served rate constant would be small. It should be pointed out, however, that trace metals markedly accelerate the degradation of corticosteroids in the pharmaceutically important pH range. The presence of these impurities should be a prime factor in steroid stability considerations.

SUMMARY

1. The decomposition of prednisolone in aqueous solution was markedly accelerated by contaminants present in buffer reagents. Evidence has been presented which strongly indicates that the contaminants were trace metals. However, no attempt was made to identify the metals or to determine the nature of their influence on the degradative reactions.

2. Addition of a sequestering agent provided a method to isolate and quantitate the rate of the apparent metal-catalyzed reaction.

3. The rate of the apparent metal-catalyzed reaction was pH independent above pH 7 and below pH 5 and exhibited a first-order dependency on hydroxide-ion in the intermediate range.

4. In the presence of sequestering agent, the reaction rate was strongly dependent on hydroxide-ion concentration above pH 8 and only slightly dependent at lower pH values.

REFERENCES

(1) Mason, H. L., *J. Biol. Chem.*, **124**, 475(1938).
(2) Velluz, L., *et al.*, *Bull. Soc. Chim. France*, **1947**, 123.
(3) Herzig, P. T., and Ehrenstein, M., *J. Org. Chem.*, **16**, 1050(1951).
(4) Wendler, N. L., and Graber, R. P., *Chem. Ind. London*, **1956**, 549.
(5) Caspi, E., Schmid, W., and Wittstruck, T. A., *Tetrahedron*, **16**, 271(1961).
(6) Lewbart, M. L., and Mattox, V. R., *Nature*, **183**, 820(1959).
(7) Conbere J., (Merck and Co., Inc.), U. S. pat. 2,773,077 (1956).
(8) Weijlard J., (Merck and Co., Inc.), U. S. pat. 2,773,-078(1956).
(9) Lewbart, M. L., and Mattox, V. R., *J. Org. Chem.*, **28**, 2001(1963).
(10) Arth, G. E., Beyler, R. E., and Sarett, L. H. (Merck and Co., Inc.), U. S. pat. 3,068,250(1962).
(11) Guttman, D. E., and Meister, P. D., THIS JOURNAL, **47**, 773(1958).
(12) Lewbart, M. L., and Mattox, V. R., *J. Org. Chem.*, **28**, 1773(1963).
(13) *Ibid.*, **28**, 1779(1963).

Ultraviolet Spectrophotometric Estimation of Arylglycolate Drugs

By LESTER CHAFETZ*

Oxidation of arylglycolic acids to carbonyl compounds affords ultraviolet chromophores which make possible the spectrophotometric estimation of the acids with greatly increased sensitivity and selectivity. Oxidative spectrophotometric methods for representative arylglycolic acids were studied; the procedures were applied to the estimation of some arylglycolate drugs in dosage forms.

SALTS OF mandelic acid have been employed as urinary antiseptics, and several arylglycolate esters are used in medicine for antispasmodic, mydriatic, psychotropic, and other pharmacological activities. A study of spectrophotometric procedures was carried out using mandelic acid, benzilic acid, α-cyclopentylphenylglycolic acid, and α-cyclopentyl-2-thiopheneglycolic acid. The application of the procedures to the assay of representative arylglycolate drugs is reported.

Phenylglycolic acids and their esters have benzenoid ultraviolet spectra which are neither sufficiently intense to afford sensitivity in determination nor sufficiently characteristic to serve for identification (1). The majority of the analytical methods reported for arylglycolate drugs are based on the presence of a tertiary amine or quaternary ammonium function in the alcohol moiety, and few of the methods are selective for unhydrolyzed drug (2–8).

Received January 9, 1964, from Neisler Laboratories, Inc., Decatur, Ill.
Accepted for publication April 14, 1964.
* Present address: Drug Systems Research, University of Arkansas Medical Center, Little Rock.
The author acknowledges the competent technical assistance of Messrs. Marvin B. Hansen and Robert S. Yamamoto.

A number of workers have described procedures for oxidation of arylglycolic acids with decarboxylation to carbonyl compounds. The reagents used included "zinc manganite" (9–11), sodium bismuthate (12), *N*-bromosuccinimide (13), lead tetraacetate (14), periodate (14–16), and ceric sulfate (17–19). Some of these oxidative procedures were made the basis of titrimetic assay methods.

