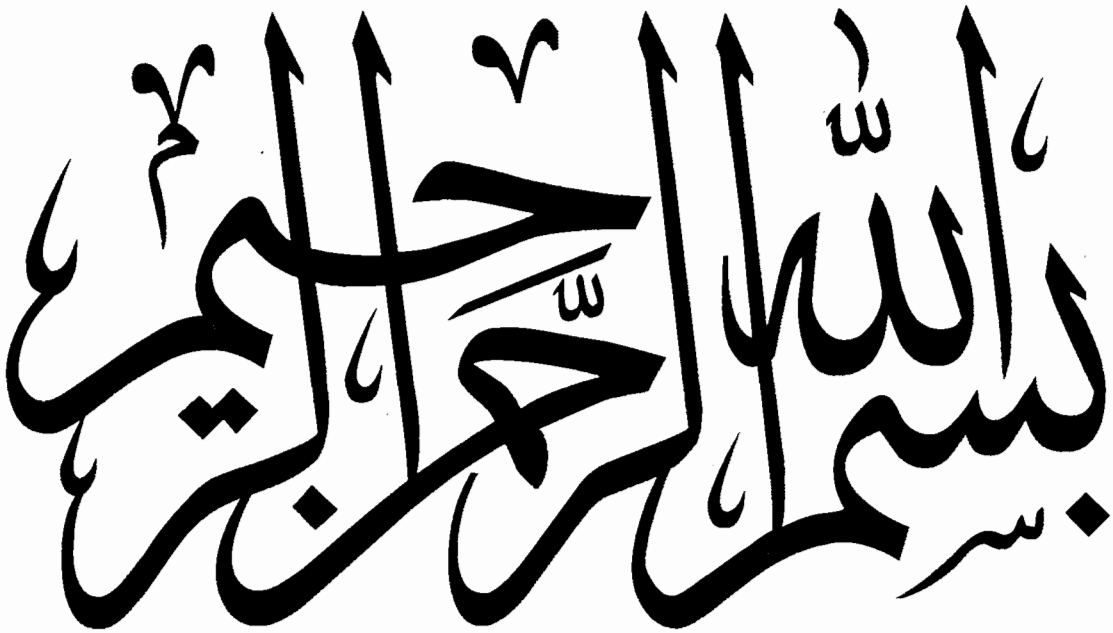

بسم الله الرحمن الرحيم

این گزارش نتیجه طرح پژوهشی با عنوان

سنتز فنل فتالئین

است که در یکصد و سیزدهمین جلسه مورخه ۸۲/۱۱/۱۹
بتصویب نهایی شورای پژوهشی دانشگاه صنعتی شاهرود
رسیده است .

عنوان

پژوهش

در روش‌های سنتز
شناساگرشیمیایی

فنل‌فتالئین

مجری طرح : دکتر سید علینقی طاهری
طرف قرارداد : دانشگاه صنعتی شاهرود
محل اجرای طرح : دانشگاه صنعتی شاهرود
تاریخ تهیه گزارش : ۱۳۸۲/۹/۱۵

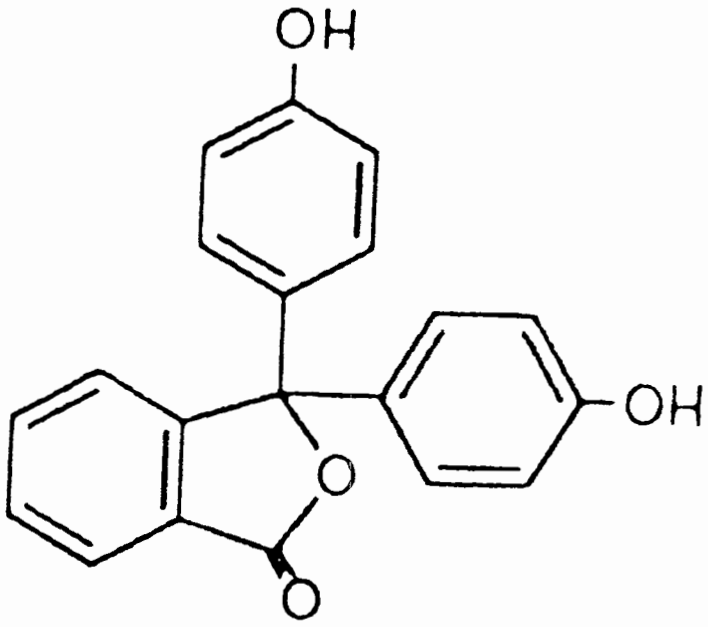
چکیده

بررسی سنتز فنل‌فتالئین از طریق واکنش فنل با انیدریدفتالیک نشان می‌دهد که واکنش بدون کاتالیزگر انجام نمی‌پذیرد. کاتالیزگرهای گوناگون نیز باید با بررسی تمام جوانب انتخاب شوند زیرا فنل(یکی از مواد ا ولیه‌ی واکنش) می‌تواند با کاتالیزگرهای اسیدی مانند اسیدسولفوریک به راحتی واکنش دهد. همچنین بعد از تشکیل فنل‌فتالئین نیز امکان سولفوناسیون وجود دارد. متون شیمی ضمیمه نیز مشتقات فنل‌فتالئین مخصوصا ترکیبات سولفونه شده را گزارش کرده‌اند. لذا بهترین کاتالیزگر اسیدفسفریک_تشخیص داده شده است .

فهرست مطالب

مقدمه

شناساگرهای شیمیایی ترکیباتی شیمیایی هستند که برای تعیین نقطه پایانی با قابل مشاهده نمودن تغییر رنگ محلول در واکنش‌های اسید و باز به روش حجم‌سنجی به کار می‌روند.
جدول ارائه شده در صفحه ۵ تعداد زیادی از اینگونه ترکیبات را نشان می‌دهد . همانگونه که در جدول مشاهده می‌شود،این ترکیبات در محیط های اسیدی و بازی دارای رنگ‌های متفاوتی بوده و همچنین در محدوده‌ی مشخصی از pH کاربرد دارند.



معرفی فنل‌فتالئین به عنوان یک شناساگر شیمیایی

فنل‌فتالئین که دارای نام‌های شیمیایی

Di-p-dioxydiphenylphthalide

یا

3,3-Bis(p-hyroxyphenyl)phthalide

یا

3,3-Bis(4-hydroxyphenyl)-1(3H)-isobenzofuranone

است،ترکیبی است که دارای بلورهای سفید رنگ یا سفید کمی متمایل به زرد می‌باشد،بی‌بواست، در هوا کاملا پایدار است،و در دمای ۲۶۳-۲۶۱ درجه سانتی‌گراد ذوب می‌شود.۱ گرم آن در ۱۵ میلی‌لیتر اتانول یا ۱۰۰ میلی‌لیتر دی‌اتیل اتر حل می‌شود(ضمیمه‌های ۱و۲) .

Indicators

The following table lists indicators commonly used for visible end-point determinations.

