

Direct Conversion of Benzyl Alcohol to Amines via Lewis Acid Activation

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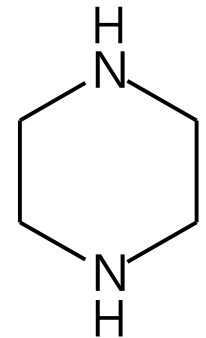
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Outline

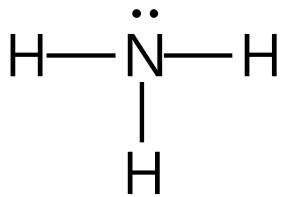
- Background
- Current Amine Syntheses
 - Alkylation
 - Gabriel Amine Synthesis
 - Azido Reduction
- Proposed Research
- Experimental Conditions/Precedence
- Summary

Background

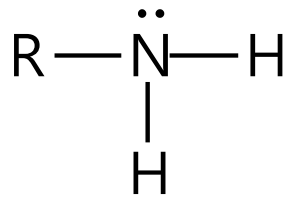
- Derivatives of Ammonia
- Can be primary (1°), secondary (2°), or tertiary (3°)
- Can be cyclic or acyclic
- Form quaternary ammonium salts



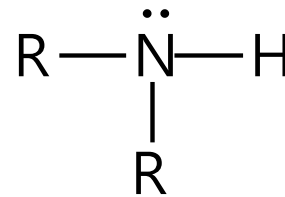
piperazine



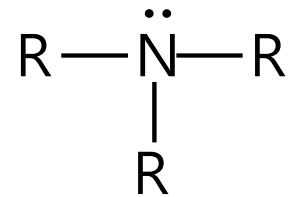
ammonia



primary amine



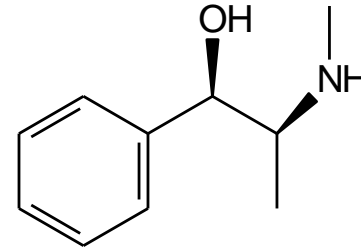
secondary amine



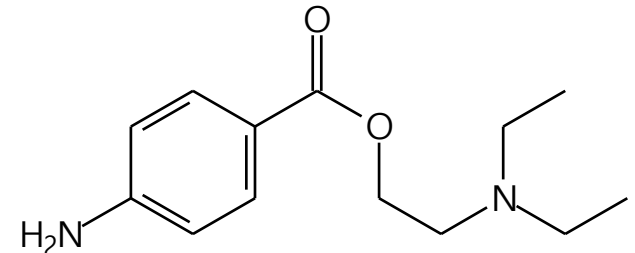
tertiary amine

Applications

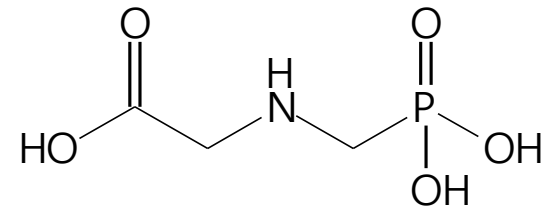
- Pharmaceuticals
 - Ephedrine
 - Novocaine
 - Fentanyl
- Agricultural Sciences
 - Herbicides
 - Pesticides



ephedrine



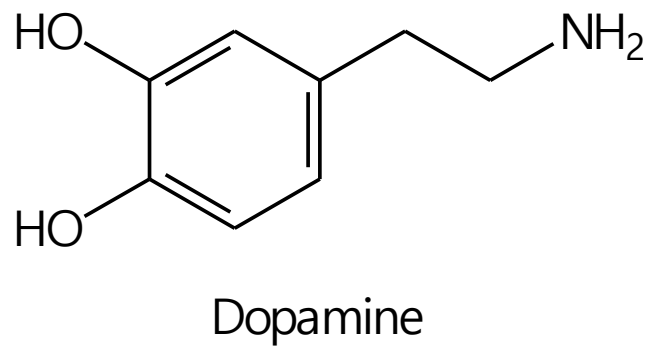
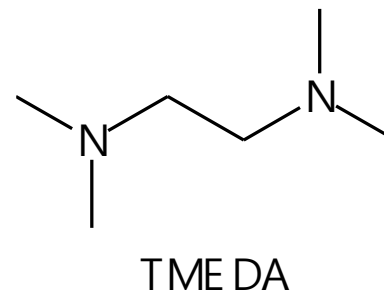
Novocaine



