Question by Question Report for Part III 2024

IDPs

For each IDP course a student takes, they answer two 45-minute questions. These are marked out of 25 and the totals added. This total mark is then scaled and contributes to Paper 1 and Paper 3.

Atmospheric Chemistry and Global Change (Chiara Giorio)

Q1- this question was answered well by the majority of the students and the average mark ended up being above target. There was a mistake in the paper but I believe it was caught and communicated on time as it does not appear to have negatively affected any student. Part b of the questions had the highest average mark (86.9%).

Q2- the students found this question more challenging and the average mark is below target. Part a of the question (recalling concepts from the notes) as well as part ciii (calculations of lifetime of Ox) were not answered well in general (average mark below 25%). Part b of the question was answered well by the majority of students (average mark 90%) while the other parts were around the target average. There were two mistakes in this paper on part c of the question. I have assigned more marks for correct equations and fewer marks for numerical answers. In a couple of cases, it appeared that the student did not receive all the corrections in time so I took that into account in the marking.

Q3- This question was more focussed on deriving expression related to aerosol-climate interactions rather than chemistry. This question was answered well by the majority of the students and the average mark ended up being above target. Part bi and ci were answered very well by the majority of students (average marks around 88-95%).

PAPER 1.

Question 1. Advanced Polymer Chemistry.

The students did well on part (a) but often polymer end-groups were not considered. In (b), most students had the right idea but failed to mention why the polymer would planarize in the solid state. In part (c) students in general had difficulty understanding the chemical transformations that were occurring. Most students understood a D-A cycloaddition was occurring but did not realise that a second cycloelimination could occur to give a fully conjugated polymer. The justification of band-gap changes with structure was mostly OK as was the discussion on GPC elution times.

Question 2. Inorganic Materials

Parts (a) and (b) were done well by almost all candidates although not many put the g value for Ni(II) in context with the many examples encountered in the lectures and supervisions. Most candidates also answered (c) well, recognising that the cluster is unfrustrated. Almost all candidates were able to draw appropriate molecular orbital diagrams to rationalise ferromagnetic and antiferromagnetic coupling but fewer commented on the low temperate at which χT deviated from its limiting high-temperature value and the relationship to the weak coupling. There were fewer good answers to part (e) with candidates missing the competition between the short, strong ferromagnetic pathway and the longer, weaker antiferromagnetic ones. Part (f) was the most challenging, with few candidates able to rationalise the data by reference to the fiel-dependence of the magnetic ground state, which has been covered frequently in a number of other contexts.

Question 3. Bio-inorganic Chemistry

Disappointing answers to, particularly, parts a and b, meant that no one got close to maximum. Both of the topics of these questions were covered in the first 2 lectures and were fundamental to the rest of the course, yet no one identified the correct answers. Part a was particularly poorly answered and showed the students are pre-programmed to regurgitate answers to related questions they have seen before.
In part d) ii) only one answer considered the role of the tyrosine relegation as part of the mechanism, in addition to protonation of the peroxy species.

Question 4. Soft Matter- from Molecules to Materials

This question was largely qualitative. Most students provided good explanations for the different parts, showing a good understanding of self-assembling monolayers and their role in soft materials.

Question 5. Energy Landscapes and Soft Matter

(a-d)
This question had a good range of marks, although the average was slightly lower than expected. A contributing factor was that many answers to the "bookwork" parts (a, d) lacked detail and explanations were not very clear. Parts (b, c) had mostly good attempts; many students had a good grasp of the scientific ideas but made small mistakes in the algebra.

Question 6. Stereo-controlled Organic Synthesis

6a (i): Large spread in answer quality. Many students ambitiously used the unprotected iodoethanol as the terminating electrophile without realising that the enolate would simply be protonated instead. Students electing to trap the intermediate as a silyl enol ether would find that it is quite an unreactive nucleophile towards alkylation. The use of a tosylated iodoethanol may be possible in theory, but in practice would be marred by poor chemoselectivity/side reactivity (e.g. dimerisation).

6a (ii): Generally well answered. The best answers discussed why the cycloreversion gave the E olefin as the major product.

6a (iii): Generally well answered. The best answers discussed that geometric constraints from the tether leads to the observed exo-selective product arising from [4+2] cycloaddition

6(b): Many people got the right idea of an acid-catalysed cyclisation with an intermediate cation and an NBS-like electrophile. The location of the double bond in the product is an important feature of the reaction. The selectivity in part (ii) was more challenging: the product suggests the rate determining step.

Question 7. Computer Simulation Methods in Chemistry and Physics

This question was answered excellently by four responders and satisfactory to well by the rest. The mean mark was 14.1 and a standard deviation of 4.4. Students were deducted marks if their answers were just factual, e.g. "the structure factor of the solid has more defined peaks than that of the liquid" and failed to provide a detailed explanation as to why that happens.

Question 8. Main Group Organometallics

a) i-iii

The mean mark was 6.0/10 for part a. Generally, the question was done quite well.
Part i) proved mixed. Identifying **1** was generally straightforward. Dearomatised **2** proved somewhat more difficult, with many candidates not doing the required 1,2-addition and several of those who did, gallating the ring instead of the N, which overlooked relative electronegativity. There was some confusion over gallium bonding; neutral, trivalent in **2** and anionic, tetravalent in **3**/**4**.
Part ii) was quite variable. Many candidates offered a 4-membered ring containing LiC_2Ga but added little other detail to explain stabilisation of the Li. Only a few answers included polymer formation.
Part iii) was generally attempted quite well. The simpler dearomatiation caused more issues even though it's just a one-step process. Perhaps this was because dearaomatising the ring was a less straightforward concept than deprotonating it. The multistep ring-metallation was generally described well, with most candidates grasping how the TMT process worked. The base was correctly identified in most cases. Some candidates drew the whole process in a rather concerted way, that was a bit confusing. However, this was marked correct.

b)

This was generally answered very well with most candidates recognising the mixed oxidation state compound Ga+[GaCl4]- with each Ga+ coordinating to two benzene units as was described in the lecture notes for the analogous chloro-compound.