Indicator	Chemical name	Acid color[1]	pH range	Basic color[1]	Preparation of stock solution[2]
methyl violet	mixture of tetra-, penta-, and hexamethyl-*p*-rosaniline hydrochloride salts	Y	0.15-3.2	V	0.01-0.05% in water
cresol red (acid range)	*o*-cresolsulfonphthalein	R	0.2-1.8	Y	Dissolve 100 mg in 2.65 ml 0.1*N* NaOH, dil to 100 ml with water
metanil yellow	4′-anilinoazobenzene-*m*-sulfonic acid, sodium salt	R	1.2-2.3	Y	0.01-0.1% in water
m-cresol purple (acid range)	*m*-cresolsulfonphthalein	R	1.2-2.8	Y	Dissolve 100 mg in 2.65 ml 0.1*N* NaOH, dil to 100 ml with water
xylenol blue (acid range)	*p*-xylenolsulfonphthalein	R	1.2-2.8	Y	Dissolve 40 mg in 0.98 ml 0.1*M* NaOH, dil to 100 ml with water
thymol blue (acid range)	thymolsulfonphthalein	R	1.2-2.8	Y	Dissolve 100 mg in 2.15 ml 0.1*N* NaOH, dil to 100 ml with water
tropeolin OO	4′-phenylaminoazobenzene-4-sulfonic acid, sodium salt	R	1.3-3.2	Y	1% in water; 0.4% in 50% aq alc[3]
quinaldine red	2-(*p*-dimethylaminostyryl)quinoline ethiodide	C	1.4-3.2	R	0.1% in alc or 90% aq ethanol[3]
α-dinitrophenol	2,4-dinitrophenol	C	2.0-4.7	Y	0.1% in 70% aq alc[3]
methyl yellow; dimethyl yellow	*p*-dimethylaminoazobenzene	R	2.9-4.0	Y	0.1% in 90% aq alc[3]
bromophenol blue	3,3′,5,5′-tetrabromophenolsulfonphthalein	Y	3.0-4.6	Pu	Dissolve 100 mg in 1.5 ml 0.1*N* NaOH, dil to 100 ml with water
tetrabromophenol blue	tetrabromophenol tetrabromosulfonphthalein	Y	3.0-4.6	B	Dissolve 100 mg in 1.01 ml 0.1*N* NaOH, dil to 100 ml with water
bromochlorophenol blue	3,3′-dibromo-5,5′-dichlorophenolsulfonphthalein	Y	3.0-4.6	Pu	Dissolve 40 mg in 0.69 ml 0.1*M* NaOH, dil to 100 ml with water
Congo red	diphenyl-4,4′-bis-(2-azo-1-naphthylamine)sulfonic acid, sodium salt	B	3.0-5.2	R	0.1% in water
methyl orange	4′-dimethylaminoazobenzene-4-sulfonic acid, sodium salt	R	3.1-4.4	O	0.04-0.1% in water
p-ethoxychrysoidine hydrochloride	4-ethoxy-2′,4′-diaminoazobenzene hydrochloride	R	3.5-5.5	Y	0.1% in 90% aq alc[3]; 0.2% in alc
naphthyl red	α-naphthylaminoazobenzene	R	3.7-5.0	Y	0.1% in ethanol or 70% aq alc[3]
alizarin sodium sulfonate	dihydroxyanthraquinone sodium sulfonate	Y	3.7-5.2	V	0.1% in water
bromocresol green	3,3′,5,5′-tetrabromo-*m*-cresolsulfonphthalein	Y	3.8-5.4	B	Dissolve 100 mg in 1.45 ml 0.1*N* NaOH, dil to 100 ml with water
γ-dinitrophenol	2,5-dinitrophenol	C	4.0-5.8	Y	0.1% in 70% aq alc[3]
methyl red	4′-dimethylaminoazobenzene-2-carboxylic acid	R	4.4-6.2	Y	Dissolve 100 mg in 3.7 ml 0.1*N* NaOH, dil to 100 ml with water; 0.1% in alc
lacmoid		R	4.4-6.4	B	0.2% in alc
chlorophenol red	3,3′-dichlorophenolsulfonphthalein	Y	4.8-6.4	Pu	Dissolve 100 mg in 2.35 ml 0.1*N* NaOH, dil to 100 ml with water
benzoyl auramine G		V	5-5.6	Y	0.25% in methanol
bromocresol purple	5,5′-dibromo-*o*-cresolsulfonphthalein	Y	5.2-6.8	Pu	Dissolve 100 mg in 1.85 ml 0.1*N* NaOH, dil to 100 ml with water
bromophenol red	3,3′-dibromophenolsulfonphthalein	Y	5.2-6.8	R	Dissolve 40 mg in 0.78 ml 0.1*M* NaOH, dil to 100 ml with water
p-nitrophenol		C	5.6-7.6	Y	0.1% in water; 0.2% in alc
bromothymol blue	3,3′-dibromothymolsulfonphthalein	Y	6.0-7.6	B	Dissolve 100 mg in 1.6 ml 0.1*N* NaOH, dil to 100 ml with water
phenol red	phenolsulfonphthalein	Y	6.4-8.2	R	Dissolve 100 mg in 2.85 ml 0.1*N* NaOH, dil to 100 ml with water
rosolic acid; aurin	*p*-quinonemono(bis-4-oxyphenylmethide)	Y	6.6-8.0	R	0.2% in 50% aq alc[3]
neutral red	3-amino-6-dimethylamino-2-methylphenazinium chloride	R	6.8-8.0	Y	0.1% in 70% aq alc[3]
quinoline blue	cyanine	C	7.0-8.0	V	1% in alc

Indicators (Continued)

Indicator	Chemical name	Acid color[1]	pH range	Basic color[1]	Preparation of stock solution[2]
cresol red (basic range)	*o*-cresolsulfonphthalein	Y	7.0-8.8	R	Dissolve 100 mg in 2.65 ml 0.1*N* NaOH, dil to 100 ml with water
α-naphtholphthalein		C	7.3-8.7	G-B	0.1% in alc or 70% aq alc[3]
tropeolin OOO; α-naphthol orange	α-naphtholazobenzene-*p*-sulfonic acid, sodium salt	Y	7.4-8.9	P	0.1% in water
m-cresol purple (basic range)	*m*-cresolsulfonphthalein	Y	7.4-9.0	Pu	Dissolve 100 mg in 2.65 ml 0.1*N* NaOH, dil to 100 ml with water
ethyl bis(2,4-dinitrophenyl)acetate		C	7.5-9.1	B	satd soln in 1:1 acetone-alc
thymol blue (basic range)	thymolsulfonphthalein	Y	8.0-9.6	B	Dissolve 100 mg in 2.15 ml 0.1*N* NaOH, dil to 100 ml with water
xylenol blue (basic range)	*p*-xylenolsulfonphthalein	Y	8.0-9.6	B	Dissolve 40 mg in 0.98 ml 0.1*M* NaOH, dil to 100 ml with water
o-cresolphthalein	di-*o*-cresolphthalide	C	8.2-9.8	R-V	0.04% in 50% aq alc[3]
phenolphthalein	di-*p*-dioxydiphenylphthalide	C	8.2-9.8	P	0.1% in alc or 60% aq alc[3]
thymolphthalein	dithymolphthalide	C	9.3-10.5	B	0.1% in 80% aq alc[3]
α-naphtholbenzein	dimethylphenolphthalein	Br	9.8-11.0	G-B	0.1% in alc
alizarin yellow GG; salicyl yellow	3′-nitro-4-oxyazobenzene-3-carboxylic acid, sodium salt	Y	10.0-12.1	Br-Y	0.1% in ethanol or water
alizarin yellow R	4′-nitro-4-oxyazobenzene-3-carboxylic acid, sodium salt	Y	10.0-12.1	R	0.1% in water
Nile blue	diethylaminonaphthophenazoxonium sulfate	B	10.1-11.1	R	0.1% in water
nitramine	2,4,6-trinitrophenylmethylnitramine	C	10.8-13.0	Br	0.1% in 70% aq alc[3]
tropeolin O	2′,4′-dioxyazobenzene-4-sulfonic acid, sodium salt	Y	11.0-12.7	R-Br	0.1% in water
Poirrier blue C4B	triphenylrosaniline sulfonic acid, sodium or potassium salt	B	11.0-13.0	Pu	0.1% in water
indigo carmine	indigotin-5,5′-disulfonic acid, disodium salt	B	11.5-14.0	Y	0.25% in 50% aq ethanol[3]
trinitrobenzene		C	12.0-14.0	O	0.1% in 70% aq alc[3]

[1]The indicator colors are abbreviated as follows: B, blue; Br, brown; C, colorless; G, green; O, orange; P, pink; Pu, purple; R, red; V, violet; and Y, yellow.
[2]One to five drops of the indicator stock soln should be added to every 10 ml soln to be titrated.
[3]When preparing the aq alc solns, it is important to dissolve the indicator in alc first and then dil with water to the indicated conc. For example, to make a 0.1% soln in 70% aq alc, dissolve 100 mg indicator in 70 ml alc, then add 30 ml water.

References

I. M. Kolthoff, *Acid-Base Indicators* (Macmillan, New York, 1937).
I. M. Kolthoff, V. A. Stenger, *Volumetric Analysis* **vols. I, II** (Interscience, New York, 2nd ed., 1942).
R. G. Bates, *Determination of pH* (Wiley & Sons, New York, 1954).
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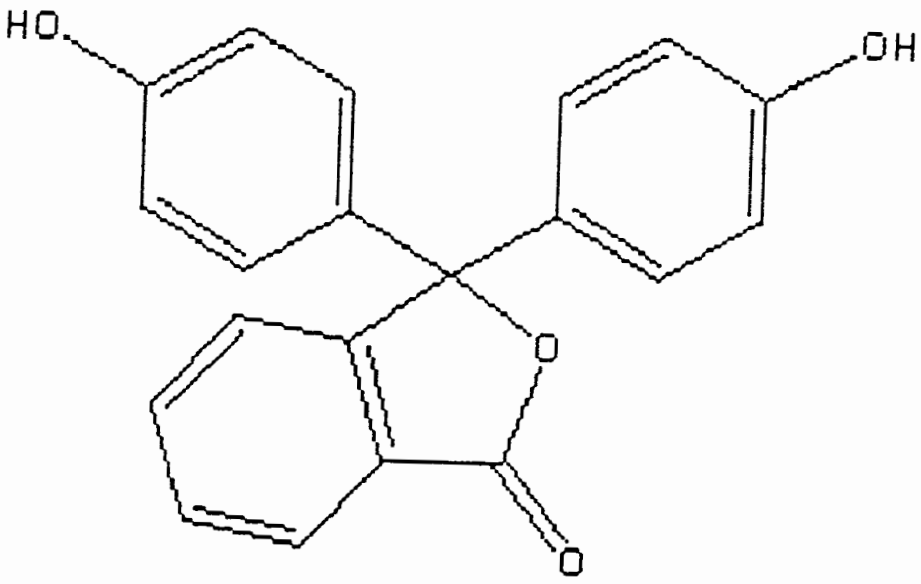
F. J. Green, *The Sigma-Aldrich Handbook of Stains, Dyes, and Indicators* (Aldrich, Milwaukee, Wisconsin, 1990).

