazole (7) (25%), the indoxyl (9), (3%), and *N*-(*m*-chlorobenzoyl)-*o*-aminophenol (11) (9%), m.p. 169—170 °C, together with recovered (5) (27%). Carbazole and the ketoamide (8) were not isolated from the reaction mixture. The structures of compounds (7) and (9) were confirmed by direct comparison with authentic samples. The structure of the aminophenol derivative (11) was deduced from its spectral data (see Experimental section) and confirmed by direct comparison with an authentic sample prepared from *o*-aminophenol and *m*-chlorobenzoyl chloride. In order to establish the precursor of compound (11), the oxidation of (7) and the ketoamide (8), probable intermediates in the formation of (11), with *m*-CPBA was carried out under similar conditions. Although the oxidation of compound (8) did not proceed, the 4a*H*-carbazole (7) gave an unstable intermediate (17) (14%) (Scheme 1) as well as the phenol (11) (42%), the indolone (9) (8%), and cyclohexane-1,2-dione (24%). In contrast to the perbenzoic acid oxidation of compound (7) which produces (8), the latter ketoamide was not obtained from this oxidation. The isolated intermediate (17) was found to give compound (11) and cyclohexane-1,2-dione, in 82 and 77% yield respectively, on treatment with silica gel in methylene dichloride at room temperature. The structure of (17) was confirmed from the above hydrolysis and the spectral data (see Experimental section). These results indicate that the aminophenol (11) is derived from the intermediate (17) which is formed by the oxidation of the carbazole (7). The oxidation of (7) with *m*-CPBA to the intermediate (17)

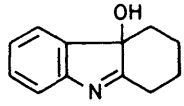

(1)

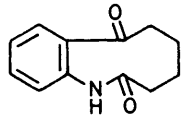

(2)

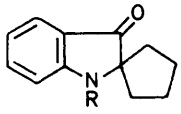

(3)

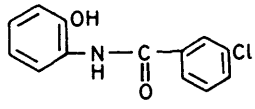

(4)

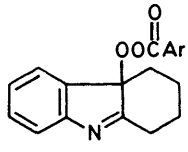

(5) R = H
(6) R = Me

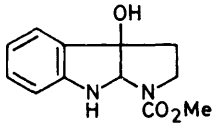

(7)

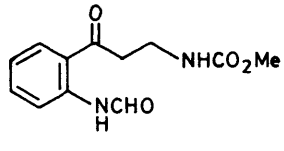

(8)

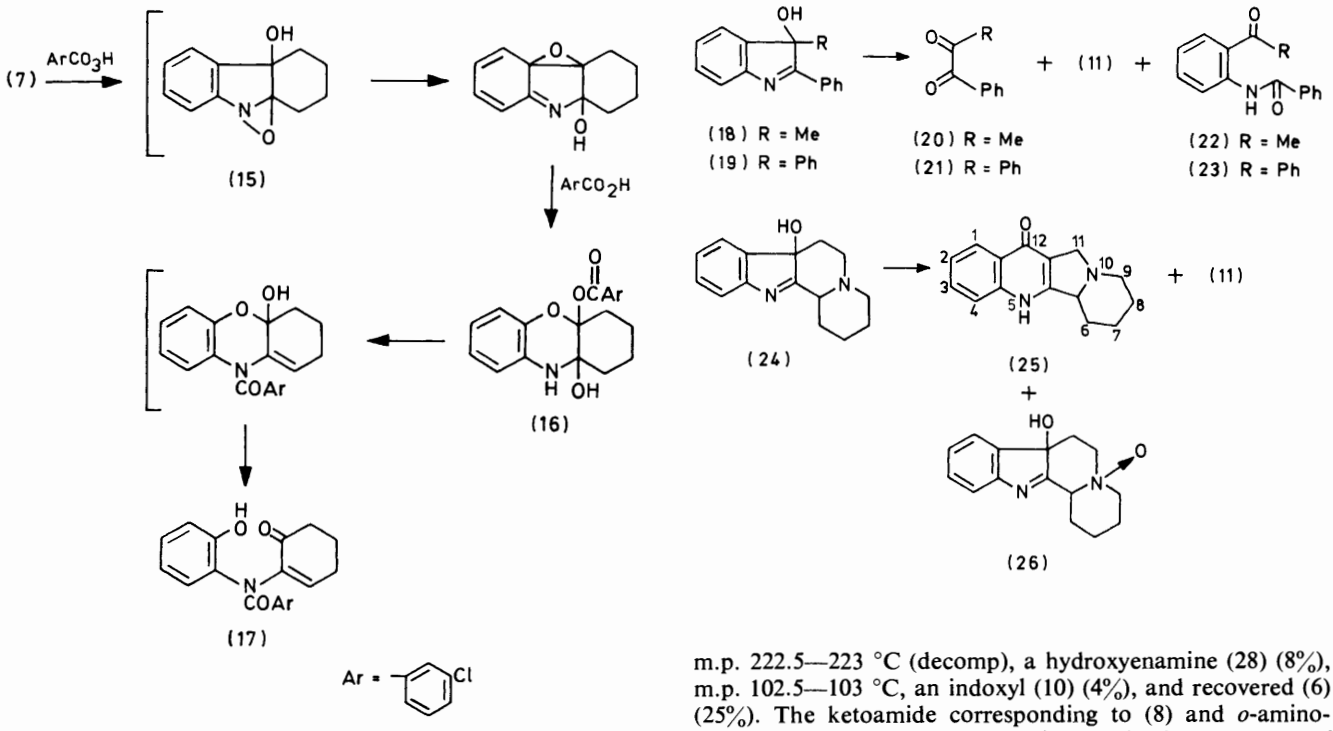

(9) R = H
(10) R = Me


(11)


