KEY WORDS: COCAMIDOPROPYL BETAINE, SYNTHESIS, ANALYSIS, PURITY

• *This paper presents the methods for producing coca-midopropyl betaine (CAPB), an important secondary surfactant in cosmetic formulations, household cleaners, dishwashing agents and technical applications. With the widespread use of CAPB, more analytical methods to determine its contents and byproducts are needed. The authors describe the current methods to determine CAPB purity and other characteristics.*

• *Cet article présente les méthodes de production de la cocamidolpropylbétaïne (CAPB), un tensio actif complémentaire important des formulations cosmétiques, des produits d'entretien et de vaisselle et de divers produits techniques. Par suite de l'emploi trés large de la CAPB, davantage de méthodes analytiques se révèlent nécessaires pour déterminer sa teneur et ses sous produits. Les Auteurs décrivent les méthodes habituelles pour évaluer la pureté de la CAPB ainsi que d'autres caractéristiques.*

• *Diese Arbeit präsentiert Methoden der Produktion von Cocamidopropyl Betainen (CAPB), ein sekundär wichtiges Tensid in kosmetischen Formulierungen, Haushaltsreinigern, Gesschirrspülmitteln und technischen Anwendungen. Mit der breiten Verwendung von CAPB werden mehr analytische Methoden, um die Inhaltsstoffe und Nebenproduckte zu bestimmen, benötigt. Die Autoren beschreiben die aktuellen Methoden um die Reinheit und andere Eigenschaften von CAPB zu ermitteln.*

• *En este artículo se presentan los métodos para producir cocoamido propil betaína (CAPB), un tensioactivo secundario importante en formulación cosmética, en detergentes caseros, en lavavajillas, y en aplicaciones técnicas. El empleo generalizado de CAPB hace necesario disponer de métodos analíticos para determinar sus contenidos y subproductos. Los autores describen los métodos corrientemente empleados para determinar la pureza de CAPB y otras características.*

Cocamidopropyl Betaine

Methods for producing CAPB and new analytical methods for determining purity and side-product composition

B. Grüning, PhD, D. Käseborn and H.I. Leidreiter, PhD
Th. Goldschmidt AG, Essen, Germany

There are many detergent and foaming surfactants available for toiletries on the market. However, only a handful of products need to be considered to focus on the raw materials that have a strong market. Of these, the most important are the anionic surfactants, such as lauryl sulfates and lauryl ether sulfates.

A range of secondary surfactants has been developed for use with these efficient and cost-effective primary surfactants. In general, formulators use secondary surfactants to improve the properties of the primary surfactants and to optimize product performance. The most important secondary surfactant is cocamidopropyl betaine (CAPB), also called coco fatty acid amidopropyl betaine.[16,17] Since its introduction into the market in the 1960s, CAPB has become essential in surface-active formulas.

Benefits: Combining primary surfactants with CAPB reduces skin and mucus membrane irritation,[9,10,15,21] improves the conditioning properties of hair shampoos[14,19] and produces a pleasant, smooth skin feel. Formulas that include CAPB thicken easier, develop better foam and give a better cleaning performance than formulas without CAPB.[4]

The use of CAPB in efficacious, mild dishwashing liquids and oral hygiene products are the latest examples of CAPB's versatility. Its excellent toxicological profile, which has been documented by many investigations and reports in the past few years, is one reason for its success in dentifrice products.[12]

Despite the widespread use of CAPB, no comprehensive documentation of its synthesis, analysis and minor components exists. By reviewing the synthetic process, we can also document its composition and byproducts. We will also assess new analytical methods, such as the direct quantitative determination of CAPB.

Production Methods

Amide formation: The methods for producing fatty acid amidopropyl betaines basically follow a scheme that has shown validity for some time. Forming the fatty acid amide is the first step (Figure 1-1); carboxymethylating the amide is the second (Figure 1-2).