Relatively few candidates recognised the isoelectronic relationship between the bent, 14-electron Ga(C6H6)22+ unit and the bent SnCp2 system. Full marks were awarded to even an incomplete MO diagram for this system. Partial marks were given to those who at least showed some of the bonding interactions between Ga+ and C6H6. Many candidates showed instead, the MO diagram for a half-sandwich complex.

Most candidates who answered part (b) correctly also scored full marks for part (c), by recognising the lowering of energy due to bending and sp-mixing. Partial marks were given to candidates who discussed things like d-orbital availability on Cr and interactions between Ga+ and GaBr4- providing stabilising interactions.

Question 9. Aromatic Heterocycles and Medicinal Chemistry

This was a popular question and was answered by all candidates who answered either or both of the M9 questions on paper 2. The standard of answers was high, and some harsh marking was needed to achieve the target average mark.

Part (a) - Most candidates had a good idea of what was going on here. However, marks were deducted for sloppy or over-abbreviated mechanisms, incorrect protonation states, and for not explaining the selectivity in enough detail. Conditions are acidic here, so kicking out ethoxide ions (for example) generally resulted in loss of a mark.

Part (b) - This mechanism was well-known, and most candidates picked up all three marks.
Part (c) - Most candidates could work out what was going on and drew a sensible mechanism. Occasionally marks were lost due to mechanistic errors such as doing S_N2 instead of S_NAr, or deprotonating the amine nucleophiles with K_2CO_3 to generate an R_2N^- species prior to attack (very unlikely given the pKa values, and so quite harshly penalised in order to achieve the target average). However, in most cases it was necessary to use the amount of detail given on selectivity to achieve the required mark distribution.
Part (d) - This part was generally well answered, with most candidates recognising an aldol-type process and correctly identifying the product.
Part (e) - Almost everyone picked up the mark here by identifying the required azide.

Question 10. Catalysis in Synthesis

a) This question was generally well attempted and the best answers were able to rationalise not only absolute stereochemistry but also diastereoselectivity as well as how the racemic starting material can lead to high ee in the product through a dynamic kinetic resolution.

b) All candidates were able to have a decent go at this and many saw the disconnections. Accuracy of the answers varied and use of catalytic asymmetric reactions. Most saw the sharpless and some saw that this could be used to send the other stereocentre from the acetaldehyde supplied, rather than trying to use another asymmetric step, using diastereocontrol.

Question 11. Electronic Structure of Solid Surfaces

Part (a) required an explanation of the principle behind NEXAFS experiments, and their application to the particular problem set out in the question. Candidates generally answered fairly well but lost some marks for lack of clarity and/or minor errors (e.g. failing to mention the need for synchrotron light, not distinguishing between sulphur-edge or carbon-edge measurements, etc). In part (b) most candidates identified the data related to inelastic tunnelling spectroscopy and went on to give the correct attribution for peaks in the spectra; occasional marks were lost for a variety of minor errors and omissions that defy easy summary here. Just over half of the candidates gained full marks for part (c) and most others lost only a few marks due to numerical errors when following essentially the correct methodology. Finally, the majority of attempts at part (d) were broadly correct, but again with marks lost for avoidable errors.

Question 12. Chemical and Synthetic Biology

This exam was written by Prof. Bernardes and by myself, and was structured in two blocks, the first one focusing on chemical biology and click chemistry reactivity and the second one in synthetic biology. On one hand and with rare exceptions, (maybe only one student in the entire cohort) all the students achieved almost a perfect score in the first part, so there is very little for me to comment on that part.

In the section related to synthetic biology while the students did well overall, most part of them failed in the question related to designing the overhangs for a Golden Gate assembly using type II S restriction enzymes. To my understanding, this was the most difficult question and was designed to discern top students. The second question that also caused some trouble for the students was the last one, where they had to rationalise the effect of the incorporations of a single nucleotide in a promoter, coding sequence and terminator. This question implied a coherent knowledge of molecular biology and gene expression. Finally, the questions where they had to describe the structure of a plasmid and the differences in transcription and translation between prokaryotes and eukaryotes were answered well.

Question 13. Solid Electrolytes

This was achieved after I re-marked my part (c) in order to try to increase the mark. However, this was so poorly answered on the whole that I felt I could not in all conscience do any more.

Part (a): This part of the question was answered quite well by practically all candidates. Several students did not quote correctly the master equation by making unnecessary assumptions regarding the occupation probabilities, transition rates and number of nearest neighbours.

Part (b): This part was answered moderately well. Quite a few candidates gave the general definitions for the bulk and single-particle diffusion coefficients which were not required. Also, some of the students did not give an explanation for the blocking factor in the expression for the single-particle diffusion coefficient, and nobody stated that it has been derived in the low-density limit of diffusing particles.

Part (c): This part was answered pretty poorly on the whole, with many candidates simply regurgitating (sometimes irrelevant) facts rather than thinking about the answers, and not answering specific aspects (e.g. although the question was explicitly related to batteries for EVs, nevertheless, several candidates instead discussed H2/O2 fuel cells). Most candidates managed to mention some or most of the advantages of solid over liquid electrolytes. Very few correctly answered the question of what are the specific challenges of using solid electrolytes in battery applications. Several identified low ionic conductivity as a problem (but none related this to charging rate); a few identified electrolyte/electrode interfaces as a problem (however, in the context of H2/O2 fuel cells), but didn't relate it to recharge-cycling limitations.

