H3 CHEM ① SPECTROSCOPY

NIGEL FONG -

① PRINCIPLES

(a) Spectroscopy & Light

Spectroscopy = study of intx of EM rad w/ matter
↳ absorb/emit ... tell us str features

Light: $E = hf = \frac{hc}{\lambda}$ since $c = f\lambda$

(b) Quantized energy

- Energy quantized, particle can only assoc w/ discrete E.
- To Δlvl, abs packet of E exactly = ΔE betw lvls.

Electronic Elvl	100+ kJ/mol	UV/vis	100-700nm	Δorbital
Vibrational	22 kJ/mol	IR photn	5000nm	Δ vib Elvl
Rotational	<1 kJ/mol	Microwave	a/mm-10mm	Δrota Elvl

NMR ... intx $\vec{B}$ w/ magnetically acte nucler

② UV/VIS

(a) Molecules UV/VIS acte

Require relate small energy gap (too large ΔE: out of range)
$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$ $n \rightarrow \sigma^*$ } Need n or π e⁻

↑conjugate, ↓energy gap ($\pi \rightarrow \pi^*$), longer abs λ
Multiple possb $\pi \rightarrow \pi^*$: Multiple abs bands

Lone pair: $n \rightarrow \pi^*$ gap < $\pi \rightarrow \pi^*$ gap : longer λ

If large enough λ : visible abs

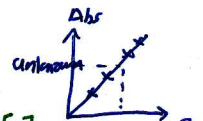
(b) Quantificatn

Lambert-Beer: $A = \lg \frac{I_0}{I}$, $T = \frac{I}{I_0} \times 100$ (I_0 = incident, I = emerging)

: $A = \varepsilon c l$ (A: abs, ε: molar absorbtivity · dm³ mol⁻¹ cm⁻¹, c: conc, l: path length: cm)

2 component mixture: $A = \varepsilon_1 c_1 l + \varepsilon_2 c_2 l$ — measure 2 λ to find rel c.

Calib
1. Run UV/VIS of cpd & other in mix
2. Choose λ w/ ↑abs of cpd but ↓abs of contam.
3. Prep std solns to cover range of conc
4. Run sol @ same wavelength
5. Plot calib curve: abs vs c
6. Mea. abs of unknown, read [ ]



Deviations
1. Chem Δ: dissociatn / associatn / cplx / polym
2. Δ refractv index of medium since too ↑ conc
3. Polychromatic instead of mono
4. Stray light

③ IR SPEC

(a) Wavenos

$\bar{\nu} = \frac{1}{\lambda}$ all in cm⁻¹.

(b) Origin of abs

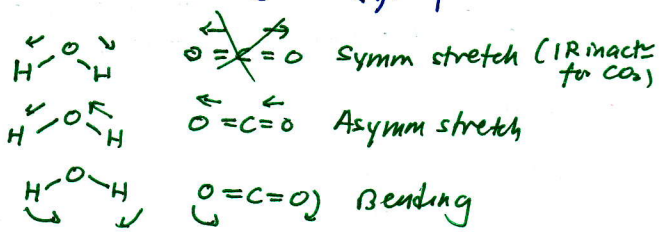
PRINCP
- Vib E of molec quantized, each vib occurs @ specific freq corres to E gap
- IR abs only when freq rad = freq vib
- When energy abs, vib w/ freq = rad freq ↑amplitude

IR-ACTV
- Vib modes resulting in Δdipole moment (IR acte)
- N atoms, 3N-6 vib (minus IR inacte ones)

VIB TYPE
- Stretch - asymm
  - symm
- Bend - scissoring
  - wagging
  - Twisting
  - Rocking

↑ Energy

EG



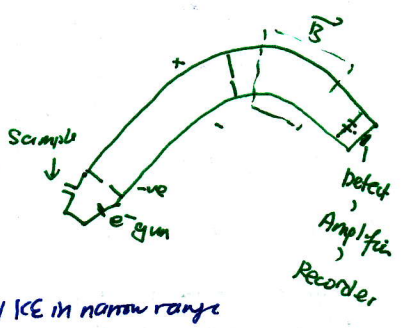
FREQ
- ↑m, ↓freq — light C-H ↑freq
- Stronger bond: ↑freq

(c) Interp

3500	Broad	-OH	2250	C≡N	1650 w C=C
3400	2 abs	$-NH_2$	2150	C≡C	1600-1500 Arom
	1 abs	$-N^{\prime}_{H}$	1810	Acid Cl	
3200	sp^2, sp	C-H	1780 +2	Anhyd	Deloc/conj shifts abs lower
3000	sp^3	C-H	1735	Ester	
2800	Aldehyde	C-H	1725	Aldehyde	1200 C-O
			1715	Ketone	
			1680	Amide	

