Safety in Research Articles

A Tale of Two Times

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RISK & SAFETY SOLUTIONS

On safety warnings

- "Review and analysis of safety policies of chemical journals" Grabowski, LE, Goode, SR, *Journal of Chemical Health & Safety*, May/June **2016**, 30-35
- "…injuries could be avoided by adding a few cautionary words to the procedure."

- "Safety as a Core Value" Langerman, N, *Journal of Chemical Health & Safety*, May/June **2016**, 48-49
- "Safety and Ethics" Langerman, N, *Journal of Chemical Health & Safety*, May/June **2015**, 44-45

RISK & SAFETY SOLUTIONS

The Quest…

- Is benzene always planar?
  - 1987/88 tale *(predates Lab standard & Cal/OSHA enforcement at UC)*
  - 2018 tale…

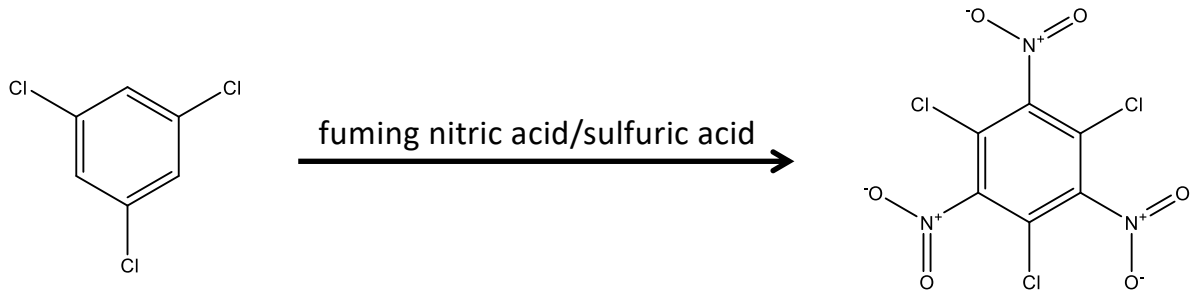
RISK & SAFETY SOLUTIONS

Creating localized pi-bonds in benzene

- Electrophilic aromatic substitution
  - trichlorobenzene, fuming nitric acid, sulfuric acid
- Nucleophilic aromatic substitution
  - ammonia
- Alkylation
  - Dimethylamine, ethanol, chloroform, hexane
    - Recrystallization, hexanes, ethanol
  - Diethylamine, ethanol, chloroform, hexane

RISK & SAFETY SOLUTIONS

On the road to non-planar benzene



Reference:

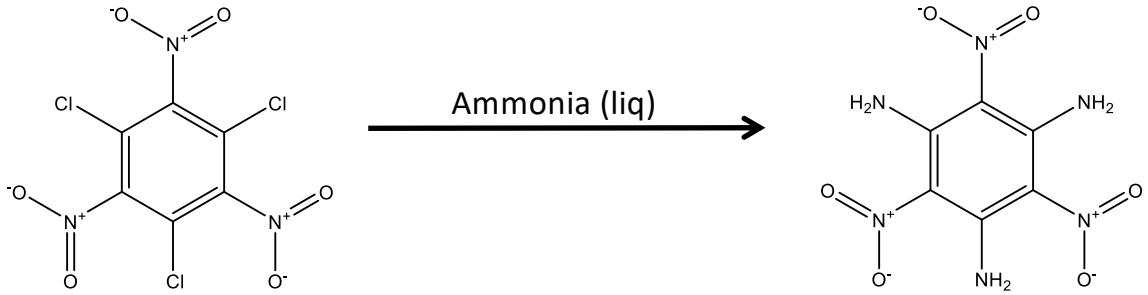
Hill, M.E.; Taylor, F. J. Org. Chem. 1960, 25, 1037

Hazards?