Question 14. Supra-molecular Chemistry and Self-Organisation

Many had a sense that the activation barrier in (a) was key, and articulated this idea well enough for full or almost-full marks. Translating this concept to the asymmetrical rotation in (b) was a bit trickier, with some not bringing to bear the key insight that light absorption allowed for unidirectional rotation. The mechanism in (c) caused a few to stumble, but most got at least partial credit for understanding that chemical energy input allowed for unidirectional rotation.

Question 15. Chemical Dynamics and Machine Learning

Part (a) on scattering theory was only fairly answered by the 7 candidates. Marks were lost in part (i) for not defining the scattering plane. Part (ii) was well answered with all candidates correctly setting up and evaluating the integral. Parts (iii)-(iv) were poorly answered, with candidates forgetting the definition of the differential cross section and only 2 candidates managing to obtain the correct results for the differential cross section in part (v).

Part (b) was poorly answered by the candidates, even though marks could have been gained for writing the form of the restricted partition function (and/or its relation to the potential of mean force) and for recognizing the Gaussian integrals. Surprisingly, part (c.i) and (c.ii) were reasonably well answered, though a surprising number struggled with basic recall of the transition state theory formula for the rate constant in terms of the PMF. Part (c.iii) was relatively well answered, with most students recognizing Kramer's turnover. While most students recognized the dependence on the friction, most failed to consider the effect of the curvature at the top of the barrier.

Question 16. Total Synthesis

The first part was a series of Pd catalysed reactions. Students were expected to provide a mechanism and explain the selectivity of the outcome. This wasn't a difficult question, but the key was detail. Most failed to provide a sufficient level of detail on the mechanistic aspects. Not many provided an acceptable explanation for the chemo and regioselectivity aspects, and virtually no one provided any comment on the ligands that were used, other than the basic notes-type comments. Overall, no outstanding answers but few disasters either.

The second part was about stopping the reaction and providing a rational stereochemical explanation. Most spotted the two reactions needed, although many got them the wrong way round, which was a surprise. Mechanistic and stereochemical detail was generally lacking. Why is a particular enol silane geometry formed, for example. Most provided a reasonable explanation for the rearrangement, but there were very few good attempts at explaining the stereochemical outcome that required an appreciation of what happened in the first step to direct the TS in the second step. Overall, good, but not stellar.

Getting the averages were fairly easy for all questions.

Question 17. Biosynthesis

This question worked well. In (a) the mechanism for forming B from A was in the notes and most students were able to get this right and forming C instead is obvious. D is a bit more challenging but most saw the rearrangment at a late stage that gives the right skeleton.

Part (b) was more challenging and weaker students struggled to get satisfactory answers, thus giving a good spread of marks. Good answers will have recognised that G, H, & I can all be made by the same initial steps with minor variations towards the end of the mechanism and then they could spot that a late-stage alternative cyclisation followed by rearrangement would give F. Students who focussed first on F alone mostly failed to find a way to make it or found a pretty implausible way that had nothing in common with the mechanisms that were needed to form G, H & I.

Question 18. Frontiers of Atomistic Simulation Techniques

General comments: Overall, in my second year of running and marking a course in Cambridge, I have seen some improvement in the quality of the responses compared to last year. Still very few students tackled my questions. Students seemed more comfortable with maths-related questions and for the most part struggled in explaining and writing about principles and concepts in a coherent manner. I think the students should learn to write about principles at an earlier point in the education.

5 students answered this question. The first part (a) on general simulation techniques was answered rather poorly. The students seemed confused by the question and for the most part did not answer the question with appropriate breadth. Parts b-f were answered well on the whole.

PAPER 2.

Question 19. Advanced Polymer Chemistry

The students did very well on parts (a) and (b); only a few candidates had issues identifying the correct end groups on part (a). In part (b) however, a number of candidates assumed use of a specific Ru-based olefin catalyst which was not part of the question and, therefore, did not understand the importance of functionality at both ends of the polymer. Part (c) required students to read the question and understand how a hydroamination catalyst might function with the polymer as well as a hydrogenation catalyst: approximately 2/3 of them were able to do this correctly. Parts (d) and (e) required some critical thinking about both the structure of the formed ABA block copolymers as well as their chemical function w.r.t. external temperature, solvent and/or pH. 15-20% of the students were able to get these completely correct.

Question 20. Advanced Polymer Chemistry

The lack of student responses to this question was surprising considering that the exact mechanism for ATRP of styrene and for MMA were shown in class, as well as phase diagrams for phase separation of a mixture of two homopolymers and what happens when a compatibilizer is added. The final part of this question (f) required students to put together knowledge about changes in hydrophobicity to hydrophilicity of a portion of the copolymer and how this might affect the diblock copolymer's assembly in water. Again, something that was described during the lectures but not explicitly. It is difficult to write a summary about this question as there were only 5 responses, 3 rather poor (5.5, 10 and 11.5) and 2 excellent (22.5 and 24).

Question 21. Inorganic Materials

Part (a) was done well by all candidates with the exception of one who was unable to determine the correct number of *f* electrons. Part (b) caused a few issues with a surprising number of students not seeing that there must be antiferromagnetic coupling between Tb and the ligand due to finite overlap of *f* orbitals with the ligand π^*; this had knock-on effects due to calculating the wrong ground-state spin for which candidates were not penalised. Allowing for this problem, sections (d) and (e) were well answered. Answers to part (c) were rather superficial, with few candidates commenting on why g values of 1.5 and 2.0 turned out to be accurate. Most candidates were able to do a good job of part (f) but almost all answers to (g), which expanded on the same theme, were unfocused and missed the important points.

