An Arsenic-containing Nucleoside from the Kidney of the Giant Clam, *Tridacna maxima*

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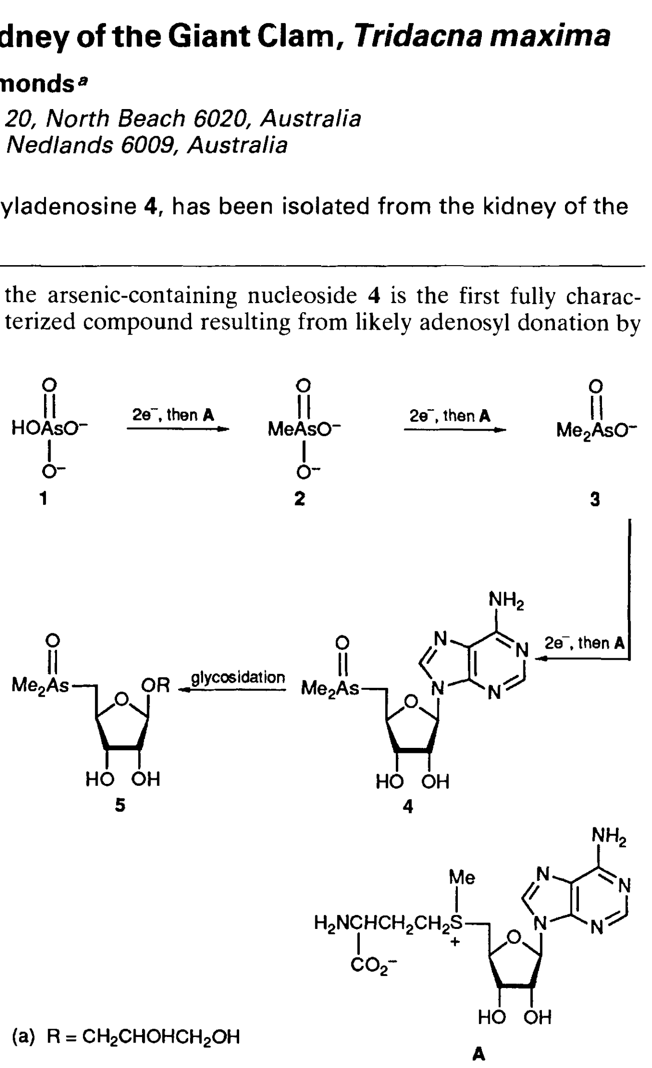
An arsenic-containing nucleoside, 5′-deoxy-5′-dimethylarsinyladenosine **4**, has been isolated from the kidney of the giant clam, *Tridacna maxima*.

Arsenic is naturally present in seawater at concentrations of 2–3 μg dm^{-3}, chiefly as arsenate. The major forms of arsenic in marine algae are dimethylarsinylribosides[1] **5a–e** which are probably metabolised to arsenobetaine ($Me_3As^+CH_2CO_2^-$, the usual form of arsenic in marine animals[2]) within food-chains. It has been proposed[1] that algae biosynthesise dimethylarsinylribosides from absorbed oceanic arsenate by mechanisms first described by Challenger[3] for the biosynthesis of trimethylarsine by microorganisms, and involving *S*-adenosylmethionine (AdoMet)[4] as the methyl donor and the nucleoside **4** as a key intermediate. The giant clam, *Tridacna maxima*, contains symbiotic algae in its tissues, and products of algal metabolism are found in its large accumulatory kidney.[5,6] We here report the isolation of 5′-deoxy-5′-dimethylarsinyladenosine **4** from the kidney of *Tridacna*.

Gel permeation and buffered ion-exchange chromatography of an aqueous–methanol extract of *Tridacna* kidneys (initially 700 g wet wt., ≈220 μg As g^{-1}) separated several major and minor arsenic compounds as determined by graphite furnace atomic absorption spectrophotometry. The chromatographic properties of the major arsenicals suggested they were identical with dimethylarsinylribosides previously isolated from *Tridacna* kidneys[6] and from other algal sources.[7]

A minor arsenic compound was purified by buffered cation-exchange chromatography and TLC, and obtained as a glass (1.5 mg). It was identified as the novel 5′-deoxy-5′-dimethylarsinyladenosine **4** by a comparison of the ^1H, ^{13}C NMR and IR spectra with those of a synthetic specimen, prepared by treatment of 5′-chloro-5′-deoxyadenosine with Me_2AsNa and then H_2O_2 (ref. 8).†

Although AdoMet-derived adenosyl–iron complexes have been proposed as intermediates in some enzyme reactions,[9] the arsenic-containing nucleoside **4** is the first fully characterized compound resulting from likely adenosyl donation by



(a) R = $CH_2CHOHCH_2OH$

(b) R = $CH_2CHOHCH_2SO_3H$

(c) R = $CH_2CHOHCH_2O\overset{O}{\overset{\|}{P}}OCH_2CHOHCH_2OH$ (with OH below P)

(d) R = $CH_2CHOHCH_2OSO_3H$

(e) R = $CH_2\underset{NH_2}{C}HCH_2SO_3H$

Scheme 1 Proposed biosynthetic pathway for dimethylarsinylribosides. The order of the alkylation steps shown here is considered the most likely. All arsenicals in the proposed pathway have been identified from algal sources.

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† **4**, $[\alpha]_D$ +54.2° (*c* 3.0, MeOH); δ_H (300 MHz, D_2O) 1.69, 1.70 (6 H, 2 s, Me_2As), 2.69 (1 H, dd, $J_{5',5'}$ 13.9, $J_{4',5'}$ 3.8 Hz, 5′-H), 2.79 (1 H, dd, $J_{5',5'}$ 13.9, $J_{4',5'}$ 10.7 Hz, 5′-H), 4.38 (1 H, dd, $J_{2',3'} = J_{3',4'} =$ 5.0 Hz, 3′-H), 4.47 (1 H, m, 4′-H), 4.95 (1 H, dd, $J_{1',2'} = J_{2',3'} =$ 5.0 Hz, 2′-H), 6.06 (1 H, d, $J_{1',2'}$ 5.0 Hz, 1′-H), 8.23, 8.29 (2 H, 2 s, 2-, 8-H); δ_C (75.5 MHz, D_2O) 14.2, 14.7 (Me_2As), 34.4 (C-5′), 73.0, 74.4 (C-2′,-3′), 78.8 (C-4′), 88.4 (C-1′), 118.8 (C-5), 140.2 (C-8), 148.5 (C-4), 152.7 (C-2), 155.3 (C-6); ν_{max}/cm^{-1} 1649s, 1577s, 1479, 1420, 1333, 1302, 1252, 1132, 1051, 852s. Satisfactory elemental analyses were obtained.

AdoMet to an acceptor other than tripolyphosphate. As such it fulfils a prediction made by Cantoni[10] that AdoMet could possibly serve as an adenosyl donor to other suitable acceptors. The biosynthetic pathway for dimethylarsinylribosides may now be described as shown in Scheme 1. Reduction and oxidative methylation of arsenate **1** in two stages would give dimethylarsinic acid **3** which, on reduction and oxidative adenosylation, would yield the key intermediate **4**. Glycosidation by reaction with available metabolites would then give the range of dimethylarsinylribosides **5a–e** that have been identified from algal sources.

No metabolic function has been proposed for organoarsenic compounds found in algae, and it has been suggested[1] that they represent merely end-products of a process for detoxifying adventitiously acquired arsenate. The presence in *Tridacna* (as a result of algal metabolism) of an arsenic-containing nucleoside suggests the possibility that arsenic has a more important biochemical role than has hitherto been supposed.

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