

## Part III Questions Reports from Markers Jun 2021

### Paper 1 – questions are marked out of 20

#### Question 1

The students did reasonably well on this question and were able to readily identify the polymers prepared from a set of monomers and reaction conditions. They also were able to explain the differences between the growth kinetics for a standard polycondensation (step-growth) vs a metal catalysed chain growth polymerisation. The students were mostly able to recall the cis/trans isomerisation of polyacetylene (c). A small percentage deviated considerably from this answer and suggested incorrect cyclisations. Few students were able to give convincing and comprehensive suggestions for proving this chemistry has occurred, that vast majority correctly stating that you could measure the electrical properties (which is not a very direct method of proving double bond geometry). However overall the students performed relatively well overall on this questions demonstrating a good overview of different types of polymers and their chemistry.

29 attempts, average mark 15.6, std.dev. 3.3

#### Question 2

Part (a). Most candidates gave good descriptions of the antiferromagnetic chain behaviour seen for  $x=0$  and a few carried on to explain the doped behaviour too. Many misinterpreted the strong increase in susceptibility with decreasing temperature as ferro- rather than paramagnetic behaviour.

Part (b). This was generally very well done with almost all candidates able to see the correct ground state. Application of the Lacorre equation was patchier with some sign and arithmetic errors, but overall a good performance.

27 attempts, average mark 12,3, std.dev. 3.9.

#### Question 3

This Q was a different format from previous years, with 9 separate short answer questions covering a wider range of the course content. I had warned the students of this. It generally worked as a means of generating a wider distribution of marks than previous years. Most questions required recall of mechanistic information or concepts. Most answers were the length I expected – some students wrote way more than necessary. There were no great issues with any part of the question and none were misinterpreted. There were a couple of scripts from students who can't have attended the course.

29 attempts, average mark 13.4, std.dev. 3.0, Max 20, Min 7.5.

#### Question 4

This question was answered very well by most students. In part (a), most gave very good explanations of the information that can be obtained from the PDF. Part (b) the students were given three sets of data to try and make sense of the material. Whilst the question was phrased to try and lead the students through (EDX, ED, XRD), some students tried to tackle the XRD straight away which lead to some difficulties. The EDX was generally very well done, with most students getting full marks or nearly full marks from those available. Likewise – the identification of the tetragonal phase from the electron diffraction pattern was well done. Most students then lost marks trying to bring this information together to explain the XRD.

Some students realised that the XRD can then be used to identify the second phase, and located the FCC pattern within it. Very few commented on the relative intensities of the two phases (relating to the concentration) or the relative peak widths (allowing a comment about the relative size of the crystallites). Almost no-one used the tetragonal lattice parameters to calculate the positions of the peaks expected in the tetragonal phase and realised that the material appears to be BCT, due to the fact that with X-rays the Ni and Zn are almost indistinguishable.

21 attempts, average mark 13.9, std.dev. 3.3.

### Question 5

Soft Matter: parts a,b,c,d

This question covered fairly standard material (except for (c)) and was done quite well. In particular: (a) had some nice explanations. The computations in (b) were mostly accurate. Most students didn't realise that the electrostatic term in (c) means that a macroscopic crystal is no longer the state of minimal free energy (instead a finite cluster minimises the free energy). Answers to (d) were mostly quite comprehensive.

For the energy landscapes parts e to g the answers covered the full range from poor to excellent. Nearly all the candidates were able to describe the master equation approach in part e. Most of the candidates realised what the equilibrium conditions were in part f, but only a few of them solved the simple detailed balance equations properly. For part g, only a couple of candidates remembered that the sum of eigenvalues is the trace of the matrix, although the zero eigenvalue for equilibrium was recalled correctly by more of the class.

15 attempts, average mark 11.9, std.dev. 3.4.

### Question 6

38 answers. (a) This question proved to be reasonably well done, particularly in providing clear 3D representations of stereochemistry. There was a distinction between a very good answer (correctly assigned configuration of the new stereocentres and convincing conformational representation of transition states), a satisfactory answer (half correct) and answers where the assigned configuration was incorrect but the overall mechanism was at least plausible. This led to quite a wide distribution of marks as intended.

(b)

38 attempts, 12.6 average mark, std.dev. 3.1

### Question 7

The question was answered by 10 students with a mean of 16.35 and a SD of 2.70. Most students showed good understanding of the methods for numerical integration, with most mistakes/misunderstandings shown on section b) where they had to write a pseudo code for Monte Carlo integration, and in c) where they had to discuss weighting functions and importance sampling.

10 attempts, average mark 16.4, std.dev. 2.6.

### Question 8

(a) was done moderately well. Mean mark 6.1/10

(i) Complex **B** was correctly identified by quite a few candidates. Those who struggled with it often didn't chelate the carboxylate group and instead used the N (or in some cases a C) to bond to Li.

(ii) The essential structure of **C** proved straightforward. However, there was a wide variation in explanations of relative M-O bond lengths and many candidates failed to relate the longer bonds to ligand chelation. Several answers clearly were influenced heavily by the diagrams of  $t\text{BuLi}_4$  in the lecture handout. Few answers drew parallels between the 8-membered ring in **B** and the transannulation of the 8-membered rings making up the dimeric components in **C**.

(iii) Most candidates got one mark for this, though many failed to see the link between greater ionicity and reduced bonding directionality.

(b) This question was a simple recall of information from the lecture notes. Most candidates knew the central concepts, though the level of detail and explanation varied *e.g.* inclusion of labelled MO diagram.

(c) Most candidates had a decent recall of the structure of  $\text{Ga}_2\text{Cl}_4$  when dissolved in benzene though very few remembered the formation of a Ga-Ga bond in the presence of a donor ligand. Credit was given to chemically sensible structures such as  $[\text{GaCl}_4]_2[\text{Ga}(\text{dioxane})]_2$ .

(d) Very few could arrive at the correct structure for  $(\text{RGaCl})_4$  and none could remember the structure of  $\text{S}_4\text{N}_4$  which was covered in 1B. Even without knowing the structure, very few candidates could show the subunits were isoelectronic. Marks for this part of the question were reduced with more credit being awarded to part b.

21 attempts, average mark 12.5, std.dev. 3.1.