Spectrophotometry of the carbonyl compound products of the oxidation of arylglycolic acids appeared to offer a promising means for analysis of arylglycolate drugs. The increase in ultraviolet absorption effected by thus obtaining a carbonyl group in conjugation with an aromatic ring is evident in a comparison of the molar absorptivities, ϵ, of the acids with values reported in the literature for the carbonyl compounds. Mandelic acid has $\epsilon_{max.}$ 212 and benzaldehyde $\epsilon_{max.}$ 14,000 (20); benzilic acid has $\epsilon_{max.}$ 538 and benzophenone $\epsilon_{max.}$ 19,500 (21); and α-cyclopentylphenylglycolic acid has $\epsilon_{max.}$ 276 compared with $\epsilon_{max.}$ of 12,900 (22) for cyclopentyl phenyl ketone.

EXPERIMENTAL

A study of the oxidation of arylglycolic acids was carried out using sodium metaperiodate and ceric sulfate solutions. The spectra of the carbonyl compounds were measured in hydrocarbon solvents to eliminate interferences from polar compounds and to provide the most characteristic spectra. The extent of formation of carbonyl compounds was estimated from the relation % carbonyl product = 100 ϵ_A/ϵ_C, where ϵ_A = molar absorptivity calculated from the concentration of the arylglycolic acid and its absorbance after oxidation, and ϵ_C = molar absorptivity, literature value, of carbonyl compound which results from the oxidation.

Reagents and Supplies.—A 2% solution of sodium metaperiodate (Matheson, Coleman & Bell No. 879) and a 0.2 *M* ceric sulfate solution in *N* sulfuric acid, prepared by dissolving 12.6 Gm. of ceric ammonium sulfate (Fisher C-249) in 50 ml. of distilled water and 3 ml. of concentrated sulfuric acid and diluting to 100.0 ml., were used as oxidants. Hexane (Phillips high purity grade) and isooctane (Phillips pure grade 2, 2,4-trimethylpentane) were satisfactory as spectrophotometric solvents. Mandelic acid (Matheson, Coleman & Bell No. 5474), benzilic acid (Eastman No. 36), α-cyclopentylphenylglycolic acid,[1] and α-cyclopentyl-2-thiopheneglycolic acid[2] were used as test compounds. Homatropine methylbromide U.S.P., poldine methylsulfate,[3] oxyphencyclimine hydrochloride,[4] and penthienate bromide[2] were used as standards for tablet analysis. Homatropine methylbromide tablets[5] and locally purchased tablets of cyclandelate, poldine methylsulfate, oxyphencyclimine hydrochloride, and penthienate bromide N.F. were used to test the method.

Equipment.—A Bausch & Lomb spectronic 505 ratio recording spectrophotometer and a Beckman DU spectrophotometer were used in this study. The wavelength calibration was the same for both instruments, and absorbance measurements agreed within 1%. All absorbance measurements were made using 1-cm. silica cells. Other equipment included a Burrell model BB wrist-action mechanical shaker, a Thelco model 16 oven, and standard laboratory glassware.

Development of Periodate Oxidation Procedure.—Preliminary trials were conducted using mandelic acid as the test compound. The observation of Courtois (16) that elevated temperature was necessary to effect measurable oxidation of the acid to benzaldehyde was confirmed. The acidity of the reaction mixture was an important variable; no yield of benzaldehyde could be detected when saturated sodium bicarbonate was added, but addition of 3 *N* hydrochloric acid resulted in good yields. Heating mixtures of 2.0 ml. of 5 mg./100 ml. mandelic acid, 2.0 ml. of periodate, and 0.1 ml. of 3 *N* acid in glass-stoppered tubes in a boiling water bath for varying periods of time, cooling, and extracting with 20.0 ml. of hexane afforded an apparent 94% yield of benzaldehyde in 15 minutes and 85% in 45 minutes. It was concluded that the aldehyde was further oxidized. This problem was circumvented by including 20.0 ml. of isooctane in the reaction mixture to extract the product as it formed. Isooctane boils at boiling water temperature, and spectra in isooctane are identical with those in hexane. The procedure was applicable to benzilic acid, α-cyclopentylphenylglycolic acid, and α-cyclopentyl-2-thiopheneglycolic acid and to their ester drugs after saponification. Low or negligible amounts of carbonyl product were obtained by reaction with unhydrolyzed ester drugs.

