Tetrahedron, Vol. 37, pp. 1813 to 1817, 1981
Printed in Great Britain

0040-4020/81/091813-05$02.00/0
Pergamon Press Ltd.

# THE PREPARATION OF 1-BENZOYL-6,7-DIMETHOXY-5-KETO-1,2,2a,3,4,5-HEXAHYDROBENZ[cd]INDOLE

IOANNIS K. STAMOS[1]

The National Hellenic Research Foundation, Athens 501/1, Greece

(*Received UK 18 November 1980*)

**Abstract**—The synthesis of 1 - benzoyl - 6,7 - dimethoxy - 5 - keto - 1,2,2a,3,4,5 - hexahydrobenz[cd]indole (**10**) is described. Reduction of the pyrrole ring of 3 - (5',6' - dimethoxy - 3' - indolyl)propanoic acid (**6**) with borane pyridine complex and a proton source, followed by N-benzoylation furnished the corresponding indoline derivative 3 - (1' - benzoyl - 5',6' - dimethoxy - 3' - indolinyl)propanoic acid (**7**). This acid was cyclized with PPA to the target tricyclic ketone (**10**).

It has been reported that certain 12 - hydroxyergoline derivatives are highly active antiserotonin agents both *in vitro* and *in vivo*,[2] and such compounds have been prepared by the oxidation of the corresponding ergoline derivatives with potassium nitrosodisulfonate.[3] At least one such a derivative has been identified as an exceedingly active metabolite of methergoline,[4] and such hydroxylated intermediates have been proposed as relevant metabolic transformations of ergometrine and lysergic acid diethylamide.[5]

An hydroxylated metabolite of Lergotrile has also been isolated and characterized as the 13 - hydroxylergotrile, and reported to be about 100 times more active than the parent compound in inhibiting the release of prolactine from the anterior pituitary *in vitro*.[6] Lergotrile itself is an anti-Parkinson agent[7] and the tricyclic amine 4 - (di - n - propyl)amino - 1,3,4,5 - tetrahydrobenz[cd]indole inhibited prolactin secretion and dopamine binding, and it has been prepared from the tricyclic ketone 1 - benzoyl - 5 - keto - 1,2,2a,3,4,5 - hexahydrobenz[cd]indole (**12**) in several steps.[8] This tricyclic ketone has also served as the key intermediate for the total synthesis of lysergic acid[9] as well as the synthesis of some ergot alkaloids with interesting pharmacological properties.[10]

Thus, we have pursued the synthesis of OMe derivatives of **12** and herein we describe the preparation of one of them.

