84. A New Synthesis of Coprine and O-Ethylcoprine

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Coprine (1), a toxin of the mushroom Coprinus atramentarius, was synthesized starting from the 2-amino- and 1-carboxy-protected L-glutamic acids 4 and 12. Compound 4 was first decarboxylated by a radical chain reaction to bromide 5 which underwent ring closure to cyclopropanecarboxylate 6 on treatment with NaH (Scheme 1). Subsequent oxidative electrolysis of 7 to form tert-butyl N-(1-ethoxycyclopropyl)carbamate (8) and acidic hydrolysis yielded the 1-aminocyclopropanol hydrochloride (9). Selective cleavage of the amino-protecting group of 8 (→ 10 or 11), coupling of the corresponding amine 13 with L-glutamic acid 12, and acidic hydrolysis of the resulting L-glutamine derivative 17 yielded O-ethylcoprine (3) and coprine (1).

Introduction. – The common inky cap (Coprinus atramentarius Bull.) is an edible and palatable mushroom which has been known for many years to cause a severe oversensitivity to EtOH after consumption [1]. The symptoms of poisoning occurring after drinking alcoholic beverages with or after a meal that includes C. atramentarius are similar to that of the drug disulphiram (Antabuse®) [2]. In 1975, the causative agent named coprine (1), was isolated from the fruiting body of C. atramentarius independently by two groups [3]. Subsequent biochemical and pharmacological studies showed that coprine is a potent in vivo inhibitor of the NAD+ dependent aldehyde dehydrogenase (ALDH; EC 1.2.1.3), whereas the product of metabolic hydrolysis of the γ-carboxamide group, 1-aminocyclopropanol (2), inhibits ALDH in vivo and in vitro [4].

Two years after its isolation, Lindberg et al. confirmed the structure of coprine (=N′-(1′-hydroxycyclopropyl)-L-glutamine; 1) by reporting a synthetic route yielding the natural product and some related cyclopropanone derivatives [5]. Its congener O-ethylcoprine (=N′-(1′-ethoxycyclopropyl)-L-glutamine; 3) showed a similar effect on ALDH as coprine and proved to be very useful for recent studies on alcohol metabolism [6].

Here, we report a new synthesis of coprine (1) and O-ethylcoprine (3) and the details of the synthesis of 1-aminocyclopropanol (2) that was already reported in a preliminary communication [7].
Results and Discussion. – First, the development of a new synthesis for the N,O-di-substituted cyclopropane moiety comprising the structural and pharmacological key feature of coprine (1) and O-ethylcoprine (3) was envisaged. The intuitively simplest starting material for the synthesis of cyclopropanone hemiaminal derivatives would probably be cyclopropanone itself. Unfortunately, several investigations showed that these hemiaminals are too reactive to be trapped and isolated in sufficient amounts [8]. An alternative approach implies the degradation of larger molecules to the desired size. We, therefore, decided to use an 1-aminocyclopropane-1-carboxylic-acid derivative as starting material.

A simple and high-yielding synthesis of 1-aminocyclopropane-1-carboxylic acid [9] starting from the commercially available 2-amino- and 1-carboxy-protected L-glutamic acid 4 (Scheme 1) afforded a suitable precursor, i.e., 1-[(tert-butyloxy)carbonylamino]-cyclopropane-1-carboxylic acid (7). Acid 4 was decarboxylated by a radical chain reaction in the presence of BrCCl₃ to bromide 5 which, upon treatment with NaH, underwent γ-elimination to cyclopropanecarboxylate 6. Hydrogenolytic debenzylation furnished 7 in up to 68% overall yield from 4.

Scheme 1

![Scheme 1](image_url)

The decarboxylation of acid 7 was investigated next. The oxidative radical chain reaction using tris(phenylthio)antimony, air (O₂), and H₂O to form the nor-alcohol, as reported by Barton et al. [10], was not successful, even when applied to the more stable model compound 2-[(tert-butyloxy)carbonylamino]isobutyric acid (Boc-Aib); although decarboxylation took place, the product was unstable under the conditions used and fragmented into tert-butyl carbamate and acetone [11]. However, anodic oxidative decarboxylation of 7 according to Hofer and Moest [12] gave the corresponding cyclopropanone N-acyl O-alkyl hemiaminal 8 in 79% yield (Scheme 1). This type of two-electron oxidation is known to provoke particularly N-acylated α-amino acids to decarboxylate; efficient substitution of the well stabilized intermediate acyliminium ion by a nucleo-
phile takes place under exceptionally mild conditions [13]. In the present case, replacement of COOH by OEt was achieved with EtOH acting as solvent and nucleophile. Comparison of the physical and spectral data of product 8 with published data for 8 obtained by photochemical synthesis [14] confirmed the structure.