glyphosate "RoundupTM"

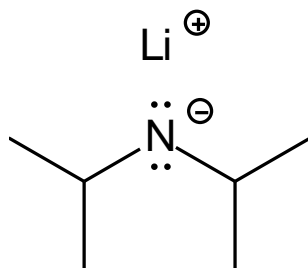
Applications Continued

- Industry
 - Photography developers
 - Water proofing agents
 - Fabric softeners
 - Chelating agents
 - Metal ligands
- Biological
 - Neurotransmitters
 - Amino acids
 - Proteins
 - Nucleotides

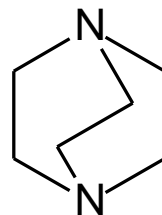


Amine Reagents in Organic Synthesis

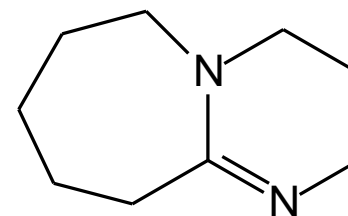
Amines are commonly used as bases and catalysts in organic reactions.



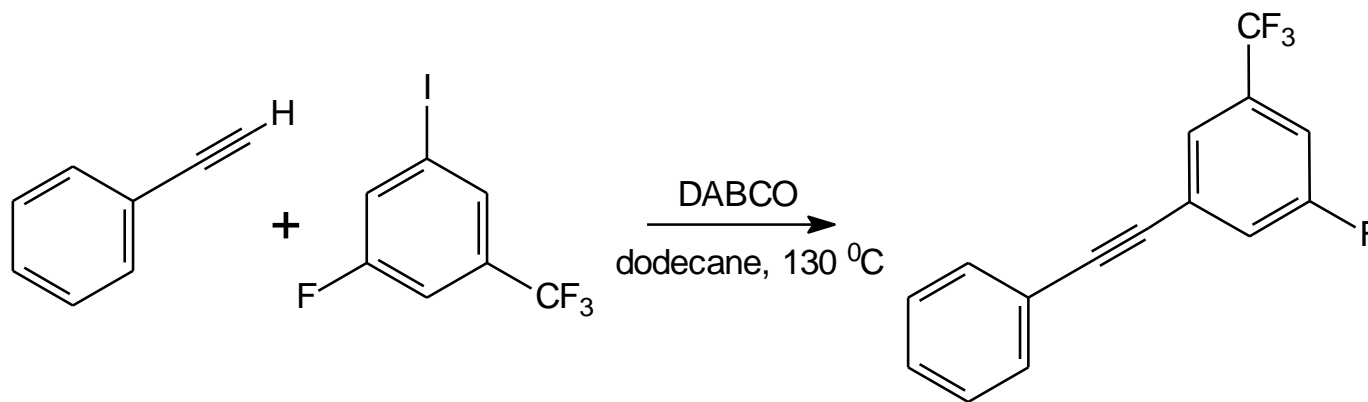
LDA



DABCO



DBU



Sonogashira coupling

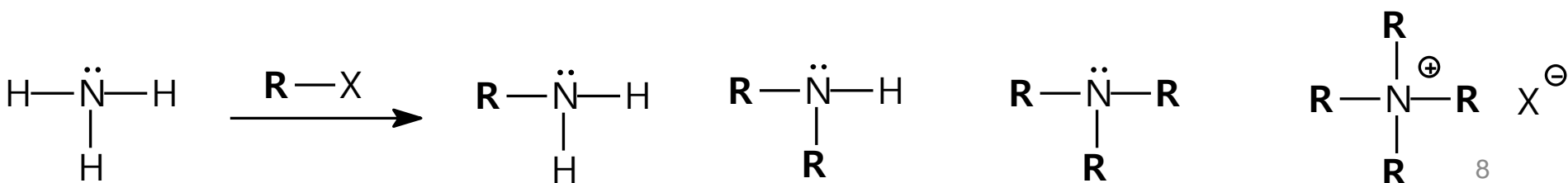
Current Amine Syntheses*

- Alkylation*
- Gabriel Amine Synthesis*