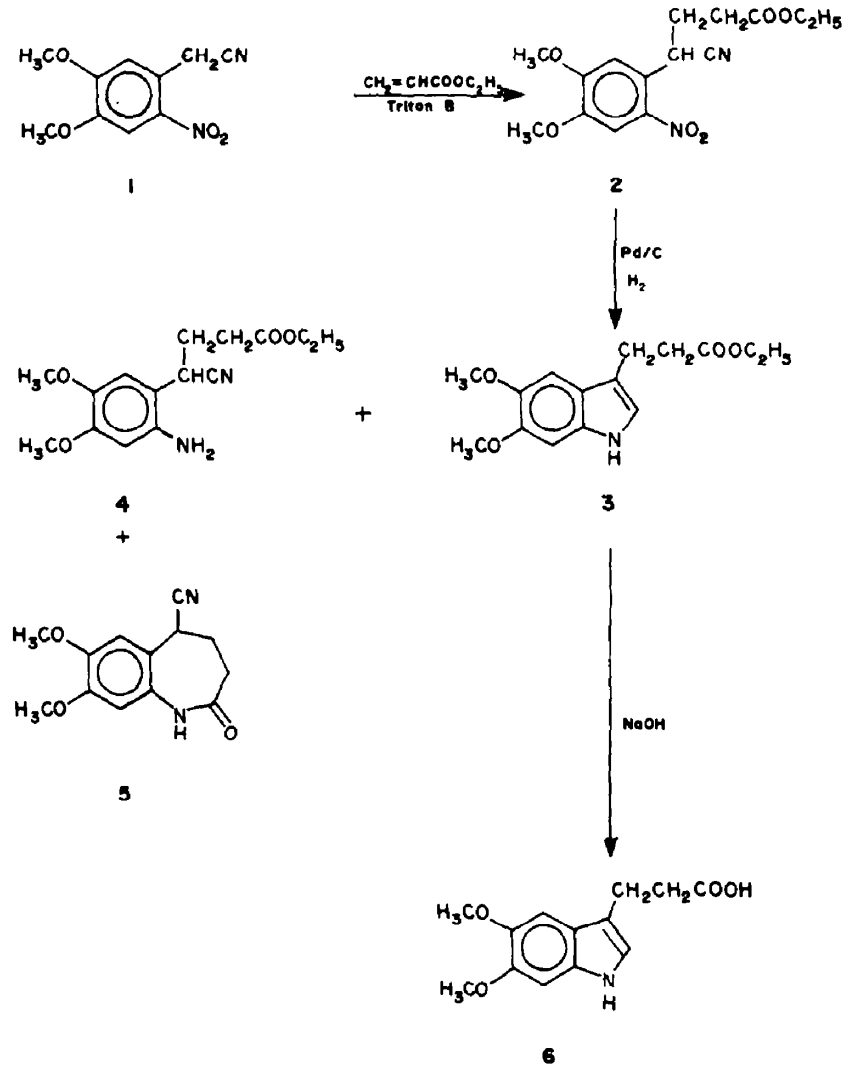
The indole ring system of **3** was formed by hydrogenation-hydrogenolysis of the ethyl 4 - cyano - 4 - (4',5' - dimethoxy - 2' - nitrophenyl)butyrate (**2**), which was in turn obtained as a pale yellow syrup from the 4,5 - dimethoxy - 2 - nitrophenylaceto - nitrile (**1**) and ethyl acrylate in the presence of a base.[11] Along with **3**, the aniline **4** and the hitherto underscribed benzazepine **5** were obtained as minor byproducts. The interesting compound **5** was easily identified by spectroscopic and elemental analysis and by comparison of its spectra with those of the 6-membered homologue.[12] The IR spectrum of **5** shows the typical nitrile absorption at 2240 $cm^{-1}$ and a CO lactam band at 1670 $cm^{-1}$, an expected shift to lower frequencies as compared to the 6-membered homologue (1685 $cm^{-1}$). Also the pattern of the NH three characteristic bands at 3320, 3200 and 3100 $cm^{-1}$ is identical with those at 3360, 3240 and 3130 $cm^{-1}$ of the 6-membered homologue.[12]

Straightforward hydrolysis of the ester (**3**) with NaOH in $H_2O$–dioxane gave the acid **6** in good yield as white crystals of m.p. 138–9° as compared to the reported[11] 124–6°. Its structure was verified by spectroscopic data and elemental analysis.

For the reduction of the pyrrole ring of **6** the reagant borane–pyridine complex in the presence of dilute HCl was found to be convenient to us over the alternative catalytic hydrogenation under high pressure. The indolinyl acid formed was subsequently benzoylated in the same pot with benzoyl chloride according to Schotten–Baumann method. The produced indolinyl acid (**7**) which is soluble in hot water was contaminated with considerable amount of benzoic acid. An attempted steam distillation could not remove the benzoic acid sufficiently. The two acids were separated by controlling the pH of their alkaline solution. The IR and NMR spectra are consistent with the expected structure **7** with only a discrepancy in the shape of the signals of the two OMe groups.[13]

When the acid **7** was treated with $SOCl_2$[14] under inert atmosphere and then with $SnCl_4$, the expected target ketone (**10**) was not formed. Instead, the tricyclic and unstable[15] ketone (**9**) was produced in 50% yield. This result suggests that dehydrogenation of the indolinyl acid (**7**) took place, probably during its treatment with $SOCl_2$, forming the pyrrole double bond which undergoes nucleophilic attack under the Friedel–Crafts conditions. In order to verify this assumption, the indolyl acid (**8**) was prepared by dehydrogenation of indolinyl acid (**7**) with $MnO_2$, and was subsequently subjected to the same reaction conditions as above with $SOCl_2$ and $SnCl_4$. Again this time the ketone (**9**) was produced in the same yield as above. It is noteworthy that in the intramolecular cyclization reactions mentioned above we were not able to isolate any product resulting from the attack of the acylium cation on the 4-position either of **7** or **8**. It could be assumed that such products were formed in minor amounts if at all, in spite of the enhanced electron density on 4-position (adjacent OMe's) as compared to the 2-position (adjacent benzoyl). Such failures are known in the literature[16,17] and it could be argued here that stereochemical strain could play a significant role for the formation of the cyclic carbonium ion intermediates over the electronic preference. Similar results have been observed in the benzofuran ring system in which intramolecular cyclization on the 4-position did not occur when the furan double bond was present.[17]

