1. Introduction

Amino alcohols have been prepared industrially since the 1930s. However, large-scale production started only after 1945, when alkoxylation with ethylene oxide and propylene oxide replaced the older chlorohydrin route. In industry, amino alcohols are usually designated as alkanolamines. Ethanolamines (aminethanols) and propanolamines (aminopropanols) are by far the most important compounds of this group. Both are used widely in the manufacture of surfactants and in gas purification [1–6].

2. Ethanolamines

Monoethanolamine \[141-43-5\] (1) (MEA; 2-aminoethanol), diethanolamine \[111-42-2\] (2) (DEA; 2,2′-iminodiethanol), and triethanolamine \[102-71-6\] (3) (TEA; 2,2′,2″-nitrilotriethanol) can be regarded as derivatives of ammonia in which one, two, or three hydrogen atoms have been replaced by a CH₂CH₂OH group.

Ethanolamines were prepared in 1860 by Wurtz from ethylene chlorohydrin and aqueous ammonia [7]. It was only toward the end of the 19th century that an ethanolamine mixture was

|   | 405 | 405 | 410 | 410 | 411 | 411 | 411 | 411 | 413 | 413 | 414 | 414 | 414 | 415 | 416 | 417 | 417 | 418 | 418 | 418 | 418 | 418 | 420 | 420 | 421 | 421 | 421 | 424 | 425 | 427 | 428 |
separated into its mono-, di-, and triethanolamine components; this was achieved by fractional distillation.

Ethanolamines were not available commercially before the early 1930s; they assumed steadily growing commercial importance as intermediates only after 1945, because of the large-scale production of ethylene oxide. Since the mid-1970s, production of very pure, colorless triethanolamine in industrial quantities has been possible [117–119]. All ethanolamines can now be obtained economically in very pure form.

The most important uses of ethanolamines are in the production of emulsifiers, detergent raw materials, and textile chemicals; in gas purification processes; in cement production, as milling additives; and as building blocks for agrochemicals [120]. Monoethanolamine is an important feedstock for the production of ethylenediamine and ethylenimine.

2.1. Properties

2.1.1. Physical Properties

Monoethanolamine and triethanolamine are viscous, colorless, clear, hygroscopic liquids at room temperature; diethanolamine is a crystalline solid. All ethanolamines absorb water and carbon dioxide from the air and are infinitely miscible with water and alcohols. The freezing points of all ethanolamines can be lowered considerably by the addition of water. Some physical properties of ethanolamines are listed in Table 1.

2.1.2. Chemical Properties

Because of their basic amino group and the hydroxyl group, ethanolamines have chemical properties resembling those of both amines and alcohols. They form salts with acids, and the hydroxyl group permits ester formation. When mono- and diethanolamine react with organic acids, salt formation always takes place in preference to ester formation. With weak inorganic acids, e.g., H2S and CO2, thermally unstable salts are formed in aqueous solution. This reaction of ethanolamines is the basis for their application in the purification of acidic natural gas, refinery gas, and synthesis gas [1], [8]. In the absence of water, monoethanolamine and diethanolamine react with CO2 to form carbamates:

\[ 2 \text{HOCH}_2\text{CH}_2\text{NHR} + \text{CO}_2 \rightarrow \text{HOCH}_2\text{CH}_2\text{CH}_2\text{NRCOOH} \]

\[ \cdot \text{RHNCCH}_2\text{OH} \]

R = H or CH2OH

Triethanolamine does not form a carbamate.

By metal-catalyzed amination, the hydroxyl group of monoethanolamine can be replaced by an amino group to form ethyleneamines such as ethylenediamine [107-15-3], diethylenetriamine [111-40-0], piperazine [110-85-0], and aminoethylethanolamine [111-41-1] [9], [10]:

\[
\text{H}_3\text{N} + \text{NN}_2 + \text{H} + \text{NN}_2 \quad \text{NH}_2
\]

\[
+ \text{H}_3\text{N} \quad \text{NH} + \text{OH}
\]

### Table 1. Physical properties of ethanolamines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mr</th>
<th>mp, °C</th>
<th>bp (101.3 kPa), °C</th>
<th>Density, ρ (20 °C), g/cm³</th>
<th>Heat of vaporization (101.3 kPa), kJ/kg</th>
<th>Specific heat, c_p, kJ kg⁻¹ K⁻¹</th>
<th>Cubic expansion coefficient, K⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoethanolamine</td>
<td>61.08</td>
<td>10.53</td>
<td>170.3</td>
<td>1.0160</td>
<td>848.1</td>
<td>2.72</td>
<td>7.78 × 10⁻⁴</td>
</tr>
<tr>
<td>Diethanolamine</td>
<td>105.14</td>
<td>28.0</td>
<td>268.5</td>
<td>1.0912 (30 °C)</td>
<td>638.4</td>
<td>2.73</td>
<td>5.86 × 10⁻⁴</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>149.19</td>
<td>21.6</td>
<td>336.1</td>
<td>1.1248</td>
<td>517.8</td>
<td>2.33</td>
<td>4.82 × 10⁻⁴</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>Viscosity (20 °C), mPa·s</th>
<th>n_20⁰</th>
<th>Surface tension (20 °C), N/m</th>
<th>Flash point, °C</th>
<th>Ignition temperature, °C</th>
<th>Temperature class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoethanolamine</td>
<td>23.2</td>
<td>1.4544</td>
<td>0.049</td>
<td>94.5</td>
<td>410</td>
<td>T2</td>
</tr>
<tr>
<td>Diethanolamine</td>
<td>389 (30 °C)</td>
<td>1.4747</td>
<td>0.0477</td>
<td>176</td>
<td>365</td>
<td>T2</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>930</td>
<td>1.4852</td>
<td>0.0484</td>
<td>192</td>
<td>325</td>
<td>T2</td>
</tr>
</tbody>
</table>

a According to DIN 53 217.
b According to DIN 51 758.
c According to DIN 51 794.
d According to VDE 0165. Ethanolamines do not belong to any hazard class according to VbF (regulation governing flammable liquids).
Considerable quantities of monoethanolamine are converted into ethylenimine (aziridine [151-56-4]) by adding sulfuric acid and cyclizing the hydrogensulfate with sodium hydroxide or by using heterogeneous catalysts [121] (→ Aziridines) [11], [12]:

\[
\begin{align*}
\text{H}_2\text{N} & \text{OH} \xrightarrow{\text{H}_2\text{SO}_4} \\
\text{H}_2\text{N} & \text{OSO}_2\text{H} \xrightarrow{\text{NaOH}} \text{H}_2\text{N} \text{CH}_3 \text{CH}_2 \text{OH}
\end{align*}
\]

As primary and secondary amines, monoethanolamine and diethanolamine also react with acids or acid chlorides to form amides. The amine first reacts with the acid, e.g., stearic acid, to form a salt, which can be dehydrated to the amide by heating:

\[
\text{NH}_2\text{CH}_2\text{CH}_2\text{OH} + \text{C}_17\text{H}_{35}\text{COOH} \rightarrow \text{NH}_2\text{CH}_2\text{CH}_2\text{OH} \rightarrow \text{NH}_2\text{CH}_2\text{CH}_2\text{COOH} + \text{H}_2\text{O}
\]

When the ethanolamides of fatty acids are heated at fairly high temperature with removal of water, oxazolines are formed:

\[
\text{O} \quad \text{H} \quad \text{N} \quad \text{OH} \quad \text{R} \quad \text{N} \quad \text{O} \quad \text{H}_2\text{O}
\]

Formaldehyde reacts with monoethanolamine and diethanolamine to form hydroxymethyl compounds, which can be reduced to the \(N\)-methyl derivatives [14] (see Section 3.2).

Monoethanolamine reacts with carbon disulfide to form 2-mercaptothiazoline [96-53-7][15]:

\[
\text{H}_2\text{N} \text{OH} + \text{CS}_2 \rightarrow \text{HS} \quad \text{N} \quad \text{S} \quad \text{H} \quad \text{OH}
\]

The hydroxyl groups of ethanolamines can be replaced with chlorine by reaction with thionyl chloride or phosphorus pentachloride. The chloroethylenamines formed are hazardous because of their skin toxicity. For example, tris(2-chloroethyl)amine has been used as a gas in warfare (N-lost). Bis(2-chloroethyl)amine is obtained in good yield by reaction of diethanolamine with thionyl chloride:

\[
\begin{align*}
\text{HN} \text{OH} + 2 \text{SOCl}_2 & \rightarrow \text{HN} \text{Cl} + 2 \text{SO}_2 + 2 \text{HCl}
\end{align*}
\]

Reaction of triethanolamine with ethylene oxide gives unstable alkaline quaternary compounds and the corresponding stable ethers [122]. For example, undistilled triethanolamine prepared from mono- or diethanolamine always contains some triethanolamine monoglycol ether [16].

Mono- or diethanolamine can also be used as the amine component in aminolkylation, the so-called Mannich reaction, which is very important in the biosynthesis of many alkaloids [17].

\[
\begin{align*}
\text{HOCH}_2\text{CH}_2\text{NH} \quad \text{OH} \quad \text{H}_2\text{N} \text{OH} \rightarrow
\end{align*}
\]

Catalytic dehydrogenation of diethanolamine leads to iminodiacetic acid, an important building block for agrochemicals [120].

\[
\begin{align*}
\text{HN} \quad + \text{HONO} \rightarrow \text{O} = \text{N} \quad \text{N} \quad + \text{H}_2\text{O}
\end{align*}
\]

\[
\begin{align*}
\text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH}
\end{align*}
\]

\[
\begin{align*}
\text{HN} \quad + \text{HONO} \rightarrow \text{O} = \text{N} \quad \text{N} \quad + \text{H}_2\text{O}
\end{align*}
\]

\[
\begin{align*}
\text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH}
\end{align*}
\]

Monoethanolamine and triethanolamine can form complexes with transition metal ions (e.g., chromium, copper, nickel, cobalt, and iron); some of these complexes are water-soluble [123–125].

2.2. Production

Ethanolamines are produced on an industrial scale exclusively by reaction of ethylene oxide with excess ammonia, this excess being considerable in some cases [19].

The reaction of ethylene oxide with ammonia takes place slowly and is accelerated by water. Anhydrous procedures employ a fixed-bed catalyst consisting of an organic ion-exchange resin or thermally more stable acidic inorganic clays or zeolites [20–23].
In all conventional processes, reaction takes place in the liquid phase, and the reactor pressure is usually sufficiently large to prevent vaporization of ammonia and ethylene oxide at the reaction temperature. In current procedures, ammonia concentrations in water between 50 and 100%, pressures up to 16 MPa, reaction temperatures up to 150 °C, and an excess up to 40 mol of ammonia per mole of ethylene oxide are used. The reaction is highly exothermic; the enthalpy of reaction is about 125 kJ per mole of ethylene oxide [24]. The following competing reactions occur:

\[ \text{NH}_3 \quad + \quad \text{O} \quad \rightarrow \quad \text{H}_2\text{N} - \text{OH} \]

\[ \text{H}_2\text{N} - \text{OH} \quad + \quad \text{O} \quad \rightarrow \quad \text{H} - \text{N} - \text{OH} \]

\[ \text{H} - \text{N} - \text{OH} \quad + \quad \text{O} \quad \rightarrow \quad \text{HO} - \text{N} - \text{OH} \]

Side reactions forming tetrakis(hydroxyethyl) ammonium hydroxide or any ethers are of no importance in the synthesis [126]. The kinetics of these reactions have been studied [25].