(12)


(13)


(14)



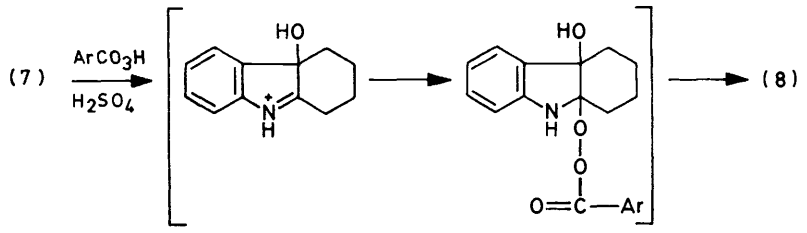
Scheme 1.

might proceed *via* a Baeyer–Villiger-type rearrangement of a peroxidic intermediate such as (12) to form a 1,4-benzoxazine (16). However, the oxidation of a hydroxypyrroloindole (13) with *m*-CPBA in methylene dichloride did not give an *o*-aminophenol derivative, but gave the ketoamide (14), and similar oxidation of cumyl alcohol did not proceed. Therefore formation of a peroxidic intermediate such as (12) is not plausible. Another possible oxidation site in (7) may be the C=N double bond to form the oxaziridine (15). Rearrangement of this compound to form the 1,4-benzoxazine (16), followed by O,N-acyl migration, could lead to (17), as shown in Scheme 1. Formation of (11) was also observed in the oxidation of the hydroxyindolenines (18), (19), and (24) with *m*-CPBA in methylene dichloride or chloroform. However, these oxidations also gave the ketoamides (22) and (23) or the quinoline (25), which were not obtained in the oxidation of (7), as by-products.

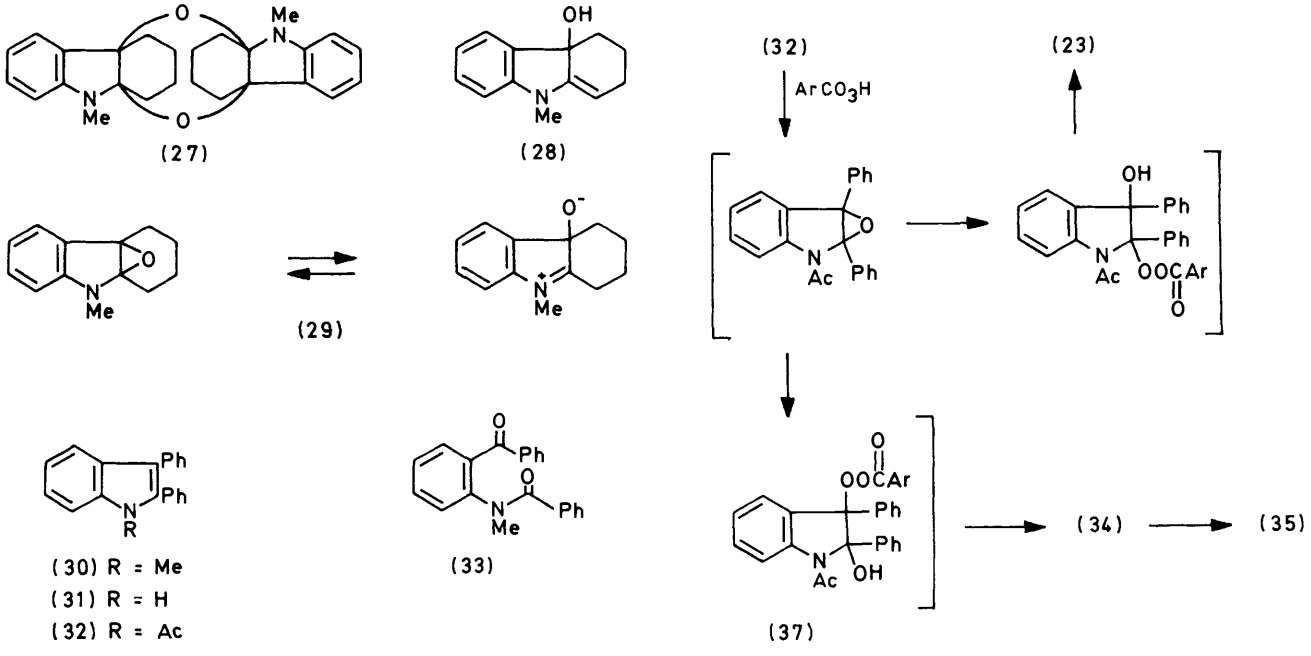
In order to clarify the difference between the results obtained by the oxidation of (7) with perbenzoic acid as opposed to *m*-CPBA, we repeated the perbenzoic acid oxidation following Witkop's procedure, and obtained the same result [formation of (8)]. The above difference in results suggested that the trace amount of sulphuric acid must direct the reaction course. Therefore, we carried out the oxidation of (7) with *m*-CPBA in chloroform containing a small amount of sulphuric acid cooled under ice, and obtained the ketoamide (8) in 78% yield, thus demonstrating that the difference in results on using perbenzoic acid rather than *m*-CPBA was not due to the nature of reagents, but depended on the reaction conditions. Protonated hydroxyindolenine facilitates the addition of perbenzoic acid or *m*-CPBA to the C=N double bond, and the ketoamide (8) is obtained by subsequent cleavage [8] as shown in Scheme 2.

