SYNTHESIS OF 4,4- AND 5,5-DISUBSTITUTED 4,5-DIHYDRO-6*H*-CANTHIN-6-ONES* ** ***

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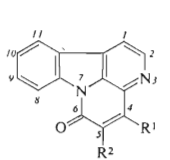
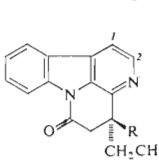
The paper describes regiospecific synthesis of 4,4- and 5,5-disubstituted 4,5-dihydro-6*H*-canthin-6-ones *III* and *XVIII*, starting from half-esters of 2,3-disubstituted succinic acids, *V* and *XIV*. The formation of the anomalous 5,5-disubstituted canthin-4,6-diones *XVII* is ascribed to oxidation of the intermediate *XIX*. The ^{1}H NMR spectra of the compounds prepared are discussed.

Canthin-6-ones constitute a family of tetracyclic indole bases, derived from the simplest representative *I*, whose structure has been confirmed by synthesis[1]. Some of them, including the base *I*, were isolated from certain plant species of the families *Rubiaceae*, *Rutaceae* and *Simaroubaceae*[2,3]. The known methods for preparation of compounds of this type, their 4,5-dihydro derivatives or more hydrogenated substances[1,4], lend themselves, as a rule, to special cases only. The most general method thus far employed for syntheses of canthinones *IIa* and *IIb*, starting from ethylsuccinic anhydride and tryptophan[5], is not quite satisfactory, mainly for its non-regiospecificity. The impossibility of its application to synthesis of 4,4-disubstituted canthin-6-ones is obvious at first sight. This paper describes regiospecific syntheses



I, $R^1 = R^2 = H$
IIa, $R^1 = C_2H_5$, $R^2 = H$
IIb, $R^1 = H$, $R^2 = C_2H_5$



IIIa, $R = CH_2CH_2CH_3$
IIIb, $R = CH_3$
VIIIa, $R = CH_2CH_2CH_3$,1,2-dihydro
VIIIb, $R = CH_3$, 1,2-dihydro

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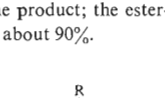
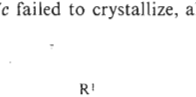
of 4,4- and 5,5-disubstituted 4,5-dihydro-6*H*-canthin-6-ones; in devising the method we considered Taylor's note[6] on synthesis of the racemic base *IIIa*, which is a degradation product of eburnane alkaloids.

The synthesis of 4,4-disubstituted canthin-6-ones *III* started from 2-allyl-2-ethylsuccinic anhydride[7] (*IVa*) and 2-ethyl-2-methylsuccinic anhydride (*IVb*). These were heated with methanol (*c.* 1·3 mol-equivalents) to give the corresponding ester-acids *Vb* and *Vc* in yields 67·4% and 91·5%, respectively. These yields are higher than with the current procedures based on the reaction of acid anhydrides with methanol, catalysed by sodium methoxide[8], or on the acid-catalysed partial esterification of succinic acid with methanol[9]. The unsaturated ester-acid *Vc* was hydrogenated on the Adams catalyst to 2-ethyl-2-propyl-3-methoxycarbonylpropanoic acid (*Va*) in an almost quantitative yield. However, only the ester-acid *Vb* was obtained as a crystalline product; the ester-acids *Va* and *Vc* failed to crystallize, although their purity was about 90%.



IVa, R = $CH_2CH{=}CH_2$
IVb, R = CH_3

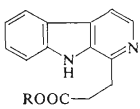


Va, $R^1 = CH_2CH_2CH_3$, $R^2 = OH$, $R^3 = OCH_3$
Vb, $R^1 = CH_3$, $R^2 = OH$, $R^3 = OCH_3$
Vc, $R^1 = CH_2CH{=}CH_2$, $R^2 = OH$, $R^3 = OCH_3$
VIa, $R^1 = CH_2CH_2CH_3$, $R^2 = Cl$, $R^3 = OCH_3$
VIb, $R^1 = CH_3$, $R^2 = Cl$, $R^3 = OCH_3$
XIIIa, $R^1 = CH_2CH_2CH_3$, $R^2 = R^3 = OCH_3$
XIIIb, $R^1 = CH_3$, $R^2 = R^3 = OCH_3$
XIIIc, $R^1 = CH_2CH{=}CH_2$, $R^2 = R^3 = OCH_3$
XIVa, $R^1 = CH_2CH_2CH_3$, $R^2 = OCH_3$, $R^3 = OH$
XIVb, $R^1 = CH_3$, $R^2 = OCH_3$, $R^3 = OH$
XVa, $R^1 = CH_2CH_2CH_3$, $R^2 = OCH_3$, $R^3 = Cl$
XVb, $R^1 = CH_3$, $R^2 = OCH_3$, $R^3 = Cl$

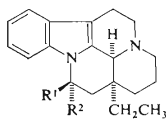
VIIa, R = $CH_2CH_2CH_3$
VIIb, R = CH_3

The ester-acids *Va* and *Vc* were quantitatively converted, by reaction with oxalyl chloride[10], into the corresponding acyl chlorides *VIa* and *VIb*, which were allowed to react, without having been isolated, with tryptamine in a medium of pyridine. The obtained N-[2-(indol-3-yl)ethyl]-2-alkyl-2-ethyl-3-methoxycarbonylpropanamides *VIIa* and *VIIb* were cyclized according to Bischler and Napieralski by the action

of phosphorus oxychloride and polyphosphoric acid to 1,2,4,5-tetrahydrocanthin-6-ones, *VIIIa* and *VIIIb*. Polyphosphoric acid induces the formation of the D ring; with phosphorus oxychloride alone this ring closure practically did not occur. However, it is desirable that it should occur before dehydrogenation of the C-ring, since compounds of type *IX* are known[11] to resist attempts at their cyclization. The structures of the tetracyclic azomethines *VIIIa* and *VIIIb* follow from their spectral properties.



