Spectrophotometric Determination of Aspirin by Transacetylation of 4-Aminophenol

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Aspirin transacetylates 4-aminophenol, yielding acetaminophen (*N*-acetyl-4-aminophenol), which can be determined by its oxidation to an orange-yellow product either by iodylbenzene in acetone when the absorbance is measured at 430 nm or by photometric titration with 2-iodylbenzoate in acetone–water medium at 444 nm. Salicylic acid, salicylamide, oxyphenbutazone, caffeine, and sodium hydrogen carbonate do not interfere. Drug mixtures of acetaminophen and aspirin have been analyzed by determining acetaminophen alone directly with iodyl reagents and then determining acetaminophen plus aspirin after 4-aminophenol reaction; aspirin is found by difference.

As an aromatic ester, aspirin (acetylsalicylic acid) has a good leaving group and is thus relatively susceptible to hydrolysis to salicylic and acetic acids (*1–3*) and other acyl transfer reactions, the catalytic effect being shown by the ortho carboxyl group and by the presence of moisture or basic substances (*4, 5*). It is this phenomenon that accounts for the instability of aspirin in the pharmaceutical preparations (*2*). According to an extensive survey of aspirin tablets (*6*), levels of salicylic acid can be similar to those of acetylsalicylic acid, and under certain conditions a large number of other products can be formed (*6–9*).

In recent formulations aspirin is dispensed with acetaminophen, caffeine, and oxyphenbutazone. Methods, e.g., titration with a base in nonaqueous media (*10*), nitrozation followed by alkalization (*11*), and bromimetry (*12*) are general reactions and cannot be used in the presence of salicylic acid or for compound tablets. Colorimetry (*13*), fluorometry (*5*), GC (*14, 15*), and room-temperature phosphorimetry (*16*) have been used in many methods but HPLC is convenient for monitoring salicylic acid simultaneously with aspirin and other active ingredients (*17–20*). Conversion of aspirin into salicylic acid during sample preparation is a vexing problem and it can limit the accuracy of determination. Attempts to obviate or minimize errors from this source include injection of sample within a few minutes of its preparation (*21*), extrapolation of results back to time zero (*5*), preparation of calibrated standards with matching amounts of aspirin (*7*), selection of solvents to minimize salicylic acid formation (*4, 20, 22*), and separation of aspirin from product ingredients that accelerate its degradation (*22*). Complex formulations have been analyzed by ultraviolet absorption after separation of their constituents by partition chromatography (*23–25*).

During a project to analyze multicomponent drugs without preseparation of their constituents (*26–31*), we aimed to determine aspirin in the presence of salicylic acid and other active constituents of drug formulations. It was found that aspirin quickly trans acetylates 4-aminophenol to produce acetaminophen (*N*-acetyl-4-aminophenol), which can be determined spectrophotometrically by its reaction with iodylbenzene or titrated photometrically with 2-iodylbenzoate. Any acetaminophen already present with aspirin can be determined by reaction with iodyl reagents without treatment of drug with 4-aminophenol.

EXPERIMENTAL SECTION

Reagents. Iodyl reagents were synthesized by the procedure described by Fieser and Fieser (*32*) and by the bromate oxidation method of Banerjee et al. (*33*) modified as follows:

Iodylbenzene. To a mixture of 20 g of iodobenzene, 200 mL of 40% v/v sulfuric acid and 50 mL of anhydrous acetic acid, heated on a boiling water bath, there was added slowly a solution of 15 g of potassium bromate in 150 mL of warm water during a period of 30 min with vigorous stirring (in a fume chamber). The heating was continued for 90 min during which all the bromine evolved was removed. After cooling, the supernatant liquid was decanted, the product (oily owing to unreacted iodobenzene) was washed with water, macerated with 50 mL of chloroform, filtered, and washed with chloroform to furnish a silky white solid, mp 222 °C (decomposition). The product obtained in this way (12 g, 50% yield) was found to be 98% pure by iodometric analysis (*32*).

