SYNTHESIS OF 2-[N-(2-METHYLPROPANOYL]-N-PHENYLETHYLGLUTARIMIDE

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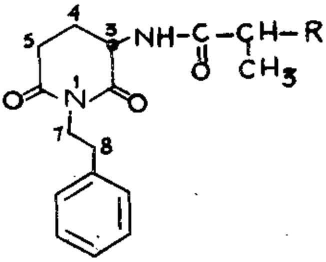
The structure of the glutarimide peptide (I) isolated from Croton humilis has been confirmed by synthesis.

Recently we reported the isolation of a 1:1 mixture of $C_{17}H_{22}N_2O_3$ and $C_{18}H_{24}N_2O_3$ compounds from Croton humilis, and on the basis of spectral and degradative studies proposed the structures (I) and (II) respectively.[1]



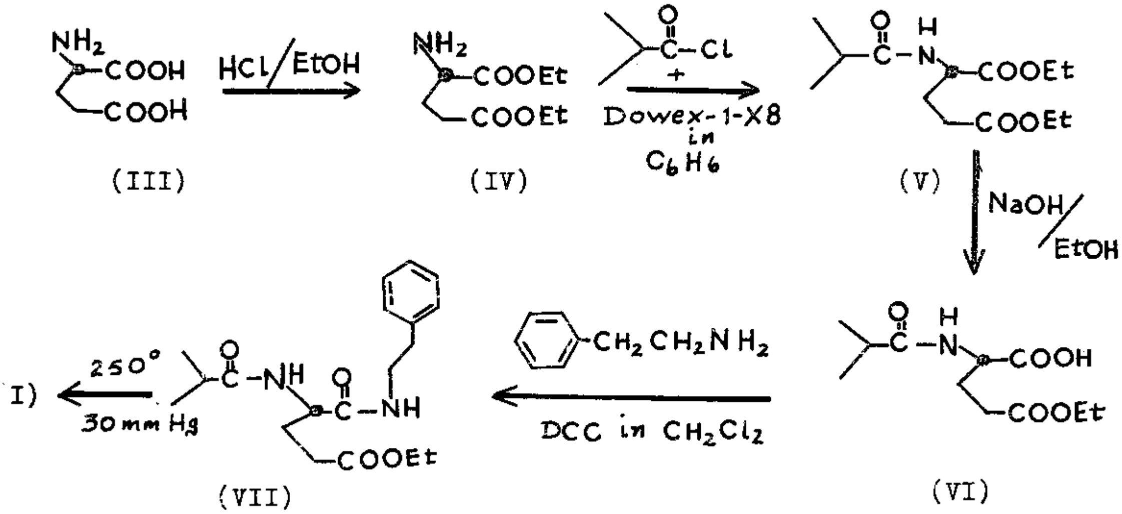
[(I), R = CH_3; (II), R = CH_2CH_3].

We have now been successful in separating these compounds. The $C_{17}H_{22}N_2O_3$ glutarimide had m.p. 148-155°, $[\alpha]_D + 11°$, ($CHCl_3$), λ_{max}^{EtOH} 210 nm (ϵ 17,560), $\nu_{max}(CHCl_3)$ 3390 (amide), 2899, 1724 (glutarimide), 1681, 1493, 1339, 1156, 1148 $cm.^{-1}$. ORD (c, 0.48 in MeOH): $[\alpha]_{589} + 16.8°$, $[\alpha]_{500} + 16.4°$, $[\alpha]_{400} + 16.0°$, $[\alpha]_{350} + 12.5°$

$[\alpha]_{300}$ + 10°, $[\alpha]_{250}$ + 3.0°. The NMR (60 M Hz in $CDCl_3$) showed signals at δ 7.27, (s, 5H; aromatic), 6.37 (bs, 1H; NH), 4.45 (m, 1H; C-3), 4.05 (m, 2H; C-7), 2.62 to 2.97 (m, 2H; C-8), 2.75 to 1.4 (5H; C-4, C-5 and isopropyl-C$\underline{H}$), 1.15 (d, 6H, J = 7.5 Hz; isopropyl methyl groups); M^+ 302.162 (9%): Calculated for $C_{17}H_{22}N_2O_3$, 302.163.

The $C_{18}H_{24}N_2O_3$ homolog, had m.p. 121-122°, $[\alpha]_D$ + 7.3° ($CHCl_3$), λ^{EtOH}_{max} 210 nm (ε 18,540), ν_{max}($CHCl_3$), 3390, 2899, 1724, 1681, 1493, 1342, 1156, 1148 cm^{-1}; M^+ 316.180 (66%), $C_{18}H_{24}N_2O_3$ requires 316.179.

We have been able to make configurational assignments on the basis of acid degradation and ORD measurements.[2] Structural confirmation is now reported by way of the synthesis of (I), which was identical in all respects with the natural product. (m.p., $[\alpha]_D$, t.l.c., IR). By starting with L-(+)-glutamic acid (III), the synthesis was achieved in an overall yield of 2.5% and is shown schematically below.[3]



There is only one other case reported of the presence of a glutarimide from a plant source.[4] This compound, julocrotine, $C_{18}H_{24}N_2O_3$, is diasterioisomeric with (II), and occurs in *Julocroton montevidensis* Klotzsch.

Acknowledgement

We wish to thank Professor J.P. Kutney and Mr. G. Eigendorf, University of British Columbia, Canada, for determining the mass spectra of compounds (I), (II) and (VII).

REFERENCES

1. J.P. Kutney, F.K. Klein, G. Eigendorf, D. McNeill and K.L. Stuart, *Tetrahedron Letters*, 1971, 4973; ibid 1972, 250.

2. K.L. Stuart, D. McNeill, J.P. Kutney, F.K. Klein and G. Eigendorf, *Tetrahedron*, submitted.

3. Satisfactory analytical data were obtained for key compounds reported.

4. T. Nakano, C. Djerassi, R.A. Corral and O.O. Orazi, *J.Org.Chem.*, 1961, 26, 1184.

Received, 14th July, 1973