For CAPB, the first step reacts 3-aminopropyl-dimethylamine (DMAPA) with either fatty acids, fatty acid methyl esters or directly with natural fats (fatty acid glycerin esters). The predominant source oils used — hydrogenated coconut oil and, occasionally, hydrogenated palm kernel oil — deter

First presented in April 1996 at the Forum Cosmeticum in Salzburg, Austria. Published in German in *Parfümerie und Kosmetik*, **77** 244 (1996)

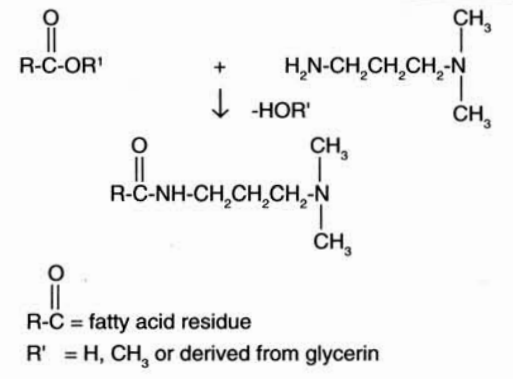


Figure 1-1. Betaine production, amidation

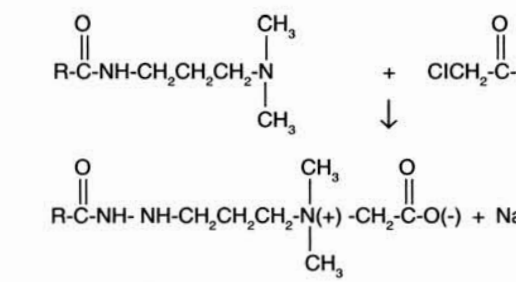


Figure 1-2. Betaine production, carboxymethylation

Table 1-1. Fatty acid composition of CAPB

Fatty acid (chain length)	*Weight % (approx values)*
8	7
10	6
12	49
14	19
16	9
18	10

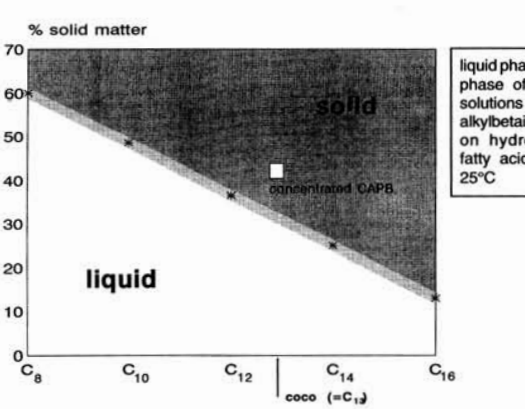


Figure 1-3. Flowability of aqueous betaine solutions

mine the fatty acid composition of the betaine, which corresponds to that of the oil. Table 1-1 outlines the typical fatty acid composition of CAPB.

To use DMAPA most efficiently and avoid large amounts of liquid waste, you should recycle the amine, which is partly distilled from the reaction medium together with the methanol or water formed, during the transformation of fatty acid methyl esters or fatty acids.

Amide purification: When CAPB synthesis starts from fat, glycerin forms as a by-product. As glycerin has no negative effect on most applications and may even be desired, a glycerin content of 2 to 3% is normal in betaine solutions. If desired, some glycerin can be removed from the amidoamine by phase separation, for a glycerin content around 1%.

The DMAPA used in the amidation reaction, present in excess, can be distilled out of the amidoamine to around 0.05% remaining. All amidoamines, whether derived from fatty acid esters or fatty acids, contain small amounts of non-amidated fatty acid that are carried over into the betaine.

Specialty betaines: Fatty acids and fatty acid methyl esters with fatty acid compositions that correspond with natural oils can be used to produce betaines. Betaines with special fatty acid compositions can also be made, including lauric acid amidopropyl betaine, caprylic/capric acid amidopropyl betaine and betaines from topped fatty acids that contain no or only very few short-chain components.

Carboxymethylation: The amidoamine is carboxymethylated in aqueous medium with chloroacetic acid or its sodium salt. The reaction leads directly to the betaine, normally obtained as a 30% aqueous solution. Sodium chloride, formed as a by-product, is present in most betaine solutions at approximately 5%. Apart from the reaction with the tertiary nitrogen atom, the chloroacetic acid can also be hydrolyzed in a side reaction that forms glycolic acid. The glycolic acid content can reach levels of more than 1% in the betaine solution; however, the level is typically considerably lower (about 0.1%).

During the past few years, research on the production of betaines has primarily concentrated on improving the carboxymethylation process. These efforts have focused on manufacturing purer products and minimizing by-products. Other efforts have focused on increasing concentration levels or reducing the water content in betaine solutions; these efforts all primarily involve fine-tuning the carboxymethylation step.

Minimizing contaminants: As the tertiary amines are consumed during carboxymethylation, the pH value falls considerably. This slows the reaction rate proportionally because free amines are also removed from the reaction medium by protonation as well as carboxymethylation. By maintaining an alkaline pH throughout the reaction, carboxymethylation can be carried out faster and more completely, with less amidoamine in the final product.[22] This technique can give amidoamine contents of less than 0.3% in the betaine. Some types of CAPB have higher amidoamine contents, up to 3%, for special applications.

