*Tetrahedron* Vol 39, No. 22, pp 3749 to 3753, 1983
Printed in Great Britain

0040-4020/83 $3.00 + .00
Pergamon Press Ltd

# SYNTHESIS OF VINCA ALKALOIDS AND RELATED COMPOUNDS—XVII[1]

## CHIRAL SYNTHESIS OF VINCA ALKALOIDS FROM L-TRYPTOPHAN

LAJOS SZABÓ, JÁNOS SÁPI, KATALIN NÓGRÁDI, GYÖRGY KALAUS and CSABA SZÁNTAY*
Department of Organic Chemistry, Technical University, Budapest Gellért-tér 4. H-1521, Budapest, Hungary

and

Central Research Institute for Chemistry, Hungarian Academy of Sciences Budapest, Pusztaszeri ut 59–67. H-1525, Budapest, Hungary

(*Received in USA 7 January* 1983)

**Abstract**—Starting from L-tryptophan two chiral syntheses of the 3*S*, 17*S*-lactam **11**, an intermediate for the preparation of (+)-vincamine and its derivatives, were elaborated in good overall yield and with an optical purity of 96%.

We have recently published the asymmetric synthesis of the tetracyclic ester **1b**, in which an optically active starting material, L-tryptophan isopropyl ester was used.[2] In the asymmetric syntheses to be described in the present paper, in order to facilitate hydrolysis, the methyl ester **1a** was used, which was prepared by analogy with **1b**,[2] as follows. L-Tryptophan methyl ester[3a,b] was acylated with 2-ethyl-5-chlorovaleryl chloride in pyridine under mild conditions, and the optically active amide formed in 78% yield was cyclized with phosphoryl chloride to the corresponding $\beta$-carboline. As the free base, the latter underwent spontaneous cyclization on standing at room temp in $CH_2Cl_2$, to yield the tetracyclic iminium salt **1a**. The product showed high specific rotation[4a,b] and was isolated as the perchlorate **1a**.

Note that it is only after removal of the chiral center derived from L-tryptophan that the efficiency of the asymmetric induction can conveniently be determined. Therefore we measured only specific rotation values of the intermediates, including iminium salts, up to that point.

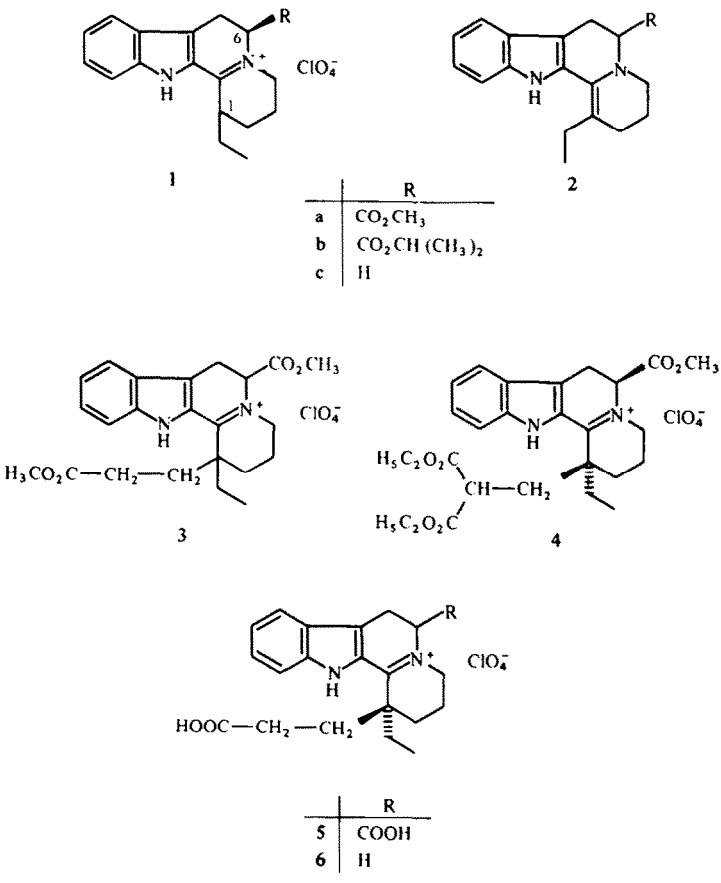
In our previous investigations we found that the enamine **2b**, derived from the iminium salt **1b** with base (e.g. aq NaOH), underwent complete racemization and gave therefore with methyl 2-acetoxyacrylate a racemic C-1 alkylated compound.[2] Similarly, when the iminium salt **1a** was reacted with methyl acrylate in the presence of 0.9 eq of $Et_3N$, the adduct (**3**) was again racemic. Racemization is triggered by the generation of a stable C-6 carbanion adjacent to the ester group, while enamine formation requires a C-1 carbanion, which is only conceivable in a kinetically controlled reaction. Since the latter species should be captured without much delay it is necessary to select more electrophilic olefins than those mentioned above. A kinetically controlled reaction may be favoured by a strong and bulky base (e.g. KOBu$^t$), used in catalytic quantities. Under such conditions, methyl acrylate does not react with the iminium perchlorates **1**, while the more reactive diethyl methylenemalonate or acrolein do.