Question 22. Inorganic Materials

Answers to (a)(i) were rather superficial and not many candidates were willing to discuss *why* the susceptibility goes through an maximum and then falls. In (ii) there were some decent descriptions of the Bonner-Fischer approach to the susceptibility of a chain but some were quite garbled. In (iii)most candidates did a good job of applying mean field theory and discussing its suitability. Part (b) was generally well done apart from a failure to recognise that g for Mn(II) will be very close to 2.0, hence the value for exclusively Co(II) can be determined from the Curie constant. In (c)(ii) some candidates made the problem more difficult than it needed to be by trying to predict the form of the neutron diffraction patterns, rather than focus on what they would look like in different temperature ranges. Despite being very similar to a supervision question, (iii) caused a surprising number of problems.

Question 23. Bio-inorganic Chemistry

Small sample, but given the time I spend discussing reorganisation energy, the answers were underwhelming. Only one student saw the key idea behind part c) which involved partial folding upon metal binding allowing recognition of DNA.

Question 24. Bio-inorganic Chemistry

Remarked to get average down from 19.1 initially. Most students breezed the supposedly more challenging part (b), but didn't answer part c) very well. Only one or two scripts mentioned that the mechanism needs significant ligand changes to the metal and hence will be slower with Cadmium than zinc.

Question 25. Soft Matter – from Molecules to Materials

Q25 focused on polymer behaviour and a discussion of elementary concepts from rheology on the basis of the Kelvin-Voight model. This question was in general well answered, including the numerical part where most students obtained the correct answer.

Question 26. Soft Matter – from Molecules to Materials

Q26 was quite long, but most students were able to complete the entire question well. The focus was on colloid behaviour in fields and associated soft matter concepts, which were generally well understood by the students.

Question 27. Energy Landscapes and Soft Matter

There were three answers to this question. All three candidates managed to complete all parts of the question correctly, and each of them is awarded most of the marks. Clearly this is a self-selected group of students who were confident enough to take on a mathematical question, where it was possible to achieve close to full marks. The formulae in the question probably discouraged less mathematical students from attempting it, so there are no weaker answers.

Question 28. Energy Landscapes and Soft Matter

This question was done quite well. The average is slightly lower than expected but it seems that several students were suffering with time pressure which may account for this. Answers for the "bookwork" questions (a,b) were often rather vague, which tends to lose marks unnecessarily. Question (d) is a tricky derivation but most students made good efforts. In answering (e,f), quite a few students seemed to overlook the previous assumption of part (c), that the particle is tethered to the wall by a spring. In this case an important aspect of the physical motion is that it remains always close to the wall, contrary to what happens for a freely diffusing particle.

Question 29. Stereo-controlled Organic Synthesis

29a: Students should recognise that acetal formation step requires a kinetically-controlled diastereoselective cyclisation onto an oxocarbenium ion. The best performing students drew and analysed competing diastereomeric transition states leading to the major (and minor) products. Second half of the question (LDA + alkylation) was well answered.

29b: Well answered

29c: Most students accurately drew and (crucially) analysed the competing transition states in setting the enolate geometry. While most accurately drew the transition state leading to the syn-aldol product, few considered how the adjacent enolate stereocentre controls the overall facial selectivity in the aldol addition.

29d: Generally well answered.

29e: Many students only considered either regio- or diastereoselectivity in their answer, rather than both elements, which stopped many from achieving full marks.

29f: Generally poorly answered; partial marks were given to students providing some degree of rationalisation. Students needed to fully analyse competing interactions in diastereomeric transition states that contribute to the high selectivity shown. Many students erroneously invoked the Houk Model as the major contributor for diastereoselection, which requires a cis-1,2-disubstituted alkene to achieve very high levels of selectivity, and did not notice severe A1,3 diaxial interactions between the Me group and the OiPr ligands on the boron Lewis acid disfavouring the minor transition state.

Question 30. Stereo-controlled Organic Synthesis

Generally, a high standard of answer.

a) Photochemical electrocyclic, driven by energy from photon which can only be absorbed by starting material. 2πs + 2πs disrotatory Woodward Hoffmann allowed under photochemical conditions. Few people considered why it cannot be thermal (4πa).

b) Good answers on the whole. Find a role for both the Lewis acid and the base. Few people thought about the geometry of the new double bond.

c)i) Straightforward Wittig
c)ii) Acidic conditions. Explain selectivity for carbonyls and double bond as well as mechanism
c)iii) Kinetic vs thermodynamic control is most plausible explanation.

d) The formation of the intermediate F is complex and was marked generously. 2+3 cycloaddition and hydrolysis lead to the product.

Question 31. Computer Simulation Methods in Physics and Chemistry

This question was answered well by many students and excellently by two. Students were deducted marks if their MC algorithm missed key steps, e.g., the computation of periodic boundary conditions were not considered in the estimation of the total energy, or if they were just factual, e.g. "we consider PBC here" and failed to provide detailed steps of how you can actually consider PBC in the algorithm.

Question 32. Computer Simulation Methods in Physics and Chemistry

This question was only answered by two students. One student answered it excellently, the other answered it well. Marks were deducted if the steps in the MD algorithm were not well detailed or were incorrect, also if information was only given as factual, e.g. “sampling improves with simulation steps” but failed to explain why.

