A solvent is a **liquid** that serves as the medium for a reaction. It can serve two major purposes:

- (Non-participatory) to dissolve the reactants. Remember "like dissolves like"? Polar solvents are best for dissolving polar reactants (such as ions); nonpolar solvents are best for dissolving nonpolar reactants (such as hydrocarbons).
- (Participatory) as a source of acid (proton), base (removing protons), or as a nucleophile (donating a lone pair of electrons). The only class of solvents for which this is something you generally need to worry about are polar protic solvents.

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Solvents

So what does "polar" and "non-polar" mean?

- Polar solvents have large dipole moments ("partial charges"); they contain bonds between atoms with very different electronegativities, such as oxygen and hydrogen (-O-H).
- Non polar solvents contain bonds between atoms with similar electronegativities, such as carbon and hydrogen (C-H, think hydrocarbons, such as gasoline). Bonds between atoms with similar electronegativities will lack partial charges; it's this absence of charge which makes these molecules "non-polar".

There are two common ways of measuring this polarity: One is through measuring a constant called "dielectric constant" or <u>permitivity</u>. The greater the dielectric constant, the greater the polarity (water = high, gasoline = low). A second comes from directly measuring the "dipole moment".

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Solvents

Some solvents are called "protic" and some are called "aprotic". What makes a solvent a "protic" solvent, anyway?

- Protic solvents have O-H or N-H bonds. Why is this important? Because protic solvents can participate in <u>hydrogen bonding</u>, which is a powerful intermolecular force. Additionally, these O-H or N-H bonds can serve as a source of protons (H+).
- There ain't such a thing as a non-polar protic solvent.
- Aprotic solvents may have hydrogens on them somewhere, but they lack
 O-H or N-H bonds, and therefore cannot hydrogen bond with themselves.

Solvents

Nonpolar solvents:

- These solvents have low dielectric constants (<5) and are not good solvents for charged species such as anions.
- However diethyl ether (Et₂O) is a common solvent for Grignard reactions; its lone pairs are Lewis basic and can help to solvate the Mg cation.

Nonpolar solvents		Dielectric Dipole constant Moment		e It
\sim	Pentane	1.8	0.00	D
\sim	Hexane	1.9	0.00	D
\bigcirc	Cyclohexane	2.0	0.00	D
\bigcirc	Benzene	2.4	0.00	D
CH3	Toluene	2.3	0.36	D
CHCI ₃	Chloroform	4.8	1.04	D
CH ₃ CH ₂ - <mark>Ö</mark> -CH ₂ CH ₃	Diethyl ether (Et ₂ O)	4.3	1.15	D

Nonpolar solvents:

Two specific applications:

Pentane: Formation of organolithium reagents

Br Li (2 equiv) pentane + LiBr

Diethyl Ether: Formation of Grignard reagents



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Solvents

"Borderline" Polar aprotic solvents:

Two examples:

CH2CI2: Halogenation of alkenes



putting CH_2CI_2 or $CHCI_3$ or CCI_4 here differentiates this reaction from those where the solvent can add (see below)

 $\ensuremath{\text{THF}}\xspace$: as solvent in Grignard reactions. Also as solvent for enolate formation with LDA.



Solvents

"Borderline" Polar aprotic solvents:

- These solvents have moderately higher dielectric constants than the nonpolar solvents (between 5 and 20).
- Since they have intermediate polarity they are good "general purpose" solvents for a wide range of reactions.
- They are "aprotic" because they lack O-H or N-H bonds.

\rightarrow They don't participate in			Dielectric constant	Dipole Moment
reactions: they serve only as the medium.	CH ₂ Cl ₂	Dichloromethane	9.1	1.60 D
	\sim	Tetrahydrofuran (THF)	7.5	1.75 D
		Ethyl acetate	6.0	1.78 D

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Solvents

Polar aprotic solvents:

- These solvents all have large dielectric constants (>20) and large dipole moments, but they do not participate in hydrogen bonding (no O-H or N-H bonds).
- Their high polarity allows them to dissolve charged species such as various anions used as nucleophiles (e.g. CN(-), HO(-), etc.).
- The lack of hydrogen bonding in the solvent means that these nucleophiles are relatively "free" in solution, making them more reactive. → These solvents do not participate in the reaction.

Polar aprotic solvents:

Polar aprotic solvents		Dielectric constant	Dipole Moment
	Acetone	21	2.88 D
Ч Ц	N,N-Dimethylformamide (DMF)	38	3.82 D
H₃C−C≣ <mark>N</mark> ∶	Acetonitrile (MeCN)	37	3.92 D
	Dimethyl sulfoxide (DMSO)	47	3.96 D

Common applications of these solvents:

Acetone, DMF, Acetonitrile, DMSO: As solvents in S_N2 reactions

DMSO



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Solvents

Polar protic solvents:

- Polar protic solvents tend to have high dielectric constants and high dipole moments.
- Furthermore, since they possess O-H or N-H bonds, they can also participate in hydrogen bonding.
- These solvents can also serve as acids (sources of protons) and weak nucleophiles (forming bonds with strong electrophiles).
- They are most commonly used as the solvent for their conjugate bases. (e.g. H₂O is used as the solvent for HO(-); EtOH is used as the solvent for EtO(-).)