Finally, the partially saturated benzoindole derivative (**7**) was readily cyclized to the desired ketone (**10**) by



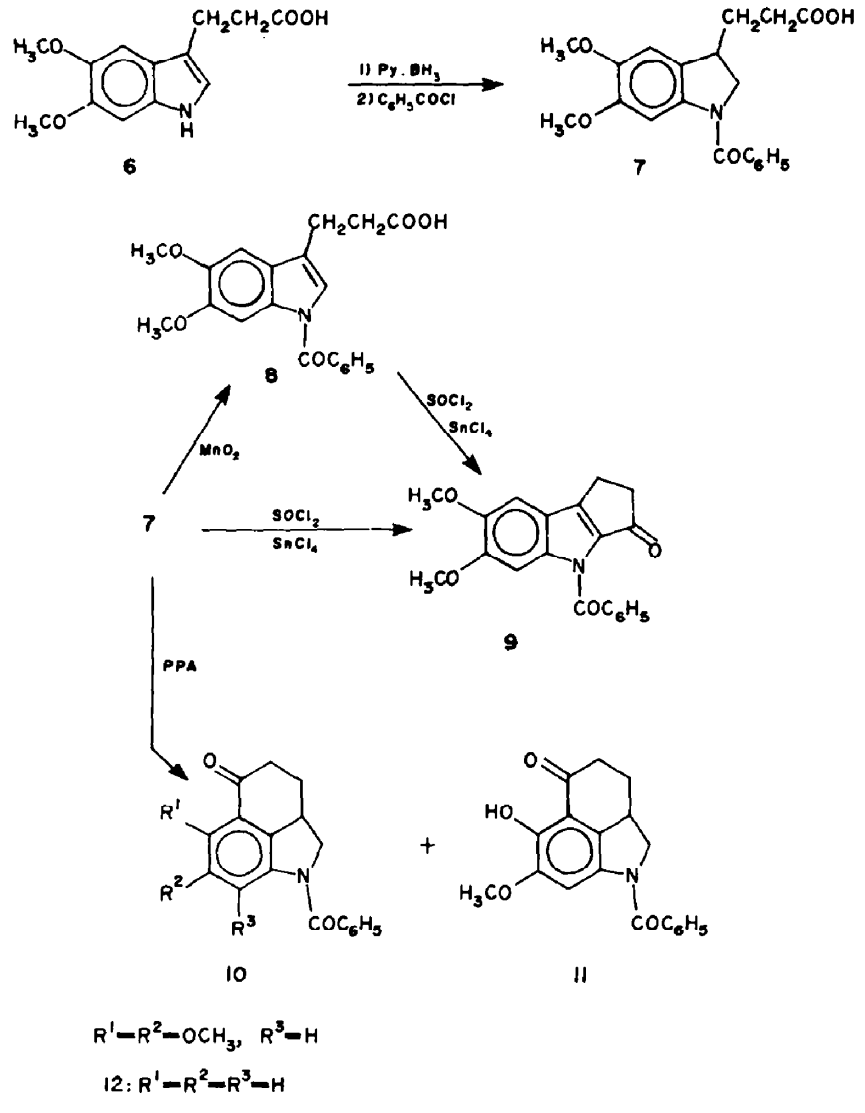

treatment with polyphosphoric acid. As expected in such cyclizations involving carbonium ion next to an OMe group, partial demethylation took place at the 5-position to form the ketone **11** as a byproduct.