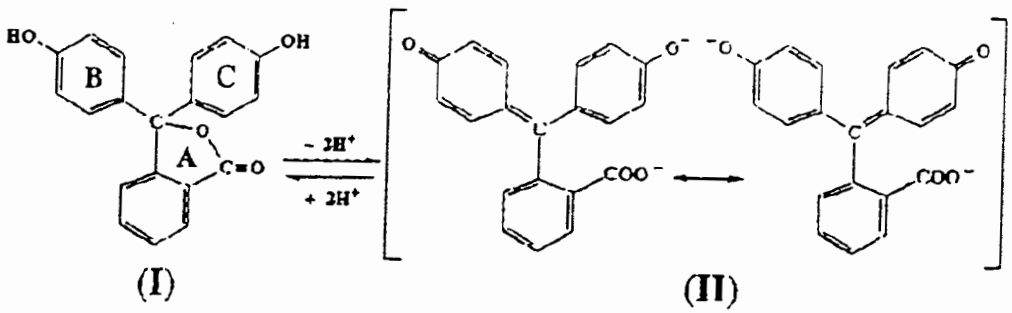
ساختمان فنل‌فتالئین

در مطالعه‌ی ساختمانی ، فنل‌فتالئین نوارهای کششی OH را در Cm^{-1} ۳۳۲۹،۳۲۹۱ و۳۳۸۳ در طیف مادون قرمز از خود نشان می‌دهد(ضمیمه ۲).
نوار قوی در $۱۷۳۷Cm^{-1}$ که دارای قله‌ای به‌صورت شانه در $۱۷۱۸Cm^{-1}$ است مربوط به ارتعاشات کششی عامل کربونیل گروه لاکتون می باشد(شکل لاکتونی فنل‌فتالئین در زیر نشان داده شده است). طیف‌های مادون قرمز فنل‌فتالئین تجارتی و سنتز شده در ضمیمه ۲ آورده شده‌است).



اثر pH بر روی ساختمان فنل‌فتالئین

از خصوصیات ویژه‌ی شناساگرهای شیمیایی این است که تغییرات رنگ آنها در محدوده‌ی طول موج‌های ناحیه‌ی مرئی صورت می‌گیرد، و آن تابع pH محیط است . تغییر رنگ فنل‌فتالئین با تغییر pH مربوط به تغییر ساختمان فنل‌فتالئین از شکل لاکتون(I) به شکل رزونانسی دی‌آنیونی(II) است .



(I) (II)

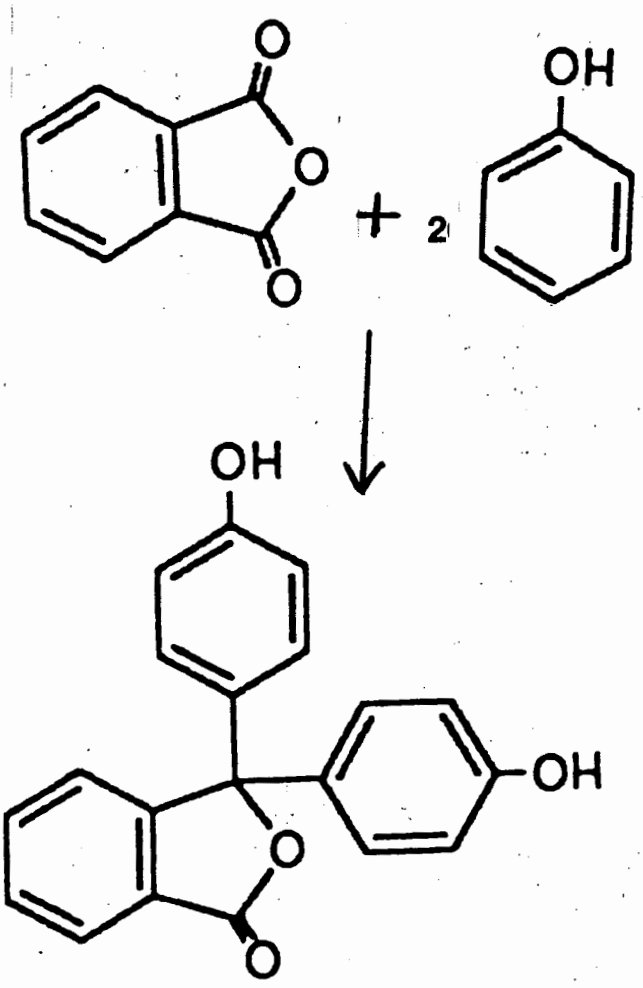
بررسی روش‌های سنتز

نگاهی به ساختمان فنل‌فتالئین و مطالعه و بررسی مطالب ارائه شده در متون علمی شیمی نشان می‌دهد که مواد اولیه‌ی مورد نیاز برای سنتز این ترکیب چیزی به جز فنل و انیدریدفتالیک نمی‌تواند باشد، لذا سنتز با این ترکیبات شروع گردید .

بررسی کاتالیزگرهای گوناگون برای سنتز فنل‌فتالئین

در ابتدای طرح بنا شد واکنش بدون کاتالیزگر و فقط با حرارت دادن دو مول فنل با یک مول انیدریدفتالیک(بر اساس معادله‌ی واکنش زیر) آغاز گردد، سپس نتایج مورد بررسی قرار گیرد و آنگاه بر اساس نتایج بدست آمده ، استفاده از کاتالیزگرهای گوناگون بررسی شود.
قابل ذکر است که دلیل استفاده از انیدریدفتالیک به‌جای اسیدفتالیک این است که بتوان واکنش را بدون کاتالیزگر ، همانند بسیاری از واکنش‌های انیدریدها ، به جای یک مول دی اسید یا دو مول اسید تک ظرفیتی به انجام رساند . لذا ابتدا واکنش بدون کاتالیزگر انجام شد.

معادله‌ی واکنش سنتز فنل‌فتالئین



جزئیات روش‌های گوناگون سنتز فنل‌فتالئین با استفاده از کاتالیزگرهای گوناگون

ـــــ **در آزمایش اول** ، فنل و انیدریدفتالیک با یکدیگر ذوب شدند ، اما واکنشی صورت نگرفت .**

ـــــ **در آزمایش دوم** ، فنل وانیدریدفتالیک در متانول حل شده و به روش بازگردان حرارت داده شد . در این آزمایش نیز واکنشی صورت نگرفت .

ـــــ **در آزمایش سوم** ، به جای متانول از تولوئن (که دارای نقطه جوش بالا تری است) استفاده شد . اما این نیز تاثیری در نتایج واکنش نداشت .

ـــــ **در آزمایش چهارم** ، واکنش با استفاده از کاتالیزگر کلرید آهن(III) و حلال متانول انجام گرفت، اما نتیجه بهتری بدست نیامد. احتمال داده شد که شاید مقدار کاتالیزگر کافی نبوده است . اما تکرار آزمایش با مقدار بیشتری از کاتالیزگر نیز محصول تولید نکرد.

ـــــ **در آزمایش پنجم** ، نیاز واکنش به دمای بالاتر بررسی شد و برای این کار از حلال تولوئن(با نقطه جوش بالا) استفاده گردید ، اما واکنشی انجام نگرفت.

ـــــ با توجه به نتایج بدست آمده در بالا تصمیم براین شد که کاتالیزگر تغییر داده شود. برای این منظور از اسید سولفوریک استفاده شد.

شرح آزمایش:

انیدریدفتالیک(۱گرم،۷ ۰/۰۰ مول) و فنل(۱/۳گرم،۰/۰۱۴مول) در متانول (۲۰ میلی‌لیتر) حل شده و به آن اسید سولفوریک(۰/۵میلی‌لیتر) اضافه شد،سپس مخلوط به مدت ۶ ساعت حرارت داده شد.اما واکنشی انجام نگرفت. لذا حلال تغییر داده شد، و این بار از تولوئن استفاده شد،که خوشبختانه نتایج مثبتی بدست آمد.پس از مدتی رسوب خمیری شکلی تشکیل شد . رسوب با آب گرم شستشو داده شد ، سپس در اتانول حل شد و از آن Tlc گرفته شد، که با محصول تجارتی مطابقت داشت. همچنین محصول متبلور شده طیف UV گرفته شد که تشکیل فنل‌فتالئین را تا ئید کرد.

ازحرارت دادن رسوب خمیری شکل با اتر در آب جوش ، محلول بنفش رنگی بدست آمد. تبخیر این محلول ،جامد بنفش رنگی بر جا گذاشت که طیف UV آن با طیف UV نمونه تجاری مطابقت داشت. دلیل بنفش رنگ بودن این ترکیب مشخص نیست،اما ممکن است به‌دلیل وجود نا خالصی فنل‌فتالئین سولفونه شده باشد.

** **محلول فنل‌فتالئین رنگ محلول رقیق هیدروکسید سدیم را ارغوانی می‌کند. از این آزمایش برای تشخیص فنل‌فتالئین تشکیل شده ، در تمام آزمایشات استفاده شده است .**

۱- سنتز فنل‌فتالئین با استفاده از کاتالیزگر اسیدسولفوریک

ابتدا انیدریدفتالیک (۰/۰۲۹۷مول ،۴/۴ گرم) و فنل (۰/۰۵۹۶مول،۵/۶ گرم) در یک بالن ته گرد (۱۰۰ میلی‌لیتر) ریخته شد و به آن تولوئن(۳۰ میلی‌لیتر) اضافه شد ، سپس اسید سولفوریک غلیظ (۱ میلی‌لیتر) به آن اضافه گردید . رنگ محلول داخل بالن قرمز متمایل به قهوه‌ای شد .
دستگاه برای رفلاکس آماده شد و مخلوط واکنش به مدت حد اقل ۴ ساعت رفلاکس گردید . باید دقت داشت که اگر محلول داخل بالن توسط یک همزن مغناطیسی به‌هم‌زده شود ، واکنش بهتر ، کامل تر و سریع تر صورت می‌گیرد . بعد از مدتی دو فاز تشکیل شد. بعد از سرد شدن، بلور های صورتی رنگ فنل‌فتالئین تشکیل گردید (محلول الکلی آن رنگ محلول هیدروکسیدسدیم را ارغوانی کرد) .