Question 33. Main Group Organometallics

The question was attempted by 12 candidates. Marks varied from 3-23, though two were (low) outliers, and excluding these marks varied from 8-23. The mean mark was 13.3 (from 12 scripts) or 15.2 (from 10 scripts). Overall, the question appears to have been quite challenging, largely on account of parts c) and d).
The first part was fairly straightforward and could be taken straight out of the notes. Many candidates scored 3/3 for this part, though some suggested Mg was in group 3.
The second part proved generally straightforward, with only identification of **D** proving a significant challenge. At this point, many candidates suggested a cyclised organomagnesium that formed an adduct with the phosphine instead of cleaving the ring in **B** and then satisfying the exposed Mg with a Cl and the $R(Me)_2C$ with PPhCl. This suggests that maybe the final product (provided in the question) was not really being looked at. Obtaining that from $ClMgC(Me)_2CH_2CH_2C(Me)_2PPhCl$ would be conceptually simple by eliminating **C**.
Parts c) and d) were conceptually quite similar. Generally, the early parts of both questions were handled reasonably, though candidates quickly got confused towards the end of either question. In part c), **E** was generally readily identified, and **F**-**H** were not too problematic, though solvation caused some difficulties and not all candidates considered the possibility of multiple THF molecules being present. Most answers included a reasonable observation about the solid-state structure of **E**(THF). Part d) was rather more complex and proved quite challenging. **J** and **K** were quite often identified, but the spirocycle **I** proved hard to identify (some candidates appeared unfamiliar with the term ‘spirocycle’). Many candidates also struggled to see that $\mathbf{M}_2$ is essentially just solvated **I**. Quite a few answers also included suggestions in which the normal valency of Mg was not obeyed. For example, on several scripts either 1 or 3 groups were attached to Mg without a charge being added. This suggested candidates were losing sight of some basic chemical principles (i.e. that Mg is in group 2) when focusing on getting the addition to work out for the DOSY calculations.

Question 34. Main Group Organometallics

Part (a) was generally answered very well. Most students gave a comprehensive account of the main synthetic approaches and the relationship between higher temperatures and larger cluster sizes. A few candidates mistakenly described organometallic compounds of Al(II).

a) This section introduced a new oxidation state: Al(0). Many candidates did not recognise this and proceeded to describe reactions of Al(I). Those who spotted the neutral Al were able to recognise the presence of an unpaired electron and draw possible structures. The most common form presented was the triangular sp^2 form. Most who also presented the sp form placed the unpaired electon in an sp orbital. Not many candidates showed Al to alkene back bonding and of those who did, most also placed the unpaired electron in the outward-pointing sp orbital.

b) Most candidates presented a symmetrical η^2-type structure similar to alkene binding to a metal centre. Some gave a double addition with two alkyne units. However, they struggled to explain the two different coupling constants giving dd. The stronger candidates did present asymmetrical structures with the unpaired electron correctly located on one of the carbon atoms and two different ^{1}H nuclei giving dd.

c) This was generally answered well with most candidates recognising back-bonding weakening the C-O bond and orbital overlap becoming less effective as the group is descended.

d) Most candidates could recognise the symmetry in the product molecules from the number of NMR signals (for which credit was awarded) but the majority could not deduce the correct structures which matched chemical shifts of the ^{13}C environments. More candidates managed to deduce the structure and mechanism of formation of **E** than **D**, which was a particularly challenging example, having an unusual four membered ring formed by cycloaddition across remote C=C groups.

Question 35. Aromatic Heterocycles and Medicinal Chemistry

The standard of answers was very high, so it was necessary to mark very harshly in order to achieve the target average mark.

Part (a) - Most people recognised this as a standard Vilsmeier acylation and had little difficulty producing a good mechanism. A wide variety of spellings of Vilsmeier were seen, but as the name was not required no marks were lost or gained for this. Many candidates gave a good account of the selectivity, illustrating (with a range of happy and sad benzene rings) how attack at C2 would disrupt the aromaticity of the benzene ring while attack at C3 did not and was therefore preferred. The subsequent alkylation step was also a standard reaction and was generally answered well.
Part (b) - Despite featuring much less in recent tripos questions than the similar van Leusen pyrrole synthesis, most people were familiar with the TosMIC oxaxole synthesis and could give a good mechanism. Where marks were lost it was generally for sloppy or incorrect mechanisms, for example it was not uncommon to 'lose' a negative charge from one of the intermediates. The majority of candidates recognised part (ii) as a Fischer indole synthesis and were able to give a good mechanism. Those who did not proposed some rather exotic chemistry but were still nevertheless able to pick up a few marks for some of the steps. Pleasingly, with only a couple of exceptions, everyone avoided drawing an SN2 mechanism at an acetal (or hemiaminal ether), about which a clear warning was given in IB.
Part (c) - This part of the question was intended to be more challenging, but many good answers were seen. Many candidates were uncertain of the structure of the trifyl group ($CF_3SO_2^-$) and it was common to see trifluoroacetic anhydride or Ts_2O used instead of Tf_2O. There were similar issues with NBS. I had intended these structures (and others, such as Bn) to be included in the question (they were removed by the examiners) and so did not penalise incorrect structures being used on this

occasion. Most candidates were able to suggest a mechanism for the ANRORC-style ring opening of the triflated pyridine, with both ionic and pericyclic versions both being seen (and credited). Many candidates were also able to propose a good mechanism for the bromination step, and a variety of mechanisms (some more plausible than others) were seen for the reclosing of the pyridine ring; anything reasonable was accepted. The most challenging bit was probably explaining the selectivity of the bromination; this was perhaps most simply done by noting that attack at the observed position gives the most conjugated and hence most stable iminium ion intermediate, but other explanations were also considered. The last part was also generally well done. Almost everyone realised that the nucleophile would attack the triflated isoquinoline at C1 and most correctly deduced the structure of the product. As some candidates pointed out, the question should really have specified that the 'one aromatic ring and one non-aromatic ring' said to be present was not including the benzyl groups.

