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Identification of Drugs and Other Toxic Compounds from Their Ultraviolet Spectra. Part II: Ultraviolet Absorption Properties of Thirteen Structural Groups

This paper continues an effort which was initiated [*1*] to simplify the identification of drugs and common organic poisons from their ultraviolet (UV) spectra. To accomplish this end, compounds have been placed in groups according to similarities in the molecular structure. More specifically, compounds with the same unsaturated, conjugated parts of the molecule have been placed in the same group. Compounds in each group therefore have similar UV absorption characteristics and show similar pH and solvent effects. Sixteen groups were studied in Part I [*1*]. This paper will deal with 13 structural groups consisting primarily of drugs and drug precursors presently available legally or illegally in the United States. Practical reviews dealing with approaches to interpretation of UV data are found in Refs *1-6*. Theoretical aspects of spectrophotometry are covered in Refs *7-10*. References containing a substantial number of illustrated spectra include *11-16*.

Methods

Ultraviolet spectra illustrated in Figs. 1-3 were recorded using either a Bausch & Lomb Model 200, a Beckman Acta IV, or a Perkin-Elmer 202 spectrophotometer. Concentrations of compounds illustrated in Figs. 1-3 may be calculated from data presented in Tables 2-4. Each block of Figs. 1-3, although accurately depicting the spectrum of one compound, is characteristic of that group of compounds which has the same letter-number designation in Table 1. For example, if an unknown compound matches that of nicotine (Fig. 1, Block G1), the unknown compound could be one of several compounds listed in Table 1 under G1.[3] The compounds in some structural groups have indistinguishable spectra, while in other groups the compounds have noticeable absorption differences. Similarities and differences within each group can be studied in Tables 2-4.

Properties of UV absorption which were used to characterize the different groups are: (1) overall appearance of the absorbance (log 1/transmittance) versus wavelength (λ) scan or "profile" from 200 to 340 nanometres (nm) in aqueous solution, (2) the effect of pH change, (3) the effect of decreased solvent polarity relative to water as a solvent, and (4) the intensity

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[3] Lettering begins with "G" in this paper because the letters A through F were used to designate groups in Part I [*1*].

TABLE 1—*Compounds in the different structural groups.*

G1	Brompheniramine		Pentachlorophenol		Butabarbital
	Carbinoxamine		Pentazocine		Butalbital
	Chlorpheniramine		Phenol		Butallylonal
	Cotinine		Phenomorphan		Butethal
	Doxylamine		Phenylephrine		Cyclobarbital
	Nicotinamide		Thymol		Cyclopentobarbital
	Nicotine		Tyramine		Heptabarbital
	Nicotinic acid		Tyrosine		Hydroxyphenobarbital
	Nicotinyl alcohol				Pentobarbital
	Nikethamide	H2	*p*-Acetamidophenol		Phenobarbital
	Nornicotine		*p*-Aminophenol		Probarbital
	Pheniramine		Chlorzoxazone		Propallylonal
			Edrophonium chloride		Secobarbital
G2	Isoniazid		Phentolamine		Talbutal
	Nialamid		Zoxazolamine		Vinbarbital
G3	Chloropyrilene	H3	Acetylsalicylic acid	J2	Hexobarbital
	Chlorothen		*p*-Hydroxybenzaldehyde		Mephobarbital
	Halopyramine		*p*-Hydroxybenzoic acid		Metharbital
	Methapyrilene		Methylparaben		Methohexital
	Phenyramidol		Methyl salicylate		
	Pyrilamine		Phenyl salicylate	J3	Methalital
	Thenyldiamine		Propylparaben		Methitural
	Thonzylamine		Salicylamide		Thiamylal
	Tripelennamine		Salicylic acid		Thiopental
			Salicylsalicylic acid		
H1	Amylmetacresole			J4	Acetylcarbromal
	Benzestrol	I1	Amydricaine		Allantoin
	p-Chlorcresole		Amylocaine		Apronalide
	p-Chlorophenol		Benzoic acid		Bemegride
	Chloroxylenol		Benzoylecgonine		Bromisovalum
	p-Cresole		Cocaine		Carbromal
	Bamethan		Eucaine		Cycloheximide
	Butylated hydroxytoluene		Di-*n*-butylphthalate		Diphenylhydantoin
	Cyclazocine		Dipiperocaine		Ethosuximide
	Cyclorphan		Hexylcaine		Glutethimide
	Dienestrol		Hippuric acid		Methetoin
	Estradiol		Phaltan		Phenglutarimide
	Estriol		Phthalate esters		
	Ethinylestradiol		Piperocaine	K	Ascorbic acid
	p-Hydroxyamphetamine		Meprilcaine		Cortisone acetate
	p-Hydroxyphenylacetic acid		Tropacocaine		Dexamethazone
	p-Hydroxyphenylethanol				Hydrocortisone
	p-Hydroxyphenylpropionic acid	I2	*N*-Acetylaminobenzoic acid		β-Methasone
	p-Hydroxytoluene		Cyclomethycaine		Norethisterone
	Isoxupine		Dyclonine		Prednisone
	Ketobemidone		Procarbazine		Progesterone
	Levallorphan				Santonin K
	Levorphanol	J1	Allobarbital		Spironolactone
	Mestranol		Allylbarbital		Testosterone
	Metaraminol		Alphenal		
	Nylidrin		Amobarbital		
	Oxedrin		Aprobarbital		
	Oxymetazoline		Barbital		

of the absorption bands. Molar absorptivity (ε) values shown in Tables 2-4 and in the Appendix were determined by the authors or abstracted from references given. The practical and often used 1%, 1-cm absorbance values, $E^{1\%}_{1\,cm}$ or $A^{1\%}_{1\,cm}$ as used in Refs *3, 12,* and *17,* can be calculated from the relationship:

$$\varepsilon = (E^{1\%}_{1\,cm})\,(0.1)\,(\text{molecular weight})$$

Sources of absorbance data for Tables 2-4 and the Appendix include Refs *2, 5, 9, 10, 13-15,* and *16-25,* and especially *3, 11, 12,* and *17.* The differences in ε values reported by different authors probably arise from differences in degree of purity of samples analyzed and instrumental differences. The differences in wavelength of maximum absorbance (λ_{max}) reported are more than likely experimental differences. Wavelength maxima and absorbances given in Table 2 were authenticated from two or more literature sources. On reviewing the literature it became apparent to the authors that there was good agreement among different authors on absorbance values for very common and easily purified compounds, but often poor agreement with rare and expensive compounds. Furthermore, solvent differences may or may not account for spectral differences reported. For example, aqueous 0.1*N* HCl, 0.1*N* H_2SO_4, and 0.5*N* H_2SO_4 are identical solvents in most spectrophotometric measurements; 0.05*N* to 0.5*N* aqueous NaOH are alike as solvents above 235 nm but different below this wavelength due to end absorption; ethanol and methanol are alike as solvents, as are hexane, *iso*octane, and cyclohexane.