### Question 9

All candidates who answered either or both of the M9 paper 2 questions also attempted this question, as did one additional candidate. This question was generally well answered, so some harsh marking was needed to give the target average.

(a) Most candidates could make some progress with this pyrazole synthesis, but relatively few realised that the product of step (i) would be a Michael acceptor (Knoevenagel condensation product). Frequently the product after the first step was implied to be an acetal, which would then not be expected to react with the hydrazine in the second step. Most candidates made at least one sensible comment about regioselectivity, although it was rare for all aspects to be commented on. A few candidates generated the wrong regioisomer in their mechanisms (due to having the terminal N of the hydrazine attacking the trifluoromethyl ketone) and apparently did not notice that their product was different to that given in the question, perhaps not helped by writing "TM" after their final arrow rather than actually drawing their product. There were also other instances throughout the question where candidates wrote " $\rightarrow$  TM" at the end of their mechanism when the curly arrows of their last step did not give the TM, and in general it would seem wise to actually draw the product of the last step in order to avoid this kind of mistake.

(b) Most candidates realised that this was some kind of van Leusen or Barton-Zard style synthesis and were able to produce a good mechanism. The most significant error was to omit the negative charge on the  $\text{sp}^2$  carbon following the cyclisation step. There were also some interesting representations of the carbonate ion, including as  $\text{CO}_3^-$  (not  $2^-$ ), and with a lone pair on carbon acting as a base to form  $\text{H}-\text{CO}_3^-$ .

(c) This question featured a Pfitzinger quinoline synthesis; as this was not covered in the lectures a particular mechanism was not required and the task was simply to devise a plausible suggestion. A wide range of mechanisms were proposed, and all reasonable suggestions were accepted. Besides the generally accepted mechanism (amide hydrolysis,

enamine formation, cyclisation), these included various aldol reactions before or after the amide hydrolysis, or the first step being the (deprotonated) amide nitrogen attacking the ketone. A few candidates got stuck (often because their first step did not help them get to the product, for example if they began by having the enolate of the ketone attacking the amide of the isatin). Otherwise, any lost marks were mainly due to over-abbreviated mechanisms and incorrect protonation states (including the appearance of protonated alcohols despite the basic conditions).

(d) Most candidates recognised a Fischer indole synthesis and were able to produce a good mechanism, but a substantial number did not and hence were not able to make significant progress. The latter often began their mechanism with the aniline attacking "NO<sub>2</sub><sup>+</sup>" (or occasionally NO<sup>+</sup>) on the benzene ring, and then proposed some rather exotic mechanistic steps to get to the product. Those who followed the Fischer synthesis generally scored well. Most candidates had some idea of how to remove the Boc group and picked up some credit here.

47 attempts, average mark 12.9, std.dev. 3.5, Max 18, Min 4

### Question 10

For part (a), a good proportion of students spotted that the C-Cl would be the weakest and most likely to undergo oxidative addition with the Pd(0) complex formed. From here there were several plausible options that candidates could have explored, and appropriate credit was given. Heck type pathways were one option although top answers saw that this created a situation in which the necessary beta hydride elimination would not be possible and so alternative pathways would need to be found. Appropriate credit was given for reasonable answers.

For part (b), almost all students saw that an enamine would be formed and there were a variety of answers from this point forward. Very good answers would explain that the enantioselectivity outcome depended upon what side the enamine forms on before capture by the electrophilic oxidant. Credit awarded for reasonable rationales of selectivity.

34 attempts, average mark 13.2, std.dev. 3.1

### Question 11

Most students gave overall good answers. Determining the size of the adsorber polymer was challenging for some students.

28 attempts, average mark 13.6, std.dev. 1.84.

### Question 12

Twenty-seven candidates attempted this question, achieving a quite disappointing average mark of just 10.22. The range of marks was extremely broad, however, spanning from 1 to 19. In fact, the distribution of marks was somewhat bimodal, with a peak around 9-11 marks, and a secondary peak around 16 marks. Parts (a), (b) and (c) appear to have presented a variety of challenges to several candidates, with errors including: (i) failing to count correctly the number of atoms of each type in the unit cell; (ii) failing to count correctly the number of dangling bonds associated with each type of atom; (iii) failing to count correctly the number of electrons in each dangling bond, especially when the structure included some homonuclear bonds; and (iv) failing to consider charge transfer between atoms as a means of eliminating partial occupancy of dangling bonds. Arguably,

the geometry involved in this question was a little trickier than that involved in, say Q12 from Paper 1 in 2019, or Q13 from Paper 1 in 2016, so candidates who had considered those past papers ought to have been able to achieve reasonable marks here. It is interesting to note that the number of candidates tackling this question slightly exceeded the number of candidates who sought supervisions for this course.

27 attempts, average mark 10.2, std.dev. 3.9.

### Question 13

This question was answered well, in total thirty one candidates answered this question. The highest mark was 17.5/20 and the lowest mark was 9.5/20. Part (a) of the question was answered well. Part (b) was answered well but a number of candidates failed to recognise the covalent warhead on the PROTAC molecule. Part (c) was also answered well but the level of explanation in this part of the question varied. The lowest mark of 9.5/20 did not have enough written for their answers throughout their question. Overall I was happy with how this question was answered.

31 attempts, average mark 14.2, std.dev. 2.25.

### Question 14

(a) Most candidates satisfactorily answered the first three parts of this part of the question, which was book-work from the lectures. However, none could make the conceptual leap to answer the last part of the question, which went beyond the lectures, where the trapping of generated holes by  $\text{Fe}^{2+}$  ions, situated on lattice sites in the  $\text{Fe}_{1-x}\text{O}$  material, to produce  $\text{Fe}^{3+}$  ions is an alternative defect mechanism.

(b) Most candidates wrote down correct defect reactions for the aliovalent doping of  $\text{FeO}$  by  $\text{Na}_2\text{O}$  and  $\text{Al}_2\text{O}_3$ , which were straightforward extensions of similar reactions in other systems given in the lectures. Most also inferred correctly the relative likelihood of the reactions taking place for the two dopants, considering the relative radii of the  $\text{Na}^+$ ,  $\text{Al}^{3+}$  and  $\text{Fe}^{2+}$  ions given in the question.