RISK & SAFETY SOLUTIONS

Non-planar benzene next step:

Nucleophilic aromatic substitution



Reference:

Chance, JM, et al. *J. Am. Chem. Soc.* ***1989****, 111,* 5944-5946

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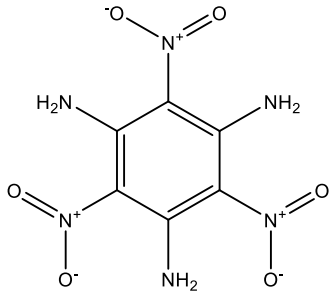
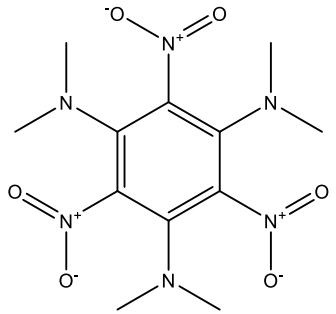
Non-planar benzene next step:

Alkylation



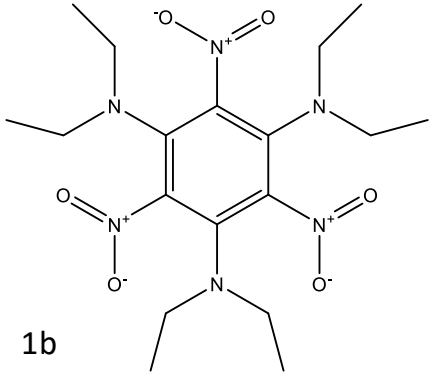
1c

dimethylamine/ethanol



1a

diethylamine/ethanol



1b

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Published Hazards?

- Chance, JM, et al. *J. Am. Chem. Soc.* ***1989****, 111,* 5944-5946

"Tris(dialkylamino)trinitrobenzenes are, in general, explosive! Extreme care should be taken when handling these materials. Do not prepare or store large quantities of these compounds. It is unadvisable to store these compounds in ground glass stoppered vials. Even though we have had no accidental detonations of 1a or 1b, we have been able to detonate a few milligrams of 1a by striking it with a ball peen hammer on a hard surface."

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What about today?

- GHS Hazard codes and statements part of information about each chemical
  - Included in SDS
  - Inform precautions
  - Communicate in publications

- Chemicals (developed by Risk & Safety Solutions, University of California)