Benzoic acid is readily available in high purity and numerous authors have reported absorbance values. The average value from six authors (laboratories) of the major band in aqueous acid solution is 11,318 ± 315, which is a relative standard deviation of ±2.8%. The maximum reported is 229.3 ± 1 nm. A secondary maximum occurs at 272 to 273 nm (aqueous acid). Benzoic acid is a convenient substance for calibration of a spectrophotometer in the ultraviolet range.

Group Characteristics Examined

A number of common antihistamines, nicotine, nicotinic acid, and nicotinamide comprise Group G1. Those compounds in G1 which have a second ring substituent show a definite maximum near 220 nm, as does chlorpheniramine (see G1 of Fig. 1). Extracts of liver and urine often exhibit a G1 absorption profile due to the presence of nicotinamide, nicotine, cotinine, and other nicotine metabolites. Group G2 compounds show marked absorption differences between acid and alkaline scans, clearly providing the analyst with a basis of qualitative identification of the group. Group G3 consists of antihistamines possessing a pyridine ring with an amine auxochrome. Spectra of the individual compounds show minor differences in positions of maxima and in relative band intensities ($\varepsilon_{240}/\varepsilon_{310}$).

A large number of compounds possess structural features of Group H1 (see Fig. 2), including a number of drugs and drug metabolites and certain artifacts of autopsy specimens [*13*]. Many of the Group H1 compounds have spectra which are practically indistinguishable. Compounds in Group H2 show more individual differences. Blocks H3 in Fig. 2 show a considerable difference in spectra between positional isomers *p*-hydroxybenzoic acid and *o*-hydroxybenzoic acid (salicylic acid).

Group I1 compounds all have a similar UV absorption pattern, although minor differences exist. Precautions should be made in analyzing this group in basic solution to

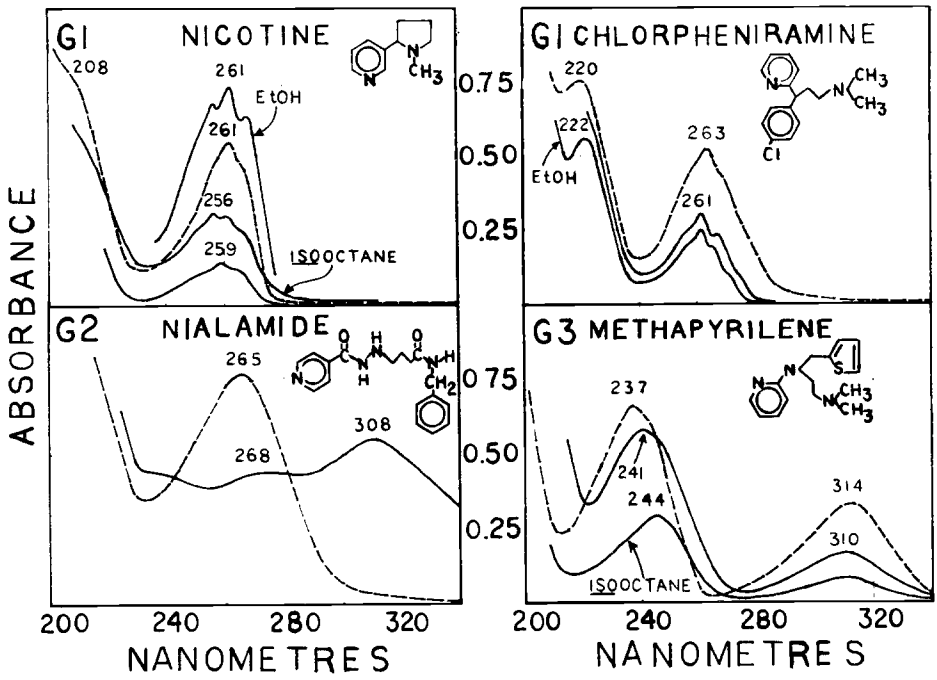

FIG. 1—*Ultraviolet spectra of pyridine derivatives (G1), hydrazides (G2), and pyridylamino compounds (G3). The dotted line traces the absorption versus wavelength scan in aqueous 0.1N HCl; a solid line traces the absorption in aqueous 0.1N NaOH; additional solid lines are marked individually. Concentrations of individual compounds vary in each block, but can be calculated from molar absorptivity values given in Table 2. A list of compounds in each group shown is given in Table 1.*

prevent splitting of the ester bond, a reaction known as "saponification." For example, cocaine is at least 50% hydrolyzed to acidic products in 5 min in 0.5*N* NaOH on a steam bath. Group 12 compounds have substantial individual differences.

Barbiturates are represented in Groups J1 (5,5′-disubstituted), J2 (1,5,5′-trisubstituted), and J3 (thiobarbiturates). Barbiturates are perhaps the class of drugs most frequently analyzed by UV spectrophotometry. Representative scans of each group are shown in Fig. 3. Table 3 summarizes UV absorption data on barbiturates which have been marketed in the United States since 1968. Barbiturates of Group J1 show only minor differences in λ_{max} of the 240, 254, and 215-nm bands. The 215 band seen in neutral or acidic solution arises at least partially from $n \rightarrow \sigma^*$ transitions of nitrogen atoms in the barbiturate ring. While differences in spectra of individual barbiturates may be noted with high purity standards [25], it would be hazardous to identify individual barbiturates on the basis of such differences. This is particularly true for "street drugs" and biological extracts.

