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Farnesylamine from the Ant *Monomorium fieldi* Forel

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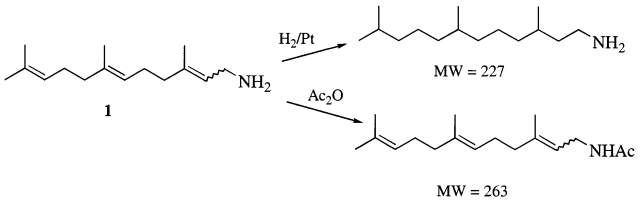
Abstract: (2*E*)- and (2*Z*)-Farnesylamine were detected in the extracts of the myrmicine ant *Monomorium fieldi* Forel from Australia. Their structures were established by direct comparison with synthetic (2*E*)- and (2*Z*)-farnesylamine. This finding of a sesquiterpene is unique in a genus known to produce unbranched fatty acid derived alkaloids and amines. Additionally, while farnesylamine has not been reported from natural sources, the synthetic material has been shown to have a variety of biological activities.

Monomorium fieldi Forel is an ant that is widely distributed in Australia. The ant belongs to the *M. monomorium* species group, which has an extensive radiation throughout Africa, Asia, and the Pacific region, including Australia. The number of taxa belonging to this group is likely to be well over 100, possibly more, and 17 species have been recorded for Australia.[1] The biology and behavior of *M. fieldi* and its relatives have been little studied, but *M. fieldi* is believed to be a generalist predator. However, several other members of the species group are known to include a large proportion of seeds and other plant material into their diet. Activity of a related ant, *M. rothsteini* Forel, at food sources includes "gaster flagging" to deter other ants from the food supply.[2] This behavior is also found in other *Monomorium* species and may occur in *M. fieldi* as well.[3]

Three collections[4] of 15−20 worker ants in methanol were analyzed by gas chromatography−mass spectrometry using a Shimadzu QP-5000 GC−MS equipped with an RTX-5, 30 m × 0.25 mm i.d. column. The instrument was programmed from 60 to 250 °C at 10 °C/min. Analysis of the methanol extracts showed two components in equal amounts with nearly identical mass spectra. MS *m*/*z* (rel %): 206 (1), 189 (3), 179 (3), 161 (3), 152 (4), 138 (5), 136 (5), 121 (6), 119 (3), 107 (6), 93 (15), 84 (15), 81 (12), 70 (21), 69 (62), 57 (15), 55 (15), and 41 (100). Treatment of a small sample of this extract with acetic anhydride produced a pair of monoacetamides with identical mass spectra. MS *m*/*z* (rel %): 263 (1, M^+), 248 (1), 220 (1), 209 (3), 194 (5), 189 (4), 161 (3), 148 (2), 136 (6), 136 (12), 121 (6), 107 (12), 93 (28), 84 (57), 69 (48), 60 (21), 43 (60), and 41 (100). The formation of the acetamides, $M^+ = 263$, suggested primary or secondary amines, MW = 221. Hydrogen was bubbled through a small portion of the extract containing ca. 1 mg of PtO_2 to provide a single peak by GC−MS, suggesting a primary amine. GC−MS *m*/*z* (rel %): 227 (2, M^+), 212 (2), 184 (3), 170 (2), 156 (1), 142 (2), 140 (3), 126 (6), 125 (8), 114 (18), 100 (7), 97 (7), 84 (12), 83 (14), 73 (12), 70 (30), 69 (24), 57 (39), 56 (38), 55 (66), 45 (68), 44 (60), 43 (100), and 41 (90). These data together suggested that the components in the natural extract were a pair of isomeric amines, $C_{15}H_{27}N$ (MW = 221), containing three double bonds. Furthermore, the mass spectrum of the saturated natural material was different from that reported for a straight-chain amine such as pentadecylamine,[5] showing branching by losses of CH_3 and C_3H_7 but not C_2H_5 and the ion at $m/z = 114$ ($M - C_8H_{17}$). A sample of (2*E*)- and (2*Z*)-farnesylamine (**1**)[6] prepared from a commercial mixture of (2*E*)- and (2*Z*)-farnesol (Aldrich Chemical Co.) had mass



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spectra and retention times identical to the compounds in the extract from *M. fieldi*. Samples of the synthetic farnesylamines also formed the same pair of acetamides and hydrogenated amine as the natural material.

This finding is remarkable for two reasons. In the first place, finding sesquiterpene amines in ants of the genus *Monomorium* is unique, and a literature search for farnesylamine failed to show its previous detection in a natural source. It is well documented that the venoms of ants in the genus *Monomorium* contain alkaloids having unbranched carbon chains,[7] presumably products of the polyacetate pathway, as has been demonstrated for similar alkaloids found in the closely related ant genus *Solenopsis*.[8] Additionally, while isoamylamines and amides have been detected in the ponerine genus *Mesoponera*,[9] and monoisoprenoid alkaloids have been detected in the myrmecine genera *Harpagoxenus* and *Leptothorax*,[10] the acyclic primary amines detected in *Monomorium* to date have had unbranched carbon skeleta.[11]

Second, while the biological activity of ant-derived amines has been investigated sporadically,[7] the previous preparations of farnesylamine (**1**) have been solely for that purpose, and its biological activity has been extensively studied. Farnesylamine has been shown to inhibit arthropod molting and reproduction,[12] inhibit squalene synthesis,[13] inhibit the growth of malignant PAP2 cells,[14] inhibit pancreatic cancer,[15,16] modulate human T cells,[17] induce apoptosis in hepatoma cells,[18] and have antiosteoporotic activity,[19] among others. Clearly, the activity of farnesylamine as a defensive chemical for *M. fieldi* needs investigation.

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