ALKANOLAMINES FROM NITRO ALCOHOLS

1. Introduction

The nitro alcohols (qv), obtained by the condensation of nitroparaffins (qv) with formaldehyde [50-00-0], may be reduced to a unique series of alkanolamines (β-amino alcohols):

$$\mathrm{RCH_2NO_2} + \mathrm{CH_2O} \longrightarrow \mathrm{R}\underset{\displaystyle \mathrm{NO_2}}{\underset{|}{\mathrm{C}}}\mathrm{HCH_2OH} \xrightarrow{[\mathrm{H}]} \mathrm{R}\underset{\displaystyle \mathrm{NH_2}}{\underset{|}{\mathrm{C}}}\mathrm{HCH_2OH}$$

The condensation may occur one to three times, depending on the number of available hydrogen atoms on the α-carbon of the nitroparaffin, giving rise to amino alcohols with one to three hydroxyl groups. A comprehensive review of these compounds has been published (1).

Many members of this series are known, based on nitroparaffin condensations with aldehydes of longer chain length than formaldehyde. However, only the five primary amino alcohols discussed in the following are manufactured on a commercially-significant scale. N-Substituted derivatives of these compounds

Table 1. **Commercial Alkanolamines**

Name	Common designation	Molecular formula	Molecular weight	CAS Registry Number	EINECS Number
2-amino-2-methyl-1-propanol	AMP	$C_4H_{11}NO$	89.14	[124-68-5]	204-709-8
2-amino-2-ethyl-1,3-propanediol	AEPD[a]	$C_5H_{13}NO_2$	119.16	[115-70-8]	204-101-2
2-dimethylamino-2-methyl-1-propanol	DMAMP	$C_6H_{15}NO$	117.19	[7005-47-2]	230-279-6
2-amino-2-(hydroxymethyl)-1,3-propanediol[b]	TRIS AMINO[a]	$C_4H_{11}NO_3$	121.14	[77-86-1]	201-064-4
2-amino-2-methyl-1,3-propanediol	AMPD	$C_4H_{11}NO_2$	105.16	[115-69-5]	204-100-7
2-amino-1-butanol	AB[a]	$C_4H_{11}NO$	89.14	[96-20-8]	202-488-2

[a] AB, AEPD, and TRIS AMINO are trademarks of ANGUS Chemical Company.
[b] Common name is tris(hydroxymethyl)aminomethane.

also have been prepared, but only 2-dimethylamino-2-methyl-1-propanol is available in commercial quantities (Table 1).

2. Physical Properties

Physical properties of the six commercial alkanolamines are given in Table 2. Because 2-amino-2-methyl-1-propanol (AMP) and 2-amino-2-ethyl-1,3-propanediol (AEPD) melt near room temperature and usually contain some water, they may be semisolid pastes, rather than crystalline solids. Water-diluted forms of both these alkanolamines are marketed because such solutions remain liquid at lower temperatures than do the pure compounds, eg, AMP-95, which contains 5% water, solidifies at $-2°C$.

These compounds are highly soluble in water. AMP, AB, AEPD, and DMAMP are completely miscible in water at 20°C; the solubility of AMPD is

Table 2. **Properties of Alkanolamines**

Compound	Boiling point, °C	Melting point, °C	Specific gravity	pH of 0.1 M aqueous solution	pK_a at 25°C
AMP	165[a]	30–31	0.934[b]	11.3	9.72
AEPD	152–153[c]	37.5–38.5	1.099[b]	10.8	8.80
DMAMP	160[a]	19	0.90[d]	11.6	10.2
TRIS AMINO	219–220[c]	171–172	N.A.[e]	10.4	8.03
AMPD	151–152[c]	109–111	N.A.[e]	10.8	8.76
AB	178[a]	−2	0.944[b]	11.1	9.52

[a] At 101.3 kPa (1 atm).
[b] At 20/20°C.
[c] At 1.3 kPa (10 mm Hg).
[d] At 25/25°C.
[e] N.A. = Not applicable.

250 g/100 mL H_2O at 20°C. They are generally very soluble in alcohols, slightly soluble in aromatic hydrocarbons, and nearly insoluble in aliphatic hydrocarbons; tris(hydroxymethyl)aminomethane is appreciably soluble only in water (80 g/100 mL at 20°C) and methanol.