Group J4 covers glutarimides, ureides, and hydantoins which contain an acidic hydrogen atom. With such compounds, a conjugated system is formed in aqueous base, leading to relatively strong but ill-defined absorption between 225 and 250 nm. Some compounds in Group J4 have phenyl substituents and thus show benzenoid absorption

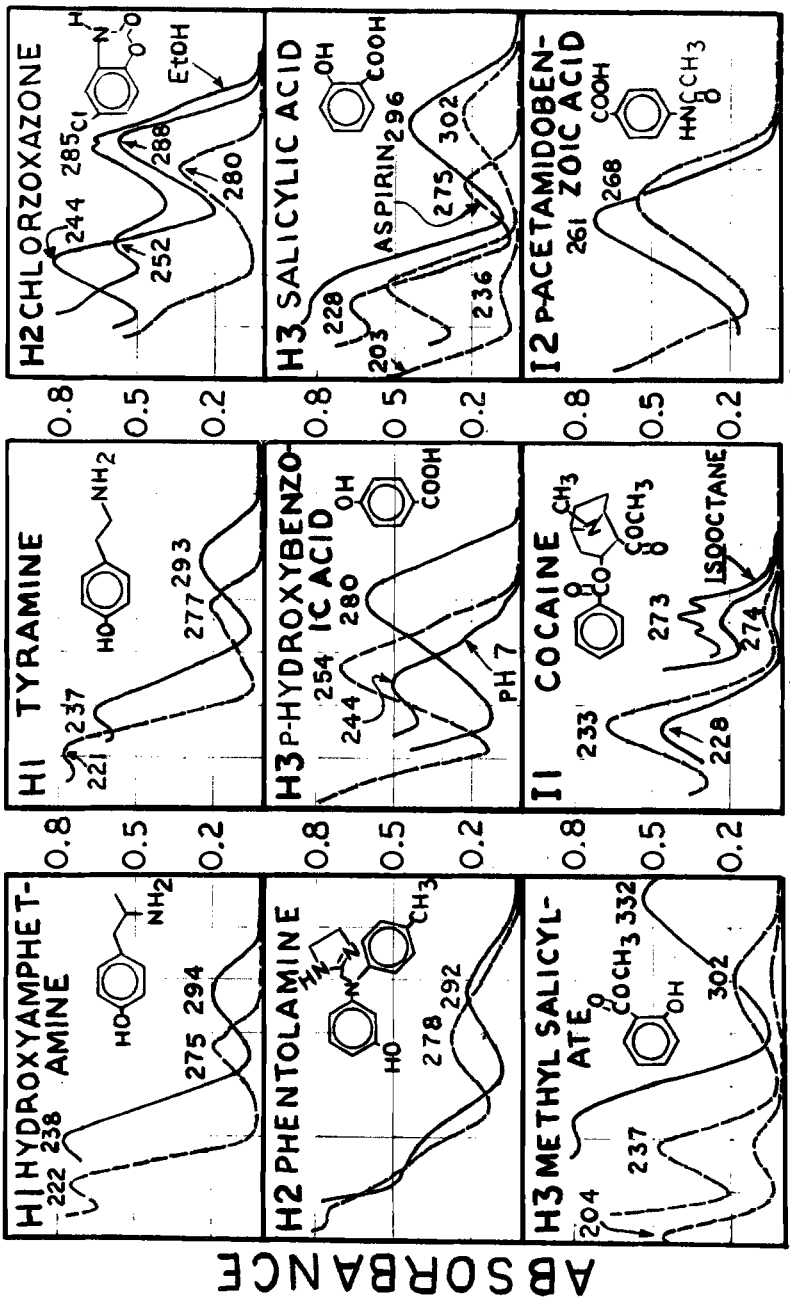

FIG. 2—*Ultraviolet spectra of variously substituted phenols (H1, H2, and H3) and benzoic acid derivatives (I1 and I2). Solvents for the compounds are represented as in Fig. 1. The H3 scans are shown at two concentrations in acidic solution in order to show all absorption bands above 200 nanometres (nm).*

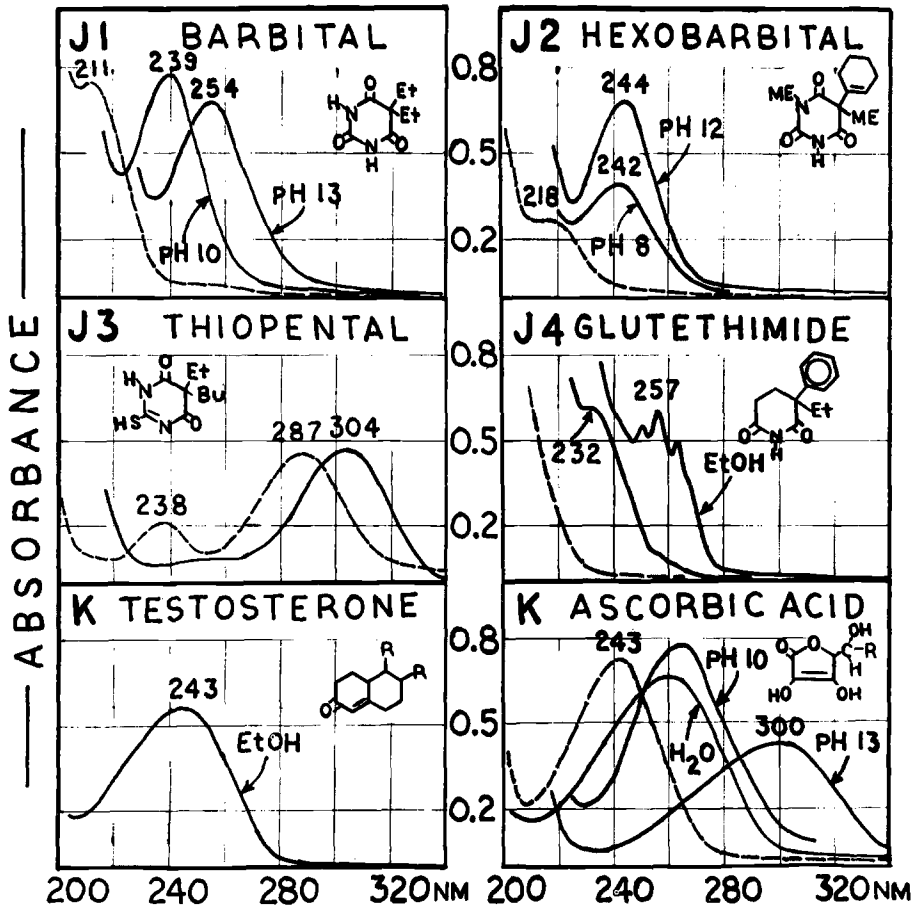

FIG. 3—*Ultraviolet absorption spectra of barbiturates (J1, J2, and J3), imides (J4), and conjugated ketones (K). Solvents for the compounds are represented as in Fig. 1. All scans are in aqueous solution except the two marked "EtOH," meaning 95% ethanol.*

[*1*]. Carbromal, a bromoureide, does not have a maximum in alkaline, neutral, or acidic solution, but does show gradually increasing absorbance from 260 to 200 nm.

Steroids (Group K) are the largest class of drugs which has a carbonyl group conjugated with a carbon-carbon double bond (the enone function). Absorption data on several steroids are given in Table 4. Ascorbic acid (Fig. 3) has an enone group, but apparently rearrangements occur in basic solution, leading to very different absorption characteristics.