2-Iodylbenzoic Acid. A solution of 9 g of potassium bromate in 100 mL of hot water was added during a period of 20 min to a boiling mixture of 12 g of 2-iodobenzoic acid, 50 mL of anhydrous acetic acid, and 100 mL of 40% v/v sulfuric acid and refluxed for 90 min during which all the bromine evolved was removed. The product obtained on cooling was filtered and washed with water to furnish 13 g (90% yield) of 2-iodylbenzoic acid, mp 222 °C (decomposition), having a purity of 95% as determined by iodometry (*32*).

2-Iodylbenzoate. A 0.01 M solution was prepared by dissolution of 2.8 g of the free acid reagent in a slight molar excess of potassium hydroxide (0.7 g in 50 mL of water) and diluting to volume in a 1-L calibrated flask. It was standardized iodometrically.

$$O_2I{\cdot}C_6H_4{\cdot}CO_2^- + 4I^- + 5H^+ \rightarrow 2I_2 + I{\cdot}C_6H_4{\cdot}CO_2H + 2H_2O$$

Alternatively, a known amount of analytical reagent grade acetaminophen (*N*-acetyl-4-aminophenol) is photometrically titrated with the reagent (as described below), the two substances reacting in a 1:1 molar ratio. The strength of 2-iodylbenzoate determined by two methods agreed within 0.2%.

Samples. High-purity samples of aspirin and acetaminophen were used. All drug samples tested were fresh.

Apparatus. A Pye Unicam SP 8-100 spectrophotometer was used.

Procedures Using Iodylbenzene. *Determination of Aspirin: Preparation of Calibration Graph.* In a 50-mL round-bottomed flask fitted with a reflux water condenser, 100 mg of accurately weighed aspirin is combined with about 200 mg of 4-aminophenol and 20 mL of ethanol and the mixture is swirled to effect dissolution and refluxed gently for about 20 min. After cooling, the contents are transferred to a 50-mL calibrated flask and diluted to the mark with acetone. A 2-mL portion is further diluted to 50 mL with acetone and 1–6-mL aliquots of this solution are each diluted to about 6 mL with acetone and stirred for 1 min with about 50 mg of powdered iodylbenzene in 10-mL beakers. The colored solution is filtered through a small fluted Whatman No. 41 filter paper into a 10-mL calibrated flask, the residue is washed with acetone, and the filtrate is made up to the mark with the same solvent. The absorbance is measured at 430 nm in a 1-cm cell against acetone.

Drug Samples. A known number of tablets are ground to a fine powder and an accurately weighed portion of powder containing about 100 mg of aspirin is combined with about 200 mg of 4-aminophenol and 20 mL of ethanol and the mixture is refluxed. The cooled solution is filtered (to remove starch, etc.) through Whatman No. 41 filter paper into a 50-mL calibrated flask and made up to the mark with acetone. It is further diluted

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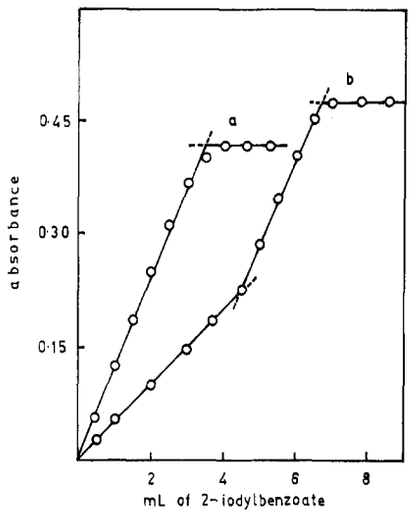


Figure 1. Photometric titration curves of acetaminophen (a) and aspirin (b) with 2-iodylbenzoate.

and treated for color development by the procedure described above.

Determination of Aspirin and Acetaminophen in Drug Formulations. To prepare a calibration graph for acetaminophen, 10 mg of accurately weighed acetaminophen is dissolved in acetone in a 50-mL calibrated flask and made up to the mark; 1–5-mL portions are each diluted to about 5 mL and stirred with about 50 mg of powdered iodylbenzene in 10-mL beakers for 1 min, the solutions are filtered into a 10-mL calibrated flask, the filtrate is diluted with acetone to the mark, and the absorbance is read at 430 nm against acetone.