The two ketones thereby obtained were separated by alumina chromatography and characterized by their spectroscopic data and elemental analysis. The region of their NMR spectrum due to their alicyclic hydrogens is compatible with the region of the NMR spectrum due to the alicyclic hydrogens of an authentic sample of the ketone **12**. Ketone **10** showed the absorption of its CO group at 1680 $cm^{-1}$ in the IR spectrum, whereas the CO absorption of the ketone **11** has shifted to 1640 $cm^{-1}$ due to its strong intramolecular H–bonding. Likewase, the HO-band of **11** is absent in the IR spectrum, whereas, it shows up in its oxime derivative at 3440 $cm^{-1}$ along with the N–OH band at 3220 $cm^{-1}$.

## EXPERIMENTAL

M.pts were taken on a Buchi m.p. apparatus and are uncorrected. IR spectra were recorded on a Beckman IR-33 spectrophotometer. PMR were recorded on a Varian 60A or EM-360A 60 MHz spectrometer and except where noted, in $CDCl_3$ solvent. Chemical shifts are reported in ppm relative to TMS as internal standard.

*Ethyl 4 - cyano - 4 - (4',5' - dimethoxy - 2' - nitrophenyl)butyrate* (**2**). To a soln of **1**[12] (12.8 g, 58 mmol) in 200 ml abs EtOH and 20 ml dioxane was added 13 g (130 mmol) ethyl acrylate and 5 ml Triton B (40% in MeOH). The dark red soln was stirred for 2.5 hr in a water bath 80–85° and then its volume was reduced to about half using water pump and a water bath at 40–50°. The soln was cooled, neutralized with dil HCl, diluted with benzene–EtOAc (500 ml, 1:1), the organic layer was washed well with water, dried ($Na_2SO_4$) and the solvent evaporated on a rotary evaporator in a water bath at 40–50°. The dark residual oil was chromatographed on Florisil using petroleum ether (40–60°), petroleum ether–benzene (1:1), and then benzene. A deep red semisolid material (0.7 g) was eluted with benzene containing EtOAc. The fractions of petroleum ether–benzene and benzene were combined, evaporated on a rotary evaporator and the residual yellow oil was subjected to high vacuum. At 45°/0.4 mm Hg a colorless liquid was distilled off. The residual syrup was chromatographed on Florisil using benzene to give the product as a pale yellow syrup (17 g, 91%). It distills at 220°/0.3 mmHg with darkening. IR (film) $\nu$=2240(CN), 1730(CO) $cm^{-1}$. Proton NMR $\delta$ 1.25(t, 3H, C–$CH_3$), 2.5(m, 4H, $CH_2CH_2$), 3.98(s, 3H, $OCH_3$), 4.05(s, 3H, $OCH_3$), 4.15(q, 2H, $OCH_2$), 5.0(t, 1H, >CH–CN), 7.20(s, 1H, aromatic), and 7.75 (s, 1H, aromatic). Anal. Calc. for $C_{15}H_{18}N_2O_6$: C, 55.90; H, 5.59; N, 8.69. Found: C, 55.81; H, 5.65; N, 8.82%.




*Ethyl 3 - (5',6' - dimethoxy - 3' - indolyl)propanoate* (3). A soln of 2 (11.27 g, 35 mmol) in 200 ml reagent grade EtOAc containing 4 g 10% Pd/C was shaken under $H_2$ at 43–46 lb and about 80° for 3 hr. The mixture was allowed to cool before taking it out the hydrogenator, filtered, the catalyst was washed with benzene and the combined soln was diluted further with benzene and extracted excaustively with 10% HCl. The extracts were saved. The organic layer was dried ($Na_2SO_4$), concentrated and chromatographed on Florisil (benzene containing EtOAc). Evaporation of the solvent gave 3 as a syrup which crystallized from ether–petroleum ether (40–60°) to give white fluffy crystals of m.p. 85–6°, (7.6 g, 78%). IR (KBr) 3360(NH) and 1770 $cm^{-1}$ (C=O). Proton NMR $\delta$=1.23(t, 3H, C–$CH_3$), a multiplet centered at $\delta$ 2.9(4H, $CH_2CH_2$), 3.83(s, 3H, $OCH_3$), 3.92(s, 3H, $OCH_3$), 4.18(q, 2H, $OCH_2$), 6.82(s, 1H, aromatic), 6.9(s, 1H, pyrrole ring hydrogen), 7.05(s, 1H, aromatic) and 8.25(s, 1H, NH). (Found: C, 64.91; H, 6.93; N, 5.01. Calc. for $C_{15}H_{19}NO_4$: C, 64.98; H, 6.86; N, 5.05%).