Phenothiazines, xanthines, coumarins, quinolines, sulfonamides, chlorothiazides, opiates, benzodiazepines, and ergotamines will be reported on in Part III of this series.

TABLE 2—*Ultraviolet absorption data on a number of compounds in each of 13 structural groups.*

Compound and Molecular Weight[a]	Wavelength Max in			Molar Absorbance Data			
	Aqueous Acid	Aqueous Base	Other Solvent	Wavelength	Absorbance[b]	Solvent[c]	Ref
Group G1							
Brompheniramine—319.3	224,[d] 265, dil. HCl	261, dil. NaOH	261, methanol	265	8 750	H_3O^+	3
				265	8 200	H_3O^+	14
				224	12 500	H_3O^+	14
				261	5 900	OH^-	12
Carbinoxamine—290.8	220, 264, 0.1*N* H_2SO_4	260, 0.1*N* NaOH	260, methanol	263	7 600	H_3O^+	15
				261	5 700	OH^-	12
Chlorpheniramine*—274.8	220, 264, 0.1*N* HCl	223, 261, 0.1*N* NaOH	223, 261, ethanol	see the Appendix			
Doxylamine—270.2	261, 0.1*N* H_2SO_4	260, 0.1*N* NaOH	260, ethanol	262	5 700	H_3O^+	3
				260	2 700	OH^-	3
Nicotinamide*—122.1	261, 0.1*N* HCl	261, 0.1*N* NaOH	262, ethanol	260	5 200	H_3O^+	13
				261	3 000	OH^-	13
Nicotine*—162.2	208s,[e] 262, 0.1*N* HCl	259, 0.1*N* NaOH	215s, 259, ethanol	261	4 200	OH^-	17
				262	5 600	H_3O^+	15
Nicotinic Acid—123.1	261, dil. HCl	262, dil. NaOH	262, ethanol	261	3 400	H_3O^+	12
				262	2 100	OH^-	12
Nikethamide—178.2	264, 0.5*N* H_2SO_4	262, 0.5*N* NaOH	...	263	4 900	H_3O^+	3
				263	3 900	OH^-	15
Pheniramine—240.3	265, 0.5*N* H_2SO_4	262, 0.1*N* NaOH	...	266	7 500	H_3O^+	3
				261	5 000	OH^-	3
Group G2							
Isoniazid—137.2	265, 0.1*N* H_2SO_4	240, 296, 0.1*N* NaOH	263, ethanol	265	5 800	H_3O^+	11
				266	5 200	H_2O	3
Nialamid*—298.3	265, 0.1*N* HCl	240, 268, 308, 0.1*N* NaOH	...	see the Appendix			
Group G3							
Chlorothen*—295.9	238, 312, 0.1*N* H_2SO_4	243, 308, 0.1*N* NaOH	243, 304, ethanol	238	18 500	H_3O^+	11
				312	9 500	H_3O^+	11
Methapyrilene*—261.4	237, 313, 0.1*N* HCl	240, 310, 0.1*N* NaOH	244, 310, *iso*octane	see the Appendix			
Phenyramidol—214.3	237, 310, 0.1*N* H_2SO_4	241, 297, 0.1*N* NaOH	...	236	14 500	H_3O^+	15
				237	15 500	H_3O^+	12
				309	7 600	H_3O^+	12

Pyrilamine—285.4	238, 281, 313, 0.1*N* H_2SO_4	248, 283, 312, 0.1*N* NaOH	247, 310, ethanol	239	18 100	H_3O^+	12
				314	8 240	H_3O^+	12
				247	18 600	ethanol	17
				310	4 600	ethanol	17
Thenyldiamine—261.4	239, 314, 0.1*N* H_2SO_4	245, 311, 0.1*N* NaOH	244, 307, ethanol	239	19 200	H_3O^+	3
				315	8 350	H_3O^+	3
				244	18 000	ethanol	17
Thonzylamine—286.4	235, 273, 281, 313, 0.1*N* H_2SO_4	244, 273, 281, 313, 0.1*N* NaOH	243, 313, ethanol	235	26 200	H_3O^+	11
				313	4 500	H_3O^+	11
				243	24 000	ethanol	17
				313	3 360	ethanol	17
Tripelennamine—255.4	238, 313, 0.1*N* H_2SO_4	248, 311, 0.1*N* NaOH	247, 307, ethanol	238	13 600	H_3O^+	17
				313	8 100	H_3O^+	17
Group H1							
p-Hydroxyamphetamine*—151.2	222, 275, 281s, 0.1*N* HCl	238, 294, 0.1*N* NaOH	225, 276, ethanol	222	7 900	H_3O^+	12
				274	1 420	H_3O^+	12
p-Hydroxyphenylacetic acid—152.0	222, 275, 281s, 0.1*N* HCl	241, 294, 0.1*N* NaOH	...	222	4 900	H_3O^+	13
				274	1 100	H_3O^+	13
				294	2 600	OH^-	13
p-Hydroxyphenylpropionic acid—166.0	222, 275, 282s, 0.1*N* HCl	238, 294, 0.1*N* NaOH	...	222	6 800	H_3O^+	13
				275	1 500	H_3O^+	13
Hydroxytoluene—108.0	214, 276, dil. HCl	237, 292, dil. NaOH	279, 286s, cyclohexane	237	6 800	OH^-	10
				292	3 500	OH^-	10
Levallorphan—283.4	226s, 278, 285s, 0.1*N* H_2SO_4	240, 299, 0.1*N* NaOH	229, 282, ethanol	226	4 700	H_3O^+	3
				278	2 100	H_3O^+	3
				240	8 850	OH^-	3
				299	3 030	OH^-	3
Levorphanol*—257.4	228s, 279, 285s, 0.1*N* HCl	240, 299, 0.1*N* NaOH	...	240	8 800	OH^-	12
				299	3 100	OH^-	12
				279	2 200	H_2O	17
Metaraminol—167.2	221, 272, 280s, 0.1*N* H_2SO_4	237, 290, 0.1*N* NaOH	...	237	7 600	OH^-	12
				272	1 870	H_3O^+	12
Nylidrin—299.4	222, 273, 0.1*N* H_2SO_4	242, 290, 0.1*N* NaOH	225, 276, ethanol	242	10 900	OH^-	12
				273	1 440	H_3O^+	12
				276	1 630	ethanol	17
Pentazocine*—285.4	218, 278, 283s, 0.1*N* HCl	239, 297, 0.1*N* NaOH	...	298	3 200	OH^-	3
				278	1 940	H_3O^+	3

