

other than inspiration only. The lower vertebrates, which are 'stiff-necked' and incapable of swinging the head from side to side have more widely separated nares, both relatively and absolutely when compared with other small vertebrates, than the higher forms which have a flexible post-cranial skeleton. This would appear to be an adaptation for tropotactic olfactory perception. Higher vertebrates are already adapted in such a way that klinotaxis is readily accomplished. The question then arises, why do snakes and tubenosed bats – both flexible necked types – resemble the lower vertebrates in so far as they have widely spaced nostrils? The answer lies in their specialized life styles. Prior to striking, snakes gain information about the precise location of their prey by vision, infra-red detection and by

sampling the air with the bifid tongue. The precise role of the olfactory system, rather than the accessory olfactory organ of Jacobson to which the tongue carries scented particles, is not known but presumably a lateral head shaking would make the final attack less successful. Widely spaced nostrils give the snake the best chances for olfactory information to come through stereolfaction. Tubenosed fruit bats locate ripe fruit from among unripe fruit by olfaction³, and since detection and selection has to be made while on the wing it seems likely that tropotaxis is beneficial inasmuch as it does not necessitate physical movement of the head which would likely interfere with flight stability.

Further support for the contention that lower vertebrates have to rely upon stereolfaction comes from many species of fish themselves. Tubular nares, which effectively increase the base for triangulation, are found in a number of species including the bichir *Polypterus bichir*, catfish *Nemacheilus barbatula* and the eel *Anguilla anguilla*. In other species the small vertical flap of tissue standing between the incurrent and exhalant nares, called the pavilion, serves to catch and direct downwards water from the faster moving layers not immediately in contact with the body. In this manner the 2 streams of sampled water come from as widely separated sources as possible.

Although the data expressed in this paper are morphometric and not behavioural, there seems no other reasonable interpretation explaining the position of the external nares of vertebrates.

Table 2. Absolute internarial separation (in mm) for a sample of 133 genera of small vertebrates

	Number of specimens	Separation (mm)	± SE
Teleosts	20	10.3	4.2
Urodeles	9	4.2	2.2
Anurans	12	4.6	1.5
Snakes	18	7.1	2.8
Lizards	30	4.1	2.5
Birds	12	4.0	1.5
Tree shrews	14	2.9	1.0
Insectivores			
Marsupials			
Rodents	8	3.0	1.4
Tube nosed fruit bats	4	12.1	1.5
Tube nosed insectivorous bats	6	4.6	0.6

See legend to table 1.

1 G.H. Parker, Bull. Bur. Fish. Wash. 33, 61 (1914).

2 G. von Békésy, J. appl. Physiol. 19, 369 (1964).

3 G.M. Allen, Bats. Harvard University Press, Boston (1939).

Mitosis in the haemocytes of *Sarcophaga ruficornis* (Diptera)¹

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Summary. Among the haemocytes of *Sarcophaga ruficornis*, only the prohaemocytes divide. Injection of phytohaemagglutinin-P induces 100% prohaemocytes to undergo mitosis but does not induce mitosis in other cells. Mitotic stages other than the prophase are apparently very short lived.

It is generally believed that among the different kinds of haemocytes found in insects, the prohaemocytes alone divide and the other types of cells are derived from the differentiation of these stem cells². However, the question is by no means settled. For instance, Arnold³ has reported the division of plasmatocytes and spheroidocytes in *Ephesia kuhniella*; Arnold and Sohi⁴ noted the division of granular haemocytes in *Malacosoma disstria*; and Nittono⁵ observed the division of spherule cells in *Bombyx mori*.

In smears of haemolymph drawn from the different stages in the life history of *Sarcophaga ruficornis*, we have observed mitotic figures only in the prohaemocytes, and also noted that the maximum percentage of dividing cells (about 20% of prohaemocytes) occurs in the freshly moulted 3rd instar larva. Mitotic figures were not observed in any other type of cells although closely adhering pairs of cells of various kinds and binucleate cells, giving a false impression of division, were occasionally encountered.

The possibility existed that the number of cells actually dividing, other than the prohaemocytes, in the circulating haemolymph is so small that they are missed in the

examinations. Therefore, we used a mitotic stimulator, phytohaemagglutinin-P, to induce their division. 0.05 ml of a 2% aqueous solution of phytohaemagglutinin-P was injected per larva into the freshly moulted 3rd instar larval stage, and haemolymph was drawn out 4, 8, 22 and 26 h after the injection for preparing smears. It was noted that the percentage of prohaemocytes undergoing mitosis suddenly increased within 4 h after the injection of the mitotic stimulator from 20% to about 84% and 22 h after the injection all the circulating prohaemocytes were in one stage or the other of mitosis. Until 26 h after the injection, all the prohaemocytes were in dividing stages. None of the other types of cells were, however, seen undergoing mitosis in any preparation even after the treatment with the mitotic stimulator. This shows that haemocytes other than the prohaemocytes in *S. ruficornis*, viz. plasmatocytes, granular haemocytes and spherule cells, do not have the competence to undergo mitosis. The table gives the percentage of prohaemocytes showing mitosis after different intervals after the injection of the mitotic stimulator, and the stages in which they were observed.

