Pyrrolidone-Based Surfactants (a literature review)[1]

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ABSTRACT: As the alkyl group of N-alkylated pyrrolidones is increased to C_8P, surface-active properties become important. The resulting surfactant can interact synergistically with an anionic surfactant. This interaction is based on the electronegativity of the pyrrolidone carbonyl oxygen which can accept a proton to form a pseudoquaternary ammonium ion that can form an ion pair with large anions (i.e., anionic surfactants). The resulting ion pair is further stabilized by hydrophobic bonding between the two alkyl chains. In addition, pyrrolidone can electrostatically interact with aromatics, hydrogen-bond to nonionics, and, in essence, associate electrostatically/hydrophobically similarly to polyvinylpyrrolidone. This interaction of the pyrrolidone functional group can be transposed from one surfactant hydrophobe structure to another. This paper reviews the literature concerning the addition of pyrrolidone to a variety of hydrophobes of interest to both industrial and academic researchers. The chemistry of selected surface-active pyrrolidone derivatives, prepared from butyrolactone, aminoethylpyrrolidone, epoxypropylpyrrolidone, chloromethylpyrrolidone and itaconic acid, is reviewed. Pyrrolidone is a versatile substituent, capable of enhancing the performance of a variety of surfactant structures by improving water solubility, compatibility and solvency in a compact head group that favors surfactancy. In addition, the pyrrolidone ring, when incorporated into derivatives, usually reduces toxicity.
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KEY WORDS: N-alkyl-2-pyrrolidones; fatty amidoalkyl-2-pyrrolidones; N-chloromethyl-2-pyrrolidone; N,N-dimethyl-N-[(2-pyrrolidonyl) methyl] N-(3-Stearamidopropyl) ammonium chloride; 4-carboxy-n-alkyl-2-pyrrolidone.

Lactams occur in nature in such familiar structures as the penicillins and the skin moisturizing factor, PCA (pyrrolidone 5-carboxylic acid), and 2-pyrrolidone itself can occur naturally or as an intermediate in metabolic pathways (1). Because it is found in biological systems, it is no wonder that it contributes improved mildness to derivatives (2).

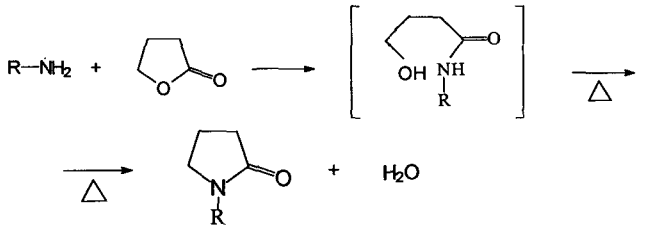
Pyrrolidone chemistry became commercially important when Reppe developed an industrially feasible synthetic route in the 1930s (3). He recognized that because of its hydrophilicity it would contribute water solubility to derivatives (4), and this eventually led to two products of commercial importance: N-methyl pyrrolidone (C_1P) (5), a nontoxic super solvent and polyvinylpyrrolidone, an ultra-low irritation complexing polymer (6).

N-SUBSTITUTED PYRROLIDONES

Preparation. N-Substituted pyrrolidones can be conveniently prepared by the condensation of primary amines and butyrolactone (Scheme 1). As long as the primary amine will stand up to the 200–300°C temperatures necessary to dehydrate and cyclize the hydroxybutylamide intermediate, a wide variety of amines can be employed (7). Alkoxylation of 2-pyrrolidone with ethylene oxide and/or propylene oxide (EO)/(PO) or α-olefin epoxides by alkali-catalyzed anionic polymerization also has been explored (8,9).

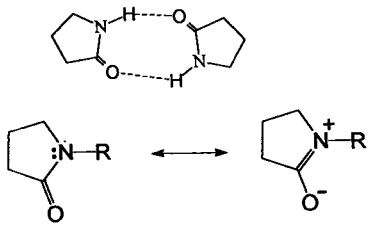
Structure. Pyrrolidone is a planar, five-membered lactam that exhibits maximum orbital overlap and, hence, charge separation. The dipole moment of C_1P has been measured at 4.06D and is higher than 2-pyrrolidone (10) because the unsubstituted lactam participates in dimerization like carboxylic acids. (Scheme 2). However, substitution of the proton on the lactam with an alkyl group removes this potential for self-association by hydrogen bonding. The polarity of the N-substituted lactam fosters strong hydrogen bonding and compatibility with organic molecules and solvents, especially water. This results in "super-solvency", and C_1P is by definition the most active member. Extending the alkyl chain only dilutes this "super-solvency" without eliminating the property.

Because pyrrolidone can have two canonical forms, the lactam is resonance-stabilized and resistant to hydrolysis. Inspection of each suggests that pyrrolidone can be compared to other surfactants such as betaines, amine oxides, and open-chain amides. The similarity is that a negative charge exists centered on the electronegative oxygen and a positive charge on the nitrogen (enhanced by electron-releasing N-alkyl



SCHEME 1

[1]Winner of the 1994 Samuel Rosen Memorial Award.



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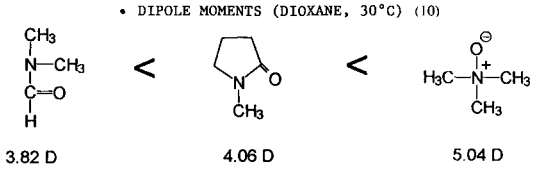


SCHEME 3

groups). Amine oxides, betaines, sultaines, and phosphobetaines have full charges, while N-substituted pyrrolidones are partially charged, but with greater charge separation compared to acyclic amides because of restricted rotation and favorable orbital overlap (Scheme 3).

Chemistry. As previously reported (11–13), extending the N-alkyl chain to approximately C_8P results in significant surface activity. This reaches a maximum at $C_{12}P$ to $C_{14}P$ and drops off above $C_{14}P$ because of minimal water solubility. Figure 1 suggests that C_8P–$C_{12}P$ all exhibit a critical micelle concentration (CMC). However, Rosen *et al.* (14) have shown that, for highly purified samples, insolubility as measured by increased absorbance in visible light (at 600 nm) indicates phase separation before the CMC (although nothing separates from solution at these low concentrations). Moreover, earlier studies (15,16) also found $C_{12}P$ too insoluble to reach the CMC, which could only be clearly delineated if the solution was acidified with HCl. Under those conditions, the pyrrolidone is sufficiently protonated and soluble. However, this restriction, due to insolubility, is of little significance when C_8P–$C_{18}P$ are employed in mixed micelles in actual usage. In addition, electron-rich nucleophilic anions, such as NaI and NaSCN, increase water solubility because the cationic charge is stabilized in the presence of electron-rich anions or at low pH, while NaCl or $NaNO_3$ has a salting-out effect. These interactions are similar to those reported for polyvinylpyrrolidone (PVP). C_nP and PVP are comparable in the sense that PVP can be viewed as containing pyrrolidone groups attached to a long chain. Many investigators have demonstrated that PVP interacts with large anions, such as dyes, phenolics, anionic surfactants, and iodide, by both electrostatic and hydrophobic interactions (17). Like a surfactant, the PVP backbone is surrounded by hydrophobically-bound water, sometimes referred to as iceberg water (18). Large anions are not only stabilized by ionic interaction as the pyrrolidone carbonyl oxygen protonates (enthalpic), but by discharge of bound water (entropic).

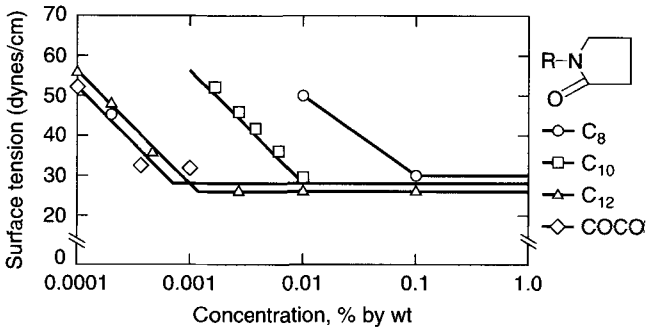


FIG. 1. Surface tension of aqueous solutions of Surfadone® (ISP, Wayne, NJ) N-alkyl pyrrolidones (All measurements made with distilled monodisperse N-substituted pyrrolidones prepared from single-cut amines or whole coco distribution).

Commercially available (19) C_8P and $C_{12}P$ are prepared from linear, single-cut distilled amines and exhibit the typical properties listed in Table 1. They are fractionated by distillation and, hence, are pure materials with more than 97% monodispersed N-alkyl-2-pyrrolidones and usually more than 99% total N-alkyl-2-pyrrolidone. C_8P has a low solidification point and a high boiling point. This suggests that it may be considered for applications where volatility (VOC) concerns exist (20).