TABLE 2—*Continued.*

Compound and Molecular Weight [a]	Wavelength Max in			Molar Absorbance Data			
	Aqueous Acid	Aqueous Base	Other Solvent	Wavelength	Absorbance [b]	Solvent [c]	Ref
Phenol—94.1	211, 270, dil. HCl	235, 287, dil. NaOH	213, 266, 277, 279, cyclohexane	211	6 200	H_2O	2
				270	1 420	H_2O	2
				235	9 400	OH^-	2
				287	2 600	OH^-	2
Phenomorphan—247.5	219, 279, 284s, 0.1*N* HCl	242, 300, 0.1*N* NaOH	230, 281, ethanol	279	1 520	H_3O^+	3
Phenylephrine—167.0	221, 273, 282s, 0.1*N* H_2SO_4	238, 292, 0.1*N* NaOH	275, ethanol	237	4 300	OH^-	12
				272	1 390	H_3O^+	17
				292	3 040	OH^-	17
Thymol—150.0	218, 273, 279s, 0.1*N* H_2SO_4	239, 290, 0.1*N* NaOH	275, chloroform	239	7 050	OH^-	12
				290	3 450	OH^-	12
Tyramine*—137.2	221, 277, 0.1*N* HCl	235, 293, 0.1*N* NaOH	...	275	1 230	H_3O^+	12
Group H2							
p-Acetamidophenol—151.2	242, 281s, 0.1*N* H_2SO_4	257, 292s, 0.1*N* NaOH	248, 287s, ethanol	242	12 100	H_3O^+	15
				257	11 300	OH^-	17
p-Aminophenol—109.1	221, 278, 283s, dil. HCl	240, 308, dil. NaOH	234, 302, methanol	272	1 430	H_3O^+	17
Chlorzoxazone*—169.6	220s, 280, 286, 0.1*N* HCl	244, 288, 0.1*N* NaOH	232s, 252, 274, 280, ethanol	279	5 090	H_3O^+	3
				243	7 120	OH^-	3
Edrophonium chloride—203.0	217, 273, H_2O	235, 293, 0.1*N* NaOH	223, 246, 275, ethanol	217	5 900	H_2O	12
				273	2 270	OH^-	16
				293	3 640	OH^-	16
Zoxazolamine—168.6	229, 278, 285, 0.1*N* H_2SO_4	242, 286, 0.1*N* NaOH	244, 285, ethanol	242	12 800	OH^-	11
				286	7 590	OH^-	11
				229	10 600	H_3O^+	11
Group H3							
Acetylsalicylic acid*—180.2	228, 275, 0.1*N* HCl	242, 296, 0.1*N* NaOH	228, 275, isopropanol	275	1 190	ethanol	12
				278	1 340	chloroform	17
p-Hydroxybenzaldehyde—122.1	222, 284, 0.1*N* H_2SO_4	238, 330, 0.1*N* NaOH	...	222	10 500	H_3O^+	13
				284	15 000	H_3O^+	13
				330	26 000	OH^-	13
p-Hydroxybenzoic acid—138.1	208, 255, 0.1*N* HCl	222, 280, 0.1*N* NaOH	201, 251, ethanol	see the Appendix			

Methylparaben—152.1	255, 0.1*N* H_2SO_4	224, 294, 0.1*N* NaOH	258, ethanol	255	16 000	H_3O^+	17
				295	23 000	OH^-	17
Methyl salicylate*—152.1	204, 237, 302, H_2O, pH 6	244, 232, H_2O, pH 13	237, 306, isopropanol	204	30 000	H_3O^+	authors
				237	9 100	H_3O^+	authors
				302	3 700	H_3O^+	authors
				330	4 560	OH^-	12
Salicylamide*—137.1	202, 236, 298, 0.1*N* HCl	242, 328, 0.1*N* NaOH	235, 302, ethanol	242	7 400	OH^-	15
				236	7 800	ethanol	17
				328	6 040	OH^-	17
Salicylic acid*—138.1	203, 237, 301, 0.1*N* HCl	238, 296, 0.1*N* NaOH	204, 236, 307, ethanol	236	8 800	H_2O	authors
				295	4 150	H_2O	authors
				296	3 520	OH^-	authors
Phenyl salicylate*—214.2	205s, 241, 307, 0.1*N* HCl	245, 340, 0.1*N* NaOH	...	205	41 000	H_3O^+	authors
				241	13 300	H_3O^+	authors
				307	4 500	H_3O^+	authors
				340	6 400	OH^-	authors
Group I1							
Benzoic acid*—122.1	229, 272, 280s, 0.1*N* HCl	224, 261, 268, 276s, 0.1*N* NaOH	232, 274, 282, cyclohexane	231	11 400	H_3O^+	17
				229	11 400	H_3O^+	authors
				272	960	H_3O^+	authors
Cocaine*—303.4	233, 274, 277s, 0.1*N* HCl	227, 270, 276s, 0.1*N* NaOH	267, 273, 280, *iso*octane	see the Appendix			
Di-*n*-butylphthalate—278.3	229, 275, 281s, 0.1*N* HCl	...	227, 274, 281s, ethanol	224	8 260	methanol	14
				274	1 260	methanol	14
Hexylcaine—261.4	232, 275, 281, 0.1*N* HCl	273, 280s, 0.1*N* NaOH	229, 274, 281, methanol	232	11 000	H_3O^+	3
Hippuric acid*—179.2	228, 267s, 0.1*N* HCl	230, 270s, 0.1*N* NaOH	225, *iso*octane	228	11 600	H_3O^+	authors
				267	900	H_3O^+	authors
Piperocaine—261.4	232, 275, 0.1*N* H_2SO_4	225, 274, 0.1*N* NaOH	...	232	16 400	H_3O^+	3
				274	840	H_3O^+	12
Group I2							
N-Acetylaminobenzoic acid—179.0	210s, 268, 0.1*N* HCl	261, 0.1*N* NaOH	270, 286s, isopropanol	261	50 000	OH^-	authors
				268	58 000	H_3O^+	authors
Cyclomethycaine—359.5	210, 268, 0.1*N* H_2SO_4	260, 0.1*N* NaOH	...	see the Appendix			
Dyclonine—289.4	222, 283, 0.1*N* H_2SO_4	278, 0.1*N* NaOH	278, methanol	221	9 320	H_3O^+	3
				278	20 300	methanol	17
				282	17 500	H_3O^+	17
Procarbazine*—221.3	232, 270s, 0.1*N* HCl	235, 0.1*N* NaOH	...	232	12 900	H_3O^+	authors

