

Unit 3: Unit Processes I

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3.1 Unit processes: chemistry as an industrial operation

A unit process is a family of chemical conversions sharing a transformation and, crucially, a family resemblance in how they are run at scale: the reagents, equipment, hazards and controls repeat from product to product. Nitration always brings mixed acid, exotherm management and drowning out; hydrogenation always brings flammable gas, pressure and catalyst handling. This unit teaches the three oxidative and electrophilic workhorses the syllabus selects: nitration, halogenation and oxidation. Unit 4 completes the set with reduction, fermentation and the kinetic discipline that ties process chemistry together.

3.2 Nitration: nitrating agents and mixed acid

Nitration introduces the nitro group, NO_2 , into an organic molecule, most valuably onto aromatic rings, where it is both a functional group in its own right (nitro drugs such as chloramphenicol, nifedipine intermediates and the nitroimidazoles carry it) and the standard gateway to aromatic amines by reduction. The common **nitrating agents** are:

- **Mixed acid:** concentrated nitric acid with concentrated sulfuric acid, the industrial default for aromatic nitration.
- **Concentrated or fuming nitric acid alone**, for reactive substrates or where sulfuric acid would damage the molecule.
- **Nitric acid in acetic acid or acetic anhydride** (acetyl nitrate generated in situ), a milder system for sensitive or highly reactive rings.
- **Alkali metal nitrates with sulfuric acid**, generating nitric acid in situ.
- **Nitronium salts** such as nitronium tetrafluoroborate, laboratory reagents that deliver the electrophile directly.
- For **O nitration** (nitrate esters such as glyceryl trinitrate and isosorbide dinitrate) the same mixed acid esterifies hydroxyl groups rather than substituting on a ring, and for **N nitration** it produces nitramines; the three modes (C, O and N nitration) share equipment and hazard thinking but differ in chemistry.

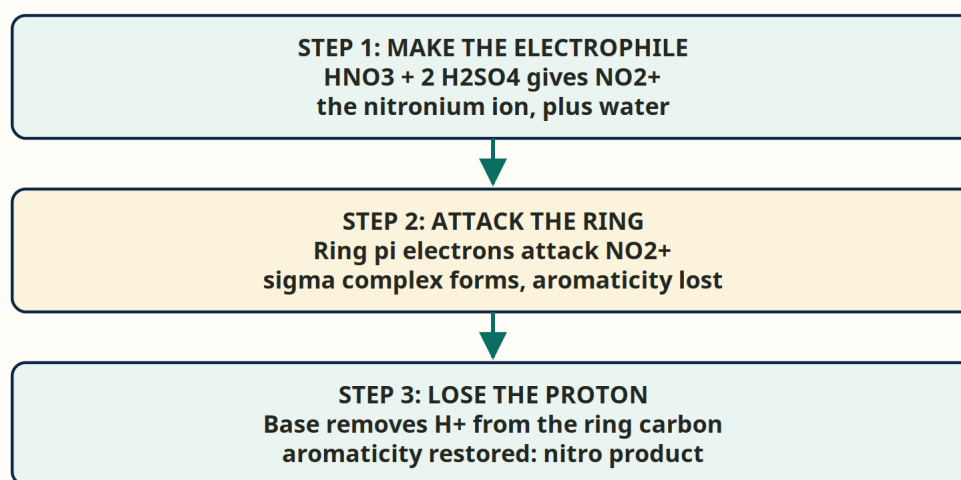
Mixed acid works because sulfuric acid does three jobs: it protonates nitric acid and drives its conversion to the **nitronium ion**, NO_2^+ , the true electrophile; it absorbs the water formed in the reaction, keeping the medium strongly acidic and the nitronium concentration high (spent acid strength is therefore a process variable, falling as nitration proceeds); and it provides a high boiling, heat absorbing medium that dissolves or suspends the aromatic substrate. Acid ratios are chosen for the substrate's reactivity: an activated ring nitrates in weaker acid, a deactivated ring needs stronger acid, higher nitronium concentration and often more forcing conditions, with the corresponding step up in hazard.

3.3 Mechanism of aromatic nitration

The mechanism is the standard electrophilic aromatic substitution, and its three steps are the examination core:

- 1 **Generation of the electrophile.** Nitric acid is protonated by sulfuric acid and loses water to give the linear nitronium ion, NO_2^+ . In shorthand: $\text{HNO}_3 + \text{H}_2\text{SO}_4$ gives NO_2^+ plus HSO_4^- plus H_2O (a second sulfuric acid molecule carries the proton balance in the full equation).
- 2 **Attack on the ring.** The pi system of the aromatic ring attacks the nitronium ion, forming the resonance stabilised sigma complex (arenium ion or Wheland intermediate), in which aromaticity is temporarily lost and the positive charge is delocalised over the ortho and para positions relative to the site of attack. This step is normally rate determining.
- 3 **Loss of the proton.** A base in the medium (bisulfate or water) removes the proton from the carbon bearing the nitro group, aromaticity is restored, and the nitroaromatic product leaves the sequence.