Available technical literature (19) records the surfactant properties of these commercial samples. A plot of surface tension vs. concentration (Fig. 1) can be compared to a similar plot obtained by Rosen *et al.* (14), with samples that are of greater purity (Fig. 2). As can be readily seen, the commercial and highly purified samples produce comparable plots. Likewise, surfactant parameters, such as the minimum area per molecule at the aqueous solution/air interface and the pC_{20} (a measure of efficiency), are also comparable to Rosen's results (Table 2). This is not unexpected because of

TABLE 1
Typical Physical Properties of Surfadone® Nonionics[a]

	Surfadone LP-100 (C_8P)	Surfadone LP-300 ($C_{12}P$)
Alkylpyrrolidone (% minimum)	97	97
Water (% maximum)	1	1
Physical form (25°C)	Clear to slightly hazy liquid	Clear to slightly hazy liquid
Color (APHA maximum)	100	100
Boiling point (°C)	100 (0.3 mm Hg)	145 (0.2 mm Hg)
Density (g/cc)	0.92	0.90
Solubility parameter ($J^{1/2}/cm^{3/2}$)	19	18.7
Flash point (°F)	246	240
Solidification point (°C)	–25	10
Thermal gravimetric analysis[b]	175	225

[a]Surfadone® from ISP (Wayne, NJ). APHA, American Public Health Association (Washington, D.C.).

[b]Air: 10°C/min; temperature at which 10% weight loss occurs (by volatilization). Products do not decompose, even up to 275°C, in the absence of air.

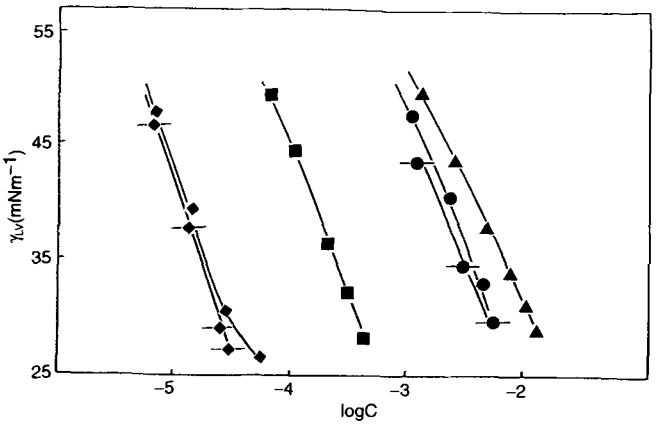


FIG. 2. Surface tension vs. log molar concentration of surfactant in aqueous solution at 25°C: ♦, $C_{12}P$ in pure water; -♦-, $C_{12}P$ in 0.1 M NaCl; ■, $C_{10}P$ in pure water; ●, C_8P in pure water; -●-, C_8P in 0.1 M NaCl; ▲, C_26P in pure water (Ref. 14).

the relatively high purity of the commercial products. Rosen's group included the branched material $C_{2.6}P$ for comparison and reports an A_{min} of 46.5 and pC_{20} of 3.0. This indicates that branching disrupts the close packing observed with linear hydrophobes. Not until $C_{14}P$ is there an indication of further compromise of close packing.

Rosen *et al.* (14) calculated the cross-sectional area of molecular models while assuming a vertical orientation at the aqueous solution/air interface. He found the value to be 34×10^{-2} nm^2, which is close to actual results, indicating close packing for linear alkyl groups. This is similar to other low hydrophile–lipophile balance surfactants, such as $C_8H_{17}OCH_2CH_2OH$; however, when compared to $C_{12}H_{25}$-$(OC_2H_4)_8$-OH, $C_{12}P$ occupies half the area at the interface. As expected for nonionics/zwitterionics, adding electrolyte (NaCl) has little effect on this parameter.

Rosen points out the interesting observation that the methylenes of the pyrrolidone ring contribute little to hydrophobicity of the molecule. He comes to this conclusion by comparing C_8P to $C_8OC_2H_4OH$ and $C_{10}P$ and $C_{12}P$ to $C_{10}CHOHCH_2CH_2OH$ and $C_{12}CHOHCH_2CH_2CH_2OH$, respectively. The result is that pyrrolidone behaves as a hydrophilic group, and the N-alkyl group determines the hydrophobicity. This may not be true when caprolactam is substituted for pyrrolidone.

As the interfacial tension against a hydrocarbon, such as, hexadecane, is concerned the partition coefficient (CH/CW) shows that, upon addition of electrolyte (NaCl), there is a sharp increase in solubility into the organic phase, especially as the hydrophobe chainlength increases. C_8P is more efficient in this regard (larger pC_{30}) because of greater partitioning into water.

Draves wetting results for 0.1% mixtures are illustrated in Figure 3. It shows that C_8P is the most active wetting agent at four seconds. This ability to wet can be transferred in combination with poorer wetting surfactants and polymers (Table 3). If this effect is due to synergy remains to be determined, but when the solubility of $C_{12}P$ is increased by formulation in suitable mixed micelles, wetting and foaming dramatically improve. Preliminary results in our laboratory suggest that the same mixed micelle interaction exists between alkyl pyrrolidones and aromatic-containing nonionics (APE) and their phosphate ester derivatives.

Zhu *et al.* (21) was also able to demonstrate the synergistic interaction of $C_{2.6}P$, C_8P, $C_{10}P$, and $C_{12}P$ with linear alkylbenzene sulfonate (LAS). In this study, the C_8P proved to be the most effective in enhancing foaming and wetting with LAS.

C_8P is the most effective wetting agent of the series tested and can improve the wetting of a variety of other materials, especially water-dispersible or soluble polymers. For example, hair-care polymers, such as those employed in mousses, gels, pumps, and sprays, are now being formulated with more water and less alcohol. In water, after alcohol evaporation during use, wetting times can be poor, resulting in poor spreading on the hair. C_8P rectifies this problem and improves drying time and over-all hold (22).

C_8P's ability, when properly formulated, to improve wetting without causing foam is an important feature that is commonly associated with the acetylenic diols. C_8P, however, has superior efficacy (pC_{20}) which has been confirmed by measuring dynamic surface tension. C_8P at a surface age of one second($\gamma_{1\,s}$) has been measured by the maximum bubble pressure method and compared to samples of dioctylsulfosuccinate and the acetylenic diol, Surfynol 104 (Air Products,

TABLE 2
Surfactant Parameters

Alkyl chain	Linear alkylpyrrolidones[a] A_{min}	pC_{20}	CMC	Minimum surface tension in aqueous solutions (dynes/cm)	Minimum interfacial tension heptane/H_2O (dynes/cm)	Hydrophilic–lipophilic balance
C_8	38	3.14	9.4×10^{-3}[b]	28	11 (0.1%)	6
C_{10}	36	4.19	8.9×10^{-4}[c]	27	25 (0.01%)	5.5
C_{12}	34	5.30	4.54×10^{-5}	26	22 (0.01%)	3
C_{14}	55	5.70	—	—	—	—
COCO	35	5.40	3.16×10^{-5}	27	18 (0.01%)	4
Cocamidoethyl	45	5.03	1.5×10^{-4}	27	6 (0.01%)	5

[a]A_{min}; pC_{20}, efficiency measure; CMC, critical micelle concentration.
[b]pH 0.4.
[c]pH 0.6.

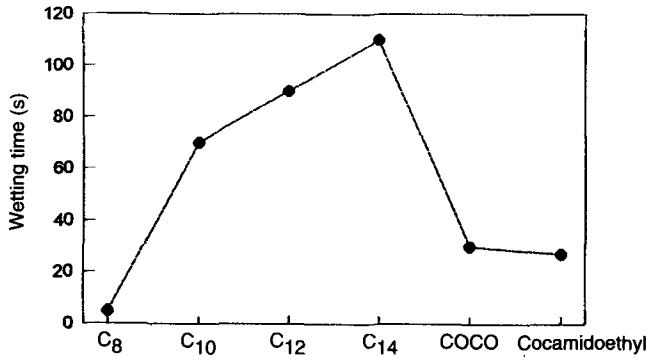


FIG. 3. Drave's Wetting of N-Alkylpyrrolidones At 0.1% (by wt).

TABLE 3
Wetting Potentiation of C_8P Draves wetting test, 0.1% s[a]

CTFA Name	Surfactant C_8P	
	Surfactant alone	50:50 Blend
Poloxamer 182[b]	>300	41
Poloxamer 407[b]	>300	48
Nonoxynol 30[c]	>300	13
Dodecylphenol[c] + 6EO	>300	44
Polysorbate 20[d]	>300	33
Nonoxynol-9 phosphate[c]	>142	20
Sodium dodecyl diphenyloxide disulfonate[e]	103	11
LAS (DDBSA)	9	4

[a]CTFA, Cosmetic, Toiletry and Fragrance Association; LAS, linear alkylbenzene sulfate; DDBSA, dodecylbenzene sulfonic acid. Oher abbreviation as in Table 1.
[b]BASF, Parsippany, NJ.
[c]Rhone Poulenc, Cranbury, NJ.
[d]ICI, Wilmington, DE
[e]Dow, Midland, MI.

TABLE 4
Dynamic Surface Tension (surface age of one second)

	Surfadone[a] LP-100	Surfadone LP-300	Surfynol 104	DSS
Minimum static surface tension (dynes/cm)	28	26	33	26
Dynamic surface tension $\gamma_{1\,s}$ (dynes/cm)	29[b]	—	35[b]	31.5[c]
Draves wetting @ 0.1% (s)	3.5	>300	12	2
Hydrophile–lipophile balance	6	3	4	—

[a]DSS (Cytec, Wayne, NJ). Other company source as in Table 1.
[b]Saturated solution.
[c]0.1% Solution.