TABLE 2—*Continued.*

Compound and Molecular Weight[a]	Wavelength Max in			Molar Absorbance Data			Ref
	Aqueous Acid	Aqueous Base	Other Solvent	Wavelength	Absorbance[b]	Solvent[c]	
Group J3							
Thiamylal*—243.3	238, 287, 0.1*N* HCl	304, 0.1*N* NaOH	...	287	22 000	H_3O^+	authors
				304	22 700	OH^-	authors
Thiopental*—242.3	238, 288, 0.1*N* HCl	304, 0.1*N* NaOH	237, 287, ethanol	see the Appendix			
Group J4							
Acetylcarbromal—279.1	...	237, 0.1*N* NaOH	210, ethanol/H_2O (1/1)	210	13 400	H_2O	3
				237	9 100	OH^-	3
Bemegride—155.2	220, inflection, H_2O, pH 2	231, 0.1*N* NaOH	231, methanolic KOH, pH 11	232	4 600	OH^-	14
				228	7 300	OH^-	12
Bromisovalum—221.3	...	228, 0.1*N* NaOH	228, ethanol	228	3 600	OH^-	3
Diphenylhydantoin*—252.3	257, 264, 268, 0.1*N* HCl	235, 0.1*N* NaOH	258, methanol	257	740	H_3O^+	3
				235	5 300	OH^-	12
Ethosuximide—141.2	...	218, H_2O, pH 12	221, 248, ethanol	248	120	ethanol	3
				218	>3 000	OH^-	3
Glutethimide*—217.3	257, 251, 263, 0.1*N* HCl	232, 0.1*N* NaOH	257, 261, 263, ethanol	256	430	H_2O	12
				232	16 000	OH^-	authors
Methetoin—218.3	...	234, 0.1*N* NaOH	256, 263, ethanol	256	260	ethanol	12

[a] Molecular weights are given so that molar absorbance values may be converted to 1%, 1-cm cell absorbances ($A^{1\%}_{1\,cm}$ or $E^{1\%}_{1\,cm}$). Starred (*) compounds were analyzed spectrophotometrically by the authors.

[b] Molar absorptivity values (ε).

[c] Solvents are abbreviated as follows: H_3O^+ is diluted aqueous HCl or H_2SO_4, 0.01 to 0.5 normal; OH^- is dilute aqueous NaOH or KOH, 0.05 to 0.5 normal; ethanol may refer to 95% ethanol or absolute ethanol.

[d] The strongest absorption band is underlined when more than one band is present.

[e] The small "s" indicates a shoulder.

TABLE 3—*Ultraviolet absorption of barbiturates in buffered aqueous and alcoholic solution.*

Compound and Molecular Weight	Wavelength Max at pH [a]			Absorptivity [b] at pH 10.3	Ratio [c] 240/255	Ref
	10.3	13.6	1			
Group J1						
Allobarbital—208.2	240	255	212s [d]	10 000	1.36	authors
	240			9 200		25
Allylbarbital—224.3	240	254	212s		1.41	authors
	240			9 300		3
Alphenal—244.2	238	256	257, 263, 235s	11 000	1.39	authors
	240			9 800		25
Amobarbital—226.3	239	254	211.5	10 200	1.36	authors
	239	254	210s	10 000		12, 14
Aprobarbital—210.2	240.5	256	211s	9 700	1.43	authors
				9 700		14
Barbital—184.2	240	254.5	211s	10 400	1.36	authors
	240		209s	10 100		12, 14
Butabarbital—212.3	240	255		10 100	1.45	authors
	239.5	254	210s	9 500		12, 14
Butalbital—224.3	240	255	212s	10 000	1.34	authors
Butallylonal—303.2	242	257	...	8 500	...	25
Butethal—212.3	239	254		9 800	1.34	authors
	239		210	9 900		14, 25
Cyclobarbital—236.3	240	255	...	10 000	...	25
	240			9 600		14
Cyclopentobarbital [e]—234.3	242	253	...	9 500	1.35	authors
Heptabarbital—250.3	239	255	...	10 100	1.29	authors
	240			10 000		25
Hydroxyphenobarbital—248.2	246, 293	251, 293	275, 225	...	...	18
Pentobarbital—226.3	240	254.5	211s	10 500	1.44	authors
	240		210s	10 000		14

TABLE 3—*Continued.*

Compound and Molecular Weight	Wavelength Max at pH[a] 10.3	13.6	1	Absorptivity[b] at pH 10.3	Ratio[c] 240/255	Ref
Phenobarbital—232.2	240	256	257, 220s	10 500	1.31	authors
	241			10 600		14
Probarbital—198.2	239	254	211	7 600	1.40	authors
	240			8 800		12, 25
Secobarbital—238.3	241.5	256	212s	9 600	1.40	authors
	240.5		214s	9 900		14, 25
Talbutal—224.3	240	255		9 600	1.43	authors
	212s		212s	9 600		14
Vinbarbital—224.3	240	255	211s	10 000	1.27	authors
	240.5			10 100		14
Group J2						
Hexobarbital—236.3	244	244	218s	7 300	na[f]	authors
	243		220s	7 900		authors
Mephobarbital—246.2	245	245	222s. 257. 264	7 000	na	authors
	245.5			7 800		14, 15
Metharbital—198.2	243.5	243.5	218	8 700	na	authors
	244	244	220s	8 600		12, 14
Methohexital—262.3	248	248		6 800	na	authors
	246		218	7 600		14

[a] The authors of this paper adjusted the pH to 10.3 with phosphate buffer to obtain the 240 ± 1 nm max. References *3* and *25* cite a pH 10 borate buffer, and Ref *14* employed methanol adjusted to pH 11 as the solvent. The 255 ± 1 nm max was recorded in 0.45*N* NaOH. The lower max was obtained by the authors in 0.1*N* HCl, and by Ref *14* in methanol.

[b] Molar absorptivities are given. Where more than one reference is cited, the absorptivities are averaged.

[c] Absorptivity ratio at the two wavelengths of maximum absorbance in alkaline solution, 240 and 255 nm.

[d] The small "s" indicates a shoulder.

[e] Other names are cyclopentenylallylbarbital and cyclopal.

[f] Group J2 barbiturates have a single max above pH 9; therefore a ratio does not apply (na).

