Evaluating Alternate Raw Materials and Processes

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Fragrance ingredients have life cycles in the hundreds and even thousands of years. The evaluation of these products, processes and alternate raw material sources is a complex and continuous process which, when successful, can lead to competitive advantages that pay dividends for decades. Superior raw material strategies have created the leaders in our industry today.

However, these strategies can be upset by new safety or scientific results as well as by changes in political and social concerns. The rapid changes in the world today present unparalleled threats and opportunities.

I wish to share with you some of the techniques I use to navigate this unstable environment. A realistic understanding of the current and near term future situation can lead to more successful projects as well as helping to orderly exit those areas where one is unlikely to win in the long term. We all hope to find areas in which we can do something much better than others, thereby gaining both the material benefits and the psychological benefits of being a winner. In today's world, this type of winning benefits us all.

Before getting into the nuts and bolts, I would like to provide some anecdotal evidence of the value of such analysis.

During the 1970s, severe shortages, extraordinarily high prices and sales of water instead of essential oil, convinced many that synthetics would replace most natural materials. Being a major producer of clove leaf-derived eugenol, I had to decide if we should also move in this direction. Since I was already planning to attend the International Essential Oil Congress in Kyoto Japan, I decided to also visit Indonesia to study the economics of producing clove leaf oil.

This visit saved me hundreds of thousands of dollars in wasted R&D. Panic buying was the sole reason for increased prices. Furthermore, the Indonesian Government was planting huge numbers of clove trees in order to reduce imports of clove buds for their cigarettes. Since wives and children collected the fallen leaves in their spare time, labor costs for producing clove leaf oil were almost nil. Families sold their leaves to a local collector, who brought them to the local distillery which used spent leaves for fuel and a mud dammed stream for water. A simple, efficient system that completely beat any synthetic process. After the speculative crash, clove leaf oil and its derivatives remained readily available at reasonable prices for decades.

However, all was not rosy. A side trip organized by a new friend from Kyoto, revealed that technology transfer was under way to Indonesia. A new plant using Western know-how was being built to locally convert clove leaf oil to eugenol and isoeugenol. Local *daily* wages were less than our *hourly* wages at home.

By analyzing the market for eugenol, we found that we could retain some sales, even at higher prices, but only in the very small segment of the market requiring chemically purified eugenol. Losing three quarters of our business was not a recipe for success. We had to do more.

Recent catalyst discoveries in the oxo process permitted this carbon monoxide petrochemical process to be run at low pressures rather than at the hundreds of atmospheres previously required. With less expensive low-pressure equipment, several fragrance raw materials could be made much cheaper with the oxo process than by the then current methods of manufacture.

Carbon monoxide is an interesting raw material in that it is a poisonous gas that can be made very cheaply, but only in very capital intensive, large factories. At that time, the smallest generator cost about US$3.5 million to produce thousands of tons of CO for aboutUS$0.35 per kilo. CO was available in cylinders throughout the world for aboutUS$35 a kilo. However, only in the USA was CO available in tube trailers for aboutUS$3.50 per kilo. It turned out that tube trailer transport of CO was not legally permitted in Europe or Japan and was not available elsewhere.

Helped by a local university professor, we succeeded in developing a process and an odor acceptable product. Since our USA competitors could readily imitate our innovation, we had to develop a strategy to capitalize on our advantage before being imitated.

From discussions with perfumers, we found that our target product was limited in usage both geographically and functionally by its strong odor characteristics. It could not be used in large concentrations without destroying a fragrance and it was only used where a preference for its odor type was well developed. This product was clearly limited by function not price. Lower prices would not appreciably increase tonnage.

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If we could quickly capture most of the limited tonnage we could optimize our production cost and profitably defend against our competitor's counterattack. By combining major price cuts with large sales incentives, one of our salesmen was able to build a family room with fireplace while our company captured 80% of the world market.

Process development and market research took more than two years and during the market battle, selling prices dropped by 50%, but this became one of our most profitable products. It more than made up for the business we had lost to Indonesia and my fellow employees did not have to take a pay cut or worse. When our major competitor finally bought from us and a large would-be competitor with an on-site generator closed their research activities, I knew we had won.

What Did We Learn?

