1. **Title of the module**
   Synthetic Chemistry Module 2 – GSKCHEM2

2. **School or partner institution which will be responsible for management of the module**
   GSK

3. **The level of the module (Level 4, Level 5, Level 6 or Level 7)**
   HE Level 4 / NQF Level 7

4. **The number of credits and the ECTS value which the module represents**
   15 credits

5. **Which term(s) the module is to be taught in (or other teaching pattern)**
   Summer

6. **Prerequisite and co-requisite modules**
   *Pre-requisite: GSK/Chem 1 – Synthetic chemistry Module 1*

7. **The programmes of study to which the module contributes**
   This is a recommended module for the Postgraduate Certificate in Professional Development.

8. **The intended subject specific learning outcomes.**
   **On successfully completing the module students will be able to:**

   **Aromatic Chemistry**
   8.1 Understands the theory of aromaticity and is familiar with the special properties which this imparts on aromatic compounds.
   8.2 Is familiar with electrophilic aromatic substitution, including the mechanism, the different substituents which can be introduced, the directing and activating / deactivating effects of existing substituents on further substitution.
   8.3 Understands the synthetic value of directed metalation of aromatic compounds and can provide examples of directing groups.
   8.4 Demonstrates awareness of nucleophilic aromatic substitution, including the severe limitations of the reaction, and of aromatic Sn1 reactions.
   8.5 Can provide details of the formation of aryl metals and of the different metals which can be employed. Is aware of the synthetic utility of such species and can provide examples. Understands how directed ortho-metalation has made a significant additional contribution to the utility of this reaction type.
   8.6 Is aware of methodologies for aromatic nucleophilic and electrophilic amination.
   8.7 Can correctly identify the products of Birch reduction and is aware of the factors which influence reactivity and regioselectivity.

   **Reactions of Heterocycles**
   8.8 Is familiar with the presence of heterocycles in commercial drug molecules and can provide examples.
   8.9 Can correctly identify a number of nitrogen, oxygen, sulphur and mixed heterocycles.
   8.10 Understands the electronic configuration in various nitrogen heterocycles and can use this to predict basicity (or lack of).
   8.11 Able to identify and rationalise the electrophilic and nucleophilic reactivity of heterocycles, including favoured positions for the reactions.
   8.12 Recognises the importance of tautomerism in the reactivity of heterocycles.
   8.13 Is able to provide examples where the metalation of heterocycles extends their synthetic utility, including examples of both ring and $\alpha$-benzylic metalation.

   **Phosphorus and Sulphur**
8.14 Understands the benefits which the lower electronegativity of phosphorus and sulphur (cf oxygen and nitrogen), the longer bonds formed to carbon and the multiple valencies and coordination states bring to organic synthesis and can exemplify.
8.15 Can identify methods for the formation of organophosphorus reagents – reduction of P(V) to P(III) and vice versa, ligand exchange on phosphorus with examples.
8.16 Is able to exemplify substitution (Mitsunobu) and halogenation (PX₅, PX₃, POX₃ etc) reactions. Demonstrates knowledge of the use of phosphorus reagents in olefination reactions – Wittig, Emmons-Horner and Wadsworth-Emmons – and can identify the phosphorus species involved in each.
8.17 Can provide details of phosphorus mediated alkene synthesis, including the Wittig reaction and similar variants. Understands the key role played by phosphorus in these reactions and the way in which reaction conditions can influence formation of cis or trans alkene isomers.
8.18 Understands how sulphur can behave as both an electrophile and a nucleophile in different reactions and can provide examples of each.
8.19 Can provide details of the Julia olefination reactions (Marc or Sylvestre or both) and of Corey’s reagent(s).
8.20 Is aware of the use of sulphoxides as chiral auxiliaries and can provide an example.
8.21 Demonstrates knowledge of the use of dithianes for carbonyl ‘umpolung’, including dithiane formation and deprotection procedures.