Mechanism of aromatic nitration in three steps



Step 2 is normally rate determining; its rate law is first order in ring and in NO_2^+

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Figure: Aromatic nitration is electrophilic substitution: the nitronium ion is the electrophile, the sigma complex the intermediate, and step 2 is normally rate determining.

Orientation follows the standard rules of electrophilic substitution: existing substituents direct the incoming nitro group according to their activating or deactivating character, and the nitro group itself is strongly deactivating and meta directing, which is why controlled mononitration of a ring that already carries a nitro group needs planning, and why polynitration becomes progressively harder and more hazardous as it proceeds.

3.4 Kinetics of aromatic nitration

The kinetics are examinable because they change with the medium, and the change teaches mechanism. In concentrated sulfuric acid, where nitronium formation is essentially complete, the rate law is **second order overall: rate equals k times $[\text{ArH}]$ times $[\text{NO}_2^+]$** , first order in the aromatic and first order in the electrophile, consistent with the ring attack being rate determining. In media of lower acidity, or in organic solvents, the formation of the nitronium ion itself can become the slow step; the observed rate then becomes **independent of the concentration and even the identity of the aromatic substrate (zero order in ArH)**, because every nitronium ion formed is captured at once. Between these limits, acidity of the medium is the master variable: rate profiles against sulfuric acid concentration pass through a maximum as rising acidity first generates more nitronium ion and then begins to protonate and deactivate the substrate itself. Process consequences are immediate. Because rate depends on nitronium concentration, which

depends on acid strength, and acid strength falls as water forms, a batch nitration slows as it runs unless composition is controlled; because the reaction is strongly exothermic, dosing the substrate or the acid at a controlled rate and holding temperature are what keep the rate, and therefore the heat output, within the cooling capacity of the vessel.

3.5 Process equipment for technical nitration

Technical nitration equipment is designed around one fact: nitration is fast, strongly exothermic and capable of thermal runaway, and the charge contains both a strong oxidising acid and an oxidisable organic compound. The classical batch **nitration** is a jacketed, corrosion resistant (now stainless steel or enamelled) vessel with cooling through jacket and often internal coils, powerful agitation to disperse the organic phase through the acid and prevent local hot spots, temperature alarms and trips, a charge system that doses substrate or mixed acid at a controlled rate with automatic cut off on cooling failure or over temperature, and an emergency **drowning (quench) tank** into which the entire contents can be dumped into water if control is lost. After reaction, the mixture passes to separators where spent acid and nitro product split by gravity; the product is washed (water, then dilute alkali to remove residual acid and phenolic by products) and the spent acid goes to recovery. **Continuous nitrators** (cascade or tubular designs) hold a far smaller inventory of reacting material and offer better heat removal, and modern practice increasingly moves nitration into continuous equipment for exactly that reason. The defences in depth are the examination points: small effective inventory, dose control, cooling with margin, agitation monitoring (a stalled stirrer lets unreacted layers accumulate and react at once on restart), and a rehearsed quench.

