

PIPEROLACTAM D, A NEW ARISTOLACTAM FROM
INDIAN PIPER SPECIES

SANJAY J. DESAI, ROHIT CHATURVEDI, AND NEWAND B. MULCHANDANI*

Bio-Organic Division, Bhabha Atomic Research Centre, Trombay, Bombay 400 085, India

ABSTRACT.—A new alkaloid was isolated from the cold EtOH extracts of *Piper attenuatum* and *Piper boehmerifolium* and has been characterized as 10-amino-2-hydroxy-3,4-dimethoxyphenanthrene-1-carboxylic acid lactam **1**.

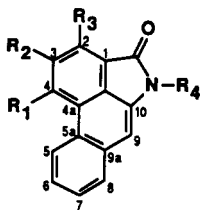
Aristolactams, a small group of compounds found mainly in the Aristolochiaceae, have also been reported from some members of the Annonaceae, Menispermaceae, and Monimimaceae (1). Recently, we reported the isolation of aristolactams from Indian *Piper* species (2,3). In continuation of this work, we report the presence of a new aristolactam, named piperolactam D **1**, from *Piper attenuatum* (Cas.) DC. and *Piper boehmerifolium* Wall (Piperaceae).

Piperolactam D **1**, obtained as a yellow crystalline solid, gave a molecular ion peak at eims m/z 295 (100%) suggesting $C_{17}H_{13}NO_4$. It exhibited uv absorption peaks characteristic of a phenanthrene chromophore. An alkali-induced bathochromic shift suggested the presence of a phenolic group. The presence of a hydroxyl band (3390 cm^{-1}) was confirmed in the ir spectrum. Appearance of ir bands at 3180 (NH), 1690, and 1650 cm^{-1} (C=O) suggested the presence of a lactam. Acetylation of **1** yielded a diacetate, $C_{21}H_{17}NO_6$, $[M]^+$ 379, which further supported the

presence of -OH and -NH groups. Methylation of **1** with CH_2N_2 furnished a compound identical with piperolactam C **2** (co-tlc, ms) (3) suggesting that **1** is a phenolic analogue of **2**. The 500 MHz 1H -nmr spectrum of **1** showed two methoxy signals at δ 3.85 and 4.40, each integrating for three protons. The absence of a C-2 proton signal in **1**, when compared with **3-5** (2), indicated a 2,3,4 trisubstituted pattern. The aromatic region of the spectrum closely resembled those of aristolactams unsubstituted at positions 5-9 (4). Therefore, the two methoxy groups were determined to be in ring A. The methoxy signals in **1** (δ 3.85 and 4.4) were at variance with the other two possible isomeric structures **6** [δ 3.98 and 4.03 (2)] and **7** [δ 4.17 and 4.62 (4), δ 4.16 and 4.61 (5)]. Therefore, the two methoxy groups were assigned to the C-3 and C-4 positions. In addition, the up-field methoxy signal (δ 3.85), due to the shielding effect of the C-2 hydroxyl, was assigned to C-3. Thus, structure **1** was established as 10-amino-2-hydroxy-3,4-dimethoxyphenanthrene-1-carboxylic acid lactam.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined on a Fisher-Johns apparatus and are uncorrected. The uv spectra were obtained in MeOH on a Shimadzu uv-visible 240 spectrophotometer. The ir spectra were taken from KBr pellets on a Perkin-Elmer 783 ir spectrophotometer. The 1H -nmr spectrum was recorded in DMSO- d_6 (δ in ppm), using TMS as internal standard on a Bruker Spectrospin 500 MHz spectrometer. Eims were recorded on Shimadzu gc/ms-QP 1000A at 70 eV. Elemental analyses