Detailed, knowledgeable, unbiased information and analysis were critical to properly assess the situation and to gain the conviction needed to act decisively. Within our industry, the most useful information is often unavailable except through substantial amounts of direct individual effort. Flexibility and an inquiring mind are key criteria.

Understanding the constraints on the usage of an item is extremely important. Is usage limited primarily by price or by function? A function-limited material will not grow in any substantial way even with major price reductions. However, major price reductions on a material whose usage has been limited primarily by price may, after a three to five year development period, explode in usage, straining or exceeding production capacity and drawing in excessive competition.

This happened to hexyl cinnamic aldehyde, when we reduced its price to below that of amyl cinnamic aldehyde. Perfumery input indicated that HCA could be used at much higher concentrations than ACA but was not because of its higher price. Since our competitive position was stronger on HCA than on ACA, we decided to risk a lower price even though it initially lowered profits without increasing volume. However, after several years, the gamble paid off in spectacular increases in tonnage and profits.

Diverse and iconoclastic perfumer input is absolutely necessary to adequately assess this type of market possibility. Can the ingredient concentration be doubled or tripled? Can the concentration be 5%, 10% or even more without destroying a fragrance compound? Is the odor type broadly acceptable and applicable? What would be used if this material were not available, or if something else were available at a much lower or higher price? If competitive materials have been available for a long time, why have the usage patterns developed as they have?

Perfumer responses to these types of questions can provide a pretty good idea of a potential future market.

In performing the initial cost/benefit analysis, assume that R&D efforts will be successful. Make the detailed financial analysis giving best possible and worst imaginable results. Do not miss the hidden costs of safety testing or potential environmental risks. Do not discount unusual or non-traditional competition. It has been amazing to me, how many financially disastrous projects could have been predicted with more realistic and detailed analysis. On the other hand, many potentially great projects are killed by excessively pessimistic forecasts coming from slanted or outdated perspectives. By establishing the widest range of best and worst, it becomes easier to kill those projects that will fail financially even if technically successful as well as keep alive projects that have the potential of greatness.

Finally, be realistic about time. The life cycle of most fragrance raw materials is in the hundreds of years and the introduction period is also very long. An entirely new material may take a decade or more to move out of the development stage and into the growth part of its life cycle. Even for materials that are widely known to perfumers a radical change in price will take three to four years and more likely five to seven years before growth accelerates. The reasons for this lie in the cycle time for perfumery projects. Barring sudden supply or safety problems, a major project, which could strongly benefit from your 'wonderful new fragrance value', may not come up for a year or two. Then product testing will chew up six to twelve months before a trial roll out. Following successful trials, the full roll out may be a year later.

Then, if successful, everyone will analyze the product and find that they must immediately use the winning ingredient. When they find that expanding production will delay delivery until next year (at best) they may shift to a substitute, possibly forever.

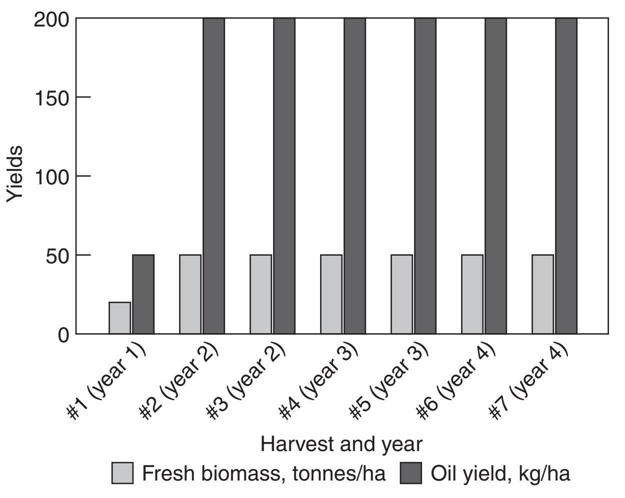
Good advanced planning and close customer contact can greatly help to successfully manage the often-chaotic transition from the development part of the life cycle to rapid growth. Pre-engineered expansion plans, short communication links and rapid response times can help avoid killing a product through bumbled deliveries. Pre-ordering of long lead-time items can save many months when big demand hits, often costing only a small percentage of the total development cost. The benefits of good planning are well worth the effort.