IX



X, $R^1R^2 = O$
XI, $R^1 = OH$, $R^2 = COOCH_3$
XII, $R^1 = OH$, $R^2 = CO_2H$

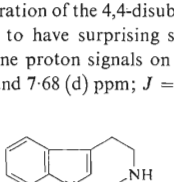
The desired 4,4-disubstituted 4,5-dihydro-6*H*-canthin-6-ones *III* were obtained in satisfactory yields from the azomethines *VIII* by a brief heating with selenium to a temperature higher than 300°C *in vacuo*. The structure of the base *III* was demonstrated by comparison with (−)-(*S*)-4-ethyl-4-propyl-4,5-dihydro-6*H*-canthin-6-one ((−)-*IIIa*), which had been prepared by an analogous dehydrogenation of (−)-(20*S*)-eburnan-16-one[12], accessible from (+)-vincamine (*XI*) *via* the corresponding vincaminic acid[12] (*XII*) by oxidative degradation with lead tetraacetate[13] or the Fétizon reagent[14]. The ^{1}H NMR spectra of the bases *III* contained the two-proton signal of methylene protons in the grouping —CO—CH_2—C—, as a singlet at 3·02 ppm in the base *IIIa* and as AB q at 3·15 and 2·90 ppm in the base *IIIb*.

The starting compounds for the synthesis of 5,5-disubstituted bases were again 2-alkyl-2-ethyl-3-methoxycarbonylpropanoic acids, *Vb* and *Vc*, which were first converted by diazomethane into the corresponding dimethyl esters *XIIIb* and *XIIIc*; the saturated dimethyl ester *XIIIa* was easily obtained by hydrogenation of dimethyl 2-allyl-2-ethylbutanedioate (*XIIIc*) on the Adams catalyst.

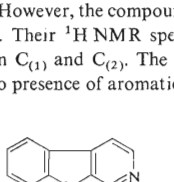
The diesters *XIIIa* and *XIIIb* were subjected to selective alkaline hydrolysis with 1·2 equivalents of potassium hydroxide in aqueous methanol at 50°C; the hydrolysis afforded high yields of the isomeric ester-acids, *viz* 3-methoxycarbonyl-3-methyl-pentanoic acid (*XIVb*) and 3-ethyl-3-methoxycarbonylhexanoic acid (*XIVa*). These were smoothly converted by reaction with oxalyl chloride into the corresponding ester-chlorides, *XVa* and *XVb*. The crude ester-chlorides were allowed to react with tryptamine in the presence of a base, to give the corresponding tryptamides,

XVIa and *XVIb*. The reaction conditions that had been used for preparation of the isomeric tryptamides *VII* failed to give good results in this case. However, under the conditions of the Schotten–Baumann reaction, with aqueous potassium carbonate as the base, the reaction proceeded smoothly and gave a good yield in either case.

To cyclize the amides *XVI* we chose the same conditions as had been employed in the preparation of the 4,4-disubstituted bases *III*. However, the compounds isolated were found to have surprising spectral properties. Their ^{1}H NMR spectra lacked the methylene proton signals on $C_{(4)}$, as well as on $C_{(1)}$ and $C_{(2)}$. The AB quartet (δ 8·50 (d) and 7·68 (d) ppm; J = 6·5 Hz) pointed to presence of aromatic hydrogens



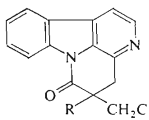
XVIa, R = $CH_2CH_2CH_3$
XVIb, R = CH_3



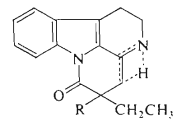
XVIIa, R = $CH_2CH_2CH_3$
XVIIb, R = CH_3

on $C_{(1)}$ and $C_{(2)}$. These facts, along with the UV spectra, having maximum at 353, 305, 268 and 230 nm, suggested a conjugated pyrido[3,4-*b*]indole chromophore. The IR spectra had two bands in the region of the carbonyl stretching vibration (*e.g.* at 1 710 and 1 690 cm^{-1} with *XVIIa*), which, along with the molecular mass (M^+) and the above-given ^{1}H NMR data, have allowed the compounds studied to be identified as 5-alkyl-5-ethyl-4,5-dihydro-6*H*-canthin-4,6-diones, *XVIIa* and *XVIIb*.

The canthin-6-ones *XVIII* can also be obtained by this method, but the dehydrogenation by selenium only proceeds with the crude product of the Bischler–Napieralski reaction (not chromatographically purified). The structures of these bases were demonstrated unequivocally by spectral methods: a sole absorption band of the carbonyl vibration in the IR spectrum (at 1 710 vm^{-1} with *XVIIIa* and 1 700 cm^{-1} with *XVIIIb*), the diagnostic signal of $C_{(4)}$-methylene protons in the ^{1}H NMR spectrum (a singlet at 3·39 ppm with *XVIIIa* and AB quartet at 3·48 and 3·18 ppm with *XVIIIb*) and mass spectrometry data. It can be inferred that the crude product from the reaction of the ester-amides *XVI* is to be assigned the structure *XIX*, which accounts for the ready formation of canthindiones *XVII* by oxidation and dehydrogenation in the course of the isolation. The high sensitivity of the postulated intermediate *XIX* to oxidation, starting in all probability by an attack on the 4-position, is evident from the fact that the corresponding diones *XVII* were detected in the crude product of Bischler–Napieralski reaction even by TLC analysis.

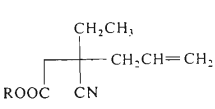


XVIIIa, R = $CH_2CH_2CH_3$
XVIIIb, R = CH_3

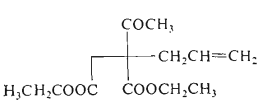


XIX

Derivatives of 2,2-disubstituted succinic acids. As can be seen from Table I, the methylene protons in the grouping —CO—C—CH_2—CO— resonate in the region 2·30 – 2·90 ppm, except for the acyl chloride *XVa*, in which this signal is shifted by electronegativity of the —CO—Cl group as far as 3·28 ppm. In compounds with the Et–Me substitution, as a result of chemical non-equivalence, the signal of these protons forms an AB quartet (^2J = 14 – 16 Hz), whereas in compounds with the Et–Pr substitution these protons invariably appear as a singlet. This behaviour can be attributed to a difference in symmetry between the two series of conformers. With the Et–Me substitution the free rotation of the methyl group brings about an asymmetrical location of the two carboxyl groups toward the methylene group, which, in turn, causes chemical nonequivalence of the two hydrogens. By contrast, in compounds with Et–Pr substitutions the rotations of the methylene groups of the two substituents are hampered and the molecule can arrange itself into the sterically and energetically optimum conformation, where the two carboxyl residues are placed symmetrically to the methylene group protons (singlet).