Hydrolysis of 8 with 1.4N HCl at 60° led to the crystalline, but hygroscopic hydrochloride 9, a stabilized form of 1-aminocyclopropanol (2), in 86% yield [7]. Many reagents were recommended in the literature for the selective cleavage of the acid-labile Boc protection [15]. The removal with CF₃COOH/CH₂Cl₂ 1:1 at 0° yielded trifluoroacetate 10 in 89% yield and deprotection with 1.2N HCl in AcOH at room temperature the corresponding hydrochloride 11 (92%).

The next step in the synthesis of coprine (1) and O-ethylcoprine (3) was the coupling of acid 12 and the labile amine 13. The latter had to be generated in situ from the ammonium salts 10 or 11 by adding 1 equiv. of base (Scheme 2). Several electron-withdrawing groups Y were tested for the activation of the carboxyl group in 12. First, the classical mixed-anhydride method was carried out using 14 (obtained from 12 by isobutyl chlorocarbonate treatment in THF at -15° [16]) to which 13 (obtained from 10 and Et₃N in dimethylformamide at room temperature) was added dropwise and stirred for 30 min at -15°. After 2 h at room temperature and chromatography, the desired coupling product 17 was obtained in a yield of only 19%. Activation of 12 with dicyclohexylcarbodiimide (DCC) and 1H-benzotriazol-1-ol (BtOH) [17] (→ 15) and generation of 13 from 11 (in THF at 0°) with Hünig’s base resulted in 8.5% of pure 17, after multiple chromatographic purifications to remove the dicyclohexylurea formed on activation. Using [[(1H-benzotriazol-1-yl)oxy]tris(dimethylamino)phosphonium hexafluorophosphate (BOP) as activating reagent [18] (→ 15 + hexamethylphosphoric triamide) and in situ generation of 13 from 11 with Et₃N, the coupling yield after 18 h at room temperature was still low (18%); presumably, amine 13 decomposed faster than it substituted the activating group Y. Therefore, the highly reactive reagent 1,1'-carbonylbis(3-methylimidazolium) triflate, developed by Rapoport and coworkers [19], was used to activate 12.
and the cationic intermediate 16 and amine 13 (generated in situ from 10) gave coupling product 17 in 28% yield in 2 h at 10°. As no alternative fast coupling reagents are known to be useful for sterically hindered amines, no further attempts were made to improve this step of the synthesis.

The Boc and t-Bu protecting groups of 17 were removed using 1.2M HCl at 40°, and after ion-exchange chromatography, the pharmacologically interesting O-ethylcoprine (3) was obtained in 78.5% yield. Under more rigorous acidic conditions at 60°, the EtO group was also hydrolyzed to give coprine (1) in 73% yield. The physical and spectral data of 1 and 3 were in good agreement with the data reported in [5], and the 400-MHz 1H-NMR spectra of the mixture of synthetic and natural 1 supported the established structure [11]. Thus, coprine (1) and O-ethylcoprine (3) were obtained in 9.7 and 10.5% overall yield, respectively, starting from both commercially available L-glutamic acids 4 and 12.

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Experimental Part

General. All reagents and chemicals were purified and dried by standard procedures. Electrochemistry: potentiosstat/galvanostat (62 V/max. 1 A) and Pt electrodes (5.5 cm²) were used in an undivided cell with cooling and under slight stirring. THF was distilled over Na/K prior to use and transferred with syringes. TLC: Alugram SIL G/UV 254 (Macherey-Nagel), RP-18 F254 (Merck), aluminium oxide UV 254 (Fluka), and cellulose UV 254 (Fluka) plates; detection under UV light where possible; by I₂, or with 5% (v/v) H₂SO₄ in MeOH or 2% (w/v) ninhydrin in EtOH-followed by heating. Column chromatography (CC): silica gel 60 (Merck, 0.063–0.200 mm or 0.040–0.063 mm). Flash chromatography (FC): silica gel 60 (Chemische Fabrik Uetikon, 0.030–0.075 mm). Ion-exchange chromatography: Amberlite CG-120-II (Fluka; strong cation-exchange resin) and Amberlite CG-400-II (Fluka; strong anion-exchange resin). M.p.: Kofler block; corrected. [α]D: Perkin-Elmer-781 spectrometer; δ in cm⁻¹. NMR: Varian-EM-360 (1H, 60 MHz), Varian-Gemini-300 (1H, 300 MHz; 1C, 75 MHz), or Varian-VXR-400 (1H, 400 MHz; 13C, 101 MHz) spectrometer; δ in ppm downfield of TMS (=0.00 ppm) or rel. to sodium 3-(trimethylsilyl)propionate (δ(H) 0.00 ppm, δ(C) 1.70 ppm) for D₂O solns.: coupling constants in Hz. MS: VG 70-250; in m/z (rel. intensity (%)).