Following are examples of detailed evaluations for two materials that, in my opinion, represent substantial opportunities for profitable development. One involves new natural plant sources for safrole and the other examines possible modifications to the Story Process to provide a low cost route to a potential major macro cyclic musk.

Alternative New Natural Sources of Safrole

Safrole is the primary raw material source for the production of heliotropine and for piperonyl butoxide (PBO). The latter is synergist for natural pyrethrum, which is currently the only insecticide allowed for use in food stores.

Figure 1. Piper—typical average yields (Brazil and elsewhere) at a planting density of 45,000 plants/HA for non-selected planting stock



Production of natural safrole has traditionally depended on the destructive harvesting of wild trees, *Ocotea pretiosa* in Brazil and certain *Cinnamomum* species in China and some neighboring countries. Unfortunately, world demand

Table 1. Comparative gross returns from Piper and some other low unit-value, bulk-volume traded oils growable in a similar climate

	Oil output over three years (kg/ha)	Nominal sale price ($/kg)	Gross returns over three years ($/ha)	Economic lifetime of plot (years)
Piper	850	5	4,250	? (est. min. of 6)
citronella	400	5	2,000	3
medicinal eucalyptus	300	5	1,500	15

Table 2. Costing of production for a new crop (indicative breakdown for commercial farming of Piper)

Capital investment costs (Year 1)	Approx. % of total cost
(a) Plantation establishment (land preparation, plant multiplication, field planting, etc.)	40
(b) Farming equipment	30
(c) Distillery and other infrastructure	30
Annual operational costs (Year 2 +)	**Approx. % of total cost**
(a) Cultivation and harvesting	50
(b) Distillation and sales	50

for safrole, which now totals around 2,000 tons per year, is rapidly leading to the extinction of the traditional tree sources.

Synthetic processes can be used to make safrole and its derivatives, but at generally higher costs than the current market prices. However, in spite of high costs, prospective shortages for natural safrole have driven PBO manufacturers to seriously consider plans for total synthesis.

A competitively priced natural and renewable source could help develop the market further by providing stable pricing and assured supply. During the 1990's two species of plants have emerged as potential commercial sources:

- In China's Sichuan Province, 'Rock cinnamom' (*Cinnamomum petrophyllum*; syn. *C. pauciflorum*)- a relative of the traditional Asian sassafras tree - has been domesticated and is now in early commercial development. This provides an oil from the non-destructive harvesting of leaf starting three years after planting and annually thereafter.
- In the Southern Amazon region of Brazil, domestication and evaluation of a perennial shrub, *Piper hispidinervium*, was initiated in 1990 under a British government aid project. This also contains safrole in its leaves but the first harvest can be taken in the first year of planting and two or three annual harvests are possible thereafter. Trials in Southern Africa and China have been made since the mid-1990s.

How Does One Evaluate the Viability of a New Crop?

The steps necessary for the evaluation of the viability of production by a farmer / distiller of a new species involve:

- Collection of seeds from wild plants.
- Creating a nursery.
- Multiplying the plant stock.
- Establishing large trial plots on the potential production site.
- Harvesting and distilling on a pilot commercial scale over several years.

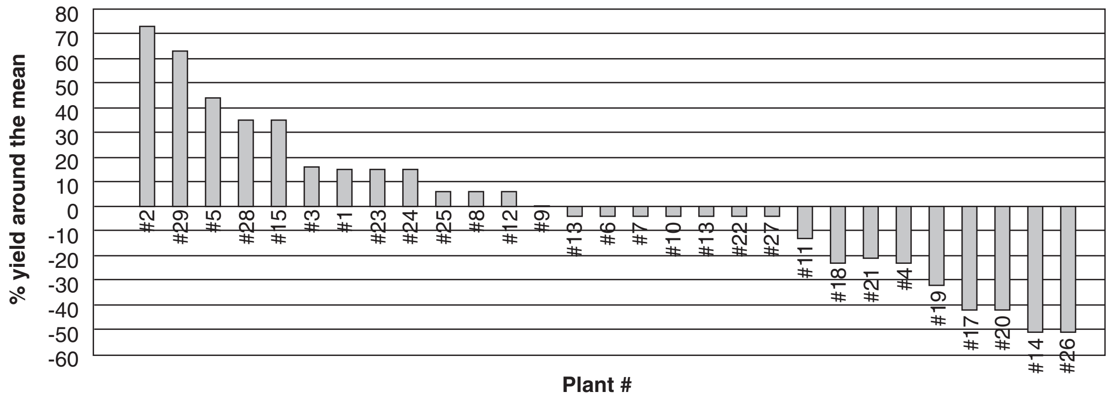


Figure 2. Means of Improving Returns—Elite Plant Selection with Piper

- Assessing field performance (yields and oil quality acceptability) and means of improving productivity.
- Carrying out an economic evaluation.