XXa, R = Me
XXb, R = Et



XXI

As studies of models have shown, derivatives of the series Et–All (ABq) behave analogously to the series Et-Me. The apparent exceptions of compounds[7] *XX* and *XXI* are due to other effects. For example, in esters of 3-ethyl-3-cyano-5-hexenoic acid (singlets at 2·62 or 2·60 ppm) they are caused by a strong shielding effect of the adjacent cyano group. Finally, comparison of chemical shifts of the carboxyl proton shows that its value is diagnostic for specification of an isomer, since the difference is 1·3 to 1·5 ppm (Table I).

EXPERIMENTAL

The boiling points and melting points (Boetius microblock) are not corrected. The analytical samples were dried for 6 h at room temperature and a pressure of 1·4 Pa. Purity of the compounds was checked by thin-layer chromatography on commercial silica gel GF_{254} plates (Merck, F.R.G.) in appropriate solvent systems, or by gas chromatography in an apparatus Chrom III IKZ (Labora, Czechoslovakia). Column chromatography was carried out employing neutral silica gel (Merck, F.R.G.) and aluminium oxide (Reanal, Hungary). Preparative thin-layer chromatography was carried out on plates 20 × 20 cm, the thickness of silica gel GF_{254} being 1 mm, in a system benzene–chloroform–methanol 90 : 45 : 10. The ultraviolet spectra were

TABLE I

^{1}H NMR spectra of derivatives of 2-substituted 2-ethylsuccinic acids

Substituent	Formula	Protons —CO—CH_2—C—		
		δ, ppm	multiplicity	^2J (c/s)
n-C_3H_7	*Va*[a]	2·50	s	—
CH_3	*Vb*[b]	2·78	ABq	15·5
		2·44		
$CH_2CH{=}CH_2$	*Vc*[c]	2·72	ABq	15·0
		2·48		
n-C_3H_7	*XIVa*[d]	2·65	s	—
CH_3	*XIVb*[e]	2·89	ABq	16·0
		2·41		
n-C_3H_7	*XIIIa*	2·63	s	—
CH_3	*XIIIb*	2·83	ABq	16·0
		2·39		
$CH_2CH{=}CH_2$	*XIIIc*	2·70	ABq	15·0
		2·46		
n-C_3H_7	*XVa*	3·28	s	—
$CH_2CH{=}CH_2$	*IVa*[f]	2·95	ABq	16·5
		2·60		
CH_3	*IVb*	2·88	ABq	15·5
		2·51		
n-C_3H_7	*VIIa*	2·50	s	—
CH_3	*VIIb*	2·82	ABq	16·0
		2·30		
n-C_3H_7	*XVIa*	2·35	s	—
CH_3	*XVIb*	2·62	ABq	14·0
		2·04		

[a] Chemical shift of the proton —CO_2H (δ ppm) 11·48, [b] 11·30, [c] 11·40, [d] 9·90, [e] 10·00, [f] reference[7].

measured in methanolic solutions using a spectrophotometer SPECORD UVIS (Zeiss, Jena, G.D.R.) and are expressed in wavelengths of the absorption maxima, λ (nm), and in the corresponding values of $\log \varepsilon$. The infrared spectra were taken with a spectrophotometer UR 10 (Zeiss, Jena, G.D.R.). The ^{1}H NMR spectra were measured using an apparatus BS 487 (Tesla, Czechoslovakia); the chemical shifts are given in the δ scale (ppm), with tetramethylsilane as internal standard. The mass spectra were measured with a high-resolution mass spectrometer of double focusation MS 902 (AEI, Great Britain), the energy of ionizing electrons being 70 eV. The values of specific rotation were measured with a subjective polarimeter (Zeiss, Jena, G.D.R.) at a wave length of 578 nm and a temperature of 21·5—23°C.

2-Ethyl-2-methylsuccinic Anhydride (*IVb*)

To 36·5 g (0·228 mol) of 2-ethyl-2-methylbutanedioic acid[15] was added 53·7 g (0·684 mol) of acetyl chloride, and when the reaction had died down the mixture was slowly heated to the boil, at which it was kept for 1 h. After evaporation of the volatile components *in vacuo* the residue was distilled on a 15 cm long Vigreaux column. Yield 25·5 g (78·7%) of an oily product boiling at 107 to 108°C/1·1 kPa, purity by GLC 98%. IR spectrum in CCl_4: 1 848, 1 790 cm^{-1} (anhydride). ^{1}H NMR spectrum in $CDCl_3$: 2·88, 2·51 (2 H, ABq, J = 15·5 Hz; C—CH_2—CO—); 1·29 (3 H, s; CH_3—C); 0·89 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C).

2-Allyl-2-ethyl-3-methoxycarbonylpropanoic Acid (*Vc*)

A mixture of 2-allyl-2-ethylsuccinic anhydride[7] (*IVa*, 20·2 g, 120 mmol), methanol (6·65 ml, 164 mmol) and 17 ml of benzene was slowly brought to the boiling point, at which it was kept for 8 h. After cooling down the mixture was distributed between benzene (200 ml) and a 6% aqueous solution of sodium hydrogen carbonate (200 and 20 ml). The aqueous phase was re-extracted with benzene (30 ml), acidified with 10% hydrochloric acid under cooling, and the separated oil was taken into benzene (200 and 2 × 25 ml). The dried organic phase was distilled to evaporate the solvent; yield 22·1 g (91%) of an oily product (purity by GLC 89%), which was directly employed in the next reaction. (Attempts at crystallization failed and the benzylisothiuronium salt was not crystalline either; distillation at 115°C/30 Pa gave a mixture with the starting anhydride in a ratio of 3 : 1). IR spectrum in CCl_4: 2 620 (CO_2H), 1 730, 1 710 (C=O), 1 631 cm^{-1} (C=C). ^{1}H NMR spectrum in $CDCl_3$: 11·40 (1 H, bs; COOH); 5·05 (1 H, d, J = = 10·0 Hz; *cis*-H—CH=CH—CH_2); 5·02 (1 H, d, J = 15·0 Hz; *trans*-H—CH=CH—CH_2); 3·64 (3 H, s; $COOCH_3$); 2·72, 2·48 (2 × 1 H, ABq, J = 15·0 Hz; C—CH_2—CO—); 2·48 (2 H, bd, J = 7·0 Hz; CH_2=CH—CH_2); 1·70 (2 H, q, J = 7·0 Hz; CH_3—CH_2—C); 0·88 (3 H, t J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 200 (M^+, $C_{10}H_{16}O_4$).

