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A new alkaloid, pandanamine; finding of an anticipated biogenetic intermediate in *Pandanus amaryllifolius* Roxb

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Abstract—A novel alkaloid having a symmetrical structure, which was anticipated to be a biogenetic precursor of pandamarilactonines and pandamarilactone-1, was found in the fresh leaves of *Pandanus amaryllifolius* Roxb.

The genus *Pandanus* belonging to the family Pandanaceae comprises about 600 species which are widely distributed in tropical and subtropical regions and many of which have been used as traditional folk medicines.[1] In a recent pharmacological survey, the hypoglycemic effect of the extract of *Pandanus odorus* was found.[2] During our chemical study on the secondary metabolites in *Pandanus* plants,[3] we recently reported the isolation of new pyrrolidine alkaloids, pandamarilactonines-A (**1**) and -B (**2**), from *Pandanus amaryllifolius*.[4] When considering how those alkaloids, as well as pandamarilactone-1 (**3**),[3a] might be formed in the plant, we can postulate the existence of a symmetrical secondary amine (**4**) as a precursor molecule,[4] which

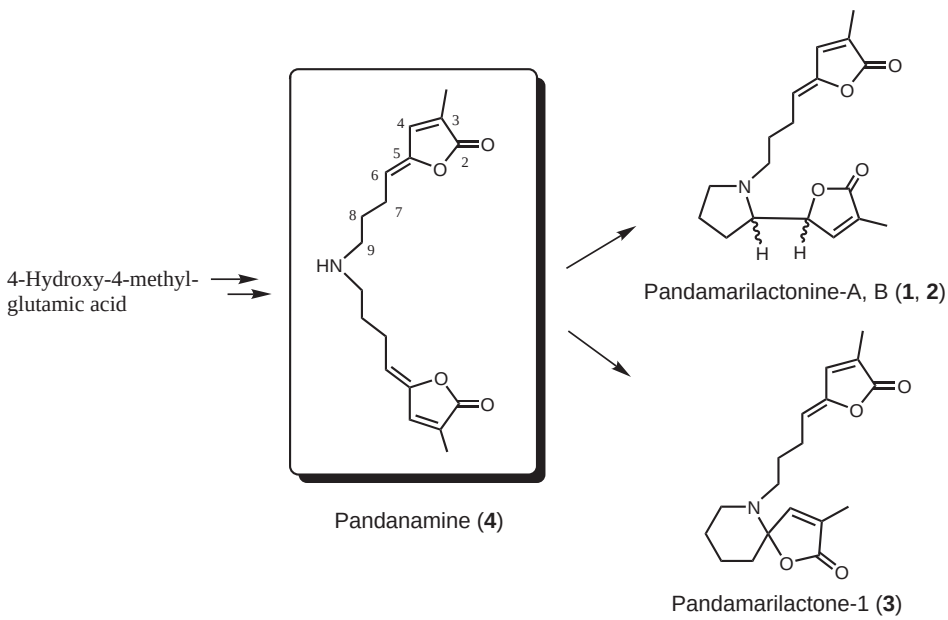

Figure 1. Hypothetical biogenetic route of the *Pandanus* alkaloids.

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undergoes intramolecular cyclization to give the alkaloids (**1**–**3**). To support this biogenetic hypothesis, we reinvestigated the polar alkaloidal fraction of *P. amaryllifolius* in order to find the anticipated alkaloid (**4**) (Fig. 1). We report here the first finding and structure elucidation of the targeted alkaloid.

The alkaloidal fraction, which was prepared by conventional procedure from an EtOH extract of the fresh leaves of *P. amaryllifolius*, was subjected to silica gel column chromatography. The polar part, obtained after elution of the fractions containing pandamarilactonines, was further purified by using reverse-phase column chromatography to give the secondary amine (**4**)[5] as an amorphous powder (0.21% based on the crude alkaloid fraction). The new compound **4**, named pandanamine, gave an m/z 318.1721 $[M+H]^+$ in a high-resolution FABMS spectrum, establishing the molecular formula as $C_{18}H_{23}NO_4$. The appearance of nine signals in the ^{13}C NMR spectrum was indicative of the symmetrical structure of the new alkaloid. The characteristic ^1H and ^{13}C NMR signals {δ 7.03 (2H, d, $J=1.5$ Hz, H-4), 5.14 (2H, dd, $J=7.9$, 7.9 Hz, H-6), 1.99 (6H, s); δ 170.9 (C-2), 129.8 (C-3), 137.8 (C-4), 149.3 (C-5), 111.3 (C-6), 10.5 (C-21)} and the UV absorption at 273 nm indicated the presence of a γ-alkylidene-α-methyl-α,β-unsaturated γ-lactone moiety. Analysis of COSY, HMQC and HMBC spectra established that one of the terminal carbons in a three-carbon methylene chain was connected with the sp^2 carbon (C6) of the γ-alkylidene-γ-lactone moiety and another one was attached to the nitrogen atom. The differential NOE experiment between H-4 and H-6 demonstrated the *Z* configuration in the γ-alkylidene-α,β-unsaturated γ-lactone moiety. All the above findings enabled us to compose the symmetrical molecular structure of the new alkaloid (**4**).

The new alkaloid (**4**) was identical with the synthetic compound,[4] which was previously prepared as a synthetic intermediate of pandamarilactonines, by direct comparison of the chromatographic behavior and high-resolution MS, ^1H and ^{13}C NMR spectra.

As we have postulated the presence of the alkaloid (**4**) as a biogenetic common precursor of pandamarilactonines (**1** and **2**) and pandamarilactone-1 (**3**),[4] we were able to find the targeted alkaloid in nature by the present study, which strongly supported the final stage of the hypothetical biogenetic pathway of the alkaloids (**1**–**3**).

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5. Natural pandanamine (**4**): an amorphous powder. R_f value; 0.2 [SiO_2, solvent system: 10% MeOH in $CHCl_3$]. UV (MeOH) λ_{max} nm (log ε): 273 (1.15), 242 (sh), 203 (1.86). IR (neat) ν_{max} cm^{-1}: 1760 (lactone). FABMS (NBA) m/z; 318 $[M+H]^+$. HR-FABMS (NBA): calcd for $C_{18}H_{23}NO_4$: 318.1704, found: 318.1721. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.03 (2H, d, $J=1.5$ Hz, H-4), 5.14 (2H, dd, $J=7.9$ and 7.9 Hz, H-6), 3.04 (4H, dd, $J=7.9$ and 7.6 Hz), 2.44 (4H, ddd, $J=7.6$, 7.6 and 7.3 Hz), 1.97–1.92 (4H, m), 1.99 (6H, d, $J=0.9$ Hz, -CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9 (C-2), 149.3 (C-5), 137.8 (C-4), 129.8 (C-3), 111.3 (C-6), 47.7 (C-9), 25.4 (C-8), 23.1 (C-7), 10.5 (-$\underline{C}H_3$).