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Solvents

Polar Protic Solven	ts	Dielectric constant	Dipole Moment
:NH3	Ammonia	~25	1.4 D
СН ₃ н– <mark>Ӧ</mark> -Ċ-СН ₃ ĊН ₃	t-Butanol	12	1.7 D
H− <mark>Ö</mark> −CH₂CH₂CH₃	n-Propanol	20	1.68 D
н−ё–сн₂сн₃	Ethanol	25	1.69 D
н- <mark></mark> -сн ₃	Methanol	33	1.70 D
	Acetic acid	6.2	1.74 D
н- <mark>о</mark> -н	Water	80	1.85 D

Solvents

Polar protic solvents are hydrogen-bond donors





Common uses:

All: As the solvent for their conjugate bases

e.g. NH_2^{\ominus}/NH_3 EtO $^{\ominus}/EtOH$ HO $^{\ominus}/H_2O$

t-BuO / t-BuOH

All: As weak nucleophiles, in the presence of strong electrophiles (such as acid)



H₂O



- These types of solvents are by far the most likely to participate in reactions.
- There are many examples where a polar protic solvent such as water, methanol, or ethanol can serve as the nucleophile in a reaction, often when a strong electrophile (such as an acid) is present.

- Hydrogen bonding solvents (protic solvents) tend to decrease the reactivity of nucleophiles(reduce nucleophilicity); polar aprotic solvents, on the other hand, do not.



The order of nucleophilicity $\underline{in\ polar\ protic\ solvents(with\ HB)}$ increases going down the periodic table



 \rightarrow Polar <u>protic</u> solvents tend to <u>favor elimination (E2)</u> over substitution (S_N2).

Solvents

- Every nucleophile with a full negative charge is in the reaction with some sort of metal counterion (typically Na, Li or K).
- Aprotic polar solvents(DMSO, DMF, acetonitirle) cause solvation of the counterion occurs, exposing the nucleophile, with its anionic charge, to need to react even more.



 The nucleophile is destabilized and faster to react.(needs to find something to react with!)

The order of nucleophilicity in polar aprotic solvents(no HB) decreases as we go down the periodic table



 \rightarrow Polar aprotic solvents tend to <u>favor substitution (S_N2)</u> relative to elimination (E2)

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Solvents

Solvent:

The case when you have a alkyl halide with a strongly basic nucleophile:

The fact that we are using a polar protic/aprotic solvent is the crucial piece of information that determines the reaction.



(If 1° R-X, the reaction will almost certainly be S_N2) Primary - rule out SN1, E1 Strong - rule out SN1, E1

Polar aprotic - SN2 favored over E2

Secondary - can't rule out Strong - rule out SN1, E1 Polar Protic - E2 favored over SN2

(3° R-X are too hindered for the S_N2) Tertiary - rule out SN2 Neutral- rule out SN2, E2 **Polar Protic**

Solvents

SN1/SN2/E1/E2 : Key factors to consider

Question 1: Is the carbon containing the leaving group methyl (only one carbon), primary, secondary, or tertiary?

• Rule #1: If primary, the reaction will almost certainly be SN2

[prominent, commonly encountered exceptions: 1) a bulky base such as tBuOK will tend to give elimination products [E2]; 2) primary carbons that can form relatively stable carbocations may proceed through the SN1/E1 pathway.] Also – methyl carbons always proceed through SN2.

• Rule #2: If tertiary, the reaction cannot be SN2. [Because tertiary alkyl halides are too hindered for the SN2. Depending on the type of nucleophile/base, it will either proceed with concerted elimination [E2] or through carbocation formation [SN1/E1]

SN1/SN2/E1/E2 : Key factors to consider

Question 2: Does the nucleophile/base bear a negative charge?

• Rule #3: Charged nucleophiles/bases will favor SN2/E2 pathways [i.e. rule out SN1/E1]. [So, for example, if SN2 has already been ruled out [e.g. for a tertiary carbon, according to Question 1] then the reaction will therefore be E2. This is the case for tertiary alkyl halides in the presence of strong bases such as NaOEt, etc. The strength of the [charged] nucleophile/base can be important! An important special case is to be aware of charged species that are weak bases [such as CI, N3, -CN, etc.] these will favor SN2 reactions over E2 reactions].

• Rule #4: If a charged species is <u>not</u> present, the reaction is likely to be SN1/E1. [so if the only reagent is, say, H2O or CH3OH you are likely looking at carbocation formation resulting in an SN1/E1 reaction.]

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Solvents

SN1/SN2/E1/E2 : Key factors to consider

Question 3: Is the solvent polar protic or polar aprotic?

• Rule #5: All else being equal, polar aprotic solvents favor substitution [SN2] over elimination [E2]. Polar protic solvents favor elimination [E2] over substitution [SN2].

[Note that this rule is generally only important in the case of trying to distinguish SN2 and E2 with a secondary alkyl halide and a charged nucleophile/base. This is not meant to distinguish SN1/E1 since these reactions tend to occur in polar protic solvents, which stabilize the resulting carbocation better than polar aprotic solvents.]

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Solvents

SN1/SN2/E1/E2 : Key factors to consider

Question 4: Is heat being applied to the reaction?

• Rule #6: Heat favors elimination reactions.

[This only becomes an important rule to apply when carbocation formation is indicated and we are trying to decide whether SN1 or E1 will dominate. At low temperatures SN1 products tend to dominate over E1 products; at higher temperatures, E1 products become more prominent.]