*5 - Cyano - 7,8 - dimethoxy - 2 - oxo - 2,3,4,5 - tetrahydro - 1H - 1 - benzazepin* (5). Elution of the above column with $CHCl_3$ and concentration of the fraction gave white crystals of m.p. 191–2°, (0.52 g, 6%). IR (KBr) 3320, 3200, 3100(NH), 2240(C≡N) and 1670 $cm^{-1}$. Proton NMR $\delta$=2.43(m, 4H, $CH_2CH_2$), 3.90(s, 3H, $OCH_3$), 3.95(s, 3H, $OCH_3$), 4.15(t, 1H, >CH–CN), 6.70(s, 1H, aromatic) 7.12(s, 1H, aromatic) and 9.12(s, 1H, NH). (Found: C, 63.55; H, 5.81; N, 11.26. Calc. for $C_{13}H_{14}N_2O_3$: C, 63.41; H, 5.69; N, 11.38%).

*Ethyl 4 - cyano - 4 - (2' - amino - 4',5' - dimethoxyphenyl)butyrate*, (4). The above dark red aqueous extracts were neutralized with $Na_2CO_3$ aq under cooling and in the presence of benzene–EtOAc. The organic layer was dried ($Na_2SO_4$) concentrated and chromatographed on Florisil (benzene containing ether or EtOAc). The red syrup obtained after evaporation of the solvent was chromatographed on silica gel using ether. Evaporation of the solvent immediately gave a pale tan colored syrup which acquires a red color after prolong exposure to air (0.92 g, 9%). IR spectrum (film) gave three bands at 3460, 3380 and 3280 $cm^{-1}$; the shape of these three NH stretching bands are similar with those of aniline; 2240(C≡N), and 1730 $cm^{-1}$ (C=O). Proton NMR $\delta$ = 1.25(t, 3H, C–$CH_3$), 2.20(m, 2H, $\rangle$C–$CH_2$), 2.58(t, 2H, $CH_2CO_2$), 2.80(s, 6H, $OCH_3$), 3.92(m, 3H, $NH_2$, $\rangle$CH–CN), 4.25(q, 2H, $OCH_2$), 6.37(s, 1H, aromatic), and 6.85(s, 1H, aromatic). (Found: C, 61.42; H, 6.97; N, 9.68. Calc. for $C_{15}H_{20}N_2O_4$: C, 61.64; H, 6.85; N, 9.59%).

*3 - (5',6' - Dimethoxy - 3' - indolyl)propanoic acid*, (6). Into a soln of 24 g NaOH in 600 ml water and 150 ml dioxane was dissolved 30.47 g (0.11 mol) of 3 and the soln was gently refluxed for 2 hr. It was cooled in an ice bath, diluted with water, and

acidified slowly to about pH 4 with dil HCl. The white ppt was filtered, washed with water and air dried to give 24 g (87.6%) of the acid. A small portion of this product was dissolved in MeOH–$CHCl_3$, filtered through short column of silica gel and the solvents were rotary evaporated. The residue was dissolved in $CHCl_3$ and the product was crystallized out as a white solid by the addition of a little petroleum ether to give the analytical sample for spectroscopic data, m.p. 138–9° (lit.[11] m.p. 124–6°). IR (KBr) 3520(OH), 3360(NH) and 1710 $cm^{-1}$ (C=O). PMR ($CDCl_3$–DMSO–$d_6$) a multiplet centered at δ 2.78(4H, $-CH_2CH_2-$), δ = 3.78(s, 3H, $-OCH_3$), 3.80(s, 3H, $-OCH_3$), 6.92(s, 1H, aromatic), 6.96(s, 1H, pyrrole ring hydrogen), 7.03(s, 1H, aromatic), 10.53(s, 1H, NH). (Found: C, 62.81; H, 6.03, N, 5.42. Calc. for $C_{13}H_{15}NO_4$: C, 62.65; H, 6.02; N, 5.62%).

