AMINES, CYCLOALIPHATIC

1. Introduction

Cycloaliphatic amines are comprised of a cyclic hydrocarbon structural component and an amine functional group external to that ring. Included in an extended cycloaliphatic amine definition are aminomethyl cycloaliphatics. Although some cycloaliphatic amine and diamine products have direct end use applications, their major function is as low cost organic intermediates sold as moderate volume specification products.

2. Physical Properties

For simple primary amines directly bonded to a cycloalkane by a single C–N bond to a secondary carbon the homologous series is given in Table 1. Up through C_8 each is a colorless liquid at room temperature. The ammoniacal or fishy odor

Table 1. **Properties of Primary Aminocycloalkanes**

Cycloaliphatic amine	CAS Registry Number	Molecular formula	Boiling point, °C	Flash point, °C	Specific gravity, g/mL	Refractive index, n_D
cyclopropylamine	[765-30-0]	C_3H_7N	49	−26	0.824	1.4210
cyclobutylamine	[2516-34-9]	C_4H_9N	82	−4	0.833	1.4363
cyclopentylamine	[1003-03-8]	$C_5H_{11}N$	108	17	0.863	1.4478
cyclohexylamine	[108-91-8]	$C_6H_{13}N$	134	32	0.868	1.4565
cycloheptylamine	[5452-35-7]	$C_7H_{15}N$	169	42		1.4724
cyclooctylamine	[5452-37-9]	$C_8H_{17}N$	190	80	0.928	1.4804
cyclododecylamine	[1502-03-0]	$C_{12}H_{25}N$	280[a]	121		

[a] Melting point 27°C.

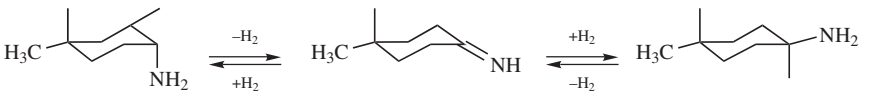
Table 2. **Properties of Substituted Aminocycloalkanes**

Cycloaliphatic amine	CAS Registry Number	Molecular formula	Boiling point, °C	Flash point, °C
1-methylcyclohexylamine	[6526-78-9]	$C_7H_{15}N$	140	
2-methylcyclohexylamine	[7003-32-9]	$C_7H_{15}N$		22
(±)*cis*-2-methylcyclohexylamine	[2164-19-4]	$C_7H_{15}N$	154	
(±)*trans*-2-methylcyclohexylamine	[931-10-2]	$C_7H_{15}N$	150	
(+)*t*-2-methylcyclohexylamine	[29569-76-4]	$C_7H_{15}N$		
(−)*t*-2-methylcyclohexylamine	[931-11-3]	$C_7H_{15}N$		
3-methylcyclohexylamine	[6850-35-7]	$C_7H_{15}N$		24
(±)*cis*-3-methylcyclohexylamine	[1193-16-4]	$C_7H_{15}N$	153	
(±)*trans*-3-methylcyclo-hexylamine	[1193-17-5] [6321-23-9]	$C_7H_{15}N$	152	
4-methylcyclohexylamine	[17746-6]	$C_7H_{15}N$		27
cis-4-methylcyclohexylamine	[2523-56-0]	$C_7H_{15}N$	154	
trans-4-methylcyclohexylamine	[2523-55-9]	$C_7H_{15}N$	152	
3,3,5-trimethylcyclohexylamine	[15901-42-5]	$C_9H_{19}N$	180	60
4-*tert*-butylcyclohexylamine	[5400-88-4]	$C_{10}H_{21}N$	213	79
N-methylcyclohexylamine	[100-60-7]	$C_7H_{15}N$	149	30
N-ethylcyclohexylamine	[5459-93-8]	$C_8H_{17}N$	165	44
N,N-dimethylcyclohexylamine	[98-94-2]	$C_8H_{17}N$	159	42
N,N-diethylcyclohexylamine	[91-65-6]	$C_{10}H_{21}N$	194	58
dicyclohexylamine	[101-83-7]	$C_{12}H_{23}N$	256	96
N-methyldicyclohexylamine	[7560-83-0]	$C_{13}H_{25}N$	265	101
1-adamantylamine	[768-94-5]	$C_{10}H_{17}N$	[a]	

[a] Melting point 207°C.

and high degree of water solubility decrease with increased molecular weight and boiling point for these corrosive, hygroscopic mobile fluids.

When additional substituents are bonded to other alicyclic carbons, geometric isomers result. Table 2 lists primary (1°), secondary (2°), and tertiary (3°) amine derivatives of cyclohexane and includes CAS Registry Numbers for cis and trans isomers of the 2-, 3-, and 4-methylcyclohexylamines in addition to identification of the isomer mixtures usually sold commercially. For the 1,2- and 1,3-isomers, the racemic mixture of optical isomers is specified; ultimate identification by CAS Registry Number is listed for the (+) and (−) enantiomers of *trans*-2-methylcyclohexylamine. The 1,4-isomer has a plane of symmetry and hence no chiral centers and no stereoisomers. The methylcyclohexylamine geometric isomers have different physical properties and are interconvertible by dehydrogenation–hydrogenation through the imine.



cis-1,4 *trans*-1,4

Table 3 lists cycloaliphatic diamines. Specific registry numbers are assigned to the optical isomers of *trans*-1,2-cyclohexanediamine; the cis isomer is achiral at ambient temperatures because of rapid interconversion of ring

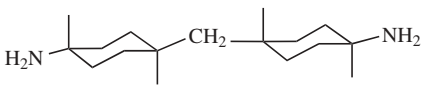
Table 3. **Properties of Cycloaliphatic Diamines**

Diamine	CAS Registry Number	Molecular formula	Boiling point[a], °C	Flash point, °C
cis,trans-1,2-cyclohexanediamine	[694-83-7]	$C_6H_{14}N_2$	183	75
cis-1,2-cyclohexanediamine	[1436-59-5]	$C_6H_{14}N_2$	182	72
(±)*trans*-1,2-cyclohexanediamine	[1121-22-8]	$C_6H_{14}N_2$		
(+)*trans*-1,2-cyclohexanediamine	[21436-03-3]	$C_6H_{14}N_2$		
(−)*trans*-1,2-cyclohexanediamine	[20439-47-8]	$C_6H_{14}N_2$		
cis,trans-1,3-cyclohexanediamine	[3385-21-5]	$C_6H_{14}N_2$		91
cis-1,3-cyclohexanediamine	[26772-34-9]	$C_6H_{14}N_2$	198	
trans-1,3-cyclohexanediamine	[26883-70-5]	$C_6H_{14}N_2$	203	
methylcyclohexanediamine	[28282-16-0]	$C_7H_{16}N_2$	99 (1.66)	83
cis,trans-1,3-cyclohexanediamine,2-methyl	[13897-56-8]			
cis,trans-1,3-cyclohexanediamine,4-methyl	[13897-55-7]			
cis,trans-1,4-cyclohexanediamine	[1436-59-5]	$C_6H_{14}N_2$	181	80
cis-1,4-cyclohexanediamine	[15827-56-2]	$C_6H_{14}N_2$		
trans-1,4-cyclohexanediamine	[2615-25-0]	$C_6H_{14}N_2$	197	71
cis,trans-1,8-menthanediamine	[80-52-4]	$C_{10}H_{22}N_2$	210	102
cis,trans-1,3-di(aminomethyl)cyclohexane	[2579-20-6]	$C_8H_{18}N_2$		106
cis-1,3-di(aminomethyl)cyclohexane	[10304-00-8]		114 (1.07)	
trans-1,3-di(aminomethyl)cyclohexane	[10339-97-6]		117 (1.33)	
cis,trans-1,4-di(aminomethyl)cyclohexane	[2549-93-1]	$C_8H_{18}N_2$	245	107
cis-1,4-di(aminomethyl)cyclohexane	[10029-09-9]	$C_8H_{18}N_2$		
trans-1,4-di(aminomethyl)cyclohexane	[10029-07-9]			
cis,trans-isophoronediamine	[2855-13-2]	$C_{10}H_{22}N_2$	252	112
methylenedi(cyclohexylamine)	[1761-71-3]	$C_{13}H_{26}N_2$	162 (2.40)	>110
isopropylidenedi(cyclohexylamine)	[3377-24-0]	$C_{15}H_{30}N_2$	182 (1.32)	>110
3,3′-dimethylmethylene-di(cyclohexylamine)	[6864-37-5]	$C_{15}H_{30}N_2$	160 (0.27)	174
cis,trans-tricyclodecanediamine[b]	[68889-71-4]	$C_{12}H_{22}N_2$	~314	165

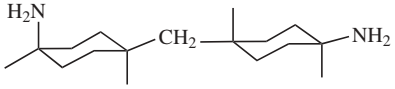
[a] At 101.3 kPa unless otherwise indicated by the value (in kPa) in parentheses. To convert kPa to mm Hg, multiply by 7.5.
[b] (4,7-Methano-1*H*-indene-dimethaneamine, octahydro).

conformers. Commercial products are most often marketed as geometric isomer mixtures, though large differences in symmetry may lead to such wide variations in physical properties that separations by classical unit operations are practicable, as in Du Pont's fractional crystallization of *trans*-1,4-cyclohexanediamine (mp 72°C) from the low melting (5°C) cis–trans mixture.