All the reaction steps have about the same activation energy and show a roughly quadratic dependence of the reaction rate on the water content of the ammonia–water mixture used. Therefore, product composition depends solely on the molar excess of ammonia and not on water content, reaction temperature, or pressure [26]. The product distribution as a function of the molar ratio of the reactants is shown in Figure 1 [27].

Unconsumed ammonia and water are separated from the products in a distillation line downstream of the reactor and are recycled. In large-scale continuous single-line plants, the requirement for low energy use (i.e., operation with minimum steam consumption) determines both the transport of heat from the reactor and the design of the thermally integrated distillation line (Fig. 2).

Product distribution of the three ethanolamines can be controlled by appropriate choice of the ammonia : ethylene oxide ratio. A higher diethanolamine or triethanolamine content can also be obtained by recycling monoethanolamine or diethanolamine to the reactor or by treating them with ethylene oxide in a separate unit [127], [128].

For safety reasons, ethylene oxide must be metered into the ammonia stream; in the reverse procedure, ammonia or amines may cause ethylene oxide to undergo an explosive polymerization reaction.

In all industrial processes, complete conversion to the three ethanolamines, without significant formation of byproducts, is achieved. Therefore, feedstock costs are independent of the type of production process. On the other hand, manufacturing costs and, in particular, energy costs depend to a large extent on the product composition desired, plant design, and degree of thermal integration.

2.3. Quality Specifications

Today, all ethanolamines are prepared with > 99 % purity. Water, the two other ethanolamines, and a small amount of triethanolamine glycol ether are minor components; all other impurities are in the ppm range. Table 2 gives specifications for commercial ethanolamines.

Purity is determined by gas chromatography, and the residual water content by the Karl Fischer method. After pretreatment, the N-nitrosamine content can also be determined by gas chromatography with a thermal analyzer.

2.4. Uses

Surfactants. Ethanolamines are used widely as intermediates in the production of surfac-
tants, which have become commercially important as detergents, textile and leather chemicals, and emulsifiers [2–6]. Their uses range from drilling and cutting oils to medicinal soaps and high-quality toiletries [28] (Fig. 3).

Properties of ethanolamine derivatives can be varied within wide limits by appropriate choice of the ethanolamine, the acid component, and their ratio. Synergistic effects in complex emulsifier systems can be obtained by simultaneous use of different combinations of amines and acids. Ethanolamines, particularly triethanolamine, which had presented problems with regard to color, are now produced in sufficient purity that no color problems arise when they are treated with acids or heated [29–32].

Ethanolamine-based surfactants can be formulated as weakly basic or neutral products and are therefore particularly well tolerated by the skin; this is especially true for triethanolamine soaps. Moreover, they are noncorrosive and can be used on virtually all textiles without damage. Ethanolamine soaps prepared from oleic acid, stearic acid, lauric acid, or caprylic acid are constituents of many toiletries and medicinal soaps.

Ethanolamine soaps produced from fatty acids are among the most industrially important emulsifiers. They are used in cosmetics [33], polishes, shoe creams, car care products, drilling and cutting oils, and pharmaceutical ointments. Ethanolamine soaps combined with wax and resins are used as impregnating materials, protective coatings, and products for the care of textile and leather goods.

Ethanolamine soaps obtained from alkylaryl-sulfonic acids, preferably alkylbenzenesulfonic acids, or from alcohol sulfates are growing

Table 2. Specifications of commercial ethanolamines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Purity, wt %</th>
<th>ρ (DIN 51 757), g/cm³</th>
<th>Color (DIN-ISO 6271), APHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoethanolamine</td>
<td>&gt; 99</td>
<td>1.016 (20 °C)</td>
<td>≤ 10</td>
</tr>
<tr>
<td>Diethanolamine</td>
<td>&gt; 99</td>
<td>1.0912 (30 °C)</td>
<td>≤ 20</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>&gt; 99</td>
<td>1.1248 (20 °C)</td>
<td>≤ 30</td>
</tr>
</tbody>
</table>

Figure 2. Flow sheet for the production of ethanolamines
a) Aqueous ammonia tank; b) Tubular reactor; c) Ammonia and ammonia solution columns; d) Dehydration column; e) Vacuum fractionation columns

Figure 3. Percentage consumption of ethanolamines according to use (1996)
steadily in importance and dominate the market for household cleansers [34]. The use of linear alkyl groups instead of branched chains in these products has resulted in greater biodegradability.

Fatty acid ethanolamides and products obtained by further ethoxylation have foam-stabilizing ability and are therefore important additives for detergents [35], [36]. Diethanolamides obtained from coconut fatty acids and from oleic acid are used industrially. These amides were first described in 1937 [37]. Liquid detergents are based predominantly on triethanolamine [38–40].

In the manufacture of leather, ethanolamine-based chemicals are used for dressing, dyeing, and finishing. For paints and coatings, ethanolamines are employed both in production and in softeners and paint removers.

**Corrosion Inhibitors.** Diethanolamine and triethanolamine are important components of corrosion inhibitors, particularly in coolants for automobile engines, as well as in drilling and cutting oils. They are also employed as additives in lubricants.

When the corrosion inhibitor sodium nitrite and diethanolamine are used together, N-nitrosamines may form. These nitrosamines are carcinogenic; therefore, sodium nitrite and diethanolamine or triethanolamine should not be used simultaneously.

**Gas Purification.** Large amounts of ethanolamines, principally diethanolamine, are used in absorptive gas purification to remove weakly acidic components. For example, hydrogen sulfide and carbon dioxide are removed from natural gas, refinery gas, and synthesis gas [1].

**Intermediates.** A substantial portion of the monoethanolamine is used as a starting material in the preparation of ethylenimine and ethylenediamine. Ethylenimine is converted to polyethylenimine, an important chemical in paper technology. Diethanolamine is used as a building block for agrochemicals (e.g., Glyphosate).

**Cement Additives.** Since the 1960s, aqueous solutions of triethanolamine and triethanolamine acetate have been used as milling additives in cement production [41]. During grinding of the clinker in ball mills, the small amount of triethanolamine added prevents agglomeration and cushioning of the grinding medium by saturating the surfaces of the freshly broken particles. Like other milling additives (e.g., various glycols), they reduce the power required for milling the clinker. The milling of virtually all high-quality portland cement involves milling additives. In addition to assisting the milling process, triethanolamine also improves the flow properties and setting behavior of the cement [42].

### 2.5. Economic Aspects

Large-scale, economical production of ethanolamines from ethylene oxide and ammonia in large, single-line plants has greatly promoted their use in many industrial sectors. In 1999, world ethanolamine capacity was about $1.09 \times 10^6$ t/a (Table 3). About 50% of world production is monoethanolamine; 30–35%, diethanolamine; and 15–20%, triethanolamine.

### 3. N-Alkylated Ethanolamines

$N$-Alkylated ethanolamines are amino alcohols that contain a secondary or tertiary nitrogen atom and one or two hydroxyl groups.

![Chemical structure](image)

Numerous compounds with different properties and uses can be synthesized by varying the alkyl group.

### Table 3. Approximate ethanolamine capacity and production in 1998

<table>
<thead>
<tr>
<th>Region</th>
<th>Capacity, 10^3 t/a</th>
<th>Estimated production, 10^3 t/a</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>569</td>
<td>456</td>
</tr>
<tr>
<td>Mexico</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Western Europe</td>
<td>275</td>
<td>242</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>123</td>
<td>68</td>
</tr>
<tr>
<td>South America</td>
<td>50</td>
<td>16.8</td>
</tr>
<tr>
<td>Total</td>
<td>1017</td>
<td>759</td>
</tr>
</tbody>
</table>
3.1. Properties

3.1.1. Physical Properties

*N*-Alkylated ethanolamines are generally liquid and have a faint amine-like odor. They tend to discolor on prolonged storage, especially if exposed to air, light, and temperatures above 40 °C. This tendency to discoloration can be reduced substantially by the use of additives when purifying the products by distillation, or by pretreating the crude products before distillation [43–45]. *N*-Alkylated ethanolamines are partially to readily soluble in alcohol, water, acetone, glycols, glycerol, and glycol ethers. They are only sparingly soluble or even insoluble in non-polar solvents, e.g., aliphatic hydrocarbons. 2-Dimethylaminoethanol [108-01-0] (N,N-di-methylethanolamine) and 2-diethylaminoethanol [100-37-8] (N,N-diethylethanolamine) form azeotropes with water; *N*-methyldiethanolamine [105-59-9] does not form an azeotrope. All *N*-alkylethanolamines are hygroscopic and also absorb CO₂ from air. Physical properties of typical compounds are listed in Table 4.

3.1.2. Chemical Properties

The chemical properties of *N*-alkylated ethanolamines are very similar to those of unsubstituted ethanolamines (see Section 2.1.2). They form unstable salts with inorganic acids such as CO₂ and H₂S [129–131]. Salts with organic acids give a neutral to weakly basic reaction. *N*-Alkylated ethanolamines also react with acids or acid derivatives to give the corresponding esters. Important products are dimethylethanolamine acrylate [2439-35-2] and diethylethanolamine acrylate [2426-54-2], which are used as intermediates in the synthesis of flocculating agents.

Secondary *N*-alkylethanolamines also react with acids to form acid amides. The reaction of *N*-alkylethanolamines with ethylene oxide to give longer chain alkoxy derivatives gives low yields.

3.2. Production

Industrially, *N*-alkylated ethanolamines are produced almost exclusively by batchwise or continuous reaction of primary, secondary, or tertiary amines with ethylene oxide [46–48]. For safety reasons, ethylene oxide must be added to the amine, never vice versa (see Section 2.2). Depending on the product involved, reaction temperature varies from 50 to 170 °C and pressure from 0.2 to 4 MPa. Water accelerates the reaction.

Figure 4 shows a flow sheet for the batchwise production of alkanolamines. The procedure is also suitable for the manufacture of isopropanolamines (see Chap. 5); in this case, propylene oxide is used instead of ethylene oxide.

The oxygen-free reaction kettle (a) is filled with the amine raw material from the stock tank (b); water is added in an amount of 10 – 60 %, based on the amine; and the kettle is heated to a minimum temperature around 50 °C. Metering of ethylene oxide is then begun, the feed rate depending on the removal of heat and the operating pressure of the reaction kettle.

The optimum amount of ethylene oxide in relation to starting amine is determined by cost-effectiveness (byproducts, work-up costs). When addition of ethylene oxide is complete, the minimum reaction temperature is maintained for some time to ensure that the product discharged from the reactor is free of ethylene oxide. The reaction mixture is separated by fractional distillation. Unconverted amine and water are removed as the first fraction and recycled to the subsequent batch. Pure alkanoamines are obtained by distillation under reduced pressure.

