of a DMF-d_7 solution of this polymer, by ^{1}H NMR (250 MHz) at 100 °C, further revealed that it was 72% isotactic, 15% syndiotactic, and 13% atactic in nature.[19]

Polymer-encased vesicles, such as those derived from DODAM, combine the best features found in synthetic membrane models with those of polymerized analogues; i.e., they retain a monomeric lipid assembly and are stabilized by polymeric counterions. For model studies that focus on the orientational properties and chemical effects of biomembranes, such vesicles may prove extremely valuable.[20] Moreover, the antiviral activity, tumor growth inhibition, and interferon induction associated with poly(acrylic acid) suggest that DODAM and related vesicles may serve as unique polymeric drugs as well as drug carriers.[21] Finally, the ready availability of polymerizable surfactants of the type described herein should greatly facilitate the entry of other workers into the polymerized vesicle area.

Efforts now under way are aimed at expanding this new and unique class of vesicles and applying it to drug delivery, membrane modeling, and solar energy conversion.

Registry No. DODAM, 89346-15-6; DODAM (homopolymer), 89346-16-7.

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On the Origin of the Isocyano Function in Marine Sponges[1]

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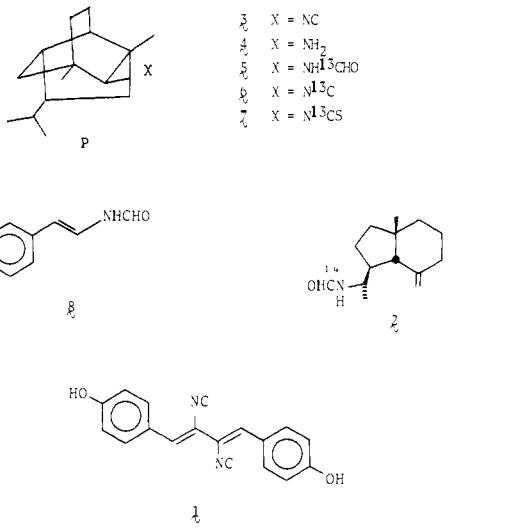
The biogenetic origin of the isocyano function has posed an intriguing, yet unsolved question ever since the first naturally occurring isocyano compound, the *Penicillium* metabolite xanthocillin (**1**), was characterized.[2] Labeling experiments by Achenbach and Grisebach[3] proved that tyrosine furnished the backbone of **1**, but neither formate nor methionine were incorporated into the isocyano group. Later, when we encountered in a sponge an isocyanosesquiterpene and a -diterpene, each accompanied by a formamide and an isothiocyanate, we[4] and others[5] conjectured that the formamides might well be the proximate precursors of the isocyanides. Sodano and co-workers[6] disproved this hypothesis. They injected an ethanolic solution of ^{14}C-labeled



axamide (**2**) into the sponge *Axinella cannabina*, which had been placed in a 10-L aquarium, yet failed to detect labeled isocyanide after 5 days. Up to 15% of radioactivity was recovered in the formamide.

In our experiments on the origin of the isocyano function in sponges, we left the animal, *Hymeniacidon* sp., in its natural habitat until completion of the experiment.[7] We used scuba to embed ^{13}C-labeled precursor encased in double gelatin capsules in the live animal. At the conclusion of the experiment, we removed the sponge and analyzed the extract by GC-MS. In this fashion we confirmed Sodano's[6] earlier finding that the formamide is not a precursor of the isocyanide. We further showed that the isothiocyanate also is not transformed into the isocyanide. We sucessfully demonstrated that, instead, both formamide and isothiocyanate are biosynthesized from isocyanide. In analogy with the xanthocillin experiments,[3] we also found that formate is not used by the sponge as a source of the isocyano carbon.

The labeled precursors were synthesized from 2-isocyanopupukeanane (**3**), mp 78–83 °C, isolated as previously described[8] from *Hymeniacidon* sp.,[9] as shown in Scheme I; the sponges were collected by scuba at Shark's Cove, Oahu, at −10 to −15 m.

Incorporation experiments were conducted at Shark's Cove, Oahu. For each experiment a relatively small sponge (estimated wet wt about 200 g) was selected, and a nearby animal was used as control. Labeled precursors were placed inside two gelatin capsules and carried to the dive site in a plastic jar. An incision was made in the sponge with a sharpened spatula. The capsule was quickly inserted and the incision was capped with a piece of sponge from a nearby animal.[10] At the end of the incubation (1 or 2 weeks) the sponge and a control animal were harvested and frozen until workup. Each sponge was extracted with acetone, the extract partitioned with hexane, and the organic layer injected into the Grobb injection port interfaced with a 30-m DB-5 fused silica capillary column (J&W Scientific), which was coupled to a Finnigan MAT OWA Model 30B mass spectrometer. Since labeled and unlabeled compounds coeluted, the criterion for incorporation was the enhancement of the $M^+ + 1$ and $M^+ + 1 -$ Me peaks, since few other fragments below m/z 217/216 retain the functional group. In the experiments with ^{13}C-labeled **5** and

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(11) A 200-g sponge normally yields 500 mg of **3**, 20 mg of PNHCHO, and 90 mg of PNCS. In order to detect a 4% enhancement of the M + 1 peak of **3**, with an assumed 10% uptake of label, one should feed 40% of labeled **3** (≡**6**). Our instrumentation detects a 1% enhancement. The case for the less abundant constituents is much more favorable.