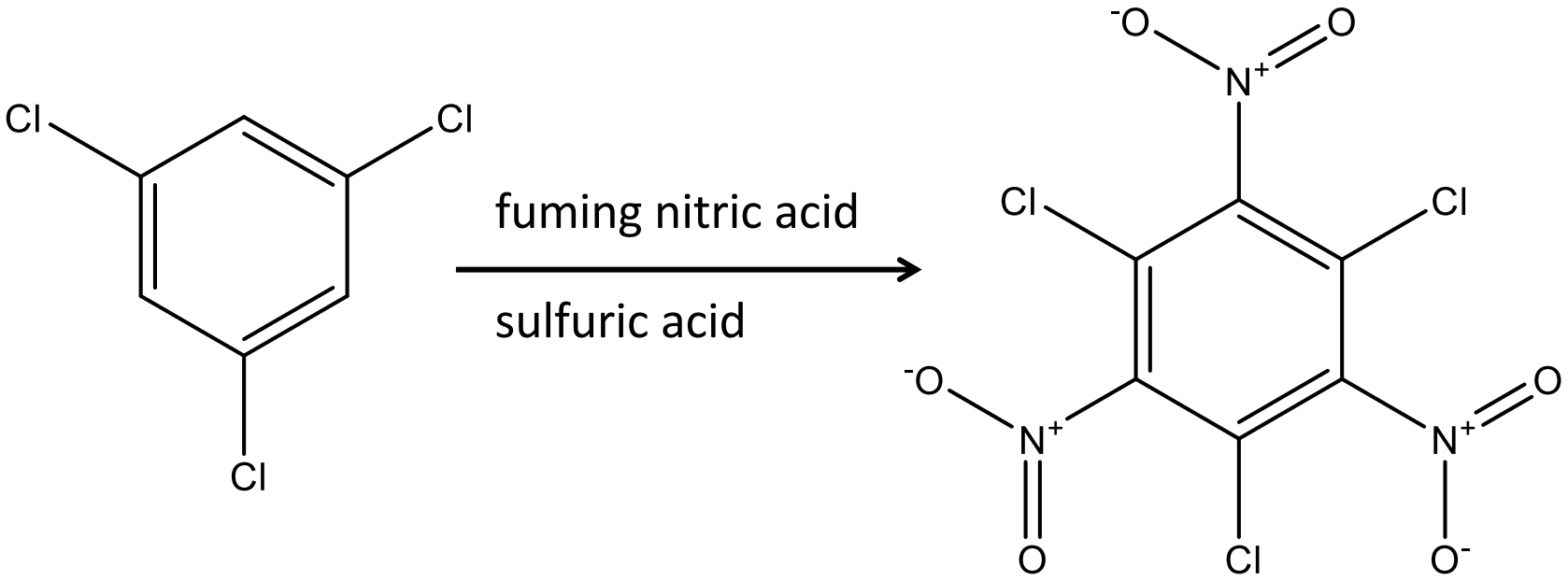
Booth 525

RiskandSafetySolutions.com

- For novel compounds, no hazard codes exist. The explosive nature of the trinitro-triaminobenzene compounds cannot be extracted from reactant Hcodes

RISK & SAFETY SOLUTIONS

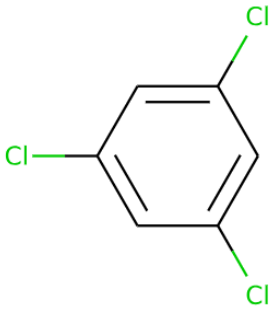
Electrophilic aromatic substitution



Electrophilic aromatic substitution hazards: trichlorobenzene

1,3,5-Trichlorobenzene

Toxic : Inhalation



CAS #

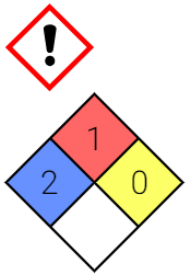
108-70-3

Molecular Formula

$C_6H_3Cl_3$

Physical State

solid



Chemical Information

Molecular Weight	Flash Point
181.45 g/mol	107 deg. C
Boiling Point	**Melting Point**
208 to 208 deg. C	56 to 60 deg. C

Hazard Statements

H302 - Harmful if swallowed (Category 4)
H312 - Harmful in contact with skin (Category 4)
H315 - Causes skin irritation (Category 2)
H319 - Causes serious eye irritation (Category 2A)
H332 - Harmful if inhaled (Category 4)
H335 - May cause respiratory irritation (Category 3)

H402 - Harmful to aquatic life (Category 3)
H412 - Harmful to aquatic life with long lasting effects (Category 3)

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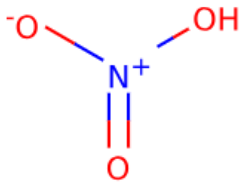
Electrophilic aromatic substitution hazards: fuming nitric acid

Nitric acid reagent grade, fuming, >90%

CFATS : Release
CFATS : Theft
Corrosive
Extremely Hazardous Substance
Oxidizers : Class 3

CAS #
7732-18-5, 7697-37-2, 10544-72-6

Molecular Formula
HNO_3



Physical State
liquid

Chemical Information

Molecular Weight
63.01

Flash Point
N/A

Boiling Point
120.5 to 120.5

Melting Point
N/A

Hazard Statements

H272 - May intensify fire; oxidizer. (Category 2)

H290 - May be corrosive to metals (Category 1)
H318 - Causes serious eye damage (Category 1)
H314 - Causes severe skin burns and eye damage. (Sub-category 1A)

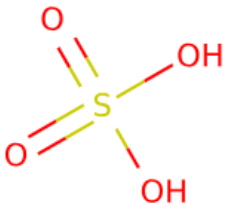
H333 - May be harmful if inhaled (Category 5)