*Reaction of the iminium salt* **1a** *with diethyl methylenemalonate*

When the iminium perchlorate **1c** was reacted with highly electrophilic olefins in the presence of a catalytic amount of KOBu$^t$, the C-1 alkylated adducts were isolated in good yield.[1,5] Accordingly, the optically active iminium perchlorate **1a** could be alkylated with diethyl methylenemalonate in the presence of a catalytic amount of KOBu$^t$ for 0.5–1 hr, and gave the perchlorate of the optically active adduct **4** in 96% yield. The adduct was used in the next step without purification.

The crucial point in asymmetric syntheses starting from L-tryptophan esters is the elimination of the derived chiral center after its temporary utilization. In recent years several new methods have been suggested for the removal of ester groups originating from the optically active starting materials.[6a–d] Since in our case we had several ester groups in the molecule none of these methods seemed to be practical, and this led to the development of a very simple and efficient method of decarboxylation.

First the crude iminium perchlorate **4** was hydrolysed with 10% aq HCl and then by alkali. This was accompanied with the loss of $CO_2$ and gave, in 92% yield, the dicarboxylic acid **5** as the iminium salt, showing considerable optical activity. Hydrolysis and decarboxylation in a two-step procedure was required because the ester group at C-6 failed to be hydrolysed by acid, whereas in alkali **4** suffered deep-seated transformations.




| | R |
|---|---|
| a | $CO_2CH_3$ |
| b | $CO_2CH(CH_3)_2$ |
| c | H |

| | R |
|---|---|
| 5 | COOH |
| 6 | H |

Scheme 1.

It could be anticipated that a positive charge such as that located at the N adjacent to C-6, would facilitate decarboxylation. In fact, on heating the salt **5** to 160–170° in decalin, vigorous evolution of $CO_2$ was observed and after 30 min the monocarboxylic acid **6** was obtained in almost quantitative yield. Specific rotation of the product ($[\alpha]_D^{25} = -19°$, $[\alpha]_{546}^{25} = -20°$) indicated considerable excess of one of the enantiomers of **6** (containing a single center of chirality). Determination of the chirality of the predominant enantiomer and its enantiomeric purity required, however, transformation of **6** to a compound of known absolute configuration.