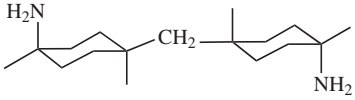
Two-ring cycloaliphatic diamines such as methylenedi(cyclohexylamine) (MDCHA), historically misnamed bis(*p*ara-amino cyclohexylmethane), or PACM, also exhibit critically dependent fundamental physical properties as a function of configurational isomerism, the simplest and most important being melting point.



trans, *trans*
[*6693-29-4*]
mp 65°C
(**1**)



cis, *trans*
[*6693-30-7*]
mp 36°C
(**2**)



cis, *cis*
[*6693-31-8*]
mp 61°C
(**3**)

3. Chemical Properties

Cycloaliphatic amines are strong bases with chemistry similar to that of simpler primary, secondary, or tertiary amines. Upon reaction with nitrous acid, primary amines evolve nitrogen and generate alcohols; secondary amines form mutagenic nitrosamines. Substituted amides are formed under forcing Schotten-Baumann alkaline conditions from primary and secondary amines using acid chlorides; benzamides from benzoyl chloride distinguish 1° and 2° from 3° amines. The Hinsberg test using benzenesulfonyl chloride differentiates water soluble primary amine sulfonamide derivatives from insoluble secondary amine derivatives; tertiary amines are unreactive. Oxidation of secondary carbon primary amines proceeds through hydroxylamine (CH–NHOH) to oxime (C=NOH) and ultimately to the nitroalkane ($CH-NO_2$). Hydrogen peroxide generates amine oxides from tertiary cycloaliphatic amines.

Salt formation with Brønsted and Lewis acids and exhaustive alkylation to form quaternary ammonium cations are part of the rich derivatization chemistry of these amines. Carbamates and thiocarbamates are formed with CO_2 and CS_2, respectively; the former precipitate from neat amine as carbamate salts but are highly water soluble.

Primary cycloaliphatic amines react with phosgene to form isocyanates. Reaction of isocyanates with primary and secondary amines forms ureas.

Dehydration of ureas or dehydrosulfurization of thioureas results in carbodiimides. The nucleophilicity that determines rapid amine reactivity with acid chlorides and isocyanates also promotes epoxide ring opening to form hydroxyalkyl- and dihydroxyalkylamines. Michael addition to acrylonitrile yields stable cyanoethylcycloalkylamines.

Cycloaliphatic diamines react with dicarboxylic acids or their chlorides, dianhydrides, diisocyanates and di- (or poly-)epoxides as comonomers to form high molecular weight polyamides, polyimides, polyureas, and epoxies. Polymer property dependence on diamine structure is greater in the linear amorphous thermoplastic polyamides and elastomeric polyureas than in the highly crosslinked thermoset epoxies (2–4).

4. Manufacture and Processing

Cycloaliphatic amine synthesis routes may be described as distinct synthetic methods, though practice often combines, or hybridizes, the steps that occur: amination of cycloalkanols, reductive amination of cyclic ketones, ring reduction of cycloalkenylamines, nitrile addition to alicyclic carbocations, reduction of cyanocycloalkanes to aminomethylcycloalkanes, and reduction of nitrocycloalkanes or cyclic ketoximes.

Secondary alcohols are aminated to secondary amines by dehydration catalysts or under H_2 pressure using metal dehydrogenation catalysts such as Ni or Co. The latter process becomes mechanistically equivalent to reductive alkylation of ammonia, though no hydrogen is consumed. Cyclohexylamine (CHA) is commercially produced from cyclohexanol [108-93-0] by reaction in the vapor phase with NH_3 and H_2. Controlled alkyl:ammonia, hydrogen ratios over metal dehydrogenation catalysts on solid supports at 160–200°C and 1350–2000 kPa (196–290 psi) at gas hourly space velocities of 1000–2500 vol/vol are analogous conditions to those of the preferred manufacturing process for other secondary aliphatic amines. Reduction of ammonia to cyclohexanol feed ratios in the fixed bed vapor phase process promotes dicyclohexylamine (DCHA) coproduction.

Reductive amination of cyclic ketones, or reductive alkylation of ammonia, is a general route to cycloaliphatic amines (5). Use of pressurized hydrogen and metal catalyst is the process technology of choice commercially; alternative (6) hydrogen sources include formic acid. Batch liquid-phase reaction technology predominates because cyclic ketone volatilization in the presence of ammonia leads to by-product-forming aldol condensations; higher molecular weight alicyclic ketones such as 2-adamantanone [700-58-3] are insufficently volatile. Short contact time (1–30 s), high temperature (to 275°C), and atmospheric vapor-phase reaction conditions for production of cyclohexylamine from mixtures of cyclohexanol and cyclohexanone [108-94-1] over heated copper chromite–nickel catalyst with an ammonia:alkyl ratio of 3.3:1 and hydrogen:alkyl ratio of 6.5:1 have, however, been claimed (8).

Aniline [62-53-3] ring reduction produces cyclohexylamine. Alternative historical synthetic routes and early (1905–1931) metal-catalyzed hydrogen additions under hydrogen pressure have been well reviewed (9). Increased efficiencies compared to those with Ni and Co catalysts are available from the

more precious elements of the same subgroup, Ru and Rh. Batch reaction giving >90% selectivity to CHA with <5% DCHA may use 1–3% of supported precious metal catalyst and neat substrate. Representative reaction conditions are 100–150°C with 1400–3500 kPa (200–500 psi) H_2 requiring 4–20 hours. Subsequent distillation may be batch or continuous. CHA fractionation from trace reaction by-product lights, then from recoverable DCHA and distillate heavies is done under reduced pressure. CHA has been made directly from phenol at low H_2 plus NH_3 pressure using rhodium catalyst in batch reactions (10) and in the vapor phase over nickel (11). Reaction selectivity to CHA is but 56% with 37% DCHA in the latter case.

Reductive amination of cyclohexanone using primary and secondary aliphatic amines provides *N*-alkylated cyclohexylamines. Dehydration to imine for the primary amines, to endocyclic enamine for the secondary amines is usually performed *in situ* prior to hydrogenation in batch processing. Alternatively, reduction of the *N*-alkylanilines may be performed, as for *N,N*-dimethylcyclohexylamine from *N,N*-dimethylaniline [121-69-7] (12,13). One-step routes from phenol and the alkylamine (14) have also been practiced.

Dicyclohexylamine may be selectively generated by reductive alkylation of cyclohexylamine by cyclohexanone (15). Stated batch reaction conditions are specifically 0.05–2.0% Pd or Pt catalyst, which is reusable, pressures of 400–700 kPa (55–100 psi), and temperatures of 75–100°C to give complete reduction in 4 h. Continuous vapor-phase amination selective to dicyclohexylamine is claimed for cyclohexanone (16) or mixed cyclohexanone plus cyclohexanol (17) feeds. Conditions are 5–15 s contact time of <1:1 ammonia:ketone, ~3:1 hydrogen:ketone at 260°C over nickel on kieselguhr. With mixed feed the preferred conditions over a mixed copper chromite plus nickel catalyst are 18-s contact time at 250°C with ammonia:alkyl = 0.6:1 and hydrogen:alkyl = 1:1.