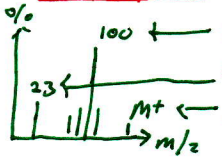
④ MASS SPEC

(a) Instrumentatn

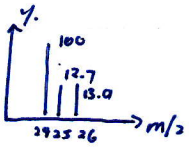


1. Vapourise sample in oven
2. Electron ioniz fr e⁻ gun
3. Accel by $\vec{E}$ field
4. Electroanalyz: select ion w/ ICE in narrow range
5. Pass thru EM pole ... deflected.
6. For given $\vec{B}$, ions of certain m pass thru slit, hit collector plate.

(b) Isotopic peaks



100 ← Base peak (set as 100%.)
Abundance as % of base peak
M+ ← M+: give Mr of sample



REL ISOTOPIC MASS

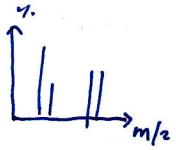
$$A_r(Mg) = \frac{100(24) + 12.7(25) + 13.9(26)}{100 + 12.7 + 13.9}$$

* Odd no ⇒ N atom

M+1 PEAK ⇒ no. of C

$$n_c = \frac{100}{1.1}\left(\frac{A_{M+1}}{A_M}\right)$$

1.1% ^{13}C
A(M+1) ↑ w/ n_c.



M+2 & M+4 PEAK

$^{35}Cl : {}^{37}Cl$ 3 : 1 } M 9 ; M+2 6 ; M+4 1

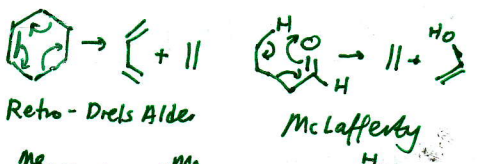
$^{79}Br : {}^{81}Br$ 1 : 1 } M 1 ; M+2 2 ; M+4 1

- High-res mass spec gives up to 5 sf
  - ↳ quadrupole mass analyz: ion oscillate bet 4 V rods; stable osc: certain m pass thr
  - ↳ Det molec F: A_rs not exact whole no

(c) Fragmentn

Commun frag: 15 CH_3; 18 H_2O; 29 CHO *stable; 77 C_6H_5; 91 $C_6H_5CH_2$; 105 C_6H_5CO

Rearrangement:



(4) NMR

(a) Principles

- Nucleus of proton spins & gen mag moment
- $\vec{B}_{applied}$: Mag moment of proton align w/ / against $\vec{B}_{app}$
- To switch: lower E spin state → align w/ $\vec{B}_{applied}$; higher E s.s → align against. } Abs radio freq rad
- Exact freq abs dpd on chem env of proton.

(b) Measurmt of chem shift

- Diff to measure abs $\vec{B}_{abs}$ w/ suff accuracy ... differ by $\frac{1}{100}$ Tesla
- More acc: measure relative $\Delta\vec{B}$ wrt TMS (tetramethylsilane)

- δ = Dist downfield fr TMS
- Use δ for easy comparison
  - ↳ $\Delta B \propto \vec{B}_{o\,app}$.
  - Diff NMR mac diff op freq
  - B mea. und diff ins diff.
  - Need comp indep of

$$\delta = \frac{B - B_{TMS}}{B_o} \times 10^6$$

- Use TMS
  - ↳ 12 eqv H: ↓[TMS] ↑ sharp sig
  - ↳ V. upfield: x interfere
  - ↳ Chem inert, ↓bp - easy removal
  - ↳ Solb in org solv

(c) EN & shifts : shielding

- e^- in chem env around H gen $\vec{B}$ opposing $\vec{B}_{applied}$.
- $B_{effect} = B_{app} - B_{induced}$: shielding ↓ B_{eff}.
- To bring shielded H to res at particular freq, need ↑ $\vec{B}_{app}$.
- Equivalent H = replace H by X ... same cpd — same sig
- ↑ EN atoms withdraw e^--density, deshielding ... downfield
- Closer to H ... deshield

(d) Diamagnetic anisotropic

- In molec w/ C=C / C≡C, circ of πe^- gen $\vec{B}$ field.
  - If $\vec{B}_{induc}$ oppos $\vec{B}_{applied}$ ... shielded ↓ B_{eff}
  - If $\vec{B}_{induc}$ reinforce $\vec{B}_{applied}$ ... deshielded ↑ B_{eff}.