RISK & SAFETY SOLUTIONS

Electrophilic aromatic substitution hazards: sulfuric acid

Sulfuric acid

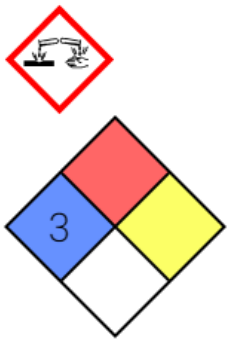
Corrosive
Extremely Hazardous Substance



CAS #
7664-93-9

Molecular Formula
N/A

Physical State
liquid



Chemical Information

Molecular Weight	Flash Point
98.08 g/mol	N/A
Boiling Point	**Melting Point**
290 to 290	N/A

Hazard Statements

H314 - Causes severe skin burns and eye damage. (Sub-category 1A)
H290 - May be corrosive to metals (Category 1)
H318 - Causes serious eye damage (Category 1)

H303 - May be harmful if swallowed (Category 5)

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Signal words

- **Danger** - Indicates death or serious injury will result if proper precautions are not taken.

- **Warning** - Indicates death, serious injury or property damage can result if proper precautions are not taken.

- **Caution** - Indicates some injury or property damage may result if proper precautions are not taken

RISK & SAFETY SOLUTIONS

Electrophilic aromatic substitution reactant hazards

By Category:

- H318 - Causes serious eye damage (Category 1)
- H314 - Causes severe skin burns and eye damage. (Sub-category 1A)
- H290 - May be corrosive to metals (Category 1)
- H315 - Causes skin irritation (Category 2)
- H272 - May intensify fire; oxidizer. (Category 2)
- H319 - Causes serious eye irritation (Category 2A)
- H335 - May cause respiratory irritation (Category 3)
- H402 - Harmful to aquatic life (Category 3)
- H412 - Harmful to aquatic life with long lasting effects (Category 3)
- H332 - Harmful if inhaled (Category 4)
- H312 - Harmful in contact with skin (Category 4)
- H302 - Harmful if swallowed (Category 4)
- H303 - May be harmful if swallowed (Category 5)
- H333 - May be harmful if inhaled (Category 5)

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Thesis

- Category 1 → “Danger”
- Category 2 → “Warning”
- Category 3 → “Caution”

RISK & SAFETY SOLUTIONS

Electrophilic aromatic substitution

- **Danger**: Reactants cause serious eye and skin damage and are corrosive to metals

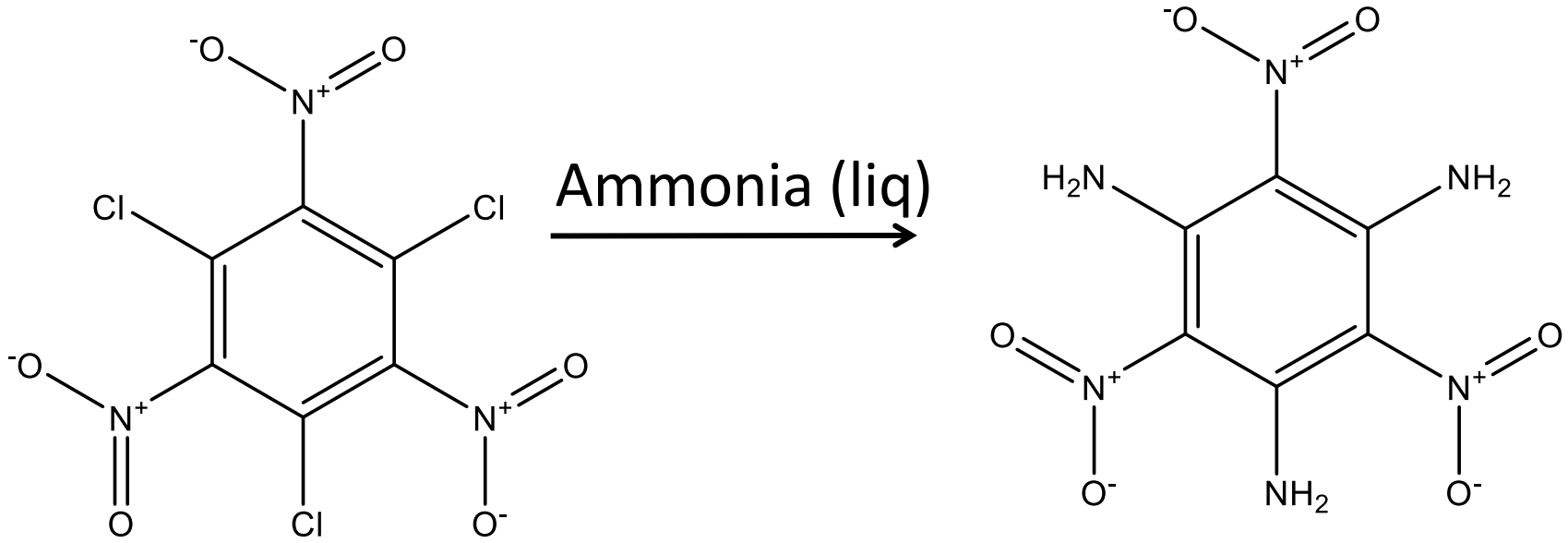
- **Warning**: Reactants include oxidizers which intensify fire