(c) With part (c), the candidates did not have major difficulties. Typical drawbacks were related to that some candidates did not mention that the effective diffusion rate is calculated as the inverse of the mean of inverse rates. In some scripts, the "bottle-neck effect" was described as trapping in a deep minimum, which certainly prevents the diffusion, but a high barrier from just one side of the well is actually sufficient for reducing the diffusion in 1D.

12 attempts, average mark 13.8, std.dev. 3.4.

### Question 15

The majority inferred an incorrect 'M1L1' structure for product D, going through sometimes-elaborate mental gymnastics to justify the observations (particularly the 1:11 19F integration ratio). Where these gymnastics made sense marks were given.

20 attempts, average mark 11.1, std.dev. 3.9.

### Question 16

Six answers to this question. One candidate was presumably out of time, and just wrote four sentences, and picked up four marks.

The other answers produced generally correct comments and suggested improvement strategies in part b. The marks basically reflect the number of details in the answer. 6 attempts, average mark 11.4, std.dev. 6.4.

### **Question 17**

Both parts of this question were very doable, although in general they weren't answered terribly well. Poor explanations of stereochemistry in (a) were common. In (b) very few answered it fully correctly, but in general the answers were along the right lines. The average mark was easy to hit and the spread of marks were probably what was to be expected.

19 attempts, average mark 13.1, std.dev. 3.06,

### **Question 18**

Parts (a)(i) and (ii) were generally well answered. Most students saw **A** as the product of oxidative dimerization of a naphthalene diol/triol and saw that the naphthalene could be made by a polyketide pathway. Some were unsure of details of the polyketide pathway. Answers to (a)(iii) were more mixed ranging from perfect answers to candidates that had no recollection. Part (b) was poorly done with most doing simultaneous decarboxylation of glycine and attack on the C=O of the thioester (which was only given 2 of the 4 marks). This is despite this course emphasising on many occasions that decarboxylation is not possible without an appropriately placed electron-withdrawing group. The solution to use PLP was only proposed by about a quarter of students.

22 attempts, average mark 13.4, std.dev. 3.6.

## **Paper 2 – questions are marked out of 25**

### **Question 19**

The overall performance on this question was okay but not great. The students were mostly able to identify, with good reasons, which polymer might be crystalline and which might be amorphous, and in general draw reasonable DSC heating curves. Often, differences in T<sub>g</sub> were overlooked. In general the students were able to calculate the DP for the polymers (part b) which was something taken straight from the lectures. The students struggled with part c where often differences in hydrodynamic radius were overimagined (there is not much difference between the two polymers). Additionally, the students were in general not able to link the fact that the polymers would have different solubilities and therefore different likelihood to aggregate. They had difficulty on part d where they needed to draw the monomer and the reaction conditions to arrive at a polythiophene with narrow PDI. This was also something that should have been straightforward. Nevertheless, even with a majority of unsatisfactory answers to part d, most were able to give a reasonable answer to part e. For part f, most of the students could identify which polymer had the wider band-gap. However, a significant percentage compared A and B, instead of A and C.

15 attempts, average mark 12.7, std.dev. 4.5.

### **Question 20**

Unfortunately, the students did not perform very well on this question, even though there were a substantial number of points taken directly from the lectures, such as part a! In fact, only 1-2 correct answers were received for this initial part of the question. Indeed, the entire question was centred around a ABA triblock copolymer architecture and many

students disregarded this and tried to develop elastomers using random co-polymers that would incorporate both lactic acid and lactone subunits. Even with partial points being awarded for such an approach the overall performance on this question was relatively poor in comparison to previous years.

14 attempts, average mark 13.9, std.dev. 3.9.

### Question 21

Parts (a) and (b) both required use of Curie-Weiss law to determine the arrangement of ions in spinel-structure compounds. There were some good answers to part (a) but many candidates slipped up on basic coordination chemistry, failing to see that Mn(III) must have greater crystal field splitting than Mn(II), so a combination of high spin Mn(III) and low spin Mn(II) isn't sensible. Most candidates got to sensible solutions for part (b)(i) and (ii). In part (iii) few candidates were able to expand a fragment of the spinel structure and therefore couldn't get sensible answers for the number of nearest neighbours. Nor did many candidates provide a complete answer as to whether Mean Field Theory is appropriate. Part (iv) and (v) were well answered but no-one managed to see that cobalt carbonate is the source of the canting in (vi) although there were many sensible other suggestions.

20 attempts, average mark 15.2, std.dev. 4.1.

### Question 22

(a)(i) was done well by almost all candidates but (ii) was surprisingly difficult. Many candidates didn't see that the Cu-L link via O must be different to the Cu-L link via N. More worryingly many candidates thought it was possible to simplify the spin Hamiltonian because of the cluster's symmetry. Most answers to (iii) were good, but some candidates ignored the instruction to ignore M-M interactions.

Part (b). Candidates tended to focus on the shape of the plot and any possible coercive field rather than investigating the size of the saturation magnetisation.

17 attempts, average mark 16.6, std.dev. 3.3.

### Question 23

A question in 3 parts marked out of 6, 8 and 11. After an initial scan of the papers I was worried that they found part c too difficult since only four figured out that the nitrating agent was peroxyxynitrite, so I thought about changing the balance of marks to 8, 9, 8. Trialing this altered scheme gave too high an average so I went back to the original mark scheme and arrived at the distribution below. No-one gave a perfect answer to all three parts but the final part c) did prove good at determining those who could think through the mechanism clearly and apply all the principles delivered in the course. One person gave a perfect simple mechanism. I was a bit disturbed how many students treated NO as NO<sup>+</sup> from the outset and therefore using it as a reductant was never a possibility. Half of part a) proved quite instructive too; the tyrosinase mechanism, which was given in a very superficial picture in the handout, revealed those who understood which direction electrons would flow, from substrate to peroxide, and those that didn't think about it.

Scripts Ave 16.6 SD 3.5

26 attempts, average mark 16.3, std.dev. 3.6, Max 23, min 9.5.

### Question 24

Perceived as more difficult perhaps because of the amount of text needing reading. Numbers small so difficult to read anything into the answers but in general the recall bits of the question were poorly done. Had people recognized it, part c) was pretty easy once they had read all the question. The only thing that was disappointing was the number of students who don't really understand what reduction potentials are and why they vary. This reinforces my belief that we need a focused section in 1A or 1B chemistry that addresses the fundamentals of redox reactions. After first marking, the average was below 16. I remarked to raise the average by 0.4 so that Q23 and 24 had similar averages. 8 attempts, average mark 16.3, std.dev. 4.7, Max 24.5, Min 11.