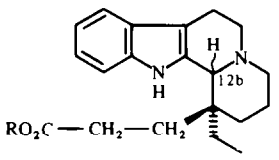
Hydrogenation of **6** in DMF over 10% Pd/C, evaporation, and treatment of the mixture of saturated epimeric acids **7** and **8** by phosphoryl chloride at room temp gave by intramolecular acylation[7] the *cis*-**11** and *trans*-lactams **12** in 40 and 14% yield respectively (after separation by layer chromatography). Specific rotation of the *cis*-lactam **11** being relatively low and highly solvent and temperature dependent, it was transformed with KOMe/MeOH into the methyl ester **9**, which proved to be of 96% optical purity ($[\alpha]_D^{22} = -116°$, lit.[7]: $[\alpha]_D^{20} = -121°$). Its sign of rotation proved unambigously that the configuration of the lactam **11** was (3*S*, 17*S*). This compound can be converted by known procedures to (+)-vincamine and (+)-apovincaminic acid esters.[7]

*Reaction of the iminium salt* **1a** *with acrolein*

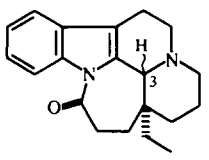
Reaction of the optically active iminium salt **1a** with highly reactive acrolein was also studied. In a synthesis of homoeburnamine, the iminium salt **1c** was reacted with acrolein by Buzás *et al.*[5]

To a suspension of **1a** in $CH_2Cl_2$, first acrolein, and then a catalytic amount of KOBu$^t$ was added. Working up the reaction mixture after 2 hr gave the optically active adduct **13** in 88% yield. This was followed by transformation of the carbinolamine to the unsaturated lactam **14** by means of chromium(VI) oxide adsorbed onto silica gel.[8] It is of interest that racemic (±)-**14** (15%) could be separated from the dextrorotatory **14** (56%) ($[\alpha]_{546}^{22} = +204°$) by crystallization.

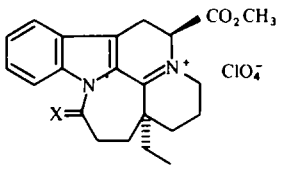
Hydrolysis of the (+)-lactam **14** with aqueous ethanolic NaOH resulted in cleavage of the lactam ring and formation of the unsaturated dicarboxylic acid **5** ($[\alpha]_{546}^{22} = +40°$) in 68% yield. The acid **5** was thermally decarboxylated without purification, as described above, to provide the iminium salt **6** in 96% yield. Specific rotation of the product was 90% as compared with the one described under A.



| | R | 12bH |
|---|---|---|
| 7 | H | α |
| 8 | H | β |
| 9 | $CH_3$ | α |
| 10 | $CH_3$ | β |



| | 3-H |
|---|---|
| 11 | α |
| 12 | β |



| | X |
|---|---|
| 13 | OH, H |
| 14 | O |

Scheme 2.

## CONCLUSIONS

The chiral syntheses reported here demonstrate that the chiral center of L-tryptophan induces the formation of chiral centers in lactam **11**, as required for its transformation to natural Vinca alkaloids.

With respect of the efficiency of the asymmetric syntheses described in this paper, two points have to be emphasized:

(1) Michael reactions with the iminium salt **1a** are highly diastereoselective.

(2) Initiation of the reaction by a sufficiently small amount of the right kind of base enables one to avoid totally or at least to a high degree racemization of the chiral center at C-6 of the iminium salt **1a** prior to alkylation.

It was possible to demonstrate a clear correlation between stereoselectivity and the electrophilic character of the olefin (i.e. the rate of addition). When using the highly electrophilic diethyl methylenemalonate, **1a** is alkylated so rapidly that racemization at C-6 is suppressed. Reaction with the slower reacting, less electrophilic acrolein is in turn preceeded by partial racemization at C-6.

## EXPERIMENTAL

IR spectra were recorded on Spectromom 2000 spectrometer. Mass spectra were taken on an AEI-MS-902 (70 eV, direct insertion) mass spectrometer. M.ps are uncorrected.