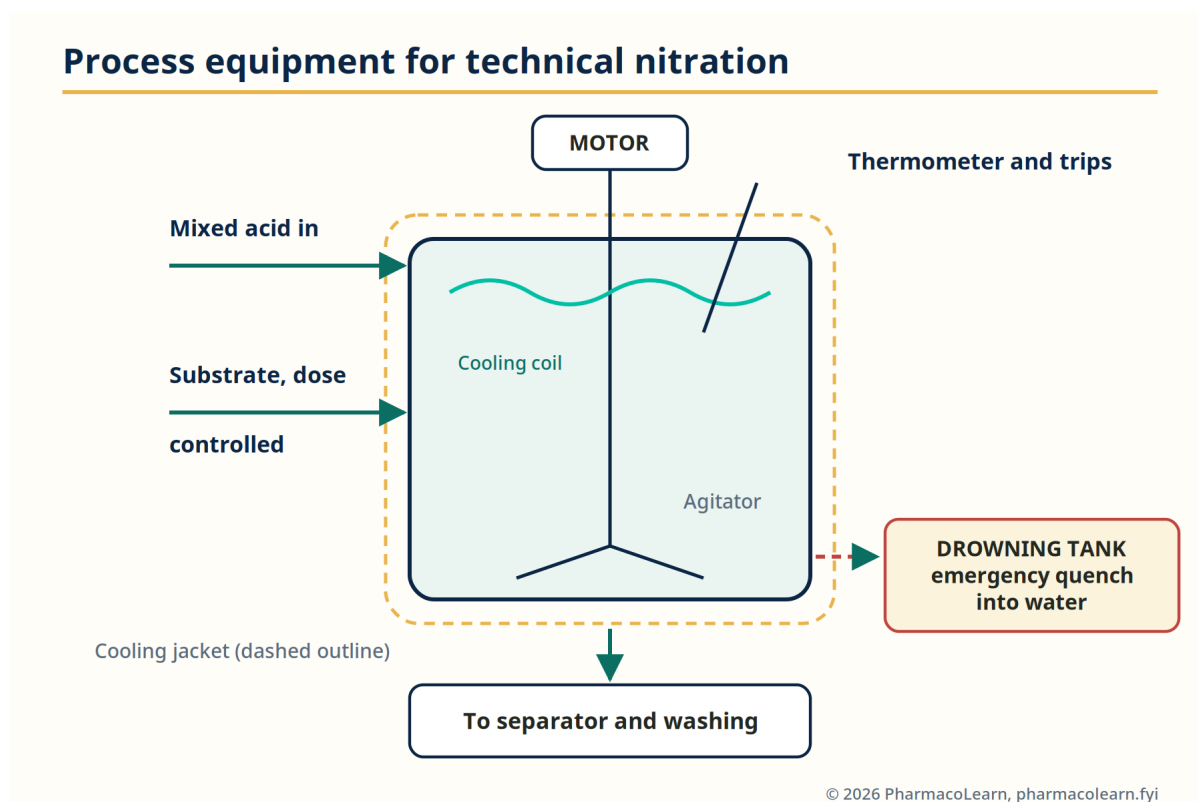


Figure: Equipment for technical nitration: dose control, cooling with margin, agitation and temperature trips, and a drowning tank if control is lost.

3.6 Halogenation: types and kinetics

Halogenation installs chlorine, bromine, iodine or fluorine. The syllabus asks for kinetics, types and catalytic halogenation, with an industrial case study.

Types of halogenation, organised by mechanism:

- **Free radical substitution**, typically side chain chlorination and bromination of alkyl aromatics and alkanes: initiated by light or heat or radical initiators, proceeding by a chain of initiation, propagation and termination steps. Benzylic chlorination of toluene to benzyl chloride is the textbook case.
- **Electrophilic aromatic substitution**: ring chlorination and bromination, requiring polarisation of the halogen, usually by a Lewis acid catalyst (ferric chloride, ferric bromide, aluminium chloride) which generates the effective electrophile; iodine, the least reactive, needs an oxidising co reagent to become electrophilic.
- **Addition to multiple bonds**: chlorine and bromine add across alkenes and alkynes (bromine addition is the classical unsaturation test); hydrogen halides add by ionic (Markovnikov) or radical (peroxide effect) pathways.
- **Replacement reactions**: hydroxyl replaced by halogen using thionyl chloride, phosphorus halides or hydrogen halides; diazonium replaced by halogen in the Sandmeyer and related reactions; halogen exchange (the Finkelstein reaction, and fluoride exchange processes) for iodides and fluorides.
- **Fluorination** stands apart: elemental fluorine is too violent for most substrates, so industry uses halogen exchange on chlorinated precursors, Balz Schiemann chemistry for aryl fluorides, and specialised reagents at fine chemical scale.

Kinetics of halogenations follow their mechanisms. Radical chain chlorination shows the signature of its class: an induction period while inhibitor (oxygen is a common one) is consumed, a rate governed by initiation rate and light intensity, long chain lengths (many product molecules per initiation event), and abrupt sensitivity to inhibitors and vessel surface. Electrophilic ring halogenation is typically first order in the aromatic and first order in halogen under catalysis, with the catalyst order and the rate determining step (formation of the sigma complex) following the same pattern as nitration; bromination is more selective than chlorination because bromine is the less reactive, more discriminating electrophile, a fact process chemists use when a single isomer is wanted.

3.7 Catalytic halogenation and the industrial case study

Catalytic halogenation names the processes in which a catalyst makes the halogen reactive enough, or selective enough, for manufacture: Lewis acids (FeCl_3 , AlCl_3 , FeBr_3) for aromatic substitution; supported metal and metal chloride catalysts for vapour phase chlorinations; hydrogen chloride oxidation catalysis (the Deacon principle, oxidising HCl back to chlorine) where chlorine economy matters; and phase transfer or iodine catalysis in exchange reactions. The case study the syllabus asks for is taught with the standard example used across the literature, **the chlorination of toluene**, because one substrate demonstrates that conditions, not the reagent, choose the product. In the presence of a Lewis acid catalyst such as ferric chloride, in the dark and at moderate temperature, chlorine attacks the ring and gives ortho and para chlorotoluenes, intermediates for further elaboration. Under light, heat or radical initiation, with no Lewis acid, the same chlorine attacks the side chain and gives benzyl chloride, and with excess chlorine benzal chloride and benzotrichloride, the hydrolysis precursors of benzyl alcohol, benzaldehyde and benzoic acid respectively. The process lessons generalise: catalyst and condition selection are selectivity decisions; the reactor for a photochemical radical chain (illuminated, inhibitor free feed) is a different machine from the reactor for a catalysed ring substitution (dark, dry, corrosion resistant); and exotherm and hydrogen chloride handling dominate the engineering of both.