2-Ethyl-3-methoxycarbonyl-2-propylpropanoic Acid (*Va*)

The acid *Vc* (6·50 g, 32·8 mmol) dissolved in 75 ml of methanol was hydrogenated under a moderate overpressure in the presence of the Adams catalyst. After 1 h 836 ml (106%) of hydrogen was taken up. The mixture was filtered and distilled. The residue was repeatedly dissolved in benzene and taken to dryness *in vacuo*; when it reached a purity of 88% by GLC (6·1 g, 92%) it still failed to crystallize and was used for the reaction without more purification. IR spectrum in CCl_4: 2 630 (COOH), 1 730 and 1 700 cm^{-1} (C=O). ^{1}H NMR spectrum in $CDCl_3$: 11·48 (1 H, bs; COOH); 3·60 (3 H, s; $COOCH_3$); 2·50 (2 H, s; C—CH_2—COO—); 1·70 (2 H, q, J = 7·0 Hz; CH_3—CH_2—C); 0·89 (3 H, def. t; CH_3—CH_2—C); 0·82 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 202 (M^+, $C_{10}H_{18}O_4$).

2-Ethyl-2-methyl-3-methoxycarbonylpropanoic Acid (*Vb*)

A mixture of the anhydride *IVb* (24·8 g, 0·175 mol) and methanol (8·5 ml, 0·21 mol) was heated to 110°C in the course of 1·5 h and kept at this temperature for 1 h. Distillation *in vacuo* yielded 26·9 g of a residue containing 90% of the product (GLC). Crystallization from hexane gave a product (20·5 g, 67·4%) melting at 70·5–72°C and boiling at 111–113·5°C/60 Pa (rep.[8] m.p. 71·9–72·4°C and b.p. 93–94°C/27 Pa). For $C_8H_{14}O_4$ (174·2) calculated: 55·16% C, 8·10% H; found: 55·29% C, 8·01% H. IR spectrum in $CHCl_3$: 2 680 (—COOH), 1 740 (ester), 1 718 cm^{-1} (—COOH). ^1H NMR spectrum in $CDCl_3$: 11·30 (1 H, bs; COOH); 3·63 (3 H, s; $COOCH_3$); 2·78, 2·44 (2 H, ABq, J = 15·5 Hz; C—CH_2—CO—); 1·25 (3 H, s; CH_3—C); 0·88 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C).

Tryptamides *VII*

A mixture of the ester-acid *V* (10 mmol), oxalyl chloride (13·2 mmol) and benzene (10 ml) was allowed to stand at room temperature for 3 h, then kept at 40°C for 0·5 h. Repeated evaporation with benzene *in vacuo* left an almost quantitative yield of the crude acyl chloride, which was dissolved in 5 ml of pyridine and added dropwise under stirring and cooling to 0°C, in the course of 0·5 h, to a solution of tryptamine (10·5 mmol) in 18 ml of pyridine. The stirring was continued for 7·5 h at room temperature; the mixture was then distilled to remove the solvent and 140 ml of chloroform was added. The solution was successively washed with 5% hydrochloric acid (70 and 30 ml), water (30 ml), 2·5% ammonium hydroxide (60 and 20 ml), water (30 ml) and brine (30 ml). After drying with anhydrous sodium sulphate the solution was concentrated by distillation. The residue, slowly crystallizing at room temperature, was dissolved in chloroform and filtered through a small column of silica gel (8 g). The concentrated eluate was crystallized from a mixture chloroform–ether–hexane, giving tryptamide *VII*, uniform in TLC.

N-[2-(*Indol*-3-*yl*)*ethyl*]-2-*ethyl*-3-*methoxycarbonyl*-2-*propylpropaneamide* (VIIa) was obtained from the ester-acid *Va* in a yield of 54·3%; m.p. 107·5–109·5°C. For $C_{20}H_{28}N_2O_3$ (344·4) calculated: 69·74% C, 8·19% H, 8·13% N; found: 69·21% C, 8·28% H, 8·13% N. UV spectrum: 293 (3·76), 284 (3·82), 275 (3·78), 224 (4·58). IR spectrum in $CHCl_3$: 3 500 (NH free), 3 340 (NH assoc.), 1 735 (ester), 1 655 (amide I—CO), 1 522 cm^{-1} (amide II — NH). ^1H NMR spectrum in $CDCl_3$: 10·90 (1 H, bs; indole NH); 7·60 (1 H, bt; CO—NH—CH_2—); 3·51 (3 H, s; $COOCH_3$); 2·80 (2 H, bt; CO—NH—CH_2—CH_2—C); 2·50 (2 H, s; C—CH_2—$COOCH_3$); 0·79 (3 H, def. t; CH_3—CH_2—CH_2); 0·70 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 344 (M^+, $C_{20}H_{28}N_2O_3$).

N-[2-(*Indol*-3-*yl*)*ethyl*]-2-*ethyl*-3-*methoxycarbonyl*-2-*methylpropaneamide* (VIIb) was obtained from the ester-acid *Vb*; yield 57·7%, m.p. 98·5–100°C. For $C_{18}H_{24}N_2O_3$ (316·4) calculated: 68·33% C, 7·65% H, 8·85% N; found: 68·26% C, 7·71 H, 8·80% N. UV spectrum: 291 (3·58), 283 (3·67), 275 inflex. (3·63), 223 (4·53). IR spectrum in $CHCl_3$: 3 500 (NH free), 3 360 (NH assoc.), 1 738 (ester), 1 655 (amide I — CO), 1 525 cm^{-1} (amide II — NH). ^1H NMR spectrum in $CDCl_3$: 8·60 (1 H, bs; indole NH); 6·00 (1 H, bt, J = 5·0 Hz; CO—NH—CH_2); 3·58 (3 H, s; $COOCH_3$); 2·95 (2 H, t, J = 7·0 Hz; CO—NH—CH_2—CH_2—C); 2·82, 2·30 (2 H, ABq, J = = 16·0 Hz; C—CH_2—$COOCH_3$); 1·52 (2 H, m; CH_3—CH_2—C); 1·13 (3 H, s; CH_3—C); 0·78 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 316 (M^+, $C_{18}H_{24}N_2O_3$).

4,4-Dialkyl-1,2,4,5-tetrahydro-6*H*-cathin-6-ones (*VIII*)

A stirred mixture of the tryptamide *VII* (1·5 mmol), phosphorus oxychloride (7 ml) and polyphosphoric acid (19 g, 83% w/w of phosphorus pentoxide) was heated to 110–120°C for 1·25 h.