### Question 25

This question was answered well by most students, with most issues being restricted to specific parts of the questions. In part (a), whilst students mentioned position and intensity, few students commented on the effect of symmetry in the structure on peak intensity. Further, very few students made the leap to what information can still be obtained from this type of fit and what information would be lost. Part (b) was the best answered part of the question, with only a few students missing the effect of the neutron scattering lengths on the pattern of intensities observed. Error carried forward (ECF) marks were given for the peak positions, if the wrong "strong" peaks had been identified. For part (c) most students were able to give a good account of the peak splitting and the multiplicities (though some miscounted) – though many missed commenting on the fact that there would be a change in the peak position (particularly for the {111} case – which does not split). Part (d) was quite well handled, although there was some mis-indexing of the peaks. Error carried forward marks were still given for lattice parameters calculated from misassigned peaks. Part (e) was well handled, with marks mainly lost for non-conversion of peak widths to radians. In part (f) whilst most people realised that least squares was a possibility, there was no expansion given (e.g. the equation for minimisation, or the linear plot that could be drawn). 16 attempts, average mark 16.7, std.dev. 3.8.

### Question 26

On the whole Q26 was answered relatively well. Part (a) was bookwork with varying quality of explanations – with some students missing the part of the question asking for a comparison to an X-ray experiment. In part (b) marks were dropped either for not showing how to go from the power spectrum to the corrected image, or for not explaining how the constants in the PCTF could be calculated. Part (c) was pretty well answered, but almost all students did not state whether the motif absences would be maintained. Unfortunately, there was a mistake in part (d) referring to "Diamond" rather than "Silicon". However, all (bar one) of the students either stated that the two structures were analogous and therefore the patterns should be the same (albeit with different spacings due to different lattice parameters), or carried on as if the question had asked for Silicon (as was intended). Error carried forward (ECF) marks were given, based on the absences calculated in the previous part of the question. In fact, this part therefore had the highest average mark. Part (e) was variable in the quality of the answer – mainly marks were lost due to the steps from the diffracted beams wave function to image intensity, rather than due to setting up the problem. Many students used the specific case and worked through it, whilst some used a general periodic object and then put in the specific case details at the end. Both methods of answering were valid and



awarded marks. Part (f) was the worst answered part of this question, as students commented on either the effect on the diffraction pattern, or the image, but not both; therefore most students only achieved half of the available marks for this question. 16 attempts, average mark 16.4, std.dev. 4.3.

### Question 27

This question turned out to be quite tricky but many students made good attempts. In (a)(i) it is important not to forget the constant of integration. There was a small typo in (b), the second virial coefficient should be  $B_2 = v/2$ , but this did not seem to cause any serious problems. It is important to use spherical polar co-ordinates when computing the averaged volumes in (b). Some answers to (c) were quite short, perhaps indicating a lack of time.

14 attempts, average mark 16.0, std.dev. 2.7.

### Question 28

The descriptive parts of the question were generally done well, and all the candidates produced a correct disconnectivity graph in (b). In contrast, the calculations in parts (c) and (d) were not carried through correctly, even by the candidates using the correct formulae. The interpretations in part (e) were reasonable, and some candidates realised that their numerical results in (c) and (d) must be wrong from thinking about the  $C_v$  plot. None of candidates noted the quantitative low temperature limit.

5 attempts, average mark 13.2, std.dev. 0.75.

### Question 29

31 answers. This question was generally well done, although part (d) proved testing in the convincing 3D depiction of highly-ordered transition states to rationalise the observed stereocontrol for the transannular cycloadditions. Almost all candidates gave a reasonable synthesis of B, although several got mixed up with oxidation states. In part (b), a sizeable number ignored the context of the total synthesis of A and the implied need for an asymmetric aldol approach (Evans style), and just generated C in racemic form as the syn aldol adduct. There were a few odd answers for G, involving alkene epoxidation, rather than selenoxide formation and elimination, which then derailed part (d). Overall, this question served to test the 3D manipulation of organic structures, mechanistic reasoning, functional group interconversions and stereochemical aspects.

31 attempts, average mark 17.0, std.dev. 4.3.

### Question 30

The cycloaddition might be endo or exo depending on the double bond geometry of the three-atom component. Very few people spotted the 1,5 hydride shift, despite it being in the lectures. Selectivity in double bond hydroboration, which is probably an electronic effect, had few good explanations. The varying outcomes from the similar reactions in part (b) were outlined well, but the reasons for the selectivity were explained less well.

16 attempts, average mark 16.4, std.dev. 4.5.

### Question 31

Most students answered the question at a high level, with most problems occurring on the first section where they had to write a pseudo code for Monte Carlo simulations.

4 attempts, average mark 15.6, std.dev. 2.9

### Question 32

For a full score, I was looking at perfect answers that did not contain any errors in the derivations or showed misunderstandings. Most parts were answered correctly, with most mistakes appearing on subsections c) and d) and f).

8 attempts, 18.6 average mark, std.dev. 3.4.

### Question 33

The question was generally done less well than hoped for and was marked a little generously. Part (b) was handled better than part (a). Throughout though, quite a few of the required structures were drawn incompletely or inaccurately when looked at in detail.

(a) The lithium cadmate was handled reasonably though the presence of only TMP groups on Cd confused some. Most candidates had a reasonably good go at identifying **A**, which was a rather unusual species. Most answers included that fact that it was some kind of agglomerate of  $\text{TMPLi}$  and  $\text{LiCl}$ , though the behaviour of the solvent proved harder to explain. The final part of (a) was generally poorly done. Few candidates saw that the idea would be to lithiate anisole and then try to react that with a cadmium species in a separate step. Generally, the relevance of the NMR data was appreciated, though without doing the stepwise metalation the NMR on its own would prove nothing about a TMT mechanism.