۲- سنتز فنل‌فتالئین با استفاده از کاتالیزگر اسیدفسفریک

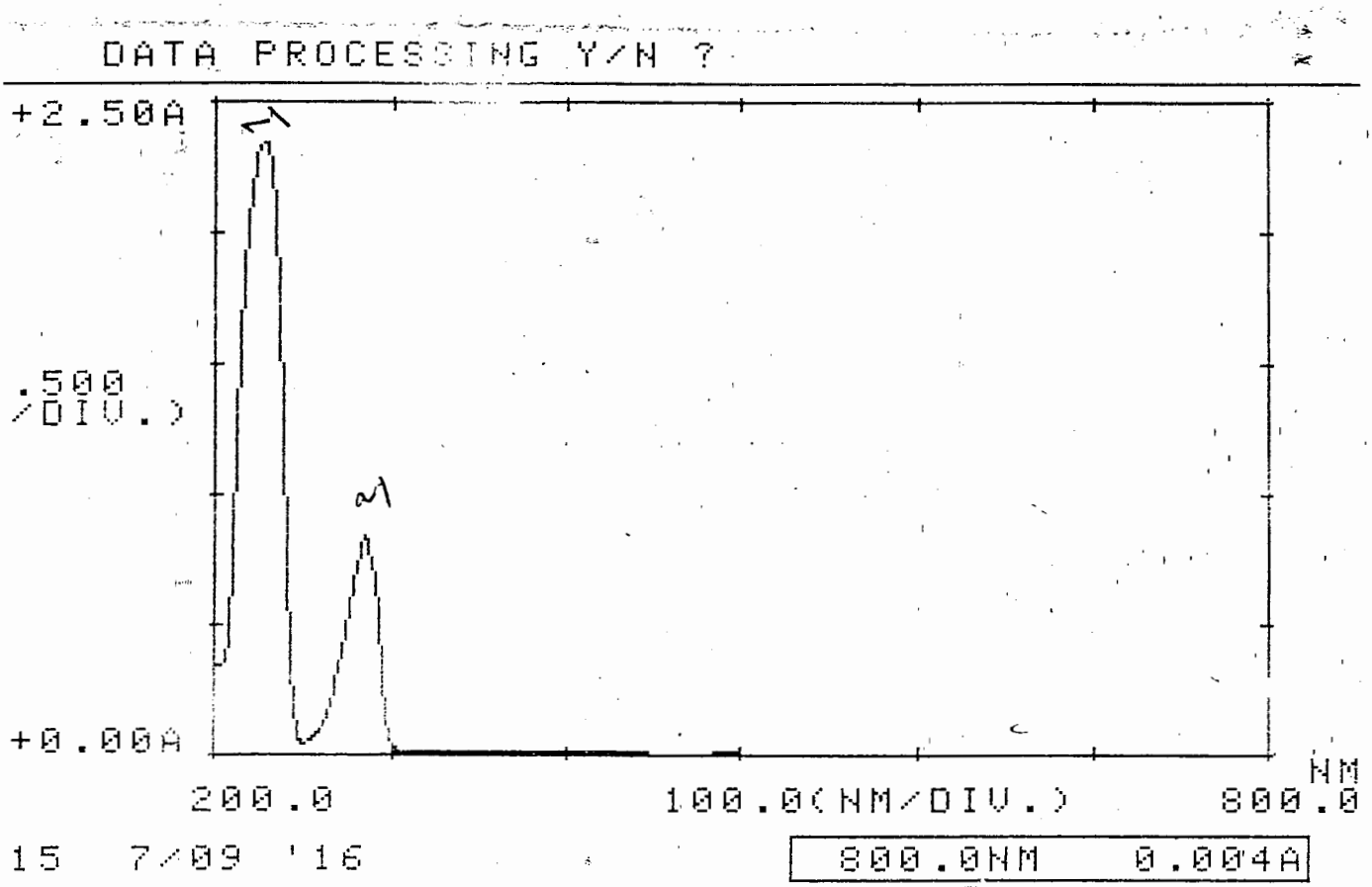
ابتدا انیدریدفتالیک (۰/۰۱۴۷مول ،۲/۲ گرم) و فنل (۰/۰۲۹۸مول،۲/۸ گرم) در یک بالن ته گرد (۵۰ میلی‌لیتر) ریخته شد و به آن تولوئن(۱۵ میلی‌لیتر) اضافه شد ، سپس اسید فسفریک (۱ میلی‌لیتر) به‌عنوان کاتالیزگر به آن اضافه گردید . سپس مخلوط واکنش به مدت ۲۴ ساعت رفلاکس شد . در حین رفلاکس، مخلوطی دو فازی ایجاد شد . فاز بالایی بی رنگ بود اما فاز زیرین قهوه‌ای رنگ و روغنی بود . هر دو فاز در در محیط بازی ارغوانی می‌شوند . دو فاز از یکدیگر جدا شدند و به هر دو آب مقطر اضافه شد تا رسوب سفید رنگی حاصل گردید که در فاز آلی حل می‌گردد . دو فاز آبی و آلی از یکدیگر جداسازی شدند و فاز آلی تبخیر گردید . رسوب حاصله فنل فتالئین است که احتمال دارد حاوی انیدرید فتالیک واکنش نداده نیز باشد . طیف UV رسوب حاصل با طیف UV فنل‌فتالئین تجارتی شباهت بسیاری دارد .
خالص‌سازی بیشتر ترکیب به‌صورت زیر انجام گرفت . انیدریدفتالیک در آب گرم حل می‌شود . لذا رسوب بدست آمده در آب جوش ریخته شد، و دمای آب به مدت ده دقیقه ثابت نگاه‌داشته شد و سپس محلول داغ صاف گردید. طیف‌های IR و NMR نمونه بدست‌آمده حذف انیدریدفتالیک را مورد تایید قرار داد .
طیف IR انیدریدفتالیک در منطقه Cm^{-1} ۱۸۴۵-۱۶۱۲ چند قله از خود به‌نمایش می‌گذارد،که از قله‌های Cm^{-1} ۱۸۴۵ و Cm^{-1} ۱۷۴۹ می‌توان برای شناسایی آن استفاده نمود . طیف نمونه خالص‌سازی شده این قله‌ها را دیگر نشان نمی‌دهد.
طیف NMR نمونه خالص‌سازی شده در منطقه ppm ۷/۷۰-۷/۵۲ چند قله از خود به‌نمایش می‌گذارد،که مربوط به پروتون‌های آروماتیکی فنل‌فتالئین می‌باشد(کلیه طیف‌ها ارائه شده‌است) .

ارزیابی نتایج حاصله

بررسی سنتز فنل‌فتالئین از طریق واکنش فنل با انیدریدفتالیک نشان می‌دهد که واکنش بدون کاتالیزگر انجام نمی‌پذیرد. کاتالیزگرهای گوناگون نیز باید با بررسی تمام جوانب انتخاب شوند زیرا فنل(یکی از مواد ا ولیه‌ی واکنش) می‌تواند با کاتالیزگرهای اسیدی مانند اسیدسولفوریک به راحتی واکنش دهد. همچنین بعد از تشکیل فنل‌فتالئین نیز امکان سولفوناسیون وجود دارد. درمتون شیمی ضمیمه مشتقات فنل‌فتالئین مخصوصا ترکیبات سولفونه شده آن گزارش شده است. لذا بر خلاف آنچه که در متون علمی شیمی آمده، بهترین کاتالیزگر اسیدفسفریک تشخیص داده شده‌است که واکنش می‌تواند با راندمان تقریبا ۵۰٪ انجام گیرد. خوشبختانه مواد اولیه‌ای که وارد واکنش نشده‌اند قابل بازیافت بوده و می‌توانند برای مصرف مجدد مورد استفاده قرار گیرند. در پایان با توجه به نتایج مثبت بدست آمده در سنتز آزمایشگاهی، پیشنهاد می‌شود تا طی طرح پژوهشی جدیدی بهبود راندمان و نحوه بازیافت مواداولیه و مطالعات تولید نیمه صنعتی و اجرای آن بررسی شوند تا جوابگوی نیازهای داخلی کشور باشیم.