- 1 $R_1=R_2=OMe, R_3=OH, R_4=H$
- 2 $R_1=R_2=R_3=OMe, R_4=H$
- 3 $R_1=R_2=OMe, R_3=R_4=H$
- 4 $R_1=OMe, R_2=OH, R_3=R_4=H$
- 5 $R_1=OH, R_2=OMe, R_3=R_4=H$
- 6 $R_1=OH, R_2=R_3=OMe, R_4=H$
- 7 $R_1=R_3=OMe, R_2=OH, R_4=H$

were carried out on a Carlo Erba Model 1106 Elemental Analyzer. Si gel (230–400 mesh size, Acme India) was used for vacuum liquid chromatography. Fractions from cc in each case were separately combined on the basis of their tlc patterns as detected by uv light (254 and 365 nm).

PLANT COLLECTION, EXTRACTION, AND ISOLATION.—The whole dried plant material (2 kg each) of *P. attenuatum* and *P. boehmerifolium* was obtained from M/s United Chemicals and Allied Products, Calcutta, with whom the voucher specimens are available. The plant materials were extracted successively with petroleum ether and EtOH by percolation. The extracts were concentrated under reduced pressure. Subsequent column and tlc separation over Si gel [CHCl_3 -MeOH (19:1), *R_f* 0.55] afforded **1** (*P. attenuatum*, 6 mg; *P. boehmerifolium*, 7 mg) in pure form.

PIPEROLACTAM D [1].—Yellow crystalline solid, mp 226–227° ($\text{C}_6\text{H}_6/\text{MeOH}$); uv λ max nm (log ϵ) (MeOH) 225 (4.68), 269 (4.92), 293 (4.59), 337 (4.35), 373 (4.10); uv λ max nm (log ϵ) (MeOH + KOH) 235 (4.83), 266 (4.51), 294 (4.81), 329 (4.27), 362 (4.33), 381 (4.30); ir ν max (KBr) cm^{-1} 3390, 3180, 1690, 1650, 1405, 1260; eims *m/z* (%) [M]⁺ 295 (100), 280 (55), 252 (28.2), 277 (13.4), 276 (12.1), 266 (14.1), 234 (13.6), 209 (20.5), 153 (19), 152 (12), 149 (16.4), 166 (16.9), 119 (19); ¹H nmr ($\text{DMSO}-d_6$) δ 3.85 (3H, s, OMe), 4.40 (3H, s, OMe), 7.24 (1H, s, H-9), 7.53 (2H, m, H-6 and H-7), 7.95 (1H, m, H-8), 9.26 (1H, m, H-5), 10.8 (1H, s, NH). *Anal.* calcd for $\text{C}_{17}\text{H}_{13}\text{NO}_4$, C 69.15, H 4.41, N 4.75; found C 69.17, H 4.36, N 4.68%.

ACETYLATION OF 1.—Pure **1** (3 mg) was dissolved in pyridine (0.5 ml) and treated with Ac_2O (0.5 ml). The reaction mixture was allowed to stand at room temperature overnight and after usual workup yielded a viscous mass purified by tlc over Si gel: yellow crystalline solid, mp 192–193° (petroleum ether/ C_6H_6); ir ν max cm^{-1} (KBr) 1790, 1740, 1720, 1640, 1480, 1400, 1380, 1310, 1280, 1190, 1160, 1150, 1090, 1080, 1020; eims *m/z* (%) [M]⁺ 379 (45.7), 358 (5.6), 337 (89), 295 (96), 280 (67), 277 (22), 266 (17), 252 (21), 236 (21.6), 209 (17.1), 180 (13.6), 152 (13.6), 105 (39). *Anal.* calcd for $\text{C}_{21}\text{H}_{17}\text{NO}_6$, C 66.49, H 4.49, N 3.69; found C 66.46, H 4.43, N 3.64%.

ACKNOWLEDGMENTS

SJD and RC are grateful to the DAE for the award of Senior Research Fellowships. Thanks are also due to the operator of the 500 MHz FT-nmr National Facility, TIFR, Bombay, for recording the spectra.

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Received 10 July 1989