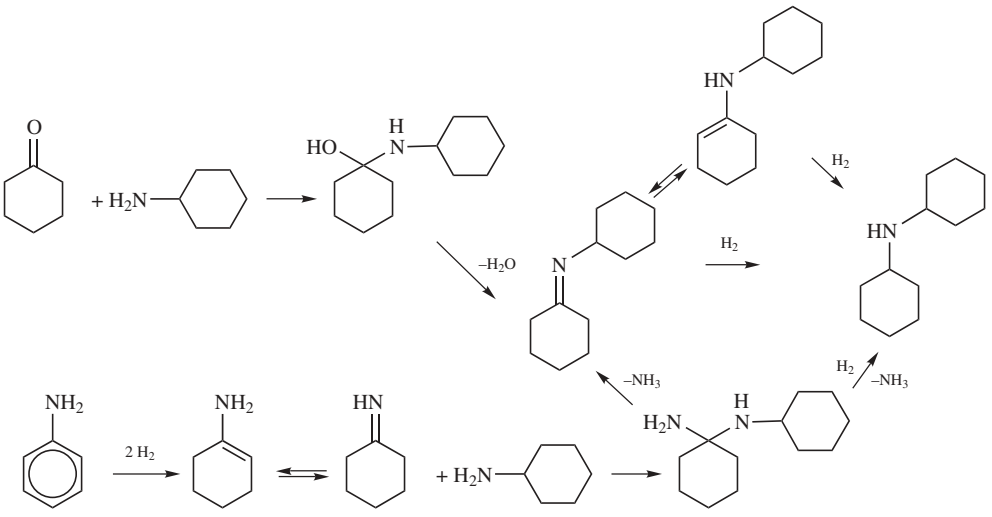
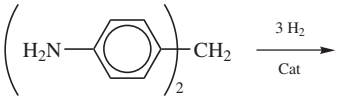


Fig. 1. Routes to dicyclohexylamine (DCHA).

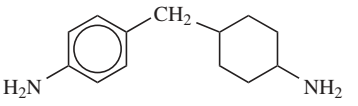
DCHA is normally obtained in low yields as a coproduct of aniline hydrogenation. The proposed mechanism of secondary amine formation in either reductive amination of cyclohexanone or arene hydrogenation illuminates specific steps (Fig. 1) on which catalyst, solvents, and additives moderating catalyst supports all have effects.

Alkali moderation of supported precious metal catalysts reduces secondary amine formation and generation of ammonia (18). Ammonia in the reaction medium inhibits Rh, but not Ru precious metal catalyst. More secondary amine results from use of more polar protic solvents, $CH_3OH > C_2H_5OH > t\text{-}C_4H_9OH$. Lithium hydroxide is the most effective alkali promoter (19), reducing secondary amine formation and hydrogenolysis. The general order of catalyst proclivity toward secondary amine formation is $Pt > Pd \gg Ru > Rh$ (20). Rhodium's catalyst support contribution to secondary amine formation decreases in the order carbon > alumina > barium carbonate > barium sulfate > calcium carbonate.

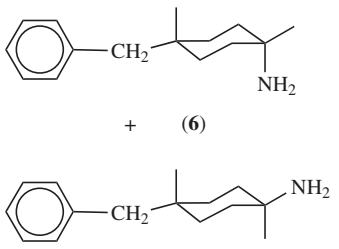
Methylenedianiline **(4)** (MDA) [101-77-9] hydrogenation to methylenedi (cyclohexylamine) generates first the *cis*-**(6)** and *trans*-**(7)** isomers of half-reduced 4-(*p*-aminobenzyl)-cyclohexylamine **(5)** [28480-77-5], a differentially reactive diamine offered in developmental quantities by Air Products and Chemicals.



(**4**)



(**5**)



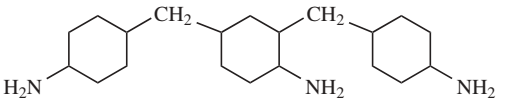
(**7**)

Addition of H_2 to the aromatic ring occurs cis, yielding a kinetic product subject to isomerization to the more thermodynamically stable trans isomer. Subsequent hydrogen addition to the remaining aromatic ring then produces the three fully reduced isomers **(1–3)**. Catalyst systems were first optimized for efficient maximum trans isomer production (21–23). Batch reaction conditions using Ru on alumina catalyst for obtaining the thermodynamic mixture of product isomers were 200°C and 28–35 MPa (4000–5000 psi). Improved yields, including isomerization to a 50/40/10 mixture of **(1,2,3)**, are enhanced by Ru alkali moderation (13,24,25).

Conditions cited for Rh on alumina hydrogenation of MDA are much less severe, 117°C and 760 kPA (110 psi) (26). With 550 kPa (80 psi) ammonia partial pressure present in the hydrogenation of twice-distilled MDA employing

2-propanol solvent at 121°C and 1.3 MPa (190 psi) total pressure, the supported Rh catalyst could be extensively reused (27). Medium pressure (3.9 MPa = 566 psi) and temperature (80°C) hydrogenation using iridium yields low *trans*/*trans* isomer MDCHA (28). Improved selectivity to alicyclic diamine from MDA has been claimed (29) for alumina-supported iridium and rhodium by introducing the tertiary amines 1,4-diazabicyclo[2.2.2]octane [280-57-9] and quinuclidine [100-76-5].

Direct production of select MDCHA isomer mixtures has been accomplished using ruthenium dioxide (30), ruthenium on alumina (31), alkali-moderated ruthenium (32) and rhodium (33). Specific isomer mixtures are commercially available from an improved 5–7 MPa (700–1000 psi) medium pressure process tolerant of oligomer-containing MDA feeds (34). Dimethylenetri(cyclohexylamine) **(8)** [25131-42-4] is a coproduct.

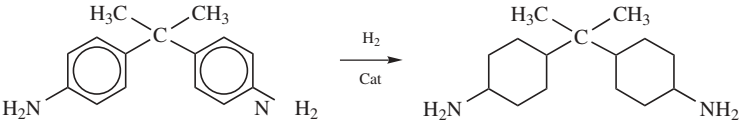


(**8**)

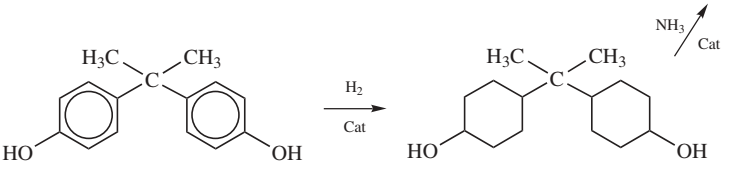
Continuous solvent-free hydrogenation of MDA over alkaline-earth-supported metals at 240°C and 25 MPa (3600 psi) has been described (35) as well as a similar high pressure process employing diluent solvent (36). MDA with isomeric impurities and oligomeric contaminants has been hydrogenated in a continuous flow system to advantage by first pretreating with Ni catalyst (150°C), then sequentially performing Ru hydrogenation at 185–200°C and 18 MPa (2600 psi) (37) (see also METHYLENEDIANILINE).

Batch syntheses comparable to those used for MDA produce 3,3′-dimethylmethylenedi(cyclohexylamine) marketed under the trade name Laromin C-260. The starting aromatic diamine, 3,3′-dimethylmethylenedianiline [838-88-0], is prepared from *o*-toluidine [95-53-4] condensation with formaldehyde. Similarly 3,3′-dimethyldicyclohexylamine [24066-10-2] may be produced (38) from *o*-tolidine [119-93-7] derived from *o*-nitrotoluene [88-72-2]. The resultant isomer mixtures are dependent on reduction conditions as in MDA hydrogenation.

Isopropylidenedi(cyclohexylamine) (PDCHA) (10) may be made by precious metal hydrogenation of isopropylidenedianiline **(9)** [2479-47-2], the condensation product of acetone [67-64-1] and aniline, commonly termed bisaniline A. A number of metal catalysts have been shown effective in an alternative route, the amination of isopropylidenedi(cyclohexanol) **(12)** [80-04-6] (39,40), the ring reduction product of bisphenol A **(11)** [80-05-7]. Ruthenium has been used for both the bisphenol ring reduction (210°C, 24 MPa H_2 = 3500 psi) and then a subsequent amination following ammonia addition. Batch amination of the cycloaliphatic diol **(12)** over a Co–Mn phosphoric acid–modified catalyst is only accomplished by initially pressurizing to 5 MPa (700 psi) with H_2, then adding NH_3 to a new autoclave pressure of 30 MPa (4350 psi) at 170°C, removing the water of reaction by venting, and cycling H_2 and NH_3 anew.