When primary amines are used, a mixture of *N*-alkylethanolamines and *N*-alkyldiethanolamines is always formed:

\[
\text{R}_2 \text{NH} + \text{O} \rightarrow \text{R}_2 \text{N} - \text{O} - \text{R} \\
R = \text{alkyl}
\]

The larger the excess of amine, the lower is the proportion of *N*-alkyldiethanolamines. If *N*-alkylethanolamines are desired, a continuous process is usually preferred for economic reasons. Excess amine is distilled from the reaction product and recycled.
### Table 4. Physical properties of N-alkylethanolamines

| Compound                        | CAS registry number | mp, °C | bp (101.3 kPa, °C) | Density\(^{\text{a}}\) ρ, (20 °C) g/cm\(^3\) | Cubic expansion coefficient, K\(^{-1}\) | Heat of vaporization, kJ/kg | Specific heat, kJ kg\(^{-1}\) K\(^{-1}\) | Specific electrical conductivity, Ω\(^{-1}\) cm\(^{-1}\) | Viscosity \(η^{20}\), (20 °C), mPa · s | Surface tension (20 °C), mN/m | Flash point, °C | Ignition temperature, °C | Temperature class |
|---------------------------------|---------------------|--------|---------------------|---------------------------------------------|------------------------------------------|-------------------------------|------------------------------------------|-------------------------------------------------|---------------------------------|------------------|--------------------|------------------|
| Methylethanolamine             | [109-83-1]          | 75.11  | ca. –3              | 159                                         | 0.939 – 0.942                            | 7.8 × 10\(^{-4}\)              | 564.4                                    | 2.55                             | 3.33 × 10\(^{-6}\) (25 °C) | 13.0              | 1.4389             | 34.4             | ca. 74              | 350              | T2 |
| Methyldiethanolamine           | [105-59-9]          | 119.17 | ca. –21             | 247                                         | 1.038 – 1.041                            | 7.5 × 10\(^{-4}\)              | 418.7                                    | 1.72                             | 8.1 × 10\(^{-7}\) (20.3 °C) | 101               | 1.4694             | 27.1             | ca. 38              | 235              | T3 |
| Dimethylethanolamine           | [108-01-0]          | 89.14  | –70°                | 134                                         | 0.887                                     | 1.35 × 10\(^{-3}\)             | 454.3                                    | 2.30                             | 3.8 × 10\(^{-7}\) (24.5 °C) | 3.85              | 1.4296             | 29.2             | ca. 46              | 260              | T3 |
| Diethylethanolamine            | [100-37-8]          | 117.19 | –70°                | 162                                         | 0.883 – 0.889                            | 1.07 × 10\(^{-3}\)             | 383.9                                    | 2.42                             | 1.1 × 10\(^{-3}\) (25 °C) | 5                 | 1.4417             | 29.9             | ca. 38              | 265              | T3 |
| n-Butylethanolamine            | [111-75-1]          | 117.19 | –2.1                | 199                                         | 0.8917                                    | 7.6 × 10\(^{-4}\)              | 397.7                                    | 2.45                             | 2.9 × 10\(^{-7}\) (22 °C) | 19.7              | 1.4435             | 33.9             | ca. 30              | 260              | T3 |
| n-Butyldiethanolamine          | [102-79-4]          | 161.25 | –45°                | ca. 270                                     | 0.970                                     | 7.7 × 10\(^{-4}\)              | 329.5                                    | 2.26                             | 6.3 × 10\(^{-7}\) (22 °C) | 75.9              | 1.462              | 33.9             | ca. 130             | 260              | T3 |
| Dibutylethanolamine            | [102-81-8]          | 173.30 | –75°                | 222 – 234                                   | 0.860                                     | 8.1 × 10\(^{-4}\)              | 277.6                                    | 2.32                             | 9.5 × 10\(^{-7}\) (22 °C) | 7.4                | 1.4444             | 26.3             | ca. 96              | 240              | T3 |
| Cyclohexylethanolamine         | [2842-38-8]         | 143.23 | 37.5                | 235                                         | 0.9797                                    | 7.6 × 10\(^{-4}\)              | 327.2                                    | 2.45                             | 2.0 × 10\(^{-8}\) (25.1 °C) | 317               | 1.4860             | 39.5             | ca. 122             | 270              | T3 |
| Cyclohexyltriethanolamine      | [4500-29-2]         | 187.29 | 297                 | 112                                         | 1.0339                                    | 6.6 × 10\(^{-4}\)              | 319.0                                    | 2.30                             | 6.6 × 10\(^{-4}\) (40 °C) | 815               | 1.4830             | 40.1             | ca. 172             | 255              | T3 |
| 1-(2-Hydroxyethyl)piperazine   | [103-76-4]          | 130.19 | 24                  | 112 (1.33 kPa)                               | 1.0592                                    | 7.5 × 10\(^{-4}\)              | 411.1                                    | 2.00                             | 6.1 × 10\(^{-4}\) (40 °C) | 1040              | 1.110              | 38.3             | ca. 135             | 280              | T3 |
| 4-(2-Hydroxyethyl)morpholine   | [622-40-2]          | 131.18 | 1.5 – 2             | 224                                         | 1.0714                                    | 8.1 × 10\(^{-4}\)              | 342.7                                    | 1.91                             | 4.7 × 10\(^{-3}\) (40 °C) | 26.6              | 1.4783             | 40.8             | ca. 148             | 205              | T3 |
| Hydroxyethylalanilene          | [122-98-5]          | 137.18 | –30°                | 224                                         | 1.0954                                    | 1.14 × 10\(^{-3}\)             | 439.2                                    | 2.08                             | 1.4783             | 40.8              | 1.5796             | 148.2            | ca. 194             | 205              | T2 |
| Ethylhydroxyethylanilene       | [92-50-2]           | 165.24 | 37                  | 270                                         | 1.030                                     | 7.3 × 10\(^{-4}\)              | 86                                       | 2.14                             | 1.4783             | 139              | 335.7              | 84               | ca. 139             | 335              | T2 |
| N-Ethylethanolamine            | [110-73-6]          | 89.14  | –5.8                | 167                                         | 0.914                                     |                                |                                | 15.1                             |                                |                                | 78                | 330                | 84               | T2 |
| N-Propylethanolamine           | [16369-21-4]        | 103.17 | –0.5                | 180 – 181                                   | 0.973                                     |                                |                                | 20.9                             |                                |                                | 84                | 290                | T3               | |
| Hydroxyethylpiperidine         | [3040-44-6]         | 129.21 | 16.7                | 198 – 203                                   | 1.0161                                    |                                |                                | 1.804                            |                                |                                | 83                | 240                | T3               | |
| Dihydroxyethylanilene          | [120-07-0]          | 181.24 | 52                  | 346                                         | 1.0161                                    |                                |                                | 1.27                             |                                |                                | 200               | 380                | T2               | |
| tert-Butylethanolamine         | [4620-70-6]         | 117.19 | 40 – 43             | 176 – 177                                   | 0.8576                                    |                                |                                | 1.27                             |                                |                                | 5.9               | 345                | T2               | |
| tert-Butyldiethanolamine       | [2160-93-2]         | 161.25 | 44 – 47             | 136 – 139                                   | 0.9556                                    |                                |                                | 1.48                             |                                |                                | 21.0              | 148                | 300              | T3 |

\(^{a}\)Pour point.  
\(^{b}\)Hazard class AI (VbF).  
\(^{c}\)Hazard class AI (VbF).
With secondary amines, only one product is formed:

\[
R^1\text{NH}_2 + OH \rightarrow R^1\text{N} = \text{OH}
\]

\[R^1, R^2 - \text{alkyl}\]

Trialkylammonium Chlorides yield the corresponding 2-hydroxyethylammonium chlorides. One of the commercially most important salts is choline chloride \([67-48-1]\) (Choline):

\[
\text{H}_3\text{C}_+ + \text{H}_2\text{C} = \text{NHCl}^- + \text{O} \rightarrow \text{H}_3\text{C} \text{CH}_2\text{N} = \text{OH} \text{Cl}^-
\]

Choline chloride can also be prepared from trimethylamine and ethylene chlorohydrin, but this route has no commercial significance.

Another common method of preparing \(N\)-alkylethanolamines is by \(N\)-alkylation of ethanolamines \([49]\). Methyl derivatives can also be obtained by reacting monoethanolamine or diethanolamine, or their homologues, with formaldehyde and then reducing the hydroxymethyl compound:

\[
\text{HN} + \text{H}_2\text{C}=\text{O} \xrightarrow{\text{Cat.}} \text{H}_2\text{C} \text{N} \text{OH}
\]

Pure components are obtained from the crude products by distillation.

The reaction of epichlorohydrin with amines to give \(N\)-alkylethanolamines is of only minor commercial importance.

### 3.3. Quality Specifications

Table 5 lists specifications of commercial products. Purity is almost always measured by gas chromatography.

### 3.4. Uses and Economic Aspects

\(N\)-Alkylethanolamines are used mainly as intermediates, especially in the production of pharmaceuticals such as the local anesthetics procaine (diethylethanolamine 4-aminobenzoate \([59-46-1]\)) and tetracaine (dimethylethanolamine 4-butyraminobenzoate \([136-47-0]\)), crop protection agents, and flocculants (dimethylethanolamine acrylate) \([50]\). They are also important in the preparation of chemicals for the paper and leather industries. Use of \(N\)-alkylethanolamines in the production of plastics has risen substantially in recent years.

Direct uses of \(N\)-alkylethanolamines, especially methyldiethanolamine \([51]\), include gas purification methods for removing acidic gases...
Choline chloride is very important in the animal feedstuff industry ([52]). World production was ca. 160 000 t/a in 1999.

Annual worldwide demand for N-alkylethanolamines (excluding choline chloride) ranges from 2 to 15 000 t, depending on the product and application. Some products in the category of more than 1000 t/a are N,N-dimethylethanolamine, N,N-diethylethanolamine, 1-(2-hydroxyethyl)pipperazine derivatives, N-methyldiethanolamine, and N-methylethanolamine.

4. Isopropanolamines

The propanolamines described here are propanol derivatives containing one amino group. They have the following general formulas:

\[
\begin{align*}
\text{4} & \quad \text{R} = \text{H, C}_2\text{H}_5\text{OH} \\
\text{5} & \quad \text{R} = \text{H, C}_2\text{H}_5\text{OH}
\end{align*}
\]

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4-(2-Hydroxyethyl)morpholine, 1-(2-Hydroxyethyl)piperazine, 1-(2-Hydroxyethyl)piperidine derivatives, N,N-dimethylethanolamine, N,N-diethylethanolamine, and N-methylethanolamine.