For the analysis of mixtures of aspirin and acetaminophen in drug formulations, two determinations are necessary on two separate portions of the blended drug.

Portion 1. The powdered drug containing about 10 mg of acetaminophen is stirred with 30 mL of acetone, the mixture is filtered into a 50-mL calibrated flask and diluted to volume, and a 2-mL portion is treated for color development as described for preparation of the calibration graph for acetaminophen. This determination yields acetaminophen alone.

Portion 2. The powdered drug containing not more than 150 mg of the sum of aspirin and acetaminophen is analyzed by the method described for the drug samples of aspirin. Aspirin is obtained by the difference of absorbance as calculated from

$$\text{absorbance for aspirin} = \text{ABS}_2 - \left[\frac{D_1 w_2}{D_2 w_1}\,\text{ABS}_1\right] \qquad (1)$$

where ABS_1/D_1 and ABS_2/D_2 are absorbance values/total dilution for portion 1, w_1 mg, and portion 2, w_2 mg, respectively.

Procedures Using 2-Iodylbenzoate. *Determination of Aspirin.* A known number of tablets are weighed and ground to a fine powder. An accurately weighed portion containing 3–10 mg of aspirin is combined with about 50 mg of 4-aminophenol and 20 mL of ethanol and refluxed for 20 min. The cooled soltuion is mixed with 30 mL of acetone, filtered into a photometric titration cell, treated with 1 mL of 5% v/v sulfuric acid, and diluted to about 80 mL with water. The absorbance is set to zero or minimum at 444 nm and the solution is titrated with 0.01 M 2-iodylbenzoate measuring absorbance after each increment. The end point is determined graphically by plotting absorbance (corrected for dilution) against the volume of titrant added (Figure 1)

$$\text{aspirin, mg/tablet} = \frac{180VMA}{w} \qquad (2)$$

where V is the volume of 2-iodylbenzoate (molarity M) used, w is the weight (mg) of sample taken for analysis, and A is the average weight (mg) of a tablet.

Determination of Aspirin and Acetaminophen in Drug Formulations. Two analyses are necessary using two separate accurately weighed portions of the blended tablet each containing not more than 0.1 mmol of the intended compound.

Portion 1. Portion 1 was stirred with 30 mL of water for 5 min and filtered into a photometric titration cell, the residue was washed with 5 mL of water, the filtrate was combined with 1 mL of 5% v/v sulfuric acid diluted to about 80 mL with acetone, and photometrically titrated with 0.01 M 2-iodylbenzoate at 444 nm.

Portion 2. Portion 2 was mixed with about 50 mg of 4-aminophenol and 20 mL of ethanol, refluxed for 20 min, cooled, diluted with 25 mL of water, filtered into a photometric cell, and photometrically titrated with 0.01 M 2-iodylbenzoate at 444 nm as described previously

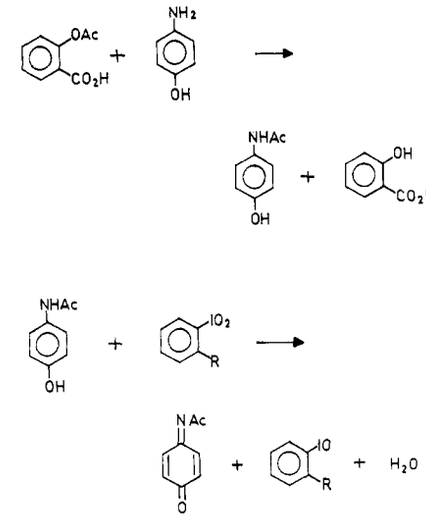
$$\text{acetaminophen, mg/tablet} = \frac{151V_1MA}{w_1} \qquad (3)$$

$$\text{aspirin, mg/tablet} = 180MA\left[\frac{V_2}{w_2} - \frac{V_1}{w_1}\right] \qquad (4)$$

where V_1 and V_2 are the volumes of 2-iodylbenzoate (molarity M) required for the titration of portion 1, w_1 mg, and portion 2, w_2 mg, respectively, of the powdered tablet, and A is the average weight (mg) of a tablet.