Benzyl 4-Bromo-2-(tert-butyl ox y)carbonylamino)cyclopropane-1-carboxylate (5). To a soln. of 1-benzyl N-[(tert-butyl oxy)-car bonyl]-L-glutamate (5.0 g, 14.83 mmol; 4, Novabiochem) in THF (75 ml), N-methylmorpholine (1.65 ml, 14.83 mmol) and isobutyl chlorocarbonate (146 ml, 1.483 mol) and isobutyl chlorocarbonate (95%; 2.05 ml, 14.83 mmol; Fluka) were added successively at -15°. The mixture was stirred for 5 min, a soln. of 1-hydroxy pyridine-2(1H)-thione (2.26 g, 17.80 mmol) and Et₃N (2.48 ml, 17.80 mmol) in THF (50 ml) added dropwise, and the heterogeneous mixture stirred for 30 min at -15°. After filtration of the N-methylmorpholinium chloride, the filtrate was evaporated and the resulting yellow oil dissolved in BrCCl₃ (146 ml, 1.483 mol) and irradiated for 45 min at r.t. with a 125-W tungsten lamp. The brownish mixture was evaporated and the residue purified by FC (pentane/CH₂Cl₂ 2:3; then CH₂Cl₂): 4.137 g (75.0%) of 5. The colorless crystals were recrystallized from pentane. M.p. 53–55° (20); 53°. IR (KBr): 3380 (OH), 3020w (CH), 2990m (CH), 2950m, 1765s (CO), 1685s (NCO), 1515s (NCO II), 1440m, 1370m, 1295m, 1250~1, 1215m, 1155s. 1H-NMR (400 MHz, CDCl₃): 1.44 (s, t-Bu); 2.22 (m, CH₂(3)); 2.42 (m, CH₂(4)); 3.40 (dt, J = 5.2, 2, H – C(2)); 5.11 (br, d, J = 2, NH); 5.19 (d, J = 2.8, PhCH₂); 7.26–7.40 (m, 5 arom. H). H-SO₄ in MeOH or 2%. UV (Fluka), Varian-Gemini-300, Varian-EM-360 (1H, 60 MHz), Varian-VXR-400 (1H, 400 MHz; 1C, 101 MHz) spectrometer; δ in ppm downfield of TMS (=0.00 ppm) or rel. to sodium 3-(trimethylsilyl)propionate (δ(H) 0.00 ppm, δ(C) 1.70 ppm) for D₂O solns.: coupling constants in Hz. MS: VG 70-250; in m/z (rel. intensity (%)).