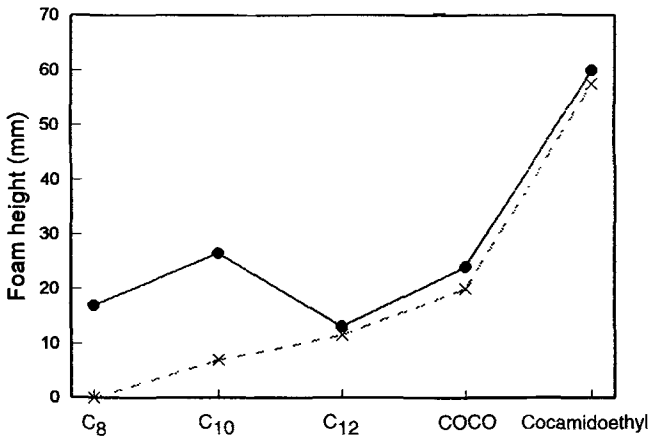


FIG. 4. Ross–Miles foam heights for N-alkylpyrrolidones. COCO, coconut (typical coconut alkyl distribution). ●, Initial; X, final.

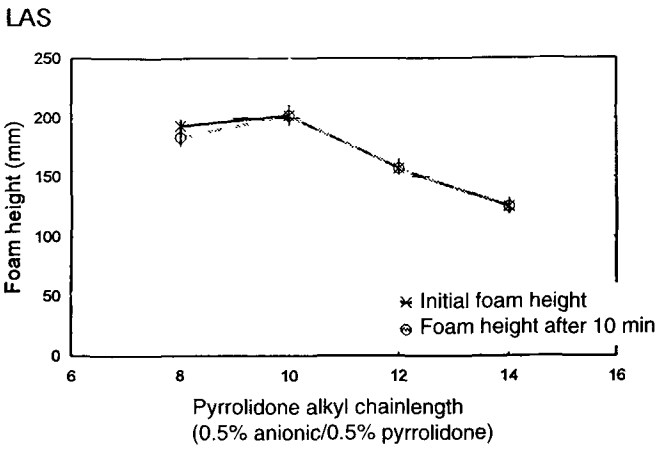


FIG. 5. Foaming properties (Ross–Miles). LAS, linear alkyl sulfate.

Philadelphia, PA) (Table 4) (23). At a concentration of 0.1%, C_8P will reduce surface tension to 33 dynes/cm (29 dynes/cm at its maximum solubility of 0.124%) which is comparable to the best wetting agents. Therefore, C_8P can be expected to not only increase wetting of adhesives and coatings but, upon dry-down, to be soluble in the organic phase, reducing the possibility of rewetting with its associated problems.

Comparison of the commercial C_8P–$C_{14}P$ products for foaming is illustrated in Figure 4. Generally, foaming is poor. However, in combination with high-foaming anionics, such as LAS, C_8P–$C_{10}P$ indicate foam enhancement (Fig. 5), which correlates with Rosen *et al.* (21,24) findings concerning synergy with LAS and $C_{12}SNa$. Table 5 is a tabulation of their results for ß (the interaction parameter in mixed monolayers at the surface). Synergy (25,26) in foaming depends upon this parameter. To exhibit synergy in surface tension reduction efficiency (when a given surface tension value can be attained at a mixed surfactant concentration less than that for either component surfactant by itself), values for B^{∞} must be negative and less than the absolute value of $\ln C_p^{\circ}/C_2^{\circ}$, where C_p° and C_2° are the molar concentrations of the N-alkyl-2-pyrrolidone and the second surfactant, required to yield that same surface tension value. "Synergy in surface tension reduction effectiveness exists when the surfactant mixture at its CMC reaches a lower surface tension than that attained at the CMC of either surface-active component of the mixture by it-

TABLE 5
Molecular Interaction and Synergism Parameters at 25°C (Π = 32 mN M^{-1})[a]

System	Interface	β^{α}	$\lvert \ln C_p^o/C_2^o \rvert$
C_8P–$C_{12}SNa$	H_2O–air	–2.6	1.68
C_8P–$C_{12}SNa$	H_2O–parafilm	–2.1	1.41
C_8P–$C_{12}SNa$	H_2O–teflon	–2.0	1.17
C_8P–$C_{12}SNa$	0.1 M NaCl (aq.)–air	–3.1	0.23
C_8P–$C_{12}SNa$	0.1 M NaCl (aq.)–parafilm	–2.9	0.32
C_8P–$C_{12}SNa$	0.1 M NaCl (aq.)–teflon	–2.5	0.25
C_8P–$C_{12}SNa$	0.1 M NaCl (aq.)–hexadecane	–1.7	0.66[b]
$C_{10}P$–$C_{12}SNa$	0.1 M NaCl (aq.)–hexadecane	–2.3	0.32[b]
$C_{2.6}P$–LAS	H_2O[c]–air	–4.0	1.87
C_8P–LAS	H_2O[c]–air	–3.8	0.99
$C_{10}P$–LAS	H_2O[c]–air	–3.8	1.54
$C_{12}P$–LAS	H_2O[c]–air	–3.1	4.0

[a]Reference 24. Abbreviations as in Tables 1 and 3.
[b] $\lvert \ln(F_2F_1^oC_{P,t}^o/F_1F_2^oC_{2,t}^o) \rvert$.
[c]Na^+ concentration held constant at 0.005 M with NaCl.

TABLE 6
Ross–Miles Foam Height: C_8P + LAS (0.25% total surfactant concentration 25°C, Na^+: 0.008 N)[a]

Wt% C_8P	Initial height (cm)	5 min (cm)
0	183	180
9.2	185	182
19.7	190	187
36.4	195	190
57.2	194	187
76.4	194	187
91.6	194	192
100	17	10

[a]Abbreviations as in Tables 1 and 3.

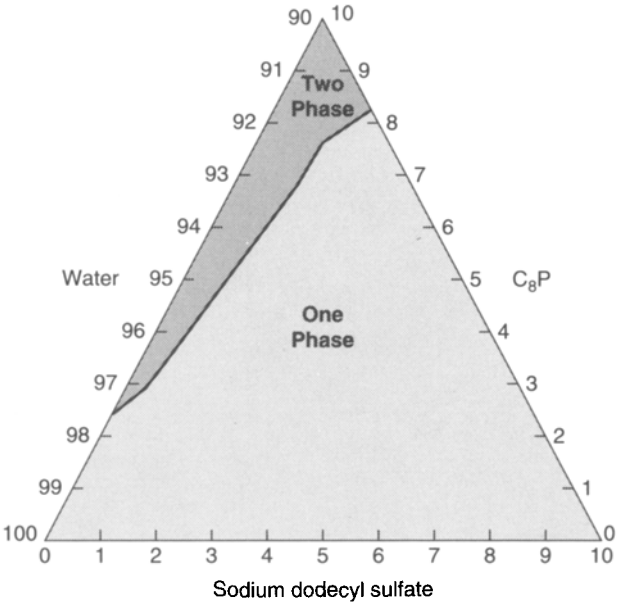


FIG. 6. C_8P/sodium dodecyl sulfate/H_2O phase diagram. Abbreviation as in Figure 2.

self" (Ref. 26). Table 5 summarizes Rosen's values and clearly shows that the conditions are met for C_8P-$C_{10}P$ but not for $C_{12}P$ and, presumably, higher alkyl analogues, for synergy in surface tension reduction efficiency.

Rosen found that small amounts of LAS and presumably other high-foaming anionics are all that is needed to generate significant foam. A mixture of C_8P/LAS with 91.6% C_8P foams as well as 100% LAS (Table 6). Hornby and Jon (23) have evaluated the phase diagram for C_8P/sodium dodecyl sulfate (SDS)/H_2O (Fig. 6) and show that small amounts of SDS will solubilize the formulation (27). Rosen's results show C_nP to be more interactive with LAS than with SDS (Table 5) because of the greater hydrophobic effect of the hydrophobic group of LAS. In conclusion, Rosen points out that the combination of C_8P–$C_{12}SNa$ in 0.1 M NaCl at the H_2O–air interface exhibits the maximum degree of synergism, as predicted from maximizing the quantity $(\beta^6 - |\ln C^0_1/C^0_2|)^2 / \beta^6)$. C_8P–LAS (H_2O–air), also listed in Table 5, illustrates the same trend for LAS.

Shampoo formulations. In concentrates, $C_{12}P$ will enhance the viscosity of typical shampoo anionics, such as ALS, SLES, SLS, AOS, and TEALS, and will thicken in response to added electrolyte (Figs. 7 and 8; Table 7) which is not surprising when considering the structural comparison to amine oxides, betaines, etc., that are currently employed in commercial formulations (28,29) to perform this function.