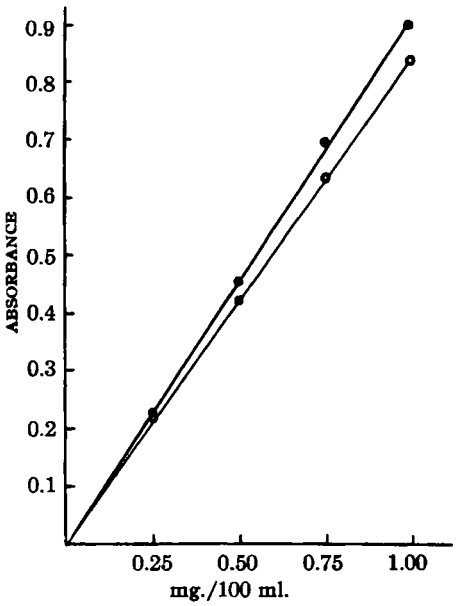

Fig. 1.—Beer's law adherence of mandelic acid oxidized to benzaldehyde. Key: ●, by 0.1 *M* ceric sulfate; ○, by 0.078 *M* ceric sulfate.

Development of Ceric Sulfate Oxidation Procedure.—Initial trials were based on the findings of Mathur and Rao (19) that oxidation of mandelic acid is activated by light. A mixture of 2.0 ml. of 5 mg./100 ml. mandelic acid, 2.0 ml. of 0.1 *M* ceric sulfate titrant (23), and 20.0 ml. of hexane was shaken 15 minutes in the light supplied by a 200-w. tungsten filament bulb at a distance of 20 cm. Benzaldehyde was evident in the spectrum of the filtered hexane phase in quantitative yield. The yield was not diminished, however, when light was totally excluded by wrapping the reaction flask in aluminum foil. Subsequent experiments were conducted in room light.

The effect of extracting the carbonyl product as it formed was determined by oxidizing benzilic acid in the presence and in the absence of hydrocarbon solvent. Unlike benzaldehyde, benzophenone would be expected to be stable under oxidizing conditions. The yield of benzophenone in the absence of extractant was 77% of that obtained when extractant was included in the reaction mixture.

Use of a 0.08 *M* ceric sulfate reagent gave 90% of the benzaldehyde obtained when mandelic acid was oxidized with 0.1 *M* reagent, but Beer's law was followed with both concentrations as shown in Fig. 1. Similarly, a quantitative amount of benzophenone was produced when benzilic acid was oxidized with 0.1 *M* reagent, but 94% of that amount was evident with an 0.08 *M* concentration of

Obtained through the courtesy of:
[1] E. F. Kluchesky, Lakeside Laboratories, Inc.
[2] M. E. Auerbach, Sterling-Winthrop Research Institute.
[3] J. Kleis, McNeil Laboratories, Inc.
[4] W. H. Lasar, Chas. Pfizer & Co., Inc.
[5] B. A. Marty, Neisler Laboratories, Inc.

TABLE I.—COMPARISON OF SPECTRAL DATA FOR OXIDIZED ACIDS WITH LITERATURE DATA FOR THE CARBONYL PRODUCTS

Oxidized Acid	Solvent	$\lambda_{max.}$, mμ	ε	Carbonyl Compd.	Solvent	$\lambda_{max.}$, mμ	ε	Ref.
Mandelic	Hexane	242	13,200	Benzaldehyde	Hexane	242	14,000	(20)
		248	11,100			248	12,500	
		280	810			280	1,400	
		289	610			289	1,200	
Benzilic	Isooctane	248	19,800	Benzophenone	Isooctane	248	19,500	(21)
						276s	2,460	
α-Cyclopentyl-phenylglycolic	Isooctane	239	15,500	Cyclopentyl phenyl ketone	Isooctane	238	12,900	(22)
		278	1,000			278	930	
		286	830			286	760	
α-Cyclohexyl-phenylglycolic[a]	Isooctane	239	13,100	Cyclohexyl phenyl ketone	Isooctane	239	12,000	(22)
		279	870			278	915	
		287	630			287	710	
α-Cyclopentyl-2-thiopheneglycolic	Isooctane	258	9,450	Methyl[b] 2-thienyl ketone	Isooctane	256.5	9,800	(24)
		275	7,700			273	7,250	

[a] Saponified oxyphencyclimine HCl was used. [b] Data for cyclopentyl 2-thienyl ketone were not available.

oxidant. To assure maximum sensitivity and to obviate standardizing the reagent, a 0.2 *M* ceric reagent was employed.

