Organic Chemicals from Marine Sources

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Abstract

Research opportunities for organic chemicals from the sea can be divided into three classes: near-term (less than 5 yrs to fruition), more distant, and very speculative, long-term opportunities. This paper describes some of these opportunities and gives the authors' view on their possibilities for success. Near-term projects might include development of by-products from the fish and macroalgae industries, process improvements, development of new materials for aquaculture, and the development of new products such as unusual sugars, polysaccharides, carotenoids, and algal lipids. More distant opportunities could include energy farming, pharmaceuticals, polysaccharides to be used for oil production and transport, chemicals to control fouling, and agricultural chemistry for marine systems. Longterm opportunities are more speculative and include increased exploitation of marine organisms as representing a tremendous untapped gene pool, using or mimicking the ability of many marine organisms to selectively extract useful elements from seawater, using bacteria from rift geothermal sources to utilize $\mathrm{H}_{2}\mathrm{S}$, exploiting unique algal photosynthetic systems, and controlling the movements of marine animals during harvesting by using pheromones and communication systems.

This conference has summarized some of the interesting characteristics of marine organisms as sources of food and chemicals. The predominate point of view has been that of enthusiasts who are knowledgeable in marine biology. This paper

will cover some material which has been presented previously. It differs from previous presentations in starting from a chemist's perspective. The authors wish, in particular, to inject several practical questions into these discussions:

- (1) What products which might be obtained from marine sources are actually needed, and at what price can one afford to make them?
- (2) Can marine biotechnology compete with more conventional areas of biotechnology for increasingly scarce research funds? For example, it appears likely that, given sufficient time and effort, genetic engineering of algae could become a reality. It is even possible that genetically engineered algae could be found which would flourish in the wild. Are the best opportunities for research in biotechnology to be found in algae, or in working with industrially useful organisms such as the yeast Saccharomyces or the bacterium Bacillus subtilis?
- (3) What will be the response of the chemical industry to initiatives from within marine biology? For example, if a good new microalgae source for β -carotene were found, could the market absorb the additional product or would the current chemical producers of this substance lower their prices and undercut the new technology?
- (4) Will biotechnology create new products and new markets? If applied biology were merely to lower the price slightly and make slightly more available materials that are already being made in other ways, the actual contribution to the economy would not be large.

This paper will present a framework for consideration of these questions, beginning with an overview of present products and the economic constraints which apply to them. Possible areas of opportunity in commodity, specialty, and pharmaceutic chemicals will be explored. The paper will conclude by suggesting some worthwhile roles that modern biology and biotechnology could play in this area.

The possible roles of marine products and marine biotechnology can be explored by beginning with basic societal needs (Figure 1). What really could make a difference in the way the world runs? Marine biotechnology may make its greatest contribution to the production of biomass, which could be used as a feedstock for chemicals, chemical intermediates, fuels, or a combination of these. There are, of course, already very well-developed terrestrial sources of biomass. Nonetheless, there is a large commercial opportunity in this area which has so far not materialized outside of food production.

Current Production of Chemicals from Marine Sources

Table I lists the most important commercial marine products now produced, considered as organic chemicals. The most important product is clearly food, i.e., proteins. Algal

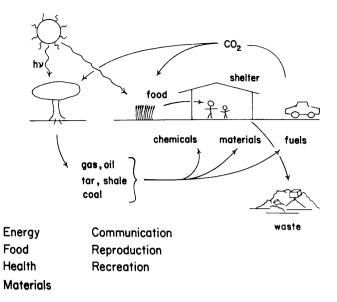


Figure 1. Basic societal needs

Table I. Present products considered as organic chemicals

	Quantity (1b)	Price (\$/1b)
Food (finfish, shellfish = protein; amino acids)	∿ ₁₀ 11	> 0.25
Algal polysaccharides (algin, carrageenan, agar)	∿ 108	3 - 7
Fish oils (fatty acids)	$\sim 10^6$	^ .135 15
Ethylene		∿ 0.25
Glucose		∿ 0.15

(Prices from Chemical Marketing Reporter)

polysaccharides (phycocolloids) are interesting and of significantly higher per weight value. Fish oils (13 to 14 cents per pound), which may presently be considered as a byproduct of the fish meal industry, are less important and are one of the least valuable oil products (compare soybean oil at