Question 36. Aromatic Heterocycles and Medicinal Chemistry

This question was slightly less popular than Q35 (36 scripts compared to 48). All but two of the candidates attempting this question also attempted Q35. It was generally well answered, though perhaps not quite as well as Q35 as (unlike for Q35) it was not necessary to make extensive adjustments to the mark scheme in order to achieve the target average.

Part (a) – This featured a Knorr pyrrole synthesis. This was covered in the lectures, although perhaps not as prominently as some of the other syntheses. Intermediate D was therefore provided as a hint and to allow candidates to attempt the second part of the reaction even if they could not do the first part. Most candidates knew what to do with the $NaNO_2/H^+$ reagents and successfully identified intermediate B although a few tried to do a nitration instead of a nitrosation. A range of possible tautomers of B were seen, all of which were accepted. Most candidates could make a good attempt at the condensation of D with C to give the pyrrole.

Part (b) - Most people had some idea of what oral bioavailability was about, although in many cases the definition offered was a little too vague or imprecise. Most candidates knew Lipinski's rules but accurately applying them under exam conditions proved difficult and many incorrect molecular masses, numbers of N and O atoms, and numbers of NH/OH protons were seen. The simplest answer for part (iii) (which was given by several candidates) was probably to suggest that the drug might be transported across membranes by a transport protein. However, a number of other explanations are also possible, and anything reasonable received credit. Some candidates wrote rather more than was justified by the single mark available. In part (iv), most people realised that the arginine side chain would be positively charged (although a few candidates drew lysine instead of arginine). No-one spotted that compound F would be likely to be negatively charged at pH 7 as a result of the N-acyl sulfonamide-like NH group being deprotonated, while many seemed to think that the molecule as drawn was already negatively charged (perhaps due to not spotting the formal 2+ charge on the sulfur).

Part (c) - The mechanism of P450 hydroxylation was well known and part (i) was well answered by almost everyone. The N-dealkylation in part (ii) was also generally done well, while a range of possible mechanisms, some more plausible than others, were proposed for the formation of metabolite L. A process similar to the paracetamol oxidation discussed in the lectures was the expected answer (and, indeed, some candidates did note the similarity to paracetamol) but other possible routes were also accepted. For the final part, the expected answer (metabolism leading to L) was chosen by just over half of the candidates. K also proved a popular choice, with the acetone byproduct or (less commonly) the secondary amine product of the N-dealkylation being proposed to give rise to toxicity. Credit was given for any answer that was sufficiently justified.

PAPER 3.

Question 37. Catalysis in Synthesis

a) This question was generally well attempted although care needed to be taken to follow through the various intermediates and not make mistakes in the carbon frameworks of the final structures, which was quite common.

b) Generally the role of pi allyl palladium chemistry was well appreciated here. Clearly indicating the stereochemical course of part ii in terms of inversion with oxidative addition and external attack on the pi allyl intermediate differentiated students to some extent.

c) Most candidates saw the basic premise but there was variability here in the details such as where transmetallation first occurs and the need to preserve the geometry of the double bond during this. Quite a few made mistakes in this aspect although some realised for the second part and corrected.

d) Many candidates found this challenging and failed to see the possibility to form a cation adjacent to the alkyne if the latter were cobalt complexed. This could then be used to initiate an epoxide opening cascade. Credit was given for reasonable attempts using other approaches.

Question 38. Catalysis in Synthesis

a) A good proportion of students saw that this needed a chiral lewis acid to activate the aldehyde to attack by the silyl enol ether and many of these chose chiral boron compounds. Some tried to use organocatalysis which was not productive pathway as would not be able to regenerate catalyst although reasonable credit was given for rationale of TSs.
b) Some proportion of students saw that the product was derived from Sharpless epoxidation of a symmetrical bis allyic alcohol and that this could be derived from the SMs given quite readily, through HWE. Others didn’t see this and provided other asymmetric oxidation methods that would be less suitable.
c) Candidates saw to varying degrees the various important points here which involved identifying quadrant diagram, that curtin Hammett is in operation as its Rh dipamp and that H2 comes from the same face as the metal. Credit was given for plausible fitting of the substrate into the quadrant diagram and highest marks went to those who identified all of the above aspects.
d) Most candidates got this to some extent, especially given the clue provided relating to epimerisation of the alpha chloro aldehyde. A few tried to do the opposite way around which was not productive, but on the most part well done with variation in how well things were rationalised and the dynamic kinetic aspect explained.

Question 39. Electronic Structure of Solid Surfaces

Part (a) required a qualitative explanation of the purpose and operating principle of the Mott polarimeter, as covered in the notes and lectures, and most candidates scored well; dropped marks were mainly the result of minor slips and/or lack of clarity. Part (b) was more challenging, requiring manipulation of a model density-of-states function that was similar (but not identical) to one seen in the supervision questions. Just over half of the candidates gained full marks here, and most of the remainder lost only a few marks due to relatively minor slip-ups. Marks for part (c) were generally quite well correlated with marks for the preceding part, since the underlying concept of the question carried through. Performance on part (d) was rather variable, with roughly a third of candidates gaining full or nearly full marks and roughly a third gaining none or very few. The concepts involved were similar to those invoked in parts (b) and (c) but in a slightly more convoluted situation, hence the slightly lower marks here. Finally, part (e) was probing for an account of the extended Blyholder model, as discussed in the notes and lectures, but while most candidates correctly realised this, there was considerable variation in the clarity of answers and the degree to which the general idea was linked with the specific example in the question.