- **Caution**: Reactants are harmful to aquatic life

RISK & SAFETY SOLUTIONS

Non-planar benzene next step:

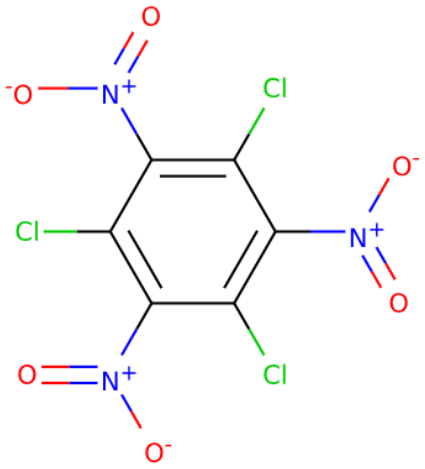
Nucleophilic aromatic substitution



Nucleophilic aromatic substitution hazards: trichloro-trinitrobenzene

1,3,5-TRICHLORO-2,4,6-TRINITRO-BENZENE

Toxic : Oral



CAS #

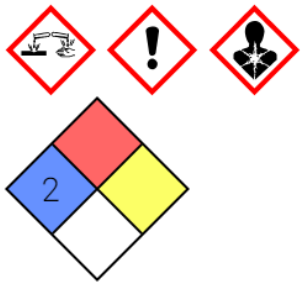
2631-68-7

Molecular Formula

$C_6Cl_3N_3O_6$

Physical State

solid



Chemical Information

Molecular Weight	Flash Point
316.442	N/A
Boiling Point	**Melting Point**
N/A	N/A

Hazard Statements

H318 - Causes serious eye damage (Category 1)

H317 - May cause an allergic skin reaction. (Category 1)

H302 - Harmful if swallowed (Category 4)

H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled. (Category 1)

H316 - Causes mild skin irritation (Category 3)

RISK & SAFETY SOLUTIONS

Nucleophilic aromatic substitution hazards: ammonia

Ammonia

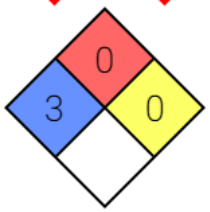
Corrosive
Extremely Hazardous Substance

NH_3

CAS #
7664-41-7

Molecular Formula
H_3N

Physical State
gas (gaseous)



Chemical Information

Molecular Weight
17.03 g/mol

Flash Point
132 deg. C

Boiling Point
-33 to -33 deg. C

Melting Point
-78 to -78 deg. C

Hazard Statements


H221 - Flammable gas (Category 2)


H280 - Contains gas under pressure; may explode if heated (Compressed Gas)


H314 - Causes severe skin burns and eye damage (Category 1B)
H318 - Causes serious eye damage (Category 1)


H331 - Toxic if inhaled (Category 3)