Alkanolamines have high boiling points; under normal ambient conditions, their vapor pressures are low. Only DMAMP (see Table 2) forms an azeotrope with water, which boils at 98°C and contains 25% by weight of DMAMP. According to current DOT regulations, AMP, AMP-95, DMAMP, DMAMP-80, AEPD, and AB are all classified as combustible liquids.

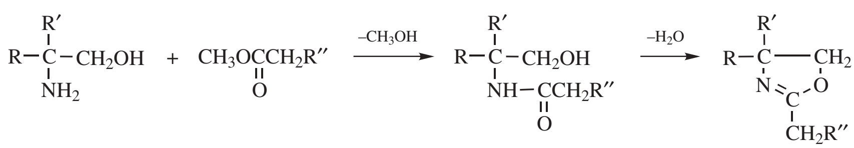
DMAMP and AMP are among the most strongly basic commercially-available amines. The dissociation constants of these materials appear in Table 2. All alkanolamines have slight amine odors in the liquid state; the solid products are nearly odorless.

3. Chemical Properties

The alkanolamines discussed here exhibit the chemical reactivity of both amines and alcohols, as is the case with other alkanolamines. Typically, they attack copper, brass, and aluminum, but not steel or iron. Alkanolamines are useful as amination agents; however, the reactivity of both the amino and alcohol group must be considered in attempting any specific synthetic scheme with them.

With mineral acids, the alkanolamines form ammonium salts which hydrolyze readily in the presence of water and dissociate upon heating. Fatty acids, such as oleic acid, give soaps which are highly efficient emulsifying agents with important industrial uses, particularly the soaps of AMP (see EMULSIONS; SURFACTANTS).

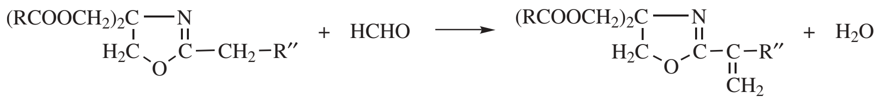
On heating, an alkanolamine soap first dehydrates to the amide; this is also obtained from the methyl ester of the fatty acid by heating with the alkanolamine at 60°C in the presence of a catalytic amount of sodium methoxide. Methanol is removed under partial vacuum. At higher temperature, the amide is dehydrated to an oxazoline.



where for AEPD, R = C_2H_5, R′ = CH_2OH and for TRIS AMINO, R = R′ = CH_2OH

These oxazolines have cationic surface-active properties and are emulsifying agents of the water-in-oil type. They are acid acceptors and, in some cases, corrosion inhibitors (see CORROSION). Reactions of AMP with organic acids to create oxazoline functionality are useful as a tool for determination of double-bond location in fatty acids (2), or for use as a carboxylic-acid protective group in synthesis (3,4). The oxazolines from AMPD, AEPD, and TRIS AMINO contain hydroxyl groups that can be esterified easily, giving waxes (qv) with saturated acids and drying oils (qv) with unsaturated acids.

Formaldehyde reacts with the hydrogen on the α-carbon of the fatty acid from which the oxazoline was formed to yield a vinyl monomer that can be polymerized or utilized for synthesis (5). Thus, esters of the oxazoline formed from TRIS AMINO undergo the reaction:

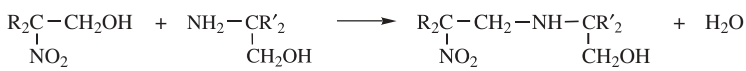


These products are useful for modification of alkyd resins (qv), preparation of paint vehicles, and copolymerization with other monomers.

Substitution on the amino group occurs readily, giving bases stronger than the parent amines.

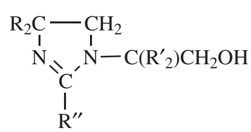
$$R{-}NH_2 + 2\,HCHO \xrightarrow{2\,H_2} R{-}N(CH_3)_2 + 2\,H_2O$$

Alkanolamines react with nitro alcohols to form nitrohydroxylamines (6).