Benzyl l-(tert-Butylox y)carbonylamino)cyclopropane-1-carboxylate (6). NaH (55–60% in oil; 58.6 mg, ≥ 1.34 mmol) was twice suspended in hexane (5 ml) and the gray soln. removed carefully. The pure NaH under Ar was suspended in THF (10 ml) and cooled to -78°. Slowly, 5 (250 mg, 0.67 mmol) in THF (5 ml) was added dropwise. After the addition (30 min), the mixture was allowed to gradually warm up to r.t., stirred for 5 h at r.t., and then treated with sat. NH₄Cl soln. (20 ml) and extracted with CH₂Cl₂ (3 × 25 ml). The combined org. phase...
was washed with brine (20 ml), dried (Na2SO4), and evaporated: 179 mg (91.7%) of 6. The colorless crystals were recrystallized from (i-Pr)2O, m. p. 116–118°C (IR (KBr): 3350s (NH), 3030w (CH), 2920w (CH), 2995m (CH2), 2940w, 1740 (CO), 1690s (NCO I), 1515s (NCO II), 1450m, 1360m, 1300s, 1270m, 1190s, 1150s, 755s, 695s. 1H-NMR (400 MHz, CDCl3): 1.12–1.22 (m, 2H, CH2(2),CH(3)); 1.42 (s, t-Bu); 1.52–1.64 (m, 2H, CH2(2),CH(3)); 5.31 (s, PhCH2); 5.17–5.20 (br. s, NH); 7.28–7.42 (m, 5 atm. H). CI-MS (NH3): 3.09 (2.4, [M + NH4]+); 292 (3, [M + H]+); 253 (42.5, [M – (t-Bu) + NH4]+); 235 (23, [M – (t-Bu)OH]); 218 (10.5), 192 (100, [M – Boc]+); 108 (62.5), 91 (45), 58 (10.5). Anal. calc. for C13H12NO4 (291.35): C 65.96, H 7.26, N 4.81; found: C 66.11, H 7.30, N 4.76.

1-[(tert-Butyloxy)carbonylamino]cyclopropene-1-carboxylic Acid (7). To a soln. of 6 (1.75 g, 6.0 mmol) in MeOH (30 ml), 10% Pd/C (175 mg; Fluka) were added at 0°C. The mixture was hydrogenated at r.t./1 atm. After 90 min (calc. amount of H2 (146.5 ml) consumed), the mixture was filtered through Celite 335 and the filtrate evaporated: 1.185 g (98%) of 7. Colorless crystals. M.p. 176–177.5°C. IR (KBr): 3600–2750s (br., OH), 3300s (NH), 3200s (NH), 3100m, 3030w (CH), 3010w (CH), 2980m (CH), 2960m, 2850m, 1700s (br., CO, NCO I), 1645s (NCO II), 1485m, 1410s, 1370s, 1200s, 1160s, 1080s, 930m, 780m. 1H-NMR (60 MHz, CD2OD): 0.8–1.2 (2H, CH(2),CH3(3)); 1.25–1.5 (m, 2H, CH(2),CH3(3)); 1.4 (s, t-Bu); 4.7–5.2 (br. s, NH). CI-MS (NH3): 219 (1.9, [M + NH4]+); 202 (2.7, [M + H]+); 163 (50.5, [M – (t-Bu) + NH4]+); 145 (53.7, [M – (t-Bu)OH]); 119 (6.1), 102 (100, [M – Boc]+); 86 (8), 58 (12.7). Anal. calc. for C13H12NO4 (291.22): C 53.72, H 7.51, N 6.96; found: C 53.65, H 7.60, N 6.85.

tert-Butyl N-[(1-Ethoxycyclopropyl)carbamate] (8). To a soln. of 7 (0.402 g, 2.0 mmol) in abs. EtOH (50 ml) in an undivided electrolytic cell with Pt-electrodes, 0.98 mmol NaOEt in EtOH (408 pl, 0.4 mmol) were added at 0°C. The electrolysis was performed under light stirring and a constant current of 0.4mA. The MeOH (30 ml), 10% Pd/C (175 mg; Fluka) was added dropwise to a soh. of 1.2~HCI/AcOH at 10°C. After evaporation, the filtrate evaporated, and the filtrate evaporated: 0.51 g (98%) of 8. Colorless crystals. M.p. 41–42°C (14): 44–45°C. IR (KBr): 3360 (NH), 2990 (CH), 2965m (CH), 1710s (br., NCO I), 1520 (NCO II), 1400m, 1370s, 1270m, 1240m, 1070s, 950m, 855m. 1H-NMR (400 MHz, CDCl3): 0.94–0.99 (m, 2H, CH2(2),CH3(3)); 1.07–1.14 (m, 2H, CH2(2),CH3(3)); 1.18 (t, J = 7.2, CH2O); 1.47 (s, t-Bu); 3.64 (q, J = 7.2, 2H, CH2O); 5.4–5.6 (br. s, NH). CI-MS (NH3): 219 (14.4, [M + NH4]+); 202 (17.7, [M + H]+); 163 (100, [M – (t-Bu) + NH4]+); 146 (45.0, [M – (t-Bu)OH]); 102 (14.0, [M – Boc]+); 73 (21.3), 56 (18.9). Anal. calc. for C13H15NO4 (201.27): C 59.68, H 9.52, N 6.96; found: C 58.98, H 9.70, N 6.85.