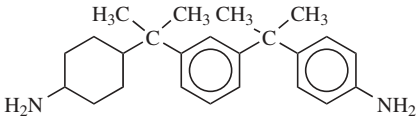
(**9**) (**10**)



(**11**) (**12**)

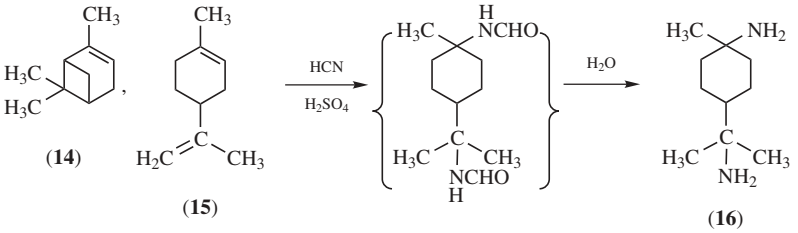
Trickle bed reaction of diol **(12)** using amine solvents (41) has been found effective for producing PDCHA, and heavy hydrocarbon codistillation may be used to enhance diamine purification from contaminant monoamines (42). Continuous flow amination of the cycloaliphatic diol in a liquid ammonia mixed feed gives >90% yields of cycloaliphatic diamine over reduced Co/Ni/Cu catalyst on phosphoric acid-treated alumina at 220°C with H_2 to yield a system pressure of 30 MPa (4350 psi) (43).

Cycloaliphatic diamines such as **(13)** [115172-12-8] which retain some aromatic character have been made from end-ring hydrogenation (44) of 1,3-bis (*p*-aminocumyl)benzene [2687-27-6], the double alkylation adduct of aniline to *m*-diisopropenylbenzene [3748-13-8] (45) using Ru catalysts (46).



(**13**)

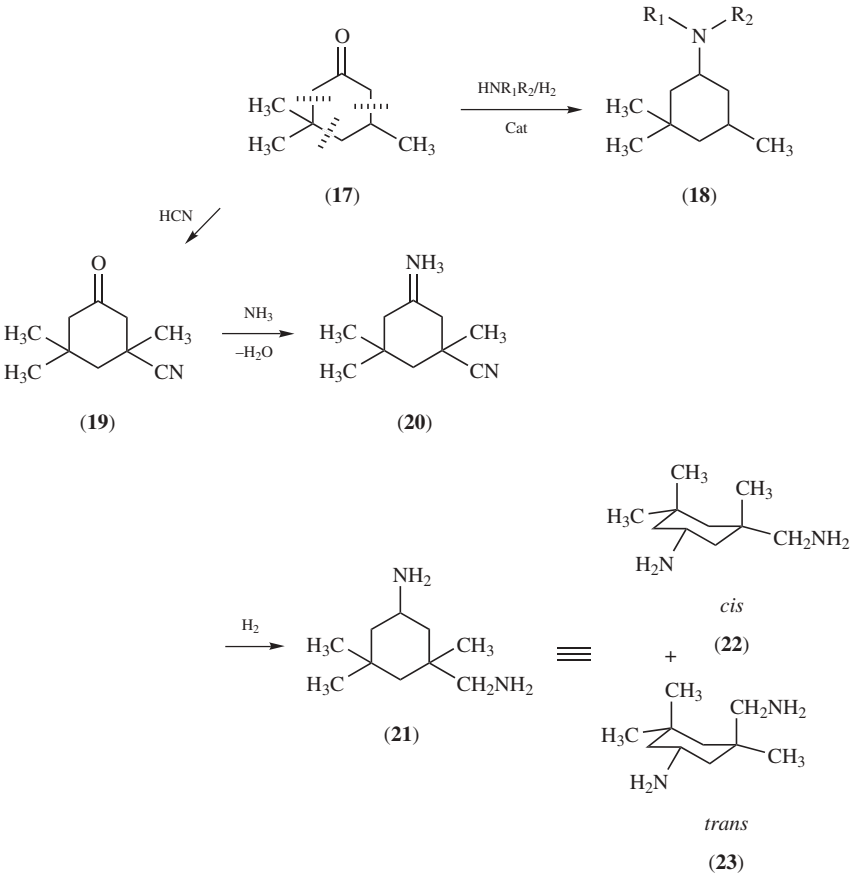
Cycloaliphatics capable of tertiary carbocation formation are candidates for nucleophilic addition of nitriles. HCN in strong sulfuric acid transforms 1-methyl-1-cyclohexanol to 1-methyl-1-cyclohexylamine through the formamide (47). The terpenes pinene **(14)** [2437-95-8] and limonene [5989-27-5] **(15)** each undergo a double addition of HCN to provide, after hydrolysis, the cycloaliphatic diamine 1,8-menthanediamine **(16)** (48).



(**14**) (**15**) (**16**)

1-Adamantylamine is prepared from the corresponding alcohol or bromide by bridgehead cation generation in the presence of acetonitrile (49). Selective hydrolysis of the resultant acetamide to the rigid cycloaliphatic amine by acid or base is difficult.

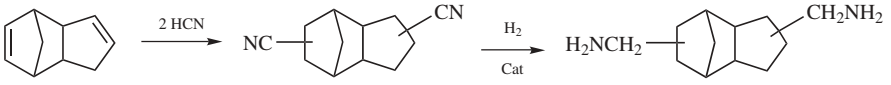
Acetone's cyclic trimer, isophorone **(17)** [78-59-1], has reacted directly with ammonia (Ra Ni, 120°C), methylamine, (Pt/C, 100°C) and dimethylamine (Pd/C, 95°C) at 2400–3450 kPa H_2 pressure to form 3,3,5-trimethylcyclohexylamines **(18)**, where R_1, R_2 = H, alkyl (50). The double bond is hydrogenated simultaneously with the imine:



3-Aminomethyl-3,5,5-trimethylcyclohexylamine **(21)**, commonly called isophoronediamine (IPD) (51), is made by hydrocyanation of **(17)** (52), (53) followed by transformation of the ketone **(19)** to an imine **(20)** by dehydrative condensation of ammonia (54), then concomitant hydrogenation of the imine and nitrile functions at 15–16 MPa (~2200 psi) system pressure and 120°C using methanol diluent in addition to H_2 and NH_3. Integrated imine formation and nitrile reduction by reductive amination of the ketone leads to alcohol by-product. There are two geometric isomers of IPD; the major product is *cis*-**(22)** [71954-30-5] and the minor, *trans*-**(23)** [71954-29-5] (55).

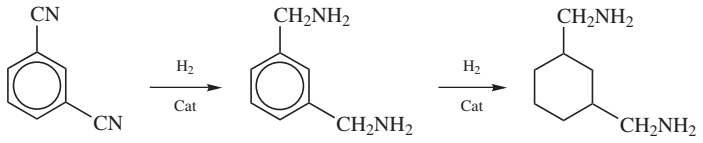
1,2-Cyclohexanediamine's commercial origin is its presence as a minor 0.1 – <1% coproduct of hexamethylenediamine [124-09-4] produced by hydrogenation of adiponitrile [111-69-3]. Fractional distillation by up to four columns in a series is routine commercial practice to purify nylon grade acyclic diamine; the crude cycloaliphatic diamine requires further refining before use as a specification intermediate.

Dicyclopentadiene **(24)** [77-73-6] is an inexpensive raw material for hydrocyanation to **(25)**, a mixture of 1,5-dicarbonitrile [70874-28-1] and 2,5-dicarbonitrile [70874-29-2], then subsequent hydrogenation to produce tricyclodecanediamine, TCD diamine **(26)**. This developmental product, a mixture of endo and exo, cis and trans isomers, is offered by Hoechst.



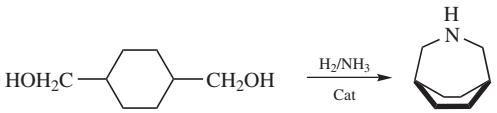
(**24**) (**25**) (**26**)

Di(aminomethyl)cyclohexanes are potentially available from large volume starting materials. The 1,3-isomer **(29)** may be produced by reduction of *m*-xylylenediamine **(28)** [1477-55-0] or directly upon exhaustive hydrogenation of isophthalonitrile **(27)** [626-17-5].