Boron and Silicon

8.22 Understands the ways in which the electronic configuration of boron, as an element and in compounds, governs organoboron chemistry – Lewis acidity, acceptance of lone pairs from reaction partners.
8.23 Is able to identify a number of boron based reducing agents and provide details of their relative reactivity / selectivity, including the use of chiral boron reagents for asymmetric reduction – to include hydride reagents and hydroboration.
8.24 Demonstrates knowledge of the use of allylboranes and vinylboranes in organic synthesis.
8.25 Is familiar with the key role which boronic acids play in the formation of C-C bonds and can exemplify.
8.26 Understands how the longer Si-X bond lengths (cf C-X), the increased electropositivity of silicon (cf carbon) and the availability of d-orbitals for penta- and hexa- valency are responsible for the useful synthetic properties of silicon reagents.
8.27 Can provide details of the use of silanes as reducing agents – hydrosilylation, including an asymmetric example.
8.28 Is familiar with the role of silyl enol ethers as stable enolate equivalents, including how these can be generated.
8.29 Demonstrates knowledge of how the ability of silicon to stabilise a β-positive charge makes vinylsilanes, arylsilanes and allylsilanes useful synthetic tools and can provide examples of their use.
8.30 Recognises that silicon can also stabilise an α-negative charge and can provide examples of the use of silicon stabilised anions.
8.31 Is familiar with the Peterson olefination reaction and how different conditions for the elimination step can provide different olefin isomers.

Rearrangements

8.32 Demonstrates knowledge of nucleophilic rearrangements involving an electron deficient carbon terminus, including details of the different migrating groups – alkyl, hydride, carbanion and carbene and can identify 2 named examples with mechanisms (e.g. Wagner-Meerwein, Pinacol, Favorskii, Wolff, Arndt-Eistert).
8.33 Provides details of nucleophilic rearrangements to a heteroatom terminus and can identify examples involving nitrogen (e.g. Beckmann, Curtius, Schmidt, Hoffmann) and oxygen (Baeyer-Villager).
8.34 Is aware of acid catalysed rearrangements around aromatic rings and side chains and can provide 1 example.
8.35 Recognises that electrophilic rearrangements are much less common than their nucleophilic counterparts and that the migration origin for the former is a heteroatom capable of stabilising a negative charge at the \( \alpha \)-position.
8.36 Can provide information on polar sigmatropic rearrangements, specifically either the 3,3 variant (Fischer indole) or 5,5 variant (benzidine).

**Physical Organic Chemistry**

8.37 Understand the concepts and equations associated with the kinetic and thermodynamic control of reactions (kinetics, equilibrium).
8.38 Understand the differences that occur in certain reactions depending on whether they are carried out under kinetic or thermodynamic control.
8.39 Know the approximate pKa values of common functional groups.
8.40 Be able to make an appropriate choice of base for a reaction based on knowledge of the pKa of the material being deprotonated.
8.41 Understand the concepts of solubility and distribution.
8.42 Awareness of the effects different solvents can have on reaction outcome and why.
8.43 Is able to give an example of how a reaction mechanism might be elucidated (e.g. isotope effects).
8.44 Understand reaction rates and key related concepts (e.g. Curtin-Hammett principle, Hammond’s postulate).
8.45 Demonstrate an understanding of the concept of catalysis and effect on rates of reaction.

9. **The intended generic learning outcomes.**

**On successfully completing the module students will be able to:**

**Aromatic Chemistry**

9.1 Demonstrate a thorough understanding of the principles of aromaticity, the classical reactions of aromatic molecules, and their importance in synthetic organic chemistry (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.2 Understand the mechanisms and synthetic applications of catalytic carbon-carbon bond forming reactions onto aromatic systems (e.g. Heck, Still, Suzuki etc.), applying knowledge gained in other sessions of the modules (A2, B1a, B1c, B1d, B1f, B1g)
9.3 Understand the mechanisms and synthetic applications of modern methods used to react amines, alcohols, etc. with aromatic systems (e.g. Buchwald-Hartwig chemistry) (A2, B1a, B1c, B1d, B1f, B1g).
9.4 Select appropriate reactions/methods to achieve the synthesis of selected targets, as appropriate (A1, A4, B1b, B1e, B1h, B2j, Cm, Cn, Co, Cq, Cs, Ct).