Table 5. Specifications for commercial N-alkylethanolamines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Boiling range 5 – 95 mL°, °C</th>
<th>Purity° (min.), %</th>
<th>Water content°, %</th>
<th>Color°, APHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethylethanolamine</td>
<td>133.5 – 135.5</td>
<td>99.8</td>
<td>&lt; 0.05</td>
<td>15</td>
</tr>
<tr>
<td>Diethylethanolamine</td>
<td>161.5 – 163</td>
<td>99.5</td>
<td>&lt; 0.05</td>
<td>15</td>
</tr>
<tr>
<td>Methyllethanolamine</td>
<td>158.5 – 160.0</td>
<td>99.0</td>
<td>&lt; 0.1</td>
<td>10</td>
</tr>
<tr>
<td>Methyleneethanolamine</td>
<td>115.5 – 118</td>
<td>99.0</td>
<td>&lt; 0.2</td>
<td>50</td>
</tr>
<tr>
<td>4-(2-Hydroxyethyl)morpholine</td>
<td>223 – 225</td>
<td>99.0</td>
<td>0.2</td>
<td>40</td>
</tr>
<tr>
<td>1-(2-Hydroxyethyl)piperazine</td>
<td>121 – 123 °</td>
<td>99.0</td>
<td>0.2</td>
<td>40</td>
</tr>
<tr>
<td>1-(2-Hydroxyethyl)piperidine</td>
<td>92 – 96 °</td>
<td>99.5</td>
<td>0.1</td>
<td>40</td>
</tr>
<tr>
<td>Hydroxyethylnalmine</td>
<td>282 – 287</td>
<td>99.0</td>
<td>0.3</td>
<td>100 – 150</td>
</tr>
<tr>
<td>Ethylethanolamine</td>
<td>167</td>
<td>99.5</td>
<td>0.2</td>
<td>15</td>
</tr>
<tr>
<td>Ditethylarolamine</td>
<td>226 – 228</td>
<td>99.0</td>
<td>0.2</td>
<td>40</td>
</tr>
<tr>
<td>Butylethanolamine</td>
<td>196 – 198</td>
<td>99.5</td>
<td>0.1</td>
<td>15</td>
</tr>
<tr>
<td>N-Prolylethanolamine</td>
<td>180 – 181</td>
<td>99.5</td>
<td>&lt; 0.1</td>
<td>10</td>
</tr>
<tr>
<td>Butyldiethanolamine</td>
<td>264 – 278</td>
<td>99.0</td>
<td>&lt; 0.3</td>
<td>10</td>
</tr>
<tr>
<td>tert-Butylethanolamine</td>
<td>178</td>
<td>99.0</td>
<td>&lt; 0.3</td>
<td>10</td>
</tr>
<tr>
<td>tert-Butyldiethanolamine</td>
<td>136 – 139 (1.6 kPa)</td>
<td>99.0</td>
<td>&lt; 0.3</td>
<td>10</td>
</tr>
</tbody>
</table>

°DIN 51 751.
°DIN 53 406.
°Determined by gas chromatography.
°Determined by Karl Fischer method.
°According to DIN-ISO 6271.

(CO$_2$, H$_2$S). Choline chloride is very important in the animal feedstuff industry (→ Choline) [52]. World production was ca. 160 000 t/a in 1999.

Annual worldwide demand for N-alkylethanolamines (excluding choline chloride) ranges from 2 to 15 000 t, depending on the product and application. Some products in the category of more than 1000 t/a are N,N-dimethylethanolamine, N,N-diethylethanolamine, 1-(2-hydroxyethyl)piperazine derivatives, N-methyldiethanolamine, and N-methylethanolamine.

4.1. Properties

4.1.1. Physical Properties

Isopropanolamines are hygroscopic, virtually colorless substances with a slight amine-like odor. They are readily soluble in water, ethanol,
glycol, and acetone but only slightly soluble in hydrocarbons and diethyl ether. Monoisopropanolamine is more soluble than monoethanolamine in organic solvents; it forms a miscibility gap with heptane and toluene.

Diisopropanolamine and triisopropanolamine undergo thermal decomposition above ca. 170 °C and can therefore be distilled only at reduced pressure. The freezing points of diisopropanolamine and triisopropanolamine can be greatly depressed by adding a small amount of water. All isopropanolamines have at least one asymmetrically substituted carbon atom and thus can be optically active. The commercial products are racemic mixtures.

Important physical data are listed in Table 6 and safety data in Table 7.

### 4.1.2. Chemical Properties

The properties of amines and alcohols are combined in isopropanolamines, and these compounds exhibit typical reactions of both functional groups; the amino group can be primary, secondary, or tertiary. In chemical behavior, isopropanolamines differ only slightly from the ethanolamines described in Section 2.1.2.

Isopropanolamines react with acidic gases (H₂S, CO₂) in aqueous solution to form salts, which decompose to the starting materials when heated. This effect is utilized in the purification of natural gas and synthesis gas. The salts of strong acids, such as HCl or H₂SO₄, are crystalline compounds.

Diisopropanolamine sulfate eliminates water at elevated temperature to form 2,6-dimethylmorpholine sulfate [54].

The sodium salt of the sulfuric acid half-ester of monoisopropanolamine undergoes cyclization when heated, and propylenimine is formed [55]:

\[
\begin{align*}
\text{H}_3\text{N}\text{SO}_3\text{Na} & \xrightarrow{\text{Heat}} \text{H}_2\text{C} = \text{N} + \text{NaHSO}_4
\end{align*}
\]

Fatty acids, such as stearic acid, react with isopropanolamine at room temperature to form neutral, waxlike isopropanolamine soaps. In reactions above 140 °C and with elimination of water, amides are formed preferentially, and minor amounts of fatty esters [56] are produced in a side reaction. Complete esterification can be effected

<table>
<thead>
<tr>
<th>Table 6. Physical properties of propanolamines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compound</strong></td>
</tr>
<tr>
<td>1-Amino-2-propanol (d,l) [78-96-6]</td>
</tr>
<tr>
<td>2-Amino-1-propanol (d,l) [6168-72-5]</td>
</tr>
<tr>
<td>Monoisopropanolamine&lt;br&gt; <em>(a)</em></td>
</tr>
<tr>
<td>Diisopropanolamine&lt;br&gt; <em>(b)</em></td>
</tr>
<tr>
<td>Triisopropanolamine&lt;br&gt; <em>(b)</em></td>
</tr>
</tbody>
</table>

*(a)* Commercial isomer mixture consisting of ca. 94 % 1-amino-2-propanol and 6 % 2-amino-1-propanol.

*(b)* Commercial isomer mixture.

<table>
<thead>
<tr>
<th>Table 7. Safety data for isopropranolamines [53]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoisopropanolamine</strong></td>
</tr>
<tr>
<td>Flash point, °C</td>
</tr>
<tr>
<td>Ignition temperature, °C</td>
</tr>
<tr>
<td>Explosion limits, vol %</td>
</tr>
<tr>
<td>Vapor pressure, kPa</td>
</tr>
</tbody>
</table>
by reaction with acyl chlorides in the presence of pyridine [57]. The reaction of esters with isopropanolamines above 100 °C gives amides [58]:

\[ \text{H}_3\text{C}=-\text{NH}_2 + \text{O} \equiv \text{C}=\text{O} \rightarrow \text{A}_{\text{R}}\text{R}_2 \]

\[ \text{H}_3\text{C}=-\text{NH}_2 + \text{R}_1\text{R}_2 \rightarrow \text{H}_3\text{C}=\text{O} \text{CH}_2\text{CH}_2\text{NR}_1\text{R}_2 + \text{H}_2\text{O} \]

R\text{R}_1, R\text{R}_2 \equiv \text{alkyl}

When thionyl chloride is used as a reactant and chloroform as the solvent, the hydroxyl group can be exchanged for chlorine. Isopropanolamine is converted to 2-chloropropylamine [59], which is obtained in good yield.

Isopropanolamine and diisopropanolamine react with epoxides to give mixed isopropanolamines. The amino group is several times more reactive than the hydroxyl group [60]. In the presence of suitable catalysts such as sodium hydroxide or sodium alkoxides, the epoxide reacts preferentially with the hydroxyl group to form polyethers [61]. Alkylating substances, e.g., alkyl halides or dimethyl sulfate, give N-alkylated derivatives [62].

Isopropanolamine can be converted to 1,2-diaminopropane by catalytic amination under pressure (→ Amines, Aliphatic, Section 8.1.2.). Aldehydes and ketones react with the primary nitrogen atom of isopropanolamine to form a Schiff base.

\[ \text{CH}_2\text{CH}(-\text{OH})\text{CH}_2\text{NH}_2 + \text{RCHO} \rightarrow \text{CH}_2\text{CH}(-\text{OH})\text{CH}_2\text{N} \equiv \text{CHR} + \text{H}_2\text{O} \]

Formaldehyde reacts with isopropanolamines to form the corresponding hydroxymethyl compounds, which can be converted to the methyl derivatives by catalytic hydrogenation.

Compounds containing an active hydrogen atom undergo a Mannich reaction with formaldehyde and an isopropanolamine that has a primary or secondary amino group.

\[ (\text{CH}_3)_2\text{C} = \text{O} + \text{HCHO} + \text{HNR}_1\text{R}_2 \rightarrow \text{CH}_3\text{C} = \text{O} \text{CH}_2\text{CH}_2\text{NR}_1\text{R}_2 + \text{H}_2\text{O} \]

R\text{R}_1 = \text{H}, \text{C}_3\text{H}_6\text{OH}; R\text{R}_2 = \text{C}_3\text{H}_6\text{OH}

Diisopropanolamine reacts with nitrous acid or its salts to form N-nitrosamines. Isopropanolamines react with optically active acids, such as tartaric acid, to form diastereomeric pairs of salts; this enables the separation of isopropanolamines into their enantiomeric forms [63].

The use of trisopropanolamine as an esterification catalyst has been suggested [64].

### 4.2. Production

Isopropanolamines are produced like ethanolamines (see Section 3.2, Fig. 4), by treating propylene oxide with NH3 in the liquid phase in a continuous or batchwise procedure [65], [66]. The product is always a mixture of 1-amino-2-propanols and 2-amino-1-propanols, with the 1-amino isomers being the major component.

Industrially, the manner in which the propylene oxide ring is cleaved, and hence the isomer ratio of isopropanolamines, cannot yet be controlled.

Excess ammonia (about 2 – 20 mol per mole of propylene oxide) facilitates removal of the reaction heat (about 93 kJ/mol) and reduces the amount of polypropoxylated byproducts. This amount also depends on the relative reaction rates of propylene oxide with any amines present in the mixture.

Reaction temperatures can vary from 50 to 150 °C but are preferably around 100 °C. The resulting pressure can be reduced by adding water (ca. 10 – 60 %). Water and hydroxyl-containing compounds such as alcohols, phenols, and alkanolamines (autocatalysis) accelerate the reaction [67].
A continuous procedure is used for large-scale production, e.g., of monoisopropanolamine and diisopropanolamine [68], [69]. This procedure is similar to that used to produce ethanolamines (see Section 2.2).

The most important manufacturers of isopropanolamines are Air Products, BASF, Bayer, Sasol, and ICI in Western Europe, and Dow Chemical in the United States.

### 4.3. Quality Specifications

Because isopropanolamines are manufactured, sold, and used worldwide, the commercial products differ only slightly in delivery specifications. Typical specifications are listed in Table 8.