(**27**) (**28**) (**29**)

The 1,4-isomer has been similarly generated from terephthalonitrile [623-26-7] (56) using a mixed Pd/Ru catalyst and ammonia plus solvent at 125°C and 10 MPa (100 atm). It is also potentially derived (57) from terephthalic acid [100-21-0] by amination of 1,4-cyclohexanedimethanol **(30)** [105-08-8]. Endocyclization, however, competes favorably and results in formation of the secondary amine **(31)** 3-azabicyclo[3.2.2]nonane [283-24-9] upon diol reaction with ammonia over dehydration and dehydrogenation catalysts (58):



(**30**) (**31**)

5. Shipment

Shipment of these liquid products is by nitrogen-blanketed tank truck or tank car. Drum shipments are usually in carbon steel, DOT-17E.

6. Economic Aspects

Cycloaliphatic amine production economics are dominated by raw material charges and process equipment capital costs. Acetone (isophorone), adiponitrile, aniline, and MDA are all large-volume specification organic intermediates bordering on commodity chemicals. They are each cost-effective precursors.

Reductive alkylations and aminations require pressure-rated reaction vessels and fully contained and blanketed support equipment. Nitrile hydrogenations are similar in their requirements. Arylamine hydrogenations have historically required very high pressure vessel materials of construction. A nominal breakpoint of 8 MPa (~1200 psi) requires yet heavier wall construction and correspondingly more expensive hydrogen pressurization. Heat transfer must be adequate, for the heat of reaction in arylamine ring reduction is ~50 kJ/mol (12 kcal/mol) (59). Solvents employed to maintain catalyst activity and improve heat-transfer efficiency reduce effective hydrogen partial pressures and require fractionation from product and recycle to prove cost-effective.

Production of cyclohexylamine reflects this balance of raw material versus operating cost structure. When aniline cost and availability are reasonable, the preferred route is aniline ring reduction; alternatively the cyclohexanol amination route is chosen.

Demand for cyclohexylamine should remain the same as current demand at 7030×10^3 t (15.5×10^6 lb) (60).

Price history for 1995–2000 was a high of $0.69/kg ($1.52/lb) and a low of $0.64/kg ($1.40/lb). Both on the same basis: list, tech., tanks delivered (60).

Cyclohexylamine's market has become stagnant as its major applications are losing ground. Since the ban in the U.S. on cyclamate sweeteners in the 1970s (cyclohexylamine's biggest market at that time), there has been an overcapacity in the market (60).

7. Specifications, Standards, and Quality Control

Liquid cycloaliphatic amines and diamines have exacting purity and color standards. Almost all are sold to specification, not performance standards. Use as isocyanate precursors requires low water content criteria for these hygroscopic fluids, hence nitrogen blanketing is often specified for product sampling as well as storage and transport.

Contaminant by-products depend upon process routes to the product, so maximum impurity specifications may vary, eg, for CHA produced by aniline hydrogenation versus that made by cyclohexanol amination. Capillary column chromatography has improved resolution and quantitation of contaminants beyond the more fully described packed column methods (61) used historically to define specification standards. Wet chemical titrimetry for water by Karl Fisher or amine number by acid titration have changed little except for their automation. Colorimetric methods remain based on APHA standards.

8. Analytical Methods

Isomer separation beyond physical fractional crystallization has been accomplished by derivatization using methyl formate to make *N*-formyl derivatives and acetic anhydride to prepare the corresponding acetamides (1). Alkaline hydrolysis regenerates the analytically pure amine configurational isomers.

Amine chromatographic analyses suffer poor resolution in many gas–liquid column separations because of strong interactions of the basic functional group and surface active components of even glass column supports. Tailing results. For close-eluting isomers, the problem is magnified. Derivatization of isomeric cycloaliphatic diamines has been reported using *N,N′*-trifluoroacetyl derivatives from reaction with trifluoroacetic anhydride (62). *N,N,N′,N′*-Tetramethyl derivatives from formaldehyde–formic acid methylation, the Eschweiler–Clarke procedural variant of the Leuckart reaction (63), avoid amide hydrogen bonding column interactions (64). A more efficient procedure has been detailed for *N,N*-dimethylformamide dimethyacetal reaction with methylene- and isopropylidene-di(cyclohexylamine) geometric isomers to form chromatographically resolvable *N*-dimethylaminomethylene derivatives (65). Improved capillary column technology allows geometric isomer resolution directly, without derivatization (34).

Wet chemical methods determining titratable amine are reported for products entering urethane (amine number as meq/g) or epoxy (AHEW = amine hydrogen equivalent weight) trade applications. For secondary amines *N*-nitrosamine contaminants are reportable down to ppb using Thermoelectron Corporation thermal energy analyzer techniques.

9. Health and Safety Factors

Cycloaliphatic amines and diamines are extreme lung, skin, and eye irritants. MSD sheets universally carry severe personal protective equipment use warnings due to the risk of irreversible eye damage. These compounds are generally not mutagenic in the Ames test, and are highly (50–500 mg/kg) to moderately (500–5000 mg/kg) toxic as graded by the Hodge–Sterner scale by acute animal testing (66) (Table 4).Use of dry chemical, alcohol foam, or carbon dioxide is recommended for cycloaliphatic amine fire fighting. Water spray is recommended only to flush spills away to prevent exposures. In the aquatic environment, cyclohexylamine has a high (420 mg/L) toxicity threshold for bacteria (*Pseudomonas putida*) (68), and is considered biodegradable, that is, mineralizable to CO_2 and H_2O, by acclimatized bacteria.

The OSHA PEL time-weighted average for cyclohexylamine is 10 ppm.

The ACGIH TLV time-weighted average is 10 ppm. Cyclohexylamine is not classified as a human carcinogen (69).

10. Uses

Cyclohexylamine is miscible with water, with which it forms an azeotrope (55.8% H_2O) at 96.4°C, making it especially suitable for low pressure steam systems in

Table 4. **Acute Toxicity of Cycloaliphatic Amines**

Cycloaliphatic amine	Rat oral LD_{50}, mg/kg
cyclohexylamine	360
dicyclohexylamine	370
N-methylcyclohexylamine	400
dimethylcyclohexylamine	348
N-ethylcyclohexylamine	590
cis,trans-1,3-cyclohexanediamine	390
methyl-1,3-cyclohexanediamine	1060
4-methyl-1,3-cyclohexanediamine	1410[a]
1,3-diaminomethylcyclohexane	880
1,4-diaminomethylcyclohexane	530
1,8-menthanediamine	700
1-adamantylamine	900
methylenedi(cyclohexylamine)	450
3,3′-dimethylmethylenedi(cyclohexylamine)	550
tricyclodecanediamine	502

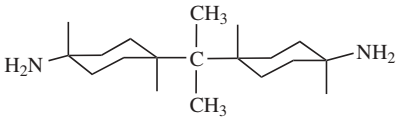
[a] Ref. 67.

which it acts as a protective film-former in addition to being a neutralizing amine.

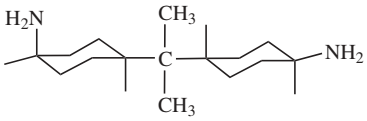
Nearly 55% of the 2000 U.S. production of 22,680 t/yr (50×10^6 lb/yr) cyclohexylamine serviced this application (60). Carbon dioxide corrosion is inhibited by deposition of nonwettable film on metal (70). In high pressure systems CHA is chemically more stable than morpholine [110-91-8] (71). A primary amine, CHA does not directly generate nitrosamine upon nitrite exposure as does morpholine. CHA is used for corrosion inhibitor radiator alcohol solutions, also in paper- and metal-coating industries for moisture and oxidation protection.