Similar oxidation of *N*-methyltetrahydrocarbazole (6) with *m*-CPBA in methylene dichloride at −60 °C was carried out to establish the effect of the *N*-substituent. Separation of the reaction mixture gave a dimeric compound (27) (34%), m.p. 222.5—223 °C (decomp), a hydroxyenamine (28) (8%), m.p. 102.5—103 °C, an indoxyl (10) (4%), and recovered (6) (25%). The ketoamide corresponding to (8) and *o*-aminophenol derivatives were not isolated. The i.r. spectrum of (28) showed the presence of an OH group (3 260 and 3 360 cm^{-1}), while its n.m.r. spectrum in $CDCl_3$ showed two allylic protons between 2.3—3.0 p.p.m. as a multiplet, and a vinyl proton at 4.85 p.p.m. as a multiplet as well as four methylene protons between 1.5—2.3 p.p.m.; its mass spectrum showed the strong molecular ion peak at *m*/*z* 201 and the dehydrated peak at *m*/*z* 183 as the base peak. The mass spectrum of the dimer (27) showed the molecular ion peak at *m*/*z* 402, the $M^+/2$ peak at *m*/*z* 201 and the base peak at *m*/*z* 185, due to removal of an oxygen atom from half of the molecule. The dimer (27) was converted into the hydroxyenamine (28) in 85% yield on treatment with 5% hydrochloric acid in methylene dichloride at room temperature. These results led to the assignment of the structure of the dimer as (27), but the stereochemistry has not been determined yet. The structure of the indoxyl (10) [9] was confirmed by direct comparison with the sample prepared from (9). These oxidation products (27), (28), and (10) may be derived from the first intermediate (29). The effect of the *N*-substituent was prominent in this case.

We next carried out a similar oxidation of 2,3-diphenylindoles. Oxidation of *N*-methyl-2,3-diphenylindole (30) with one equivalent of *m*-CPBA in methylene dichloride at −60 °C gave the corresponding ketoamide (33) in 37% yield as the sole product together with recovered (30) in 57% yield. The reaction at −15 to −20 °C increased the yield of (33) (43%) slightly. The oxidation of (30) with *m*-CPBA in methylene dichloride–0.5M-sodium hydrogen carbonate [10] at room temperature gave compound (33), in 44% yield, besides recovered (30) (52%). Under similar conditions the *N*-unsubstituted derivative (31) gave the amide (23) in 31% yield and the hydroxyindolenine (19) in 7% yield. On the other hand, the oxidation of the *N*-acetyl derivative (32) with *m*-CPBA in methylene dichloride proceeded slowly at room temperature and gave compound (23) (7%), small amounts of the 1,4-benzoxazine derivatives (34) and (35), together with recovered (32) (55%). The reaction under reflux for 8 h gave the amide (23) (14%), benzoxazines (34) (13%) and (35) (15%), and the acetyl-indole (36) (7%), as well as recovered (32) (42%). The structures of compounds (19), (23), (33), and (36) were confirmed by comparison of their



Scheme 2.



Scheme 3.

spectral data with those of known samples obtained by dye-sensitized photo-oxygenation of 2,3-diphenylindoles,[11] The 1,4-benzoxazine (34), m.p. 146.5—147 °C, gave *o*-aminophenol, benzil, and *m*-chlorobenzoic acid in good yields on treatment with 1M-sulphuric acid–methanol or 10% sodium hydroxide–methanol. The n.m.r. spectrum of (34) showed a singlet for the acetyl group at 2.25 p.p.m., two multiplets for aromatic protons at 6.40—7.00 and 7.00—8.40 p.p.m., and a broad singlet for the OH proton at 8.98 p.p.m., while its i.r. spectrum showed the presence of carbonyl groups at 1 740 and 1 695 cm^{-1}. Although its mass spectrum did not show the molecular ion peak, the above data as well as its elemental analysis supported the assigned structure (34). The 1,4-benzoxazine (35), m.p. 151—152 °C, gave *o*-aminophenol and benzil on alkaline hydrolysis. Its n.m.r. spectrum showed a broad singlet for the acetyl group at 2.00 p.p.m., and fourteen aromatic protons between 6.50—8.20 p.p.m. as multiplets; no exchangeable OH or NH proton was observed. Its i.r. spectrum showed a carbonyl band at 1 700 cm^{-1} and a C=N band at 1 674 cm^{-1}. These data as well as elemental analyses are consistent with the structure (35), but the stereochemistry is not certain. These 1,4-benzoxazine derivatives are probably derived from the peroxyester (37) by a Baeyer–Villiger type rearrangement (Scheme 3).