Purity is usually determined by gas chromatography. Depending on analytical conditions, isomeric and enantiomeric forms of isopropanolamines exhibit different numbers of peaks, which can be identified by test analyses. Derivatives obtained by reaction with trifluoroacetic anhydride can be analyzed more easily and analysis time can be reduced.

### 4.4. Uses

Possible uses of isopropanolamines are similar to those of ethanolamines; as a rule, the isopropanolamine derivatives exhibit better solubility in hydrophobic media. For example, neutralization with fatty acids, such as stearic or lauric acid, gives the corresponding soaps which are used in lubricant additives, textile finishing, and coating paper and wood [70]. Salts of isopropanolamines with fatty acids are also used as ionic emulsifiers in emulsion paints and as dispersants for pigments. Salts of isopropanolamines with alkylaryl sulfonic acids are employed as degreasers and cleaning promoters [71]. The fatty acid amides of isopropanolamines and mixtures of these with esters are frequently used in the cosmetics industry as shampoo thickeners and foam regulators [72].

Isopropanolamines are effective corrosion inhibitors in antifreezes [73] and cutting oils. Simultaneous use of nitrites should be avoided, since carcinogenic nitrosamines may form under certain circumstances. Isopropanolamines are important catalysts for urethane foams [74]. In epoxy resin systems, they have proved useful additives to curing agents [75].

Sulfur-containing isopropanolamine derivatives are used to extract metal ions, such as mercury, gold, and platinum, from salt solutions and wastewater [76].

A very important use of aqueous diisopropanolamine solutions is as a gas wash in the Adip and Sulfinol processes. Here, CO$_2$ and H$_2$S, in particular, are washed out of natural gas, synthesis gas, or coke oven gas and, after desorption, can be obtained in some cases in their pure form [77].

Monoisopropanolamine is employed extensively as an intermediate in the production of 1,2-diaminopropane (→ Amines, Aliphatic, Section 8.1.2.), while diisopropanolamine is used for the synthesis of 2,6-dimethylmorpholine [54].

#### Table 8. Minimum quality requirements for commercial isopropanolamines (as of 2000)

<table>
<thead>
<tr>
<th>Quality criterion</th>
<th>Method</th>
<th>Monoisopropanolamine</th>
<th>Diisopropanolamine</th>
<th>Diisopropanolamine containing 10% H$_2$O</th>
<th>Triisopropanolamine</th>
<th>Triisopropanolamine containing 15% H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water content, wt %</td>
<td>DIN 51 777</td>
<td>max. 0.2</td>
<td>max. 0.2</td>
<td>10 ± 1</td>
<td>max. 0.2</td>
<td>15 ± 1</td>
</tr>
<tr>
<td>Purity, %</td>
<td>GC</td>
<td>min. 99.0</td>
<td>min. 99.0</td>
<td>88</td>
<td>min. 99.0</td>
<td>84</td>
</tr>
<tr>
<td>Low boilers (max., %) (excluding H$_2$O)</td>
<td>GC</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>High boilers (max.) %</td>
<td>GC</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Color (max.), APHA</td>
<td>DIN-ISO 6271</td>
<td>20</td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Acid consumption, mL of 1 N HCl per gram</td>
<td>BS 523 : 1964</td>
<td>13.15 – 13.45</td>
<td>7.35 – 7.65</td>
<td>6.60 – 6.90</td>
<td>5.10 – 5.40</td>
<td>4.30 – 4.60</td>
</tr>
<tr>
<td>Freezing point, °C</td>
<td>BS 523 : 1964</td>
<td>ca. 2</td>
<td>ca. 39</td>
<td>ca. –10</td>
<td>ca. 58</td>
<td>&lt; -10</td>
</tr>
</tbody>
</table>

* Determined as area under GC peak.
5. N-Alkylated Propanolamines and 3-Alkoxypropylamines

N-Alkylated propanolamines can be divided into N-alkylated 1-amino-2-propanols, 2-amino-1-propanols, and 3-amino-1-propanols.

2-Amino-1-propanols and 1-amino-2-propanols are referred to industrially as isopropanolamines (Chap. 4). N-Alkylated isopropanolamines are prepared by reacting propylene oxide with the corresponding amines, which yields almost exclusively 1-amino-2-propanols [78]. Alkylated 2-amino-1-propanols have no industrial importance and are not discussed in this chapter.

5.1. Properties

5.1.1. Physical Properties

With a few exceptions, N-alkylated isopropanolamines, 3-amino-1-propanols, and 3-alkoxypropylamines are colorless liquids at room temperature. Some of them, such as cyclohexylisopropanolamine, are crystalline solids. The compounds tend to discolor on prolonged storage, especially if exposed to light, air, and heat (＞40°C). They have an amine-like odor, and absorb water and carbon dioxide. They are soluble in water, alcohol, acetone, glycol, glycerol, and glycol ethers, but only sparingly soluble in aliphatic or aromatic hydrocarbons and diethyl ether. Methyldiisopropanolamine does not form an azeotrope with water, but an azeotrope is formed upon distillation of aqueous dimethylisopropanolamine and 3-methoxypropylamine. Physical properties of N-alkylated isopropanolamines are given in Table 9 and those of 3-amino-1-propanols and 3-alkoxypropylamines in Table 10.

5.1.2. Chemical Properties

Because N-alkylated propanolamines contain hydroxyl groups and basic nitrogen, they possess the properties of both amines and alcohols. They form salts with organic and inorganic acids [79]. The sulfuric acid esters of propanolamines can be cyclized with sodium hydroxide to give propylenamines (see Section 4.1.2) [80]. Propanolamines with secondary amino groups form alkanolamides with fatty acids. Reaction of the amides with ethylene oxide gives water-soluble or easily dispersible nonionic surfactants [81]. 1-Amino-2-propanols are chiral and can be separated into enantiomers by means of appropriate reagents [63], [82]. N-Alkylpropanolamines with tertiary amino groups can be converted by means of benzoyl chloride, without the assistance of a base, into the amino alcohol ester hydrochlorides; with thionyl chloride, they give 2-chloropropylammonium chlorides.

The condensation of 3-amino-1-propanol with carbonyl compounds yields tetrahydro-1,3-oxazines [83], Schiff bases, or mixtures of both compounds. 3-Amino-1-propanol and 2-hydroxy-3,3-dimethylbutyrolactone react almost quantitatively to give panthenol [84].

Alkoxypropylamines react analogously to primary aliphatic amines. They form salts with inorganic or organic acids, and can be converted to acid amides, sulfonamides, urethanes, and Schiff bases. They can be alkylated with formaldehyde or formic acid to give dimethylamino compounds. 3-Methoxypropylamine catalyzes the addition of hydrogen cyanide to vinyl esters to give 1-cyanoethyl esters [85]. 3-Methoxypropylsulfanilylurea obtained from the 3-methoxypropylammonium salt of N,N-di(acetylsulfanilyl)urea is an oral antidiabetic agent [86].

5.2. Production

Industrially, N-alkylated isopropanolamines are prepared primarily from amines and propylene...
<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS registry number</th>
<th>M_r</th>
<th>mp, °C</th>
<th>bp (101.3 kPa), °C</th>
<th>p_c (20 °C) g/cm³</th>
<th>Cubic expansion coefficient, K⁻¹</th>
<th>Heat of vaporization kJ/kg</th>
<th>Specific heat, kJ (20 °C) K⁻¹</th>
<th>Viscosity (20 °C), mPa·s</th>
<th>nD²</th>
<th>Surface tension (20 °C), mN/m</th>
<th>Flash point, °C</th>
<th>Ignition temperature, °C</th>
<th>Temperature class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monomethyliso-propanolamine</td>
<td>[16667-45-1]</td>
<td>16667-45-1</td>
<td>89.14</td>
<td>12.5</td>
<td>149</td>
<td>0.9062</td>
<td>455.6</td>
<td>4.8 × 10⁻⁷</td>
<td>1.4340</td>
<td>28.7 (22 °C)</td>
<td>58.7</td>
<td>305</td>
<td>T2</td>
<td></td>
</tr>
<tr>
<td>Methyldiisopropanolamine</td>
<td>[4402-30-6]</td>
<td>4402-30-6</td>
<td>147.22</td>
<td>–32</td>
<td>226</td>
<td>0.945</td>
<td>329.3</td>
<td>1.4 × 10⁻⁷</td>
<td>47.3</td>
<td>1.4472 (25 °C)</td>
<td>24.5 (22 °C)</td>
<td>26</td>
<td>225</td>
<td>T3</td>
</tr>
<tr>
<td>Dimethylisopropanolamine</td>
<td>[108-16-7]</td>
<td>108-16-7</td>
<td>103.17</td>
<td>–85°</td>
<td>125.8</td>
<td>0.849 – 0.852</td>
<td>7.0 × 10⁻⁴ 393.6</td>
<td>2.45 (25 °C)</td>
<td>2 × 10⁻⁶</td>
<td>1.5</td>
<td>1.4189 (25 °C)</td>
<td>110.5</td>
<td>300</td>
<td>T3</td>
</tr>
<tr>
<td>Diethylisopropanolamine</td>
<td>131.22</td>
<td>157.5 – 159</td>
<td>0.8570</td>
<td>157.8</td>
<td>229.1</td>
<td>0.8419 &amp; 0.852</td>
<td>246.6</td>
<td>9.0 × 10⁻⁴</td>
<td>3.5</td>
<td>1.4361 (205 °C)</td>
<td>111</td>
<td>270</td>
<td>T3</td>
<td></td>
</tr>
<tr>
<td>Dibutylisopropanolamine</td>
<td>187.33</td>
<td>157.26</td>
<td>45.1</td>
<td>157.26</td>
<td>238</td>
<td>0.9365 (40 °C)</td>
<td>320.3</td>
<td>2.47 (60 °C)</td>
<td>11.5</td>
<td>1.4732 (60 °C)</td>
<td>111</td>
<td>270</td>
<td>T3</td>
<td></td>
</tr>
<tr>
<td>Cyclohexylisopropanolamine</td>
<td>215.34</td>
<td>2.0</td>
<td>157.26</td>
<td>238</td>
<td>0.9365 (40 °C)</td>
<td>320.3</td>
<td>2.47 (60 °C)</td>
<td>11.5</td>
<td>1.4732 (60 °C)</td>
<td>111</td>
<td>270</td>
<td>T3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclooctylisopropanolamine</td>
<td>185.31</td>
<td>12.85°</td>
<td>275</td>
<td>0.935</td>
<td>7.6 × 10⁻⁴</td>
<td>243.5</td>
<td>5.1 × 10⁻⁴</td>
<td>665</td>
<td>1.4902 (37.0 °C)</td>
<td>141</td>
<td>245</td>
<td>T3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclooctyldiisopropanolamine</td>
<td>243.39</td>
<td>29.6</td>
<td>318</td>
<td>0.977</td>
<td>7.4 × 10⁻⁴</td>
<td>233.95</td>
<td>5.7 × 10⁻¹¹</td>
<td>10670</td>
<td>1.4890 (38.0 °C)</td>
<td>176</td>
<td>245</td>
<td>T3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminoethylisopropanolamine</td>
<td>[123-84-2]</td>
<td>123-84-2</td>
<td>119.19</td>
<td>–38°</td>
<td>0.9868</td>
<td>145</td>
<td>1.4750 (123 °C)</td>
<td>115</td>
<td>290</td>
<td>T3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-(2-Hydroxypropyl)piperazine</td>
<td>144.22</td>
<td>–17°</td>
<td>1.0108</td>
<td>144.22</td>
<td>17</td>
<td>1.0108</td>
<td>145</td>
<td>1.4750 (123 °C)</td>
<td>115</td>
<td>290</td>
<td>T3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,4-Bis(2-hydroxypropyl)piperazine</td>
<td>202.30</td>
<td>97 – 98</td>
<td>0.9868</td>
<td>144.22</td>
<td>17</td>
<td>1.0108</td>
<td>145</td>
<td>1.4750 (123 °C)</td>
<td>115</td>
<td>290</td>
<td>T3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2-Hydroxypropyl)morpholine (12)</td>
<td>145.21</td>
<td>–47°</td>
<td>218</td>
<td>0.9868</td>
<td>144.22</td>
<td>17</td>
<td>1.0108</td>
<td>145</td>
<td>1.4750 (123 °C)</td>
<td>115</td>
<td>290</td>
<td>T3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N,N′N″-Tetrakis(2-hydroxypropyl)ethylenediamine</td>
<td>292.43</td>
<td>+11°</td>
<td>190</td>
<td>1.03</td>
<td>6.7 × 10⁻⁴</td>
<td>2.297</td>
<td>2.4 × 10⁻⁴</td>
<td>45</td>
<td>1.478 (35.1 °C)</td>
<td>201</td>
<td>285</td>
<td>T3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Pour point.
N-Alkylated 1-amino-2-propanols are formed predominantly [66], [88], [89]. The isomeric 2-amino-1-propanols are obtained only as byproducts (0.2 – 5 %, depending on the nature of the amino component). The reactions are carried out at 80 – 160 °C and pressures up to 5 MPa, batchwise or continuously. A detailed description can be found in Section 4.2. As in ethanolamine production, the oxide must be added to the amine, not vice versa (see Section 2.2). The crude reaction products are purified by continuous or batchwise distillation.

