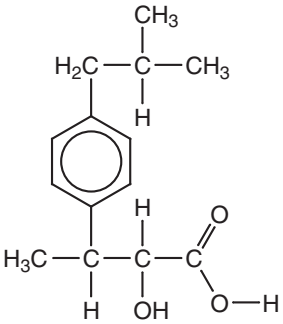
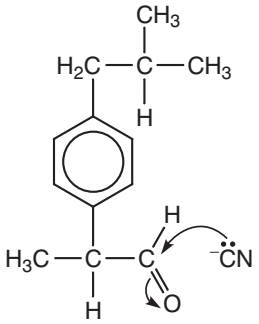
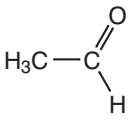
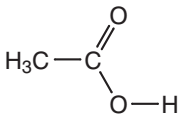
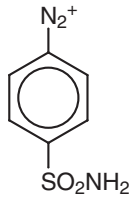
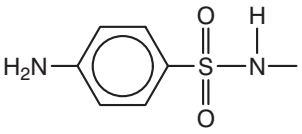
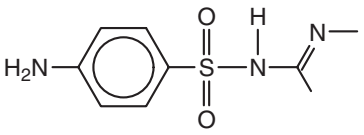
Answers to Medicines by Design End of Unit Test

Q	Answer with marks	Marking suggestions
1(a) (i)	Reflux (1); with ethanoyl chloride (1); and aluminium chloride (1)	Only award first mark if some reference to chlorides; accept 'anhydrous conditions' as an alternative to 'reflux'
1(a) (ii)	5.00 × 176/134 (1) = 6.57 g (1); (6.24/6.57) × 100 = 95.0% (1)	
1(b) (i)	Aldehyde (1)	
1(b) (ii)	Reflux (1); with acidified (1); dichromate(VI) (1)	Only award first mark if one of next two scored. Allow named acid and named dichromate, or correct formulae
1(b) (iii)	*Any one* of (1): yield is too low reagents too expensive dichromate/acid is non-selective	Accept alternative answers about difficulty of separating product/ large amounts of effluent
1(c) (i)	 (1) extra COOH; (1) rest of detail	
1(c) (ii)	Nucleophilic (1); addition (1)	
1(c) (iii)	 (1) CN^- attack; (1) electron movement to oxygen	Accept ^-CN without lone pair and curly arrow from negative charge
1(d) (i)	No (1); the peak at 1740 cm^{-1} indicates an (aliphatic) aldehyde, rather than a carboxylic acid (1); there is no broad peak at 2500–3300 cm^{-1} to show presence of O–H in carboxylic acid (1)	
1(d) (ii)	A peak at 206 (1)	
1(e) (i)	Alkali forms the salt of ibuprofen (1); which is more soluble in water than in hexane (1)	
1(e) (ii)	Add acid (1); filter off precipitate (1)	
1(e) (iii)	An additional peak at 11.0 (1); due to C**H**O (1)	

Q	Answer with marks	Marking suggestions
2(a)	 (1)  (1)	
2(b) (i)	**C** is $(CH_3)_2CHCH_2OH$ (1); two identical CH_3 groups (1) single hydrogen well away from oxygen (1) two hydrogens on carbon next to oxygen (1)	
2(b) (ii)	**A** is the most volatile (1); **A** has the smallest intermolecular forces/most compact structure (1); **A** is $(CH_3)_3COH$ (1)	

Q	Answer with marks			Marking suggestions
3(a) (i)	 (1) for diazo part (1) for rest of molecule			Allow N_2Cl
3(b) (i)	Reaction step	Reagent(s)	Conditions	Classification
	1	**conc. nitric and conc. sulphuric acid**	**<55 °C**	**substitution**
	3	**ethanoyl chloride**	room temperature	**condensation**
	5	**conc. NH_3(aq)**	room temperature	**substitution**
	6	**NaOH(aq)** (allow HCl)	reflux	**hydrolysis**
	(1) each			
3(b) (ii)	Steps 1 (1); and 4 (1)			

Q	Answer with marks	Marking suggestions
4(a) (i)	As a starting compound it showed useful activity and its structure could easily be modified (1)	
4(a) (ii)	Any *two* from (2): to avoid or reduce side-effects to reduce the effective dose to lower toxicity to find an easier synthesis to reduce the cost to widen the spectrum of activity	
4(a) (iii)	computer modelling (1)	
4(b) (i)	 (1)	
4(b) (ii)	 (1)	
4(b) (iii)	(b)(i) (1); this is the pharmaceutically active part of the molecule (1)	
4(b) (iv)	The pharmacophore has a similar structure/charge distribution to the true substrate 4-aminobenzoic acid (1) Sulphonamides bind to the active sites of enzymes (1); thus stopping them working (1)	