Deshielding outside (reinforce B) | Shielded | Deshielded | Deshielded

(e) Integrals

- Area under NMR sig ∝ No. of H.
- Given as relative peak areas

(f) Coupling

- Adj H can align w/ / against $\vec{B}_{applied}$
  - Spin w/ : reinforce $\vec{B}_{app}$ — deshielding
  - against: oppose $\vec{B}_{app}$ — shielding
  } split into doublet
- n eqv H → n+1 peaks

(g) D_2O exchange

- Greater H-b: Greater δ of H bonded to N/O
- Labile H^+: Bonded to O, N. — no splitting: rapid exchg
  - Add D_2O: R-OH + D_2O → R-OD + DOH .. sig disapp
  - δ = 4.7 may appear if HOD miscible w/ solv

(h) δ values

Start: 0.9 sp^3 C; 1.3 sp^2 C; 1.7 sp C

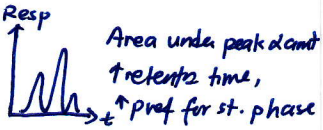
Add: +2.5 −O; +2 −N; +1 −X, −Ar, −Vinyl

Std: 2 C≡C; 5-6 C=C; 7 Arom.; 10 Aldehyd; 12 COOH

H3 CHEM ② SEP TECNQ

— MIGEL RONG —

① CHROMATOGRAPHY

TYPE	STAT PHASE	MOBILE PHASE	SEP PRINCIPLE	SAMPLE PREP	ANALYTE TYPE	ANALYSIS METHODS
Paper	Cellulose (paper) w/ assoc H_2O - v. polar/H-b	• Liq solvent drawn up by capillary action - Less polar	Solute partition bet - stat phase ( ) - mobile ph ( ) If - ↑abs to stat - ↓ mobile p solub (↑polar) ⇒ ↑retention	/ can use 2D if insuff sep ' drop solvent Dissolve in solvent Spot on start line Absorb onto stat phase Remove plate when solvent reaches top, record solvent front		• Colour • UV abs : silica impregnated w/ UV-fluorescent cpd : spots appear dark if UV-active • Beaker w/ I_2 crystal : abs by solute • Ninhydrin — proteins • Molisch (1 naphthanol, HCl) — sugars • Tollens' — reduc sug R_f = dist moved by solute / dist moved by solvent
TLC (thin-layer)	SiO_2 / Al_2O_3 - polar/H-b - Acid-base SiO_2 acidic Al_2O_3 basic → smaller size : ↑eff → ↑reproducible				e.g. org rxn intern ↓ can help to sep rxn intern cut-out silica	
GLC gas/liq	Non-volatile liq coated on small inert particles	Gas (inert) carrier g : He, N_2 Must be dry - Dry : use $CuSO_4$ (anh) - Xorg vap : activ charcoal	Sep on • Affinity for st & mob phases • Volatility Retent time also dep - Flow rate of mob - T - Length of column	- J into rubber septum - Vapourise everything in oven - Travel thru oven - If ↑ng components / sim st : mob p affinity ↳ ↑T grad. → Better & faster sep	Gas / ↑vap p @ column T ⋮ ok for T & bp once inside colm but must ↑vp	Detector : eg flame ion z Gas fr column mix w/ H_2 & air Burn — prod CH· → CHO^+ Prod current — recorded Resp  Area under peak & amt ↑retent time, ↑pref for st. phase Can collect cpnt & MS
HPLC high peform liq ch.	Uniform porous silica particles w/ surf pores to ↑surf area → Polar	Non-polar solvent	Liq mobile phase carr solute to sep thru stat phase. Solute partn bet st & mob ph based on polarities. → Non-polar elute first	No special treatmt rqd — aq samples Need to ctrl factors exactly : flow rate, inject time ...	Even those not GLC-suitab - Therm unstab • ↑polar - ↑volatile. Appn : - anal. pollutants in syn drugs - anal. Cmpt & metabolites	Other methods reqd to det output components - MS - UV/VIS - IR
Reverse-phase HPLC	Octadecyl silyl coated silica (C-18, C-8, C6) → Non-polar	MeOH / H_2O etc → Polar	→ Polar elute first			

② ELECTROPHORESIS

(a) Uses

- Measure macromolec Mr
- Sep. nuc acid & polypep
  - ↳ for seq
  - ↳ & hydrolysate of prot
- Sep prot — raise anti B
- DNA fingerprinting
- Xtensive allergy-induc chm
- Screen milk for lethal α-lactoglobulin

(b) Apparatus

- Gel — 3D polymer, spongelike
  - prop precisely ctrl
  - ↑chem stable
- Electrophoresis chamber
- Support for gel
- Power SS
- Detects / quantificates
  - ↳ e.g. bioassay, silver stain
- Extracts of prot & nec