1-Aminocyclopropanol Hydrochloride (9). A suspension of 8 (166 mg, 0.825 mmol) in aq. 1.4m HCl (10 ml) was heated to 60°C for 1 h and stirred vigorously. To the resulting homogeneous mixture (TLC (SiO2, AcOH/Buf/H2O: H2O 1:3:1); Rf 0.51 (pure), H2O (10 ml) was added and the soln. evaporated. To remove traces of HCl, the addition of H2O (10 ml) followed by evaporation was repeated 3 times. Drying at 50°C/0.02 Torr yielded 77 mg (86%) of 9. Colorless, hygroscopic salt. IR (KBr): 3600–3200s (br., OH ass.), 3300–2500s (br., NH), 2990 (CH), 1720w, 1610w, 1450w, 1350m, 1250s (C=O), 1170w, 1120w. 1H-NMR (60 MHz, D2O): 1.1–1.2 (br. m, CH2(2), CH3(3)); FAB-MS (glycine): 166 (30.1, [M + glycine]+), 132 (4.4, [C3H4 + glycine]+), 104 (30.4), 74 (100, M)+, 61 (1.4), 57 (1.5, [M – OH]+).

1-Ethoxycyclopropanolammonium Trifluoroacetate (10). To a soln. of 8 (99 mg, 0.493 mmol) in abs. CH2Cl2 (0.8 ml), CF3COOH (0.8 ml, 10 mmol) and the homogeneous solvent stirred vigorously. After 45 min (TLC (SiO2, AcOH/Buf/H2O: H2O 1:3:1); no 8 at Rf 0.49), the mixture was dissolved in AcEt (10 ml) and evaporated. To remove traces of CF3COOH, the addition of AcEt (10 ml) followed by evaporation was repeated twice. Drying at r.t./0.01 Torr for 6 h yielded 94 mg (89%) of 10. Partly crystalline salt. 1H-NMR (300 MHz, (D2)DMSO): 0.85–1.32 (m, CH2(2),CH3(3)); 1.24 (t, J = 7.2, CH2O); 3.67 (q, J = 7.2, CH2O); 8.35–9.05 (br. s, NH2). El-MS (70 eV): 102 (0.3, M)+, 95 (5.0), 87 (2.7, [M – CH]+), 86 (5.6), 73 (7.4), 69 (85.1, [M – CH2 – NH2]+), 56 (21.2, [M – EtO]+), 43 (51.4), 45 (100, EtO2). 1H-NMR (300 MHz, (D2)DMSO): 0.85–1.35 (m, CH2(2),CH3(3)); 1.25 (t, J = 7.3, CH2O); 3.62 (t, J = 7.3, CH2O); 8.7–9.5 (br. s, NH2). CI-MS (NH3): 69 (15.2, [M – CH2 – NH2]+), 60 (36.7), 56 (98.0, [M – EtO]+), 45 (56.2, EtO2), 43 (100, Ac2, Fluka), 41 (26.4, C3H8).
abs. DMF (0.1 ml) was added and 

**Novobiocin (CH₃)₂, 1730s (br., CO), 1695s (NCO I), 1545s (br., NCO II),**

TLC (cellulose, BuOH/acetone/H₂O/Et₂NH 10:5:5:2). The mixture was heated to 60°, and after 1 h stirring (TLC: R₄ 0.55; pure. M.p. 179-181° [S]: 183-184°), [α]D = + 3.3 (c = 4.4, H₂O; [5]: [α]D = + 5.2 (c = 7.8, H₂O)); [α]Boc = + 4.8 (c = 4.4, H₂O). IR (KBr): 3420 (br., NH), 3290 (NH), 3010 (CH), 2990 (CH), 1665 (br., CO, NCO I), 1590 (m), 1540 (br., NCO II), 1450 (m), 1390 (s), 1370 (m), 1260 (m), 1195 (m), 1130 (m), 1040 (m), 980 (m), 840 (s), 790 (m), 710 (m), 690 (m), 650 (m), 610 (m), 560 (m), 430 (m). Anal. calc. for C₁₉H₂₃N₂O₆ (386.49): C 59.05, H 8.87, N 7.25; found: C 59.23, H 8.65, N 7.16.