Monofunctional, cyclohexylamine is used as a polyamide polymerization chain terminator to control polymer molecular weight. 3,3,5-Trimethylcyclohexylamines are useful fuel additives, corrosion inhibitors, and biocides (50). Dicyclohexylamine has direct uses as a solvent for cephalosporin antibiotic production, as a corrosion inhibitor, and as a fuel oil additive, in addition to serving as an organic intermediate. Cycloaliphatic tertiary amines are used as urethane catalysts (72). Dimethylcyclohexylamine (DMCHA) is marketed by Air Products as POLYCAT 8 for pour-in-place rigid insulating foam. Methyldicyclohexylamine is POLYCAT 12 used for flexible slabstock and molded foam. DMCHA is also sold as a fuel oil additive, which acts as an antioxidant. Sterically hindered secondary cycloaliphatic amines, specifically dicyclohexylamine, effectively catalyze polycarbonate polymerization (73).

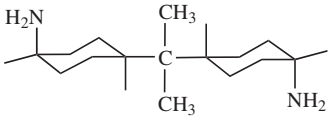
Cycloaliphatic diamines which have reacted with diacids to form polyamides generate performance polymers whose physical properties are dependent on the diamine geometric isomers (58, 74). Proprietary transparent thermoplastic polyadipamides have been optimized by selecting the proper mixtures of PDCHA geometric isomers **(32–34)** for incorporation (75):



trans, *trans*
[*28465-04-5*]
(**32**)



cis, *trans*
[*28465-03-4*]
(**33**)



cis, *cis*
[*28465-02-3*]
(**34**)

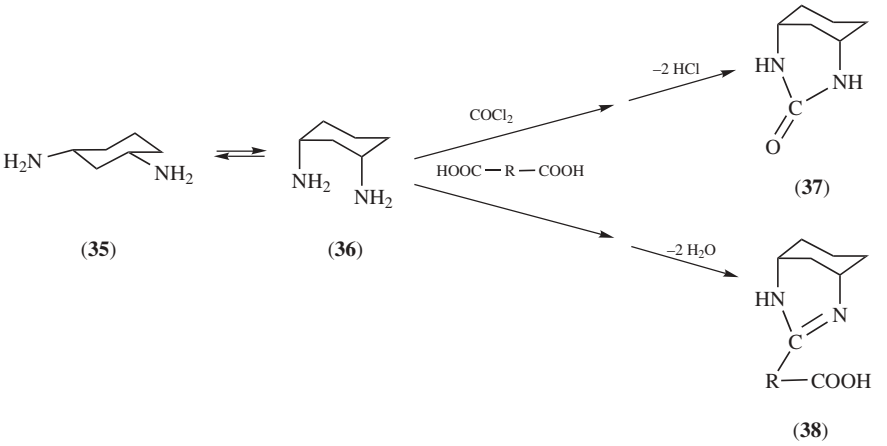
The polyamide copolymer of dodecanoic acid with methylenedi(cyclohexylamine) (MDCHA, PACM) was sold as continuous filament yarn fiber under the tradename QIANA. The low melting raffinate coproduct left after trans, trans isomer separation by fractional crystallization was phosgenated to produce a liquid aliphatic diisocyanate marketed by Du Pont as Hylene W. Upon termination of their QIANA commitment, Du Pont sold the urethane intermediate product rights to Mobay, who now markets the 20% trans, trans–50% cis, trans–30% cis, cis diisocyanate isomer mixture as Desmodur W. In addition to its use in polyamides and as an isocyanate precursor, methylenedi(cyclohexylamine) is used directly as an epoxy curative.

1,2-Cyclohexanediamine is used as an epoxy curative, (Millamine 5260). It may be adducted with epichlorohydrin to generate solventless low viscosity curatives for varnishes and surface coatings (76). Other cycloaliphatic diamines have long been modified as epoxy curatives to modify their reactivity profile (77).

MCHD from ring reduction of TDA (78,79) has been cited as an epoxy curative (80) and is available as a developmental cycloaliphatic diamine. Ring reduction of sterically hindered arylenediamines such as diethyltoluenediamine [68479-98-1] provides slower-reacting alkylated 1,3-cyclohexanediamines for polyurethane, polyurea, and epoxy use (81).

Use of 1,3-cycloaliphatic diamines as organic intermediates appears limited because of cis isomer endocyclization reactions. Ring hydrogenation of the low cost 80/20 2,4-toluenediamine/2,6-toluenediamine isomer mixture results in 4 geometric isomers of 4-methyl-1,3-cyclohexanediamine, 3 isomers of 2-methyl-1,3-cyclohexanediamine; the overall sum of methyl *cis*-1,3-diamine is ~50%. Phosgenation of the free-base or dicarbamate of hydrogenated TDA to produce methylcyclohexanediisocyanate results in low yields (82,83), possibly because of endocyclic urea formation. Diequatorial 1,3-cyclohexanediamine **(35)** is conformationally labile, and in the alternative 1,3-diaxial diamine conformation **(36)** allows facile condensation to urea **(37)**. Phosgenation of the methylcyclohexanediamine dihydrochloride, however, is efficient, giving ~90% yields of methylcyclohexanediisocyanate in 4–14 hours at 125–185°C and, depending on

solvent, pressure to 1 MPa (145 psi) (84).



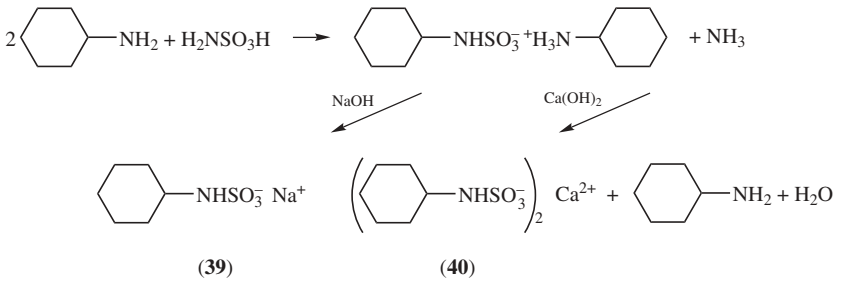
(**35**) (**36**) (**37**) (**38**)

Use of 1,3 cycloaliphatic diamines in polyamides may be similarly limited by internal amide dehydration of the conformationally labile cis isomers to form a tetrahydropyrimidine **(38)** rather than high molecular weight polyamide. 1,3-Cyclohexanediamine is, however, a component of Spandex polyureas; Du Pont uses the hydrogenation product of *m*-phenylenediamine [108-45-2] (24) captively to produce Lycra (see FIBERS, ELASTOMERIC).

1,8-Menthanediamine has been effectively reacted to form polyamides (85) and is sold in metric tons per year volume as a premium epoxy curative (86). 1-Adamantylamine hydrochloride [665-66-7] is a prophylactic against type A viral infections sold by Du Pont under the trade name Symmetrel. Cyclohexylamine derivatives as subtype selective *N*-methyl-D-aspartate antagonists useful for treating cerebral vascular disorders have been described (87).

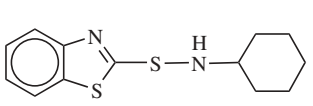
11. Derivatives

Before a 1/1/70 FDA ban, cyclamate noncaloric sweeteners were the major derivatives driving cyclohexylamine production. The cyclohexylsulfamic acid sodium salt (39) [139-05-9] and more thermally stable calcium cyclohexylsulfamic acid **(40)** [139-06-1] salts were prepared from high purity cyclohexylamine by, among other routes, a reaction cycle with sulfamic acid.

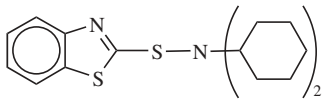


(**39**) (**40**)

Cyclohexylamine condensed with mercaptobenzothiazole produces the large volume moderated rubber accelerator *N*-cyclohexyl-2-benzothiazolesulfenamide **(41)** [95-33-0] (see RUBBER COMPOUNDING). DCHA similarly is used in preparing *N,N*-dicyclohexyl-2-benzothiazolesulfenamide **(42)** [4979-32-2]. The cyclohexylamine derivative is preferred over *tert*-butylamine [75-64-9] and morpholine sulfenamide analogues because of lower amine volatility and less nitrosamine risk respectively.



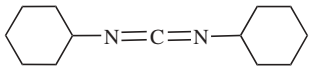
(**41**)



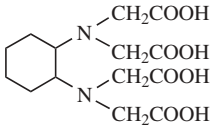
(**42**)

1,3-Dicyclohexylcarbodiimide **(43)** [538-75-0] is an important peptide-condensing agent and analytical reagent (88).

trans-1,2-Cyclohexanediamine is derivatized by Mannich reaction of formaldehyde and HCN, then hydrolyzed to the tetraacetate **(44)** [13291-61-7] and sold as a chelating agent.