After concentration *in vacuo*, 15% ammonium hydroxide was added to the mixture under cooling and stirring until it was brought to pH 12. The chloroform extracts (50 and 2 × 25 ml) were washed with water (2 × 20 ml) and brine (30 ml), dried with magnesium sulphate and concentrated *in vacuo* to an oil, which was purified by filtration through small column of silica gel (benzene–chloroform). The concentrated eluate after two runs of preparative TLC gave the base *VIII* (a glass-like substance, uniform in TLC).

4-*Ethyl*-4-*propyl*-1,2,4,5-*tetrahydro*-6*H*-*canthin*-6-*one* (VIIIa) was obtained from the tryptamide *VIIa* in a yield of 40·1%. UV spectrum: 318 (4·05), 231 (4·18). IR spectrum in CCl_4: 1 708 (lactam), 1 628 and 1 582 cm^{-1} (arom. vibration and C=N). ^1H NMR spectrum in $CDCl_3$: 8·35 (1 H, m; —N—C—$C_{(8)}$H=CH—CH=); 4·03 (2 H, t, J = 8·5 Hz; =N—CH_2—CH_2—); 2·87 (2 H, s; =N—CO—CH_2—C); 2·84 (2 H, t, J = 8·5 Hz; =N—CH_2—CH_2—); 0·88 (2 × 3 H, def. t and t, J = 7·0 Hz; $CH_3CH_2CH_2$— and CH_3CH_2—). Mass spectrum: m/z 294 (M^+, $C_{19}H_{22}N_2O$).

4-*Ethyl*-4-*methyl*-1,2,4,5-*tetrahydro*-6*H*-*canthin*-6-*one* (VIIIb) was prepared from the tryptamide *VIIb* in yield of 43·6%. UV spectrum: 318 (4·11), 230 (4·16). IR spectrum in CCl_4: 1 708 (lactam), 1 586 cm^{-1} (arom. vibration). ^1H NMR spectrum in $CDCl_3$: 8·36 (1 H, mcd; —$C_{(8)}$H—=CH—CH=); 4·00 (2 H, m; =N—CH_2—CH_2—); 2·87 (2 H, s; —N—CO—CH_2—C); 2·85 (2 H, m; =N—CH_2—CH_2—); 1·31 (3 H, s; CH_3—C); 0·90 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 266 (M^+, $C_{17}H_{18}N_2O$).

4,4-Dialkyl-4,5-dihydro-6*H*-canthin-6-ones (*III*)

a) A mixture of tetrahydrocanthinone *VIII* (0·20 mmol) and pulverized selenium (600 mg) in a dosed evacuated pipe was rapidly heated to 330°C and kept at this temperature for 9 min. After cooling it was repeatedly digested with a mixture chloroform–methanol (3 : 1). The residue of the combined organic layers was subjected to preparative TLC, giving the base *III* (a glass-like substance, uniform in TLC).

b) The crude cyclization product of the tryptamide *VII* was dehydrogenated as described under *a*). The base was isolated by filtration through a small column of silica gel, followed by two runs of TLC.

4-*Ethyl*-4-*propyl*-4,5-*dihydro*-6*H*-*canthin*-6-*one* (IIIa) was obtained from the tetrahydrocanthinone *VIIIa*; yields: 80·6% by procedure *a*) and 34·1% by procedure *b*). Except for optical rotation, the product was identical with that obtained from vincamone (*X*).

4-*Ethyl*-4-*methyl*-4,5-*dihydro*-6*H*-*canthin*-6-*one* (IIIb) was prepared from the compound *VIIIb*. Yields: 71·4% by *a*) and 32·7% by *b*). UV spectrum: 328 (3·88), 317 (3·82), 284 (4·15), 274 (4·07), 265 (4·13), 231 inflex. (4·51), 224 (4·54). IR spectrum in CCl_4: 1 708 (lactam), 1 628 and 1 580 cm^{-1} (aromatic vibrations). ^1H NMR spectrum in $CDCl_3$: 8·59 (1 H, d, J = 5·0 Hz; C=N—$C_{(2)}$.H=CH—); 8·50 (1 H, mcd, J = 8·0 Hz; C—$C_{(8)}$H=CH—CH=); 7·70 (1 H, d, J = 5·0; C=N—CH=$C_{(1)}$H—C); 3·15 and 2·90 (2 H, ABq, J = 16·5 Hz; —CO—CH_2—C); 1·63 (3 H, s; CH_3—C); 0·86 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 264 (M^+, $C_{17}H_{16}$.N_2O).

Picrate: m.p. 213—216°C (ethanol). For $C_{23}H_{19}N_5O_8$ (493·4) calculated: 55·98% C, 3·88% H, 14·19% N; found: 55·89% C, 3·95% H, 14·27% N.

(—)-(4*S*)-4-Ethyl-4-propyl-4,5-dihydro-6*H*-canthin-6-one ((—)-*IIIa*)

(—)-(20*S*,21*S*)-Eburnan-16-one (vincamone, *X*) was prepared from 360 mg (1·06 mmol) of vincaminic acid[12], either as described in ref.[13] yield 67·3%, m.p. 170·5—172°C (ethanol), [α] —90·1°

(*c* 0·55 in chloroform), or according to ref.[14] (yield 53·6%, m.p. 169·5—171·5°C (methanol).

A pulverized mixture of vincamone (*X*, 245 mg, 0·83 mmol) and selenium (950 mg) was heated in a sealed and evacuated Carius tube to 360°C for 7 min and allowed to cool down. The contents were extracted with a mixture of dichloromethane and methanol (2 : 1) and the combined organic layers were distilled to remove the volatile components; the remaining oil was filtered through a small column of silica gel (chloroform) and purified by preparative TLC; yield 159·5 mg (65·6%) of an oil, uniform in TLC. The compound was further purified by crystallization of its picrate from ethanol, m.p. 194—196°C. The salt was decomposed on a column of neutral aluminium oxide; the chloroform eluate left after evaporation 138·5 mg of the oily base *IIIa* [α] —31·4° (*c* 2·9 in chloroform); reported[1] $[\alpha]_D$ +32° (chloroform) for the enantiomer. UV spectrum (max.) 329 (3·87), 317 (3·81), 285 (4·16), 274 (4·07), 265 (4·13), 230 (4·51), 224 (4·55); (min): 322 (3·77), 293 (3·21), 280 (3·93), 272 (4·05), 244 (3·84). IR spectrum in CCl_4: 1 708 (lactam), 1 625 and 1 580 cm^{-1} (aromatic vibration). ^1H NMR spectrum in $CDCl_3$: 8·60 (1 H, d, J = = 5·0 Hz; C=N—$C_{(2)}$H=CH—); 8·50 (1 H, mcd, J = 8·0 Hz; C—$C_{(8)}$H=CH—CH=); 8·02 (1 H, mcd, J = 8·0 Hz; C—CH=CH—CH=$C_{(11)}$H—C);7·70 (1 H, d, J = 5·0 Hz; C=N— —CH=$C_{(1)}$H—C); 3·02 (2 H, s; —CO—CH_2—C); 0·85 (6 H, t, J = 7·0 Hz; $CH_3CH_2CH_2$— and CH_3CH_2—). Mass spectrum: m/z 292 (M^+, $C_{19}H_{20}N_2O$), 263, 250, 235, 221, 219, 206, 193, 140, 103.

