Iseluxine: A Novel Isoquinolinone Alkaloid from *Iseia luxurians*[§]

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A novel isoquinolinone alkaloid, iseluxine (**1**), has been isolated from the epigeal parts of *Iseia luxurians* (Moric.) O'Donell (Convolvulaceae), a climber indigenous to the tropical Americas. Structural elucidation was achieved by HRMS, ^{1}H NMR, ^{13}C NMR, and HMBC spectroscopy. N- and / or O-methyl derivatives of **1** are already known from certain Magnoliidae families, e.g., the Fumariaceae, the Lauraceae, or the Papaveraceae. Iseluxine, the "missing link" in the biosynthesis of these methyl derivatives from dopamine, is the first isoquinolinone alkaloid characterized by a catechol substructure.

Introduction

Iseia luxurians (Moric.) O'Donell is a herbaceous climber mostly distributed along river and stream margins. The monotypic American genus *Iseia* occurs from Honduras south to the northern part of Argentina (Austin, 1975) and belongs to the Cresseae tribe of the Convolvulaceae. The plants subjected to our study were cultivated in a tropical greenhouse from seeds collected in the wild, and have been harvested at the stage of 12 months. The alkaloid has finally been obtained from the aqueous phase of the plant extract.

Only small information is provided by the literature concerning the phytochemistry of *I. luxurians*. A GC-MS study of numerous convolvulaceous species revealed calystegines B_1 and B_2, hydrophilic nortropane alkaloids commonly distributed in Convolvulaceae and Solanaceae, to be present also in the leaves and the seeds of this plant (Schimming *et al.*, 1998).

Materials and Methods

Plant material

Iseia luxurians (Moric.) O'Donell, Convolvulaceae (voucher specimen Panama I/1995, Nr. 25; Institut für Pharmazie, Pharmazeutische Biologie, Freie Universität Berlin). The seeds were collected on the banks of the Panama Canal, near Gamboa, Republic of Panama, in 1995.

Extraction and isolation

Dried ground aerial parts of *Iseia luxurians* (50 g), harvested from a tropical greenhouse (Berlin) at the age of 12 months, were extracted with 600 ml MeOH (70%). After evaporation, the extract was acidified (2% aq. tartaric acid) and partitioned between H_2O and organic solvents (petrol, CH_2Cl_2, EtOAc). The aq. phase was then made alkaline (10% aq. NH_3) and extracted with $CHCl_3$-i-PrOH (3:1; v/v). The remaining aq. phase was again reduced to 50 ml *in vacuo*, simultaneously removing NH_3 from the solution. Further purification was achieved by column chromatography (LiChroprep RP-8, 40–63 µm, Merck Art. 9362) [H_2O, H_2O-MeOH mixtures, fractions 1–12]. Fractions 9–10, eluting with H_2O-MeOH (80:20; v/v), reduced to 1 ml, were submitted to preparative HPLC (LiChrosorb RP 18, 7 µm material) [H_2O-MeOH (85:15; v/v)] at 4.5 ml/min.

Iseluxine (3,4-dihydro-6,7-dihydroxy-1(2*H*)-isoquinolinone): EI-MS (70 eV, 240°), *m/z* (rel. int.): 179 [M]+ (75), 150 (100), 122 (83); HR-MS, *m/z*: 179.0584 ($C_9H_9NO_3$+., calc. 179.0582); ^{1}H NMR (400 MHz, CD_3OD): d 2.80 (2H, t, *J*=6.5 Hz, H-4), 3.43 (2H, t, *J*=6.5 Hz, H-3), 6.65 (1H, s, H-5), 7.34 (1H, s, H-8); reaction with 2,6-dichlor-

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oquinone-4-chloroimide / NH_3 (Gibbs reagent) on the TLC (silica gel, $CHCl_3$-MeOH, 4:1, detection UV 254 nm, R_f 0.45).

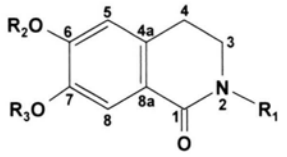
Results and Discussion

Structural elucidation of **1** (Table I) was achieved by EI-MS, HR-MS, ^{1}H NMR, ^{13}C NMR, and HMBC spectroscopy. The ^{1}H NMR showed two aromatic s hinting to a 1,2,4,5-tetrasubstituted aromatic system (d 6.65, 1H, H-5; d 7.34, 1H, H-8) and two t (d 2.80, J=6.5 Hz, H-4; d 3.43, J=6.5 Hz, H-3) for two protons, each. From the HR-MS, the molecular formula could be deduced as $C_9H_9NO_3$. HMBC measurements finally allowed total structural assignments (Table II). Thus, the isolated compound has to be 3,4-dihydro-6,7-dihydroxy-1(2*H*)-isoquinolinone, which, as a novel alkaloid, we named iseluxine. Its structure is characterized by a catechol moiety, and obviously, dopamine can be regarded as its biogenetic precursor.

Remarkably, this is the first report on an isoquinolinone alkaloid from the Convolvulaceae and even from the Solanales. The occurrence of isoquinolinones such as corydaldine, oxyhydrastinine, thalifoline, and their derivatives in certain families of the Magnoliopsida *sensu stricto* (Frohne and Jensen, 1998) (Annonaceae, Berberidaceae, Fumariaceae, Hernandiaceae, Lauraceae, Papaveraceae, Ranunculaceae) is well documented (Krane and Shamma, 1982; Shamma *et al.*, 1974; Cava and Bessho, 1966; Hussain *et al.*, 1983; Doskotch *et al.*, 1969; Chou *et al.*, 1994). However, there are only two reports on isoquinolinone alkaloids from the Rosopsida: N-methylcorydaldine (also described as 6,7-dimethoxyhydrastine) has been isolated from *Hammada articulata* (Moquin) Iljin ssp. *scoparia* Pomel, a chenopodiaceous plant indigenous to the Middle East (Benkrief *et al.*, 1990), and from *Evodia daniellii* Benth. (Rutaceae), a plant endemic to Korea (Mitsunaga *et al.*, 1991).

It should be mentioned that **1** seems to occur in the growth period up to about 12 months only, since it is not detectable in later stages of development. The potential occurrence of methylated derivatives, e.g., corydaldine, has been investigated by GS-MS measurements of all lipophilic fractions of the plant (petrol, methylene chloride, ethyl acetate), but definitely no isoquinolinones could be detected.

Table I.



Compounds	R_1	R_2	R_3
Iseluxine (**1**)	H	H	H
Northalifoline	H	CH_3	H
Thalifoline	CH_3	CH_3	H
Corydaldine	H	CH_3	CH_3
Noroxyhydrastinine	H	- CH_2 -	
Oxyhydrastinine	CH_3	- CH_2 -	
N-Methylcorydaldine	CH_3	CH_3	CH_3

Table II.

C	^{13}C NMR (100 MHz, DMSO-d_6)	HMBC-correlation
C-1	165.1 (s)	H-8
C-3	39.2 (t)	
C-4	26.7 (t)	
C-4a	121.0 (s)	H-4, H-5
C-5	113.9 (d)	
C-6	148.0 (s)*	H-5, H-8
C-7	143.7 (s)*	H-5, H-8
C-8	114.0 (d)	
C-8a	131.7 (s)	H-4, H-8

* Interchangeable.

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