3.8 Oxidation: introduction and types of oxidative reactions

Oxidation at process scale converts alcohols to carbonyls and acids, oxidises side chains, introduces oxygen into rings and cleaves double bonds, and it does so under the shadow of a simple danger: the reagents that oxidise substrates can also oxidise everything else, including the solvent and the plant's

inventory of intermediates, and over oxidation is a yield loss as well as a hazard. **Types of oxidative reactions** in the syllabus sense:

- **Dehydrogenation:** removal of hydrogen (alcohol to carbonyl is the borderline case, oxidation without oxygen insertion).
- **Oxygen insertion and hydroxylation:** adding oxygen atoms (side chain oxidation of alkyl aromatics to acids, the route by which toluene reaches benzoic acid; hydroxylation of phenols).
- **Oxidative cleavage:** breaking carbon carbon bonds (glycol cleavage, ozonolysis of alkenes, ring opening oxidations).
- **Liquid phase oxidation with oxidising agents:** the syllabus emphasis, in which the oxidant is delivered in the liquid phase: air or oxygen with metal catalysts (cobalt and manganese salts and bromide promotion in the industrial oxidation of alkyl aromatics), hydrogen peroxide systems, hypochlorite systems and permanganate or dichromate in classical processes, increasingly displaced on waste grounds.

The classical stoichiometric oxidants earned their place in textbooks and their retirement in plants: chromium and manganese reagents give excellent chemistry and stoichiometric heavy metal waste, and much of modern process oxidation is the search for catalytic, oxygen or peroxide based replacements that keep the selectivity and lose the waste.

3.9 Nonmetallic oxidising agents: hydrogen peroxide, sodium hypochlorite, oxygen and ozone

Agent	Strengths at scale	Limitations and cautions
Hydrogen peroxide, H ₂ O ₂	Clean by product (water); high active oxygen per rupee; versatile with catalysts (tungstate, titanium silicalite, peracids formed in situ)	Decomposes with heat and metal contamination, releasing oxygen; storage and dosing discipline needed; dilute forms carry much water
Sodium hypochlorite, NaOCl	Cheap, aqueous, easy to dose; the standard reagent for TEMPO catalysed oxidation of alcohols to aldehydes and acids at fine chemical scale, and for oxidative work ups	Chlorinated by products possible; gas evolution (chlorine) if acidified; strength decays in storage
Oxygen gas (and air)	The cheapest and cleanest oxidant of all; the basis of large scale liquid phase oxidations with Co/Mn catalysis	Flammable vapour mixtures above the liquid demand rigorous control of oxygen concentration; mass transfer limited; needs pressure equipment
Ozone, O ₃ (ozonolysis)	Cleaves carbon carbon double bonds with a selectivity no other reagent matches; no stoichiometric waste beyond the work up	Generated on site (cannot be stored or shipped); intensely toxic and corrosive gas; ozonides are energetic intermediates needing controlled reductive or oxidative work up

Ozonolysis deserves its mechanism note. Ozone adds across a double bond to give a primary ozonide, which rearranges to the more stable ozonide; the **work up chooses the product**: reductive work up (dimethyl sulfide, zinc in acetic acid, triphenylphosphine or catalytic hydrogenation) delivers aldehydes and ketones with aldehydes intact, while oxidative work up (hydrogen peroxide) carries aldehydes on to carboxylic acids. At scale the operation is run cold, in solution, with the ozone generated from oxygen on site and the excess destroyed at the vent, and it remains the industrial route of choice for cleaving double bonds where the carbonyl fragments are the product.

3.10 Unit 3 summary

Process	Electrophile / active species	Signature hazard	Control that defines the process
Nitration	Nitronium ion from mixed acid	Thermal runaway of an oxidiser fuel mixture	Dose control, cooling, quench tank, agitation monitoring

Process	Electrophile / active species	Signature hazard	Control that defines the process
Halogenation	Polarised halogen (Lewis acid) or halogen radical (light)	Runaway chains, HCl evolution, corrosive media	Condition selection for selectivity, feed purity, gas handling
Oxidation	O ₂ , peroxide, hypochlorite, ozone	Over oxidation, flammable O ₂ mixtures, energetic intermediates	Oxidant dosing, oxygen concentration control, work up discipline

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