H400 - Very toxic to aquatic life (Category 1)
H410 - Very toxic to aquatic life with long lasting effects (Category 1)

RISK & SAFETY SOLUTIONS

Nucleophilic aromatic substitution reactant hazards

H318 - Causes serious eye damage (Category 1)

H314 - Causes severe skin burns and eye damage (Category 1B)

H317 - May cause an allergic skin reaction. (Category 1)

H400 - Very toxic to aquatic life (Category 1)

H410 - Very toxic to aquatic life with long lasting effects (Category 1)

H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled. (Category 1)

H221 - Flammable gas (Category 2)

H331 - Toxic if inhaled (Category 3)

H316 - Causes mild skin irritation (Category 3)

H302 - Harmful if swallowed (Category 4)

H280 - Contains gas under pressure; may explode if heated (Compressed Gas)

RISK & SAFETY SOLUTIONS

Nucleophilic aromatic substitution

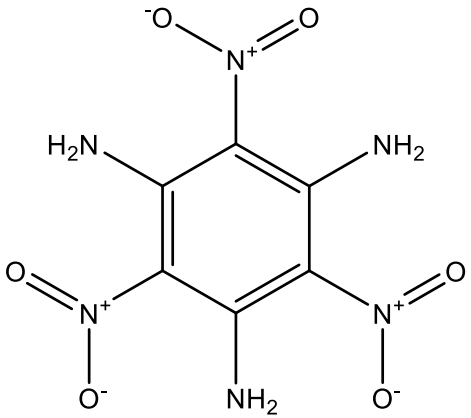
- **Danger**: Reactants cause serious eye damage & skin burns. , may cause an allergic skin reaction, Very toxic to aquatic life with long lasting effects. May cause allergy or asthma symptoms or breathing difficulties if inhaled.

- **Warning**: Reactants include flammable gas

- **Caution**: Reactants are toxic if inhaled and cause mild skin irritation

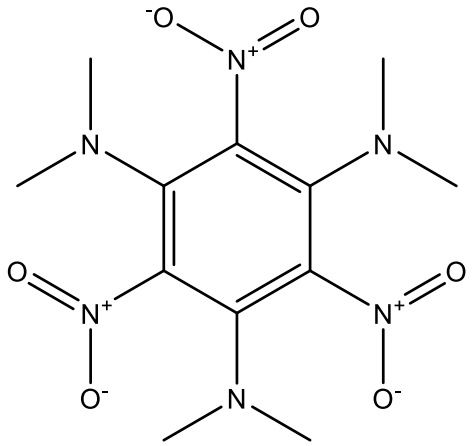
RISK & SAFETY SOLUTIONS

Alkylation



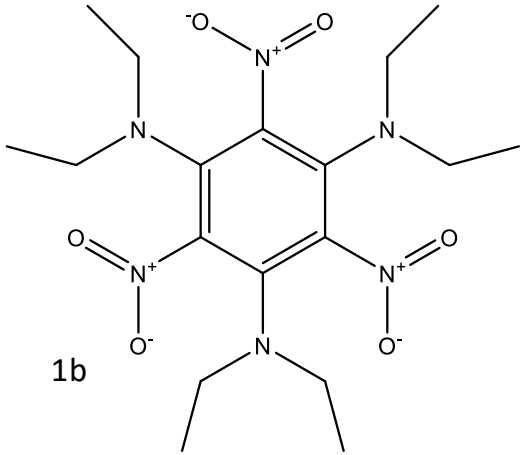
1c

dimethylamine/ethanol



1a

diethylamine/ethanol



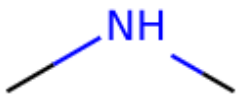
1b

RISK & SAFETY SOLUTIONS

Alkylation hazards: dimethylamine

Dimethylamine

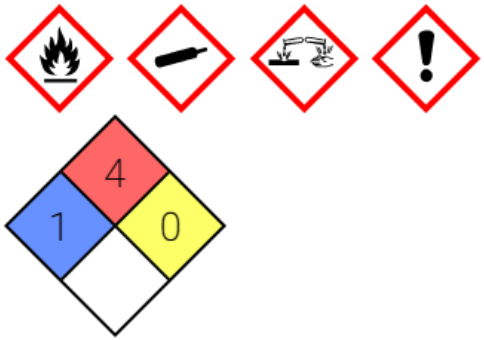
CFATS : Release Flammable Gas
Toxic : Inhalation