These results indicate that the *m*-CPBA oxidation of 2,3-disubstituted indoles gives a variety of compounds depending upon the substituents and conditions, and that all of these compounds may be derived from the 2,3-epoxide or 3-hydroxyindolenine [such as (29)] as the first intermediate.

Experimental

M.p.s are not corrected. I.r. spectra were recorded on Hitachi 215 and 295 spectrometers. U.v. spectra were recorded on Hitachi 323 and 340 spectrometers. ^{1}H N.m.r. spectra were measured with a JEOL-MH-100 spectrometer, with $SiMe_4$ as internal standard. Mass spectra were obtained using a Hitachi RMU-6 instrument. *m*-Chloroperbenzoic acid (*m*-CPBA) (Nakarai Chemicals) was used in 83% purity after iodine titration.

Oxidation of 1,2,3,4-*Tetrahydrocarbazole* (5) *with* m-*CPBA.*—*m*-CPBA (1.216 g, 5.85 mmol) in CH_2Cl_2 (250 ml) was added dropwise during 25 min to a solution of the carbazole (5) (1.00 g, 5.85 mmol) in CH_2Cl_2 (200 ml) at −60 °C with stirring. The mixture was stirred for 25 min at the same temperature until the KI–starch test gave negative results, and the cooling bath was removed. The reaction mixture was passed through a short alumina column to remove the *m*-CPBA to give a brown oil (1.09 g) which was chromatographed on a silica-gel column. Elution with benzene–CH_2Cl_2 (1 : 1) gave compound (5) (268 mg, 27%) and 2′,3′-dihydro-3′-oxospiro[cyclopentane-2′-indole] (9) (39 mg, 4%). Elution with CH_2Cl_2 gave *o*-[*N*-(*m*-chlorobenzoyl)amino]phenol (11) (130 mg, 9%) and 1,2,3,4-tetrahydro-4a-hydroxy-4a*H*-carbazole (7), (273 mg, 25%). The hydroxy-4a*H*-carbazole (7), m.p. 158—159 °C (lit.,[6] m.p. 159 °C), was identical with an authentic sample (*vide infra*) by i.r. spectra and t.l.c. behaviour. The indoxyl (9) (lit.,[6,12] m.p. 79 °C) did not crystallize, but its spectral data and t.l.c. behaviour were identical with an authentic sample prepared from compound (7) following Witkop's procedure.[6] Recrystallization of the *phenol* (11) from benzene gave colourless fine needles, m.p. 169—170 °C; $\lambda_{max.}$ (EtOH) 294.5 (ε 8 650); $\nu_{max.}$ (KBr) 3 200 (OH, NH), 1 648 (CO), 1 550, and 1 455 cm^{-1}; *m*/*z* 249 (*M* + 2, 11%), 247 (*M*$^+$, 29), 141 (35), and 139 (100); δ[$(CD_3)_2SO$] 6.60—7.20 (m, 3 H, arom H), 7.40—7.80 (m, 3 H, arom H), 7.80—8.20 (m, 2 H, arom H), and 9.56 (s, 2 H, NH + OH, exchangeable) (Found: C, 63.05; H, 3.9; N, 5.6. $C_{13}H_{10}ClNO_2$ requires C, 63.04; H, 4.07; N, 5.66%).

Alternative Synthesis of the Phenol (11).—To a stirred solution of *o*-aminophenol (670 mg, 6.38 mmol) in CH_2Cl_2 (150 ml) was added NaOH (306 mg) in H_2O (30 ml) and *m*-chlorobenzoyl chloride [prepared from *m*-chlorobenzoic acid (1.00 g, 6.38 mmol) and thionyl chloride (1.0 g)] in CH_2Cl_2 (30 ml) simultaneously during 30 min while cooled with ice. The reaction mixture was stirred for 10 min and neutralized to pH 7 with 5% HCl. The CH_2Cl_2 layer was separated, washed with H_2O and dried. Evaporation of the solvent gave the phenol (11) (1.276 g, 81%). Recrystallizations from benzene gave pure (11), m.p. 169—170 °C. This was identical with the sample obtained above by mixed m.p., i.r., spectra, and t.l.c. behaviour.