The procedure was applicable to all of the arylglycolic acids used in the study. Approximately quantitative yields were obtained.

Selectivity of the Oxidative Spectrophotometric Procedure.—Because ceric sulfate is a reagent with a high oxidation potential, it was of some interest to try the oxidative spectrophotometric procedure on a few aromatic compounds with low absorptivity. Oxidation of amphetamine provided no hydrocarbon-soluble chromophore. Benzaldehyde was identified by its characteristic spectrum after oxidation of phenylacetic acid in an amount equivalent to 11% of theoretical. Phenethyl alcohol gave 2.4%, and tropic acid about 15% of the calculated amount of benzaldehyde after oxidation and extraction. The extent of benzaldehyde formation from these compounds, unlike the arylglycolic acids, was enhanced by light; production of benzaldehyde was completely inhibited in the dark.

RESULTS AND DISCUSSION

Identity of Oxidation Products.—Ultraviolet spectra provide two criteria for identification, the position of the absorption maxima, $\lambda_{max.}$ and the intensity of absorption or absorptivity. A close correspondence of both criteria with literature values for the carbonyl compounds was found for the ceric oxidation products of phenylglycolic acids. Although no spectra data for α-cyclopentyl-2-thienyl ketone were found in the literature, the absorption curve obtained on oxidation of α-cyclopentyl-2-thiopheneglycolic acid corresponds well with data for an analog, methyl 2-thienyl ketone. Data obtained for oxidation products of the arylglycolic acids are compared with the literature values in Table I. Molar absorptivity was calculated from the concentration of acid oxidized in replicated experiments.

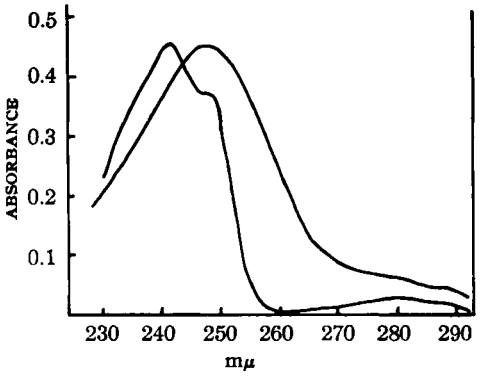

Fig. 2.—Ultraviolet absorption spectra of benzaldehyde from oxidation of mandelic acid, 0.5 mg./100 ml. (curve on left) and benzophenone from oxidation of benzilic acid, 0.5 mg./100 ml. (curve on right).

TABLE II.—SPECTRAL DATA FOR PERIODATE OXIDATION PRODUCTS OF ARYLGLYCOLIC ACIDS IN ISOOCTANE

Oxidized Acid	Oxidized, Min.	$\lambda_{max.}$, mμ	ε
Mandelic	15	242	14,080
	30		14,800
	60		15,150
Benzilic	15	248	19,380
	30		19,250
	60		20,450
α-Cyclopentylphenylglycolic	15	239	9,940
	30		11,500
	60		13,700
α-Cyclopentyl-2-thiopheneglycolic	15	258	8,020
		275	6,370

The molar absorptivities derived by ceric sulfate oxidation showed practically quantitative conversion to carbonyl compounds in 15 minutes. The periodate procedure gave yields which varied with reaction time and the structure of the glycolic acid. These data are presented in Table II.

The absorption curves for the carbonyl compounds are sufficiently characteristic to serve for identification of the arylglycolic acids, except for the α-cyclopentyl- and α-cyclohexylphenylglycolic acids. The spectra are shown in Figs. 2–4.