3 - (1' - *Benzoyl* - 5',6' - *dimethoxy* - 3' - *indolinyl*)*propanoic acid.* (7). Into a soln of 6 (21 g, 84 mmol) in 350 ml MeOH, cooled with ice-water bath was added 35 ml borane–pyridine complex and then dropwise with stirring 60 ml 12.5% HCl over a period of 25 min. The mixture was stirred for 4 hr and then for about 20–30 min with the ice-water bath removed. The progress of the reaction was monitored by the disappearance of the starting material (tlc on silica gel/EtOAc). The reaction solution was cooled again with an ice-water bath and basified slowly with NaOH pellets. The MeOH was rotary evaporated (40°), the residue was diluted with 350 ml water and extracted with 150 ml benzene. The aqueous layer was treated with 32 ml benzoyl chloride (Schotten–Baumann method), adding it in portions under stirring and occasional cooling, and keeping the soln alkaline with NaOH aq. After about 1 hr stirring, the mixture was acidified under cooling to pH6, extracted with $CHCl_3$, organic layer was dried ($Na_2SO_4$), filtered and evaporated. The syrupy residue was dissolved in $K_2CO_3$ aq, washed with $CHCl_3$ and the aqueous basic soln was neutralized with acidic acid to pH7 (litmus paper) in the presence of equal volume of $CHCl_3$ under cooling and vigorous stirring for about 1 hr. The $CHCl_3$ layer was separated and the remaining aqueous one was acidified to pH6 with dil HCl aq in the presence of equal volume of $CHCl_3$ under vigorous stirring for about 1 hr. The $CHCl_3$ layer was evaporated, the residue was dissolved in $K_2CO_3$ aq and worked up as above at pH=7. The above two $CHCl_3$ layers were combined, dried ($Na_2SO_4$), filtered and evaporated. The syrupy green residue was filtered through silica gel using EtOAc to remove the green impurities. Evaporation of the solvent gave 27 g (89%) of the product as a white solid with a greenish tinge, which still contained small amount of benzoic acid. An analytical sample was recrystallized from EtOAc–benzene to give white solid of m.p. 168–70°. IR(KBr): ν=1730 (acid C=O), and 1610 $cm^{-1}$ (amide C=O). $^1H$ NMR: δ = 1.78–2.62(m, 4H, $CH_2CH_2$), 3.17–4.43(m, 9H, $CHCH_2N$, $2CH_3O$), 6.82(s, 1H, aromatic), 7.55(s, 6H, aromatic), 10.65(s, 1H, COOH). (Found: C, 67.70; H, 6.09; N, 3.70. Calc. for $C_{20}H_{21}NO_5$: C, 67.60; H, 5.91; N, 3.94%.)

3 - (1' - *Benzoyl* - 5',6' - *dimethoxy* - 3' - *indolyl*)*propanoic acid* (8). A suspension of $MnO_2$[18] (6 g, 69 mmol) in 100 ml $CHCl_3$ and 7 (2 g; 5.7 mmol) was stirred at room temp for 48 hr. It was then filtered through Celite, the $MnO_2$ was washed with $CHCl_3$ and the combined solvent was evaporated. The residue was dissolved in $K_2CO_3$ aq, filtered, acidified and extracted with $CHCl_3$. The organic layer was dried ($Na_2SO_4$), filtered through little silica gel and evaporated. The residue was recrystallized from benzene to give the product as an off-white solid, m.p. 172–3°, 1.3 g (65%). IR (KBr): ν=1710 (acid C=O), and 1680 $cm^{-1}$ (amide C=O); $^1H$ NMR δ=2.80(m, 4H, $CH_2CH_2$), 3.90(s, 6H, $2CH_3O$), 6.96(s, 2H, overlapping aromatic–pyrrolic), 7.60(broad pseudosinglet, 5H, $C_6H_5CO$) 8.02 (s, 1 H, aromatic), 10.56 (s, 1 H, COOH). (Found: C, 67.89; H, 5.40; N, 4.10. Calc. for $C_{20}H_{19}NO_5$: C, 67.99; H, 5.38; N, 3.96%).