(b) This part was generally done a bit more strongly, though was more recognisable from the handouts. **B-H** were generally identified, though **F** and **G** proved surprisingly hard given that the relationship between Lipshutz and Gilman structures is covered clearly in handout 2. Most students correctly got **H**. Since identifying **F** proved tricky, marks were generally also dropped when attempting to describe the solid-state structure, though most answers got some points for identifying a linear Cu and THF solvation. The final part proved very hard, even allowing for the incorrect identification of **F**. Very few candidates appeared to see that the liberated THF must feature in the  $M_r$  calculation. This was a surprise, because in lectures I make a point of highlighting this issue.

6 attempts, average mark 15.5, std.dev. 3.0.

### Question 34

a) Candidates generally gave a good account of the bonding in alkyne derivatives and how it changes upon moving down the group. A fair few, however, did not notice that the question asked about alkyne derivatives rather than alkenes, and discussed the bonding in these systems instead.

b) This part of the question was also done well and showed candidates had taken note of similar examples in the lectures, especially with the reaction of  $\text{RGeGeR}$  with hexyne. Subsequent reaction with  $\text{CO}_2$  produced more varied answers that did not always make chemical sense. Most recognised the very weak aromaticity contributing to the instability of **B** though fewer also pointed out the relative strength of  $\text{Al-O}$ .

c) A good number of candidates remembered the lone-pair/empty orbital character of the Ge atoms which could react with multiple bonds. Cycloaddition across the diene resulting in the five-membered metallocycle was the most popular answer, though credit was also given to those who reacted at one double bond only to give metallocyclopropanes. Most correctly predicted lower reactivity at  $\text{M} = \text{Pb}$  due to the inert pair effect.

d) The final part of the question was answered less well, with many candidates not thinking to apply the 18e rule to find the number of electrons contributed by the Sn moiety. Of those who did, most correctly predicted linear geometry with the 3e donor unit and bent geometry as a 1e donor, though none included any backbonding from Mo to Sn p-orbital. 20 attempts, average mark 16.3, std.dev. 3.8.

### Question 35

This question was well mostly well answered, and the marking had to be quite harsh to reach the required average.

(a) This type of reaction was well-known, and the question was generally well answered.

(b) This question required an explanation of the regioselectivity, and generated some good answers including discussion of the charge distribution and shape of the LUMO in quinolines, as well as a desire to leave the benzene ring intact (as one candidate wrote, *"Wouldn't want to disrupt aromaticity of this ring"*). Other answers were a little too vague, for example simply drawing an analogy with conjugate vs direct addition without actually explaining anything, and these did not receive full marks. Many candidates were also confused about what to do with the  $\text{Me}_3\text{SiOTf}$  in the first reaction, with one commenting *"Not sure why  $\text{Me}_3\text{SiOTf}$  is necessary though, unless it's to prevent polyalkylation on the N"*, and many only having it get involved after the Grignard had attacked the quinoline. In fact, it plays an important role in activating the quinoline towards attack (the researchers who did this work reported that without any Lewis acid only recovered starting material was obtained).

(c) Most candidates correctly predicted that substitution would take place at C4, due to electron withdrawal by the ester group. As part of the question was to predict the structure of the product, it was necessary to actually draw the product formed, and not (as one candidate did) simply write "TM" instead of drawing a final structure.

(d) Step (i) of this reaction is the formation of a quinazoline, analogous to the 1,3-dicarbonyl / N-C-N pyrimidine synthesis covered in the lectures. The handout and supervision exercises included examples of urea or thiourea being used as the NCN unit and giving a (thio)pyrimidone product. However, many candidates thought that the reaction would stop at some intermediate stage before cyclisation, and then used the  $\text{POCl}_3$  in step (ii) to complete the cyclisation (Vilsmeier-style) to give an aminopyrimidine. This led to problems in step (iii) as it was then necessary to do a  $\text{S}_{\text{N}}\text{Ar}$  with only  $\text{NH}_2^-/\text{NH}_3$  as the leaving group. Other candidates generated an aminopyrimidine in step (i), and then tried to adapt the mechanism for conversion of a pyridone to a chloropyridine by  $\text{POCl}_3$  to their aminopyridine starting material, with one candidate suggesting that *"If OH can do it so can  $\text{NH}_2$ "*.

(e) Part (i) required accounting for the regioselectivity of  $\text{S}_{\text{N}}\text{Ar}$ . The preference for the 2-position can be explained in terms of the alkoxide being a hard nucleophile so preferring the more  $\delta^+$  2-position adjacent to the N; as one candidate wrote *"Both ortho & para positions can do  $\text{S}_{\text{N}}\text{Ar}$  with -ve charge delocalised onto N so can't be that"*. Others were clearly expecting the answer to be that only one Cl was in a suitable position, with one writing *" $\text{S}_{\text{N}}\text{Ar}$  cannot occur on the meta chloro position because the negative charge would not be stabilised by the pyridine N in the intermediate"* despite there being no chlorine meta to the pyridine N.

Some candidates invoked the "ortho effect" without explaining what they meant (the only "ortho effect" discussed in the lectures was relating to electrophilic substitutions on pyridine, not nucleophilic substitutions) or the "alpha effect" (again without explanation). Other candidates were not specific enough in their answers, failing to explain why the nucleophile was hard (high charge density on alkoxide) or why the C2 position on the pyridine was hard (high  $\delta^+$  due to both conjugative and inductive withdrawal).

In part (ii) most candidates identified that the bromination could be directed by the oxygen lone pair and many noted that the position ortho to the ether would be more hindered. Relatively few discussed the influence of the pyridine nitrogen on the electronics of the ring (this would direct meta to itself in an electrophilic aromatic substitution).

Metal-halogen exchange (for part iii) was covered in the lectures, but some candidates had the Grignard adding to the pyridine instead, and then somehow being lost again later. The final part involved the N vs O regioselectivity of pyridone alkylation, which was also discussed in the lectures. Most candidates appreciated that the TBAF would remove the ether protecting group (although one confused TBAF with  $\text{CF}_3\text{COOH}$  despite the structure of TBAF being given). But many then protonated their pyridone anion (despite the lack of acid) to give a neutral pyridone before adding the alkyl halide, with one such candidate adding that "*N lone pair can act as nucleophile in pyridone*". Relatively few candidates discussed the fact that the alkyl halide is a soft electrophile (and especially good at  $\text{S}_{\text{N}}2$  due to conjugation with the thiazole ring in the transition state), that the N is not too hindered (no substituent on C6) or that counterion is  $\text{Bu}_4\text{N}^+$  which would not complex the N (or indeed the O), although it was not necessary to discuss all of these factors in order to get full marks.