RESULTS AND DISCUSSION

Alkali metal salts of 2-iodylbenzoic acid when used in acetone–water medium in the presence of acids or iodylbenzene (which is insoluble in water or commonly used organic solvents) when employed as its suspension in acetone react almost instantaneously with acetaminophen yielding an orange-yellow color, the molar ratio of the reaction being 1:1 using 2-iodylbenzoate. On treatment with iodyl reagents, a reaction mixture of aspirin and 4-aminophenol also yields an orange-yellow color that has the same visible absorption spectrum (Figure 2). When treated separately, 4-aminophenol or aspirin do not produce any color with iodyl reagents. Thus, aspirin transacetalates 4-aminophenol exclusively at its more reactive amino group to form acetaminophen (*34*). The following are the plausible reactions



where R is –H (in iodylbenzene) or $-CO_2H$ (in 2-iodylbenzoic acid). The proposed 1,4-quinoneimine structure of the colored product is confirmed by its reversible oxidation–reduction reaction, which is discharge of color by reduction with ascorbic acid and reappearance of color by oxidation with an iodyl reagent, and by the fact that 4-aminophenol acetylated at both amino and hydroxyl groups does not yield any color with iodyl reagents. The possibility of acetylation of hydroxyl group in the present procedure is only remote since 4-aminophenol is taken double the amount of aspirin. The colored product absorbs maximally at 430 nm when iodylbenzene is used as a reagent in acetone, or at 444 nm when 2-iodylbenzoate is employed in acetone–water medium. In acetone, 2-iodylbenzoic acid does not produce any color and in aqueous medium the color has low intensity. However, a pronounced

Table I. Determination of Aspirin in Drug Formulations

drug	label claim, mg	found,[a] mg: iodylbenzene method (RSD)	found,[a] mg: 2-iodylbenzoate method (RSD)	found,[a] mg: Comparison method (ref)
laboratory made				
tablet no. 1[b]	101	102 (0.2)	103 (0.3)	104 (20)
tablet no. 2[c]	200	203 (0.2)	198 (0.3)	
tablet no. 3[d]	150	148 (0.5)	152 (0.4)	151 (12)
micropyrin[e]	350	338 (0.3)	336 (0.3)	339 (20)
tuxyne[f]	300	316 (0.4)	319 (0.5)	
disprin[g]	350	340 (0.4)	341 (0.3)	338 (20)
majoral	75	79 (0.2)	81 (0.2)	82 (12)
bambitini[h]	75	80 (0.3)	78 (0.2)	
anacin[i]	400	438 (0.3)	443 (0.2)	445 (12)
coldarin[j]	600	574 (0.3)	569 (0.4)	576 (12)
oxipyrin plus[k]	250	239 (0.4)	242 (0.4)	

[a] Average of six determinations; RSD, relative standard deviation. [b] Coexisting substances include caffeine (20 mg) and salicylic acid (100 mg). [c] Coexisting substance is salicylamide (50 mg). [d] Coexisting substance is sodium hydrogen carbonate (50 mg). [e] Coexisting substance is caffeine (20 mg). [f] Coexisting substances include caffeine (30 mg) and chlorpheniramine maleate (2 mg). [g] Coexisting substances include calcium carbonate (105 mg) and anhydrous citric acid (35 mg). [h] Coexisting substance is menadione (0.75 mg). [i] Coexisting substance is caffeine (30 mg). [j] Coexisting substances include phenylephrine hydrochloride (10 mg), terpin hydrate (30 mg), caffeine (30 mg), and calcium carbonate (200 mg). [k] Coexisting substances include oxyphenbutazone (100 g), diazepam (2 mg), and dried aluminum hydroxide (100 mg).