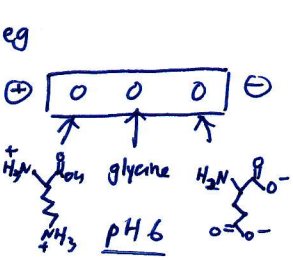
(c) Principle

- Charged substrate
  - Amino acids (charged dpd pH)
  - DNA (-ve)
- Place in wells in gel, migrate to opp-charged electrode

Rate mtg : Fricts = Attracts

- Factors affecting mobility (μ)
  1. Voltage
  2. Size
  3. Shape
  4. pH — ston
  5. Temp. may denature prot

eg

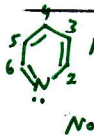
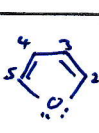
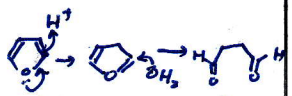
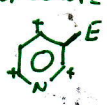
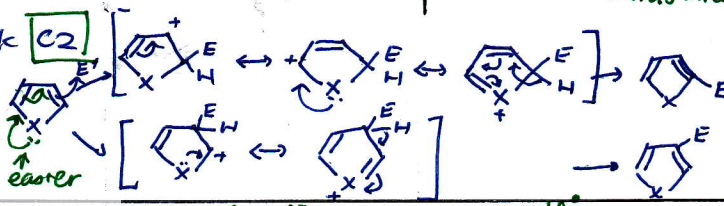


H3 CHEM ⑤ FUNC GRPS

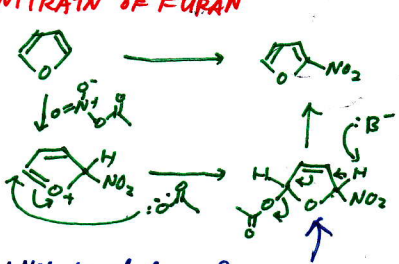
NIGEL FONG

① AROM HETEROCYCLES

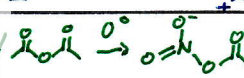
Arom ∴ Cyclic
2. Flat … max overlap … uninterrup. deloc π e⁻
3. (4n+2) e⁻

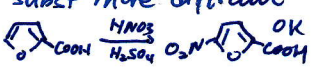
	PYRIDINE	PYRROLE	FURAN	THIOPHENE
STRUCTURE	 N: lone pair not deloc. : last e⁻ join w/ p-e⁻s Not perf symm.	 Lone pair deloc into π-system to form 6e⁻	 One lp deloc into π-sys other remains	 1 lp deloc into π-sys
AROMATICITY	Less arom than 	Res energy: 90kJmol⁻¹ Extent of deloc varies inversely w/ EN of heteroatom: furan<pyrr<thiop  …etc	Res energy: 67kJmol⁻¹ O ↑EN of O: res str w/ Ö ↓contrib O hold on to e⁻ ∴ low arom.	Res energy: 121kJmol⁻¹ • ↓EN of S • Large C-S-C ∠ less strain ↑arom
BP (=80°C)	115°C – Net dipole: pd-pd – ↑intr than benzene	129°C – only VDW (no N–H) – ↑ Dipole mom	34°C – Only VDW – ↓ Dipole Mom: no H	84°C – Only VDW – slightly id-id.
MISCIBILITY IN H_2O	Soluble – H-bonding w/ H_2O ↳ Lp free	Poor – lp deloc – But have H ↳H-b	Poor – One lp deloc – But have 1 more ↳H-b	Immiscible ↳S X H-b
BASICITY	Basic: free (not deloc) lone pair Weaker than RNH_2: sp^2 lp vs sp^3 more strongly attr by nuc, ↓ avail for bonding. ↳ Look for A-B rx.	Very weak B – lp deloc. Can protonate under [H⁺]↑ but lose aromaticity • Polym in str acid	 ↳Hydrolyse in str acid	
Nu^- AROM SUBST.	Form C2 & C4-sub  Nu^- = $\bar{N}H_2$, $\bar{O}Me$, $\bar{S}Et$			
E^+ AROM SUBST	Only w/ great difficulty e⁻-density ↓ by EWG N Cs: δ+ve … more inert to E^+ E^+ attack N: → +ve on ring further deactv Vig cond, attack C3 ↳avoid ⊕ on N 	More reactv than : lp of heteroatom stab +ve in intermediate Most reactv: N less EN lp deloc	2nd most reactv: O ↑EN, ↓del	Least reactv: S: poor orb ovlp ↓resonance ↓stab intem
		Monosub: attack C2 intem w/ +ve deloc over more atoms  easier		

NITRATN OF FURAN

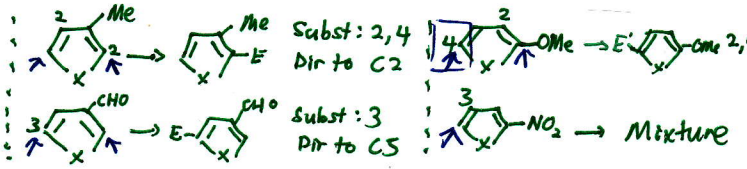


- Nitrate of furan forms stable addition pdt
- Base nec to give subst pdt
- Low arom of furan
- But w/ non-nu^- counteranion (BF_4^-) does not give adds intem.