The first evaluation step requires posing the following questions:

- Do the results - in the new microclimate and soil conditions - compare favorably with other locations?
- Do estimated gross returns compare favorably with other prospective crops for the site? If so, a more thorough cost / return evaluation is necessary.

Figure 1 and Table 1 illustrate the results for a *Piper hispidinervium* trial on a site in Southern Africa.

Since production costs inevitably vary according to the specific production site, country and the intended mode of production, a prospective commercial grower/distiller must consider a number of other critical factors:

- What is the minimum scale of production for viability, given that the product is of a low unit-value and that economies of scale apply?
- What are the labor costs for weeding and harvesting and is an investment in mechanization justified?
- Is it worthwhile to invest in irrigation in order to extend the growing season and to obtain an extra crop?
- What is the best option for boiler fuel? Buying oil or coal or wood or, alternatively, growing a eucalyptus wood lot or burning the residual biomass?

The Potential for Improving Returns

Plant productivity has a major impact on profitability. Improvement experiments can be readily performed in the field, especially with a fast growing crop like Piper. The 'research' is simple and equipment purchase can be limited to several plastic bags, a spring balance and a knife or clipper.

Figure 2 shows a typical spread of the leaf biomass yields from randomly selected individual Piper plants within a plot raised from seeds collected in the wild. The zero line represents the average leaf yield for all of the plants while the (+) and (-) figures represent the percent yield above and below the average for individuals. It can be clearly seen that a significant number of superior and very poor performing plants occur within the population.

Identification and selective multiplication of elite plants would result in yield improvement of 30% or more in a single step. Confirmation of oil yield and quality can be obtained through lab distillations and GLC analysis.

Clearly, adoption of selective breeding can make all the difference between a marginal or attractive return from Piper oil production.

Figure 3. Comparative oil yields of sichuan and Piper Oils over Years 1-6 (Piper at 45,000 plants/ha and two harvests per year)

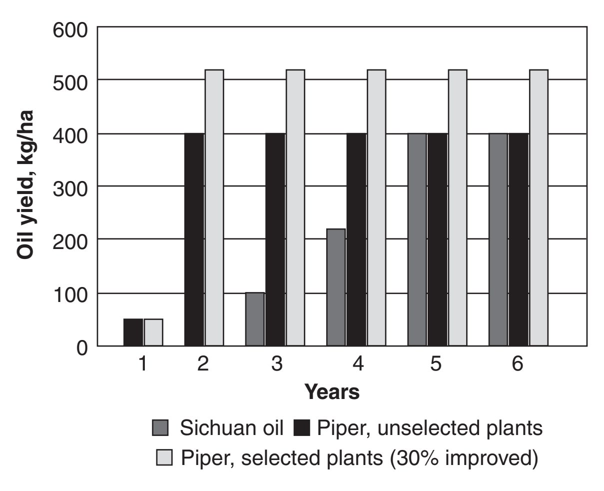
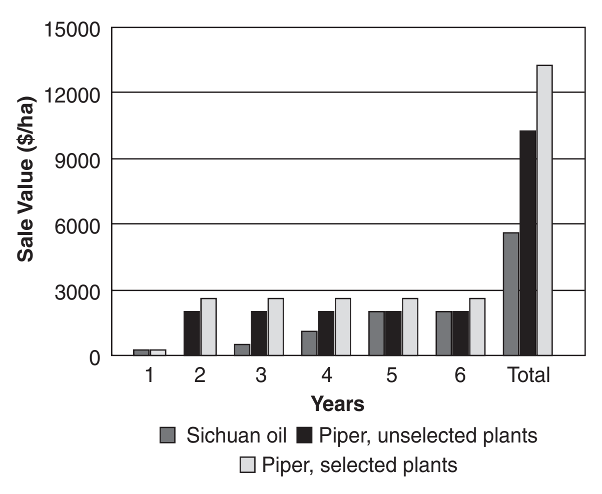


Figure 4. Sichuan vs. Piper



The Crunch Factor: Piper versus Sichuan *C. petrophyllum*

The final step in an evaluation resides on an assessment of competitiveness against the opposition.