Oxidation of Arylglycolate Drugs.—Ester hydrolysis is catalyzed by both acid and base; thus, some degree of hydrolysis might be expected under the acid oxidative conditions employed. However, the ester drugs studied were hydrolyzed only to a

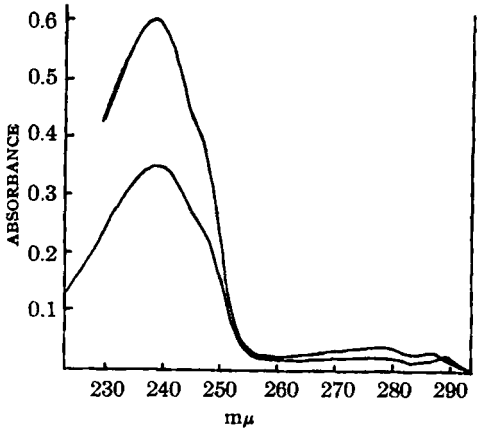

Fig. 3.—Ultraviolet absorption spectra of cyclohexyl phenyl ketone from oxidation of α-cyclohexylphenylglycolic acid, 1.165 mg./100 ml. (upper curve); and cyclopentyl phenyl ketone from oxidation of α-cyclopentylphenylglycolic acid, 0.505 mg./100 ml. (lower curve).

small extent evidenced by very low absorbances obtained when their solutions were oxidized. Heating 2.0 ml. of approximately 10 mg./100 ml. aqueous phenylglycolate solution or approximately 25 mg./100 ml. penthienate bromide with 0.1 ml. of 2.5 *N* sodium hydroxide at 80° for 15 minutes accomplished saponification efficiently. Shaking the cooled mixtures 15 minutes with 2.0 ml. of 0.2 *M* ceric sulfate and 20.0 ml. isooctane provided the data in Table III.

The precision obtained using this procedure was excellent. Measurement of the absorptivity of poldine methylsulfate had a standard deviation (S.D.) of 0.55% in five trials. Standard deviations for penthienate bromide in six trials were 0.62% at 258 mμ and 0.79% at 275 mμ.

Determination of Drugs in Tablets.—The procedure which follows was applicable to the determination of homatropine methylbromide tablets U.S.P. and commercial tablets of poldine methylsulfate and oxyphencyclimine hydrochloride.

Determine the average weight of not less than 20 tablets, and shake weighed amounts of pulverized tablet equivalent to 8–10 mg. of drug with exactly 100.0 ml. of distilled water for 15 minutes. Filter the mixture, and treat duplicate 2.0-ml. aliquots

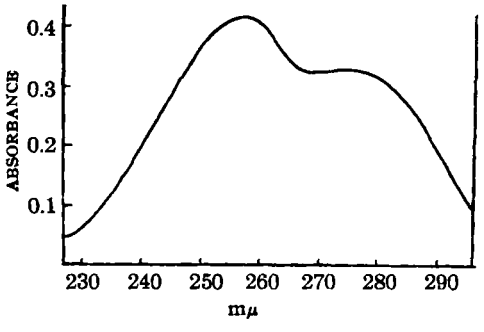

Fig. 4.—Ultraviolet absorption spectra of cyclopentyl 2-thienyl ketone from oxidation of α-cyclopentyl-2-thiopheneglycolic acid, 1.0 mg./100 ml.

with 0.1 ml. of 2.5 *N* sodium hydroxide for 15 minutes at 80° in a glass-stoppered 40-ml. centrifuge tube or 50-ml. volumetric flask. Cool to room temperature, and add 2.0 ml. of 0.2 *M* ceric sulfate and exactly 20.0 ml. of isooctane or hexane. Shake 15 minutes, and filter the solvent layer through paper. Similarly, saponify and oxidize a solution of reference drug of known concentration. Concomitantly, determine the absorbance of the sample and reference solutions in 1-cm. silica cells at the $\lambda_{max.}$ Calculate the amount of drug per tablet from the equation

$$\text{drug, mg./tablet} = \frac{A_{sample}}{A_{ref.}} \times \text{mg. std.} \times \frac{\text{av. tablet wt.}}{\text{sample wt.}}$$

(See Table IV.)

Cyclandelate.—The drug, the only ester of the group not an amine salt, has a low water solubility, but it is soluble in alcohol and ether. It was extracted from tablets with 100.0 ml. of methanol, shaking for 10 minutes. A 2.0-ml. aliquot of the filtered extract was treated with 2 ml. of water and 5 ml. of 0.05 *N* sodium hydroxide. The solution was evaporated to about 2 ml. on the steam bath.