NITRATN	Unstable to H^+: use HNO_3 /  (acetyl nitrate)		Thiopha HNO_3 ✓
ACYLATN	Unstable to H^+: use BF_3 (cat)		$AlCl_3$, $SnCl_4$ (cat)
ALKYLATN	No rx: alkylatns need stroy lewis acid.		Alkylate, $AlCl_3$, $ZnCl_2$ Give + $-SO_3H$ (30°C)
+c.H_2SO_4	Polymerm	Hydrolyse	
Br_2.	MeOH – tetrasub Diox – C2 sub		Trisub

SUBSTS. EWG subst make further subst more difficult – add stab esp pyrr & furan 

DIRECTING Directg eff heteroatom & subst compete



H3 CH ⑥ DRUGS : PRINCP.

NIGEL FONG

① DRUG-RECEPTOR INTX

(a) Principle

- Drug binds to complementary binding site (receptor)/actv site
  - └ comp bet drugs : ⊗drug & affinity det which bind
- Ligand bind to receptor, induce Δshape
  - └ Δshape to get opt binding intx
- Physiolg effect — eg open ion channel

(b) Type of binding

COVALENT | • Drug ↑reactv (eg mustards)

IONIC | • Opp charges
• Stronger in hydrophobic env
• Most impt initial

H-BOND | • Donor = "H", Acceptor = "Ö" — donate H
• Directional

ION-DIPOLE | • Charged gp distort ē cloud (even arom)

VDW | • Have to be quite close
• Hydrophobic pockets

(c) Competv & Non-comp inhibition

COMP | • Drug sim to ntl substrate, ↑affinity
• Block access to actv site — stop rxn
• Can be displaced w/ ↑ [substrate]
| ○ EG: ethylene glycol ox to oxalic acid - harmful
administer ethanol ↑↑ to comp inhibit

NON-COMP | • Irrev binding to actv site — ⊗displace w/ sub
○ EG: nerve gas, penicillin

ALLOSTERIC | • Δ conformatn by binding to allosteric site

(d) Agonist & Antagonist

AGONIST | Mimic ntl ligand → Δ recep. shape, ↑effect
• Correct binding groups in corr pos
⇒ opt isomer ✗ since recep chiral
• Correct size & shape to fit
• May bind stronger/weaker than ntl ligand

ANTAGON. | Bind well but ✗ cause phys. effect — block site
Does not distort actv site shape to give effect
⇒ Bind better than ntl ligand
• Allosteric antagonist
• Umbrella effect antagonist — bind near b. site too
└ overlap norm b. site, prevent ligand intx

② PHARMACOKINETICS & DYNAMICS

(a) Intro

Pharmacokinetics = What body does to drug
Pharmacodynamics = What drug does to body

Pharmk : Absorptn / Dist / Metabolism / Excretion

(b) Absorptn & Distributn — Use pro-drug to opt.

ORAL | • Should not taste too bad
• Chem stable in stomach HCl & proteolytic enz
• Water soluble
• Lipophilicity — pass thru cell mem of intestin villi

INHAL | • Eg anti-asthmatic drugs

TRANS DERMAL | • Eg skin patches
• Need to be lipophilic

INJ | • Enter bloodstream quickly, no barriers

TPT | • Carried in blood — soln
— assoc w/ plasma prot.
• Need to pass thru cell mem ?? — some

(c) Metabolism & Excretn

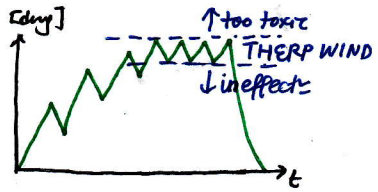
1 Metab. by blood enzymes
1st-pass metab thru liver

2 2nd-pass metab thru liver — ↑hydrophilic
⇒ for excretn thru kidney, etc

How

1. Ox. methyl gp / aryl rings / heteroatom
2. De-alkylatn.
3. Conjugatn w/ SO_4^{2-}, amino acids, sugars

(d) Therapeutic window



- Drug will be metab & excreted
- Top-up dose nec
  - └ maintain @ therap dose

(e) Tolerance & dependance

TOLERANCE = ever ↑ amt rqd to give effect
DEPENDANCE = ppl on drug — or feel withdrawal symptoms