Oxidation of the Alcohol (7) *with* m-*CPBA. Isolation of* o-N-(m-*Chlorobenzoyl*)-N-(6-*oxocyclohex*-1-*enyl*)*amino*]-*phenol* (17).—*m*-CPBA (1.062 g, 5.1 mmol) in CH_2Cl_2 (150 ml) was added to a solution of the alcohol (7) (956 mg, 5.1 mmol) in CH_2Cl_2 (100 ml) during 30 min at −60 °C. The mixture was stirred for 30 min at the same temperature until the KI–starch test of the mixture gave negative results. The t.l.c. of the mixture showed two strong spot of compounds (17) and (7) besides weak spots for (9) and (11). Evaporation of the solvent gave a brown oil (2.01 g) which was passed through a short alumina column to remove the benzoic acid. Separation of the products by a silica-gel column gave the aminophenols (17) (243 mg, 24%) and (11) (538 mg, 42%), cyclohexane-1,2-dione (138 mg, 24%), and compounds (9) (76 mg, 8%), and (7) (187 mg, 20%). Compounds (11), cyclohexane-1,2-dione, and (9) were identified by comparison with known samples. The aminophenol (17): was obtained as an unstable colourless oil, $\lambda_{max.}$ (EtOH) 233, 285, and 294 nm; $\nu_{max.}$ ($CHCl_3$) 3 370, 1 740, 1 670, 1 635, and 1 605 cm^{-1}; *m*/*z* (%) 343 (*M* + 2, 20), 341 (*M*$^+$, 53), 202 (83), 186 (58), 141 (35), and 139 (100); δ($CDCl_3$) 1.50—2.20 (m, 2 H, CH_2), 2.25—2.70 (m, 4 H, $COCH_2$ + C=CCH_2), 6.24 (t, 1 H, C=CH, *J* 4 Hz), 6.40 (s, 1 H, OH, exchangeable), 6.6—7.7 (m, 6 H, arom H), and 7.90—8.30 (m, 2 H, arom H).

Transformation of the Secondary Amine (17) *into the Primary Amine* (11).—Silica gel (2.0 g) was added to a solution of compound (17) (217 mg) in CH_2Cl_2 (15 ml) and the mixture was stirred for 2.5 h at room temperature. After removal of silica gel the mixture was evaporated to give a pale yellow solid (218 mg) which was separated by preparative t.l.c. (silica gel, CH_2Cl_2) to give compound (11) (123 mg, 82%) and cyclohexane-1,2-dione (55 mg, 77%). Both samples were identical with the samples obtained above in their i.r. spectra, mixed m.p. and the retention time in h.p.l.c. Compound (17) was also converted into the amine (11) and cyclohexane-1,2-dione on treatment with alumina–CH_2Cl_2.

Dye-sensitized Photo-oxygenation of Tetrahydrocarbazole (5). *Synthesis of the* 4a*H*-*Carbazole* (7).—A solution of compound (5) (2.00 g, 11.7 mmol) in MeOH (250 ml) was irradiated for 3.5 h with a 500-W halogen lamp in the presence of Rose Bengal (114 mg) at 4—6 °C under a stream of oxygen. Dimethyl sulphide (5 ml) was added to the mixture to reduce any hydroperoxide, and the solvent was evaporated to give a residue. This residue was put on a short alumina column and eluted with CH_2Cl_2–MeOH (100 : 3) to give a brown solid (2.28 g) which was chromatographed on a silica-gel column. Elution with CH_2Cl_2 gave the indoxyl (9) (197 mg, 9%). Elution with CH_2Cl_2–MeOH (100 : 3) gave the 4a*H*-carbazoles (7) (1.83 g, 84%) which was recrystallized from benzene to give colourless needles, m.p. 157.5—159 °C (lit.,[6] m.p. 159 °C).

Oxidation of Methyl 1,2,3,3a,8,8a-*Hexahydro*-3a-*hydroxypyrrolo*[2,3-b]*indole*-1-*carboxylate* (13) *with* m-*CPBA.*—*m*-CPBA (208 mg, 1 mmol) in CH_2Cl_2 (30 ml) was added to a solution of the ester (13) (230 mg, 1 mmol) in CH_2Cl_2 (20 ml) during 20 min at −60 °C. The mixture was stirred for 2 h at the same temperature. The methyl 2-(2-formylaminobenzoyl)-ethylaminoacetate (14) (115 mg) and starting material (13) (78 mg) were obtained by the same procedure as above. The ketoamide (14) was identified by comparison with a standard sample (t.l.c. behaviour). The *o*-aminophenol derivative was not detected.

Oxidation of Cumyl Alcohol (p-*Cymen*-7-*ol*) *with* m-*CPBA.*—*m*-CPBA (4.16 g, 20 mmol) in CH_2Cl_2 (500 ml) was added to a solution of cumyl alcohol (2.72 g, 20 mmol) in CH_2Cl_2 (50 ml) during 2 h at −60 °C. The mixture was stirred for 1.5 h at −60 °C and then for 20 h at room temperature. The t.l.c. of the mixture only showed the presence of starting materials. Dimethyl sulphide (3 ml) was added to the mixture to reduce the *m*-CPBA, and CH_2Cl_2 was distilled off. The distillate did not show the presence of acetone (2,4-dinitrophenylhydrazine test). Methylene dichloride was added to the residue and separated *m*-chlorobenzoic acid was filtered off. The CH_2Cl_2 solution was passed through an alumina column to remove the remaining *m*-chlorobenzoic acid. The CH_2Cl_2 solution was distilled to give an oil, b.p. 100—110 °C. The n.m.r. spectrum of the oil and the residue showed to be a mixture of cumyl alcohol and its dehydrated α-methylstyrene.