Agricultural formulations. The C_8 and C_{12} pyrrolidones are poorly soluble in water but will imbibe 35 and 20% water, respectively, at high surfactant concentrations (Fig. 9). However, they are soluble in a variety of solvents (Table 8) and can form reverse micelles in the presence of a polar compound or water. In addition, they have the ability to complex with polar actives by hydrogen bonding, and this can be used to an advantage in agricultural emulsifiable concentrate formulations (30,31). In addition, C_1P and C_8P or $C_{12}P$ complement each other in such formulations because C_1P can effectively increase polarity and solubility in aromatic or other solvents to dissolve typically low-solubility actives. However, C_1P is highly water-soluble and will not remain in a mixed micellar system once it is diluted with water. That is true with many emulsifiable concentrate agricultural formulations where the combination of C_1P and C_8P or $C_{12}P$ is required because of the added solubility contributed by C_1P to the concentrate, where the active is held in the oil phase by the solubilizing effect of the $C_8P/C_{12}P$ upon aqueous dilution (32). The surface-active pyrrolidones remain in the micelle, along with solvent and other stabilizing emulsifiers, and retain the active material by hydrogen bonding and/or hydrophobic interactions. $C_8P/C_{12}P$ also prevents crystallization of actives from diluted emulsions and works synergistically with the phosphate ester surfactant that is commonly found in such formulations to improve aqueous dispersibility (33–38).

Narayanan (39–41) has demonstrated that, by careful selection of cosurfactants, the necessity for solvent in emulsifiable concentrates can be essentially eliminated and the result-

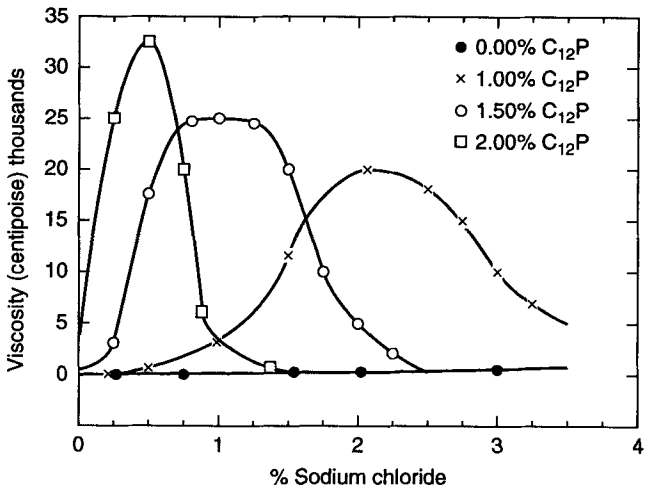


FIG. 7. Viscosity response curves of ammonium lauryl sulfate (12%).

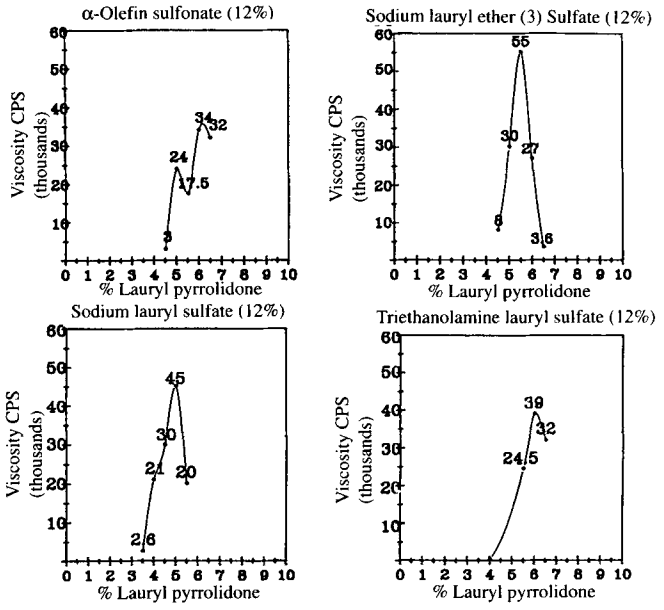


FIG. 8. Viscosity response curves of anionic surfactant and lauryl pyrrolidone (Brookfield Rvt. Spindle TC @ 10 rpm, 25°C; Brookfield Eng. Labs, Inc., Stoughton, MA).

TABLE 7
Viscosity Response (peak viscosities with N-dodecylpyrrolidone)

Anionic (12% actives)[a]	Nonionic level (%)	Peak viscosity[b] (CPS)
ALS	2.5	78 K
SLES (3 mole)	5.5	61 K
SLS	5.0	25 K
AOS	6.0	36 K
TEALS	6.0	18 K

[a]ALS, ammonium lauryl sulfate; SLES, sodium laureth sulfate; SLS, sodium lauryl sulfate; AOS, α-olefin sulfonate; TEALS, triethanolamine lauryl sulfate. [b]Brookfield RVT Viscometer (Brookfield Eng. Labs, Inc., Stoughton, MA), Helipath Stand, T-C Spindle at 10 rpm for 1 min at 25°C.

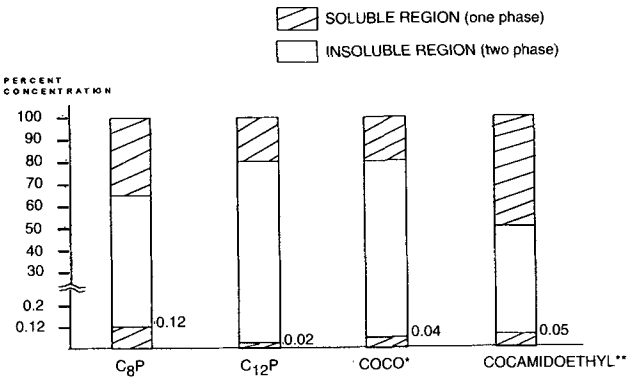


FIG. 9. Aqueous solubility of pyrrolidones. Abbreviations as in Figures 2 and 4. *, C_8, whole coconut distribution; **, C_8–C_{18}, whole coconut fatty acid distribution.

TABLE 8
Solubility of N-Alkyl Pyrrolidones (10% w/w at 25°C)[a]

Solvent	C_8/C_{12}	N-Cocoamidoethyl pyrrolidone
Acetone	S	S
Ethanol	S	S
Xylene	S	DS
Heptane	S	IS
Paraffin oil	S	IS
Stoddard solvent	S	IS
Perchloroethylene	S	S

[a]S, soluble; IS, insoluble; and DS, dispersible.

ing concentrate is formulated as a microemulsion. This is advantageous because of the elimination of potentially dangerous solvents. Table 9 compares C_1P to $C_8(C_{12})$ pyrrolidones and illustrates the differences in solubility and solvency.

Extraction of antibiotics. The formation of reverse micelles and complexation of actives by the pyrrolidone head group can be employed to extract phenolic- or carboxylic-containing antibiotics from aqueous fermentation broths into suitable organic solvents (42). Because of limited water solubility and excellent solvency, the N-alkyl pyrrolidone surfactant can be used by itself or added to another solvent, such as N-butyl acetate. After extraction, the bulk of the antibiotic is found in the organic layer (Tables 10 and 11). The active is claimed to be at least 90% pure in one extraction and can be recovered by using normal or reverse-phase silica gel chromatography or gel-filtration countercurrent distribution high-pressure liquid chromatography. The recovered lactam extractant can be reused for an economical and continuous process. Interestingly, water-soluble dyes and indicators, such as bromophenol blue or methyl orange, also can be readily extracted out of dilute aqueous solutions with C_8 or C_{12} pyrrolidones (Table 12). The ability to extract or solubilize water-soluble actives of this type is facile and clearly demonstrates the unique nature of the pyrrolidone head group.

Hard-surface cleaners. In hard-surface cleaning, C_8P, because of its wetting properties and synergy with anionic surfactant, has generated notable success, especially in glass cleaner formulations. C_8P can function much like other auxiliaries, such as short-chain fatty alcohols, to enhance microemulsification of greasy dirt (43) when formulated with

TABLE 9
Comparison of N-Methyl Pyrrolidone to N-C_8 or C_{12}

Property	Methyl	C_8–C_{12}
Surfactancy	Not surface-active	Very surface-active
Solubility parameter ($J^{1/2}/cm^{3/2}$)	22.9	19.0/18.7
Solubility in water (one phase)	Infinite	<1%
High flash point	+	+
Chem/thermal stability	+	+
Low vapor pressure	+	+
Low toxicity	+	+
Aprotic solvent	+	+
Biodegradable	+	+

TABLE 10
Solubility of Antibiotics in $C_8(C_{12})$ Pyrrolidones Weight (grams) of Antibiotic Dissolved in 100 g Solvent

Antibiotic	NBUOAc[a]	BuOH[b]	C_8 Alkyl Pyrrolidone	C_{12} Alkyl Pyrrolidone
Rifampicin	0.54	<0.30	3.34	2.0
Penicillin V	1.37	2.86	42.22	24.11
Tetracycline	<0.55	1.8	6.25	3.23

[a]*n*-Butylacetate.
[b]*n*-Butanol.