(+)-1-(3-*Indolyl*)-2-[(2-*ethyl*-5-*chloropentanoyl*)-*amino*]-2-*methoxycarbonyl ethane*. The hydrochloride of L-tryptophan methyl ester[3] (10.0 g, 39.4 mmol) was dissolved in abs pyridine (75 ml), the soln cooled to 0°, and 2-ethyl-5-chlorovaleryl chloride[2] (8.05 g, 44.0 mmol) was added dropwise. The mixture was allowed to stand at room temp for 4 days. After evaporation to dryness *in vacuo* the residue was triturated with ice-water, 5% $NaHCO_3$ aq with cooling, and with ice-water again. The solid substance was filtered off, washed with water and dried to give the amide (11.22 g, 77.8%), m.p. 97–100°. (Found: C, 62.56; H, 6.99; N, 7.67. Calc for $C_{19}H_{26}N_2O_3Cl$ (365.87): C, 62.37; H, 7.16; N, 7.65). IR(KBr): 3250 (NH), 1720 (ester CO), 1630 $cm^{-1}$ (amide CO). $[\alpha]_D^{20} = +24°$, $[\alpha]_{546}^{20} = +41°$ (*c* 1.00, $CH_2Cl_2$).

(+)-1-*Ethyl*-6β-*methoxycarbonyl*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-*a*]*quinolizine*-5-*iumperchlorate* (**1a**). To a suspension of the above amide (5.00 g, 13.7 mmol) in abs benzene (100 ml), $POCl_3$ (9.75 g, 63.7 mmol) was added, and the mixture heated under reflux for 5 hr. After evaporation to dryness *in vacuo*, the residue was washed with petroleum ether (3 × 10 ml), dissolved in $CH_2Cl_2$ (100 ml), and shaken with 5% $NaHCO_3$ aq at 0° to basify to pH 7.5–8. The separated organic layer was dried ($MgSO_4$), filtered off, and allowed to stand at room temp overnight. After evaporation to dryness under reduced pressure, the residue was dissolved in MeOH (6 ml), acidified with 70% $HClO_4$ aq to pH 3–4 and crystallized to afford iminium perchlorate **1a** (2.80 g, 49.7%), m.p. 219–220° (MeOH). (Found: C, 55.34; H, 5.84; N, 7.08. Calc for $C_{19}H_{23}N_2O_6Cl$ (410.85): C, 55.54; H, 5.64; N, 6.82). IR(KBr): 3200 (indole NH), 1735 (ester CO), 1600 $cm^{-1}$ (C=N). $[\alpha]_D^{22} = +92°$, $[\alpha]_{546}^{22} = +129°$ (*c* 1.00, $CH_2Cl_2$).

From the mother liquor another portion of **1a** (0.5 g, 8.8%) was crystallized possessing slower specific rotation. $[\alpha]_{546}^{22} = +80°$ (*c* 1.00, $CH_2Cl_2$).

(±)-1-*Ethyl*-1-*methoxycarbonyl*-*ethyl*-6-*methoxycarbonyl*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* (**3**). To a soln of **1a** (2.00 g, 4.87 mmol, $[\alpha]_{546}^{22} = +129°$) in $CH_2Cl_2$ (15 ml), methyl acrylate (1.26 g, 14.6 mmol), and $Et_3N$ (0.44 g, 4.38 mmol) were added with stirring. The stirring was continued for 24 hr at room temp. The solvent was evaporated to dryness under reduced pressure, the residue was triturated with ether (2 × 5 ml), and crystallized from MeOH (4 ml) to yield **3** (2.00 g, 82.5%) inactive adduct perchlorate, m.p. 214° (dec). (Found: C, 55.42; H, 5.70; N, 5.78. Calc for $C_{23}H_{29}N_2O_8Cl$ (496.92): C, 55.59; H, 5.88; N, 5.64). IR(KBr): 3320 (indole NH), 1745, 1720 (ester CO), 1618 $cm^{-1}$ (C=N).