3-Amino-1-propanol is obtained by hydrogenating ethylene cyanohydrin. N-Methylated 3-amino-1-propanol and formaldehyde, with subsequent hydrogenation of the adducts [90]. 3-Alkoxypropylamines are prepared from acrylonitrile by addition to alcohols and subsequent hydrogenation [91].

### 5.3. Quality Specifications

Table 11 gives the specifications for commercial N-alkylated propanolamines and 3-alkoxypropylamines. Purity is generally determined by gas chromatography.

### 5.4. Uses and Economic Aspects

N-Alkylated propanolamines and 3-alkoxypropylamines are used mainly as intermediates, especially in the preparation of crop-protection agents and pharmaceuticals. 3-Alkoxypropyla-
mones have considerable commercial importance in the preparation of dyes. \(N\)-Alkylated propanolamines and their derivatives have been employed, in the form of soaps, as lubricating oil additives, mold release agents [92], [93], textile finishes, and coatings for paper and wood [94]. The propanolammonium salts of alkaryl sulfonic acids are used as cleansing boosters and degreasing agents [95]. 3-Alkoxypropylamines are utilized as catalysts in the production of polyurethane foams and epoxy resins. 3-Alkoxypropylamines and \(N\)-alkylpropanolamines are used as corrosion inhibitors and in the preparation of aqueous polymer solutions [96–100]. Anion exchangers can be prepared by reacting cellulose with dimethylisopropanolamine and epichlorohydrin [101].

World demand for \(N\)-alkylpropanolamines and 3-alkoxypropylamines is estimated at 5000 t/a. More than 100 t/a of 3-methoxypropylamine and dimethylisopropanolamine are used.

### 6. Storage and Transportation

Alkanolamines should be stored in stainless steel containers with exclusion of air (\(O_2\), \(CO_2\)) and moisture, preferably under dry nitrogen. Storage temperature should not exceed 40 °C (50 °C for ethanolamines). Steel tanks may be used if absorption of iron (up to 10 ppm) is not important. Alkanolamines turn yellow on prolonged storage, especially in the presence of oxygen. Depending on quality requirements and sensitivity of the products, steel, stainless steel, or polyethylene containers can be used for transportation. The containers must possess airtight closures to prevent absorption of water and carbon dioxide. Zinc and other nonferrous metals are attacked by alkanolamines. For transportation, particular national regulations, such as GGVS in Germany, should be observed [102]. Rubber gloves and safety goggles should be worn when handling alkanolamines. In some cases, especially with 3-alkoxypropylamines, a full face shield and rubber clothing are advisable. For safety data of alkanolamines, see the sections on physical properties.

### 7. Environmental Protection

Ammonia- or amine-containing off-gases from alkanolamine production are either burned or purified by acid scrubbing. Very low amine concentrations (10⁻³ ppm) can be determined by modern analytical methods [103]. Wastewater from plant cleaning and acid scrubbing is treated in a sewage plant. When properly fed into a biological treatment plant, alkanolamines are readily degraded by appropriate bacteria. Spilled product should be removed with an absorptive material such as urea resin foam (Hygromull) or peat dust, which is then incinerated.

### 8. Toxicology and Occupational Health

#### 8.1. General Aspects

All alkanolamines considered here are compiled in Table 12 along with available data on acute...
<table>
<thead>
<tr>
<th>Substance [CAS no.]</th>
<th>LD50, g/kg</th>
<th>Acute toxicity</th>
<th>Local irritation</th>
<th>OEL, mL/m³ (mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanolamines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoethanolamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[114-43-5]</td>
<td>1.5 (o, rt)</td>
<td>[116], &gt;8 h (520 ppm)</td>
<td>[116], 1 – 5 min: c</td>
<td>c [116] MAK: 2 (5.1)</td>
</tr>
<tr>
<td></td>
<td>1.2 – 2.5 (o, rt)</td>
<td>[142], [142]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0 – 2.5 (d, rbt)</td>
<td>[104]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diethanolamine</td>
<td>ca. 1.6 (o,r,t)</td>
<td>[116], &gt;8 h (0.37 ppm)</td>
<td>[116], se i ≤ 15 min: n i</td>
<td>se i [116] OEL(NL): (15) sk</td>
</tr>
<tr>
<td>[111-42-2]</td>
<td>1.7 – 2.8 (o, rt)</td>
<td>[142], [142]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.1 – 12.2 (d, rbt)</td>
<td>[142], [104]</td>
<td>1471 ppm (vapor/aerosol, 2 h)</td>
<td>m/s i</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>ca. 7.2 (o, r,t)</td>
<td>[116], &gt;8 h (0.0047 ppm)</td>
<td>[116], 4 h n i</td>
<td>n i se i [116] OEL(S): (5) TLV: (5)</td>
</tr>
<tr>
<td>[102-71-6]</td>
<td>8.4 – 11.3 (o, r,t)</td>
<td>[142]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;20 (d, rbt)</td>
<td>[142]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-(2-Aminoethoxy)ethanol</td>
<td>ca. 3.4 (o, r,t)</td>
<td>[116], &gt;8 h</td>
<td>[116], c</td>
<td>se i [116] n.e.</td>
</tr>
<tr>
<td>[929-06-6]</td>
<td>ca. 2.5 (o, r,t)</td>
<td>[159]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ca. 1.3 (d, rbt)</td>
<td>[181], [159]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;3 (d, rbt)</td>
<td>[159]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkylalkanolamines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monomethylethanolamine</td>
<td>1.39 – 2.34 (o, r,t)</td>
<td>[114], [116], &gt;8 h</td>
<td>[114], 3 min: i 4 h: c</td>
<td>[132], [133], n.e., sk</td>
</tr>
<tr>
<td>[109-83-1]</td>
<td>&gt;2 (d, rbt)</td>
<td>[116], [132]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ca. 1.9 (d, rbt)</td>
<td>[132]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ca. 1.25 (d, rbt)</td>
<td>[133]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethylethanolamine</td>
<td>1.1 (o, r,t)</td>
<td>[116], &gt;7 h</td>
<td>[116], c</td>
<td>se i [116] n.e.</td>
</tr>
<tr>
<td>[110-73-6]</td>
<td>1.48 (o, r,t)</td>
<td>[114], [116]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.67 (d, r,t)</td>
<td>[116]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n-Propylethanolamine</td>
<td>ca. 1 (o, r,t)</td>
<td>[116], &gt;8 h</td>
<td>[116], 3 min: sl i</td>
<td>c</td>
</tr>
<tr>
<td>[16399-21-4]</td>
<td>&gt;0.4 (d, rbt.)</td>
<td>[116], &gt;2.9 mg L⁻¹(4 h)⁻¹</td>
<td>[116], 1 h c</td>
<td>c [116]</td>
</tr>
<tr>
<td>n-Butylethanolamine</td>
<td>ca. 1 (o, r,t)</td>
<td>[116], &gt;8 h</td>
<td>[116], 5 min: sei/c</td>
<td>c</td>
</tr>
<tr>
<td>[111-75-1]</td>
<td>Hydroxyethylaniline</td>
<td>2.73 (o, r,t)</td>
<td>[116], &gt;8 h</td>
<td>[116], n i</td>
</tr>
<tr>
<td>[122-98-5]</td>
<td>2.23 (o, r,t)</td>
<td>[140]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.06 (d, rbt)</td>
<td>[140]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimethylethanolamine</td>
<td>≥ 2 (o, r,t)</td>
<td>[116], [134], LC10 ca. 6.6 mg L⁻¹ (4 h)⁻¹</td>
<td>[132], [135], se i/c</td>
<td>se i/c [116], [135], n.e.</td>
</tr>
<tr>
<td>[108-01-0]</td>
<td>1.24 – 1.6 (o, r,t)</td>
<td>[135]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.2 (d, rbt)</td>
<td>[132]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.7 – 2.4 (d, rbt)</td>
<td>[135]</td>
<td>30 min</td>
<td>[116]</td>
</tr>
<tr>
<td>Diethylethanolamine</td>
<td>1.33 (o, r,t)</td>
<td>[116], [113], &gt;1 h</td>
<td>[116], 1 h c</td>
<td>c [116] MAK: 10 (50) sk TLV: 2 (9.6)</td>
</tr>
<tr>
<td>[100-37-8]</td>
<td>ca. 0.89 (d, gp)</td>
<td>[113]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dibutylethanolamine</td>
<td>ca. 0.6 (o, r,t)</td>
<td>[116], &gt;7 h</td>
<td>[116], &gt;5 min: i</td>
<td>se i [116] OEL (NL): (14) sk TLV: 0.5 (3.5) sk</td>
</tr>
<tr>
<td>[102-31-8]</td>
<td>1.68 (d, rbt)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-Hydroxyethylpiperazine</td>
<td>ca. 4.2 (o, r,t)</td>
<td>[116], &gt;8 h</td>
<td>[116], se i</td>
<td>se i [116] n.e.</td>
</tr>
<tr>
<td>[103-76-4]</td>
<td>≥5 (d, rbt)</td>
<td>[166]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical Name</td>
<td>CAS Number</td>
<td>Concentration</td>
<td>Test Duration (h)</td>
<td>Test Duration (min)</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------------</td>
<td>---------------</td>
<td>------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>N-Hydroxyethylmorpholine</td>
<td>[622-49-2]</td>
<td>ca. 6.8 (o, rt)</td>
<td>&gt;8 h</td>
<td>n</td>
</tr>
<tr>
<td>N-Hydroxyethylpiperidine</td>
<td>[3040-44-6]</td>
<td>1 – 2 (d, rbt)</td>
<td>&gt;8 h</td>
<td>c (&lt;3 min)</td>
</tr>
<tr>
<td>Methylidietanolamine</td>
<td>[105-59-9]</td>
<td>1.95 (o, rt)</td>
<td>&gt;5 (d, rbt)</td>
<td>mi</td>
</tr>
<tr>
<td>n-Butyldiethanolamine</td>
<td>[102-79-4]</td>
<td>0.6 – 1.0 g/kg</td>
<td>&gt;8 h</td>
<td>n</td>
</tr>
<tr>
<td>Monoisopropanolamine</td>
<td>[78-96-6]</td>
<td>4.26 (o, rt)</td>
<td>&gt;8 h</td>
<td>n</td>
</tr>
<tr>
<td>Triisopropanolamine</td>
<td>[122-20-3]</td>
<td>6.5 (o, rt)</td>
<td>&gt;8 h</td>
<td>mi</td>
</tr>
<tr>
<td>3-Dimethylamino-1-propanol</td>
<td>[3179-63-2]</td>
<td>1.86 (o, rt)</td>
<td>&gt;8 h</td>
<td>se i</td>
</tr>
<tr>
<td>Monomethylisopropanolamine</td>
<td>[16667-45-1]</td>
<td>1 (o, rt)</td>
<td>&gt;7 h</td>
<td>c</td>
</tr>
<tr>
<td>Dimethylisopropanolamine</td>
<td>[108-16-7]</td>
<td>1.36 (o, rt)</td>
<td>&gt;8 h</td>
<td>se i</td>
</tr>
<tr>
<td>Methyldiisopropanolamine</td>
<td>[4402-30-6]</td>
<td>2.15 – 3.83 (o, rt)</td>
<td>LC₅₀ &gt; 16.4 mg L⁻¹ h⁻¹</td>
<td>[116]</td>
</tr>
<tr>
<td>3-Methoxypropylamine</td>
<td>[5332-73-0]</td>
<td>6.26 (o, rt, aq. sol., pH 7)</td>
<td>8 h</td>
<td>5 min</td>
</tr>
<tr>
<td>3-Ethoxypropylamine</td>
<td>[6291-85-6]</td>
<td>1.1 – 1.5 (o, rt)</td>
<td>8 h</td>
<td>5 min</td>
</tr>
<tr>
<td>3-(2-Ethylhexyloxy)propylamine</td>
<td>[5397-31-9]</td>
<td>0.85 (o, rt)</td>
<td>8 h</td>
<td>n</td>
</tr>
</tbody>
</table>