TABLE 11
Extraction of Antibiotics from Water by $C_{12}P$

	pH of antibiotic solution	% $C_{12}P$ added to solution	% Antibiotic originally in solution	% Antibiotic extracted into $C_{12}P$ phase
Lasalocid	3	2	0.02	>80
Rifampicin	6.5	2	0.02	>80
Tetracycline	5.7	6	0.02	50
Vancomycin	10.6	2	0.025	50
Vancomycin	10.6	4	0.05	55

TABLE 12
Extraction of Dyes from Water

Active	Original concentration in water (%)	% Extracted in $C_8(C_{12})$ layer
Methyl orange	0.01	>90[a]
Bromophenol blue	0.01	>90[b]

[a]C_8 Pyrrolidone, 10% w/w, single extraction.
[b]C_{12} Pyrrolidone, 5% w/w, single extraction.

primary synergistic anionics. Because of hydrogen bonding, pyrrolidone has a strong affinity for glass, another reason for its use in this application.

Because $C_{8-12}P$ are very soluble in other nonionic surfactants especially those that are liquid under ambient temperatures, and because pyrrolidone is capable of strong hydrogen bonding, it can be employed to stabilize particulate builders in nonaqueous concentrate liquids (44). C_8P is especially effective because of wetting and synergy with the other surfactants present.

Fiber lubricants. As a fiber lubricant, lubricity can be changed by varying the length of the alkyl chain. The advantage lies in the excellent thermal stability exhibited on hot surfaces, ease of removal by water-based extraction and safety to the environment because of rapid biodegradation. Because of compatibility, C_nP's are easy to formulate and also contribute uniform wetting to the lubricant.

Fountain solutions. Fountain solutions are employed to maximize the contrast between etched and unetched regions on aluminum lithography plates. Once again, C_8P has shown an excellent ability to adhere and render the etched regions hydrophilic.

Personal care. In personal-care products, both C_8P and $C_{12}P$ have had success because they have been shown to be effective swelling and penetration-enhancing auxiliaries for hair treatments, such as dyeing, bleaching, and permanent waving (45,46). They increase the rate of treatment by accelerating wetting and, because they are pseudo-cationic in the presence of large anions such as those found in the hair, they afford some conditioning. The result is that the hair is protected during treatment.

The current interest in formulating with silicone polymers in shampoo products points out the need for emulsifiers/stabilizers. $C_{12}P$ in combination with anionic and cationic surfactants stabilizes nonvolatile siloxanes and contributes to wetting and conditioning (47).

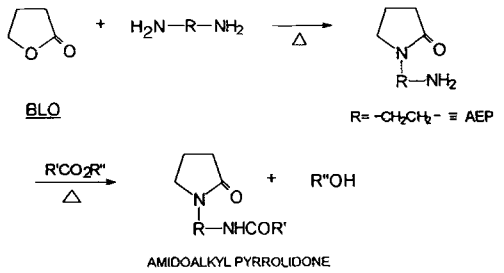
Long-chain N-alkyl pyrrolidones have been proposed for a variety of applications as diverse as skin-penetration enhancers (48,49), tick repellents (50), plant virus growth inhibitors (51), rice herbicides (52), deinking of waste paper (53), manufacturing of hydrogen peroxide (54), stabilizing additives in photographic emulsions (55), industrial microbiocides and preservatives (56), solubilizers for unneutralized chlorhexadine (57) in water, and emulsifier co-surfactant in water-in-oil emulsion polymerization (58).

Now that the substituted pyrrolidones are commercially available (Surfadone®, ISP, Wayne, NJ); additional applications in such end uses as drug solubilization, chemical processing, cosmetic, agricultural, and detergent formulations can be expected.

Toxicity. Ansell and Fowler (1) have summarized some of the extensive toxicological information available for both C_8P and $C_{12}P$. Basically, at recommended use levels of a few percent, neither derivative is an ocular or primary skin irritant. With a LD_{50} of 5.0 g/kg, vs. 2.05 g/kg for C_8P, $C_{12}P$ is the less toxic material. Both surfactants are nonmutagenic by the Ames test and noncomedogenic by the rabbit ear test. In human clinical studies, neither compound was phytotoxic or photoallergic, nor were they contact dermal sensitizers. Analytical studies failed to detect nitrosamines at a 50-ppb detection limit, and, as previously mentioned, both are highly biodegradable.

AMIDOALKYL PYRROLIDONES

The reaction of butyrolactone (BLO) with primary amines at high temperatures produces N-alkyl substituted pyrrolidones directly and is the commercial route to such derivatives. How-



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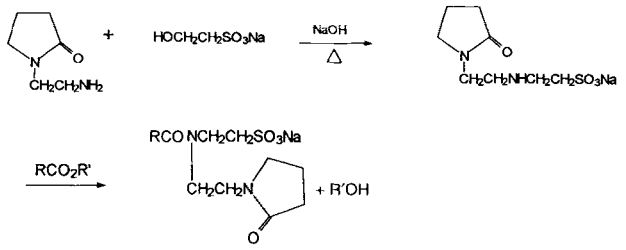


SCHEME 5

ever, other methods of incorporating the pyrrolidone nucleus also have been investigated. BLO reacts with diamines, when the diamine is in excess, to afford N-amino-alkyl pyrrolidones (AEP), which can be further condensed with fatty acids, anhydrides, acid chlorides, or esters to produce amidoalkyl pyrrolidones (59) (Scheme 4). When the fatty acids are in the surfactant range ($C_8 - C_{16}$), highly surface-active compounds are formed (60). For convenience, the surfactant and physical properties are included in the earlier tables and figures along with the N-alkyl-2-pyrrolidones, and the example shown in those charts is based on the condensate formed from distilled whole-cut coconut fatty acids and AEP. This amido derivative is more water-soluble than the corresponding N-alkyl derivative and exhibits lower interfacial tension, suggesting that by itself it would display greater detergency. AEP also can be condensed with sodium isethionate to form the N-(pyrrolidonylethyl) taurine sodium salt, which can be further condensed with lauric acid to form the N-(pyrrolidonylethyl) N-lauroyl taurine salts (61) (Scheme 5). Adding the taurine functional group to the amidoalkyl pyrrolidone results in greater water solubility and compatibility.

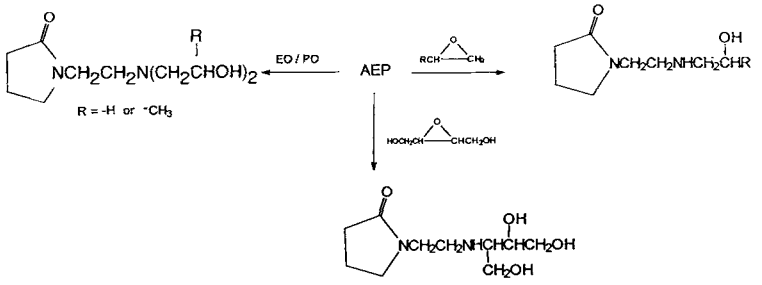
AEP also reacts with epoxides, such as fatty alpha-olefin epoxides, to produce hydroxy secondary amine surfactants. The reaction with EO, PO, or 2,3-epoxy-1,4-butanediol affords N-pyrrolidonyl ethyl amino alcohols, and such derivatives are thought to be useful as complexing aqueous solubilizers for medicinals, agricultural chemicals, iodine, and the like (62) (Scheme 6). In this reaction, the pyrrolidone functional group exhibits affinity for selected insoluble actives, and the amino alcohol contributes aqueous solubility. Obviously, AEP itself can neutralize acid-containing compounds, to improve aqueous solubility (63), and can be ethoxylated to afford tertiary amine derivatives with significant hydrophilicity.

EPOXYPROPYL PYRROLIDONE (EPP)

Pyrrolidone reacts under alkaline conditions with epichlorohydrin to form the N-epoxypropyl derivative in modest yield (64). Recently, the use of quaternary ammonium phase-transfer catalysts has been shown to improve the yield from 20–30% to about 70% (65). Although EPP can be homopolymerized (66), recently it has been employed as a building block for nonionic surfactants. EPP can be readily copolymerized with EO and PO to form a wide variety of block polyols (67). Such block polyols are surface-active complexing agents and find particular application as moisturizers in shampoo and cosmetic cream or lotion formulations (Schemes 7 and 8).

EPP will readily condense with a wide variety of hydrophobes (68), such as fatty alcohols and alkyl phenols, analogous to EO and PO. The hydrophobe is dehydrated in the presence of potassium or sodium hydroxide or the corresponding methylate, and EPP is added over time to this mixture, at 110–120°C or so. The mixture is then neutralized with glacial acetic acid and analyzed. Table 13 illustrates the observed cloud point and surface tension measurements, and Table 14 shows foam heights and Draves wetting for nonylphenol and lauryl alcohol derivatives.