Table II. Determination of Aspirin and of Acetaminophen in Drug Formulations

drug	label claim,[a] mg: I	label claim,[a] mg: II	found,[b] mg: iodyl reagents method: I (RSD)	found,[b] mg: iodyl reagents method: II (RSD)	found,[b] mg: comparison method (ref): I	found,[b] mg: comparison method (ref): II
laboratory made						
tablet no. 1	100	158	101 (0.4) *102 (0.3)*	160 (0.2) *157 (0.2)*	99 (20)	159 (20)
tablet no. 2	209	112	210 (0.4) *208 (0.3)*	111 (0.2) *210 (0.3)*	212 (20)	110 (30)
tablet no. 3	152	155	150 (0.4) *153 (0.5)*	154 (0.1) *157 (0.3)*	153 (19)	153 (19)
veganin[c]	250	250	264 (0.4) *269 (0.5)*	238 (0.2) *242 (0.2)*	261 (20)	240 (30)
safrine[d]	150	300	144 (0.4) *341 (0.3)*	280 (0.3) *133 (0.2)*	146 (19)	278 (19) 130 (30)
sarbyna strong[d]	350	125				
painkill[d]	300	150	307 (0.4) *309 (0.3)*	143 (0.4) *140 (0.1)*	304 (20)	140 (20)
panjon[d]	300	150	361 (0.5)	141 (0.4)	364 (20)	139 (30)
panbin[d]	300	150	*339 (0.5)*	*132 (0.4)*		130 (30)

[a] I, aspirin; II, acetaminophen. [b] Average of six determinations; results obtained by using iodylbenzene are italic; others were obtained by using 2-iodylbenzoate. [c] Coexisting substance is codeine phosphate (5 mg). [d] Coexisting substance is caffeine (30 mg).

hyperchromic effect without any appreciable change in λ_{max} is observed when acetone, methanol, or ethanol is used as a cosolvent with water (Figure 2). This observation has been used in the sensitive and accurate measurement of absorbance during photometric titrations with 2-iodylbenzoate. Because of the critical dependence of color absorbance on the ratio of organic solvent and water, the 2-iodylbenzoate method could not be used for the direct (nontitrimetric) determination of aspirin. With iodylbenzene as an oxidimetric reagent in acetone, the color developed has a molar absorptivity of 2.65×10^3 L mol^{-1} cm^{-1} at 430 nm, follows Beer's law in the range 0–70 μg mL^{-1} of aspirin in the final solution, remains stable up to an hour, and shows a 10% decrease after 2 h. The absorption spectrum is unaffected by the use of as high as 100-fold molar excess of iodylbenzene. The molar absorptivity for acetaminophen is 1.58×10^3 L mol^{-1} cm^{-1} at 430 nm.

It is apparent from the photometric titration curve (Figure 1) that some reducing matter is also produced along with acetaminophen by the reaction of aspirin with 4-aminophenol. This substance (which could not be identified) delays the color reaction of acetaminophen until it has completely reacted. Since the oxidation product of this unknown substance is also colored, the molar absorptivity found for aspirin is higher than that for authentic acetaminophen. The titration curve consists of two sharp breaks, the second corresponding to the acetaminophen reaction. Any acetaminophen already present with aspirin in formulations is also titrated along with that produced in reaction with 4-aminophenol, but it can be determined without any interference from aspirin by a separate titration of drug avoiding 4-aminophenol treatment. Aspirin is found by difference. Results are given in Tables I and II for the determination of aspirin when present alone or in combination with acetaminophen in drug formulations. The reliability of present methods has been checked by analyzing laboratory made tablets spiked with known amounts of aspirin and acetaminophen. For the determination of aspirin when present alone the mean error is 0.4% with relative standard deviation of 0.6%, and in the presence of acetaminophen the respective values are 0.6% and 0.8%. For the determination of acetaminophen either present alone or in mixtures with aspirin, the mean error is 0.2% with relative standard of deviation of 0.3%.