Chloroacetic acid and the dichloroacetic acid present in chloroacetic acid in small amounts are both unwanted by-products in betaines (as well as other zwitterionic or ampho-

teric surfactants, like amphoglycinates) because of their toxicity. Chloroacetic acid is almost completely depleted during the carboxymethylation reaction, but dichloroacetic acid is almost inert under the typical reaction conditions. By submitting betaines to additional post-treatment steps, the residual chloroacetic acids can be reduced. This can be achieved either by reacting at alkaline pH or by additional treatment with ammonia or amino acids that reduce the amount of monochloroacetic acid.[32]

Using sulfonating reagents is another possible way to minimize the chloroacetic acids.[30] Finally, both mono- and dichloroacetic acid can be hydrolytically decomposed simply by exposure to high temperatures (>120°C).[27] Levels of less than 5 ppm chloroacetic acid and less than 10 ppm dichloroacetic acid can be achieved. There are, however, very few products on the market that fulfill CAPB purity requirements of amidoamine content <0.3%, monochloroacetic acid <5 ppm and dichloroacetic acid <10 ppm.

Sodium chloride: Based on weight, the most important components of the marketed aqueous CAPB solutions are the betaine itself and sodium chloride. In general, sodium chloride is left in the solution as it does not interfere with most applications. In fact, sodium chloride is desirable to build viscosity in ready-to-use preparations, such as shampoos. For special applications, there are also betaine products with reduced salt contents. These can be produced by using solvents or membrane separation processes.

Flowable CAPB concentrates: Most marketed CAPB solutions contain approximately 30% active matter. This is primarily because aqueous betaine solutions form viscous, gel-like phases at slightly higher concentrations. In contrast to the situation for surfactants like lauryl ether sulfates, fluid mesophases consisting of CAPB, NaCl and water do not exist at higher concentrations. The critical concentrations above which non-flowable gel-phases are formed partly depend upon the length of the fatty-acid alkyl chains. Figure 1-3 shows this for solutions composed of stoichiometric amounts of fatty acid amidopropyl betaine and sodium chloride.

Numerous attempts have been made to obtain flowable betaine solutions with increased active matter; in some cases, by adding other surfactants.[23-25,29,31] Other ways to achieve highly concentrated betaines include adding solvents or using additional salts not normally contained in betaine solutions, such as sodium citrate, trimethylglycine (natural betaine: methanaminium, 1-carboxy-N,N,N-trimethyl-, innersalt)[28] or nitrilotriacetate.

A relatively simple way to obtain more highly concentrated betaine solutions is to adjust the free fatty acid content. By adding small amounts of fatty acid to the betaine with the amidoamine solution, you can produce betaine contents of 34-36% and detergent-active substances, including fatty acids, of 36-38%.[26]

The increase in concentrations has an important positive side effect: such betaine solutions are microbiologically stable and don't require preservatives.[26]

By spray-drying aqueous betaine solutions, it is possible to obtain highly concentrated betaine products, typically consisting of 80-85% fatty acid amidopropyl

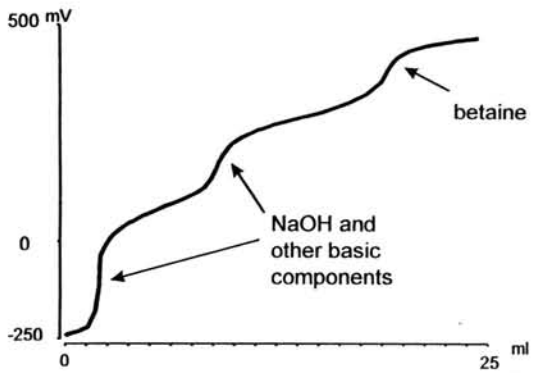


Figure 1-4. Titration of CAPB in methanol/ethylene glycol menomethyl ether with perchloric acid in dioxane

betaine, 13-15% sodium chloride and 0.3 to 3.0% water.

The details of betaine production demonstrate that marketed solutions will contain by-products. Determining the types and amounts of such incidental components helps us characterize the betaine's quality.

Analytical Methods

Water determination: Karl-Fischer titration, as described in several standard methods,[5] is still the preferred method to quickly determine the exact water content. Using modern titrators and reagents, water determination can be carried out in a few minutes. Other methods, such as oven drying at 105°C or water determination by extraction,[6] are generally more time-consuming and show a greater standard deviation than Karl-Fischer titration.