- Reductive Amination
- Alkyl Azide formation/reduction*
- Nitrile Reduction
- Amide Reduction
- Hofmann Rearrangement

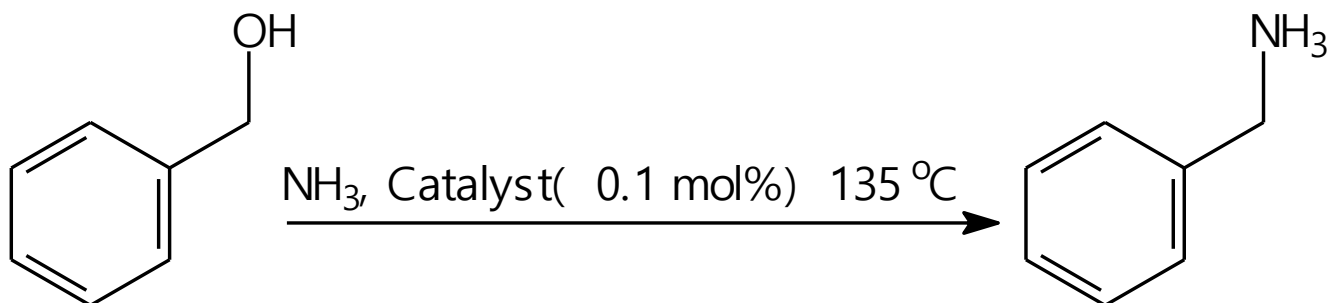
Alkylation

Treatment of an amine with an alkyl halide or alcohol electrophile resulting in N-C bond formation

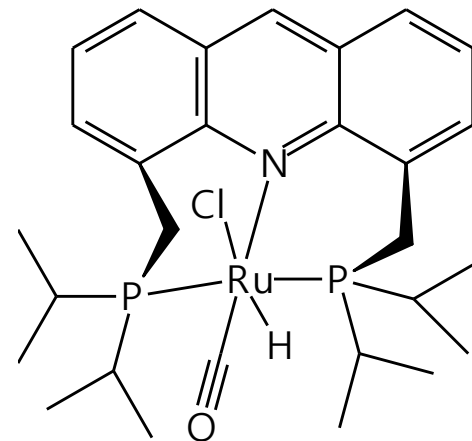
- Pros
 - Achievable on an industrial scale with select reagents
- Cons
 - Direct alkylation with alcohols often require expensive catalyst(s) and/or harsh conditions
 - Low selectivity (over-alkylation)



Harsh Conditions/Expensive Catalyst



Reaction requires specialized apparatus, high pressure, elevated temperature, and long reaction times. Limited to primary amines.