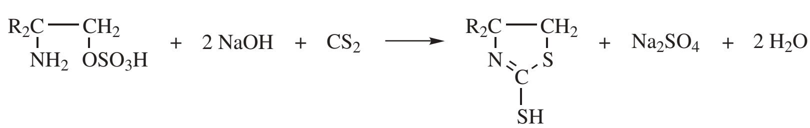


(1)

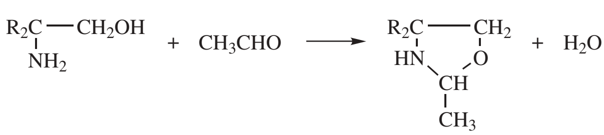
Some of these compounds show antibacterial activity. Reduction gives 2-[(2-aminoethyl)amino]ethanols that react with organic acids to form amides that, on further heating, cyclize to imidazolines (7). For example, the diamine obtained by reducing (1) reacts with an organic acid (R″COOH) to give:



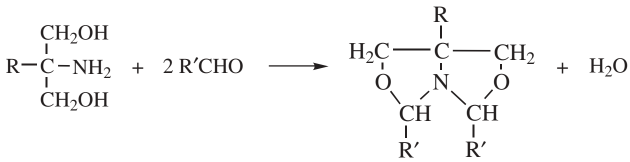
Mercaptothiazolines are obtained from the corresponding sulfate esters and carbon disulfide.



Aldehydes react with monohydric alkanolamines to give monocyclic oxazolidines

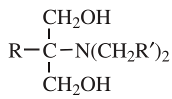


or with polyhydric alkanolamines to give bicyclic oxazolidines (8,9).



(2)

These can be hydrogenated to N,N-substituted alkanolamines. Thus (2) yields:



Oxidation of the hydroxyl group, after protection of the amine group by benzoylation, gives amino acids (8), eg, oxidation of 2-amino-2-methyl-1-propanol to 2-methylalanine [62-57-7], $(CH_3)_2CNH_2COOH$.

4. Manufacture

The reduction of nitro alcohols to alkanolamines is readily accomplished by hydrogenation in the presence of Raney nickel catalyst (1,10,11).

AMP, AEPD, and AB are purified by distillation. TRIS AMINO and AMPD are purified by crystallization. TRIS AMINO concentrate in water (40% assay) is also available.

2-Dimethylamino-2-methyl-1-propanol is manufactured from AMP by hydrogenation in the presence of formaldehyde and purified by distillation. It is marketed primarily as DMAMP-80 (water added), however.

5. Economic Aspects

Production statistics on alkanolamines are not available, but they are sold in 1000-ton quantities and are available for bulk shipment except for DMAMP, AB, TRIS AMINO, and AMPD (the latter two being crystalline solids). TRIS AMINO concentrate is available in bulk. AMPD is manufactured only in low volumes to meet limited demand in certain specialized uses.

ANGUS Chemical Company is the basic manufacturer of technical-grade TRIS AMINO. However, ANGUS and numerous processors offer recrystallized, higher purity grades of this alkanolamine for specialized applications (tris buffer; tromethamine USP).

Table 3 gives the 2002 prices for bulk quantities and the net weights packaged in drums or bags; Table 4 provides specification values.

Table 3. **2002 U.S. Prices of Alkanolamines, \$/kg**

Product	Tank car	Carload	Net weight, kg[a]
AMP	6.97	7.19	191.6 (D)
AMP-95	3.81	4.07	191.6 (D)
AEPD		5.08	204.5 (D)
AEPD-85	3.52	3.43	204.5 (D)
TRIS AMINO crystals		17.67	22.7 (B)
TRIS AMINO 40% aq.	5.98	6.09	226.9 (D)
TRIS AMINO ultrapure		22.10	50 (F)
DMAMP-80		13.44	186 (D)
AMPD		98.78	11.3,22.6 (F)
AB		9.90	193.2 (D)

[a] D = 208-L (55-gal) steel drums; B = bags; F = fiber drums.

6. Health and Safety Factors

Alkanolamines are only slightly toxic by ingestion (acute oral LD_{50} in rodents = 1.0–5.5 g/kg).