In some cases a quick method to determine the water content can be carried out with (sugar-) refractometers, but these instruments must be calibrated on products with a known water content, determined by Karl-Fischer titration.

Fatty acid amidopropyl betaine content: Until recently, the only reliable method to determine the content of fatty acid amidopropyl betaine (betaine content) in solutions was using subtraction methods. Many attempts have been made[18] to use direct titration methods, but, according to our investigations, these methods lead to inaccurate results. Many times the results are invalidated by other protonable substances, such as free amidoamine, glycolic acid, citric acid or trimethylglycine, during the titration with acids, such as perchloric acid in acetic acid.[18] Platinga et al describe a potentiometric titration with potassium hydroxide in methyl isobutyl ketone. This method is relatively slow; moreover, further interferences with water lead to a lack of accuracy. Methods that include an extraction step can yield low values due to the short-chain fatty acid amidopropyl betaines being only partially measured.

Recently a modified titration method has been proposed that allows a differentiating titration of fatty acid amidopropyl betaines by choosing the proper solvent. The basic approach and results, explained in detail in reference 13, are reviewed here.

A mixture of methanol and ethylene glycol monomethyl ether serves as the solvent for the CAPB. The CAPB is

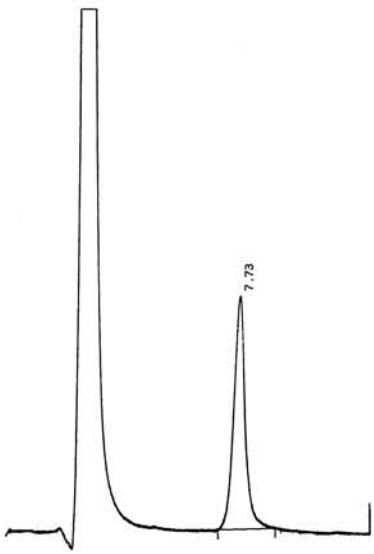
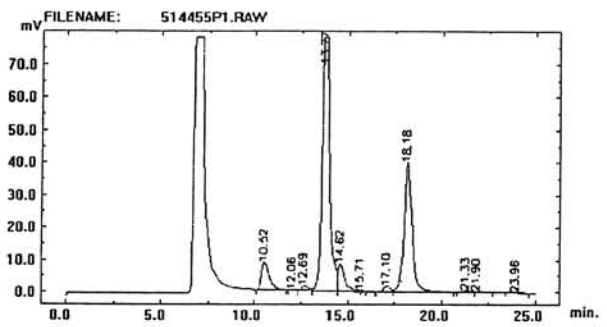


Figure 1-5. Determination of amidoamine by HPLC (peak at 7.73 min)



Peak at 10.52 min: dichloroacetic acid
13.77 min: glycolic acid
18.18 min: monochloroacetic acid

Figure 1-6. Determination of monochloroacetic acid, dichloroacetic acid and glycolic acid by HPLC

adjusted to its pure zwitterionic form with a sodium hydroxide/sodium acetate buffer. The titration uses a perchloric acid solution in 1,4-dioxane. The titration step transforms the betaine into its cationic form. The choice of the special methanol/ethylene glycol menomethyl ether solvent mixture allows an almost selective titration. The titration curves obtained can be evaluated by modern titrators without problems (Figure 1-4).[13] According to our experience, there is a relative standard deviation of approximately 0.6% using this method.

Gerhards et al have discussed alternative methods, including titration with ion-sensitive electrodes, in their publications. [13]

Sodium chloride determination: Determining the chloride concentration using potentiometic titration in dilute nitric acid with silver nitrate is one of the most reliable analytical methods applied to fatty acid amidopropyl betaine solutions.[7] The precipitation titration can be carried out reliably with a relative standard deviation of 0.4%. From the chloride concentration, the sodium chloride content is calculated.

Glycerin: As previously mentioned, glycerin is formed as a by-product during amidoamine production starting from triglycerides. The most convenient way to determine the glycerin in CAPB solutions is iodometric titration.[8] Compounds with vicinal OH-groups are cleaved by periodate, then the periodate is reduced to iodate:

$$CH_2OH\text{-}CHCH\text{-}CH_2OH + 2\ NaIO_4 \rightarrow 2\ HCHO + HCOOH + 2\ NaIO_3 + H_2O$$

The iodate forms free iodine with the addition of iodide. The free iodine is titrated with sodium thiosulfate using starch as indicator.