1. Metabolic : Body ↑ metab enz to destroy drug
Discont : t nec for [Enz] ↓
2. Pharmacody : Body Δ no of receptor to compensate for eff
3 Behavioral : Psycholog / user compensates

Sudden withdrawal : body too much enz, too many receptor
└ effect opp. of drug

Esp — Depressants : alcohol, benzodiazepines, barbiturates
— Opiates : morphine, heroin
— Stimulants : cocaine, amphetamines

③ DRUG DEVELOPMT

(a) Overview

DRUG DVP = Lead compound to just b/f human tests
DISCOVERY = Find suitable drugs

(b) ID drug target

TYPES
1. Protein – receptors
2. – enzymes
3 Lipids – cell mems, hormones
4. Carbohydrates

- Und how inf ctrl @ molec level
- No, type, eff of molec
- Find str. acts/b site

(c) Bioassay: check candidate efficacy

Checks effects
1. Effectiveness ~ affinity for target and none
2. Side-effects

Bioassays
1. Lab animals
2. GM bact / mice : w/ hum enz/recep
3. In vitro testing
4. Enz kinetics – how eff displacement/block of radioactive ligand
   \ NMR : binding strength.

(d) Lead cpd

DEF
- Has some desired pharmac acts
- Use as start pt for mod to ↑potency, selectv etc

SOURCES
1. Trad plant remedies – sep & purify
2. Ntl substrate/ligand for enz/recep
3. Existing drugs
4. Deduce molec to fit 3D shape of target
5. Random testing of comb. syn lib.

+ Then make & test analogues

(e) Testing

After bioassays & animal testing...

I Small no of healthy vol ... test safety & tolerability
II Greater no patients ... test ~~dosage~~, efficacy, ~~safety~~
III Large no patients ... test efficacy & side eff

Frequency – wait approval

(f) Modif of drug

POLARIT
- To pass thru cell mem / blood-brain barrier, need non-polar molecule (e.g. add Cl, alkyl) → Advantage possibly to keep drug fr CNS tx (but readily ox to COOH)
- Right pol for intx w/ recep! (eg. + OH)

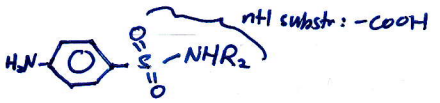
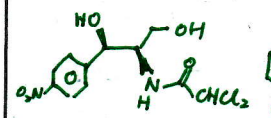
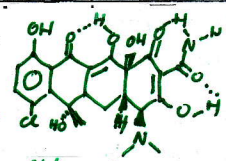
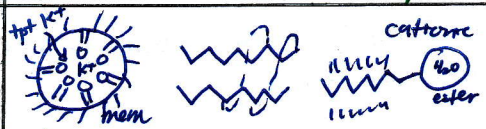
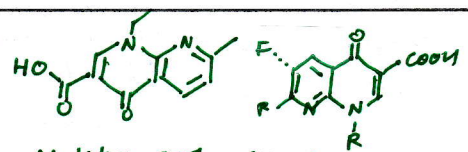
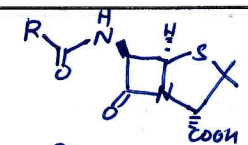
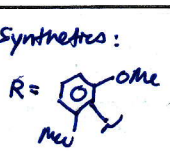
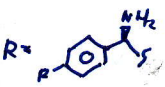
A-B
- N atoms : pKa ~ 6-8 – both ionz & non-ionz in c
  ↳ intx str w/ recep in ionized form
  pass thru p mem in unionized ↑rap eqm
- COOH : Mostly ionized (pKa 3.5)
  ↳ X pass thru cell mem (except carrier p)
  ↳ Can mask w/ ester gp (pro-drug)

ELECT EFF
- EDG: ↑basicity of amine, ↓acidity of acids (but large EDG restr H_2O access, ionz)
- Δ gp w/ anr of sim size (isostere) w/ diff e effect
  can stab ag premature metabolism

STERIC
- Bal bet ↓metabolism & ↑binding

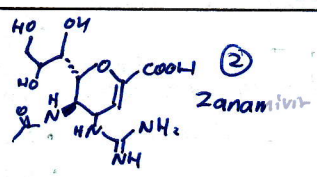
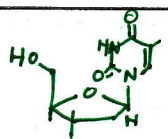
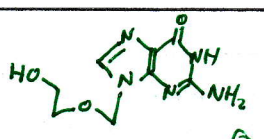
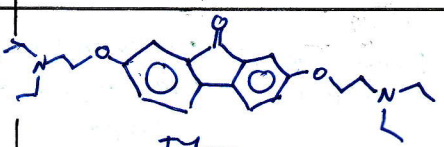
H3 CH ⑦ DRUG CLASSES