Substances that do not interfere in aspirin determination include salicylic acid, salicylamide, oxyphenbutazone, caffeine, and sodium hydrogen carbonate; others appear in the footnote to Tables I and II. *N*-Acetyl or *O*-acetyl compounds, e.g., acetanilide, phenacetin, *N*-acetylanthranilic acid, 4-*O*-acetylhydroxybenzoic acid, and hexa-*O*-acetylmannitol do not

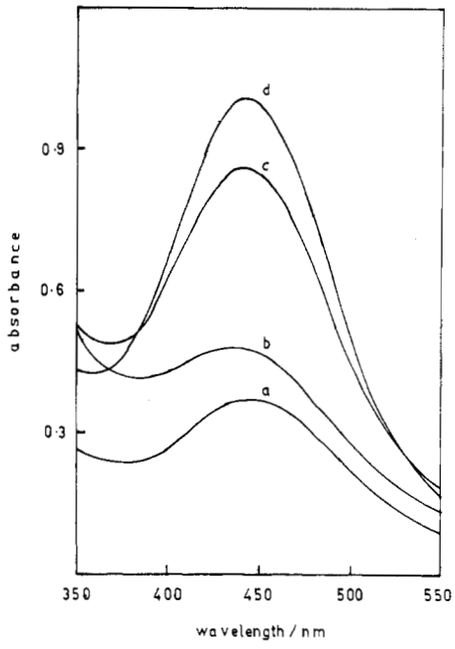


Figure 2. Absorption spectra of the colored product of acetaminophen in water (a) and in 40% acetone (d) and of aspirin in water (b) and in 40% acetone (c).

trans acetylate 4-aminophenol. The only interfering substance is acetaminophen and it should be predetermined.

Registry No. Aspirin, 50-78-2; 4-aminophenol, 123-30-8; acetaminophen, 103-90-2.

LITERATURE CITED

(1) Florey, K. In "Analytical Profiles of Drug Substances"; Florey, K., Ed.; Academic Press: New York, 1979; Vol. 8, p 1.
(2) Connors, K. A.; Amidon, G. L.; Kennon, L. "Chemical Stability of Pharmaceuticals", Wiley: New York, 1979; p 151.
(3) Kelley, C. A. *J. Pharm. Sci.* **1970**, *59*, 1053.
(4) Bundgaard, H. *Arch. Pharm. Chem., Sci. Ed.* **1976**, *4*, 103.
(5) Baum, R. G.; Cantwell, F. F. *J. Pharm. Sci.* **1978**, *67*, 1066.
(6) Kirchhoefer, R. D.; Reepmeyer, J. C.; Juhl, W. E. *J. Pharm. Sci.* **1980**, *69*, 550.
(7) Taguchi, V. Y.; Cotton, M. L.; Yates, C. H.; Millar, J. F. *J. Pharm. Sci.* **1981**, *70*, 64.
(8) Mroso, P. V.; Li Wan Po, A.; Irwin, W. J. *J. Pharm. Sci.* **1982**, *71*, 1096.
(9) Reepmeyer, J. C. *J. Pharm. Sci.* **1983**, *72*, 322.
(10) Walash, M. I.; Agarwal, S. P.; Martin, M. I. *Can. J. Pharm. Sci.* **1972**, *7*, 123.
(11) Belal, S. F.; Elsayed, M. A. H.; Elwalily, A.; Abdine, H. *Analyst (London)* **1979**, *104*, 919.
(12) Boudeville, P.; Burgot, J. L.; Chauvel, Y. *Analusis* **1983**, *11*, 406.
(13) Harris, P. A.; Riegelman, S. *J. Pharm. Sci.* **1967**, *56*, 713.
(14) Nickerly, J. G. *Anal. Chem.* **1964**, *36*, 2248.
(15) Tam, Y. K.; Au, D. S. L.; Abbott, F. S. *J. Chromatogr.* **1979**, *1974*, 239.
(16) Bateh, R. P.; Winefordner, J. D. *J. Pharm. Biomed. Anal.* **1983**, *1*, 113.
(17) Ascione, P. P.; Chrekrian, J. P. *J. Pharm. Sci.* **1975**, *64*, 1029.
(18) Gupta, V. D. *J. Pharm. Sci.* **1980**, *60*, 110.
(19) Jalal, I. M.; Sa'sa, S. I. *Talanta* **1984**, *31*, 1015.
(20) Bevitt, R. N.; Mather, J. R.; Sharman, D. C. *Analyst (London)* **1984**, *109*, 1327.
(21) Kirchhoefer, R. D.; Juhl, W. E. *J. Pharm. Sci.* **1980**, *69*, 548.
(22) Galante, R. N.; Visalli, A. J.; Grim, W. M. *J. Pharm. Sci.* **1984**, *73*, 195.
(23) "U.S. Pharmacopeia XX"; Mack Printing Co.: Easton, PA.
(24) Cunningham, C. G.; Barkan, S. *J. Assoc. Off. Anal. Chem.* **1973**, *56*, 667.
(25) Cunningham, C. G.; Barkan, S. *J. Assoc. Off. Anal. Chem.* **1974**, *57*, 728.
(26) Verma, K. K.; Gulati, A. K. *Anal. Chem.* **1980**, *52*, 2336.
(27) Verma, K. K.; Gupta, A. K. *Anal. Chem.* **1982**, *54*, 249.
(28) Verma, K. K.; Gulati, A. K. *Anal. Chem.* **1982**, *54*, 2550.
(29) Verma, K. K.; Jain, A.; Rawat, R. *J. Assoc. Off. Anal. Chem.* **1984**, *67*, 262.
(30) Verma, K. K.; Gulati, A. K.; Palod, S.; Tyagi, P. *Analyst (London)* **1984**, *109*, 735.
(31) Verma, K. K.; Tyagi, P.; Gulati, A. K. *J. Pharm. Biomed. Anal.*, in press.
(32) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley-Interscience: New York, 1967; Vol. 1 pp 507, 511.
(33) Banerjee, A.; Banerjee, G. C.; Bhattacharya, S.; Banerjee, S.; Samaddar, H. *J. Indian Chem. Soc.* **1981**, *58*, 605.
(34) Furniss, B. S.; Hannaford, A. J.; Robers, V.; Smith, P. W. G.; Tatchell, A. R. "Vogel's Textbook of Practical Organic Chemistry"; Longman: London, 1978; p 753.

