KENYATTA UNIVERSITY

UNIVERSITY EXAMINATIONS 2009/2010

SUPPLEMENTARY EXAMINATION FOR THE DEGREE OF MASTER OF SCIENCE

SCH 532: NATURAL PRODUCTS CHEMISTRY

DATE: THURSDAY, 30TH SEPTEMBER 2010 TIME: 9.00 A.M. - 12.00 P.M.

INSTRUCTIONS: ANSWER ALL QUESTIONS.

Q1 (a) Give an outline of key biochemical reactions involved in building polyketides (polyacetates) from "acetate" units. **[6 marks]**

(b) Show how the fungal metabolite orsellinic acid (I) from *Lichen* spp. and eugenone (II), a constituent of clove oil, can be derived from the appropriate polyketide chains, indicating the key reactions that may be involved (including any further modifications).

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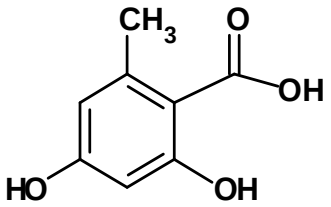
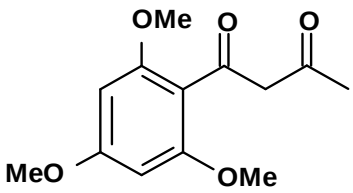


(I)

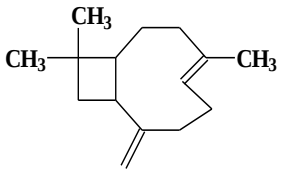


(II)

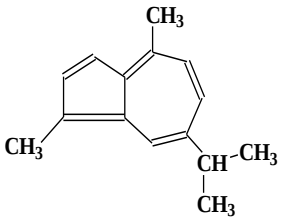
[8 marks]

(c) In a feeding experiment with [2-^{13}C]-acetate ($^{13}CH_3COO^- Na^+$), show which carbon atoms of orsellinic acid (I) would be expected to show enhanced signals in ^{13}C nmr spectrum. Which signal pattern would you expect to get if [2-^{13}C]-malonate [$^{13}CH_2(CO_2^- Na^+)_2$] is used? **[8 marks]**

Q2 (a) Identify the isoprenoid units in guaiazulene (III) and caryophyllene (IV), constituents of geranium and clove oils, respectively, clearly differentiating between 'head-to-tail' linkages and any additional C-C bonds formed or other changes involved.



(III)



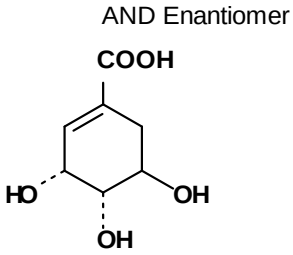
(IV)

[8 marks]

(ii) If the plant producing (IV) is treated with $^{13}CH_3COO^-Na^+$, trace the labelled ^{13}C atoms to mevalonic acid, then to isopentenyl and dimethlylallyl 5-carbon intermediates, and finally to (IV), indicating which atoms in this natural product will show enhanced ^{13}C NMR signals. **[10 marks]**

Q3. (i) Show how cinnamic acid and the amino acids phenylalanine and tyrosine (p-hydroxyphenylalanine) are biosynthesised from shikimic acid (V).

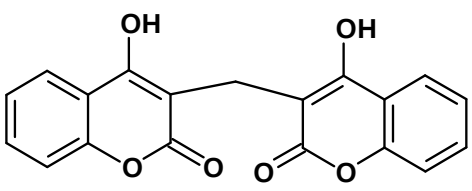
(V)



[8 marks]

(ii) Outline likely reaction pathway from cinnamic acid to dicoumarol (VI) (sweet clover constituent that causes internal bleeding in cows).

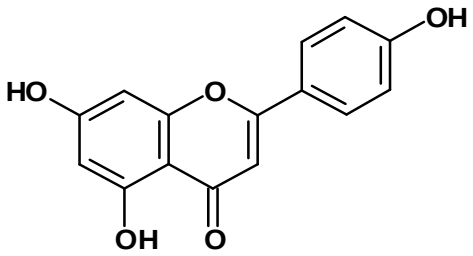
(VI)



[8 marks]

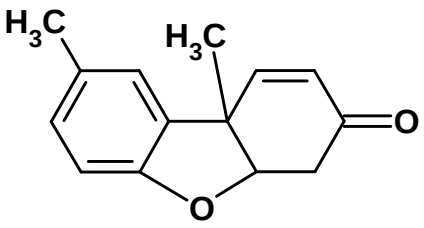
(iii) Show how a combination of shikimic and acetogenin pathways leads to the biosynthesis of naringenin (VII), a flavone found in grapefruit.

(VII)



[8 marks]

Q4. (i) Radical-mediated oxidative coupling is a key reaction in the biosynthesis of a series of complex phenolic and alkaloidal natural products. One-electron oxidation of 4-cresol (p-methylphenol) gives the coupling product (VIII), (known as 'Pummerer's ketone', which provided a model for the biogenesis of various plant secondary compounds). Outline the mechanism associated with its formation showing clearly all the key steps (including which of the alternative coupling sites in the phenoxy radical are involved).



(VIII)

[8 marks]

(ii) Explain why may free radicals be important in many human diseases? What structural features of some plant secondary metabolites in our diet make them effective scavengers of free radicals? Illustrate your answer with specific examples. **[8 marks]**