**Reactions of Heterocycles**

9.5 Demonstrate an understanding of the fundamental reactivities of the heterocyclic systems discussed, including 5- and 6-membered monocyclic heterocycles, quinolines, isoquinolines and indoles (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.6 Apply this understanding to the design of synthetic routes to key compounds (A1, B1a, B1c, B1d, B1e, B1f, B1g, B1h, B2j, Cm, Cn, Co, Cq).
9.7 Relate the properties of heterocycles with more than one heteroatom to the parent systems, understanding the similarities and differences in reactivities (B1a, B1c, B1d, B1f, B1g).

**Phosphorous and Sulphur**

9.8 Demonstrate an understanding of the principle features that distinguish phosphorous and sulphur-based reagents from others in organic synthesis (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
 MODULE SPECIFICATION

9.9 Show familiarity with a number of synthetically useful reactions of organophosphorous and organosulphur reagents (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.10 Recognise the key properties that influence the outcome of reactions of these reagents, and hence gain an ability to predict the outcome of reactions (including stereochemistry), or choose the most appropriate reagent for a given transformation (A2, A7, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).

Boron and Silicon

9.11 Understand the principle features that distinguish boron and silicon-based reagents from others in organic synthesis (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.12 Show familiarity with a number of synthetically useful reactions of organoboron and organosilicon reagents (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.13 Recognise the key properties that influence the outcome of reactions of these reagents, and hence gain an ability to predict the outcome of reactions (including stereochemistry), or choose the most appropriate reagent for a given transformation (A2, A7, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).

Rearrangements

9.14 Explain the mechanisms of polar rearrangements, in particular as exemplified by key well-known named reactions (e.g. Curtius, Beckmann, Pummerer rearrangements) (A2, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).
9.15 Appreciate the factors influencing the stereochemical outcome of these rearrangements, and apply to the design of synthetic schemes, as appropriate (A2, A7, B1a, B1c, B1d, B1f, B1g, Cm, Cn, Co, Cq).

Physical Organic Chemistry

9.16 Recognise that physical organic chemistry concepts underpin all reactions (A2, A7, B1c, B1d, B1f, B1g, Cm, Cn, Co).
9.17 Appreciate that an understanding of physical chemistry parameters is essential for planning any new/novel reactions (A2, B1c, B1d, B1f, B1g, Cm, Cn).
9.18 Appreciate the factors influencing the kinetics and/or thermodynamics of a given reaction (A7, B1c, B1d, B1f, B1g, Cm, Cn).
9.19 Understand (and where appropriate be able to calculate) key physical parameters such as pKa and equilibrium constants (A7, B1c, B1d, B1f, B1g, Cm, Cn, Co).

10. A synopsis of the curriculum

The module provides a continuing framework of learning for new staff entering the company, primarily recent Chemistry graduates. However, it is also suitable for those who have more industrial experience, but who wish to refresh and build on their knowledge and appreciation of synthetic chemistry. This group may include staff who initially joined the company without a first degree, but who have achieved an equivalent qualification by part time study.

11. Reading list (Indicative list, current at time of publication. Reading lists will be published annually)

- Lecture notes and tutorial questions are normally made available in advance of each session. Further study of the subject is encouraged and this will improve the participant’s skills in efficient and effective literature retrieval and extraction of information.