Undiluted DMAMP, AMP, and AB cause eye burns and permanent damage, if not washed out of the eye immediately. They are also severely irritating to the skin, causing burns upon prolonged or repeated contact. Of these three alkanolamines, only AMP has been studied in subchronic and chronic oral studies. The principal effect noted was the action of AMP on the stomach as a result of its alkalinity. The no-observed-effect level (NOEL) in a 1-year feeding study in dogs was 110 ppm in the diet. In general, the low volatility, and the applications for which these products are used, preclude the likelihood of exposure by inhalation.

Table 4. **Specifications for Alkanolamines**

Product	Neutral equivalent	Color, APHA, max	Water, wt %, max	Melting point, °C, min	Amine assay, %
AMP	88.5–91.0	20	0.8		
AMP-95	93.0–97.0	20	4.8–5.8		
AEPD	124.0, max	2[a,b]	3.8		
AEPD-85	none established	2[a,b]	13.0–15.0		
DMAMP-80		100	18.0–22.0		78.0–82.0[d]
AMPD[c]	103.0–107.0	50[b]	0.5	100.0	
AB		100	0.5		98.0
TRIS AMINO					
40% aqueous		5[a]			38.0–42.0[d]
crystals	121.0–122.0	40[b]	0.5	160.0	
ultrapure[e,f]		20[b]	0.2	170.0–172.0	99.9–100.1

[a] Gardner color.
[b] 20% aq solution.
[c] Residue on ignition = 0.01 wt%, max; insoluble matter = 0.01 wt%, max.
[d] By titration.
[e] Additional specifications for heavy metal content; meets USP and ACS specifications.
[f] Residue on ignition = 0.05 wt%, max; insoluble matter = 0.005 wt%, max.

AEPD is severely irritating to the eyes and should be washed out immediately on contact; it is only mildly irritating to the skin.

AMPD and TRIS AMINO, normally crystalline solids, are of less concern in terms of irritancy to skin and eyes.

The 40% aqueous solution of TRIS AMINO is nonirritating to the eyes and skin. In general, the toxicology of the alkanolamines is typical of alkaline materials, ie, the greater the base strength, the greater the effect. Neutralized alkanolamines are much less toxic; their stearate soaps, eg, have been found to be nonhazardous.

TRIS AMINO, the least toxic of this series of alkanolamines, has been studied extensively as a buffer (12). It is used in a number of pharmaceutical applications (13).

Environmentally, these alkanolamines present little problem. Only AMP has been studied in great detail, but it was found to be degradable according to OECD guidelines, to be of low toxicity to fish and microorganisms, and to be nonaccumulative. TRIS AMINO is actually added to the water used for shipment of living fish, in order to improve their viability (14).

7. Uses

Because they are closely related, the alkanolamines can sometimes be used interchangeably. However, cost/performance considerations generally dictate a best choice for specific applications.

Functional Fluids. The fatty acid soaps of alkanolamines are excellent emulsification agents for use in functional fluids such as hydraulic and metalworking fluids. For example, improved hardwater stability of a hydraulic fluid emulsion is obtained using AMP in the formulation (15). AMP has also been shown to enhance the chemical and biostability of metalworking fluids (16).

Pigment Dispersion. AMP is used widely as a pigment co-dispersant in water-based paints and paper coatings. In small amounts, it efficiently disperses pigments and improves pH and viscosity stability, corrosion inhibition, odor and dried-film properties (17). When AMP is used in conjunction with other surfactants, enhanced performance is obtained with lower levels of these ingredients in the dispersion.

TiO_2 and clay slurries which utilize AMP as part of the dispersant system are available in bulk for the paint and paper industries (see PIGMENTS). AMP has been used as a particle-surface treatment for production of TiO_2 with improved luster and dispersibility (18).

Resin Solubilizers. In general, water-soluble resins are amine salts of acidic polymers. Water-soluble coatings formulated with AMP-95 or DMAMP-80 exhibit superior performance (19,20) (see WATER-SOLUBLE POLYMERS). AMP-95, used in conjunction with associative thickeners (21) or derivatized cellulose, provides for the most efficient utilization of such thickeners.