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Table I. Incorporation Experiments with ^{13}C-Labeled Formamide 5 and Isothiocyanate 7

precursor	amount embedded	incubation period	weight of animal	PN^{13}C (6), m/z ^{13}C experiment 232/231	^{13}C experiment 217/216	control 232/231	control 217/216
5	(1) 30 mg (2) 30 mg	7 days	150 g	12/100[a]	15/100[a]	13/100	16/100
7	45 mg	15 days	108 g	13/100	16/100	13/100	16/100

[a] m/z 231 and m/z 216 are arbitrarily assigned 100% intensity.

Table II. Incorporation of [^{13}C]Formate

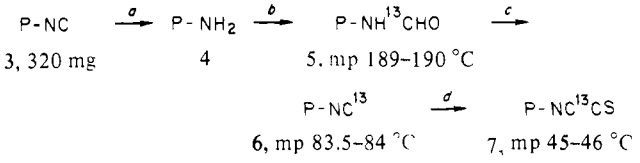
amount embedded	incubation period	wet wt animal	PN^{13}C (6), m/z experiment 232/231	experiment 217/216	control 232/231	control 217/216
(1) 102 mg (2) 102 mg	7 days 7 days	150 g 150 g	12/100	16/100	13/100	16/100

Table III. Internal distribution of C^{13}-Labeled Isocyanopupukeanane (6)[a]

sect. no.	m/z, experiment 232/231	m/z, experiment 217/216	m/z, control 232/231	m/z, control 217/216
1	15/100	15/100		
2[b]	28/100	39/100		
3	14/100	17/100		
4[b]	34/100	50/100	13/100	16/100
5	10/100	17/100		
6	12/100	16/100		
7	12/100	15/100		

[a] Approximate wet wt of animal 260 g; incubation time 14 days; wt of labeled precursor 2 × 45 mg. [b] These are the sections where the labeled precursor was imbedded.

Scheme I



[a] 6 N HCl (50 mL), reflux 4 h; 30% NaOH; distill; 140 mg (69%). [b] $H^{13}CO_2H$ (91.7% ^{13}C, Prochem), 103 mg + 117 mg 4, sealed tube, 110 °C, 10 h; 85 mg (64%). [c] 5 (497 mg) in CH_2Cl_2 (15 mL) and pyridine (1.1 mL) at 0 °C, $POCl_3$ (700 mg), 20 min at 0 °C; after 2 cycles 193 mg of 6 (42%); ν_{max} (KBr) 2099 cm^{-1} vs. PN^{12}C at 2137 cm^{-1}. [d] 6 (25 mg), S (5 mg), sealed tube, 110 °C, 16 h; after workup, 5.6 mg (18%); ν_{max} (KBr) 2166, 2101 cm^{-1}.

7 and [^{13}C]formate the whole animals were worked up.

The results are summarized in Tables I and II. The data show unambiguously that no formamide **5** or isothiocyanate **7** is transformed into labeled 2-isocyanopupukeanane (**6**)[10] (Table I) and that, in analogy with the *Penicillium* research,[2] formate is not utilized by the sponge for isocyano biosynthesis (Table II).

In the experiment with labeled 2-isocyanopupukeanane (**6**), we checked diffusion of the label by analyzing seven parallel slices. The data in Table III show that little transport of label takes place in a 2-week period. Examination of the formamide $(M^+ + 1)/M^+$ (m/z 250/249) and isothiocyanate $[(M^+ + 1)/M^+$ (264/263), $(M^+ + 1 - HS)/(M^+ - HS)$ (231/230)] peaks demonstrates unequivocally that the isocyano function is the precursor of formamide and isothiocyanate in *Hymeniacidon* sp. (Table IV). The recent demonstration by Herbert and Mann[12] that the *N*-formyl carbon in the *Streptomyces* metabolite tuberin (**8**) is biosynthesized from glycine is interesting but irrelevant in this case since we have shown that *Hymeniacidon* does not transform the *N*-formyl into the isocyano function.

Table IV. Transformation of ^{13}C-Labeled 2-Isocyanopupukeanane (6) into Formamide 5 and Isothiocyanate 7[a]

sect. no.	m/z formamide (5) 250/249	m/z isothiocyanate (7) 264/263	m/z isothiocyanate (7) 231/230
1	12/100	ND[b]	20/230
2	44/100	25/100	28/100
3	18/100	ND	15/100
4	41/100	31/100	28/100
5	ND[b]	ND	17/100
6	13/100	ND	15/100
7	ND	ND	13/100

[a] See Table III for experimental parameters. [b] ND denotes <0.8% peak enhancement.

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Isolation, Characterization, and Rearrangement of *cis*- and *trans*-*N*-Acetyl-2-amino-5,6-dimethoxy-5-methylcyclohexa-1,3-diene. Models for the Proposed Precursors of Meta-Substituted Products from Carcinogenic Aromatic Amines

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Reactions of activated derivatives of the potent carcinogen *N*-acetoxy-2-acetamidofluorene (**1**) with in vitro nucleophiles have been reported by Scribner[2] and others[3,4] to produce products

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