Oxidation of 3-*Hydroxy*-3-*methyl*-2-*phenyl*-3H-*indole* (18) *with* m-*CPBA*.—*m*-CPBA (770 mg, 4.48 mmol) in CH_2Cl_2 (250 ml) was added to a solution of the 3*H*-indole (18) (1.00 g, 4.48 mmol) in CH_2Cl_2 (200 ml) during 25 min at −60 °C. The mixture was stirred at the same temperature for 20 min and then treated as above to give methyl phenyl diketone (20) (124 mg, 21%) as an oil, *N*-(2-acetylphenyl)benzamide (22) (525 mg, 54%), m.p. 98.5—99 °C, the phenol (11) (220 mg, 23%), m.p. 169—170 °C, and the 3*H*-indole (18) (319 mg, 21%).

Oxidation of 3-*Hydroxy*-2,3-*diphenyl*-3H-*indole* (19) *with* m-*CPBA*.—*m*-CPBA (610 mg, 3.51 mmol) in CH_2Cl_2 (200 ml) was added to a solution of the 3*H*-indole (19) (1.00 g, 3.51 mmol) in CH_2Cl_2 (200 ml) during 20 min at −60 °C. The mixture was stirred for 2 h at the same temperature and then treated as above to give benzil (21) (10 mg, 5%), m.p. 90—92 °C, *N*-(2-benzoylphenyl)benzamide (23) (602 mg, 66%), m.p. 88—91 °C, and compounds (11) (76 mg, 5%), m.p. 169—170 °C, and (19) (434 mg, 20%).

Oxidation of 1,2,3,4,6,7,7a,12b-*Octahydro*-7a-*hydroxyindolo*[2,3-a]*quinolizine* (24) *with* m-*CPBA*.—*m*-CPBA (83 mg, 0.4 mmol) in $CHCl_3$ (30 ml) was added to a solution of compound (24) (97 mg, 0.4 mmol) in $CHCl_3$ (5 ml) during 1 h at −10 °C. The mixture was stirred for 30 min at the same temperature and then treated as above to give 5b,6,7,8,9,11-hexahydroindolizino[1,2-*b*]quinolin-12(5*H*)-one (25) (32 mg, 35%), m.p. 279—282 °C, 1,2,3,4,6,7,7a,12b-octahydro-7a-hydroxyindolo[2,3-*a*]quinolizine 5-oxide (26) (28 mg, 29%), compound (11) (16 mg, 16%), m.p. 169—170 °C, and the quinolizine (24) (7 mg, 7%). The quinolone (25) was identified by comparison of its i.r. spectrum with that of a standard sample. The structure of (26), a pale yellow solid, was supported by the following spectral data: $\lambda_{max.}$ (EtOH) 220, 225sh, and 267 nm; $\nu_{max.}$ (KBr) 3 350 (OH), 1 620 (C=N), 1 455, and 980 cm^{-1}; *m*/*z* (%) 258 (M^+, 7), 242 (M − O, 55), 240 (50), 223 (94), and 97 (100).

Oxidation of the 4aH-*Carbazole* (7) *with* m-*CPBA in Chloroform containing Sulphuric Acid*.—The chloroform for the reaction was shaken with 0.5M-H_2SO_4 and separated before use. *m*-CPBA (2.22 g, 10.7 mmol) in $CHCl_3$ (75 ml) was added to a solution of compound (7) (1.00 g, 5.34 mmol) in $CHCl_3$ (100 ml) during 25 min at 2—5 °C while cooled with ice. The mixture was stirred for 1.5 h and $CHCl_3$ (50 ml) added. The mixture was washed with 5% NaOH and H_2O, and dried. Evaporation of the solvent gave a brown solid (913 mg) which was recrystallized from AcOEt to give 7,8,9,10-tetrahydrobenzocyclononene-6,11(5*H*)-dione (8) (738 mg), m.p. 157—158 °C. Further (8) (108 mg, total 846 mg, 78%) was obtained from the mother-liquor by preparative t.l.c. [alumina–hexane–AcOEt (3 : 7)]. This sample was identical with a standard specimen obtained by the ozonization of compound (5) by mixed m.p. and i.r. spectra.