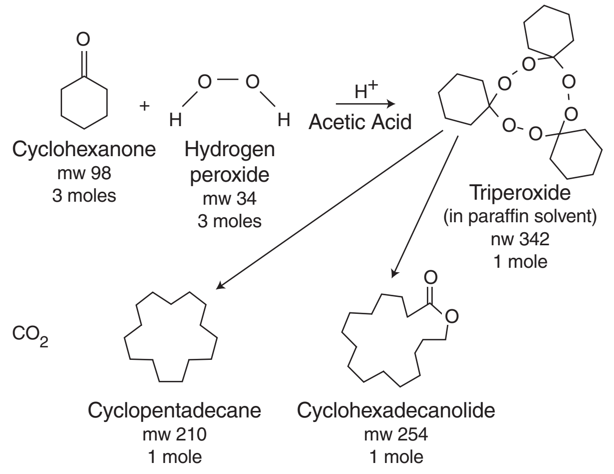
Figure 3 provides a comparison, using available information of the oil yield predicted per hectare from Sichuan *C. petrophyllum* and Piper. Note that cash flow for the Sichuan oil does not start until the third year after planting and does not match that of unselected Piper until year 5.

Figure 4 translates these figures into comparative gross returns per hectare, using a nominal sale price of US$5 per kilo:

- Piper clearly is more attractive in terms of early significant cash flow.

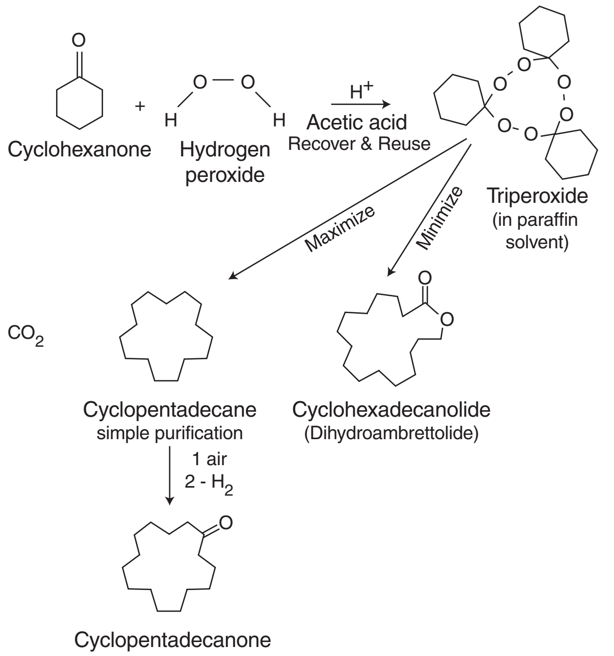
C. petrophyllum has the advantages of an expected longer economic lifetime and only one harvest operation per year (but this cannot be mechanized).

Figure 5. Summary of Story Process Chemistry



Chemical stoichiometry at 100 percent theoretical yield
294K of cyclohexaonone + 102 k of Hydrogen Proxide (100 percent) will yield 2019 of cyclopentadecane of 254 k of cyclohexadecaneolide or 105 k of cyclopentadecane and 127 k cyclohexadecanolide

Figure 6. Summary of Story Process Chemistry research objectives



The Future of Natural Safrole

At present, it is difficult to predict where we will be in 10 years:

- Will total synthesis have replaced natural safrole on the market place?

  or

- Will the Sichuan oil dominate the market?

  or

- Will the market be shared between Sichuan and Piper oils?

  and

- Will Piper oil largely be produced in South America or Asia or Africa?

Whatever the eventual outcome, it seems clear that, as for eugenol 25 years ago, total synthesis is not the only route to solve a raw material supply problem.