TABLE III.—SPECTROPHOTOMETRIC DATA CALCULATED FOR ARYLGLYCOLATE DRUGS AFTER SAPONIFICATION AND CERIC OXIDATION

Oxidized Drug	$\lambda_{max.}$, mμ	ε
Homatropine methylbromide	242	13,200
Poldine methylsulfate	248	17,700
Oxyphencyclimine hydrochloride	239	13,100
Penthienate bromide	258	9,890
	275	7,750

It was then oxidized by the ceric procedure given above and by the periodate procedure, using 0.2 ml. of 3 *N* sulfuric acid to neutralize the excess alkali and insure an acid medium. Since no pure cyclandelate was available as a reference standard, an equivalent concentration of mandelic acid was determined concomitantly, using the same dilutions and conditions. The hydrocarbon extracts were filtered and read at 242 mμ, and the amount of drug was calculated from the equation

$$\text{Cyclandelate, mg./tablet} = \frac{A_{sample}}{A_{M.A.}} \times \frac{276.36}{152.14} \times \text{mg. M.A.} \times \frac{\text{av. tablet wt.}}{\text{sample wt.}}$$

where 276.36 is the formula weight of cyclandelate and 152.14 the formula weight of mandelic acid (M.A.).

The periodate and ceric sulfate procedures yielded results which corresponded closely. The absorbances for sample and standard obtained in the periodate procedure, however, were 90% of the values obtained by ceric oxidation. (See Table IV.)

Penthienate Bromide.—Determination of the drug in tablets by the general procedure for arylglycolates presented above gave an apparent 80% of label declaration, but direct spectrophotometry (2) showed 98% was present. It was determined that penthienate bromide was incompletely ex-

TABLE IV.—ASSAY OF ARYLGLYCOLATE DRUGS IN TABLETS

Drug	mg./Tablet Declared	mg./Tablet Found	Method
Homatropine methylbromide	2.5	2.4	Ceric sulfate
Cyclandelate	100.0	99.5	Ceric sulfate
		99.2	Periodate
Poldine methylsulfate	4.0	4.0	Ceric sulfate
Oxyphencyclimine hydrochloride	10.0	10.1	Ceric sulfate
Penthienate bromide	5.0	5.0	Ceric sulfate

TABLE V.—PER CENT ARYLGLYCOLATE DRUG HYDROLYZED IN TABLET EXTRACTS

Drug	% Hydrolyzed	Procedure
Homatropine methylbromide	2.3	Ceric
Cyclandelate	17.6	Ceric
	11.6	Periodate
Poldine methylsulfate	13.8	Ceric
Oxyphencyclimine hydrochloride	4.3	Ceric
Penthienate bromide	2.1	Ceric

tracted from the tablets by shaking with 100 ml. of water. Direct spectrophotometry at the 239 mμ maximum showed the drug was completely extracted with methanol. A quantity of pulverized tablet equivalent to 5 mg. of penthienate bromide was shaken 15 minutes with 100.0 ml. of methanol. A 2.0-ml. aliquot of methanol filtrate was treated with 2.0 ml. of water and 0.1 ml. of 2.5 *N* sodium hydroxide. The solution was evaporated to 2 ml. on the steam bath, then heated 15 minutes at 80°. A reference solution of penthienate bromide treated similarly was run concomitantly. Only 92% of claim was obtained when the ceric procedure was used, and the isooctane layer after periodate oxidation was violet. Quite stable and reproducible absorbance values for the reference solution were obtained; no trace of color was seen after periodate oxidation of reference penthienate bromide or α-cyclopentyl-2-thiopheneglycolic acid. It was concluded that an excipient with strong reducing properties was present in the tablets. (The violet obtained in the periodate oxidation of the tablet extract may have been due to iodine, but it was not positively identified.) Use of 4.0 ml. of 0.2 *M* ceric reagent, instead of 2.0 ml., increased the absorbance obtained by oxidation of the tablet extract without, however, affecting the absorbance of the standard. (See Table IV.)

Stability of Arylglycolate Drugs.—Although no stability studies were performed, a semiquantitative indication of the stability of the drugs to the acid oxidative conditions was obtained by running the procedure on the tablet extracts without prior saponification. The results in Table V were derived from the ratio of the absorbance of the unsaponified to the saponified tablet extract after oxidation. Some indication was obtained that these values may be partly due to the extraction of alkaline substances from the tablet, for the extract of poldine methylsulfate tablets had pH 7.5 compared with a pH of 6.3 for an equivalent concentration of reference drug in water. A comparison of the absorbances obtained in the oxidative spectrophotometric determination on extracts from drug dosage forms and reference arylglycolate drugs, omiting the saponification step of the procedure, may provide useful stability information for pharmaceutical formulators of these compounds.