Although analysis of these materials indicates that the hydroxyl numbers are more than theoretical and that the reac-



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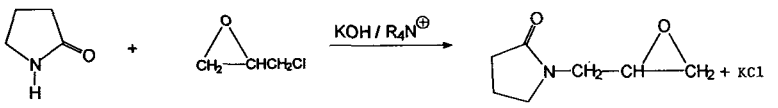

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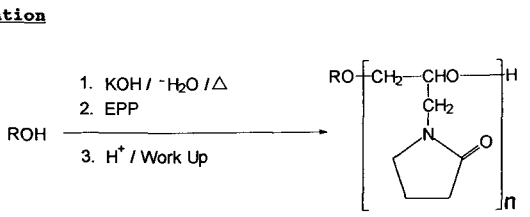


SCHEME 8

tion requires fine-tuning, the data suggest that EPP contributes hydrophilicity and produces highly surface-active compounds. However, because of increased hydrophilicity and molecular size, surface activity drops off as the amount of EPP is increased. The foaming and wetting data can be explained in the same way. However, considering pyrrolidone's proven ability to complex, those derivatives with low foam are particularly useful adjuvants for hard-surface cleaners, such as laundry detergents, metal cleaners, etching solutions, or anti-rust compositions.

These products are readily soluble in polar solvents, such as water, ethanol, and butyl cellosolve, but only partly soluble or insoluble in nonpolar solvents, much like PVP.

Iodophors based on PVP and EO adducts are well known (69); therefore, surfactants that contain pyrrolidone, such as those prepared with EPP, have the advantage of combining both functions in the same compound. In fact, PVP.I is combined in various surgical scrub and disinfectant formulations with surfactant to enhance detergent properties. Such a combination product would be expected to clean and disinfect at the same time, affording a slow release of a stabilized form of soluble iodine (70,71).

CARBOXYPYRROLIDONES

Itaconic acid condenses with primary amines to readily form 4-carboxypyrrolidone derivatives (Scheme 9). As the R group increases in chainlength into the surfactant range (C_8–C_{14}), a series of surface-active "interrupted" soaps can readily be synthesized (72). Comparison to similar sarcosine derivatives indicates nearly equivalent performance and mildness. However, the sarcosine derivatives are less expensive because of current itaconic acid economics. Interestingly, like the hydrophilic amide in sarcosines, the 4-carboxypyrrolidones form complexes with fatty quaternary derivatives that are water-soluble, presumably because the pyrrolidone solubilizes the complex. A similar effect is observed when the pyrrolidone is incorporated into a fatty quaternary derivative (described in the following section).

CHLOROMETHYL PYRROLIDONE (CMP) AND QUATERNARY AMMONIUM DERIVATIVES

CMP synthesis. CMP can be prepared from hydroxymethyl pyrrolidone (HMP) by reaction with thionyl chloride (73). The same reaction with primary alcohols is of commercial significance in the manufacture of chlorine-capped ethoxylated surfactants which are useful for low-foam applications (74). Because of nucleophilicity, with amido alcohols conversion of the intermediate thionyl ester to chloride derivative is facile, affording CMP in high yields (75) (Scheme 10).

CMP is an active alkylating agent (76,77) and will react with a wide variety of nucleophiles. The reaction with tertiary amines to form quaternary ammonium compounds is exothermic and easily carried out under anhydrous conditions. CMP

TABLE 13
Epoxypropyl Pyrrolidone (EPP)-Based Nonionic Surfactants

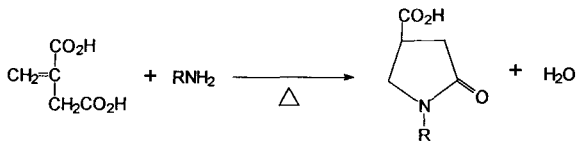
Hydrophobe	(Theoretical) moles of EPP	1% Cloud point (°C)	Surface tension minimum[a]	CMC × 10^{-2} (%)[b]
Nonylphenol (NP)	2	<0	—	—
NP	4	33	30.9	0.94
NP	6	66[c]	34.2	1.4
NP + 4 ethylene oxide (EO)	2	<0	31.9	1.0
NP + 4 EO	4	>100	30.7	1.4
NP + 15 EO	3.5	>100	38.8	1.4
Lauryl alcohol	3	<0	26.8	1.02
Lauryl alcohol	5	67–68[c]	32.6	1.25

[a]dynes/cm, 25°C (Fisher Surface Tensiomat, Model 21 DU Nou; Fisher Scientific, Fairlawn, NJ). At 0.1%, all solutions are optically clear.
[b]CMC, critical micelle concentration.
[c]10% NaCl solution.

TABLE 14
Ross–Miles Foam and Draves Wetting for EPP–Based Nonionic Surfactants[a]

Hydrophobe	Moles of EPP	0.1% Foam height MM Initial	0.1% Foam height MM After 5 min	0.1% Wetting time (s)
NP	4	32.5	30	11.2
NP	6	40.5	38	40.6
NP + 4 EO	2	26.0	17.5	27.0
NP + 4 EO	4	15.0	4.5	36.0
NP + 15 EO	3.5	81.0	71.0	41.9
Lauryl alcohol	3	63.5	54.5	17.2
Lauryl alcohol	5	18.0	9.0	127.0

[a]Abbreviations as in Table 13.



SCHEME 9

exhibits a low vapor pressure at 25°C, is easily hydrolyzed to form HMP, and, therefore, is readily eliminated by hydrolysis as an impurity after alkylation, unlike related, more hydrolysis-resistant, alkylating agents, such as benzyl or methyl chloride. CMP's physical properties are: appearance, colorless solid or liquid; melting point, 37–38°C; boiling point, 96–98°C (~0.3 mm Hg); decomposition [thermogravimetric analysis (TGA)], ≤150°C; molecular weight, 133.6. Because of its reactivity with water and the liberation of hydrochloric acid, CMP exhibits acute toxicity as a result of its corrosive action. However, it does not pose a chronic problem and does not remain in aqueous formulations or in the environment. CMP's reactivity is a direct consequence of the resonance stability of the corresponding amidomethyl carbonium ion, which can be represented by three canonical forms (Scheme 11). The N-methylene carbon is therefore electron-deficient and, hence, electrophilic. Reaction with a fatty tertiary amine can be readily accomplished neat or in anhydrous nonreactive solvents such as acetone. The reaction is essentially quantitative except for the by-products amine hydrochloride salt and HMP as a result of residual moisture (78–87).

Quaternary ammonium derivatives. Placing a pyrrolidone substituent on a fatty quaternary ammonium compound results in increased aqueous solubility. The pyrrolidone group contributes hydrophilicity equal to about two moles of EO and affords a compact substituent unlike the situations with ethoxylated amine-based quaternaries.

Models of CMP-derived quaternaries show crowding around the quaternary nitrogen, resulting in varying levels of instability. Quaternaries are known to exhibit ceiling temperatures (on-set of decomposition) or reactivity as in the Hofmann elimination. The nature of the R group or counter ion plays a crucial role with straight-chain derivatives, which exhibit the lowest ceiling temperature. Structures with an amido or ester linkage two to three carbons from the quaternary nitrogen are 15 times more stable than straight-chain derivatives and are sufficiently stable to survive a three-month accelerated aging test at 45°C. This is also the situation when the chloride counter ion is exchanged with a less nucleophilic organic sulfate or sulfonate, even with straight-chain derivatives.

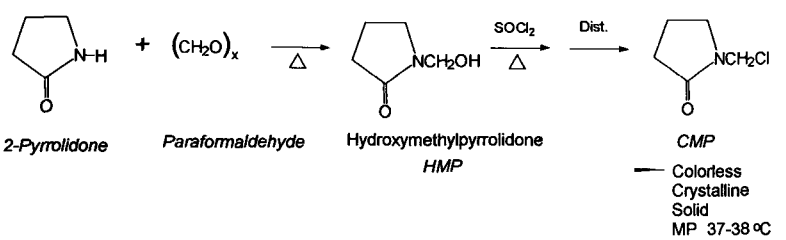
Formulation with anionic surfactant, such as SLS, ALS, or SLES, results in chloride exchange because of strong cation–anion interaction. This results in significantly improved stability, even for the N-alkyl quaternary derivatives (88) (Scheme 12). The structure of these quaternary pyrrolidonyl compounds affords interesting speculative possibilities (Scheme 13).

Inspection of the canonical forms illustrates the possibility that the carbonyl oxygen negative charge can shield the quaternary nitrogen, reducing its apparent charge in favor of a partial charge on the lactam nitrogen. This is similar to the betaines and accounts for their mildness.

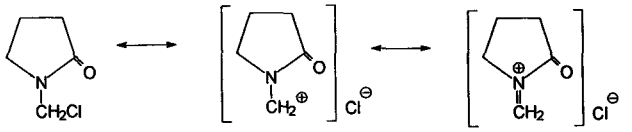
With personal-care and cosmetic applications in mind, stability concerns dictated that dimethyl stearamidopropyl [(2-pyrrolidonyl) methyl] ammonium chloride (DSPMAC) be evaluated. It was prepared from the corresponding amidoamine, which, in turn, was based on a relatively pure cut of stearic acid. The amido–amine starting raw material typically is 99% pure with a melting point of 65–70°C.

A solution of the amido amine in acetone is readily quaternized with CMP, filtered and dried. The subsequent quaternary (DSPMAC) has the following CTFA dictionary designation–stearamidopropyl pyrrolidonyl methyl dimonium chloride (Surfadone ^{R} QSP; ISP Corp., Wayne, NJ) (Scheme 14).