Table 3. The Story process—theoretical and calculated actual

	Mole ratio	Molecular weight	Theory wt/kg	Actual wt/kg	% of theory	Actual unit prices	Actual cost/kg
Ingredients :							
Cychexanone	3	98	1.23	6.3	19.5%	$1.00	$6.30
Hydrogen Peroxide 50%	3	34	0.85	4.5	19.0%	$0.60	$2.70
Acetic acid solvent			0	6.2		$0.50	$3.10
Paraffin solvent (98% recovered)			0	0.85		$0.70	$0.60
Miscellaneous							$0.80
Total RM costs :							$13.50
Estimated working costs :							$10.00
Total manufacturing cost :							$23.50
Actual Products :							
Cyclohexadecanolide		254		0.5			
Cyclopentadecanone		224		0.5			
Product mixture calculated mw :	1	239	1	1			

The Story Process

Let us now move into the musk area.

As you all know, concerns were raised during the 1990s over safety aspects of many of the most widely used synthetic musks. With DNA testing now available and environmentalists advocating greater application of the precautionary principle, who knows what the future will bring. Nature identical materials may be no safer than synthetics, but we at least know that man has been able to co-exist with them for thousands of years and they clearly biodegrade in reasonable time periods. One of the potentially lowest cost processes to manufacture nature identical macrocyclic musks is the Story Process.

The chemistry of the Story Process is shown in the Figure 5. It involves the reaction of three molecules of cyclohexanone, a widely available commodity chemical, and three molecules of the equally widely available hydrogen peroxide, to form a cyclic peroxide that is heated to decompose primarily into cyclohexadecanolide and cyclopentadecane plus carbon dioxide.

Dr. Story invented this process in the late 1960s while doing air pollution research at the University of Georgia. He was so enamored of macrocyclic musks that he went on to co-found the Story Chemical Company, which produced and sold cyclohexadecanolide, also known as dihydroambrettolide, using his process until the company was sold in the late 1970s and production was stopped.

However, times change, patents run out, and this old and possibly overlooked process may yet contain some gold and possibly even a gold mine.

Research Objectives

Cyclopentadecane, the unwanted by-product of Story's invention, can be easily and inexpensively converted with air and catalyst into cyclopentadecanone, as shown in Figure 6. Cyclopentadecanone is the principle component of Firmenich's Exaltone. Being a saturated macrocyclic ketone, cyclopentadecanone provides high odor intensity and great chemical stability while retaining the positive allure of being a nature identical material.

Perfumers have told me that if this product could be reduced in price to the range of the polycyclic musks, usage would go up dramatically. Present prices in the hundreds of dollars per kilo limit usage to only a few tons per year. The Story process, at least theoretically, presents the possibility of dramatic cost reductions.

Unfortunately, it is not easy to reach the theoretical optimum.

By examining the published literature and then tracking down Dr. Story and his colleagues with the help of the alumni office of the University of Georgia, it was possible to piece together a fairly good representation of the actual production process practiced during the 1970s.

By costing out this process with current unit prices in a less expensive part of the world, it is possible to determine that one kilo of cyclopentadecanone and cyclohexadecanolide, consisting of more than 50% cyclopentadecanone, could be produced at a production cost of approximately US$23.50 USD per kilo. Overall, this represents only 20% of the theoretical yield, approximately half of the result expected if the best published literature results were obtained for each of the five synthesis steps.

Let us systematically examine the variance of reality from the theoretical optimum and develop an action plan to reduce some of the major variances.

By examining the process in detail, it appears that there are three primary areas where there is room for substantial improvement.