و منا...التوفیق

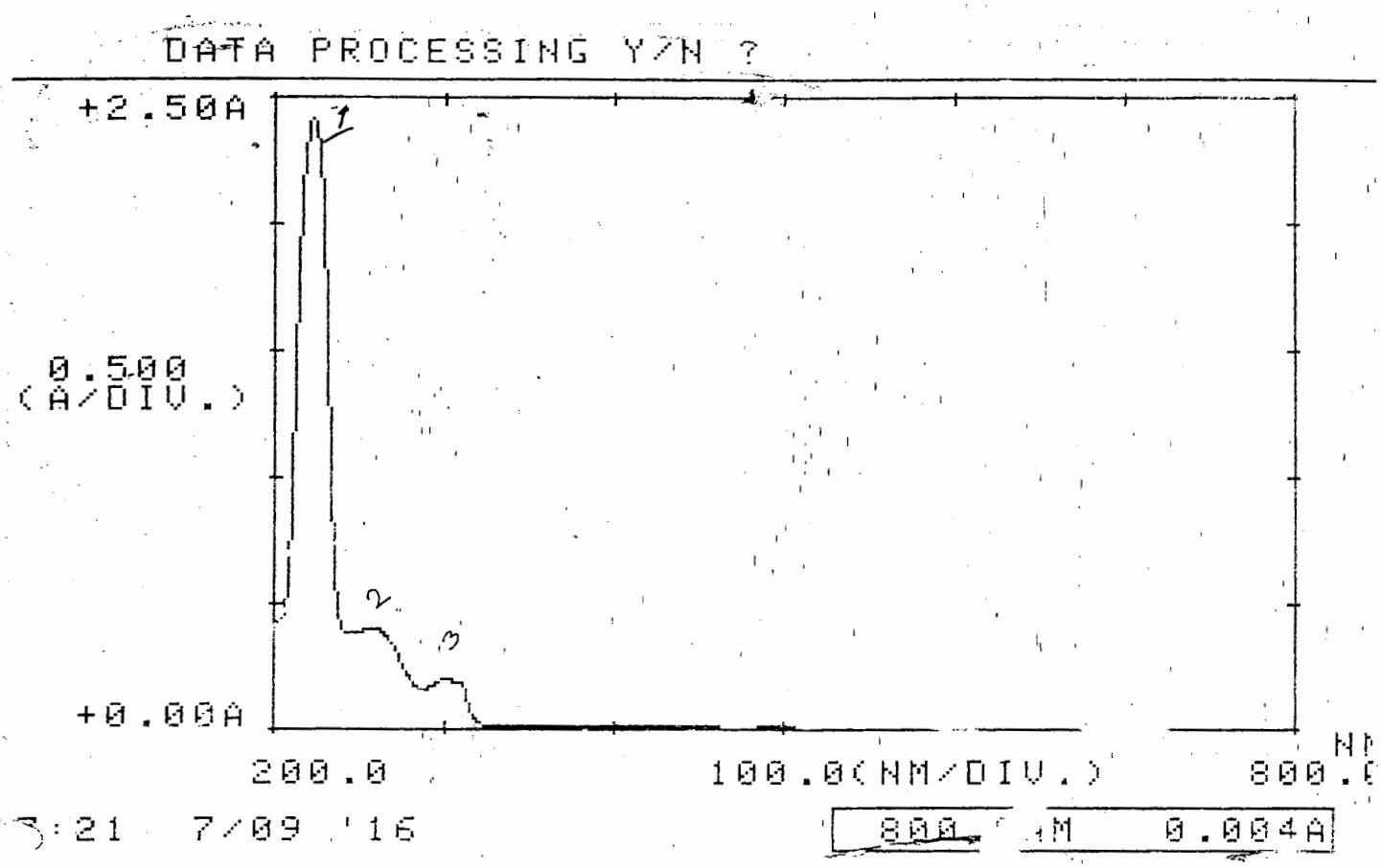
دکتر سید علینقی طاهری



*** PEAK-PICK ***

-- PEAK --		-- VALLEY --	
λ	ABS	λ	ABS
679.0	0.003	787.0	0.001
383.0	0.012	649.0	0.002
2 284.0	0.841	361.0	0.011
1 228.0	1.343	250.0	0.049

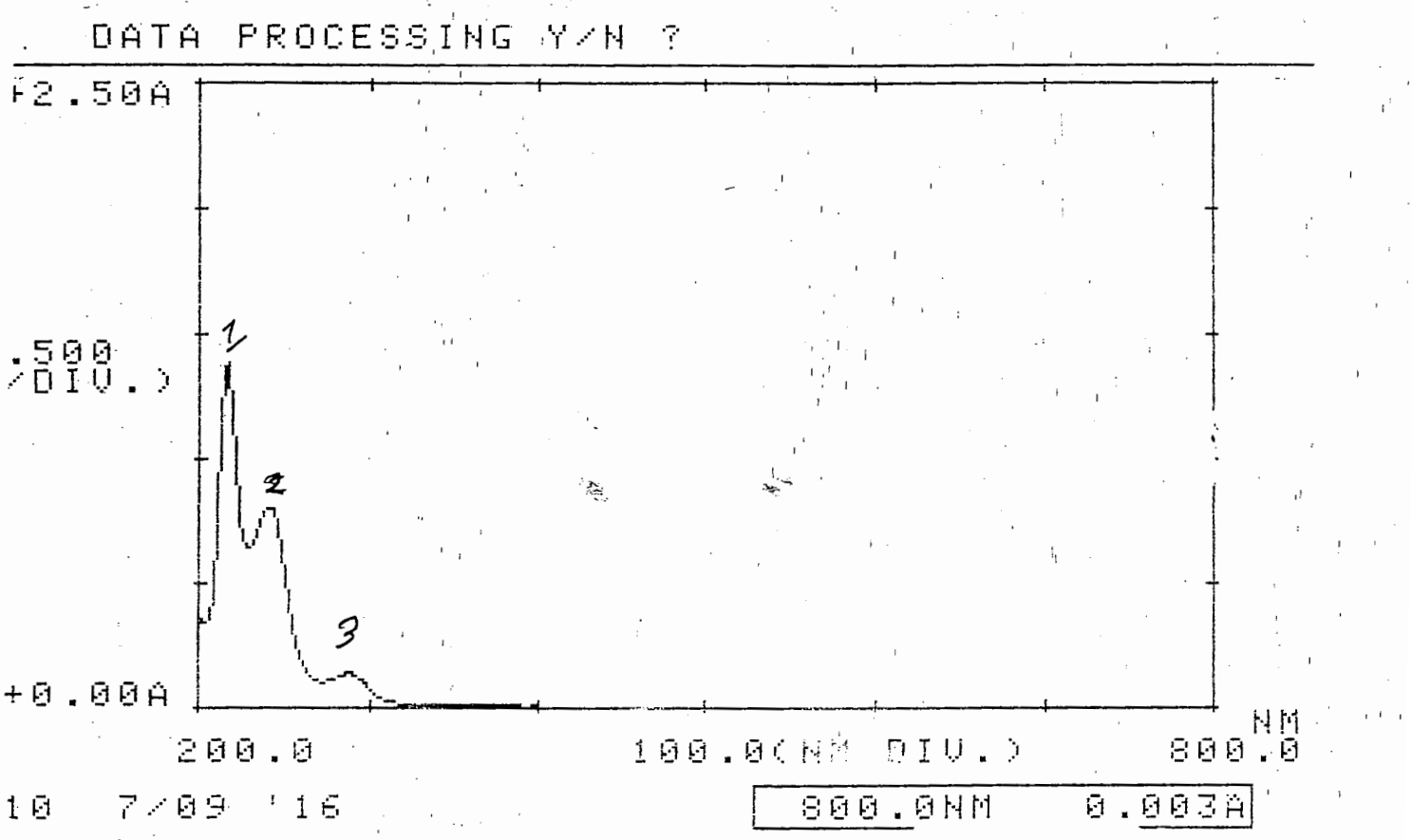
طیف ماورای‌بنفش فنل



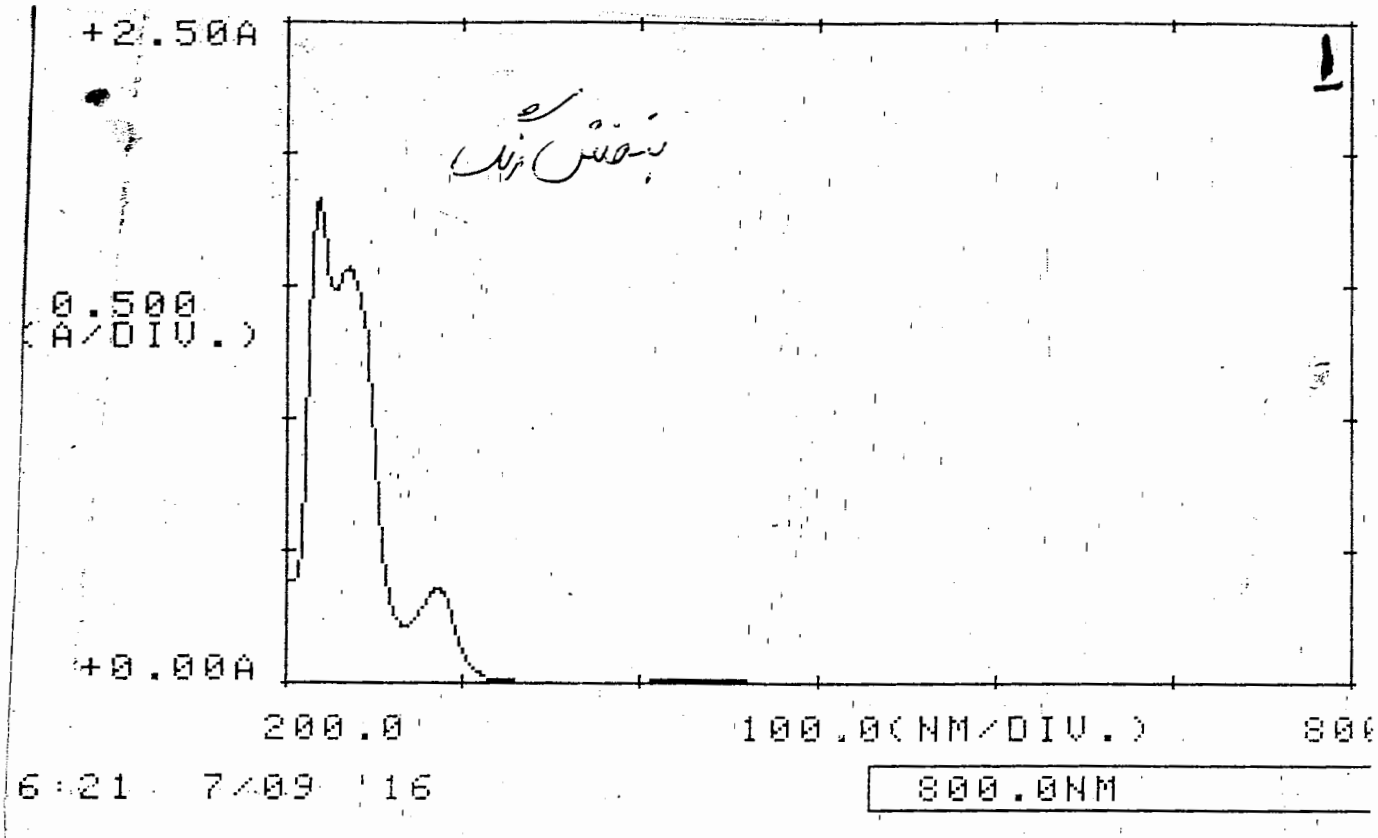
*** PEAK-PICK ***

	-- PEAK --		-- VALLEY --	
	λ	ABS	λ	ABS
	745.0	0.005	788.0	0.001
	493.0	0.008	702.0	0.002
3	301.0	0.206	467.0	0.006
2	258.0	0.398	287.0	0.156
1	223.0	2.420	245.0	0.381