44 attempts, average mark 16.4, std.dev. 3.6, Max 22, Min 8

### Question 36

This question was a little less popular than the other M9 question on this paper (Q35), and with only two exceptions everyone who answered this question also answered Q35. In general this question was better answered than last year's medicinal chemistry question, and the marking needed to be relatively harsh in order to achieve the required average.

(a) Part (a) proved straightforward for most candidates and was well answered. Where marks were lost it was generally due to not being specific enough or including enough detail.

(b) Most candidates chose to focus on the possibility that the replacement of a benzene ring by a pyridine ring in **F** might give improved  $\pi$ -stacking interactions with a group such as Phe188 on the enzyme, rather than on the possibility of extra hydrogen bonds being formed. This may have been because there was no obvious H-bond donor shown in the diagram of the crystal structure. A few candidates read 'lower  $\text{IC}_{50}$ ' to mean 'less tightly bound' (even if they had interpreted  $\text{IC}_{50}$  correctly in part (a)), and some talked about metabolic stability instead (this does not affect the  $\text{IC}_{50}$ ).

In terms of the metabolic stabilities of **F** and **G**, the expected answer was that the ester of **F** would be more susceptible to hydrolysis than the amide of **G** because esters are more electrophilic, but it was more common for candidates to suggest other explanations such as the cyclopropyl group acting as a steric shield to protect the carbonyl or the extra

Me group on the pyrrole ring in **F** being susceptible to P450 oxidation. All reasonable suggestions were accepted. Some candidates went into a lot of detail about how the metabolism would make the compound more polar and more easily removed by the kidneys (with one candidate even suggesting that "*F is smaller so more likely to be cleared through renal filtration in the kidneys whereas G is slightly bigger so it may not fit through the Bowmans capsule as easily*"), but in fact that was not relevant here because the clearance rates given referred to an *in vitro* assay (incubation of the compound with liver microsomes) as suggested by the wording of the question which said that the clearance rate was the rate of metabolism by liver enzymes, not the rate of removal from the body. Other candidates assumed that the cyclopropane ring must be important, with proposals including "*G has a reactive, electrophilic cyclopropane ring as its amide side chain. This is likely to react with nucleophilic functional groups (e.g. Ser, Thr, Cys residues on enzymes, or even with DNA) to form covalent adducts and therefore will be cleared from the body slower*".

(c) The P450 mechanism was well known, and most candidates picked up both marks here. Parts (ii) and (iii) were a little less well answered with many candidates not including enough detail about why electron-rich systems are oxidised faster (e.g. in terms of the electrophilic nature of the ferryl radical) or how a less electron rich pyrimidine ring could affect the rate of metabolism at an adjacent methylene group.

(d) Part (i), relating to protonation state, was relatively poorly answered. Few candidates mentioned  $pK_a$  values (probably the easiest way to answer the question) and those that did did not always get them right (for example "*Pyridine's pKa is greater than 7.4, so I would expect the pyridine N to be protonated in G.*") or drew the wrong conclusion (for example "*pKa of pyridine about 5 so expect G to be protonated here*" and "*Amide pKa  $\approx 12 \Rightarrow$  Deprotonated*"). A number of candidates highlighted that it would be unlikely for both pyrimidine nitrogens in **H** to be protonated, but still thought that one of them would be (despite the  $pK_a$  of pyrimidine being about 1.3 and likely even lower here due to the  $CF_3$  group). With regard to the protonation state of the amide and pyrrole nitrogens, the question could have been interpreted in terms of whether the N would be positively charged with an extra proton (the intended meaning) or in terms of whether it would be negatively charged (i.e. deprotonated). As the question was not entirely clear, both interpretations were accepted and given full credit where the reasoning and explanation was correct. ,

(ii) Most candidates knew what  $\log D$  referred to (although some of the more imaginative suggestions by those who did not included "*Water-decanol partition coefficient (Sorry)*" and "*D is the water:cyclohexane coefficient*". Many candidates only answered in terms of drugs that were weak acids, despite the previous question asking about basicity, while some produced a full derivation of equations such as  $\log D = \log P - \log (1 + 10^{(pH - pK_a)})$  and/or  $\log D = \log P - \log (1 + 10^{(pK_aH - pH)})$ . Others tried to quote these equations and got them wrong (with minus signs instead of pluses or vice versa). These results were not required for full marks, and it was probably simpler to just say that  $D = [X]_{\text{octanol}} / ([X]_{\text{water,unionised}} + [X]_{\text{water,ionised}})$ . There were some good answers to why  $\log D$  and  $\log P$  would be similar for compounds **F–H**, although some candidates gave answers that were inconsistent with what they said in part (i) regarding the likely protonation state at pH 7.4.

(iii) Accounting for the  $\log D$  values posed some difficulty for some candidates (some got confused if they focused initially on the cyclopropyl vs ethyl groups) but most were able

to pick up some marks here. It was rare for all the factors (extra methyl group in **F**, pyrimidine in **H**, and the relative hydrogen-bonding ability of amides vs esters (covered in detail in IB)) to be discussed. Marks were also lost for not including enough detail, for example not explaining why replacing the pyridine ring in **G** by a pyrimidine ring in **H** made a difference.

(iv) Most candidates knew Lipinski's rules and could apply them, although not everyone realised that they could use  $\log D$  in place of  $\log P$  because, from part (ii), the two are expected to be similar for these molecules. A few candidates quoted the  $\log D$  value for **H** instead of for **G**. The main issue was in calculating the molecular mass, with only 9 scripts out of 33 correctly calculating  $M_r = 323$  and 21 scripts stating an incorrect value ranging from 285 to 346.

32 attempts, average mark 16.7, std.dev. 3.5, Max 22, Min 8.5.

### **Paper 3 – questions are marked out of 25**

#### **Question 37**

For part (a), many students observed that this is a pi allyl palladium question. Some tried to use the enol ether instead and gave some interesting mechanistic possibilities. For (b) there were several approaches to uniting the two organic components on the palladium and appropriate credit was given for reasonable suggestions. For (c) the majority of candidates spotted that Pd(II) was to be used and that this was a Saegusa type process, but more complex than those seen in the lectures. For (d) there were several possibilities, particularly for the final cyclization step and appropriate credit was given for reasonable suggestions.