Percentage of prohaemocytes in different stages of mitosis after injection of phytohemagglutinin-P

Stage of examination	Total prohaemocyte percentage undergoing mitosis	Prophase	Metaphase	Anaphase	Early telophase	Late telophase
Early 3rd instar before treatment	20.0	-	-	-	-	-
4 h after treatment	84.1	78.9	-	-	-	5.2
8 h after treatment	78.4	67.8	7.1	-	-	3.5
22 h after treatment	100.0	80.0	20.0	-	-	-
26 h after treatment	100.0	83.3	6.1	8.8	-	1.8

The table shows that in all the stages examined, the predominantly large number of prohaemocytes undergoing division are encountered in the prophase stage and none in the early telophase stage. The small percentage of cells in the late telophase stage in the smear made 4 h after the treatment apparently represents some of the cells starting division before the treatment. In the metaphase stage, 7.1, 20 and 6.1% prohaemocytes are observed 8, 22 and 26 h after the injection while 8.8% prohaemocytes are seen in the anaphase stage only 26 h after the treatment. The obvious inference is that prophase is the longest lasting stage in the mitotic cycle of prohaemocytes of *S. ruficornis* and the anaphase and early telophase stages are the most transient. Injection of 0.02 ml of 1% colchicine in the larvae 1 h before collection of haemolymph at each one of the stages mentioned confirmed the results already cited.

We have concluded that in *S. ruficornis*, mitosis among the haemocytes is confined to the prohaemocytes, that the mitotic stimulator phytohaemagglutinin-P effectively induces mitosis in these cells and that in their mitotic cycles, stages other than the prophase are short lived and therefore observed relatively rarely.

- 1 Acknowledgment. We express our gratitude to the State Council of Scientific and Industrial Research, U.P. for the grant of financial assistance to U.S.S.
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- 4 J.W. Arnold and S.S. Sohi, Can. J. Zool. 52, 481 (1974).
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4,5,6,7-Tetrahydro-7-oxobenzo[b]thien-4-ylurea; Sulbenox¹, a novel animal growth stimulant

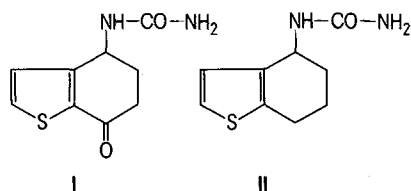
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Summary. The title compound, a metabolite of 4,5,6,7-tetrahydrobenzo[b]thien-4-ylurea, was synthesized and found to be an effective growth promoter in sheep, mice, and rats. In sheep it gave over a 6-week growth period at 15 and 60 ppm in the diet an economically and statistically significant growth response.

The increasing cost of livestock production³ and concern for the continued use of hormones, especially the synthetic estrogen diethylstilbestrol⁴, the most commonly used growth stimulant in cattle and sheep, has prompted the search for a safe drug which can improve the efficiency of raising farm animals.

We have synthesized a compound, 4,5,6,7-tetrahydro-7-oxobenzo[b]thien-4-ylurea (I), which when administered to animals increases their rate of growth. Furthermore, it appears to have a number of characteristics desirable in a compound to be used as a growth stimulant for meat-producing animals. Thus, it is not estrogenic, androgenic, or goitrogenic in standard rat tests. It is non-mutagenic in the Ames test, its LD₅₀ in rats (single oral dose) is greater than 5000 mg/kg b.wt, and at effective growth-stimulating levels the body compositions of experimental animals are normal.



Early investigations with 4,5,6,7-tetrahydrobenzo[b]thien-4-ylurea (II) indicated that II was a member of a new class of growth stimulants in sheep. Metabolism studies showed that II when administered orally to rats, sheep, and cattle was rapidly converted to 2 major metabolites, probably a ketonic and a hydroxylated material⁵, which were isolated from urine. Since I was a possible metabolite based on spectral data (NMR and CIMS), and could thereby be the active drug, synthesis and structural elucidation work was initiated.

Compound I was prepared in 37% yield by ceric ammonium nitrate oxidation of II which was obtained by allowing 4,5,6,7-tetrahydrobenzo[b]thiophen-4-amine hydrochloride to react with KOCN. It was recrystallized from methanol to give crystals melting at 245–246 °C; microanalysis for C, H, N was satisfactory and spectral data (NMR, IR, CIMS) were consistent for the structure represented by I. Comparison of spectral data and R_f values of I with those of the ketonic metabolite showed they were identical⁵.

Given orally or parenterally, I was effective in stimulating growth in female, male, and castrate male rats. When compound I was administered orally in the diet of lambs over a 6-week growing period, economically and statistically significant improvements in average daily gain and feed efficiency were elicited. These results are summarized in