*Route A*

(−)-1α-*Ethyl*-1β-(2′,2′-*diethoxycarbonyl*-*ethyl*)-6β-*methoxycarbonyl*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* (**4**). To a soln **1a** (2.00 g, 4.87 mmol, $[\alpha]_{546}^{22} = +129°$) in abs $CH_2Cl_2$ (15 ml), freshly distillated diethyl methylenemalonate (1.16 g, 6.75 mmol) and a suspension of KOBu$^t$ (30 mg, 0.268 mmol) in abs $CH_2Cl_2$ (5 ml) were added with cooling to 0–5°. The mixture was allowed to stand at room temp for 0.5–1 hr. After neutralization with HCl/EtOH the solvent was removed *in vacuo*, the residue was washed with ether (2 × 5 ml) to remove a trace of reagent, and decanted to afford (−)-**4** (2.75 g, 96.5%) as a viscous oil. IR($CHCl_3$): 3420 (indole NH), 1745, 1730 cm$^{-1}$ (ester CO). $[\alpha]_D^{23} = -10°$, $[\alpha]_{546}^{23} = -17°$ (*c* 1.00, $CH_2Cl_2$).

(±)-1α-*Ethyl*-1β-*carboxy*-*ethyl*-6-*carboxy*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* (**5**). To a soln of **4** (1.50 g, 2.57 mmol) in EtOH (10 ml), a soln of 10% HCl aq (15 ml) was added and the mixture heated under reflux for 24 hr. After evaporation to dryness *in vacuo*, the remaining oil was dissolved in EtOH (30 ml), and allowed to stand at room temp with NaOH (0.62 g, 15.45 mmol), dissolved in water (3 ml) for 4–6 hr. The solvent was evaporated under reduced pressure, the residue was dissolved in water (7 ml), and acidified with 70% $HClO_4$ aq to pH 3 with cooling. The ppt was filtered off, washed with water and dried to give **5** (1.10 g, 92%), m.p. 183° (dec). (Found: N, 6.16. Calc for $C_{21}H_{25}N_2O_8Cl$ (468.89): N, 5.98). IR(KBr): 3450–3300 (indole NH, COOH), 1715 (COOH), 1610, 1580 cm$^{-1}$ (C=N). $[\alpha]_D^{23} = +36°$, $[\alpha]_{546}^{23} = +47.5°$ (*c* 0.80, $CH_3OH$).

(−)-1α-*Ethyl*-1β-*carboxy*-*ethyl*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* (**6**). Acid **5** (1.00 g, 2.13 mmol) was heated in decalin (15 ml) at 160–170° for 25–30 min. When the $CO_2$ evolution ceased the mixture was cooled, filtered, and the solid substance washed with ether (3 × 5 ml) to afford (−)-**6** (0.88 g, 97.2%), m.p. 163° (dec). (Found: N, 6.33. Calc for $C_{20}H_{25}N_2O_6Cl$ (424.89): N, 6.59). IR(KBr): 3350 (broad, indole NH, COOH), 1710 (COOH), 1620, 1580 cm$^{-1}$ (C=N). $[\alpha]_D^{25} = -19°$, $[\alpha]_{546}^{25} = -20°$ (*c* 1.00, MeOH).

(+)-(3S, 17S)-14-*Oxo*-E-*homo*-*eburnane* (**11**) *and its* 3-*epimer* (**12**). A soln of **6** (400 mg, 0.943 mmol) in DMF (9 ml) was hydrogenated over 10% Pd/C (200 mg). When the $H_2$ consumption ceased the catalyst was filtered off, washed with DMF (5 × 2 ml) and the solvent was evaporated to dryness *in vacuo* (1–2 torr). The residue was dissolved in $POCl_3$ (3 ml) and allowed to stand at room temp for 2–3 days.

After evaporation to dryness *in vacuo*, the residue was treated with water (5 ml), basified to pH 9 with 25% $NH_4OH$ aq with cooling, and extracted with $CH_2Cl_2$ (3 × 8 ml). The combined organic layers were dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure to afford a mixture of lactams **11** and **12**, which were separated by preparative TLC (silica gel KG-60 $PF_{254+366}$, benzene:MeOH 14:3, elution with $CH_2Cl_2$:MeOH 20:1). The slower running fraction (129 mg, 44%) was crystallized from MeOH (0.5 ml) to afford (+)-**11** (117 mg, 40%), m.p. 154–155° (MeOH). Lit.[7]: m.p. 155–157°. (Found: C, 77.72; H, 7.80; N, 9.18. Calc for $C_{20}H_{24}N_2O$ (308.40): C, 77.88; H, 7.84; N, 9.08). IR(KBr): 1700 cm$^{-1}$ (lactam CO). MS *m/e*, (%): 308 ($M^+$, 100), 307 (53), 280 (14), 279 (14), 252 (22). $[\alpha]_D^{22} = +17°$ (*c* 1.00, $CH_2Cl_2$).

