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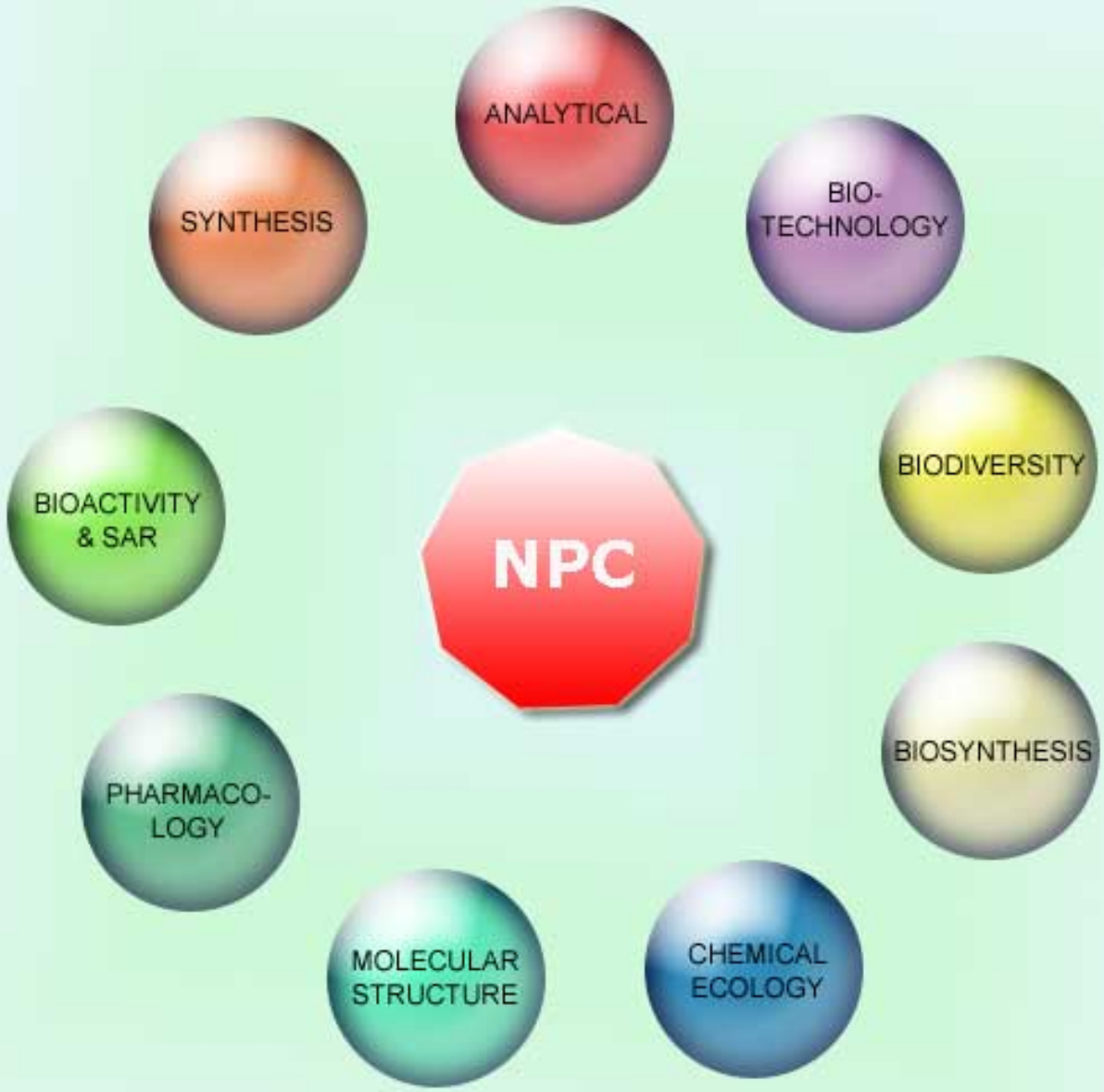

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N-(4-Methylphenyl) benzenepropanamide - the First Isolated Amide from the Genus *Paederia*

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Investigation of the stem of *Paederia foetida* (Rubiaceae) resulted in the isolation and characterization of *N*-(*4*-methylphenyl)-benzopropanamide, which was hitherto unknown as a natural product This is the first report of an amide for the genus *Paederia*.

Key words: *Paederia foetida*, *N*-(*4*-methylphenyl)-benzopropanamide, Rubiaceae, X-ray crystallography.

Paederia foetida (Rubiaceae), locally called "Gandal" in India, grows in tropical parts of India, as well as in Central and Eastern Himalayas [1]. The stem of the plant has a reputation in folklore medicine and exhibits anti-inflammatory, anti-microbial, anti-oxidative and hepato-protective properties [2]. Several iridoid glycosides and lactones (paederinin, paederoside and paederia lactone) have been isolated from the stem of this plant [3]. The present article describes the isolation and characterization of an amide (**1**) from *P. foetida* stem; this compound was hitherto unknown as a natural product.

The ethereal extract of the stem was fractionated between *n*-hexane and ethyl acetate. The ethyl acetate fraction of the extract was subjected to column chromatography over silica gel (60-120 mesh). A white solid was isolated from the *n*-hexane-ethyl acetate (9:1) fraction, which on crystallization from methanolic *n*-hexane (2%) afforded a needle shaped microcrystalline compound (**1**).