طیف ماورای‌بنفش انیدریدفتالیک تجارتی



طیف ماورای‌بنفش‌فنل‌فتالئین تجارتی



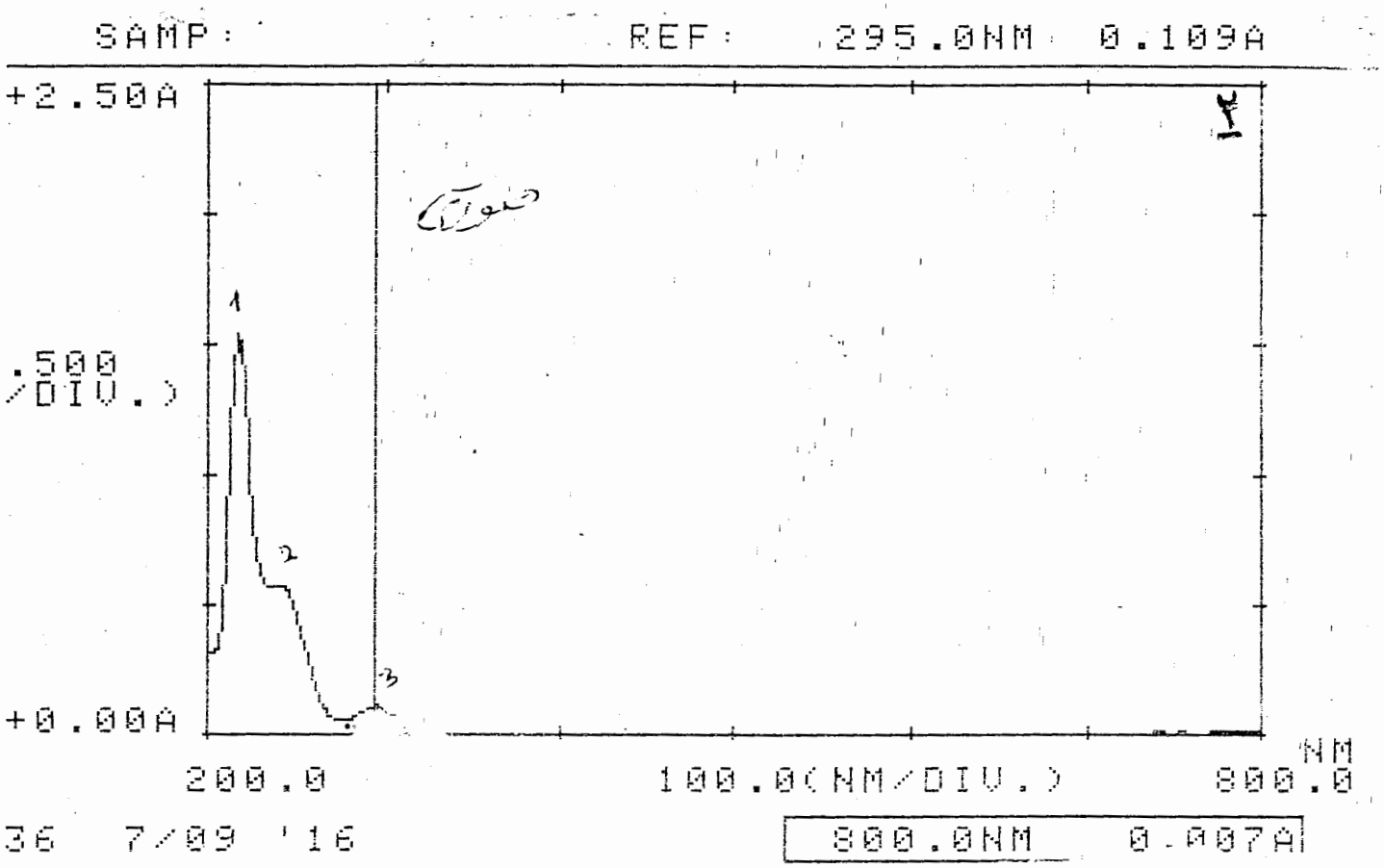
1

*** PEAK-PICK ***

-- PEAK --		-- VALLEY --	
λ	ABS	λ	ABS
717.0	0.001	744.0	-0.001
441.0	0.009	651.0	-0.002
285.0	0.358	345.0	0.004
235.0	1.565	267.0	0.211
218.0	1.824	228.0	1.481

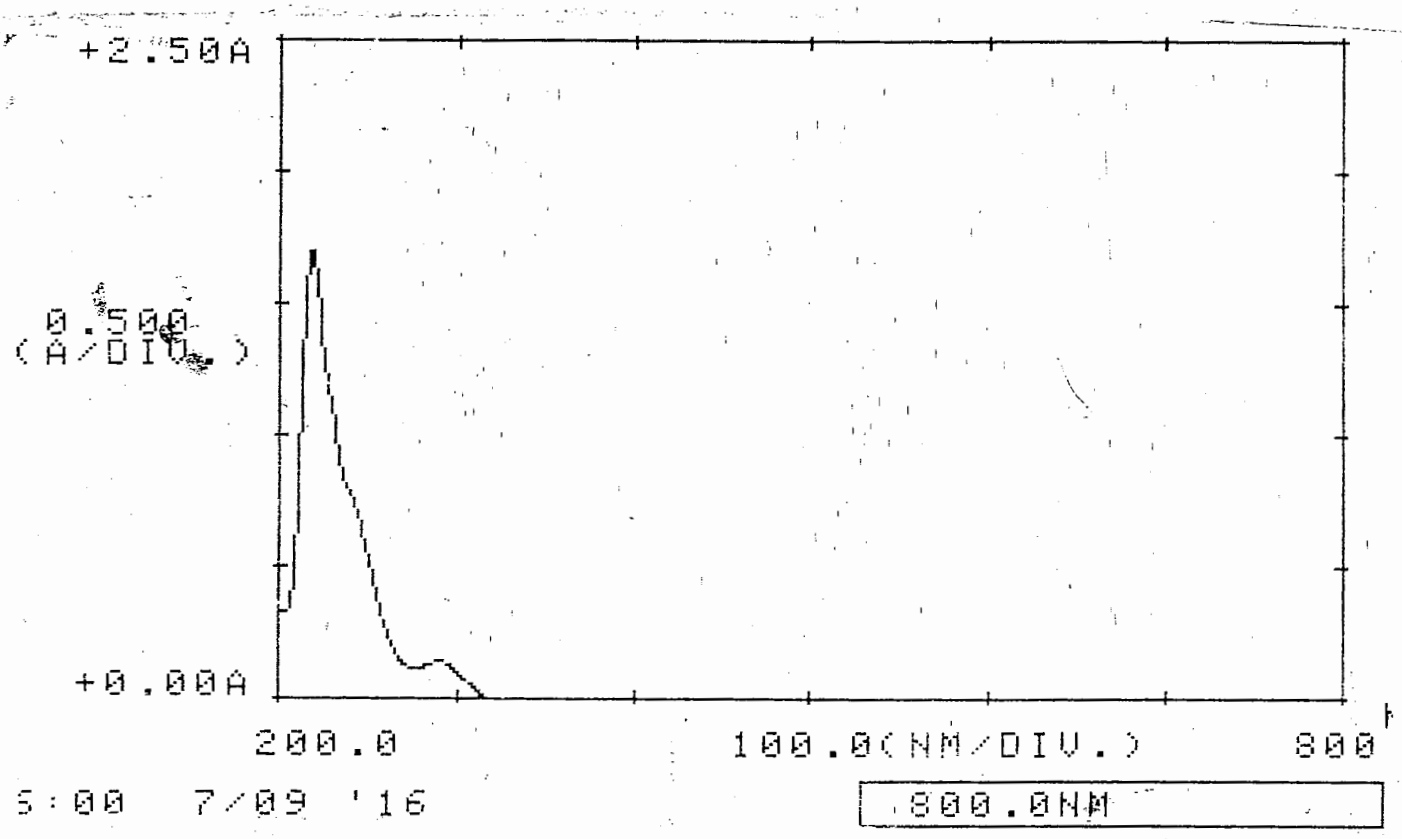
λ_{max}

طیف ماورای بنفش محصول بنفش رنگ.