Free fatty acid: The problem of determining free fatty acid concentration in CAPB solutions has still not been completely solved. As previously described, the gas chromatography (GC) method[18] extracts free fatty acids from the dried betaine using diethyl ether. After elution through a silica gel cartridge, the eluate is neutralized with tetramethylammonium hydroxide in the presence of phenolphthalein; this is then directly injected into a gas chromatograph. The formation of fatty acid methyl esters takes place in the injector of the gas chromatograph. Pentadecanoic acid was used as the internal standard. Apart from problems with the time-consuming preparation of samples, this procedure has also inexplicable problems with the reproducibility.

At this time, investigations are underway to determine the free fatty acids using a new, high-pressure liquid chromatography (HPLC) procedure. This method derivatizes the fatty acids with 2-bromoacetophenone and identifies them by reversed-phase (RP) HPLC analysis.

The total free fatty acids can also be determined with nuclear magnetic resonance spectroscopy.

Fatty acid amidoamine: A variety of methods have also been discussed to determine residual amounts of free fatty acid amidoamines.[18,11] Titration and chromatographic methods have been investigated most extensively; Käseborn explains in detail why existing titration methods cannot be satisfactorily applied to alkylamidopropyl betaines.[18]

Thin layer chromatography has shown to be a successful semi-quantitative method to determine free amidoamine. The silica gel plate can be developed in a solvent mixture of chloroform, methanol and ammonia (30/50/2), and the amidoamine is detected by means of a bromophenol blue solution.

Amidoamine can be quantitatively determined by HPLC without any problems using a special ion exchange column.[a] A 0.02 M phosphate buffer solution serves as eluent. Under these conditions, the amidoamine can be detected as a single peak, not separated according to the fatty acid composition. Figure 5 shows an example of such a determination. This method is currently being discussed by committees of the DGK[b] and GAT.[c]

By-product acids: Because of the toxicological effects of

[a]ProTens: Dr. Herbst Haudelschemiker, Ubstadt Weiher, Germany
[b]Deutsche Gesellschaft für wissenschafthiche und auuj augewandte Kosmetik (Fachgruppe Aualgtile)
[c]Gemeinschaftsausschup Teugide der Detschen Gesellschaft für Feltwisseuschaft und DIN

chloroacetic acids, researchers needed to develop new analytical methods with lower detection limits than the methods previously used, mainly ion chromatography with suppressor techniques or capillary zone electrophoresis.

For the GC methods, according to Cetinkaya[3] and Arens and Spilker,[1] the organic acids are converted to methyl esters and are detected using an electron capture detector.

HPLC detection can be carried out directly with little sample preparation other than dilution on an anion exchange column.[d] The elution is achieved with 0.01 M sulfuric acid; the detection is carried out with a UV detector at 205 nm. The detection limits are approximately 5 ppm for monochloroacetic acid and 10 ppm for dichloroacetic acid. With this method, glycolic acid can be measured at the same time. Figure 6 shows a corresponding chromatogram.

The GC methods have proved more reliable in interlaboratory tests, but the HPLC method turns out to be considerably less time-consuming and more universal, since it detects all three organic acids (glycolic and mono- and dichloroacetic) simultaneously.

DMAPA: Residual DMAPA is normally determined in the amidoamine before betaine production. With a recently developed method, however, it is also possible to detect free DMAPA in the final betaine.[2] In both the amidoamine and the betaine, DMAPA is analyzed by RP-HPLC, with UV-detection after derivatizing with phenyl isothiocyanate. This sensitive method is especially suitable for the detection of very low concentrations of DMAPA. In betaines, DMAPA occurs only in the lower ppm-level, typically from less than 5 to 20 ppm.

Fatty acid composition: With the help of the analytical methods discussed above, it is possible to characterize the quality of the process by which the fatty acid amidopropyl betaine was produced. The fatty acid composition is, however, a characteristic of the fatty raw materials used. Therefore, the fatty acid composition of the raw material used, not the CAPB, is normally analyzed.

It is also possible to characterize the product by determining the fatty acid composition of the betaine. The free fatty acids can be obtained after cleaving the amide bond by heating in concentrated hydrochloric acid. After their conversion into methyl esters by known methods (with methanol/sulfuric acid, for instance), the fatty acids can be analyzed by gas chromatography.