18 to 20 cents per pound or peanut oil at 25 cents per pound; prices from Chemical Marketing Reporter, November 15, 1982). It is interesting to compare these figures with those for two typical, high-volume organic chemicals, ethylene and glucose. On a weight basis, prices are roughly comparable for ethylene and for fish (as food). The price for ethylene is depressed now; a more realistic price might be 28 to 29 cents per pound; likewise a real price for food might be about 30 cents per pound. An important criterion for chemicals is the price per weight of fixed carbon. On this basis ethylene is about half as expensive as fish.

By contrast, consider glucose, which is principally produced from corn. Corn-derived glucose could be considered as a material competitive with marine biomass as chemical feedstock at the current price of 15 cents per pound. Note that glucose is almost as cheap as ethylene on the basis of price per unit of carbon. Nonetheless, with the possible exception of isomerization to fructose for high-fructose syrups, glucose has not made any significant impact on the commodity chemical industry.

Marine Biomass

Marine production of biomass has qualitative characteristics which differ from those of continental biomass production. Advantages of algae biomass production include the absence of water limitation, plentiful sunlight, and perhaps most importantly, the fact that the land area used to produce algae would not be needed for other uses. Advantages of algae biomass production have been reviewed by Goldman et al. (1975), Shelef and Soeder (1980), North et al. (1981), Benemann et al. (1979), Anderson, and Richmond and Preiss (1980). It might be economically feasible, but it is not going to be politically realistic to use large areas of agricultural land to grow crops to be used as chemical feedstocks rather than food while there is starvation in the world. A serious problem for marine biomass production is nutrient availability. There are many possible solutions, including growing algae in areas of natural upwelling or using sewage or runoff; the technical details of solutions remain, nonetheless, to be worked out. Another difficulty is the nature of product harvesting. In the case of macroalgae, harvesting technology is well worked out for wild strains; however, the engineering of substrates to immobilize the seaweeds and protect them from storm and wave action is not satisfactory and this lack proscribes open ocean farming. For the microalgae, low cost harvesting techniques need to be developed because the product is very dilute. A typical phytoplankton culture reaches a concentration of a few hundred milligrams of cells per liter; by contrast, fermentations of bacteria may reach 100-200 grams per liter. Of course, sunlight is free, but we seriously question whether it might not be more practical to grow corn or trees as feedstocks for fermentations to produce chemicals than to grow algae.

Marine and continental biomass productivities, measured as carbon fixed per unit area per day, may in some cases be quite similar (Table 2, Ryther 1959; Lieth 1975). Under the best circumstances sugar cane, water hyacinth, and microalgae all produce on the order of 20 to 30 grams of dry biomass per square meter per day, which corresponds to 5 to 10 grams of fixed carbon per square meter per day, or an energy equivalent of about a hundredth of a gallon of gasoline. This amount is not enough to be wildly excited about. Under favorable circumstances marine biomass may be competitive with terrestrial biomass, but will not be superior.

Economies of scale will be very difficult to achieve for marine biomass production because of engineering and logistical problems. In many processes which would use biomass for chemical production, dry product is required. Removing water is much more straightforward for land-based agriculture than for marine biomass production.

One final point to be addressed in marine biomass production is the possible role of genetic engineering and other modern biological techniques which are beginning to be applied to algae (Sherman and Guikema 1981; Rochaix and van Dillewijn 1982). In the production of biomass there are typically four steps: research (i.e., strain selection), cultivation, harvesting, and processing. This process is shown schematically in Figure 2. In marine biomass production one must ask what properties should be selected during strain selection and what are the best techniques for selecting those properties. If genetic engineering is to be used, the question of survival in the wild

Table II. Biomass productivity

Energy Fixed as Carbon; Biomass Productivity.