*Symbols:* o = oral; d = dermal; rt = rat; rbt = rabbit; gp = guinea pig; i = irritating (n = not, sl = slightly, m = moderately, se = severely); c = corrosive.

The skin irritation for the specific time of exposure to the substance is given.

OEL = occupational exposure limit: MAK (Germany, 1999), TLV (USA, 1997); NL = The Netherlands, S = Sweden; I = inhalable (total aerosol), sk = skin; n.e. = not established.

Monoisopropanolamine (d,l) [78-96-6] contains 2-amino-1-propanol (d,l) [6168-72-3].
toxicity, irritant/caustic properties, and occupational exposure limits.

Most prominent among the toxic effects of alkanolamines is their caustic/irritant action on exposed skin and mucous membranes. This effect decreases from primary to tertiary alkanolamines and is distinctly less pronounced or absent in their salts due to compensation of alkalinity. An increase in the number of hydroxyl groups further alleviates the irritant properties.

The low vapor pressure of these compounds at room temperature explains the generally low acute inhalation hazard. However, vapors formed at elevated temperatures may irritate eyes and respiratory tract. Aqueous solutions containing 1 – 10 % of monoalkanolamines such as monoethanol- and monoisopropanolamine are still irritating to eyes and skin. In principal, this also applies to the N-dialkanol derivatives, albeit to a lesser degree. Available data suggest that alkanolamines can penetrate the skin.

In general, the acute toxicity of the tested compounds is moderate to low and nonspecific; it is probably dominated by local irritant effects owing to their alkalinity. In a few cases, acute or long-term systemic symptoms may involve neuropharmacological effects that interact with acetylcholine synthesis and neurotransmitter function or neurotoxicity as a consequence of disturbed neural membrane structure.

The mutagenic potential of alkanolamines is very low. However, in the presence of nitrite or under other appropriate conditions, primary and secondary alkanolamines form nitroso compounds which may be mutagenic or carcinogenic. Existing regulatory limitations on the use of compounds need to be considered as well as work-place regulations.

The skin-sensitizing potential of alkanolamines is very low.

8.2. Ethanolamines

The chemistry, biochemistry, and toxicity of monoethanolamine (MEA), diethanolamine (DEA), and triethanolamine (TEA) have comprehensively been reviewed [142]. MEA is a natural building block of a group of important membrane components, the phospholipids, and the precursor in the de-novo synthesis of choline to form lecithin. DEA interferes with the MEA and phospholipid metabolism by replacing choline. The accumulation of atypical phospholipids appears to be the determinant in the systemic toxicity of DEA. TEA does not exhibit these properties.

There is no evidence that MEA and DEA have a sensitizing potential [142], while for TEA, occasional cases of allergic contact dermatitis were reported [108], [109]; however, no sensitizing effect was found in guinea pigs [110], [164], [142].

The majority of genotoxicity tests, including bacterial and mammalian in vitro test systems, indicate the absence of mutagenic activity in these ethanolamines [142].

Monoethanolamine. Early inhalation studies with various animal species demonstrated that the extreme irritancy of an MEA atmosphere to exposed skin and the respiratory tract resulted in pronounced discomfort and behavioral depression already at concentrations of 5 – 15 ppm (ca. 12.5 – 38 mg/m³) [142]. Nonstop inhalation for about 3 – 6 weeks of 66 – 75 ppm MEA vapors was lethal to guinea pigs and rats; 100 ppm was lethal to dogs. The liver and the kidney were identified as target organs at high doses [142]. Oral administration of 1.28 g kg⁻¹ d⁻¹ in the feed to rats for 30 – 90 d was lethal, whereas a dose of 0.64 g kg⁻¹ d⁻¹ led to changes in the liver and kidney weights; a dose of 0.32 g kg⁻¹ d⁻¹ was tolerated without any toxic effects [105], [142].

MEA produced no signs of developmental toxicity in standard developmental toxicity tests when applied orally to pregnant rats [142], [143] and dermally to pregnant rabbits [144]. This refutes the putative increases in the incidence of fetal malformations, unrelated to dose, in a previous nonstandard study [142].

Diethanolamine. All toxicity data for repeated exposure suggest that DEA can be incorporated in cell membranes and affects their stability [142]. The liver and kidneys are the major target organs, but demyelinization of nerve fibers and anemia, presumably due to altered composition of the erythrocyte membranes, is also possible. Toxic effects were observed after continuous inhalation of 25 ppm for 9 d or 6 ppm for 13 weeks (5 d/week), which was lethal to some of the exposed rats, and after a seven-week
administration to rats of neutralized diethanolamine at a concentration of 4 mg/mL in drinking water [107], [142]. Oral administration of 0.02 g kg\(^{-1}\) d\(^{-1}\) to rats for 90 d was tolerated without any signs of toxicity, whereas a dose of 0.09 g kg\(^{-1}\) caused an increase in liver and kidney weights. A dose of 170 mg kg\(^{-1}\) d\(^{-1}\) was lethal [105], [142]. A subchronic no observed adverse effect level was established at a dose of 20 – 25 mg kg\(^{-1}\) d\(^{-1}\) for oral exposure in rats [145]. In two-year dermal carcinogenicity studies, increased incidence of liver tumors was observed in mice, but not in rats [146]. Follow-up studies in two transgenic mouse lines, which were expected to exhibit enhanced sensitivity to carcinogenic substances, clearly failed to elicit any carcinogenic potential of DEA [147]. Furthermore, the development of DEA-related neoplasia in mouse liver could reasonably be explained by a non-genotoxic mechanism expressed by disruption of choline metabolism [148].

DEA was maternally toxic and fetotoxic (i.e., retarded ossification) at oral doses of 0.2 g kg\(^{-1}\) d\(^{-1}\) [142], [149], and at dermal doses of 1.5 and 0.35 g kg\(^{-1}\) d\(^{-1}\) in rats and rabbits, respectively, but failed to produce structural malformations in any test [142].

**Triethanolamine** has a low systemic toxicity, mainly restricted to the kidney as target organ [112], [142]. In contrast to DEA it is readily eliminated via the urine without undergoing appreciable metabolism. Extensive mutagenicity testing did not reveal a genotoxic effect [154], [154]. In subacute inhalation studies with rats and mice exposed to TEA aerosols over a 16-d period (0.125 – 2 g/m\(^3\), 6 h/d, 5 d per rats and mice exposed to TEA aerosols over a [154], [154]. In subacute inhalation studies with genicity testing did not reveal a genotoxic effect going appreciable metabolism. Extensive muta-tion study using mouse BALB/3T3 cells indicate a genotoxic potential [159]. A cell trans-formation assay in rat hepatocytes failed to show any signs of toxicity, whereas a dose of 0.09 g kg\(^{-1}\) caused an increase in liver and kidney weights. A dose of 170 mg kg\(^{-1}\) d\(^{-1}\) was lethal [105], [142]. A subchronic no observed adverse effect level was established at a dose of 20 – 25 mg kg\(^{-1}\) d\(^{-1}\) for oral exposure in rats [145].

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A dermal carcinogenicity study in mice suggested a significant increase in the spontaneous tumor rate of hepatocellular adenomas in the high-dose male and female groups (2 and 1 g kg\(^{-1}\) d\(^{-1}\), respectively). However, because of an infection of the animals with *Helicobacter hepaticus*, the study could not be evaluated and was abandoned as being inadequate [165]. There was no significant carci-nogenicity in rats epicutaneously administered TEA at doses from 30 to 250 mg kg\(^{-1}\) d\(^{-1}\) [165]. However, because of a marginally positive trend in the incidence of renal tubular adenomas in males, the Peer Review concluded on “equivocal evidence” in male rats [165].

**2-(2-Aminoethoxy)ethanol** (diglycolamine) applied as 10% ethanolic solution showed no skin-sensitizing activity in the Buehler test [159], [167]. The Ames test [143], [159] and a DNA repair assay in rat hepatocytes failed to indicate a genotoxic potential [159]. A cell transformation study using mouse BALB/3T3 cells was also negative [159].