4 - *Benzoyl* - 6,7 - *dimethoxy* - 1,4 - *dihydrocyclopent*[b]*indole* - 3(2H) - *one*, (9). $SOCl_2$ (2 ml) was added into a soln of 8 (1.3 g, 3.66 mmol) in 15 ml $CHCl_3$ and the solution stirred for 1 hr at room temp under $N_2$ and for 25 min in a water bath at 60°. The excess $SOCl_2$ and the solvent were evaporated under reduced pressure (water pump) in a water bath at 40°. Into the viscous brown residue was added 30 ml 1,2 - dichloroethane and then 2 ml $SnCl_4$ and the soln was stirred for 4 hr at rt under $N_2$. It was then hydrolysed with HCl in ice-water and extracted with $CHCl_3$. The organic layer was dried ($Na_2SO_4$), concentrated with a rotary evaporator at a lukewarm water bath, and chromatographed on alumina ($CHCl_3$–1% EtOH). The yellow fraction containing the product was concentrated with a rotary evaporator at a lukewarm water bath, and the product was crystallized out by adding a little petroleum ether (40–60°) to give the product as a yellow solid, m.p. 197–207°, 0.6 (48%). It was dissolved in $CHCl_3$ without heating,[15] filtered through silica gel and concentrated again as above, m.p. 206–10° (dec). IR (KBr): ν=1690 (ketone C=O), and 1620 $cm^{-1}$ (amide C=O). $^1H$ NMR δ=2.90(m, 4H, $CH_2CH_2$), 3.95(s, 6H, $2CH_3O$), 7.07(s, 1H, aromatic), 7.60(m, 5H, $C_6H_5CO$) and 7.82(s, 1H, aromatic). (Found: C, 71.83; H, 4.90; N, 4.31. Calc. for $C_{20}H_{17}NO_4$:C, 71.64; H, 5.07; N, 4.18%.)

1 - *Benzoyl* - 6,7 - *dimethoxy* - 5 - *keto* - 1,2,2*a*,3,4,5 - *hexahydrobenz*[cd]*indole* (10). A mixture of 7 (3.55 g, 10 mmol) and polyphosphoric acid (400 g) was heated for 1 hr at 85° on a hot plate under vigorous stirring. The orange-red mixture was then decomposed with ice (500 g). Into this mixture was added 500 ml $CHCl_3$ and treated with solid $K_2CO_3$ to pH 5 under cooling in an ice-water bath and diluting it with additional ice-water as necessary. The $CHCl_3$ layer was separated and the aqueous one was extracted with 200 ml $CHCl_3$. The combined organic layer was dried ($Na_2SO_4$), filtered and evaporated with a rotary evaporator at lukewarm temp. The residual oil was chromatographed on alumina ($CHCl_3$) or $CH_2Cl_2$ to give a waxy product (2 g, 59%) which was recrystallized from ether containing a few drops of $CH_2Cl_2$ and diluting the soln with a little petroleum ether (40–60°). Crystallization was induced by scratching the inside of the Erlenmeyer flask containing the soln with a glass rod to give 10 as pale yellow crystals, m.p. 120–2°, 1.7 g (50%). IR (KBr): ν=1680 (ketone C=O), and 1640 $cm^{-1}$ (amide C=O). Proton NMR δ=1.60–2.80(m, 4H, $CH_2CH_2CO$), 3.28–4.00(m, 8H, $2CH_3O$ and $CH_2N$), 4.10–4.60(m, 1H, ≡CH), 7.55(bs, 6H, aromatic). (Found: C, 71.25; H, 5.48; N, 4.21. Calc. for $C_{20}H_{19}NO_4$: C, 71.22; H, 5.64; N, 4.15%.) Its oxime: white crystals, m.p. 253–5° (dec).

1 - *Benzoyl* - 6 - *hydroxy* - 5 - *keto* - 7 - *methoxy* - 1,2,2*a*,3,4,5 - *hexahydrobenz*[cd]*indole*, (11). Elution of the above column with $CHCl_3$–MeOH (98:2) and evaporation of the solvent gave a yellow solid, 0.4 g (12%). Recrystallizatin from $CH_2Cl_2$–pet ether (40–60°) yielded clusters of yellow crystals which melted at 96–8°, solidified and melted again at 144–5°. IR (KBr): ν=1640 (ketone C=O), and 1630 $cm^{-1}$ (amide C=O). Proton NMR δ=1.60–2.80(m, 4H, $CH_2CH_2CO$), 3.20–4.00(m, 5H, $CH_3O$ and $CH_2N$), 4.10–4.50(m, 1H, >CH), 7.40(s, 1H, aromatic), 7.58(s, 5H, $C_6H_5CO$), 10.88(s, 1H, OH). (Found: C, 70.26; H, 5.41; N, 4.26. Calc. for $C_{19}H_{17}NO_4$: C, 70.59; H, 5.26; N, 4.33%.) Its oxime: white crystals, m.p. 236–7° (dec).