Sugarcane
Water Hyacinth
Macroalgae $= \begin{cases}
20-30 \text{ g dry biomass/m}^2/d \\
80-100 \text{ kcal/m}^2/d \\
\Rightarrow 0.01 \text{ gal gasoline/m}^2/d \\
\sim 2-3 \% \text{ photosynthetic} \\
\text{efficiency} \\
5-10 \text{ g C/m}^2/d \end{cases}$

Averages

Continental I.8 g/m²/d
Oceanic total 0.4
Upwelling Zones I.5

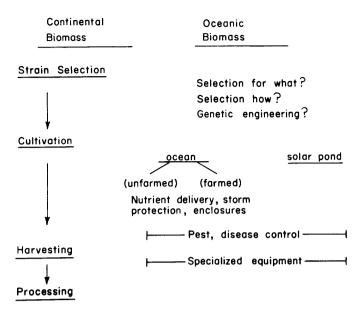


Figure 2. Steps in developing a biomass production process $% \left(1\right) =\left(1\right)$

must be addressed. It is the case with bacteria that genetically engineered strains are more fragile than the wild types. It may be necessary to control the marine environment much more closely than presently seems practical before genetic engineering will be helpful in marine biology.

The problems discussed above are in general technically solvable. In order to be sufficiently economically interesting to warrant the required research and development, however, marine biomass will require larger markets than those which are presently available. The next section will consider the sorts of products which might be candidates for large-scale production.

Chemicals Derived from Marine Biomass

There are two general strategies for marine chemicals: producing the high-value, low-volume chemicals exemplified by algal polysaccharides, or the low-value, high-volume products such as methane (i.e., energy). These will be considered in turn.

There are three commercially important algal polysaccharides – agar and carrageenans from red algae and alginic acid from brown seaweeds. These polysaccharides are produced in amounts – $1-5\times10^7$ pounds per year – which are considered intermediate—to-small quantity materials by the standards of the chemical industry (Chapman and Chapman 1979). The world markets are on the order of \$10^8 per year. This size market does not justify

a very expensive, long-term research program in biotechnology in the view of the chemical industry. It would be necessary either to expand the markets or uses or do relatively inexpensive research to increase the economics of production.

An important point about the algal polysaccharides is that their structures are complex (Figures 3, 4, and 5, Chapman and Chapman 1979; Percival and McDowell 1967). There are no competitive technologies for making these products from petroleum derived feedstocks. These products are quite secure from the standpoint of direct replacement by different technology, although they are, of course, vulnerable to replacement by materials with different structures and superior properties.

Carrageenan

Food = Gels with milk proteins

HO OH
$$OH$$
 $OSO_3^ OSO_3^ OSO_3^ OH$
 OH
 $OSO_3^ OSO_3^ OSO_3^-$

Figure 3. Carrageenan

Agar = Agarose + Agaropectin

Figure 4. Agar

Alginate

Figure 5. Alginate

A second favorable aspect of algal polysaccharides is that they are used in the food industry. The food industry is technologically underdeveloped, and these products could play a large role in a future technological expansion. The food industry is also extremely conservative, and the fact that these products are cleared for food use virtually guarantees their future acceptance.

There are certain uses for the algal polysaccharides for which there is no direct replacement. For example, carrageenan (Figure 3) forms gels with milk proteins and so is useful in stabilizing emulsions such as chocolate milk and ice cream (FMC 1977, 1981).

Agar (Figure 4), a related sulfated galactan, is uniquely important to microbiology and biotechnology. Supplies of this product are short; it is clear that world markets could absorb considerably more than the amounts presently produced, and in fact development of new uses would be dependent on and very likely to follow expansion of supplies. From the point of view of its gelling properties, the fewer sulfate and other charged groups in the agar, the better (Guisely and Renn 1977). The reaction below is enzyme catalyzed:

One could imagine isolating and cloning the gene for that enzyme and developing a bioreactor to carry out this conversion for upgrading native agar. It might be worthwhile to investigate carefully the economics of such a scheme.

Of the present commercially important polysaccharides, alginic acid (Figure 5) is the lowest in price. Its uses are

diverse, ranging from food to technology for immobilizing enzymes to coatings and sizing for textile, paper, and printing industries (Kelco 1981).