Dimethyl 2-allyl-2-ethylbutanedioate (*XIIIc*)

2-Allyl-2-ethyl-3-methoxycarbonylpropanoic acid (*Vc*, 14·0 g, 70 mmol) was refluxed with 3% hydrogen chloride in methanol (70 ml) for 5 h. After repeated evaporation with benzene the residue was dissolved in ether (70 ml) and an ethereal solution of diazomethane was added dropwise at room temperature until the mixture turned yellow. After 1-h standing the solvent was evaporated and the residue was distilled over a 15 cm long Vigreaux column; the collected fraction was a liquid boiling at 116—116·5°C/1·3 kPa (97% purity by GLC). Yield 13·8 g (92·3%). IR spectrum in CCl_4: 2 880 (OCH_3), 1 730 (ester), 1 640 cm^{-1} (C=C). ^1H NMR spectrum in $CDCl_3$: 5·00 (1 H, d, J = 10·0 Hz; *cis*-H—CH=CH—CH_2—); 4·97 (1 H, d with str., J = 15·0 Hz; *trans*-H—CH=CH—CH_2—); 3·65, 3·60 (2 × 3 H, s; $COOCH_3$); 2·70, 2·46 (2 × 1 H, d, ABq, J = 15·0 Hz; —CH_2—COO—); 2·42 (2 H, bd, J = 7·0 Hz; CH_2=CH—CH_2—); 1·65 (2 H, q, J = 7·0 Hz; CH_3—CH_2—C); 0·82 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 214 (M^+, $C_{11}H_{18}O_4$).

Dimethyl 2-ethyl-propylbutanedioate (*XIIIa*)

A solution of 6·60 g (30·8 mmol) of dimethyl 2-allyl-2-ethylbutanedioate (*XIIIc*) in 70 ml of methanol was stirred with 150 mg of the Adams catalyst in a hydrogen atmosphere at room temperature until the absorption of hydrogen had ceased (70 min, 104%). After filtration and evaporation, distillation *in vacuo* over a Vigreaux column, 15 cm long, gave 5·76 g (86·0%) of a liquid boiling at 103—105·5°C/1·1 kPa; purity by GLC 98%. IR spectrum in CCl_4: 2 880 (OCH_3), 1 721 cm^{-1} (ester). ^1H NMR spectrum in $CDCl_3$: 3·75 and 3·65 (2 × 3 H, s; $COOCH_3$); 2·63 (2 H, s; C— —CH_2—COO—); 1·72 (2 H, q, J = 7·0 Hz; CH_3—CH_2—C); 0·91 (3 H, def. t; CH_3—CH_2 —CH_2—); 0·82 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 216 (M^+, $C_{11}H_{20}$ .O_4), 201, 185, 174, 156, 143.

Dimethyl 2-ethyl-2-methylbutanedioate (*XIIIb*)

To a stirred solution of the ester-acid *Vb* (2·40 g, 13·8 mmol) in ether (30 ml) was added dropwise an ethereal solution of diazomethane until the yellow colouration remained permanent. The mix-

ture was left standing for 3 h, then the ether was removed *in vacuo*. Distillation of the residue gave 2·43 g (93·7%) of a liquid boiling at 89·5–90·0°C/1·2 kPa, purity by GLC 98%. Reported[8] b.p. 72°C/400 Pa. IR spectrum in $CHCl_3$: 1 729 cm^{-1} (ester). ^1H NMR spectrum in $CDCl_3$: 3·78 and 3·68 (2 × 3 H, s; $COOCH_3$); 2·83 and 2·39 (2 H, ABq, $J = 16·0$ Hz; C—CH_2—COO—); 1·27 (3 H, s; C—CH_3); 0·87 (3 H, t, $J = 7·5$ Hz; CH_3—CH_2—C). Mass spectrum: *m/z* 188 (M^+, $C_9H_{16}O_4$).

Ester-Acids *XIV*

A mixture of 10·0 mmol of a dister *XIII* and 12·0 mmol of potassium hydroxide in 20 ml of ethanol and 3 ml of water was heated to 50°C with an occasional stirring for 15 h. After cooling, 25 ml of water was added and the methanol was evaporated. The residue was extracted with 15 ml of ether. The aqueous phase was brought to pH 4 with 10% hydrochloric acid under cooling and extracted with ether. The combined ethereal extracts (30 and 2 × 15 ml) were washed with water (2 × 15 ml) and brine (15 ml), and dried with anhydrous magnesium sulphate. Distillation *in vacuo* left the product *XIV* as an oil (purity by GLC 96–97%).

3-*Ethyl*-3-*methoxycarbonylhexanoic acid* (XIVa) was obtained from the diester *XIIIa* in a yield of 93·8%. IR spectrum in $CHCl_3$: 2 880 (OCH_3), 2 660 (COOH), 1 721 and 1 710 cm^{-1} (C=O). ^1H NMR spectrum in $CDCl_3$: 9·90 (1 H, bs; COOH); 3·68 (3 H, s; $COOCH_3$); 2·65 (2 H, s; C—CH_2—COO—); 1·72 (2 H, q, $J = 7·0$ Hz; CH_3CH_2—C); 0·90 (3 H, def. t; CH_3—CH_2—CH_2—); 0·80 (3 H, t, $J = 7·0$ Hz; CH_3—CH_2—C). Mass spectrum: *m/z* 203 (M^+, $C_{10}H_{18}O_4$), 174, 171, 160, 156.