(**43**)

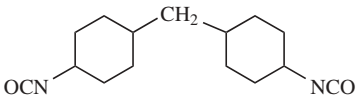


(**44**)

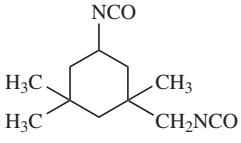
Methylenedi(cyclohexylisocyanate) **(45)** [5124-30-1] (MDCHI, Desmodur W) is the dominant derivative of MDCHA and is used in light-stable urethanes. Polyurethane physical properties are dependent on the diamine geometric isomer composition used for the derivative diisocyanate which reacts with diol (89).

Isophoronediisocyanate **(46)** [4098-71-9] made by phosgenation of IPD (90) competes effectively in this same polyurethane market, predominantly coatings, and is the major commercial application of isophoronediamine.

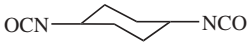
1,4-Cyclohexanediamine from hydrogenation of *p*-phenylenediamine [106-50-3] may be easily phosgenated, unlike the corresponding 1,2- and 1,3- isomers to produce a useful (92) diisocyanate for performance polyurethanes efficiently (91), particularly *trans*-1,4-cyclohexanediisocyanate [2556-36-47] **(47)** (CHDI). This diamine organic intermediate use competes with an Akzo route to *t*-CHDI from the corresponding diacid without intermediacy of the diamine.



(**45**)

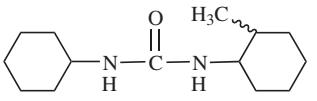


(**46**)

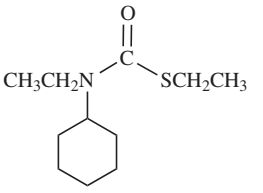


(**47**)

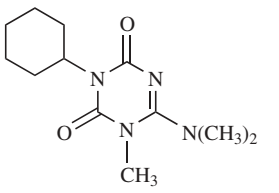
A representative agrochemical application of cycloaliphatic amines is the reaction of the commercial 30/70 cis/trans isomer mixture of 2-methylcyclohexylamine with phenylisocyanate to give the crabgrass and weed control agent Siduron (1-(2-methylcyclohexyl)-3-phenylurea **(48)** [1982-49-6] (93). The preplant herbicide Cycloate used for sugar beets, vegetable beets, and spinach, (*S*-ethyl-*N*-ethyl-*N*-cyclohexylthiocarbamate **(49)** [1134-23-2], incorporates *N*-ethylcyclohexylamine. The herbicide Hexazinone, (3-cyclohexyl-6-dimethylamino-1-methyl-1,3,5-triazine-2,4-dione **(50)** [51235-04-2]) is prepared from cyclohexylisocyanate [3173-53-3] (94).



(**48**)



(**49**)



(**50**)

BIBLIOGRAPHY

"Amines" in *ECT* 1st ed., Vol. 1, pp. 702–717, by E. F. Landau, Celanese Corporation of America; "Amines, Survey" in *ECT* 2nd ed., Vol. 2, pp. 99–116, by Richard L. Bent, Eastman Kodak Company; "Amines, Cyclic" in *ECT* 3rd ed., Vol. 2, pp. 295–308, by Kenneth Mjos, Jefferson Chemical Company; in *ECT* 4th ed., Vol. 2, pp. 386–405, by Jeremiah P. Casey, Air Products and Chemicals.

CITED PUBLICATIONS

1. A. E. Barkdoll, H. W. Gray, and W. Kirk, *J. Am. Chem. Soc.* **73**, 741–746 (1951).
2. T. F. Mika and R. S. Bauer, in C. A. May, ed., *Epoxy Resins Chemistry and Technology*, 2nd ed., Marcel Dekker, New York, 1988, 465–550.
3. H. Lee and K. Neville, in *Handbook of Epoxy Resins*, McGraw-Hill, 1967, (1982 reissue), Chapt. 7.
4. *EPON Resin Structural Reference Manual*, Shell Chemical Company.
5. W. S. Emerson, in R. Adams, ed., *Organic Reactions*, Vol. 4, John Wiley & Sons, Inc., New York, 1948, Chapt. 3, 174–255.
6. J. March, *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, 3rd ed., John Wiley & Sons, Inc., New York, 1985.
7. U.S. Pat. 3,532,748 (Oct. 6, 1970), G. W. Smith (to E. I. du Pont de Nemours & Co.).
8. U.S. Pat. 3,551,487 (Dec. 29, 1970), B. R. Bluestein, J. M. Solomon, and L. B. Nelson (to Witco).
9. T. S. Carswell and H. L. Morrill, *Ind. Eng. Chem.* **29**, 1247–1251 (1937).
10. U.S. Pat. 3,364,261 (Jan. 16, 1968), F. H. Van Munster (to Abbott).
11. Jpn. Kokai 85 239,444 (Nov. 28, 1985), H. Matsumoto, K. Hiraska, M. Hasiguchi, and H. Arimatsu (to Honshu).
12. U.S. Pat. 3,376,341 (Apr. 2, 1965), C. R. Bauer (to E. I. du Pont de Nemours & Co., Inc.).

13. U.S. Pat. 3,644,542 (Feb. 22, 1972), L. D. Brake and A. B. Stiles (to E. I. du Pont de Nemours & Co., Inc.).
14. U.S. Pat. 3,355,490 (Nov. 28, 1967), F. H. Van Munster (to Abbott).
15. U.S. Pat. 3,154,580 (Oct. 27, 1964), R. M. Robinson and W. C. Braaten (to Abbott).
16. U.S. Pat. 3,551,486 (Dec. 29, 1970), J. M. Solomon, B. Ishitsky, and B. R. Bluestein (to Witco).
17. U.S. Pat. 3,551,488 (Dec. 29, 1970), B. R. Bluestein and J. M. Solomon (to Witco).
18. S. Nishimura, T. Shu, T. Hara, and Y. Takagi, *Bull. Chem. Soc. Japan* **39**, 329–333 (1966).
19. S. Nishimura, Y. Kono, Y. Otsuki, and Y. Fukaya, *Bull. Chem. Soc. Japan* **44**, 240–243 (1971).
20. P. N. Rylander, L. Hasbrouck, and I. Karpenko, *Ann. N.Y. Acad. Sci.* **214**, 100–109 (1973).
21. A. E. Bardoll, and co-workers, *J. Am. Chem. Soc.* **75**, 1156–1159 (1953).
22. U.S. Pat. 3,347,917 (Oct. 17, 1967), W. J. Arthur (to E. I. du Pont de Nemours & Co., Inc.).
23. U.S. Pat. 3,697,499 (Oct. 10, 1972), L. D. Brake (to E. I. du Pont de Nemours & Co., Inc.).
24. U.S. Pat. 3,636,108 (Jan. 18, 1972), L. D. Brake (to E. I. du Pont de Nemours & Co., Inc.).
25. U.S. Pat. 3,697,449 (Oct. 10, 1972), L. D. Brake (to E. I. du Pont de Nemours & Co., Inc.).
26. U.S. Pat. 3,591,635 (July 6, 1971), W. J. Farrissey and F. F. Frulla (to Upjohn).
27. U.S. Pat. 3,856,862 (Dec. 24, 1974), T. H. Chung, M. L. Dillon, and G. L. Lines (to Upjohn).
28. Jpn. Kokai 75 37,758, (Apr. 8, 1975), K. Watanabe, Y. Hirai, and K. Miyata (to Mitsui Toatsu).
29. U.S. Pat. 3,914,307 (Oct. 21, 1975), S. N. Massie (to Universal Oil Products).
30. U.S. Pat. 4,394,522 (July 19, 1983), G. F. Allen (to Mobay).
31. U.S. Pat. 4,394,523 (July 19, 1983), G. F. Allen (to Mobay).
32. U.S. Pat. 4,448,995 (May 15, 1984), G. F. Allen (to Mobay).
33. Eur. Pat. Appl. 0 066 212 (Dec. 8, 1982), G. F. Allen (to Mobay).
34. U.S. Pat. 4,754,070 (June 28, 1988), J. P. Casey and M. J. Fasolka (to Air Products).
35. U.S. Pat. 3,634,512 (Jan. 11, 1972), L. Wolf, H. Corr, and K. Pilch (to BASF).
36. U.S. Pat. 3,743,677 (July 3, 1973), O. Grosskinsky and K. Merkel (to BASF).
37. U.S. Pat. 3,959,374 (May 25, 1976), M. E. Brennan and E. L. Yeakey (to Texaco).
38. E. V. Genkina, and co-workers. *Zh. Vses. Khim. Obshchest.* **14**, 475–476 (1969).
39. U.S. Pat. 3,551,485 (Dec. 29, 1970), P. Raff, H. G. Peine, L. Schuster, and K. Adam (to BASF).
40. U.S. Pat. 3,283,002 (Nov. 1, 1966), L. D. Brake (to E. I. du Pont de Nemours & Co., Inc.).
41. U.S. Pat. 4,479,009 (Oct. 23, 1984), T. K. Shioyama (to Phillips).
42. U.S. Pat. 4,399,307 (Aug. 13, 1983), T. K. Shioyama (to Phillips).
43. U.S. Pat. 4,014,933 (Mar. 29, 1977), G. Boettger and co-workers (to BASF).
44. U.S. Pat. 4,161,492 (July 17, 1979), O. Weissel (to Bayer).
45. H. A. Colvin and J. Muse, *CHEMTECH* **16**, 500–504 (1986).
46. U.S. Pat. 4,186,145 (Jan. 29, 1980), O. Weissel (to Bayer).
47. L. I. Krimen and D. J. Cota, in W. G. Dauben, ed., *Organic Reactions*, Vol. 17, John Wiley & Sons, Inc., New York, 1948, Chapt. 3, 213–235.
48. U.S. Pat. 2,632,022 (Mar. 17, 1963), M. N. Bortnik (to Rohm and Haas).
49. R. C. Fort and P. v. R. Schleyer, *Chem. Rev.* **64**, 277–300 (1964).