*Acknowledgements*—The author is indepted to Prof. G. Tsatsas of the University of Athens for use of facilities. Thanks also are due to Dr. Mantzos for performing some of the microanalysis.

## REFERENCES

[1]The National Hellenic Research Foundation Fellow 1977–80. A part of this work was performed in the laboratory of Pharmaceutical Chemistry, University of Athens, Athens, Greece.
[2]F. Arcamone, G. Franceschi, A. Glaesser and L. Dorigotti, *Ger. Pat.* 1,910,930 (1969); *Chem. Abstr.* 72, 21818z (1970).
[3]G. Franceschi and A. Vigevani, *Il Farmaco-Ed. Sci.* 33, 126 (1978); P. A. Stadler, A. J. Frey, F. Troxler and A. Hofmann, *Helv. Chim. Acta* 47, 756–9 (1964).
[4]F. Arcamone, A. Glaeser, A. Minghetti and V. Nicolella, *Boll. Chim. Farmac. Milano*, 110, 704 (1971); *Chem. Abstr.* 77, 28736h (1972).
[5]M. B. Slaytor and S. E. Wright, *J. Med. Pharm. Chem.* 5, 483–91 (1962); Z. H. Siddik, R. K. Barnes, L. G. Dring, R. L. Smith and R. T. Williams, *Biochem. Soc. Trans.* 3, 290 (1975).
[6]J. C. Parli, B. Schmidt and C. J. Shaar, *Biochem. Pharmacol.* 27(9), 1405–8 (1978).
[7]A. N. Lieberman, M. Kupersmith, E. Estey and M. Goldstein, *Lancet*, 2 (7984), 515 (1976).

[8]N. J. Bach and E. C. Kornfeld, *U.S. Pat.* 4,110,339 (1978); *Chem. Abstr.* **90**, 121415f (1979).
[9]E. C. Kornfeld, E. J. Fornefeld, G. B. Kline, M. J. Mann, D. E. Morrison, R. G. Jones and R. B. Woodward, *J. Am. Chem. Soc.* **78**, 3087–3114 (1956).
[10]A. M. Crider, J. M. Robinson, H. G. Floss and J. M. Cassady, *J. Med. Chem.* **20**, 1473 (1977); and refs therein.
[11]G. N. Walker, *J. Am. Chem. Soc.* **78**, 3698 (1956).
[12]Ioannis K. Stamos, *Synthesis* 663 (1980).
[13]In the proton NMR spectra, the signal of the MeO-group on the three *indolinyl* compounds (**7**, **10** and **11**), which is the identified as 6-MeO on **7** and 7-MeO on **10** and **11**, appears as a broadened singlet, whereas the signal of the same 6-MeO on the *indole* ring systems **3**, **6**, **8** and 7-MeO on **9**, appears as a typical intense singlet of equal intensity to the signal of the adjacent MeO-group.
[14]Commercially supplied $SOCl_2$ was used directly without any purification.
[15]In boiling $CHCl_3$, it was converted to a new yellow compound of m.p. 214–7° and 219–221°. Its proton NMR spectrum showed no alicyclic hydrogens. On long standing, up to a year, it was transformed to a white solid (m.p. 262–4°), which can be separated from intractable yellow solids by column chromatography on alumina ($CHCl_3$–EtOH, 99:1).
[16]T. Nagasaka and S. Ohki, *Chem. Pharm. Bull.* **25**, 3023 (1977). R. Neidlein and F. Moller, *Liebigs Ann.* 971 (1980).
[17]T. Horaguchi and T. Abe, *Bull. Chem. Soc. Japan* **52**, 2437 (1979).
[18]J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.* 1094 (1952).