Oxidation of 1,2,3,4-*Tetrahydro*-9-*methylcarbazole* (6) *with* m-*CPBA*. *Formation of the Carbazole Dimer* (27) *and* 2,3,4,-4a-*Tetrahydro*-4a-*hydroxy*-9-*methylcarbazole* (28).—*m*-CPBA (1.124 g, 5.41 mmol) in CH_2Cl_2 (250 ml) was added gradually to a solution of compound (6) (1.00 g, 5.41 mmol) in CH_2Cl_2 (200 ml) during 3 h at −60 °C. The mixture gave negative results to the KI–starch test. It was then passed through a short alumina column to remove the benzoic acid and gave a brown solid (882 mg). Methylene dichloride was added to the solid and the dimer (27) as an insoluble powder (276 mg) was collected. The filtrate was evaporated to give a residue which gave further (27) (98 mg, total 374 mg, 34%) as an insoluble powder when dissolved in benzene. The filtrate was evaporated to give a residue (510 mg) which was chromatographed on silica gel. Elution with benzene gave the *N*-oxide (26) (251 mg, 25%), and the indoxyl (10) (43 mg, 4%). Elution with benzene–CH_2Cl_2 (1 : 1) gave compound (28) (85 mg, 8%) and some unknown mixture. Recrystallization of compound (10) from light petroleum–diethyl ether gave pale yellow, fine needles, m.p. 65—67 °C (lit.,[9] 68—69 °C), which was identical with a sample prepared from compound (9) by methylation with NaH–CH_3I–THF by mixed m.p., i.r. and mass spectra. Recrystallization of the dimer (27) from DMF gave colourless, fine needles, m.p. 222.5—223 °C; $\lambda_{max.}$ (EtOH) 252 (ε 9 500) and 305 nm (2 800); $\nu_{max.}$ (KBr) 2 930, 1 618, 1 490, 1 180, 1 050, 1 035, and 1 000 cm^{-1}; *m*/*z* (%) 402 (M^+, 27), 201 (M^+/2, 19), 186 (18), 185 (100), 184 (19), 160 (22), and 157 (40); δ(CF_3CO_2H) 1.10—3.50 [m, 16 H, 2 × $^-(CH_2)_4^-$], 4.08 (s, 6 H, 2 × CH_3), and 7.40—7.90 (m, 8 H, arom H) (Found: C, 77.55; H, 7.65; N, 7.0. $C_{26}H_{30}N_2O_2$ requires C, 77.58; H, 7.54; N, 6.96%). Recrystallization of compound (28) from benzene gave colourless *needles*, m.p. 102.5—103 °C; $\lambda_{max.}$ (EtOH) 230 (ε 19 000), 281sh (3 300), and 289 nm (3 500); $\nu_{max.}$ (KBr) 3 260, 3 360 (OH), 1 470, and 1 070 cm^{-1}; *m*/*z* (%) 201 (M^+, 61), 184 (49), 183 (M − H_2O, 100), 182 (91), 173 (27), 168 (26), and 167 (60); δ($CDCl_3$) 1.5—2.30 (m, 4 H, CH_2CH_2), 1.70 (s, 1 H, OH, exchangeable), 2.30—3.00 (m, 2 H, C=CCH_2), 3.70 (s, 3 H, NCH_3), 4.85 (br s, 1 H, C=CH), 6.90—7.35, and 7.35—7.60 (m, 4 H, arom. H) (Found: C, 78.0; H, 7.55; N, 7.0. $C_{13}H_{15}NO$ requires C, 77.58; H, 7.51; N, 6.96).

In a similar reaction the yield of (27) was decreased to 18% and that of (28) was increased to 18% when *m*-CPBA was added during 25 min and the mixture was stirred for 20 min at −60 °C.

Hydrolysis of the Dimer (27).—A solution of (27) (100 mg) in CH_2Cl_2 (20 ml) and 5% HCl (15 ml) was stirred for 2 h at room temperature. The mixture was neutralized with 10% NaOH and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried. Evaporation of the solvent gave a pale yellow oil (28) (85 mg, 85%). Recrystallization of the oil from benzene–hexane gave compound (28) (43 mg), m.p. 101—102 °C, whose i.r. spectrum was identical with that of the sample obtained above.

Oxidation of N-*Methyl*-2,3-*diphenylindole* (30) *with* m-*CPBA*.—(i) *In* CH_2Cl_2. *m*-CPBA (734 mg, 3.53 mmol) in CH_2Cl_2 (100 ml) was added during 25 min to a solution of compound (30) (1.00 g, 3.53 mmol) in CH_2Cl_2 (100 ml) at −60 °C. The mixture was stirred for 4 h and passed through a short alumina column to give a pale yellow solid (1.09 g) which was chromatographed on a silica-gel column. Elution with benzene gave compound (30) (547 mg, 55%). Elution with CH_2Cl_2 gave *N*-(2-benzoyloxyphenyl)-*N*-methylbenzamide (33) (414 mg, 37%) which was recrystallized from benzene–hexane to give pale yellow crystals, m.p. 110—111 °C, which was identical with a sample obtained previously [11] by comparison of their i.r. spectra. The reaction at −15 to −20 °C gave *N*-acetyl-2,3-diphenylindole (32) (43%) and recovered methyl-indole (30) (55%).

(ii) *In* CH_2Cl_2–0.5M-$NaHCO_3$.[10] *m*-CPBA (734 mg, 3.53 mmol) was added during 10 min to a mixture of compound (30) (1.00 g, 3.53 mmol), CH_2Cl_2 (35 ml), and 0.5M-$NaHCO_3$ (11 ml) at room temperature. The mixture was stirred for 1 h at room temperature and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 solution was washed with 1M-NaOH and H_2O, and dried. Evaporation of the solvent gave a pale yellow solid (1.03 g). Separation of the solid on a silice-gel column gave

starting compound (30) (523 mg, 52%) and the ketoamide (33) (489 mg, 44%).

Oxidation of 2,3-*Diphenylindole* (31) *with* m-*CPBA*.—2,3-Diphenylindole (31) (500 mg) was oxidized with *m*-CPBA in CH_2Cl_2–$NaHCO_3$ as in procedure (ii) to give recovered (31) (229 mg, 56%), the ketoamide (23) (175 mg, 31%), and the hydroxy-3*H*-indole (19) (35 mg, 8%). Recrystallization of (23) from EtOH–H_2O gave pale yellow prisms, m.p. 88—89.5 °C, identical with a sample reported previously.[11] Recrystallization of (19) from benzene–hexane gave colourless prisms, m.p. 190—194 °C, which was identical with a sample reported previously [11] by comparison of their i.r. spectra.