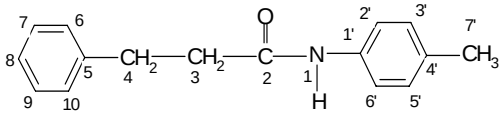

Figure 1: Structure of (**1**).

The IR (KBr disc) spectrum of **1** revealed the presence of >NH and >C=O at 3299 and 1655 cm^{-1}, respectively. The elemental composition of **1** could be ascertained as $C_{16}H_{17}NO$ from the TOF mass spectrum. This exhibited a base peak at (m/z +Na) 262.1203, corresponding to $C_{16}H_{17}NO$, and a characteristic peak $[M-C_9H_9O]^+$ at m/z 107, from which the elemental composition C_7H_8N was determined by exact mass measurements (found: 107.9367). A fragment at m/z 91.8811 indicated the presence of a substituted toluene unit and another fragment at m/z 104.9208 indicated the presence of a Ph-CH_2-CH_2 moiety. In the ^{1}H NMR spectrum, two triplets at δ 2.65 and δ 3.06 have been assigned to two adjacent methylenes, the latter being adjacent to a carbonyl group, as it resonated in a comparatively downfield region. A three-proton singlet at δ 1.71 was due to the *para*-methyl substituent at C-4 (Table 1).The ^{13}C NMR spectrum clearly showed the presence of sixteen carbon atoms in the molecule. Comparison of the ^{13}C NMR spectrum (fully decoupled) with DEPT 135^0 and DEPT 90^0 clearly indicated the presence of one methyl, two methylenes, nine aromatic methines and four quaternary carbons in the molecule, among which the signal at δ 170.24 was assigned to the carbonyl carbon. The NMR shifts of all the protons and

carbons have been depicted in Table 1. All these spectral data identify **1** as *N*-(4-methylphenyl)-benzopropanamide (Figure1).

Table 1: NMR spectroscopic shifts of the amide (**1**) in $CDCl_3$.

Position	^{1}H (δ)	^{13}C (δ)
2	–	170.24
3	3.1(t, 2H, *J* = 7.6 Hz)	39.42
4	2.65 (t, 2H, *J* = 7.6 Hz)	31.59
5	–	140.71
6, 10	7.1-7.4 (m, 10H)	128.60
7, 9	7.1-7.4 (m, 10H)	128.38
8	7.1-7.4 (m, 10H)	126.34
1′	–	133.95
2′, 6′	7.1-7.4, (m, 10H)	120.03
3′, 5′	7.1-7.4 (m, 10H)	129.41
4′	7.1-7.4 (m, 10H)	135.15
7′	1.71 (3H, s)	20.81

Finally the structure was confirmed by X-ray crystallographic analysis. The ORTEP projection is shown in Figure 2.

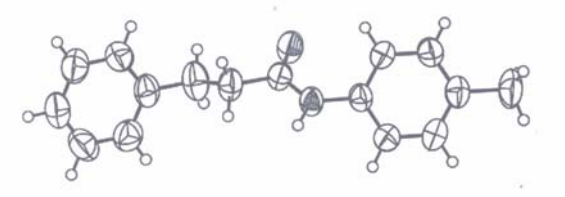

Figure 2: ORTEP projection of **1**.

In conclusion, this investigation has resulted in the first report of the isolation of *N*-(4-methylphenyl)-benzenepropanamide as a natural product.

Experimental

The melting point was determined in an electrically controlled melting point apparatus (Sunvic, UK). The IR spectrum was recorded using a Perkin Elmer RX1 FT IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ in a Bruker AVANCE 300 DIGITAL MHz NMR spectrometer. Chemical shifts were reported as δ (ppm) and the coupling constants (*J*) were given in Hz. The mass spectrum was recorded on a Qtof Micro YA 263 mass spectrometer. The X-ray crystallographic data were recorded on a Nonius CCD diffractometer operating the MoKα radiation (λ = 0.7107 Å). The crystals are monoclinic, space group $P2_1/c$, with parameters a = 14.706(3); b = 4.870(4); c = 18.965(4) Å, β = 98.14(4)°, and refined to a R = 8.9 % (for all 1468 data). Crystallographic Data for compound **1** i.e. *N*-(*4*-methylphenyl)-benzopropanamide have been deposited with the Cambridge Crystallographic Data Centre as CCDC 643303. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

Plant material: The stems of *P. foetida* were collected from the Ministry of Food and Supplies, Government of India, and compared with a voucher specimen maintained in the herbarium of Calcutta University.

Extraction and Isolation: The stem (0.53 Kg) was extracted at room temperature with ether. The ethereal fraction was concentrated under low pressure and a dark brown mass (22 g) was obtained. This was column chromatographed over silica gel (60-120 mesh) and eluted successively with *n*-hexane and *n*-hexane-ethyl acetate mixtures. The fraction obtained with *n*-hexane-ethyl acetate (9:1) afforded a white solid, which on repeated recrystallization using methanolic *n*-hexane afforded pure (57 mg) compound **1** as white needle-shaped crystals (m.p. 128^0C).

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