Question 40. Electronic Structure of Solid

Part (a) proved tricky, with no candidates achieving full marks, reflecting the fact that most failed to spot that the work function of the surface changes when the initial oxide layer is removed. Amongst those that grasped this essential point, marks were lost through lack of clarity or other minor errors. Conversely, parts (b), (c) and (d) required relatively straightforward interpretation and calculation, meaning that all but three of the candidates gained full marks. Part (e) was only slightly less well-answered, with nearly three-quarters of candidates gaining full marks and most others losing out only due to small slip-ups. There was more variability in part (f) despite this requiring only discussion of an experimental technique covered in the notes and lectures; the main discriminator, however, was clarity and accuracy of expression, rather than fundamental lack of understanding. Finally, in part (g) most candidates were able to give reasonable accounts of the various types of surface-localised states that might occur, and amongst these to rule out image and Tamm states on sensible grounds; full marks required them also to point out that any Shockley states would exist only as surface resonances due to the lack of a gap in the bulk projected states.

Question 41. Chemical and Synthetic Biology

I had 31 students completing this question, with a median mark of ~15. This is slightly below what I would expect since a number of students had difficulties in some questions I considered to be more accessible. For example, a)i) proved more difficult than expected. We did speak about the roles of sodium ascorbate and THPTA in Cu(I)-catalysed azide-alkyne cycloadditions but many students had difficulties in this question. Also a)iii) led to some less well structured answers with some examples of students showing a disulphide doing a Michael addition???, The harder of the questions b)ii) saw some good answers. This may be a result of the focus on the iEEDA topic in lectures which seemed to be really attractive to the students.

Overall, the main concepts discussed in the lectures were well understood, in particular, the topic on the IEDDA and its properties as a bioorthogonal reaction.

Question 42. Chemical and Synthetic Biology

In my opinion and based on the results, the students overall understood very well the topics discussed in the lectures. I would say that they acquired a good knowledge of synthetic biology with a special emphasis on a) methods to assemble DNA fragments (molecular cloning), b) differences in the use of bacteria, yeast and mammalian cells in the context of synthetic biology, and c) approaches to improve protein expression.

I was surprised that one of the questions that most students failed was related to writing the optimal sequence of DNA to express a specific peptide sequence. The chart with percentage usage of the codons was provided, but the students did not convert the codons to DNA, or misplaced an Adenine for Uracil.

Question 43. Solid Electrolytes

This question was disappointingly answered by the few students who attempted it. The question extended the discussion of the structure of amorphous (glassy) solids given in the lecture course, from germanium to phosphorus, thereby including the possibility of a molecular (P_4) glass as well as a cross-linked (red-P) random network.
(a) All students recognized the similarity between the layer-like crystalline polymorph, black P, and graphite in terms of atomic intercalation in battery anodes.
(b) No candidate successfully identified the $G(r)$ pair-distribution function for hypothetical amorphous white P as being a delta function at the (single) intra-molecular P-P bond length in a P_4 molecule, assuming there to be no inter-molecular correlations in the ideal disordered structure of this material.
(c) The requested derivation was book work, except that in the lectures, the expression for the structure factor, $S(K)$, as a function of the Fourier transform of $G(r)$, was not given explicitly.
(d) No student correctly sketched $S(K)$ for the case of a delta-function $G(r)$, corresponding to (b), viz a damped sinusoid, oscillating around unity and tending to zero as $K \rightarrow 0$.
(e) This part was patchily answered.
(f) Several students answered this part correctly.
(g) No student gave the correct answer for the second-neighbour coordination number (viz. 6) for amorphous red P, when a simple sketch of the atomic arrangements would have revealed the answer immediately.

Question 44. Solid Electrolytes.

There were 2 typos in Eq.(2) and Eq.(3). The very first symbol, ∂, should not be present in both equations. I suspect that the typos originated from retyping my original Latex version of the question into word document. Also, this year the examiners did not have a chance to check their questions before forwarding them to print, so that there was no chance to correct the typos.

This question did not cause many difficulties for the majority of candidates.
Part (a) was very straightforward and only very few candidates did not use an appropriate value for the activation energy barrier.
Part (b) was also very straightforward. However, in part b(i) not many candidates identified n with the probability density function. Part b(ii) did not cause practically any difficulties, although a few candidates did not explain why the expression in the exponent should be dimensionless. Part b(iii) could be answered by two ways: by using a definition of the variance for normal distribution or by substitution of the solution into original equation and finding the variance. Quite a few candidates followed the second not optimal rout.
Part (c) and especially part c(ii) was the most challenging one and only a few candidates managed to find an explicit expression for function of two dimensionless variables.

Question 45. Supra-molecular Chemistry and Self-Organisation

Many got the nuclearity of the macrocycle in part (a) off (trimer, not dimer or tetramer!) but managed nonetheless to come up with good answers for the other parts of the question. Some basic chemistry stumbles (nitrate with a lone pair on N!) led to difficulties with aspects of the question.

Question 46. Supra-molecular Chemistry and Self-Organisation

Several students had problems with the maths that would have allowed them to figure out the stoichiometry of the assemblies that form. These problems propagated through the question, although credit was granted where reasonable inferences were drawn based upon incorrect product structures.

Question 47. Chemical Dynamics and Machine Learning

This question was well attempted overall, with 6/7 of the scripts scoring a 1st or high 2.1. All candidates found parts (a), b(i) and b(iii) to be straightforward, although a few candidates neglected to substitute for <xR(t=0)> in b(i). Few candidates gave a completely satisfactory account of the timescale separations involved in the answer to b(ii). Part b(iv) was found to be more challenging, although 3 candidates gave good answers.