**O-Ethylephrim (N=⁻/⁻-Ethoxycyclopropyl)-l-glutamine; 3.** A suspension of 17 (36 mg, 0.156 mmol) in aq. 1.2 M HCl (0.5 ml) was heated to 40°. After 30 min (TCL (cellulose, BuOH/aceton/H₂O/Et₂NH 10:5:5:2): no at R₄ 0.97, H₂O (2 ml) was added and the mixture evaporated. The solid residue was purified by cation-exchange chromatography (Amberlite CG-120-Η²⁺ form, aq. 0.3N NH₃): 16.8 mg (78.5%) of 3. The colorless crystals were recrystallized from H₂O/NaOH. TLC (cellulose, BuOH/aceton/H₂O/Et₂NH 10:5:5:2): R₄ 0.55. Pure. M.p. 179-181° ([S]: 183-184°), [α]D = + 3.3 (c = 4.4, H₂O; [5]: [α]D = + 5.2 (c = 7.8, H₂O)); [α]Boc = + 4.8 (c = 4.4, H₂O). IR (KBr): 3420 (br., NH), 3010 (CH), 2990 (CH), 1665 (br., CO, NCO I), 1580 (m), 1525 (m), 1450 (m), 1390 (s), 1370 (m), 1260 (m), 1195 (m), 1130 (m), 1040 (m), 980 (m), 840 (s), 790 (m), 710 (m), 690 (m), 650 (m), 610 (m), 560 (m), 430 (m). Anal. calc. for C₁₉H₂₃N₂O₆ (386.49): C 59.05, H 8.87, N 7.25; found: C 59.23, H 8.65, N 7.16.

**Coprine (N=⁻/⁻-Hydroxypropyl)-l-glutamine; 1.** A suspension of 17 (242 mg, 0.627 mmol) in aq. 2M HCl (5 ml) was heated to 40°. After stirring for 1 h, a mixture of 3 (R₄ 0.55) and 1 (R₄ 0.33) was present according to TCL (cellulose, BuOH/aceton/H₂O/Et₂NH 10:5:5:2). The mixture was heated to 60°, and after 1 h stirring (TCL: R₄ 0.33 and traces of t-glutamic acid at R₄ 0.15), H₂O (10 ml) was added and the mixture evaporated. The solid residue was purified by cation-exchange chromatography (Amberlite CG-120-Η²⁺ form, aq. 0.3N NH₃ and anion-exchange chromatography (Amberlite CG-400-Η⁻ form, AcO⁻ form, H₂O): 29.4 mg (73%) of 1. The colorless crystals were recrystallized from H₂O/NaOH. TLC: pure. M.p. 194-197° ([S]: 197-199°), [α]D = + 5.9 (c = 2.8, H₂O; [5]: [α]D = + 7.6 (c = 4.1, H₂O)); [α]Boc = + 8.2 (c = 2.8, H₂O). IR (KBr): 3380 (br., NH), 3020 (CH), 2950 (CH), 1680 (br., CO, NCO I), 1590, 1540 (br., NCO II), 1450 (m), 1420 (m), 1390 (m), 1260 (m), 1195 (m), 1130 (m), 1040 (m), 980 (m), 825 (m). 1H-NMR (400 MHz, D₂O): 0.92-1.10 (m, 2H, CH₂(2'), CH₂(3')); 1.11-1.19 (m, 2H, CH₂(2'), CH₂(3')); 2.04 (s, traces of AcO⁻); 2.05-2.17 (m, CH(3)); 2.40 (t, J = 7.2, CH₂(3)); 2.77 (t, J = 6.6, H-C(2)). ¹³C-NMR (101 MHz, D₂O): 22.36, 25.70 (C(2'), C(3')); 30.90 (C(3)); 48.61 (C(4)); 60.82 (C(2)); 66.33 (C(1)); 179.45, 181.15 (C(5), C(11)). FAB-MS (glycerine): 405 (0.63), 317 (1.23), 262 (1.25), 244 (1.19), 240 (5.00), 225 (11.62), 203 (100, [M + H]⁺), 186 (13.10, [M + O]⁺), 166 (4.30), 157 (4.17), 148 (44.34, [Gln + H]⁺), 130 (17.53), 110 (50.58), 80 (5.27), 84 (19.79), 74 (52.29), 56 (10.44). Anal. calc. for C₁₉H₂₃N₂O₆ (202.21): C 47.52, H 6.98, N 13.85; found: C 47.31, H 6.70, N 13.89.
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