AMP is also the neutralizer/solubilizer of choice for use with acid-functional hair-fixative resins (22). AMP and TRIS AMINO are efficient neutralizers of polyacrylate (carbomer) resins used for thickening or gelling of topical pharmaceutical and personal-care products (23).

Catalysts. The alkanolamines continue to find use in blocked-catalyst systems for textile resins, coatings resins, adhesives, etc. Of particular utility in curing durable-press textiles is AMP·HCl. Other salts, such as those of the benzoin tosylate or *p*-toluenesulfonic acid, find utility in melamine- or urea-based coatings (24) (see AMINO RESINS AND PLASTICS).

Boiler Water Treatment. Alkanolamines in general provide corrosion protection for ferrous metals in many applications. When used in boiler water treatment, AMP provides excellent protection to condensate-return lines through efficient absorption of CO_2, effective distribution ratio for transport throughout the system, and minimum amine loss in the deaerating heater (25–27).

Formaldehyde Scavenging. The formation of oxazolidines from alkanolamines and formaldehyde is rapid at room temperature and provides a method for the elimination of excess free formaldehyde from products such as urea–formaldehyde resins. AEPD and TRIS AMINO are the products of choice for this purpose because 1 mol of each will react with 2 mol of formaldehyde (28).

Applications in Oil and Gas Production. AMP, as a hindered amine, is useful for removing acid-gas contaminants such as CO_2 or H_2S from gas streams (29). It also has been utilized in tertiary oil recovery to enhance removal of petroleum from marginal wells (30).

AB has also shown value in purification systems for fluid streams (31).

Biomedical Applications. TRIS AMINO is used for a number of biomedical purposes. In its pure form, it is an acidimetric standard; TRIS AMINO also is useful in biotechnology as a buffering agent for enzyme systems, industrial protein purification, and electrophoretic separations (32).

TRIS AMINO, together with ethylenediaminetetraacetic acid (EDTA), can enhance the effectiveness of antimicrobial agents and antibiotics (33).

AB, the only optically active member of this alkanolamine series, is used as a raw material for production of the anti-tuberculosis drug ethambutol[74-55-5], and in chiral synthesis/resolution of drug optical isomers (34).

Synthetic Applications. Oxazolines, which are synthesized as indicated above, have been utilized in many different applications (35). When used in resin formulations, AMP, AEPD, and TRIS AMINO can incorporate the oxazoline structure into the polymer structure (36). Because they are polyols, both AEPD and TRIS AMINO can be used in polyester-resin modification. Oxazoline alkyd films are characterized by improved performance, particularly salt-spray resistance and gloss (see ALKYD RESINS; COATINGS, SPECIAL PURPOSE, HIGH PERFORMANCE).

Other oxazolines produced from alkanolamines are useful as oil-soluble surface-active agents and corrosion inhibitors. Synthetic oxazoline waxes promote lubricity and mar-resistance of coatings.

Oxazolidines, formed by reaction of alkanolamines with aldehydes, are useful as leather tanning agents (37) and are effective curing agents for proteins, phenolic resins, moisture-cure urethanes, etc. They also find use as antimicrobial agents (38).

BIBLIOGRAPHY

"Alkanolamines from Nitro Alcohols" in *ECT* 2nd ed., Vol. 1, pp. 824–831, by R. H. Dewey, Commercial Solvents Corporation; in *ECT* 3rd ed., Vol. 1, pp. 961–967, by Robert H.

Dewey and Allen F. Bollmeier, Jr., International Minerals & Chemical Corporation; in *ECT* 4th ed., Vol. 2, pp. 26–34, by Allen F. Bollmeier, Jr., ANGUS Chemical Company; "Alkanolamines from Nitro Alcohols" in *ECT* (online), posting date: December 4, 2000, by Allen F. Bollmeier, Jr., ANGUS Chemical Corporation.