Question 48. Chemical Dynamics and Machine Learning

This is the second year of this half of the Chemical Dynamics course. Two students attempted the question, with both achieving greater than 70% (one very much so).
Part (a) examined knowledge covered in the lectures, and was well answered by both candidates. Part (b) also examined knowledge of the physical interpretation of the form of the correlation function (i.e., the correspondence between exponential decay and the Markovian approximation) and was reasonably well answered. The first part of (c) was an extension of the (a) to a perturbing force not explicitly encountered in the lectures. One candidate did not see the need to use the more general form of the response function derived in (a) and instead attempted to use the formula appropriate for (the different) perturbing force specified in (a). Both candidates did well on the final two parts of (c).

Question 49. Total Synthesis

Generally answered fairly well. The difficultly of the question lay in three parts (a), (e) and (f).

(a) Involved a ‘how do you make the starting material’ problem, which naturally attracted a lot of variety. A couple were excellent, most a bit long winded but acceptable and a few were fraught with problems

(e) the reality was this the crux to this question was heavily covered in the lectures and yet it was surprising how few got it completely right. Instead, many got there by a protracted process, which was credited with most of the marks but not all. Some came up with some rather ‘inventive’ solutions. Only a few made no effort and so most of the attempts accrued marks

(f) probably the hardest part because it used uv light to generate radicals, a couple got it, but most failed to appreciate the light and radical aspects

Marking to the average was fairly easy. No disasters, one very good script, a couple of very good ones and then most hovered +/- two marks from the average

Question 50. Total Synthesis

With the low numbers answering this question, nothing is statistically relevant. I actually thought this was a slightly easier question and was surprised more people didn't answer it.

(a) This was easy and most people got it right with a couple of aberations…..
(b) Not many provided the detail required in terms of mechanism. Only one student spotted the intramolecular Diels Alder and very few ended up at the right product and most stopped at an isomeric product having failed to spot the reactivity patterns. Arguably, I could have provided another clue, but I thought it would be fairly obvious. So overall, a rather averagely answered question
(c) This was also not very well answered and I thought this was fairly logical. If they could identify which C-H bond was most acidic, the rest should have been fairly straightforward as it was just a series of Michael additions. Many made this very difficult for themselves by not applying logic.
(d) Again, average. The number of people who are seemingly incapable of spotting what should be an obviously over strained product was remarkable. Most failed to notice that C–N bond formation would give an impossible structure, but because that's what they learned that's the way they went. I think only two got this right.

Overall, this was a logical set of questions that in reality, could have all been answered very well. Instead, it was generally very average. I was surprised.

Question 51. Biosynthesis

Only 4 students attempted this question and it was poorly done. With such low numbers, one cannot know if these were weak students or the question was too hard.

In (a) three of the students saw that B could be made from 2 molecules of A but none saw that C could be too and that a fairly simple late-stage modification of the pathway to B would give C. In retrospect it would have been sensible to give the students a bit more help (a) by telling them that the proposed pathways to B, C & D all start from two molecules of A, and (b) by drawing C in chair-form so it looked more like B (or by drawing B and D so they looked more like C).

In (b) none of the students interpreted the spectrum correctly. One skipped this part, one concluded all 8 carbons are labelled, and the other two correctly deduced that six carbons were labelled but either did not try to analyse the couplings or got them wrong.

All students got some marks for (c) but were too vague to get full marks.

Part (d) was answered well.

In (e) students were meant to come up with a minor modification of their previously suggested pathways that made them consistent with the information in (a), (b), (d) and (e). None of them managed this. One said their previous pathway was consistent (which it wasn't), one skipped this part, one could see their proposals were not consistent but could not suggest any alternative, while the fourth came up with a modification that made one half consistent but not the other.

None of the students tried to show how lysine plus E (known precursors of both halves) could be converted into A (a known precursor of one half).

One script was unfinished and got low marks, which accounts for the low average.

Question 52. Biosynthesis

Part (a) was answered quite well. All recognised the polyketide origin of A, though a couple thought the aromatic ring would be of different origin, which it is not and which does not work well. All but two showed they knew the basic steps of polyketide chain extension. Some did not explicitly answer the last question in this part but they only lost one mark if the pathway they had shown would imply the correct answer. For formation of the ether linkages I thought good students might come up with the epoxide-opening cascade by themselves but only one student did and said that was because they had seen it in a textbook. However only one mark was lost if students could suggest a not-so-good but still plausible alternative, which most did.

Parts (b) and (c) were poorly done as many did not think through the implications of the pathway they had shown for retention or loss of deuterium atoms and/or were unaware the need in places to epimerise R-centres to S-centres (with loss of deuterium) in propionate-derived units.

Part (d) required students to say how deuterium could be detected in (c) as well as with the precursors mentioned in (d). Many failed to do the former and lost half of the marks.

Part (e) was badly done with only a couple of students remembering the succinyl CoA to methylmalonyl CoA rearrangement (which was in lectures).

Several scripts were unfinished and got low marks, which accounts for the low average.

Question 53. Frontiers in Atomistic Simulation Techniques

General comments: Overall, in my second year of running and marking a course in Cambridge, I have seen some improvement in the quality of the responses compared to last year. Still very few students tackled my questions. Students seemed more comfortable with maths-related questions and for the most part struggled in explaining and writing about principles and concepts in a coherent manner. I think the students should learn to write about principles at an earlier point in the education.

Only 2 students answered this question. They put in good/decent answers. It’s hard to tell why the question was so unpopular.

Question 54. Frontiers in Atomistic Simulation Techniques

This was attempted by 6 students. Students did fairly well at this question making valiant attempts at both part a (DFT) and part b (machine learning). One student did particularly well, showing a very pleasing command of the material and a clear ability to answer the questions with both words and maths.