In order to justify a large research program in the area of polysaccharides, it will be necessary to define areas of future potential. Some specific opportunities include the following:

- (1) Enhanced oil recovery is a potentially very large market for polysaccharides if their properties are appropriate and they can be produced cheaply enough.
- (2) Certain polysaccharides, e.g., the lipopolysaccharide emulsan from the bacterium Acinetobacter calcoaceticus, could be used in petroleum transport and cleaning of vessels and tanks.
- (3) All of the algal polysaccharides mentioned here may have expanding roles in biotechnology. Agar is used as a culture substrate and in its highly purified form agarose, as a separation medium. All three phycocolloids have uses in enzyme immobilization technology.
- (4) The role of polysaccharides in food processing is likely to increase.
- (5) In any situation where the viscosity or interfacial properties of an aqueous system must be modified or strictly controlled, the phycocolloids can find use. The market in such uses will depend on the relative economics of the algal polysaccharides versus other polysaccharides of plant or microbial origin.

Figure 6 summarizes some specific opportunities to improve marine polysaccharides production and economics. An important point to note is that there are many potential co-products. For example, the brown algae which produce alginic acid also contain a good deal of the sugar fucose in a polysaccharide called

Opportunities (Macroalgae)

Strain Improvement:

Classical genetics; strain development

Plant cell culture To obtain what properties?

Genetic engineering New polymers?

Production

Improved farming techniques

Enzymatic treatments

Production engineering (supercritical fluids; magnetic separation)

Other

Energy farming?

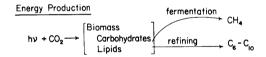
Coproduction of unusual sugars, lipids, enzymes.

Figure 6. Opportunities to improve marine polysaccharides production and economics

fucoidan. There may be a good potential market for fucose; however, no one currently makes cheap and plentiful fucose. Hence, market development would be required.

At the other end of the economic spectrum is methane, which is an extremely cheap and plentiful substance. Supplies are not unlimited, however, and schemes for methane production by anaerobic digestion of algae have been proposed. This plan is certainly technically feasible; various workers have shown that many types of algae are good digestion feedstocks (Chynoweth et <u>al</u>. 1981; Ryther <u>et al</u>. 1979; Kennan 1977; Uziel <u>et al</u>. 1975; Eisenberg <u>et al</u>. 1980, 1981). Algae contain very little refractory material such as lignin; water and sunlight are available. The chief obstacle is lowering the cost of production and harvesting enough to make methane production economical. It has been estimated that to be an economically realistic feedstock for conversion to methane, algal biomass must be produced and harvested at a cost of \$20-30 per ton (Dubinsky et al. 1979; Richmond and Preiss, 1980). This figure is presently unattainable because of difficulties with nutrient provision or harvesting. Schemes in which algae biomass production is combined with some other valuable function, such as waste treatment, are more likely to be successful. The advantages and disadvantages are summarized in Figure 7.

In between the extremes of polysaccharides and methane fall a few intermediate value products of potential interest. These products include vegetable-like oils and fatty acids from microalgae (Shifrin and Chisholm 1980), mannitol from macroalgae (Chapman and Chapman 1979), and glycerol from the salt-tolerant algae <u>Dunaliella</u> (Ben-Amotz and Avron 1980). Some of the <u>Dunaliella</u> strains contain large amounts of β -carotene; it might be worth more than the glycerol.



- Macroalgae photosynthesize efficiently; there is little lignin (or equivalent) in biomass; water and sunlight are available.
- 2) Engineering of production and harvesting are difficult and expensive; Nutrient limited.
- Combine with waste/sewage treatment?
 Combine with other power-generating schemes? (thermal gradient extraction?
 Nuclear waste heat use?)

Figure 7. Advantages and disadvantages of marine-biomass-based energy production

Marine Pharmaceuticals

The premise in discussing pharmaceuticals is that there is a large number of new compounds in the sea, and these can be screened for useful pharmacological activity. The premise is valid, but at present there are vanishingly few human or animal drugs based on or derived from compounds first identified in marine organisms (see Fenical 1982 for a review of marine natural products chemistry and Stein and Bordon 1982 for an introduction and bibliography on algae in medicine). Many of the bioactive molecules isolated from marine sources have been toxins. This predominance of toxic substances is an artifact of the methods of bioassay (that is, will a mouse or guinea pig injected with the material die?).