-- PEAK --		-- VALLEY --	
λ	ABS	λ	ABS
722.0	0.003	751.0	-0.001
472.0	0.005	652.0	0.001
287.0	0.139	464.0	0.004
241.0	0.805	273.0	0.106
216.0	1.380	229.0	0.647

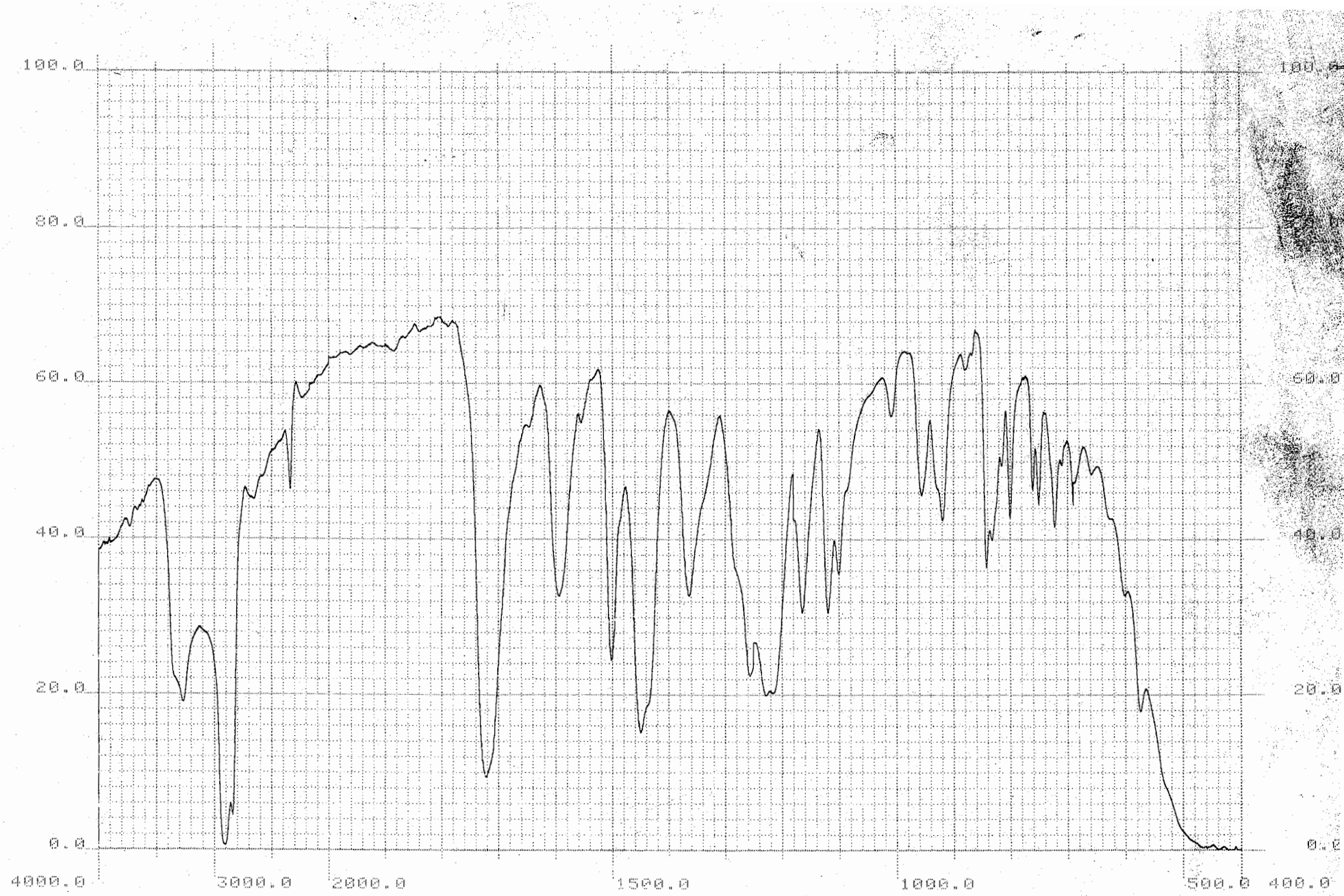
طیف ماورای بنفش محصول صورتی رنگ



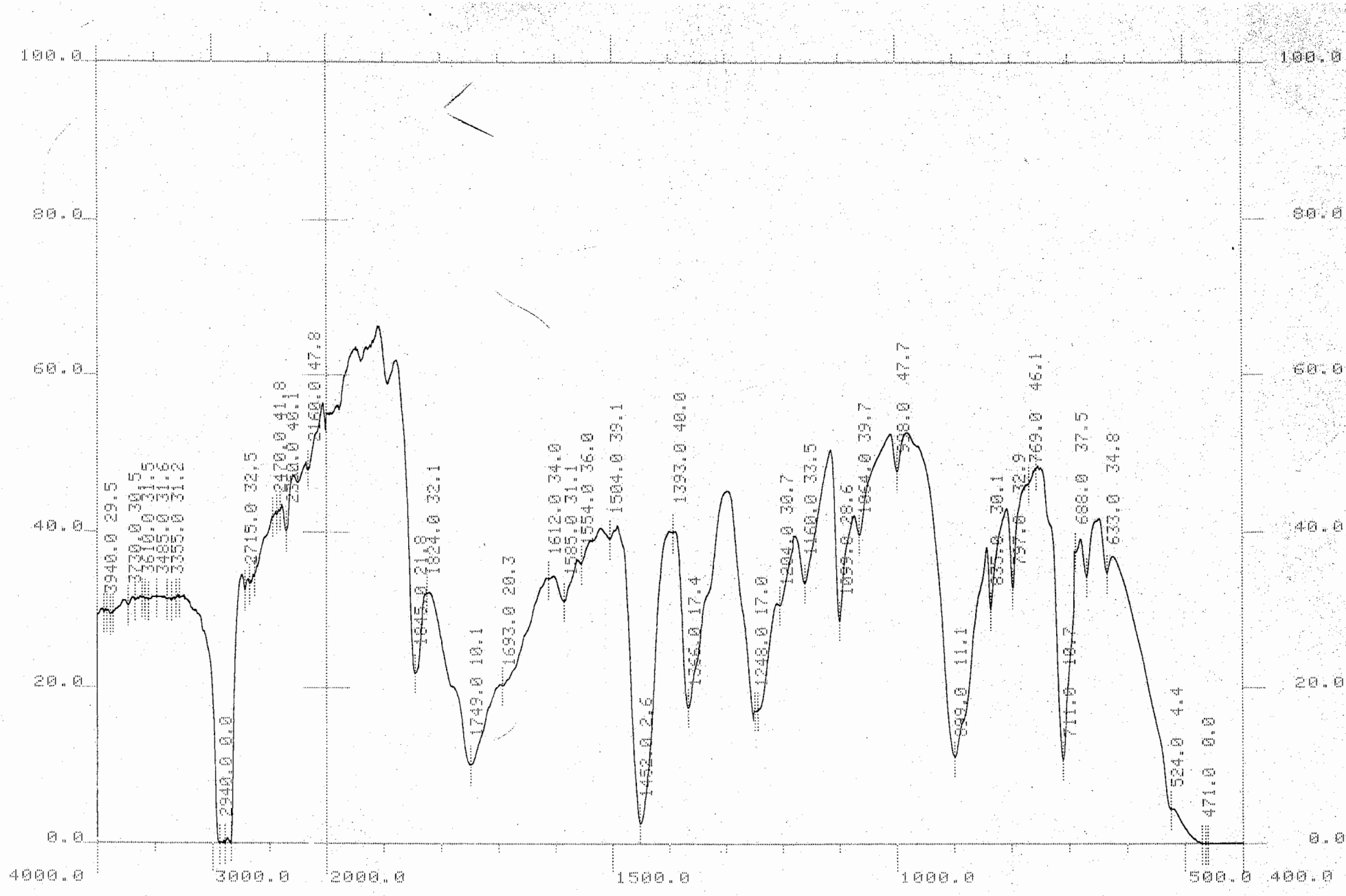
*** PEAK-PICK ***

-- PEAK --		-- VALLEY --	
λ	ABS	λ	ABS
426.0	0.006	535.0	-0.004
290.0	0.137	326.0	-0.003
218.0	1.694	277.0	0.115

طیف ماورای بنفش محصول سفید رنگ

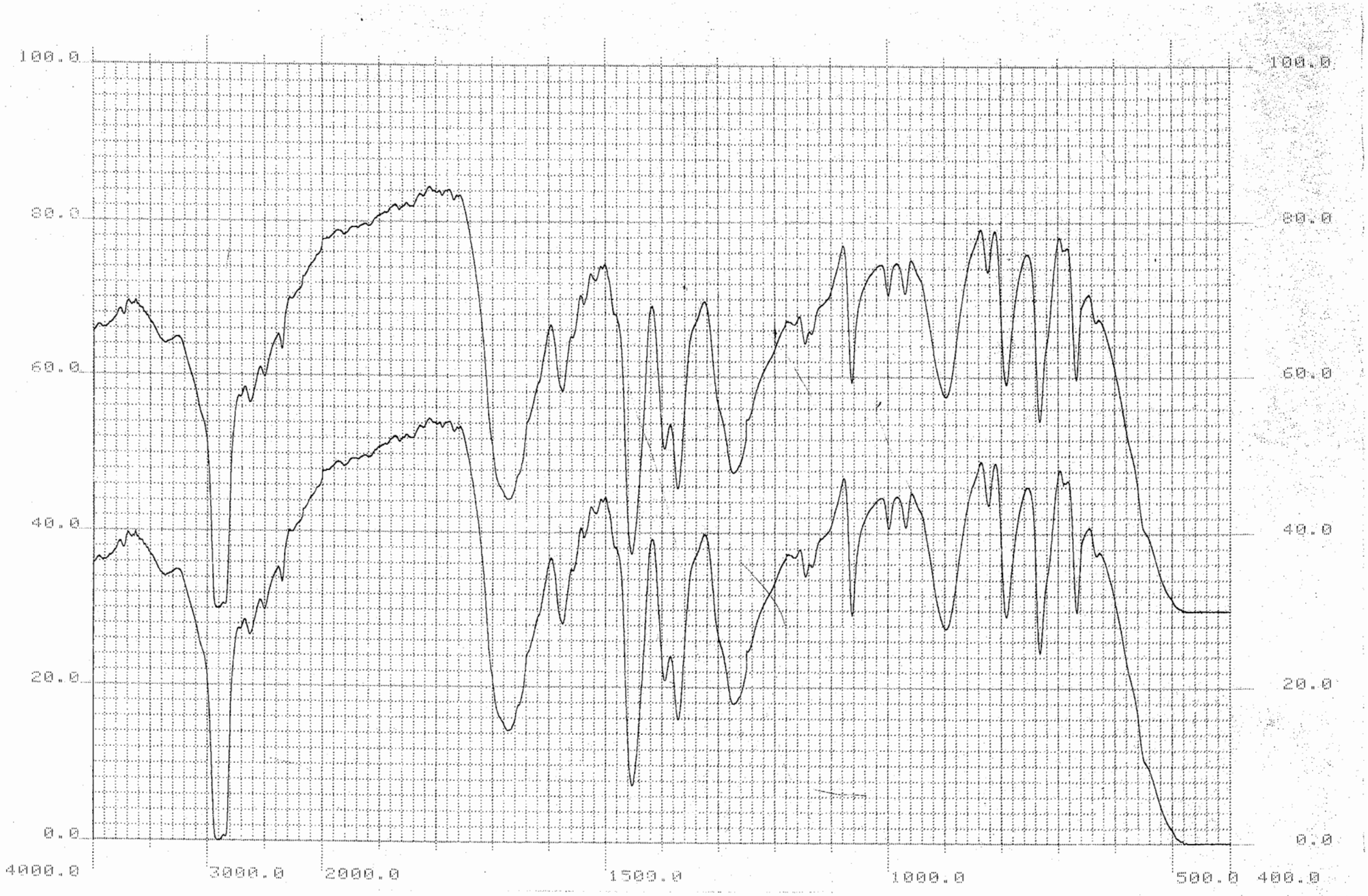


طیف مادون قرمز فنل‌فتالئین تجارتی



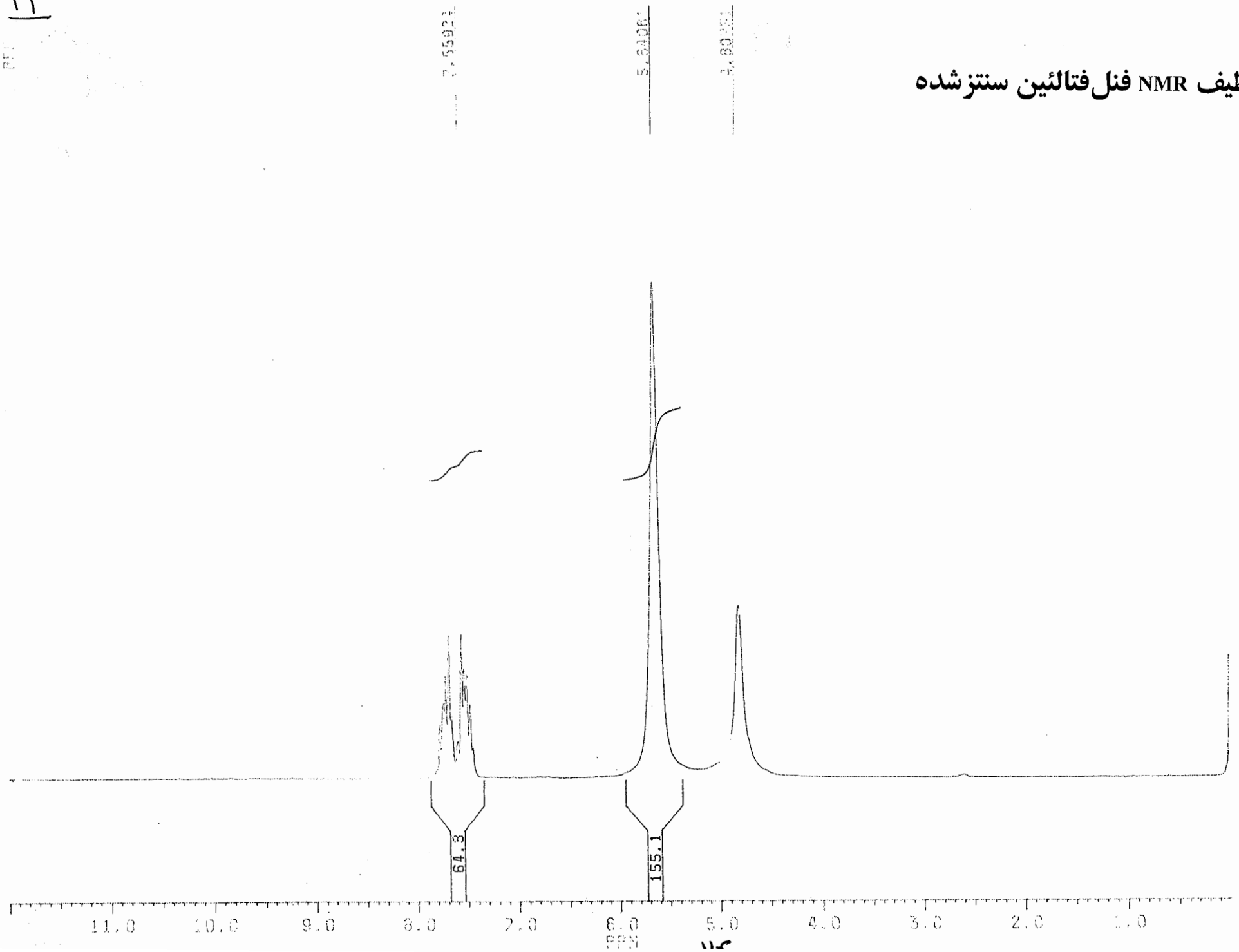
phthalic anhydride

طیف مادون قرمز انیدرید فتالئیک تجارتی



طیف مادون قرمز فنل‌فتالئین سنتزشده

طیف NMR فنل‌فتالئین سنتزشده



طیف NMR فنل‌فتالئین سنتزشده

ضمیمه ها

و

منابع

ضمیمه ۱

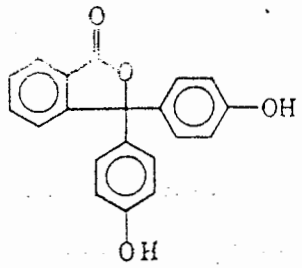
Preparation. Bisacodyl may be prepared from 2-pyridinecarboxaldehyde by condensation with phenol with the aid of a dehydrant such as sulfuric acid (5). The resulting 4,4′-(2-pyridylmethylene)diphenol is esterified by treatment with acetic anhydride and anhydrous sodium acetate. Crystallization is from ethanol.

Safety. Inhalation of bisacodyl and contact with eyes, skin, and mucous membranes should be avoided.

Uses. Bisacodyl is a contact laxative that may be given orally or rectally. It is often used for evacuation of the bowel prior to surgery or diagnostic examinations. It may obviate the need for a cleansing enema.

Plantago Seed. Plantago seed, also called psyllium seed and plantain seed, is the cleaned, dried, ripe seed of *plantaso psyllium* Linne or, *plantago indica* Linne or *plantago ovata* Forskal (blond or Indian psyllium). It is used as a bulking agent.