RECEIVED for review August 26, 1985. Accepted November 4, 1985. Thanks are due to University Grants Commission, New Delhi, for a Junior Research Fellowship to A.J.

Spectrophotometric Determination of Iron in Wines, Foods, and Minerals with 5,5-Dimethyl-1,2,3-cyclohexanetrione 1,2-Dioxime 3-Thiosemicarbazone

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A new reagent, 5,5-dimethyl-1,2,3-cyclohexanetrione 1,2-dioxime 3-thiosemicarbazone, has been synthesized and studied spectrophotometrically and a simple, rapid, selective, and sensitive method for the spectrophotometric determination of iron has been developed based upon the formation of (5,5-dimethyl-1,2,3-cyclohexanetrione 1,2-dioxime 3-thiosemicarbazone)-iron(II) complex. A violet color is formed in strongly acid medium and the absorbance is measured at 550 nm. The molar absorptivity is 8.9 × 10^3 L·mol^{-1}·cm^{-1} and the relative error is 0.5% (3 ppm of iron). The detection limit is 0.05 μg·mL^{-1} of Fe(II) and the determination limit is 0.1 μg·mL^{-1} of Fe(II). The method has been applied to the determination of iron in wines, minerals, and foods.

Thiosemicarbazones have been widely used for spectrophotometric determination of inorganic ions and their analytical applications have been reviewed (*1–3*). Thiosemicarbazones of greatest analytical interest are those that posses another complexing group. The most important of these are the *N*-pyridine, the oxime group, and the phenolic group, in adjacent position to the thiocarbonyl group. The other complexing group can be other thosemicarbazonic group. In this paper, the analytical properties and applications of 5,5-dimethyl-1,2,3-cyclohexanetrione 1,2-dioxime 3-thiosemicarbazone (DCDT) are presented.

An important section of this paper is the development of a method of determination of iron in wine. The determination

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