CAS #
124-40-3

Molecular Formula
C_2H_7N

Physical State
gas (gaseous)



Chemical Information

Molecular Weight	Flash Point
45.08 g/mol	-6.69 deg. C
Boiling Point	Melting Point
7 to 7 deg. C	-93 to -93 deg. C

Hazard Statements


H220 - Extremely flammable gas (Category 1)


H280 - Contains gas under pressure; may explode if heated (Liquefied Gas)


H318 - Causes serious eye damage (Category 1)


H315 - Causes skin irritation (Category 2)
H332 - Harmful if inhaled (Category 4)
H335 - May cause respiratory irritation (Category 3)

H402 - Harmful to aquatic life (Category 3)
H412 - Harmful to aquatic life with long lasting effects (Category 3)

RISK & SAFETY SOLUTIONS

Alkylation hazards: diethylamine

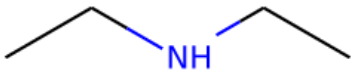
Diethylamine

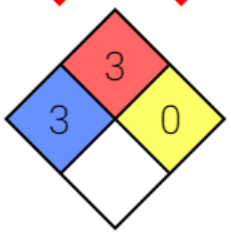
Corrosive
Flammable Liquid : IB
Toxic : Inhalation
Toxic : Dermal

CAS #
109-89-7

Molecular Formula
$C_4H_{11}N$

Physical State
liquid





Chemical Information

Molecular Weight
73.14 g/mol

Flash Point
-23 deg. C

Boiling Point
55 to 55 deg. C

Melting Point
-50 to -50 deg. C

Hazard Statements

H225 - Highly Flammable liquid and vapour (Category 2)

H314 - Causes severe skin burns and eye damage (Category 1A)
H318 - Causes serious eye damage (Category 1)

H311 - Toxic in contact with skin (Category 3)

H302 - Harmful if swallowed (Category 4)
H332 - Harmful if inhaled (Category 4)
H335 - May cause respiratory irritation (Category 3)

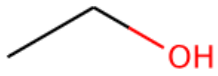
H401 - Toxic to aquatic life (Category 2)

RISK & SAFETY SOLUTIONS

Alkylation hazards: ethanol

Ethanol, ≥190 proof

Flammable Liquid : IB



CAS #
64-17-5

Molecular Formula
C_2H_6O

Physical State
liquid

Chemical Information

Molecular Weight
46.07 g/mol

Flash Point
14 deg. C

Boiling Point
78 to 78 deg. C

Melting Point
-114 to -114 deg. C

Hazard Statements

H225 - Highly Flammable liquid and vapour (Category 2)

H319 - Causes serious eye irritation (Category 2A)
H336 - May cause drowsiness or dizziness (Category 3)

H401 - Toxic to aquatic life (Category 2)

RISK & SAFETY SOLUTIONS

Alkylation hazards

- H220 - Extremely flammable gas (Category 1)
- H314 - Causes severe skin burns and eye damage (Category 1A)
- H318 - Causes serious eye damage (Category 1)
- H225 - Highly Flammable liquid and vapor (Category 2)
- H315 - Causes skin irritation (Category 2)
- H319 - Causes serious eye irritation (Category 2A)
- H401 - Toxic to aquatic life (Category 2)
- H311 - Toxic in contact with skin (Category 3)
- H335 - May cause respiratory irritation (Category 3)
- H336 - May cause drowsiness or dizziness (Category 3)
- H402 - Harmful to aquatic life (Category 3)
- H412 - Harmful to aquatic life with long lasting effects (Category 3)
- H302 - Harmful if swallowed (Category 4)
- H332 - Harmful if inhaled (Category 4)
- H280 - Contains gas under pressure; may explode if heated (Liquefied Gas)