50. U.S. Pat. 3,994,975 (Nov. 30, 1976), B. A. Oude Alink and N. E. S. Thompson (to Petrolite Corporation).
51. U.S. Pat. 3,352,913 (Nov. 14, 1967), K. Schmitt, J. Disteldorf, and W. Hubel (to Schloven-Chemie).
52. U.S. Pat. 3,270,044 (Aug. 30, 1966), K. Schmitt, J. Disteldorf, W. Hubel, and K. Rindtorff (to Hibernia-Chemie Gesellschaft).
53. U.S. Pat. 4,299,775 (Nov. 10, 1981), B. Dubreux (to PCUK).
54. U.S. Pat. 4,429,157 (Jan. 31, 1984), J. Disteldorf, W. Hubel, and L. Broschinski.
55. L. Born, D. Wendisch, H. Reiff, and D. Dieterich, *Angew. Makrol. Chem.* **171**, 213–231 (1989).
56. U.S. Pat. 4,070,399, (Jan. 24, 1978), W. A. Butte (to Suntech).
57. U.S. Pat. 3,334,149 (Aug. 1, 1967), G. A. Akin, H. J. Lewis, and T. F. Reid (to Eastman Kodak).
58. Fr. Pat. 1575505, (May 21, 1962), V. L. R. Brown, J. G. Smith and T. E. Stanin (to Eastman Kodak).
59. D. V. Sokol'skii, A. E. Temirbulatova, and A. Ualikhanova, *Zh. Prik. Khim.* **56**, 1610–1614 (1983).
60. "Cyclohexylamine, Chemical Profile", *Chemical Market Reporter*, (May 28, 2001).
61. J. G. Theivagt, P. F. Helgren, and D. R. Luebke, "Cyclohexylamine," *Encyclopedia of Industrial Chemical Analysis*, Vol. 11, John Wiley & Sons, Inc., New York, 1971, 209–219.
62. F. R. Prince and E. M. Pearce, *Macromolecules* **4**, 347–350 (1971).
63. M. L. Moore, in R. Adams, ed., *Organic Reactions*, Vol. 5, John Wiley & Sons, Inc., New York, 1949, Chapt. 7, 301–330.
64. M. W. Scroggins, L. Skurcenski, and D. S. Weinberg, *J. Chrom. Sci.* **10**, 678–681 (1972).
65. M. W. Scroggins, *J. Chrom. Sci.* **13**, 146–148 (1975).
66. T. J. Haley in N. L. Sax, ed., *Dangerous Properties of Industrial Materials*, 6th ed., sect. 1, Van Nostrand-Reinhold, New York, 1984.
67. Reference 66, p. 887 (misprinted as 1410 μg/kg).
68. K. Verschueren, ed., *Handbook of Environmental Data on Organic Chemicals*, 2nd ed., Van Nostrand-Reinhold, New York, 1983.
69. R. J. Lewis, Sr., *Sax's Dangerous Properties of Industrial Materials*, 10th ed., Vol. 2, John Wiley & Sons, Inc., New York, 2000.
70. H. L. Kahler and J. K. Brown, *Combustion*, 55–58 (1954).
71. B. Tuck and E. M. Osborn, *Chem. Ind.*, 326–331 (1960).
72. U.S. Pat. 4,473,666 (Sept. 25, 1984), F. A. Casati, D. S. Raden, and F. W. Arbir (to Abbott).
73. U.S. Pat. 4,286,086 (Aug. 25, 1981), V. Mark (to General Electric).
74. U.S. Pat. 4,794,158 (Dec. 27, 1988), M. Hasuo, H. Urabe, M. Kawai, and T. Ohsako (to Mitsubishi Kasei).
75. U.S. Pat. 3,703,595 (Nov. 21, 1972), G. Falkenstein and co-workers (to BASF).
76. U.S. Pat. 4,525,571 (June 25, 1985), C. Burba and H. Franz (to Schering AG).
77. U.S. Pat. 3,629,181 (Dec. 21, 1971), A. Heer, W. Schneider, and B. Dreher (to CIBA Limited).
78. Can. Pat. 892,636 (Feb. 8, 1972), J. M. Cross and R. V. Norton (to Mobay).
79. U.S. Pat. 3,450,759 (June 17, 1969), J. M. Cross, C. D. Campbell, and S. H. Metzger (to Mobay).
80. U.S. Pat. 2,817,644 (Dec. 24, 1957), E. C. Shokal and H. A. Newey (to Shell).
81. U.S. Pat. 4,849,544 (July 18, 1989), S. A. Culley, K. A. Keblys, and C. J. Nalepa (to Ethyl).

82. U.S. Pat. 3,351,650 (Nov. 7, 1967), J. M. Cross, S. H. Metzger, and C. D. Campbell (to Mobay).
83. U.S. Pat. 3,419,612 (Dec. 31, 1968), J. M. Cross, S. H. Metzger, and C. D. Campbell (to Mobay).
84. U.S. Pat. 3,651,118 (Mar. 21, 1972), M. Cenker and P. T. Kan (to Mobay).
85. D. L. Trumbo, *J. Poly. Sci., part A, Poly. Chem.* **26**, 1859–2862 (1988).
86. A. Sabra, J. P. Pascault, and G. Seytre, *J. Appl. Polym. Sci.* **32**, 5147–5160 (1986).
87. U.S. Pat. Appl. 2003000 4212 (Jan. 2, 2003), R. J. De Orazio and co-workers (to Warner-Lambert Company).
88. H. G. Khorana, *Chem. Ind.* 1087–1088 (1955).
89. C. A. Byrne, D. P. Mack, and J. M. Sloan, *Rubber Chem. Tech.* **58**, 985–996 (1985).
90. U.S. Pat. 3,401,190 (Sept. 10, 1968), K. Schmitt, F. Gude, K. Rindtorff, and J. Disteldorf (to Schloven-Chemie).
91. U.S. Pat. 4,256,869 (Mar. 17, 1981), H. Schulze, and co-workers (to Akzo).
92. U.S. Pat. 4,892,920 (Jan. 16, 1990), J. R. Quay and J. P. Casey (to Air Products).
93. U.S. Pat. 3,309,192 (Mar. 14, 1967), (to E. I. du Pont de Nemours & Co., Inc.).
94. U.S. Pat. 3,902,887 (Sept. 2, 1975), K. Lin (to E. I. du Pont de Nemours & Co., Inc.).

JEREMIAH P. CASEY
Air Products and Chemicals