3-*Methoxycarbonyl*-3-*methylpentanoic acid* (XIVb) was obtained from the diester *XIIIb* in a yield of 86·4%. IR spectrum in $CHCl_3$: 2 885 (OCH_3), 2 665 (COOH), 1 726 and 1 709 cm^{-1} (C=O). ^1H NMR spectrum in $CDCl_3$: 10·00 (1 H, bs; COOH); 3·71 (3 H, s; $COOCH_3$); 2·89 and 2·41 (2 × 1 H, d, ABq, $J = 16·0$ Hz; —CH_2—COO—); 1·30 (3 H, s; CH_3—C); 0·89 (3 H, t, $J = 7·5$ Hz; CH_3—CH_2—C). Mass spectrum: *m/z* 174 (M^+, $C_8H_{14}O_4$).

Tryptamide-Esters *XVI*

To 8·5 mmol of an ester-acid *XIV* in 19 ml of benzene, kept at 10°C, was added 0·87 ml (10 mmol) of oxalyl chloride and the mixture was allowed to warm up to room temperature. After the reaction had died down, the temperature was elevated to 45°C, where it was kept for 30 min. After repeated evaporation with benzene *in vacuo* there was obtained a quantitative yield of the ester-chloride *XV* (a liquid, purity by GLC 95–96%). The ester-chloride *XV* thus obtained was dissolved in 5 ml of chloroform and added dropwise under stirring and cooling in the course of 45 min to a mixture of tryptamine (1·44 g, 9·0 mmol), potassium carbonate (1·98 g, 14·3 mmol), chloroform (45 ml) and water (28·5 ml). The stirred mixture was allowed to equilibrate with room temperature, 15 ml of chloroform and 3 ml of 40% potassium hydroxide were added, the chloroform layer was separated and the aqueous layer was extracted with 15 ml of chloroform. The combined organic portions were washed with 10 ml of water, 2 × 25 ml of 6% hydrochloric acid, 2 × 20 ml of water and brine, and dried with anhydrous magnesium sulphate. After evaporation *in vacuo* the tryptamide-ester *XVI* was obtained (a chromatographically uniform product).

Chloride of 3-*ethyl*-3-*methoxycarbonylhexanoic acid* (XVa) was prepared from the ester-acid *XIVa*. ^1H NMR spectrum in $CDCl_3$: 3·71 (3 H, s; $COOCH_3$); 3·28 (2 H, s; C—CH_2—COCl); 1·80 (2 H, q, $J = 7·0$ Hz; CH_3—CH_2—C); 0·95 (3 H, def. t; CH_3—CH_2—CH_2—); 0·88 (3 H, t, $J = 7·0$ Hz; CH_3—CH_2—C).

N-[2-(*Indol*-3-*yl*)*ethyl*]-3-*ethyl*-3-*methoxycarbonylhexaneamide* (XVIa) was prepared from the ester-acid *XIVa* in yield of 67·3%; m.p. 113—115·5°C (chloroform–ether–hexane). For $C_{20}H_{28}N_2O_3$ (344·4) calculated: 69·74% C, 8·19% H, 8·13% N; found: 69·85% C, 8·23% H, 8·04% N. UV spectrum: 291 (3·68), 283 (3·75), 275 (3·73), 223 (4·52). IR spectrum in Nujol: 3 470 (free NH), 3 400 (assoc. NH), 1 721 (ester), 1 660 cm^{-1} (amide), ^1H NMR spectrum in $CDCl_3$: 8·70 (1 H, bs; indole NH); 5·95 (1 H, bt; —CO—NH—CH_2—); 3·58 (3 H, s; $COOCH_3$); 3·55 (2 H, m; —CO—NH—CH_2—CH_2—); 2·88 (2 H, t, J = 7·0 Hz; —CO—NH—CH_2—CH_2—); 2·35 (2 H, s; —NH—CO—CH_2—C); 0·82 (3 H, def. t; CH_3—CH_2—CH_2—); 0·72 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 344 (M^+, $C_{20}H_{28}N_2O_3$), 313, 172, 158.

N-[2-(*Indol*-3-*yl*)*ethyl*]-3-*methoxycarbonyl*-3-*methlpyentaneamide* (XVIb) was a glass-like substance obtained from the ester-acid *XIVb* in a yield of 65·4% UV spectrum: 292 (4·66), 284 (3·75), 275 (3·73), 224 (4·53). IR spectrum in $CHCl_3$: 3 500 (free NH), 3 400 (assoc. NH), 1 730 (ester), 1 670 (amide I — CO), 1 525 cm^{-1} (amide II — NH). ^1H NMR spectrum in $CDCl_3$: 8·60 (1 H, bs; indole NH); 6·95 (1 H, d, J = 2·0 Hz; C—NH—CH=C); 5·89 (1 H, bt; —CO—NH—CH_2—); 3·60 (3 H, s; $COOCH_3$); 2·88 (2 H, t, J = 6·5 Hz; —CO—NH—CH_2—); 2·62 and 2·04 (2 × 1 H, d, ABq, J = 14·0 Hz; —CO—CH_2—C); 1·52 (2 H, m; CH_3—CH_2—C); 1·18 (3 H, s; CH_3—C); 0·78 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C). Mass spectrum: m/z 316 (M^+, $C_{18}H_{24}N_2O_3$), 285, 144, 130.

Canthin-4,6-diones *XVII*

A stirred mixture of a tryptamide-ester *XVI* (1·2 mmol), polyphosphoric acid (8·5 g, 83% w/w of phosphorus pentoxide) and phosphorus oxychloride (10·8 g) was heated to 110°C under nitrogen for 1·5 h. The excess of phosphorus oxychloride was distilled off *in vacuo*, the mixture was cooled and decomposed under stirring and cooling by the addition of water (40 ml) and concentrated ammonia to pH 12. The chloroform extracts (50 and 2 × 20 ml) were washed with water (2 × 25 ml) and brine (2 × 25 ml), dried with anhydrous magnesium sulphate and distilled *in vacuo*. The residue was filtered through a column of silica gel (benzene–chloroform 1 — 0 : 1) and subjected to two runs of preparative TLC, giving the corresponding base *XVII* (uniform in TLC).