Oxidation of N-*Acetyl*-2,3-*diphenylindole* (32) *with* m-*CPBA*.—*m*-CPBA (1.137 g, 5.47 mmol) was added to a solution of the indole (32) (1.70 g, 5.47 mmol) in CH_2Cl_2 (100 ml) at room temperature. The mixture was refluxed for 8 h and passed through a short alumina column to remove the benzoic acid. The residue obtained on evaporation of the solvent was chromatographed on a silica-gel column. Elution with benzene–hexane (1 : 4) gave recovered (32) (706 mg, 42%) and the ketoamide (23) (235 mg, 14%). Elution with benzene gave (35) (276 mg, 15%) and *N*-acetyl-2,3-dihydro-2(3)-hydroxy-3(2)-methoxy-2,3-diphenylindole (36) (139 mg, 7%). Elution with CH_2Cl_2 gave 2-acetoxy-2,3-diphenyl-2*H*-1,4-benzoxazine *N*-acetyl-2-(*m*-chlorobenzoyloxy)-3,4-dihydro-3-hydroxy-2,3-diphenyl-2*H*-1,4-benzoxazine (34) (363 mg, 13%). Recrystallization of (36) from benzene gave colourless prisms, m.p. 193—195 °C, which was identical with a sample obtained previously.[11] Recrystallization of (35) from MeOH gave colourless *needles*, m.p. 151—152 °C; $\lambda_{max.}$ (EtOH) 251 (ε 19 000) and 292 nm (8 200); $\nu_{max.}$ (KBr) 1 710, 1 700, 1 670, 1 620, 1 600, 1 585, 1 485, 1 382, 1 330, 1 238, 1 035, and 745 cm^{-1}; *m*/*z* (%) 238 (40), 197 (27), 196 (100), 149 (25), and 105 (15); δ($CDCl_3$) 2.00 (br s, 3 H, CH_3), 6.50—7.15, 7.15—7.70, 7.70—8.20 (m, 14 H, arom. H) (Found: C, 76.85; H, 4.9; N, 4.05. $C_{22}H_{17}NO_3$ requires C, 76.96; H, 4.96; N, 4.08%).

Recrystallization of (34) from MeOH gave colourless *prisms*, m.p. 146—147 °C; $\lambda_{max.}$ (EtOH) 243 (ε 33 000) and 287sh nm (4 700); $\nu_{max.}$ (KBr) 3 355, 1 740, 1 695, 1 610, 1 535, 1 262, and 750 cm^{-1}; *m*/*z* (%) 289 (9), 238 (8), 196 (29), 140 (10), 139 (100), 133 (58), 111 (23), and 105 (60); δ($CDCl_3$) 2.25 (s, 3 H, CH_3) 6.40—7.00, 7.00—8.40 (m, 18 H, arom. H), and 8.98 (br s, OH, exchangeable) (Found: C, 69.6; H, 4.35; N, 2.85. $C_{29}H_{22}ClNO_5$ requires C, 69.67; H, 4.40; N, 2.80%).

Hydrolysis of (34) (50 mg) with MeOH–1M–H_2SO_4 (2 : 1; 12 ml) under reflux for 2.5 h gave *o*-aminophenol (7 mg, 67%), benzil (20 mg, 94%), and *m*-chlorobenzoic acid (12 mg, 79%). The hydrolysis of (34) with MeOH–10% NaOH gave the same results.

Hydrolysis of (35) (50 mg) with MeOH–10% NaOH for 2 h at room temperature gave *o*-aminophenol (9 mg, 57%) and benzil (27 mg, 88%).

Acknowledgement

We are grateful to the Ministry of Education, Science, and Culture for financial support.

References

1 B. Witkop and H. Fiedler, *Ann. Chim.*, 1947, **558**, 91.
2 B. Witkop, *Ann. Chim.*, 1947, **558**, 98.
3 A. J. Hutchison and Y. Kishi, *Tetrahedron Lett.*, 1978, 539.
4 R. J. Sundberg, 'The Chemistry of Indoles,' Academic Press, New York, 1970.
5 W. E. Savige, *Aust. J. Chem.*, 1975, **28**, 2275.
6 B. Witkop and J. B. Patrick, *J. Am. Chem. Soc.*, 1951, **73**, 2188.
7 B. Witkop and J. B. Patrick, *J. Am. Chem. Soc.*, 1951, **73**, 2196.
8 C. Ouannes and C. Thal, *Tetrahedron Lett.*, 1981, **22**, 951.
9 A. S. Bailey, R. Scattergood, and W. A. Warr, *Tetrahedron Lett.*, 1970, 2979; *J. Chem. Soc. C*, 1971, 2479.
10 W. K. Anderson and T. Veysogln, *J. Org. Chem.*, 1973, **38**, 2267.
11 M. Nakagawa, N. Ohyoshi, and T. Hino, *Heterocycles*, 1976, **4**, 1275.
12 B. Witkop, *J. Am. Chem. Soc.*, 1950, **72**, 614; M. A. Ardakani and R. K. Smalley, *Tetrahedron Lett.*, 1979, 4769.

Received 17*th May* 1982; *Paper* 2/802