Consider some interesting molecules and their possible application. Figure 8 shows the structures of palytoxin, tetrodotoxin, and brevetoxin B. These compounds are the products of very complicated biosyntheses. Genetic engineering can handle cloning and expressing the gene for one enzyme; genetically engineering an organism which could express the many enzymes which would be required to synthesize these toxins is out of the question for the next 10 to 20 years. One must, of course, ask what purpose would be served by synthesizing these molecules; the market for paralytic agents is very small!

Figure 9 shows another class of compounds of much greater commercial interest, the carotenoids. It is becoming clear that many of these compounds have interesting biological activities. The fact that these occur as photosynthetic pigments in a large number of algae (Richmond and Preiss 1980) opens up an area in which the pharmaceutic industry has specific interest. Whether this industry has the resources to go into this area now is not clear

Some problems common to all marine pharmaceuticals are the following:

- (1) Screening unfamiliar organisms may be quite difficult.
- (2) There is a supposition among organic chemists that the structures found in marine species, because there is no particular advantage associated with volatility, have a tendency to be water-soluble and non-volatile, to have high molecular weight, and to be much more difficult to work with than the compounds usually handled.
- (3) There is a broad question of target. If any unique marine antibacterial agents were found, they might or might not be useful against mammalian pathogens.

The marine environment certainly is worth continued examination as a source of new compounds, but it is uncertain what the payoff will be.

Animals

The largest industry at the moment having to do with the sea is the production of finfish and shellfish. Here there are many

Figure 8. (A) Palytoxin; (B) tetrodotoxin; (C) brevetoxin B
Source: Fenical 1982

opportunities for chemical production perhaps using biotechnol-

ogy.

The pharmaceutics markets for the aquaculture and fish principally trout and catfish - could expand. Chemicals for
reproduction control and synchronization of fertility in fish

Figure 9. Carotenoids Source: Fenical 1982

would be very useful. Communication substances, particularly to attract fish, would be desirable. These are areas which would require a large research effort.

There is also room for a great deal of fundamental work in the microbiology and enzymology of spoilage and flavor modification.

Finally, an area which clearly deserves examination is by-product development. The viscera of fish might be used as sources of enzymes and fine biochemicals rather than as pet food. For example, it has been reported that carp guts contain a small peptide factor called longevin which increases the longevity of specific pathogen-free mice (Anon. 1982). The structural elements, fins, scales, bones, and exoskeletons surely contain interesting materials. An example is chitin, a polysaccharide isolated from crab shells, which has properties which are very distinctive and potentially useful in food, technology, biotechnology, and medicine (Rha, this volume).

Materials Modification

Any surface put into the sea eventually serves as a substrate for the growth of marine organisms. Any good solution to the problem of fouling will find a huge market. Biotechnology could make a large contribution to this area, summarized in Figure 10.

Research Opportunities

Research opportunities for organic chemicals from the sea may be divided into relatively immediate (i.e., less than five years), more distant, and very long term programs.

Materials Modification for Marine Use

Corrosion, Fouling

Off-shore drilling, production, mining Thermal gradient power extraction Floating nuclear/chemical facilities Wave power extraction Defense, transportation

Surface modification to control the attachment of marine organisms. Chemical control of surface microecology. Growth of calcareous layers and cathodic protection.

Friction Reduction

Figure 10. Possible biotechnology contribution to marine materials modifications

Relatively immediate opportunities include improvement of existing industries:

- (1) Development of useful by-products from the materials that are already collected by the fish or macroalgae industry: unusual sugars, enzymes, and other biochemicals. It should be possible to find high valueadded biochemicals in these by-products of existing industries, in which all of the collection work has already been done.
- (2) Process improvement enzymatic polysaccharide modification of the sort discussed above and food quality maintenance and verification present opportunities on a practical time scale.
- (3) Materials development for aquaculture especially improved fish feeds, materials for lining aquaculture tanks, and netting to which macroalgae will attach spontaneously when they are put into the water for algae farming.