5-*Ethyl*-5-*propyl*-4,5-*dihydro*-6*H*-*canthin*-4,6-*dione* XVIIa was obtained from the tryptamide-ester *XVIa* as a glass-like substance in a yield of 33·1%. UV spectrum: 353 (3·60), 305 (3·88), 268 (3·98), 230 (4·44). IR spectrum in CCl_4: 1 710 (lactam), 1 690 (ketone), 1 650 sh (C=N), 1 630 and 1 608 cm^{-1} (aromatic vibration). ^1H NMR spectrum in $CDCl_3$: 8·85 (1 H, d, J = 5·0 Hz; C=N—$C_{(2)}$H=CH—); 8·65 (1 H, mcd, J = 8·5 Hz; —CO—N—C—$C_{(8)}$H=CH—); 8·14 (1 H, mcd, J = 8·5 Hz; C—$C_{(8)}$H=CH—CH=$C_{(11)}$H—C); 8·06 (1 H, d, J = 5·0 Hz; =N—CH=$C_{(1)}$H—); 0·79 (3 H, t, J = 7·0 Hz; CH_3—$(CH_2)_n$—); 0·77 (3 H, t, J = 6·0 Hz; CH_3—$(CH_2)_n$—). Mass spectrum: m/z 306 (M^+, $C_{19}H_{18}N_2O_2$), 292, 277, 263, 249, 235, 222, 210, 198, 182, 166, 139, 114, 84.

5-*Ethyl*-5-*methyl*-4,5-*dihydro*-6*H*-*canthin*-4,6-*dione* (XVIIb) was prepared from the tryptamide-ester *XVIb* in a yield of 32·4%; m.p. 88—91°C (benzene–light petroleum). For $C_{17}H_{14}N_2O_2$ (278·3) (calculated: 73·36% C, 5·07% H, 10·07% N; found: 73·19% C, 5·12% H, 10·16% N. UV spectrum: 351 (3·61), 305 (3·88), 269 (3·99), 231 (4·43). IR spectrum in $CHCl_3$: 1 721(lactam), 1 695 (ketone), 1 640 and 1 630 cm^{-1} (C=N and arom. vibration). ^1H NMR spectrum in $CDCl_3$: 8·85 (1 H, d, J = 5·0 Hz; C=N—$C_{(2)}$H=CH—); 8·60 (1 H, mcd, J = 8·0 Hz; —CO—N—C—$C_{(8)}$H=CH—); 8·13 (1 H, mcd, J = 8·0 Hz; C—$C_{(8)}$H=CH—CH=$C_{(11)}$H—C); 8·05 (1 H, d, J = 5·0 Hz; =N—CH=$C_{(1)}$H—); 2·21 (2 H, q, J = 7·5 Hz; CH_3—CH_2—C); 1·65 (3 H, s; CH_3—C); 0·84 (3 H, t, J = 7·5 Hz; CH_3—CH_2—C). Mass spectrum: m/z 278 (M^+, $C_{17}H_{14}N_2O_2$).

5,5-Dialkyl-4,5-dihydro-6*H*-canthin-6-ones *XVIII*

A mixture of selenium (0·90 g) and the crude (not chromatographically purified) product obtained from 1·1 mmol of a tryptamide-ester *XVI* by the procedure described for the preparation of canthin-4,6-diones *XVII* was heated *in vacuo* of a water pump to 330°C, kept at this temperature for 12 min, allowed to cool down, and extracted with a mixture of dichloromethane and methanol (1 : 1). The combined organic portions were distilled and the residue was purified by filtration through a column of silica gel (benzene–chloroform 1 : 1). After two runs of preparative TLC the base *XVIII* was a chromarographically uniform product.

5-*Ethyl*-5-*propyl*-4,5-*dihydro*-6*H*-*canthin*-6-*one* (XVIIIa) was obtained from the tryptamide-ester *XVIa* as a glass-like substance in a yield of 33·2%. UV spectrum: 330 (3·96), 3·17 (3·89), 284 (4·18), 274 (4·12), 264 (4·19), 230 inflexion (4·56), 224 (4·59). IR spectrum in CCl_4: 1 710 (lactam), 1 655 (C=N), 1 636 cm^{-1} (arom. vibration) .^{1}H NMR spectrum in $CDCl_3$: 8·60 (1 H, mcd, J = 8·0 Hz; —CO—N—C—$C_{(8)}$**H**=CH—); 8·50 (1 H, d, J = 5·0 Hz; C=N—$C_{(2)}$**H**=CH—); 8·05 (1 H, mcd, J = 8·0 Hz; C—$C_{(8)}$**H**=CH—CH=$C_{(11)}$**H**—C); 7·70 (1 H, d, J = 5·0 Hz; =N—CH=$C_{(1)}$**H**—); 3·39 (2 H, s; N—CO—C—$C_{(4)}$**H**$_2$—C); 0·99 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C); 0·80 (3 H, def. t; CH_3—CH_2—CH_2—C). Mass spectrum: m/z 292 (M^+, $C_{19}H_{20}N_2O$), 263, 250, 235, 221, 219, 206, 182, 85, 83, 58, 43, 28.

Picrate: m.p. 203—205° (ethanol). For $C_{25}H_{23}N_5O_8$ (521·5) calculated: 57·58% C, 4·45% H, 13·43% N; found: 57·51% C, 4·51% H, 13·51% N.

5-*Ethyl*-5-*methyl*-4,5-*dihydro*-6H-*canthin*-6-*one* (XVIIIb) was obtained in a yield of 30·7% from the tryptamide–ester *XVIb*; m.p. 101·5—104°C (benzene). For $C_{17}H_{16}N_2O$ (264·3) calculated: 77·25% C, 6·10% H, 10·60% N; found: 77·41% C, 6·02% H, 10·48% N. UV spectrum: 328 (3·76), 316 (3·91), 283 (4·17), 273 (4·12), 265 (4·19), 230 4·56), 224 (4·58). IR spectrum in $CHCl_3$: 1 700 (lactam), 1 635 and 1 580 cm^{-1} (C=N), and arom. vibration). ^{1}H NMR spectrum in $CDCl_3$: 8·50 (2 H, m; —CO—N—C—$C_{(8)}$**H**=CH— and C=N—$C_{(2)}$**H**=CH—); 8·00 (1 H, mcd, J = 8·0 Hz; C—$C_{(8)}$H=CH—CH=C$_{(11)}$H—C); 7·68 (1 H, d, J = 5·5 Hz; =N—CH=$C_{(1)}$**H**—); 3·48 and 3·18 (2 × 1 H, d, ABq, J = 17·0 Hz; N—CO—C—$C_{(4)}$**H**$_2$—C); 1·72 (2 H, m; CH_3—CH_2—C); 1·42 (3 H, s; CH_3—C); 0·94 (3 H, t, J = 7·5 Hz; CH_3—CH_2—C). Mass spectrum m/z 264 (M^+, $C_{17}H_{16}N_2O_2$).

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