Analysis. The standard method of analysis for fatty quater-



SCHEME 10



SCHEME 11

naries is the Epton or methylene blue two-phase titration, which relies on the insolubility of a complex of the quaternary and the anionic surfactant titrant. In the present case, this complex is too water-soluble to afford a sharp end point, and this method of analysis cannot be employed. Good results are obtained with a method based on sodium tetraphenylboron (89) or by thin-layer chromatography (90). A key feature of this quaternary is its outstanding solubility (wt/wt%, 25°C): water, 25%; ethanol, 40%; propylene glycol, 5%; mineral oil, 0.5%.

Surface tension. The surface tension vs. concentration curve in 0.1 N NaCl (passed through a SEP-PAK® silicone column to absorb impurities that are more surface-active than DSPMAC) indicates a CMC of 5×10^{-6}M, Π_{max} of 40 dynes/cm and an area/molecule at the interface of $35A^2$ (M. Rosen, private communication). This suggests that DSPMAC should exhibit significant activity as a hair conditioner because exhaustion and substantivity from dilute solution are to be expected. Figure 10 shows the surface tension/concentration curves for DSPMAC in distilled water and in 0.1N NaCl, showing the pronounced and expected effect of the common chloride ion with added electrolyte. In this case, the common ion shields the charge repulsion in the micelle and allows micelles to form at much lower concentrations, 1×10^{-5} vs. 1×10^{-4}M for distilled water. Increasing the alkyl chainlength to behenyl (60% C_{22}, 40% C_{20}), as expected, reduces the CMC to 5×10^{-4}M in distilled water.

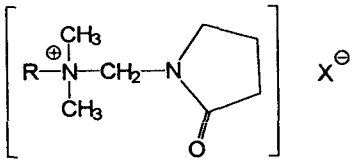
The solubility of DSPMAC in water allows easy mixing with anionics, such as ALS and SLS. In typical shampoo formulations with 12% anionic, clear solutions can be prepared with up to 5% DSPMAC. Foam is not compromised even at this level. In addition, DSPMAC will thicken mesophases much like other auxiliary surfactants such as those based on betaines, sultaines, amine oxides, and alkanolamides. Maximum viscosity is reached at a ratio of three parts anionic to one part DSPMAC, and even several percent of DSPMAC will not degrade foam as measured by the Ross–Miles test.

Performance tests and salon evaluations, rating such attributes as wet and dry combing, curl retention, static, and fly away, indicate that DSPMAC is as active and effective as competitive conditioners, such as stearalkonium chloride and dicetyldimonium chloride. However, in dry combing, it clearly has the advantage as measured by the method of Garcia and Dias (91) according to Instron combing tests. The advantage of DSPMAC is that additional benefits can be achieved by taking advantage of the ability of the pyrrolidone substituent to complex with desirable actives such as sunscreens and hair dyes (92,93). Because a significant proportion of these ingredients contain phenolic groups, they can be expected to complex with the pyrrolidone substituent and be carried onto or in the hair because of the hair's strong affinity for surface-active quaternaries. Many fragrance additives can be complexed and delivered in a similar manner (94).

The high level of water solubility of DSPMAC guarantees easy removability during subsequent shampooing. Furthermore, evaluation of toxicity indicates that, as with other pyrrolidone derivatives, DSPMAC exhibits a mild toxicity profile.

Unlike other quaternaries, such as those derived from benzyl chloride, DSPMAC and lower-molecular weight homologs do not exhibit germicidal or fungicidal activity, even at 500 ppm ("Use—Dilution" test, Association of Official Analytical Chemists). This correlates with their inherent mildness and low toxicity (Tables 15 and 16).

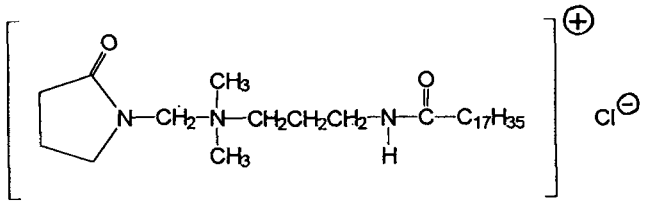
In conclusion, the pyrrolidone functional group can contribute desirable attributes to a wide variety of surfactants and other compounds. They include water solubility, solvency, polarity (low vapor pressure), and hydrogen-bonding complexation. In addition, in practically every instance pyrrolidone affords derivatives with improved mildness. This key attribute, related to other "interrupted" soaps, points clearly to utility in cosmetic, personal-care, and pharmaceutical formulations.



Order of Stability When R is: N-alkyl ($Cl^{\ominus}$) < N-alkyl ($-SO_3^{\ominus}$, $-OSO_3^{\ominus}$) < $R'CONH(CH_2)_3$ / $R'CO_2CH_2CH_2Cl^{\ominus}$ < $R'CONH(CH_2)_3$ / $R'CO_2CH_2CH_2$ ($-SO_3^{\ominus}$, $-OSO_3^{\ominus}$)

SCHEME 12

SCHEME 13



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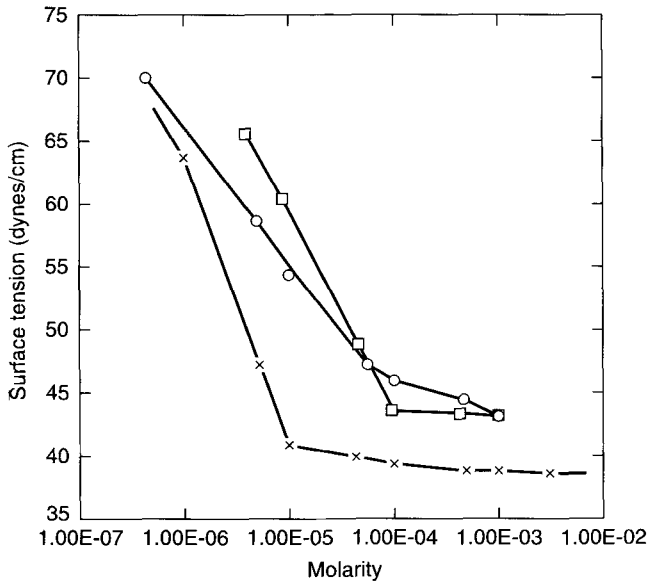

FIG. 10. Surface tension. CMC, critical micelle concentration. □, Stearamidopropyl pyrrolidonyl methyl dimonium chloride (distilled water), 1×10^{-4} M (CMC); X, stearamidopropyl pyrrolidonyl methyl dimonium chloride (0-1N NaCl) 1×10^{-4} M (CMC); ○, benehamidopropyl pyrrolidonyl methyl dimonium chloride (distilled water) $5 \times^{-4}$ M (CMC).

TABLE 15
Toxicity of Dimethyl Stearamidopropyl [(2-pyrrolidonyl)methyl] Ammonium Chloride

	Concentration	Results
Acute oral (LD_{50})	1.12 g/kg	—
Acute dermal	>2.0 g/kg	No effects
Comedogenicity	5%	Negative
Ames test	—	Negative
Mouse micronucleus	1077 mg/kg	Negative

ACKNOWLEDGMENTS

The special advice and assistance of Prof. Milton J. Rosen is greatly appreciated. The encouragement and advice of Dr. William J. Burlant was critical from the beginning in achieving commercial success.

TABLE 16
Irritation of Dimethyl Stearamidopropyl [(2-pyrrolidonyl)methyl] Ammonium Chloride

	Concentration (%)	Skin (PII)	Eye unwash 30-s wash
Stearamidopropyl Pyrrolidonyl methyl Dimonium chloride	5	1.6	Moderate Mild
Stearamidopropyl Pyrrolidonyl methyl Dimonium chloride	2	1.0	Minimal Minimal
Dicetyldimonium Chloride	5	4.08	Severe Severe