The development of new products on this time scale is also possible:

- (1) Sugars It is clear that sugar chemistry is undergoing a renaissance. Everyone is considering sugars as starting materials (Fraser-Reid 1975; Fraser-Reid and Anderson 1980; Hanessian 1979; Smith and Williams 1979), and particularly as communication substances to the immune system. Materials such as fucose can have real use as chemical intermediates, if they can be provided, even at fairly high prices.
- (2) Polysaccharides Chitin is an example
- (3) The carotenoids and their analogs
- (4) High-value algal lipids that is, equivalents of jojoba oil: materials which have the right molecular weight range to go into high-quality lubricating oils and into

detergent-grade alcohols. These materials are presently quite expensive, and their supply is severely limited. Land-based biotechnology is seen as a plausible strategy to provide new sources of oils. There is no reason at all why the same thing should not be practical using algae.

More distant areas (more than 5 years) for development include:

- (1) Energy farming This area will have to be coupled with something else, either alternative forms of energy production (e.g., thermal gradient power extraction) or waste disposal. The economics will not justify the development of a pure marine energy production industry, when there is so much difficulty developing the corresponding industry continentally.
- (2) Pharmaceuticals The principal interest here will be in screening biochemicals from the sea. It is important to remember that when an interesting compound is found, it is going to have to be something that can be synthesized in a laboratory, because one cannot duplicate the complex biosyntheses in microorganisms.
- (3) Polysaccharides for oil production and transport.
- (4) Chemicals or biotechnological processes will be required to control the problems of fouling and waste disposal.
- (5) Agricultural Chemistry for Marine Systems A fairly substantial effort in production of biologically active substances for use with marine plants and animals could be justified. The fact that this effort has not already started is a reflection of the fact that the chemical industry is only now really discovering land-based agricultural chemistry. The opportunities there and the things which are learned - particularly if one can find decent delivery systems - will justify the research in the marine environment.

Long-term opportunities are more speculative.

- (1) Clearly, the sea represents a rich source of new kinds of microorganisms for screening. A tremendous untapped gene pool exists for proteins and enzymes for use in recombinant DNA. In a major sense, this potential for new proteins and enzymatic activities may prove to be one of the most important long term contributions of marine biology to biotechnology.
- (2) Another interesting area rests on the ability of many marine organisms to extract useful elements selectively from the sea, for example, diatoms concentrate silica to the extent of about 10¹². Almost nothing is known about these marine transport systems. Their basic microbiology may, in the long term, provide the basis for important and interesting new ways of mineral or element extractions from the oceans. For example, there was quite a seriously considered scheme for growing

 $\frac{Teredo}{worm}$ worms on piles in the ocean, because the $\frac{Teredo}{worm}$ extracts vanadium from seawater. If one is willing to grow worms, then one should certainly be willing to work with organisms that have the appropriate characteristics to extract metals.

- (3) There are whole classes of organisms that live in unusual circumstances. One of the most interesting environments is the rift region spouters, which release large amounts of H₂S. A problem of society right now is utilizing H₂S; there are not many good ways to solve this problem.
- (4) Many of the marine algal systems have photosynthetic capacities which have no clear counterpart on land.
- (5) Marine pheromones and communication systems would be useful for controlling the movement of marine animals during harvesting.

We see those areas as being particularly promising. It is clear that there <u>are</u> major opportunities, but it is also clear that they are going to require much more active exploration than the corresponding opportunities on land. It is going to behoove all of us who are interested in this area to take a very careful look at the economics of proposed targets and the downstream development after the advance biology has been done, in order to come up with the projects which justify their expenses.

References

- Anderson, R.E. 1979. Biological Paths to Self-Reliance: A Guide to Biological Solar Energy Conversion, Van Nostrand Reinhold, New York, NY.
- 2. Anonymous, 1982. The elixir of life. Nature, 296:392-393.
- 3. Ben-Amotz, A. and M. Avron, 1980. In G. Shelef and C.J. Soeder, Eds., Algae Biomass, Elsevier/North Holland Biomedical Press, Amsterdam, pp. 603-610.
- Benemann, J.R., J.C. Weissman, and W.J. Oswald, 1979. Algal biomass. In A.H. Rose, Ed., Microbial Biomass, Economic Microbiology, V. 4, Academic Press, New York, NY, pp. 177-206.
- Chapman, V.S. and D.J. Chapman, 1979. The Seaweeds and Their Uses, 3rd Edition, Chapman and Hall/Methuen, New York, NY
- Chynoweth, D.P., S. Ghosh, and D.L. Klass. Anaerobic digestion of kelp. In S.S. Sofer and O. Zaborsky, Eds., Biomass Conversion Processes for Energy and Fuels, Plenum Press, New York, NY, pp. 315-338.