22 attempts, average mark 16.5, std.dev. 3.9.

#### **Question 38**

For part (a), a good number of the candidates observed that a Birch reduction followed by Sharpless AD would be appropriate although answers varied in the discussing aspects such as selectivity for which double bond after the reduction. For (b), many candidates spotted that the cyclohexene could be disconnected through Diels Alder chemistry. There were various possible strategies, such as copper box, Corey-type oxazaborolidine Lewis acid. Some students also opted to use organocatalysis. For (c), generally people saw this acted as a chiral Lewis acid and answers were differentiated largely on how well they rationalized the observed selectivity. Part (d) was attempted reasonably well and variations occurred in how well the substrate was fitted to the catalyst in terms of binding mode etc.

attempts, average mark, std.dev.

#### **Question 39**

The question was in general well answered. Most students were able to describe clearly the coil to globule transition and use their knowledge to analyse the addition of electrostatics to a polymer model.

26 attempts, average mark 16.5, std.dev. 2.4.

#### **Question 40**

The question was in general well answered. Most students demonstrated a good understanding of colloid stability and the main factors that affect it. Some students did not answer all parts of the question.

22 attempts, average mark 16.2, std.dev. 1.3.

#### **Question 41**

Nine candidates attempted this question, and achieved a somewhat pleasing average mark of 17.56, with a range of 7-24. Indeed, with the exception of one candidate who achieved a mark of 7, all other candidates scored at least 15 marks, with an average of 18.88 marks. The majority of candidates tackled Part (a) rather well, either by summing a discrete series or by integrating a continuous function. Those adopting the continuum approach needed to be particularly careful to do so consistently in the later sections, and not all were quite careful enough. Nevertheless, most candidates succeeded in answering Parts (b) and (c) accurately, using one or other approach. In tackling Part (d) a few candidates got muddled between photon energies and electron kinetic energies, accounting for some more dropped marks. Those who managed the first four parts of the question well were, on the whole, also successful in tackling Part (e), which combined concepts and methods used in the earlier sections.

9 attempts, average mark 17.6, std.dev. 4.9.

#### **Question 42**

Twenty-five candidates attempted this question, and achieved an excellent average mark of 18.52, with a range of 11-24. Parts (a)-(d) were completed by the majority of candidates in an efficient and clear manner, with relatively few errors distributed amongst the cohort. Part (e) was less well answered, in general, with some candidates failing to spot that the states described were most likely image states, and many of the remaining candidates applied only the simplest form of the equation for image state energies, which does not well approximate the stated energies from the problem. A slightly more sophisticated equation, including the effect of electrons tunnelling into the surface, would match the data better and should have been used instead. Part (f) was predominantly discursive in nature, and most candidates were able to provide a reasonable account, consistent with information from the lecture notes.

25 attempts, average mark 18.5, std.dev. 3.6.

#### **Question 43**

The students have had more difficulties than expected answering the question 43. 31 students completed the question and they scored on average 15.9 out of 25.

a) - some students instead of describing bioorthogonal cleavage of drugs from antibody drug conjugates, described endogenous triggering of drug release. Others gave complete responses with details of the antibody format and target antigen.

b)i) - most students were able to draw the mechanism based on the IEDDA reaction

ii) - students struggled with parts of the mechanism and only two were able to provide the complete correct mechanism

iii) - about 25% of students could not draw the 4+1 cycloaddition and thus were not able to provide the mechanism

c) - the majority of students provided the example of the IEDDA reaction between TCO-carbamate and tetrazine, others provided the Staudinger based mechanism for drug release and others instead of a bioorthogonal reaction, showed a self-immolative linker whose trigger was an endogenous enzyme or thiols (this was not correct).

Overall, I expected students to be able to better answer the question, but I am satisfied with the results. Some however seemed to not have read or perhaps did not understand what was being asked (example, bioorthogonal versus endogenous reaction triggers).

31 attempts, average mark 15.9, std.dev. 2.45.

#### **Question 44**

Overall this question was answered well, in total there were twenty one candidates that took this question. The highest mark was 23/25 and the lowest mark was 8/25. The first part of the question was answered well except a number of candidates concluded the heme containing enzyme was a cytochrome P450. This mechanism was covered in the lectures. Parts (b) and (c) were answered well. Two candidates obtained 8/25 for their questions, one simply did not write enough to get the marks. The second confused the first part of the question with a CYP mechanism and for the other two parts did not give enough in their answer. Overall I was happy with how this question was answered.

21 attempts, average mark 16.4, std.dev. 4.9.

#### **Question 45**

A disappointingly very small number (4) of candidates attempted this long question on the L5 Solid Electrolytes course. In previous years, many more candidates (~10-15) have attempted such questions. The range of marks attained by these four candidates was exceptionally wide, ranging from nearly full marks (23/25) to nearly no marks (3/25). Detailed remarks on the candidates' performance for various sections of the question are as follows:

a) Half the candidates made no mention of the involvement of an applied electric field in generating an ionic drift velocity, determined by the mobility.

b) Most candidates were unable to reproduce the requested book-work derivation of the Nernst-Einstein equation from the lectures. The highest scoring candidate supplied a novel derivation, which was very different from that given in the lectures.

c) This question asked for a straightforward modification of the Nernst-Einstein equation.

d) Most candidates were unable to sketch correctly the temperature dependence of the  $\text{Ag}^+$ -ion conductivity of  $\text{AgI}$  showing the discontinuity in conductivity at the  $\alpha$ - $\beta$  phase transition, instead showing – and discussing – an intrinsic- to extrinsic-behaviour crossover. Most candidates were unable to calculate correctly the  $\text{Ag}^+$ -ion concentration, knowing that the  $\alpha$ -phase has the bcc structure. Most candidates also could not see that the  $\text{I}^-$ -ion diffusion coefficient for the  $\alpha$ -phase crystal should be essentially zero, since the  $\text{I}^-$  ions, constituting the bcc crystal structure, are immobile, unlike the 'liquid-like' diffusive motion of the  $\text{Ag}^+$  ions.

4 attempts, average mark 13, std.dev. 7.1.

#### **Question 46**

The majority of candidates successfully approached this question with several students achieving very good marks.

In part (a), some of the candidates did not mention the temperature as being one of the parameters in description of diffusion.