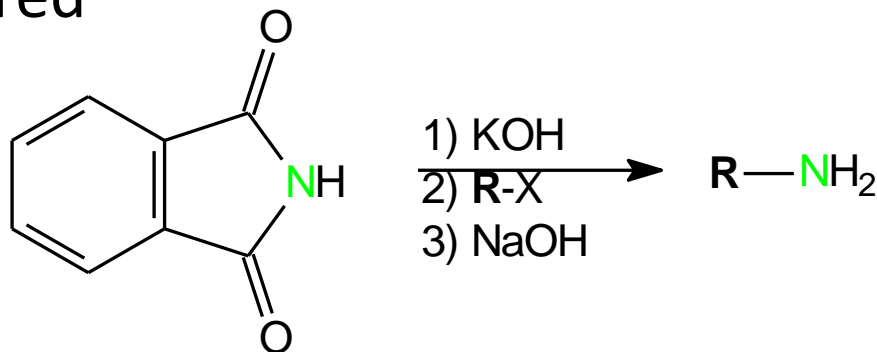


Ruthenium Catalyst Complex

Gabriel Amine Synthesis

Alcohol is converted to alkyl halide, allowed to react with a metal phthalimide, then hydrolyzed to provide the amine.

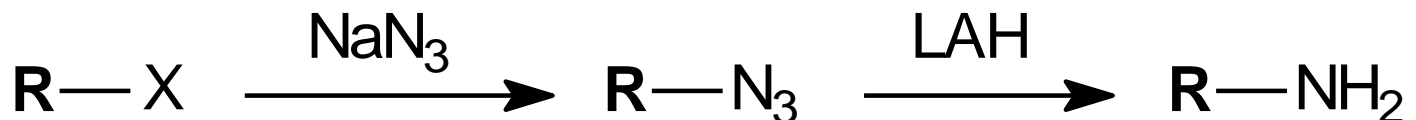
- Pros
 - Metal phthalimides are readily available
 - Selective (over-alkylation not observed)
- Cons
 - General procedure gives only 1° amines
 - Several steps required



Amines from Azides

Alkyl halide treated with sodium azide to form an azido compound. Subsequent reduction provides the corresponding amine.

- Pros
 - Sodium azide is readily available
 - Efficient and generally reliable
- Cons
 - Limited to 1° amines
 - Azides, esp. low MW azides are explosive and impact-sensitive
 - Multiple steps required



Experimental Conditions

- Proposal
 - Use benzyl alcohol as electrophilic reagent
 - Implement ZnI_2 as the Lewis acid for preliminary investigation
 - Explore ammonia as well as 1° , 2° , and 3° amines as nucleophilic reagents
 - Vary conditions (solvent, temperature, concentration, etc.) to maximize conversion.

Precedence

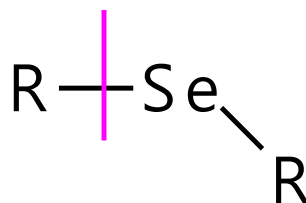
- Previously published research
 - Use of zinc halides and benzylic alcohols
- Previous nucleophiles used in parallel reactions

– Thiols

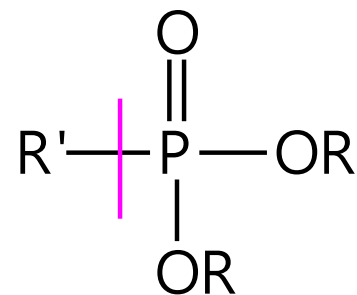
– Alcohols

– Selenols

– Phosphites



selenide



phosphonate

Periodic Table of the Elements

Skupina → ↓ Perioda	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra		104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Cn	113 Uut	114 Uuq	115 Uup	116 Uuh	117 Uus	118 Uuo
Lantanidi	57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu			
Aktinidi	89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr			

Characterization

- Thin Layer Chromatography (TLC)
- Gas Chromatography (GC)
- Infrared Spectroscopy (IR)
- Nuclear Magnetic Resonance (NMR)
- Mass Spectrometry (MS)



Summary

- Efficient and direct synthesis of amines
- Proposed Research
 - Use of ZnI_2 and benzyl alcohol
- No special apparatus required, mild conditions, inexpensive
- Various methods to check products and progress

Acknowledgements

- INBRE
- Western Wyoming Community College
- Professor Rocky Barney
- Audience