TABLE 4—*Ultraviolet absorption data on a number of Group K compounds.*

Compound and Molecular Weight	Wavelength Max	Solvent	Molar Absorptivity	Ref
Ascorbic acid—176.1	260	H_2O	...	authors
	243	0.1*N* HCl	...	authors
	265	pH 10 buffer	...	authors
	300[a]	0.1*N* NaOH	...	authors
	245	dil. HCl	9 900	3
Cortisone acetate—402.5	240	ethanol	15 700	3
	238	methanol	15 800	17
Dexamethasone acetate—434.5	240	ethanol	16 900	17
Hydrocortisone—362.5	240	ethanol	15 800	24
β-Methasone—392.5	240	ethanol	15 300	3
Norethisterone—298.4	240	ethanol	17 000	3
Prednisone—358.4	240	ethanol	15 400	3
Progesterone—314.5	240	ethanol	16 800	3
	240	methanol	17 900	17
Spironolactone—416.6	238	methanol	19 600	17
Testosterone—288.4	240	ethanol	16 200	3

[a] This max is transitory, lasting only seconds in aqueous base. After treatment with base, the max seen in neutral or acidic solution will not reappear if the solution is reacidified, indicating the enone function is destroyed in alkaline solution.

Summary

The ultraviolet absorption spectra of 13 different chemical classes of drugs and toxic organic compounds were studied. A classification system has been developed in which compounds with the same conjugated molecular system and auxochrome substituents are grouped together. Each of these groups has characteristic absorption spectra, showing similarities in the number of major bands, position of maximum absorbance, pH effects, and solvent effects. The absorption maxima and molecular absorptivities are tabulated for approximately 100 compounds, and characteristic spectra of each designated group are illustrated. Classes of drugs included in this study are pyridine derivatives, hydrazines, pyridylamine derivatives, variously substituted phenols, barbiturates, ureides, imides, hydantoins, and conjugated ketones (enones).

APPENDIX

Summary of the Ultraviolet Absorption Characteristics of Compounds in the Different Structural Groups

Group G1—Pyridine ring with alkyl or carbonyl substituent; a second aromatic ring may be present.

1. Maxima (given in nanometres, nm).
   a. Below 210 nm in H_3O^+; usually a shoulder unless a second aromatic ring with an auxochrome substituent is present, as in the example below; $\pi \rightarrow \pi^*$ transition of an E_2 band.

b. 260 ± 5 nm in aqueous solution; absorbance is approximately 1.4 times greater in H_3O^+ relative to OH^-; up to 4-nm λ_{max} shifts with pH change; $\pi \rightarrow \pi^*$ transition of B band.

2. Solvent polarity effects (water versus organic solvents)—1 to 5-nm λ_{max} shifts for B band with solvent changes: increased fine structure in less polar solvents when pyridyl nitrogen is unprotonated.

3. Example (compound having spectra typical of this group)—Chlorpheniramine.

Band Max	Molar Absorptivity	Solvent	Ref
220	10 200	0.1*N* HCl	authors
222	11 000	0.1*N* NaOH	authors
222	10 600	95% ethanol	authors
263	8 000	0.1*N* HCl	authors
260	6 500	0.1*N* NaOH	authors
261	6 600	95% ethanol	authors
261	5 900	0.2*M* H_3BO_3	12

Group G2—Hydrazides.

1. Maxima.
   a. Below 215; $\pi \rightarrow \pi^*$ transition of an E_2 band.
   b. 265 ± 2 nm in H_3O^+; maxima near 241, 268, and 306 nm in OH^- due to increased conjugation upon ionization; $\pi \rightarrow \pi^*$ transitions.
2. Solvent polarity effects—Minor relative to pH effects on λ_{max}.
3. Example—Nialamide.

Band Max	Molar Absorptivity	Solvent	Ref
265	7 500	0.1*N* H_2SO_4	11
308	7 200	0.1*N* NaOH	11
305	6 900	0.1*N* NaOH	3
265	6 000	0.5*N* H_2SO_4	15
310	6 000	0.5*N* NaOH	15

Group G3—Pyridylamino derivatives.

1. Maxima.
   a. 238 ± 2 nm in H_3O^+; 2 to 7-nm red (positive) shift and decreased absorbance in OH^-; $\pi \rightarrow \pi^*$ transition of E_2 band.
   b. 312 ± 3 nm in H_3O^+; 1 to 8-nm blue (negative) shift and decreased absorbance in OH^-; $\pi \rightarrow \pi^*$ transition of B band.
2. Solvent polarity effects—E_2 band shows slight red shift and B band a slight blue shift in going from water to less polar solvents.

3. Example—Methapyrilene.

Band Max	Molar Absorptivity	Solvent	Ref
237	16 200	0.1*N* HCl	authors
238	16 700	0.5*N* H_2SO_4	15
238	15 700	0.2*M* H_3BO_3	12
240	16 000	0.1*N* NaOH	authors
313	7 600	0.1*N* HCl	authors
308	4 200	0.2*M* H_3BO_3	12
310	3 900	0.1*N* NaOH	authors

Group H1—Phenols with one or two alkyl substituents involving saturated carbon atoms attached to the aromatic ring.

1. Maxima.
   a. 220 ± 8 nm in H_2O at pH below the compound's phenolic pK_a; circa 18-nm red shift and 1.5-fold absorbance increase in OH^-; $\pi \rightarrow \pi^*$ transition of E_2 band.
   b. 275 ± 5 nm in H_3O^+; circa 18-nm red shift and 1.7-fold increase in absorbance in OH^-; $\pi \rightarrow \pi^*$ transition of B band.
2. Solvent polarity effects—Both bands show 1 to 5-nm red shifts as solvent polarity decreases; B band shows pronounced fine structure in hydrocarbon solvents.
3. Example: *o*-catechol.

Band Max	Molar Absorptivity	Solvent	Ref
214	6 300	H_2O, pH 3	2
276	3 200	H_2O, pH 3	2
236	6 800	H_2O, pH 11	2
292	3 500	H_2O, pH 11	2

Group H2—Phenols with amine or amide substituent attached to the aromatic ring.

1. Maxima.
   a. 208 to 250-nm broad band in H_3O^+; red shift in OH^-; $\pi \rightarrow \pi^*$ transition of an E_2 band.
   b. 278 ± 8 nm in H_3O^+; red shift in OH^-; $\pi \rightarrow \pi^*$ transition of B band.
2. Solvent polarity effects—Lower band shows red shift of several nanometres in changing from H_3O^+ to ethanol or a hydrocarbon solvent.
3. Example: Phentolamine.

Band Max	Molar Absorptivity	Solvent	Ref
208	30 000	0.1*N* HCl	authors
278	8 300	0.1*N* HCl	authors
241	13 000	0.1*N* NaOH	authors
292	8 900	0.1*N* NaOH	authors
276	9 200	0.1*N* H_2SO_4	3

Group H3—Phenols with a carbonyl substituent extending ring conjugation.