Table 4. The Story Process—variance analysis and potential improvements

			$2.00 recovery in acetic acid	Increase yield by 10%	Increase yield by 20%	Increase yield by 40%		
Improvement:								
Yield as % of theory		20%	20%	30%	40%	60%	80%	100%
Ingredients:	Actual unit prices	Actual cost per kg						
Cychexanone	$1.00	$6.30	$6.30	$4.20	$3.15	$2.10	$1.58	$1.26
Hydrogen peroxide 50%	$0.60	$2.70	$2.70	$1.80	$1.35	$0.90	$0.68	$0.54
Acetic Acid solvent	$0.50	$3.10	$1.10	$0.73	$0.55	$0.37	$0.28	$0.22
Pariffin solvent (98% recovered)	$0.70	$0.60	$0.60	$0.40	$0.30	$0.20	$0.15	$0.12
Miscellaneous reagents and freight		$0.80	$0.80	$0.53	$0.40	$0.27	$0.20	$0.16
Total RM Costs:		$13.50	$11.50	$7.67	$5.75	$3.83	$2.88	$2.30
Total Working Costs:		$10.00	$10.00	$7.33	$6.00	$4.67	$4.00	$3.60
Fixed:		$2.00	$2.00	$2.00	$2.00	$2.00	$2.00	$2.00
Variable:		$8.00	$8.00	$5.33	$4.00	$2.67	$2.00	$1.60
Total Manufacturing Cost:		$23.50	$21.50	$15.00	$11.75	$8.50	$6.88	$5.90
Cyclopentadecanone: plus some cyclohexadecanolide								
Selling price with 40% gross profit		$39.17	$35.83	$25.00	$19.58	$14.17	$11.46	$9.83

Assumptions:
- That solvent and miscellaneous costs will vary directly with yield.
- That US $2.00 of the working costs are fixed and that US $8.00 varies directly with yield.

Potential Process Improvements:
- Save $2.00 per kilo by recovery of at least 70% of the value of the Acetic Acid either through recycle or alternate use.
- Improvement of yield from 20% to 30% by better temperature control in a backmixed reactor.
- Improvement of yield from 30% to 40% by elimination of crystallization purification of cyclopentadecane.
- Potential improvement through process breakthroughs to 60% yield.

Variance Analysis and Potential Improvements

The first objective is to recover the acetic acid value: During the initial reaction, acetic acid is one of two solvents used to keep the concentration of the dangerous peroxide intermediates safely out of the explosive range until decomposed by thermolysis. Much of theUS$3.10 per kilo that this solvent contributes to the product's cost may be recovered if the waste aqueous acetic acid can be recycled by distilling off excess water or recovered in some other way.

The second objective is to reduce tar, improve yield & selectivity to cyclopentadecane: Substantial high boiling tars and residues are formed during the thermolysis reaction. Since most are related to the starting materials, a reverse reaction may be occurring during the heat up period. At the highest reported temperatures, the maximum published combined yield of products was about 60% of theory with two thirds of this cyclopentadecane. At the time of commercialization, no commercial use was found for cyclopentadecane. Fractions from the 1970's are still in inventory at one of the present day successors to the Story Chemical Company. There is no evidence of any effort to determine optimal conditions to maximize this unwanted by-product.

More precise control of the heat up time, reaction temperature and residence time could be quite useful for improving the overall yield and selectivity to cyclopentadecane. A back mixed reactor system would permit rapid heat up and other temperature studies as well as screening of various catalysts. A single output product would also reduce the equipment needs to purify co-products. There is very little published work in this area, leaving much room for new discoveries and possibly patents.

The third objective is to simplify cyclopentadecane purification : Impurities interfere with the oxidation process. Crystallization was used for purification since fractional distillation did not produce adequately pure feedstock. Crystallization is one of the most costly purification methods in term of capital investment, operating costs, and product losses. An examination of alternate purification methods including a review of the methods used to purify feedstock for similar commercial oxidations may prove fruitful. A more detailed examination of the impurities removed by crystallization could help identify the problem impurities and initiate a specific treatment.

In summary, my analysis reveals the following potential:

- Save US$2.00 per kilo by recovery of at least 70% of the value of the acetic acid either through recycle or alternate use.
- Improvement of yield from 20% to 30% by better temperature control in a back-mixed reactor.
- Improvement of yield from 30% to 40% by elimination of crystallization purification of cyclopentadecane.
- Potential improvement through process breakthroughs to 60% yield.

As can be seen from this analysis (Table 4), even partial success in this research would result in being able to sell cyclopentadecanone at US$20 per kilo with a 40% gross profit. Major research breakthroughs could lead to prices in the low teens potentially even in theUS$10 per kilo range.

Would an internal cost ofUS$12 and/or a selling price ofUS$20 per kilo allow:

- cyclopentadecanone to capture a large part of the world musk market, and
- can cyclohexadecanolide either be eliminated through process modifications or used/sold at the same price?

That is a hundred million dollar question. A gold nugget, a gold mine or only fool's gold? Your decision. ■

References

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