- 7. Dubinsky, Z., S. Aaronson, and T. Berner, 1980. Some economic considerations in the culture of microalgae. In G. Shelef and C. Soeder, Eds., Algae Biomass, Elsevier/North Holland Biomedical Press, Amsterdam, pp. 819-832.
- 8. Eisenberg, D.M., W.J. Oswald, J.R. Benemann, R.P. Goebel, and T.T. Tiburzi, 1980. Methane fermentation of microalgae. In D.A. Stafford, B.I. Wheatley, and D.E. Hughes, Eds., Anaerobic Digestion, Applied Science Publishers, Ltd., London, pp. 99-111.
- 9. Eisenberg, D.M., B. Koopman, J.R. Benemann, and W.J. Oswald, 1981. Biotechnol. Bioeng. Symp., 11:429-448.
- 10. Fenical, W., 1982. Natural products, chemistry in the marine environment, Science, 215:923-928.
- FMC, 1977. Carrageenan: Monograph Number One, FMC, Springfield, NJ.
- FMC, 1981. Carrageenan: Monograph Number Two, FMC, Springfield, NJ.
- 13. Fraser-Reid, B., 1975. Some progeny of 2, 3-unsaturated sugars they little resemble grandfather glucose, Acct. Chem. Res., 8:192-201.
- 14. Fraser-Reid, B., and R.C. Anderson, 1980. Prog. Chem. Org. Nat. Products, 39:1-61.
- 15. Goldman, J.C., J.H. Ryther, and L.D. Williams, 1975. Mass production of marine algae in outdoors culture, Nature, 254:594-595.
- Guisely, K.B. and D. Renn, 1977. Agarose, FMC, Springfield, NJ.
- 17. Hanessian, S., 1979. Approaches to the total synthesis of natural products using "chiral templates" derived from carbohydrates, Acct. Chem. Res., 12:159-165.
- 18. Kelco, 1981. Kelco Algin, Kelco, Chicago, IL.
- 19. Kennan, J.D., 1977. Energy, 2:265-373.
- Lieth, H., 1975. Primary productivity in ecosystems. In W.H. Van Dobben and R.H. Lowe-McConnell, Eds., Unifying Concepts in Ecology, Dr. W. Junk B.V. Publishers, the Hague, pp. 67-88.
- 21. North, W.J., V. Gerard, and J.S. Kuwubara, 1981. Biomass

- production by freshwater and marine macrophytes. In D. Klass, Ed., Biomass as a Non-Fossil Fuel Source, ACS Symp. Series, 144:77-98.
- 22. Percival, E. and R.H. McDowell, 1967. Chemistry and Enzymology of Marine Algal Polysaccharides, Academic Press, New York, NY.
- 23. Richmond, A. and K. Preiss, 1980. The biotechnology of algaculture, Interdisciplinary Sci. Rev., 5:60-70.
- 24. Rochaix, J.-D. and J. van Dillewijn, 1982. Transformation of the green algae <u>Chlamydomonas reinhardii</u> with yeast DNA, Nature, 296:70-72.
- 25. Ryther, J.H., 1959. Science, 130:602-608.
- 26. Ryther, J.H., L. Williams, M.D. Janioak, R.W. Stenberg, and T.A. DeBusk, 1979. Biomass production of marine and freshwater plants. In 3rd Annual Biomass Energy Systems Conference Proceedings, SERI, Golden, CO.
- 27. Shelef, G. and C.J. Soeder, Eds., 1980. Algae Biomass, Elsevier/North Holland Biomedical Press, Amsterdam.
- 28. Sherman, L.A. and S.W. Guikema, 1981. Photosynthesis and cloning in cyanobacteria. In A. Hollander, Ed., Microorganisms for Chemicals, Plenum Press, New York, NY.