1. Maxima.
   a. *Ortho* substituted compounds—Separate bands in H_3O^+ at 204 ± 3, 238 ± 4, and 302 ± 6 nm; upper two bands show moderate λ_{max} shifts in OH^-.
   b. *Para* substituted compounds—Strong, broad band in mid-UV range in H_3O^+ or neutral solution; max or shoulder near 210 nm; large red shifts in OH^-.
2. Solvent polarity effects—Moderate to pronounced, depending on the compound.
3. Example—*p*-Hydroxybenzoic acid.

Band Max	Molar Absorptivity	Solvent	Ref
201	15 000	ethanol	10
251	12 300	ethanol	10
280	16 300	0.1*N* NaOH	10
210s[4]	14 000	0.1*N* HCl	authors
256	15 800	0.1*N* HCl	authors
247	13 800	H_2O, pH 7	authors
281	17 400	0.1*N* NaOH	authors

Group I1—Esters of benzoic acid and phthalic acid with no additional ring substituents.

1. Maxima.
   a. 230 ± 3 in H_3O^+; 5 to 8-nm blue shift as pH is raised; $\pi \rightarrow \pi^*$ transition of E_2 band.
   b. 274 ± 3 nm with upper shoulder in H_3O^+; fine structure more pronounced in OH^-; $\pi \rightarrow \pi^*$ transition of B band.
2. Solvent polarity effects—E_2 band shows 1 to 4-nm shifts with solvent changes; B band shows increased fine structure as solvent polarity decreases.
3. Example—Cocaine.

Band Max	Molar Absorptivity	Solvent	Ref
233	14 300	0.1*N* HCl	3
233	12 700	0.1*N* HCl	authors
233	12 400	dil. HCl	22
275	1 150	0.1*N* HCl	3
274	1 040	0.1*N* HCl	authors
227	9 600	0.1*N* NaOH	authors
270	900	0.1*N* NaOH	authors
274	1 060	dil. HCl	22

Group 12—Benzene derivatives with two ring substituents, one chromophore and one auxochrome (other than phenol).

1. Maxima.
   a. 205 to 225 nm in H_2O (maxima or shoulders); $\pi \rightarrow \pi^*$ transition.
   b. 272 ± 12 nm in H_3O^+ with 1 to 3-nm blue shift as pH is raised; $\pi \rightarrow \pi^*$ transition.
2. Solvent polarity effects—Vary with type of substituents.

[4] The small "s" indicates a shoulder.

3. Example—Cyclomethycaine.

Band Max	Molar Absorptivity	Solvent	Ref
261	19 200	dil. HCl	3
261	17 300	0.01*N* HCl	17
261	20 000	methanol	14
210	13 600	methanol	14

Group J1—Barbiturates, 5,5′-disubstituted.

1. Maxima.
   a. 240 ± 2 nm at pH 9 to 11 in aqueous or alcoholic base; 255 ± 2 nm at pH 13 to 14; $\pi \rightarrow \pi^*$ transitions.
   b. 212 ± 3-nm max, shoulder, or inflection in aqueous neutral or acidic solution; $n \rightarrow \sigma^*$ transition.
   c. 257 ± 1, 263, 268-nm benzenoid band present with phenyl-substituted barbiturates; $\pi \rightarrow \pi^*$ transition of B band.
2. Solvent polarity effects—212-nm band shows slight solvent effects.
3. Example: Pentobarbital.

Band Max	Molar Absorptivity	Solvent	Ref
240	10 500	H_2O, pH 10.3	authors
240	9 900	H_2O, pH 10	18
240	10 000	methanol, pH 11	14
242	9 700	0.001*N* NH_4OH	17
254.5	7 300	H_2O, pH 13.6	authors
211s	11 000	0.1*N* HCl	authors
210s	9 000	methanol	14

Group J2—Barbiturates, 1,5,5′-trisubstituted.

1. Maxima.
   a. 243 ± 1 nm above pH 9 in aqueous or alcoholic solution; $\pi \rightarrow \pi^*$ transition.
   b. 218 ± 2-nm max or shoulder in neutral or acidic solution; $\pi \rightarrow \sigma^*$ transition.
   c. 257 ± 1 nm as in Group J1 (1c) above.
2. Solvent polarity effects—pH effects are much more useful.
3. Example—Hexobarbital.

Band Max	Molar Absorptivity	Solvent	Ref
243.5	6 700	H_2O, pH 10.3	authors
244.5	7 900	methanol, pH 11	14
218	6 000	H_2O, pH 1	authors
220s	5 000	methanol	14

Group J3—Thiobarbiturates.

1. Maxima.
   a. 288 ± 2-nm broad max in H_3O^+ which shifts to 304 nm in OH^-.
   b. 238 ± 1-nm band in H_3O^+ which shifts to 255 nm (much weaker) in OH^-.
2. Example—Thiopental.

Band Max	Molar Absorptivity	Solvent	Ref
304	20 500	0.1*N* NaOH	authors
305	22 600	0.1*N* NaOH	12
288	18 600	0.1*N* HCl	authors
288	20 800	0.5*N* H_2SO_4	15
238	8 400	0.1*N* HCl	authors

Group J4—Imides, cyclic imides, and ureides.

1. Maxima.
   a. 228 to 242 nm in aqueous or alcoholic base; solution must be sufficiently basic to ionize the imido hydrogen, but not so strong that "end absorption" obliterates the max; $\pi \rightarrow \pi^*$ transition.
   b. 257 ± 1 nm (plus fine structure) when phenyl substituent is present; $\pi \rightarrow \pi^*$ transition of B band.
2. Example: Glutethimide.

Band Max	Molar Absorptivity	Solvent	Ref
256	430	H_2O	12
232	16 000	0.5*N* NaOH	authors
235	19 000	0.5*N* KOH	3

Group K—Ketones with a conjugated carbon-carbon double bond, an enone.

1. Maxima.
   a. 241 ± 3 nm in alcoholic solution; $\pi \rightarrow \pi^*$ transition.
   b. 310 to 320-nm broad, but very weak, band which is usually submerged by the major band; $n \rightarrow \pi^*$ transition.
2. Solvent polarity effects—Major band shows red shift with increasing solvent polarity.
3. Example—Testosterone.

Band Max	Molar Absorptivity	Solvent	Ref
240	16 200	ethanol	3
240	16 300	ethanol	21
241	18 000	ethanol	17

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