NIGEL FONG

CLASS	NAME & STR	MECH OF ACTION	PROBLEMS
①ANTI-BACT Disrupt cell metab.	 nH substr: -COOH Sulphonamide / Sulphone drugs	DHPS 4-amino benzoic acid → Dihydropteroate synthetase → folic acid ↑ Comp inhib – Bact X syn nucleic acid – Hum x syn FA, unaffected	·Eventual resist └only comp inhib. Bact ↑[subst] to rev · Coadminister w/ anr sequential blocking
Disrupt prot syn	 Chloramphenicol  Chlorotetracycline	Block prot translatn by inhibit ribosome	·Tetracycline resistance └use in animal feed · Bind to dvp teeth/bone cause weakeng/discol
p. mem Damage	 Valinomycin Gramicidin A Polymyxin B Colistin	Peptide-like → hydrophobic channel / M+ tpt hydrophob coat Make bact cell mem ↑perm to cations & small hydrophilic molecules. ↓ Upset ionic bal, fatal.	
Disrupts DNA transcp	 Nalidixic acid (fluoro) quinolones	- Inhibit gyrase enz which unwinds bact DNA for supercoil. - Stop replicatn & exp of bact DNA	
Disrupts cell wall constr.	 Penicillin Synthetases:  Methicillin I F R= II G R= III X R= IV K R= V R=  R=H ampicillin R=OH amoxycillin	Inhib X-linkg of adj chain of peptidoglycan └inhib peptide bond formation → Bind to transpeptidases which link · Cell death fr osmotic pressure · Animal cells – no cell wall · Syn penicillin: R=bulky, hinder β-lactamase	· Resist: β-lactamase hydroly – if bact X killed off tot, – transf via plasmid – worse: over-prescp, anim fee · Sol: oclm β-L inhibitor (clavulinic acid : synthetics ... · Side eff: Diarrhoea Fever ADH Vomiting Headache Rash Seizure

② ANTIVIRALS

Difficulty – metabolism linked to host, cpd targetg viruses likely to attack host
– ↑rate of mut
– cannot be killed, only stop prod.

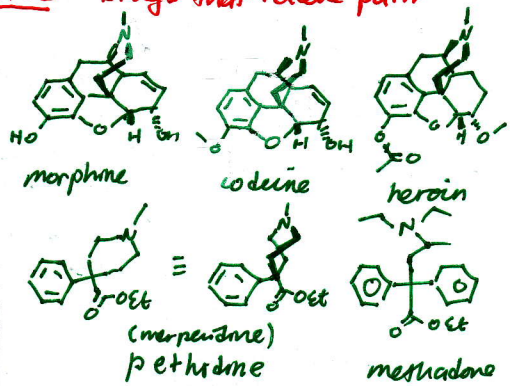
Target cpsid/prot	 Amantadine HCl ①  ② Zanamivir	1. Block ion channel in virmem 2-stop vir core dissoc & inv host 2. Inhib neuraminidase 2 particles stuck to host mem, X bud.	
Target nuc acid syn	 ① AZT (thymidine II)  ② Acyclovir (guanosine analog)	① Conv to triphosphate & incorp into DNA by rev transcriptase – but X allow cont of chain → block enz. ② Incorporate but X read to make viral mRNA 2 halt reprod	Toxicity (g ancriclovir)
Inhibit viral prot syn	 Tilorone	Induce interferon prod Inhib viral prot/mRNA syn.	Only works in mice at ē moment

CLASS	NAME & STR	MECH OF ACTION	PROBLEMS
Monoclonal antibodies	• Antibodies cloned fr 1 B-cell • B-cell + Bone marrow cancer cell (myeloma) → Hybridoma divide indef * Antibody = Protein whose in vivo syn in B-c triggered by antigen on foreign m.	• Imp precision of drug – target sp. cell by attaching monoc antibs ↓ cancer cells : diff antigen fr norm	