### 8.3. *N*-Alkyl- und *N*-Arylethanolamines

**Methylethanolamine** was not mutagenic in the Ames test [169]. Continuous inhalation exposure to 1.8 and 9.7 ppm (ca. 0.006 and 0.03 g m\(^{-3}\), respectively) for 90 d resulted in local irritation (inflammatory effects on the nasal epithelium), but no treatment-related systemically toxic findings in rats and guinea pigs. In male dogs, dose-related atrophic degenerations in the testes were noted under comparable test conditions [151]. After 32-d administration of 0.004, 0.04, and 0.4 g kg\(^{-1}\) d\(^{-1}\) in the diet to rats, relative liver weights were increased in all dose groups with slight hepatic vacuolization at the two upper levels, and slight testicular edema and atrophy in the high-dose male group [151]. There was no evidence of embryotoxic and teratogenic effects on fetuses after inhalation exposure to 150 ppm (ca 0.47 g/m\(^3\)) in pregnant rats [152].
Ethylethanolamine is reported to be negative in the Ames test [155]. After ingestion in drinking water for 30 d, mainly dose-related histopathological changes in the kidneys developed in rats, with diffuse edema in the tubular epithelia at about 0.023 g kg$^{-1}$ d$^{-1}$ and progressive degenerative lesions at higher doses; furthermore, counts of white and red blood cells were enhanced [156]. After 90-d administration, the above-mentioned effects appeared to be less pronounced at corresponding dosage [156].

In a specially designed test, ethylethanolamine applied at an oral dose of about 0.18 g kg$^{-1}$ d$^{-1}$ during the implantation period (day 1 through 6 of gestation), produced implantation losses of some 50% in pregnant rats [157].

$n$-Propylethanolamine was nonmutagenic in the Salmonella typh./E. coli reverse mutation test [158].

$n$-Butylethanolamine was nonmutagenic in the Salmonella typh./E. coli reverse mutation test [158].

Hydroxyethylaniline was nonsensitizing in the guinea pig maximization test [143] and was mutagenic in a bacterial assay using only Salmonella typh. TA 98 [143]. Methemoglobinemia developed in cats after oral and dermal exposure (54.5 and 545 mg kg$^{-1}$, respectively), a known effect of aromatic amines [116].

Dimethylethanolamine occurs as intermediate in endogenous choline synthesis and therefore interferes with phospholipid and acetylcholine metabolism. It is said to have some stimulatory effect on the CNS by influencing neurotransmitter activity [163]. No skin sensitization was induced in guinea pigs [168], and no mutagenicity in Ames tests [143], [169]. Inhalation toxicity is associated with strong local irritation of the nasal region and extreme discomfort of the exposed animals; no pathological changes of inner organs occurred in rats exposed to concentrations of up to 76 ppm (0.37 g/m$^3$) for 14 weeks [170], [171]. Likewise, there were no significant treatment-related findings in rats that received ca. 0.013 and 0.033 g kg$^{-1}$ d$^{-1}$ and successively increased doses of up to 0.67 g kg$^{-1}$ d$^{-1}$ in the diet for two years [172]. Marked neurological action was observed in dogs at repeated dietary doses of ca. 0.04 g kg$^{-1}$ d$^{-1}$ and above, expressed as tremor and head shaking followed by ataxia and convulsions at elevated doses [172]. There was no evidence of developmental effects on fetuses after inhalative exposure to maternally toxic concentrations (up to 100 ppm or 0.48 g/m$^3$) during pregnancy of rats [173].

Diethylethanolamine is also a metabolite of the local anesthetic procaine and has some pharmacological activity (vasodilatation, depression of nerve conductivity). No skin sensitization was induced in guinea pigs [168], and no mutagenicity in Ames tests [143], [169]. Inhalation toxicity is associated with strong local irritation of the nasal region and extreme discomfort of the exposed animals; no pathological changes of inner organs occurred in rats exposed to concentrations of up to 76 ppm (0.37 g/m$^3$) for 14 weeks [170], [171]. Likewise, there were no significant treatment-related findings in rats that received ca. 0.013 and 0.033 g kg$^{-1}$ d$^{-1}$ and successively increased doses of up to 0.67 g kg$^{-1}$ d$^{-1}$ in the diet for two years [172]. Marked neurological action was observed in dogs at repeated dietary doses of ca. 0.04 g kg$^{-1}$ d$^{-1}$ and above, expressed as tremor and head shaking followed by ataxia and convulsions at elevated doses [172]. There was no evidence of developmental effects on fetuses after inhalative exposure to maternally toxic concentrations (up to 100 ppm or 0.48 g/m$^3$) during pregnancy of rats [173].

Dibutylethanolamine. Five-week administration of neutralized dibutylethanolamine in drinking water in doses of 0.43, 0.20, and 0.13 g kg$^{-1}$ d$^{-1}$ (male rats) and 0.33, 0.24, and 0.14 g kg$^{-1}$ d$^{-1}$ (female rats) produced no substance-related, histopathological effects; the lowest dose was devoid of any macroscopic findings [115]. Irritation of the eyes and nose was observed after inhalative exposure of rats (70 ppm or ca. 0.5 g kg$^{-1}$ d$^{-1}$, 5 d per week, 6 h/d). This exposure was lethal to one of five animals and led to an
increase in the relative liver and kidney weights and to liver damage. A concentration of 22 ppm (ca. 0.16 g kg\(^{-1}\) d\(^{-1}\)) for 6 h/d over a period of six months was tolerated by rats without any signs of toxicity [115].

**Hydroxyethylpiperazine and Hydroxyethylmorpholine.** Hydroxyethylpiperazine [175] and hydroxyethylmorpholine [176] were nonmutagenic in an Ames test. But the latter substance is reported to exhibit some genotoxic activity by inducing DNA damage and repair in rat liver cells and cell transformation in cultured mouse embryo fibroblasts [176].

**N-Hydroxyethylpiperidine** (2-piperidino-ethanol) was not mutagenic in an Ames test with *Salmonella typh. TA100, TA98, and E. coli WP2* [177] and in a cytogenetic assay using Chinese hamster cells [178].

**Methyldiethanolamine** is reported to be nonsensitizing in a guinea pig maximization test [174] and proved to be nonmutagenic in various genotoxicity assays, including bacterial [161], [169] and mammalian cells and an in vivo micronucleus test [161]. After prolonged dermal administration to rats, no systemic effects were found up to the top dose of 0.75 g kg\(^{-1}\) d\(^{-1}\), but local changes at the treated site, characterized as acanthosis and hyperkeratosis, were induced at doses of 0.25 g kg\(^{-1}\) d\(^{-1}\) and higher. No pathological changes were noted at 0.1 g kg\(^{-1}\) d\(^{-1}\) [174].

**n-Butyldiethanolamine** was nonmutagenic in the *Salmonella typh./E. coli* reverse mutation test [158].

### 8.4. Propanolamines

**Monoisopropanolamine** induced no skin-allergic and photoallergic reactions in 150 humans tested in a repeated insult patch test [179]. Negative mutagenic results were obtained in Ames tests using *Salmonella* and *E. coli* tester strains [180], [169]. The ninefold inhalation of up to 0.24 g/m\(^3\) (5 d/week, 6 h/d) failed to produce clinical signs of intoxication or macroscopic changes in rats and mice [179]. Likewise, after 90-d feeding of 0.14 to 2.2 g kg\(^{-1}\) d\(^{-1}\) to rats, no effects were reported, but weight changes of the liver and kidney occurred at high dosage [181]. No increase in tumor incidences occurred in rats that received 1% in the feed (ca. 0.67 g kg\(^{-1}\) d\(^{-1}\)) for 94 weeks. However, in combination with 0.3% sodium nitrite in drinking water, endogenously produced nitroso compounds induced tumors [182].

**Diisopropanolamine** applied as 2% aqueous solution induced no skin-allergic and photoallergic reactions in a repeated insult patch test with 25 volunteers [179]. One case report of contact allergy has been published [183]. Dermatological testing programs using 1% diisopropanolamine in facial sunscreen resulted in two positively responding subjects out of two random collectives of 424 volunteers in total [179]. Based on a nonverifiable test report, a weakly allergic potential was concluded in guinea pigs [184]. The substance was nonmutagenic in the Ames test and induced no chromosomal aberrations in rat lymphocytes [185], [186]. When it was administered to rats at doses of 0.1–3 g kg\(^{-1}\) d\(^{-1}\) in the drinking water for 2 weeks, no symptoms were observed up to 0.6 g kg\(^{-1}\) d\(^{-1}\). The dose of 3 g kg\(^{-1}\) d\(^{-1}\) was lethal to two out of five male animals; the prominent effects for this dose group included a significant loss in body and organ weight, acute inflammation and degeneration of kidneys and urinary bladder, and general liver atrophy [138]. After four weeks of dermal exposure to up to 0.75 g kg\(^{-1}\) d\(^{-1}\), no pathological changes were noted in rats, except for skin irritation at the treated site at 0.5 g kg\(^{-1}\) d\(^{-1}\) and higher [186]. No clinical and organotoxic findings, as well as no increase in tumor incidences, were reported in rats that received 1% in the feed (ca. 0.5 g kg\(^{-1}\) d\(^{-1}\)) for 94 weeks. However, in combination with sodium nitrite in drinking water, endogenously produced nitroso compounds induced tumors [187].

**Triisopropanolamine** is reported to be nonsensitizing in humans when patch-tested as a 1.1% additive in a cosmetic lotion [179] and as such in a guinea pig maximization test [184]. It was nonmutagenic in the Ames test [169] and failed to induce chromosomal aberrations in a mouse micronucleus assay [143]. When it was administered to rats at doses of 0.1 to 0.2 g kg\(^{-1}\) d\(^{-1}\) in drinking water for two weeks, no effects
were observed at 0.1 and 0.33 g kg\(^{-1}\) d\(^{-1}\), with minor, but noncharacteristic findings at the higher doses [138]. No evidence of a fetotoxic and teratogenic potential was found in the progeny from pregnant rats exposed to oral doses reaching maternal toxicity [137], [143].

**Propanolamine** (3-amino-1-propanol) showed no skin-sensitizing potential in an early epicutaneous nonstandard test with guinea pigs [188] and no mutagenic activity in the Ames test [143], as well as in an SCE assay with CHO cells [189]. In a screening test, oral treatment of rats and cats with about 0.78 g kg\(^{-1}\) d\(^{-1}\), as well as in an SCE assay with CHO cells [188] and no mutagenic activity in the Ames test [139], two unspecified assays, a UDS assay, and a micronucleus test [139].

**3-Methoxypropylamine** caused skin sensitization in the Buehler test (5 % in ethanol) [139]. There was no evidence of mutagenic activity in the Ames test [139], [143], two unspecified assays, a UDS assay, and a micronucleus test [139].

**3-(2-Ethylhexoxy)propylamine** was reported to be nonmutagenic in the Ames test [19].

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Further Reading