The faster running fraction (41 mg, 14.1%) was crystallized from MeOH (0.3 ml) to afford *trans*- **12** (31 mg, 10.6%), m.p. 120–122° (MeOH). (Found: C, 77.70; H, 7.75; N, 9.10. Calc for $C_{20}H_{24}N_2O$ (308.40): C, 77.88; H, 7.84; N, 9.08). IR(KBr): 2780–2800 (Bohlmann bands), 1690 cm$^{-1}$ (lactam CO). MS *m/e*, (%): 308 ($M^+$, 100), 307 (47.5), 280 (12), 252 (18).

*Determination of the optical purity of* cis-*lactam* **11**. Lactam **11** (50 mg) was treated with KOBu$^t$ (25 mg) in MeOH (1 ml) at room temp for 2–3 hr. The mixture was acidified with AcOH and the solution treated with 5% $Na_2CO_3$ aq (1 ml), extracted with $CH_2Cl_2$ (2 × 2 ml), the combined organic extracts were dried ($MgSO_4$), filtered and evaporated to dryness to give **9** (58 mg). $[\alpha]_D^{22} = -116°$, $[\alpha]_{546}^{22} = -140°$ (*c* 1.16, $CH_2Cl_2$). Lit.[7]: $[\alpha]_D^{20} = -121°$ (*c* 2.02, $CH_2Cl_2$). Optical purity: 96%.

*Route B*

(+)-14-*Hydroxy*-5-*methoxycarbonyl*-3-*dehydro*-E-*homo*-*eburnane*-4-*ium perchlorate* (**13**). To a soln of **1a** (2.00 g, 4.87 mmol, $[\alpha]_{546}^{20} = +129°$) in abs $CH_2Cl_2$ (12 ml), acrolein (0.5 g, 9.04 mmol) and a suspension of KOBu$^t$ (28 mg, 0.25 mmol) in abs $CH_2Cl_2$ (6 ml) were added with cooling. The mixture was allowed to stand at room temp for 2 hr, shaken with water (2 × 5 ml), and dried ($MgSO_4$). The solvent was evaporated to dryness *in vacuo* to give **13** (2.0 g, 88.1%) in oil form, which was used without further purification. IR($CHCl_3$): 3350 (OH), 1740 (ester CO), 1590 cm$^{-1}$ (C=N). $[\alpha]_{546}^{22} = +42°$ (*c* 1.00, $CH_2Cl_2$).

(+)-5-*Methoxycarbonyl*-14-*oxo*-3-*dehydro*-E-*homo*-*eburnane*-4-*ium perchlorate* (**14**). A soln of **13** (2.00 g, 4.28 mmol) in abs $CH_2Cl_2$ (100 ml) was stirred with freshly prepared $CrO_3$ on KG–HF[8] (9 g) at room temp for 8–10 hr. The reagent was filtered off and washed with $CH_2Cl_2$ containing 2% MeOH (5 × 10 ml). The combined filtrates were evaporated under reduced pressure and the residue (1.40 g) was crystallized from a mixture of MeOH:$CH_2Cl_2$ 5:1 (5 ml) to afford racemic **14** (0.30 g, 15.2%), m.p. 179–181°. IR(KBr): 1740 (ester CO), 1720 (lactam CO), 1540 cm$^{-1}$ (C=N).

The mother liquor was evaporated to dryness *in vacuo* to give optically active **14** (1.10 g, 55.7%) in oil form. $[\alpha]_{546}^{20} = +204°$ (*c* 1.08, $CH_2Cl_2$).