These sample preparations can be avoided in two other HPLC methods.[13,18] Using these methods, alkyl distributions can be obtained directly after separation on a reversed phase column (RP 18/7 μm) with methanol/water (detection by UV at 215 nm) or using ion exchange chromatography. In the latter, the order of elution is reversed compared to the RP chromatography, with the longest-chain betaine eluted first followed by shorter-chain derivatives.

Conclusion

The described analytical methods for the determination of the main components (water and betaine), the by-products (sodium chloride, glycerin and fatty acid) and trace

[d]Aminex HPX-87 H, Bio-Zad Laboratories, Munich, Germany

components (such as fatty acid amidoamine, glycolic acid, mono- and dichloroacetic acid) are reliable and can be routinely applied. Thus the production of CAPB and related marketed forms of betaine can be carried out in a controlled manner to ensure consistent high quality. If required, these analytical methods can be supplemented by modern HPLC methods to determine fatty acid composition or by ^{1}H- and ^{13}C-NMR spectroscopy. The NMR methods repeatedly prove helpful to recognize unexpected additional components; however, trace components cannot be detected by NMR spectroscopy.

The further development of analytical methods is an essential requirement for the continued improvement of CAPB production methods and its quality as a marketed ingredient so the cosmetic and detergent industries can be offered CAPB products that satisfy the highest demands of quality and technical properties.

References

Address correspondence to B. Grüning c/o ***Cosmetics & Toiletries*** magazine, 362 South Schmale Road, Carol Stream, IL 60188-2787 USA.

1. M Arens and R Spilker, *FETT/FAT* **97** 212-214 (1995)
2. T Böhmer, private communication, submitted for publication.
3. M Cetinkaya, *Parf Kosm* **72** 816 (1991)
4. Y Chevalier, *Langmuir* **7** 848 (1991)
5. DGF — Einheitsmethoden H-III 3a (92), DIN 51777, ISO 4317, DGK-Analysenmethoden W 010.1
6. DGF — Einheitsmethoden H-III 3 (92), ISO 4318, DGK-Analysenmethoden W 011.1
7. DGF — Einheitsmethoden H-III 9 (92)
8. DGF — Einheitsmethoden E-III 3b (79)
9. X Domingo, BM Phillips, J Sanchez Leal, T Garcia and A Garbayo, *Int J Cosmet Sci* **13** 263 (1991)
10. JG Dominguez, F Balaguer, JL Parra and CM Pelejero *Goldschmidt informiert* **55** 10 (1981)
11. JJ Donkerbroek and CN Wang, *Proc 2nd World Surfactants Congress Paris*, v III (1988) p 134
12. Final report on the safety assessment of cocamidopropyl betaine, *J Am Coll Tox* **10** 33 (1991)
13. R Gerhards, I Jussofie, D Käseborn, S Keune and R Schulz, *Tenside Surf Det* **33** 8 (1996)
14. B Grüning, *Proc 3rd CESIO Int Surfactant Congress*, v 3 (1992) p 221
15. TJ Hall-Manning, GH Holland, G Rennie, P Revell, J Hinres, DA Basketter and MD Barratt, *Proc 4th CESIO Int Surfactant Congress*, v 3 (1996) p 13
16. K Hoffmann, *Jahrbuch für den Praktiker,* Verlag f chem Industrie H. Ziolkowsky (1973)
17. R Hüttinger, *Goldschmidt informiert* **32** 39 (1975)
18. D Käseborn, *Tego Cosmetics Special* 2
19. HI Leidreiter, K Jenni and C Jorbandt, *SÖFW* **120** 852 (1994)
20. JM Platinga, JJ Donkerbroek and RJ Mulder, *JAOCS* **70** 97 (1993) (published by the Am Oil Chem Soc)
21. W Seidel, *Parf Kosm* **71** 712 (1990)

Patents

22. V Bade, DE 29.26.479
23. V Bade, DE 36.13.944
24. V Bade, DE 37.26.322
25. V Bade, DE 38.26.654
26. U Begoihn, W Foitzik, B Grüning, D Käseborn and C Weitemeyer, DE 42.07.386
27. W Foitzik, B Grüning, D Käseborn and C Weitemeyer, DE 42.05.880
28. J Hamann, HJ Köhle, K Stark and W Wehner, EU 656 346
29. T Messenger, DE Mather and BM Phillips, US 4,243,549
30. H Seitz and R Vybirol, DE 42.32.157
31. G Uphues, P Neumann and A Behler, DE 43.40.423
32. G Uphues, U Ploog, K Bischof, K Kenar and P Saldek, DE 39.39.264