SUMMARY

Oxidation of arylglycolic acids to carbonyl compounds greatly increases the sensitivity of their determination by ultraviolet spectrophotometry and affords a means for identification. Periodate and ceric sulfate oxidation procedures are described which are general for arylglycolic acids.

The oxidative spectrophotometry procedure is shown to be applicable to mandelic acid, benzilic acid, α-cyclopentylphenylglycolic acid, and α-cyclopentyl-2-thiopheneglycolic acid. Assay procedures are presented for the arylglycolate drugs, homatropine methylbromide, cyclandelate, poldine methylsulfate, oxyphencyclimine hydrochloride, and penthienate bromide in tablets. The possible application of the procedure in stability studies is suggested.

REFERENCES

(1) Ernsting, M. J. E., *et al.*, *Pharm. Weekblad*, **88**, 605 (1953); through *Chem. Abstr.*, **48**, 1893*h*(1954).
(2) *Drug Standards*, **26**, 212(1958).
(3) Singleton, D. O., and Wells, G. M., *J. Pharm. Pharmacol.*, **12**, 171T(1960).
(4) Langley, P. F., *et al.*, *ibid.*, **15**, 100(1963).
(5) Rapson, H. D. C., Austin, K. W., and Cutmore, E. A., *ibid.*, **14**, 66T(1962).
(6) Bandelin, F. J., THIS JOURNAL, **37**, 10(1948).
(7) Robinson, R. H., *ibid.*, **41**, 392(1952).
(8) Robinson, R. H., Kaulfers, H. C., and Duelly, E. B., *ibid.*, **40**, 56(1951).
(9) Bister, F., and Wolff, J. H., *Arzneimittel Forsch.*, **3**, 481(1953).
(10) Ernsting, M. J. E., *et al.*, *ibid.*, **6**, 145(1956); Ernsting, M. J. E., *et al.*, *ibid.*, **12**, 632, 691(1962).
(11) Bister, F., and Wolff, J. H., *ibid.*, **2**, 423(1952).
(12) Rigby, W., *J. Chem. Soc.*, **1950**, 1907.
(13) Bakarat, M. Z., and El-Wahab, M. F. A., *J. Am. Chem. Soc.*, **75**, 5731(1953).
(14) Berka, A., and Zýka, J., *Chem. Listy*, **52**, 930(1958); through *Chem. Abstr.*, **53**, 5141*a*(1959).
(15) Berka, A., *Cesk. Farm.*, **8**, 561(1959); through *Chem. Abstr.*, **54**, 19307*c*(1960).
(16) Courtois, J., *Ann. Pharm. Franc.*, **2**, 148(1944); through *Chem. Abstr.*, **43**, 7379*d*(1949).
(17) Verma, M. R., and Paul, S. D., *J. Sci. Res. India*, **12B**, 178(1953); through *Chem. Abstr.*, **47**, 9216*d*(1953).
(18) Krishna, B., and Tewari, K. C., *J. Chem. Soc.*, **1961**, 3097.
(19) Mathur, N. K., and Rao, S. P., *Current Sci. India*, **29**, 92(1960); through *Chem. Abstr.*, **54**, 24114*g*(1960).
(20) Braude, E. A., and Sondheimer, F., *J. Chem. Soc.*, **1955**, 3754.
(21) Rekker, R. F., and Nauta, W. Th., *Rec. Trav. Chim.*, **73**, 959(1954); through Ungnade, H. E., ed., "Organic Electronic Spectral Data," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1960, p. 348.
(22) Mariella, R. P., and Raube, R. R., *J. Am. Chem. Soc.*, **74**, 521(1952).
(23) Kolthoff, I. M., and Sandell, E. B., "Textbook of Quantitative Inorganic Analysis," 3rd ed., The Macmillan Co., New York, N. Y., 1952, p. 582.
(24) A.P.I. Res. Project 44 I 8, 315(1949); through Kamlet, M. J., ed., "Organic Electronic Spectral Data," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1960, p. 90.