General


Aromatic Chemistry

Reactions of Heterocycles

Phosphorous and Sulfur

Boron and Silicon

Rearrangements

Physical organic chemistry

12. Learning and teaching methods
This module will be taught by using a lecture and tutorial format; the lectures will be delivered by external academics.
Independent learning hours will include literature searching, private study and assessment work
Total Learning hours: 150

13. Assessment methods
13.1 Main assessment methods
Successful completion of the module will require the participant to pass all aspects of the assessment process. These comprise completed tutorial problems, a written report and a viva voce examination.

The participant will be required to write a report of 2500 words maximum (minimum 2000 words), including chemical structures where appropriate. This report will exemplify how the material covered in at least two sessions from Module 2 has been (or may be) applied to an ongoing GSK research programme. Cross referencing to recently published literature and/or internal/external lectures would also be required.

The viva voce examination will be conducted by two selected senior/experienced members of staff, who are also likely to have an active involvement with our recruitment of PhD/Post-Doc qualified
chemists, and thus a good appreciation of the level of knowledge and understanding we wish to assess. To initiate the detailed science-driven discussion, the participant will be asked to discuss a particular topic of their own choosing (using visual aids, as required). Through detailed scientific questioning, the assessor will seek to establish that the participant has appropriate knowledge and understanding at Masters level. The participant will be expected to defend their position during detailed chemistry questioning. Furthermore, the assessor will seek to establish understanding of a range of material covered in other sessions of Module 2. The focus will be on a high quality issues-led discussion and debate, rather than a pre-set list of questions to be covered. This is an established practice at GSK.

The assessors will write a formal report, indicating whether the participant has successfully passed the module.

Clear guidelines and training where appropriate, will be provided to the assessors on how to conduct the viva voce examination, and the expected level of knowledge and understanding that the participant is required to demonstrate in order to pass the module. This will clearly be directly related to the Learning Outcomes described above.

The External Examiner will have access to:

- The participant’s worked solutions to tutorial questions
- The participant’s report
- The participant’s visual aids for viva voce examination
- Assessors’ report
- Any additional examples where the knowledge acquired has been applied in the workplace.

14. Map of module learning outcomes (sections 8 & 9) to learning and teaching methods (section 12) and methods of assessment (section 13)

<table>
<thead>
<tr>
<th>Module learning outcome</th>
<th>8.1 – 8.45</th>
<th>9.1 – 9.19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning/teaching method</td>
<td>Hours allocated</td>
<td></td>
</tr>
<tr>
<td>Private Study</td>
<td>120</td>
<td>X</td>
</tr>
<tr>
<td>Lectures</td>
<td>18</td>
<td>X</td>
</tr>
<tr>
<td>Tutorials</td>
<td>12</td>
<td>X</td>
</tr>
</tbody>
</table>

| Assessment method |  |  |
| ----------------- | | |
| Report           | X | X |
| Solutions to tutorial problems | X | X |
| Viva voce        | X | X |
15. Inclusive module design

GSK recognises and has embedded the expectations of current equality legislation, by ensuring that the module is as accessible as possible by design. Additional alternative arrangements for students with Inclusive Learning Plans (ILPs)/declared disabilities will be made on an individual basis, in consultation with the relevant policies and support services.

The inclusive practices in the guidance (see Annex B Appendix A) have been considered in order to support all students in the following areas:

a) Accessible resources and curriculum
b) Learning, teaching and assessment methods

16. Campus(es) or centre(s) where module will be delivered

GSK Stevenage

17. Internationalisation

Chemistry is an international subject with new compounds, reaction pathways and techniques which are discovered, developed and refined by scientists across the globe. Mastery of the subject-specific learning outcomes will equip students to apply the theories and techniques of this module in a wide range of international contexts. GSK is large multi-national organisation which enables students to appreciate the international aspects and benefits of scientific research and development. In compiling the reading list, consideration has been given to the range of materials that are available internationally and a selection of texts has been identified to complement the delivery of the material.

18. Partner College/Validated Institution

GSK Stevenage

19. University School responsible for the programme

Physical Sciences