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Alkylation Hazards

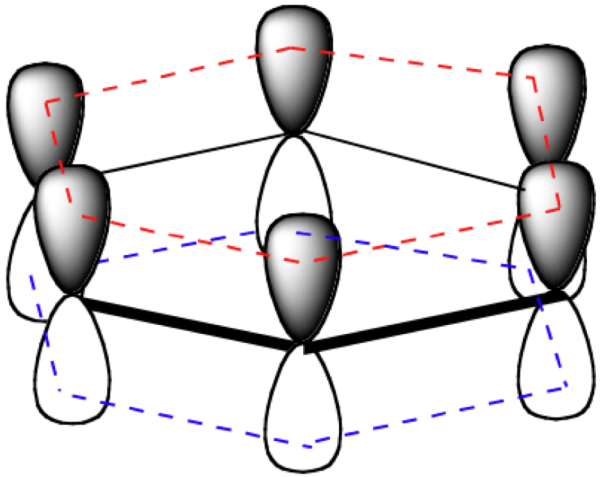
- **Danger**: Extremely flammable gas, causes severe skin burns and eye damage

- **Warning**: Highly Flammable liquid and vapor, causes skin and eye irritation, toxic in contact with skin and to aquatic life

- **Caution**: Toxic in contact with skin, may cause respiratory irritation and drowsiness or dizziness, harmful to aquatic life with long lasting effects

RISK & SAFETY SOLUTIONS

So, can you make benzene non-planar?

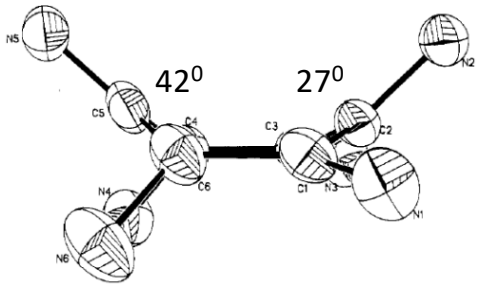


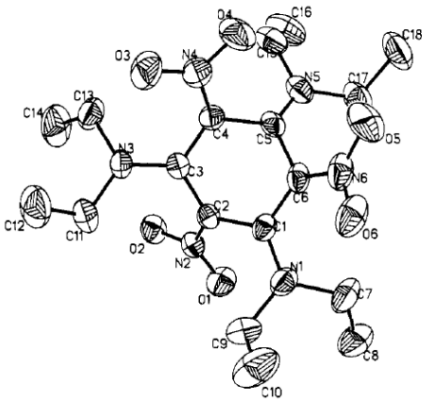
π electrons delocalized around the ring, above and below the plane

RISK & SAFETY SOLUTIONS

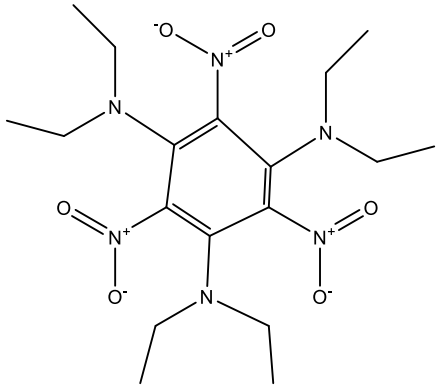
Yes

- Boat confirmation ground state





Bond	Expected	Found
C(ar)-N(ar)	1.37Å	1.34Å & 1.30Å
C(ar)-C(ar)	1.40Å	1.48Å & 1.44Å
C(ar)-NO_2	1.47Å	1.42Å & 1.40Å
N-O (nitro)	1.22Å	1.24V
C(sp^2)-C(sp^2)	1.33Å	---
C(sp^2)-N(sp^2)	128Å	---



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What are the hazards along the way?

- fires
- chemical burns
- toxic exposures &
- explosions

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Risk and Safety Solutions, University of California