(+)-1α-*Ethyl*-1β-*carboxy*-*ethyl*-6-*carboxy*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* (**5**). To a soln of **14** (750 mg, 1.60 mmol, $[\alpha]_{546}^{20} = +204°$) in EtOH (15 ml), a soln of NaOH (310 mg, 7.75 mmol) in water (1.5 ml) was added, and the mixture was allowed to stand at room temp for 2 days. After evaporation to dryness *in vacuo*, the residue was dissolved in water (5 ml), and acidified with 70% $HClO_4$ aq to pH 5 with cooling. The ppt was filtered off, washed and dried to give **5** (480 mg, 68%), m.p. 185–188° (dec). IR(KBr): 3350 (broad, indole NH, OH), 1710 (COOH), 1610, 1575 cm$^{-1}$ (C=N). $[\alpha]_{546}^{22} = +40°$ (*c* 0.45, MeOH).

(−)-1α-*Ethyl*-1β-*carboxyethyl*-1,2,3,4,6,7-*hexahydro*-12H-*indolo*[2,3-a]*quinolizine*-5-*ium perchlorate* **6**). Acid **5** (460 mg, 0.95 mmol) was heated in decalin (5 ml) at 175–180° for 20 min. The solid residue was cooled, filtered off, and washed with ether (3 × 2 ml) to afford **6** (390 mg, 96%). IR(KBr): 3350 (broad, indole NH, OH), 1710 (COOH), 1620, 1580 cm$^{-1}$ (C=N). $[\alpha]_{546}^{22} = -18°$ (*c* 1.00, MeOH).

*Acknowledgement*—Thanks are due to the Hungarian Academy of Sciences and Richter Gedeon Pharmaceutical Co. for financial support.

## REFERENCES

[1]L. Szabó, J. Sápi, Gy. Kalaus, Gy. Argay, A. Kálmán, E. Baitz-Gács, J. Tamás and Cs. Szántay, *Tetrahedron* **39**, 3737 (1983).

[2]L. Szabó, Gy. Kalaus, K. Nógrádi and Cs. Szántay, *Acta Chim. Acad. Sci. Hung.* **99**, 73 (1979).

[3a]E. Abderhalden and H. Kempe, *Zeitschrift für Physiologische Chemie* **52**, 214 (1907); [b]T. Kametani, N. Tagaki, N. Kanaya and T. Honda, *Heterocycles* **19**, 535 (1982).

[4a]L. Szabó, J. Sápi, K. Nógrádi, Gy. Kalaus and Cs. Szántay, 1*st Int. Conf. Chemistry and Biotechnology of Biologically Active Natural Products*, Vol. 3/2, p. 73. Varna—Bulgaria (1981); [b]Cs. Szántay, L. Szabó, Gy. Kalaus, P. György, J. Sápi and K. Nógrádi, *Organic Synthesis Today and Tomorrow* (IUPAC) (Edited by B. M. Trost and C. R. Hutchinson), p. 285. Pergamon Press, Oxford (1981).

[5]A. Buzas, C. Rétourne, J. P. Jaquet and G. Lavielle, *Tetrahedron* **34**, 3001 (1978).
[6a]H. Rapoport, *Stereoselective Synthesis of Natural Products, Excerpta Medica*, p. 37. Amsterdam–Oxford (1979); [b]S. Yamada, K. Murato and T. Shioiri, *Tetrahedron Letters* 1605 (1976); [c]S. Yamada and K. Okamura, *Chem. Pharm. Bull. Tokyo* **26**, 2305 (1978); [d]H. H. Wassermann, A. W. Tremper and J. S. Wu, *Tetrahedron Letters* 1089 (1979).
[7]L. Szabó, Gy. Kalaus and Cs. Szántay, *Archiv der Pharmazie* **316**, 629 (1983).
[8]E. Santiello, F. Ponti and A. Manzocchi, *Synthesis* 534 (1978).