REFERENCES

1. Ansell, J.M., and J.A. Fowler, *Fd. Chem. Toxic 26*:475 (1988).
2. Robinson, B.V., F.M. Sullivan, J.F. Borcelleca and S.L. Schwartzs, *A Critical Review of the Kinetics and Tox. of Polymers*, Lewis Publishers, 1990.
3. Copenhaver, J.W., and M.H. Bigelow, *Acetylene and Carbon Monoxide Chemistry*, Reinhold, New York, 1949.
4. Reppe, W., *Bibliogr. Tech. Rep. 10*:348 (1948).
5. *NMP-ISP NMP Bulletin*, ISP Corp., Wayne, NJ, 1990.
6. Barabas, E.S., *Encyclopedia of Polymer Science and Engineering*, Vol. 17, 2nd edn., John Wiley, New York, 1989.
7. Zienty, F.B., and G.W. Steahly, *J. Am. Chem. Soc. 69*:716 (1947).
8. Tracy, D., M. Hashem and V. Vara, U.S. Patent 4,760,152 (1988).
9. Tracy, D., and M. Hashem, U.S. Patent 4,698,412 (1987).
10. Lee, C.M., and W.D. Kumler, *J. Am. Chem. Soc. 83*:4593 (1961).
11. Login, R.B., R.K. Chaudhuri, M.M. Hashem, M.W. Helioff, D. Pritchard and R. Ruppert, WO 88/00184 (1988).
12. Login, R.B., R.K. Chaudhuri, M.M. Hashem, M.W. Helioff, D. Pritchard and R. Ruppert, U.S. Patent 5,093,031 (1992).
13. Login, R.B., R.K. Chaudhuri, M.M. Hashem, M.W. Helioff, D. Pritchard and R. Ruppert, U.S. Patent 5,294,644 (1994).
14. Rosen, M.J., Z.H. Zhu, B. Gu and D.S. Murphy, *Langmuir 4*:1273 (1988).
15. Nakagaski, M., and S. Shimabayashi, *J. Chem. Soc. Japan 11*: 2056 (1973).
16. Shimabayashi, S., and M. Nakagaki, *Ibid. 14*:547 (1976).
17. Molyneux, P., *Water-Soluble Synthetic Polymers*, Vol. 1, CRC Press, Boca Raton, 1984.
18. Kirsch, Y.E., *Prog. Poly. Sci. 18*:519 (1993).
19. *Surfadone Bulletin*, ISP Corp., Wayne, NJ, 1992.
20. Schreiner, J.L., *Spray Technology & Marketing*, January (1994).
21. Zhu, Z.H., D. Young and M.J. Rosen, *J. Am. Oil Chem. Soc. 66:998* (1989).
22. Login, R.B., C. Bires and E. Walls, U.S. Patent 5,160,729 (1992).
23. Hornby, J., and D. Jon, *Surface Active Specialty Solvents, Soap & Cosmetic Specialties*, September (1992).
24. Rosen, M.J., B. Gu, D.S. Murphy and Z.H. Zhu, *J. Colloid and Interfacial Sci.* 468 (1989).
25. Rosen, M.J., *J. Am. Oil Chem. Soc. 66*:1840 (1989).
26. Rosen, M.J., *Surfactants and Interfacial Phenomena*, 2nd edn., J. Wiley & Sons, New York, 1989.
27. Rosen, M.J., and Z.H. Zhu, *J. Am. Oil Chem. Soc. 70*:65 (1988).
28. Helioff, M.W., and S. Marsi, *Drug & Cos. Ind.*, April (1988).
29. Helioff, M.W., S. Marsi and C. Bires, *Cosmetics & Toiletries*, 80 (1988).

30. Narayanan, K.S., and R.K. Chaudhuri, *IUPAC 7th International Congress of Pesticide Chemistry*, Hamburg, 1990, pp. 77–94.
31. Narayanan, K.S., and R.K. Chaudhuri, *Pesticide Formulation and Application Systems*, Vol. II, edited by D.G. Chasin, and L.N. Borde, American Society for Testing Materials, Philadelphia, 1990.
32. Narayan, K.S., *13th Symposium of Pesticide Formulation and Application—The Pesticide Science Society of Japan*, Saitaoma Foundation Center, November 11, 1993.
33. Narayanan, K.S., and R.K. Chaudhuri, U.S. Patent 5,283,229 (1994).
34. Narayanan, K.S., R.K. Chaudhuri and M. Dhanayake, U.S. Patent 5,250,499 (1993).
35. Narayankan, K.S., R.K. Chaudhuri and M. Dhanayake, U.S. Patent 5,176,736 (1993).
36. Narayanan, K.S., R.K. Chaudhuri and M. Dhanayake, U.S. Patent 5,160,528 (1992).
37. Narayanan, K.S., R.K. Chaudhuri and M. Dhanayake, U.S. Patent 5,156,666 (1992).
38. Narayanan, K.S., R.K. Chaudhuri and M. Dhanayake, U.S. Patent 5,071,463 (1991).
39. Narayanan, K.S., U.S. Patent 5,317,042 (1994).
40. Narayanan, K.S., U.S. Patent 5,300,529 (1994).
41. Narayanan, K.S., U.S. Patent 5,298,529 (1994).
42. Login, R.B., and R.K. Chaudhuri, U.S. Patent 4,719,287 (1988).
43. Murthy, A.K., *Colloid & Polymer Science 271*:209 (1993).
44. Hull, M., and P.C. Van Der Hoeven, GB Patent 2,259, 096A (1993).
45. Bires, C., M.W. Helioff and R.B. Login, U.S. Patent 4,775,527 (1988).
46. Helioff, M.W., C. Bires and R.B. Login, U.S. Patent 4,793,994 (1988).
47. Zhou, J., and D.J. Fochtman, U.S. Patent 5,198,209 (1993).
48. Rajadhyaksha, V.J., U.S. Patent 3,991,203 (1976).
49. Rajadhyaksha, V.J., U.S. Patent 4,122,170 (1978).
50. Skinner, W.A., U. Rosentreter and T.E. Elward, U.S. Patent 4299,840 (1981); *J. Pharm. Sci. 72*:1354 (1983).
51. Dalington, W.A., U.S. Patent 3,085,931 (1963).
52. Takemkatsu, T., Japan Patent Appl. No. 92,231 (1974).
53. Mestetsky, T.S., and B.G. Webster, U.S. Patent 3,846,227 (1974).
54. Ranbom, W., U.S. Patent 4,394,369 (1983).
55. Kobayashi, R., T. Usui and T. Omura, Ger. Offen. 2,805,250 (1978).
56. Hollis, C.G., S.R. Rayudu and M.S. Whkittemore, U.S. Patent 5,250,194 (1993).
57. Merianos, J.J., and R.B. Login, U.S. Patent 5,008,038 (1991).
58. Chuang, J., U.S. Patent 5,206,316 (1993).
59. Buc, S.R., and E.P. Williams, U.S. Patent 2,945,863 (1960).
60. Diehl, F.L., U.S. Patent 3,322,675 (1967).
61. Anderson, L.R., M.M. Hashem and R.B. Login, U.S. Patent 4,918,198 (1990).
62. Anderson, L.R., M.M. Hashem and R.B. Login, U.S. Patent 4,924,006 (1990).
63. Narayanan, K.S., R.K. Chaudhuri and R.B. Login, U.S. Patent 5,221,791 (1993).
64. Sidelkovkaya, E.P., *Chim. Geterosiki Soevin 2*:212 (1968).
65. Chaudhuri, R.K., R.B. Login and D.J. Tracy, U.S. Patent 4,713,463 (1987).
66. Sidelkorskaya, F.P., *Vysokomol. Soedin Ser. B* (10/3):187 (1968).
67. Tracy, D.J., R.B. Login and M.M. Hashem, U.S. Patent 4,698,412 (1987).
68. Login, R.B., M.M. Hashem and D.J. Tracy, U.S. Patent 4,801,400 (1989).
69. Gottardi, W., *Disinfection Sterilization, and Preservation*, edited by S. Block, Lea & Febiger, Philadelphia, 1991, p. 152.
70. Tracy, D.J., M.M. Hashem and R.B. Login, U.S. Patent 4,830,851 (1989).
71. Tracy, D.J., M.M. Hashem and R.B. Login, U.S. Patent 4,842,858 (1989).
72. Murdak, A., U.S. Patent 2,757,125 (1956).
73. De Lannoy, J., U.S. Patent 4,216,221 (1980).
74. *Antarox Surfactants,* Rhone Poulenc, Cranbury.
75. Tracy, D.J., and T. Rizzo, U.S. Patent 4,792,604 (1988).
76. Narayanan, K.S., and P. Taylor, U.S. Patent 4,997,952 (1991).
77. Narayanan, K.S., and P. Taylor, U.S. Patent 5,206,386 (1993).
78. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Heilioff, U.S. Patent 4,732,990 (1988).
79. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Heilioff, U.S. Patent 4,830,850 (1989).
80. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Heilioff, U.S. Patent 4,834,970 (1989).
81. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Helioff, U.S. Patent 4,837,013 (1989).
82. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Helioff, U.S. Patent 4,883,655 (1989).
83. Login, R.B., R.K. Chaudhuri and D.J. Tracy, U.S. Patent 4,886,890 (1989).
84. Login, R.B., R.K. Chaudhuri and D.J. Tracy, U.S. Patent 5,008,104 (1991).
85. Login, R.B., R.K. Chaudhuri, D.J. Tracy and M.W. Helioff, U.S. Patent 5,110,585 (1992).
86. Login, R.B., R.K. Chaudhuri and D.J. Tracy, U.S. Patent 5,156,837 (1992).
87. Login, R.B., and R.K. Chaudhuri, U.S. Patent 5,157,126 (1992).
88. Tracy, D.J., T. Rizzo and R.B. Login, U.S. Patent 4,885,158 (1989).
89. Cross, J.T., *Analysis 90*:315 (1965).
90. Ianniello, R.M., *J. Liq. Chromatogr. 13*:1943 (1990).
91. Garcia, M.L., and J. Diaz, *J. Soc. Cosmet. Chem. 27*:379 (1976).
92. Helioff, M.W., C.D. Bires and R.B. Login, U.S. Patent 4,834,767 (1989).
93. Helioff, M.W., C.D. Bires and R.B. Login, U.S. Patent 4,871,535 (1989).
94. Chaudhuri, R.K., M.W. Helioff and R.B. Login, U.S. Patent 4,808,569 (1989).

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