③ ANALGESICS = Drugs that relieve pain

brain cannot appreciate pain

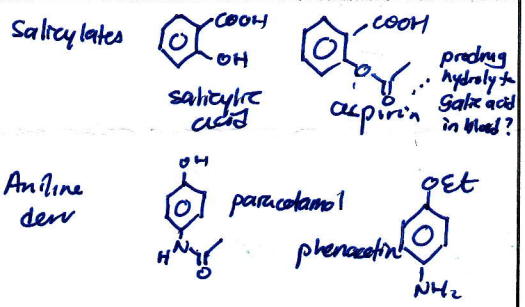
Narcotics



- Depress activ of CNS – analgesia
  - ↳ sleepiness, lethargy, loss consciousness.
- Bind to morphine receptors
  - ↳ nat ligand : endorphins
- Nec FG – 1 of 5 rings ↑ Bind to
  - Hydrophobic RHS ↑ VDW$_1$
  - Arom ring ↑ VDW$_2$
  - Basic N (ioniz) ↑ anion
  - Phenolic OH helps ↑ H-b

- Quickly causes phy dependency that is diff to reverse – toler & addic
- Side eff : constip. nausea, euphora, depression of respiratory reflex
  - ↓
  - Death fr overdose : suffocate

Non-narcotics (anti-pyretics)



Works on pain recep dir, ↓ resp to stimuli transmit pain info to brain

Arachidonic acid → Prostaglandin (cyclo-oxygenase) COX$_1$

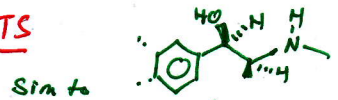
Aspirin + acylate → Salicylic acid

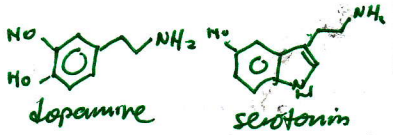
	Aspirin	Salicylic acid
Analgesic	✓	✓
Antipyretic	✓	✓
Anti-inflam	✓	✗
Anticoagulant	✓	✗

} Does not inhibit COX$_1$

	ASP	PAR
Gastroint bleeding (inhib cox, which buffers stom lining)	✓	✗
↑ Bleeding	✓	✓
Nausea/vomiting	More	Less
Suicide drug	✓	✓

④ STIMULANTS



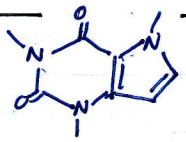


- Act on CNS, ↑ h/r & bp, mimic adr.

diff recep

	Caffeine	Nicotine	Amphetam	Adrenaline
Breathing	↑	↑	↑	↑
Heart rate	↑	↑	↑	↑
Blood p	↑	↑	↑	↑
Blood sug	↑		↑	↑
Urine vol	↑	↓	–	–
Appetite		↓	↓	–
Bronchi	Dilated		Dilated	Dilated

Caffeine

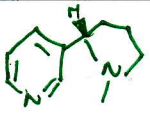


- Comp. antagonist – adenosine recep
- ↑ adren & nora release – activ recep
- Inhib cAMP-phosphodiesterase

} ↑cAMP

Diff recep diff eff.

Nicotine



Cocaine : dopamine accum in synapse, ✗ re-uptake

stim recep assoc w/ pleasure centre longer stim effect

- Agonist @ acetylcholine recep
  - ↳ stim nerve transmission, ↑ adrenal
- Cigs also ↑ alkaloids – inhibit enz that destroy dopamine } ↑dop amine
- SR : stim, ↑ mental activ, alertness

LR addiction ← psychological, physical

↑ dopamine : body ↓ cholinergic recep to keep nerve transm rate at steady level

- Dosage need ↑ for same eff
- Withdrawal : insuff recep for rapid neurotr. lvl – anxiety & tension

Amphetamine

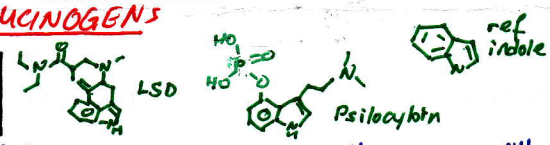
fast solub unlike adrenaline

- Open prot channel @ pre-synaptic n
  - ↳ noradrenaline & dopamine → synapse
- Release serotonin fr pre-s vesicles
- Inhibit noradr & dopamine re-uptake

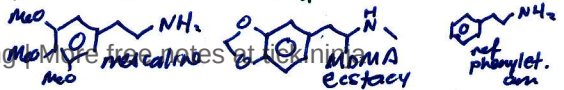
} ↑noradr, ↑serotn, ↑dopamine | ↑ nerve imp strength

⑤ HALLUCINOGENS

Indole



Phenethylamine



Agonist of serotonin recep

Agonist dopam. recep

Retard re-uptake of neurot by pre-synap

} ↑ > norm [neurot] in synapse ↳ over-stim

↑ brain nerve t parts of B not norm activ → engaged

- Delusion & vivid hallucinate
- Impair judgement & thought susceptible to accidents
- Flashbacks : exp past episod long aft drug worn off