CITED PUBLICATIONS

1. H. B. Haas and E. F. Riley, *Chem. Rev.* **32**, 373 (1943).
2. J. Y. Zhang and co-workers, *Biomed. Environ. Mass Spectrom.* **15**(1), 33 (1988).
3. A. I. Meyers and co-workers, *J. Org. Chem.* **39**(18), 2787 (1974).
4. A. I. Meyers and K. A. Lutomski, *Synthesis* **2**, 105 (1983).
5. U.S. Pat. 2,559,440 (July 3, 1951), W. A. Jordan and S. H. Shapiro (to Armour and Company).
6. H. G. Johnson, *J. Am. Chem. Soc.* **68**, 14 (1946).
7. J. L. Riebsomer, *J. Am. Chem. Soc.* **70**, 1629 (1948).
8. J. H. Billman and E. E. Parker, *J. Am. Chem. Soc.* **66**, 538 (1944).
9. M. Senkus, *J. Am. Chem. Soc.* **67**, 1515 (1945).
10. M. Senkus, *Ind. Eng. Chem.* **40**, 506 (1948).
11. U.S. Pat. 3,564,057 (Feb. 16, 1971), J. B. Tindall (to Commercial Solvents Corp.).
12. G. G. Nahas and co-workers, *Ann. NY Acad. Sci.* **92**, 333 (1961).
13. A. C. Eachus, *Chimica Oggi*, **12**(1–2), 24 (1994).
14. W. N. McFarland and K. S. Norris, *Calif. Fish Game*, **44**(4), 291 (1958).
15. U.S. Pat. 4,428,855 (Jan. 31, 1984), D. A. Law and J. Shim (to Mobil Oil Corp.).
16. U. Aumann and co-workers, *Lubricants World*, **9**(5), 20 (1999).
17. G. N. Robinson, *Paint Coatings Ind.*, **16**(10), 160 (2000).
18. Ger. Pat. 2,924,849 (Jan. 22, 1981), K. Koehler and co-workers (to A. G. Bayer).
19. M. E. Woods, *Mod. Paint. Coat.* **65**, 21 (1975).
20. Can. Pat. 1,242,182 (Sep. 20, 1988), M. A. Fentrup and co-workers (to BASF Corp.).
21. L. W. Hill and Z. W. Wicks, *Prog. Org. Coat.* **8**(2), 161 (1980).
22. U. Aumann and A. C. Eachus, *Euro Cosmetics*, **9**(3), 52 (2001).
23. U. Aumann and A. C. Eachus, *SOFW-Journal*, **125**(10), 3 (1999).
24. L. R. Gatechair, *Polym. Mater. Sci. Eng.* **59**, 289 (1988).
25. D. G. Dionisio, *Mater. Perform.* **16**(5), 21 (1977).
26. M. J. Fountain and co-workers, *Proceedings of the International Water Conference, Engineering Society of Western Pennsylvania*, 45th, 1984, p. 393.
27. C. Fernandez Palomero and J. Perez Pallares, *Rev. Soc. Nucl. Esp.* **1**(56), 27 (1987).
28. Jpn. Pat. 53/37794 (Apr. 7, 1978), K. Ebisawa and O. Matsudaira (to Hitachi Chemical Co., Ltd.).
29. G. Sartori and co-workers, *Sep. Purif. Methods,* **16**, 171 (1987).
30. U.S. Pat. 4,485,021 (Nov. 27, 1984), R. F. Purcell and R. B. Kayser (to ANGUS Chemical Company).
31. International Pat. Appl. WO 00/18492 (Apr. 6, 2000), P. C. Rooney (to The Dow Chemical Company).
32. *Biotechnology Applications of TRIS AMINO (Tris Buffer), Technology Review No. 10, ANGUS* Chemical Company, Buffalo Grove, Ill., March 1994.
33. A. C. Eachus and U. Aumann, *Pharma. Chem.* **1**(9), 56 (2002).
34. *Applications of ANGUS AB in Chiral-Drug Synthesis, Benchmark No. 54*, ANGUS Chemical Company, Buffalo Grove, Ill., August 1997.

35. J. A. Frump, *Chem. Rev.* **71**, 483 (1971).
36. U.S. Pat. 3,382,197 (May 7, 1968), R. F. Purcell (to Commercial Solvents Corp.).
37. S. das Gupta, *J. Sol. Leather Technol. Chem.* **61**, 97 (1977).
38. A. C. Eachus and co-workers, *S.D.F.W.*, (9), 337 (1991).

ALAN C. EACHUS
ALLEN F. BOLLMEIER
ANGUS Chemical Co.