In part (b), the candidates mainly successfully derived the normal distribution for position of diffusing ions. The main difficulty in this part of the question was related to an estimate of the bias in the jump probability.

10 attempts, average mark 16.5, std.dev. 6.0.

#### **Question 47**

This question touched upon a wide range of the skills required for supramolecular chemistry. There were different answers given for the various parts, such that few got close to full credit, but many acquitted themselves well. For the last two parts, where the student asserted that they did not understand circular dichroism or where these parts were left blank, these parts were discounted and the remaining 18 marks were normalised to the 25-mark scale by multiplying by 25/18.

12 attempts, average mark 17.5, std.dev. 3.9.

#### **Question 48**

It was surprising to note how many claimed a triple-helical structure for 1, despite our discussing the tetrahedral nature of this structure in lectures. Marks were given for claims of binding within this putative helicate nonetheless, where justified. Also relatively few noted that anionic 1 will lower the energy of the cationic intermediates and transition states to the formation of 3 from 2. The question appeared to give a good tour around different concepts from the course.

14 attempts, average mark 14.4, std.dev. 3.3.

#### **Question 49**

This question was well answered by most of the 11 candidates who attempted it (with a few scripts from candidates whose answers indicated that they had not attended the lecture course). Part (a) (definitions) was well answered by most candidates (although quite a few candidates were not able to sketch the time-evolution of the side-side time-correlation function. Part (b)(i) was also well answered by most, and part (b) (ii) by a substantial minority (with candidates who failed to answer this well either not attempting this part of the question or not being able to work out which bounds to put on the integral). The remaining parts of the questions (b)(iii), (iv) and (c) concerned transition-state theory and recrossing and were generally well answered.

11 attempts, average mark 17.6, std.dev. 5.7.

#### **Question 50**

One answer for this question. In part (a), some of the partial derivatives were recognisable. Similarly, in part (b), parts of the mathematical derivations were correct. The training algorithm scheme described in part (b) had some of the basic required elements.

1 attempt, average mark 14, std.dev. n/a.

#### **Question 51**

Notably many students went down the wrong path in (a). This error was given credit even though it was wrong as long as it was consistent throughout. (c) many didn't really answer this well, but the good answers were well articulated. The rest were fairly standard. I thought this was the easier of the two questions, and probably wasn't answered as well as it could have been. Average was achieved without having to adjust mark scheme

11 attempts, average mark 15.8, std.dev. 4.5.

### Question 52

I think this was the harder of the two questions and I accommodated a range of answers in some of the questions (b) was the hardest part, and very few people answered this well.

Overall, the multiple parts were included to give students a chance to pick up marks throughout. Surprisingly, many spurned that opportunity. Aside from (b) which was tough, the other parts were very 'answerable'. Again, it could have been answered better, but the target average was met without having to adjust the marking.

13 attempts, average mark 16.1, std.dev. 3.1.

### Question 53

(a) All candidates recognised that A is made by a terpene biosynthetic pathway but most gave the mevalonate pathway (1 mark lost). Bacteria use the non-mevalonate pathway. Cyclisation of A to B and C: most treated these as separate problems and generally came up with totally different mechanisms for each. A single enzyme is not going to catalyse two totally different mechanisms. The point of the question was that candidates needed to work out mechanisms to B and C that were the same for the majority of steps and just diverged in the last one or two steps (2 marks). Also quite a number proposed mechanisms that needed multiple enzymes, e.g. Types I and II terpene cyclases and oxidase and reductase, not likely to be found in a single protein.

For the change in ratio upon deuteration, almost everyone said it was due to a kinetic isotope effect (1.5 marks) but only one realised that if the enzyme-bound intermediate was by that stage already committed to forming C then it would not alter the amount of C formed. Instead the breaking of the C-D bond needed to be at the divergence point or the reactions from the divergence point to the C-D breaking step would have to be reversible, so that the intermediate could form B instead of C if formation of C was slowed by the KIE (1.5 marks).

(b) Many recognised that D is a pyrrolizidine alkaloid and gave the correct initial steps from putrescine, as given in lectures. However none apparently recalled what was also given in lectures that the biosynthesis starts in plants (Senecio species mostly) to give retronecine-based alkaloids. Then the caterpillar eats the plant and converts the alkaloids into the pheromone. Mechanisms for the loss of OH to give the methyl group were often poor.

21 attempts, average mark 15.4, std.dev. 4.2.

### Question 54

(a) Only two answers to this question and both were poor. Neither knew what was unusual about the multidomain synth(et)ases and neither even tried to produce a biosynthetic pathway that proceeded linearly from one module to the next down the "production line", extending the chain in a consistent direction. As it was marks had to be given for the right type of step even if it was in quite the wrong order, and even so the average was very low.

(b) Similarly poor answers - one started from ornithine not lysine, the other would have given the NH<sub>2</sub> in the wrong position. So neither was feasible.

2 attempts, average mark 12.0, std.dev. 2.0.

## **Paper IDP1 – questions are marked out of 25**

### **IDP1 Question 1**

The answers were, in general, disappointing. The ClO dimer polar loss cycle has appeared on previous questions but many candidates struggled. Too many talked about the role of PSCs at low temperature, rather than discussing the temperature dependence of the cycle. A disappointing number offered no argument viz-a-viz the validity of steady state in part c. 18 attempts, average mark 17.9, std.dev. 1.88.

### **IDP1 Question 2**

This was answered well with many good answers. The numerical parts of the question were handled well.

16 attempts, average mark 17.1, std.dev. 3.72.

### **IDP1 Question 3**

Overall, students did very well. Chemists achieved higher marks on average than students from other fields, the highest mark being 22 out of 25. No issues with the majority of questions, but only a few students got full part marks for question b) (i) because most talked about tropospheric mechanisms in form of aerosol indirect effects when these are not relevant in the stratosphere. Students also often talked about SO<sub>2</sub> aerosol when SO<sub>2</sub> is a gaseous aerosol pre-cursor species. This specific question was meant to separate marks. About half the students did not get the right result in (b) (iv). Several students also struggled a bit with calculating the fraction that is oxidised in the atmosphere to produce sulfate aerosol in (d) (i), but nothing unexpected overall.

10 attempts, average mark 19.1, std.dev. 1.58.