Phenolphthalein. ***Properties.*** Phenolphthalein (4), 3,3-bis(*p*-hydroxyphenyl) phthalide [*77-09-8*], is a white or faintly yellowish-white crystalline powder. It is odorless, stable in air, and it melts not lower than 258°C. Phenolphthalein is practically insoluble in water; one gram is soluble in 15 mL alcohol and 100 mL diethyl ether.



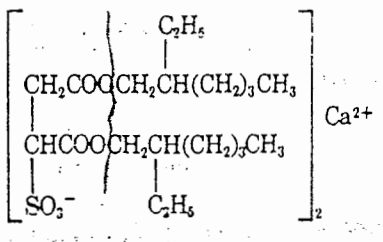
(4)

Preparation. Phenolphthalein may be prepared by mixing phenol, phthalic anhydride, and sulfuric acid, and heating at 120°C for 10–12 h. The product is extracted with boiling water, then the residue dissolved in dilute sodium hydroxide solution, filtered, and precipitated with acid.

Analysis. Official assay methods are reported in the USP (1).

Uses. Phenolphthalein is a cathartic drug, and the basis of many laxatives. It may cause red urine if alkaline, and may cause rash.

Dioctyl Calcium Sulfosuccinate. ***Properties.*** Dioctyl calcium sulfosuccinate (5), calcium salt [*128-49-4*] of 1,4-bis(2-ethylhexyl)sulfosuccinate, also known as Surfak, is a white amorphous solid having the characteristic odor of octyl alcohol. It is very slightly soluble in water, and very soluble in alcohol, polyethylene glycol 400, and corn oil.



(5)

ANALYTICAL SCIENCES JUNE 1999, VOL. 15

Crystal Structure of Phenolphthalein

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We have studied the molecular structures of various organic dyes by the vibrational spectroscopies.[1] Our recent research interests have been focused on the inclusion phenomena of the phthalein dyes in various organic hosts. As a part of our study, the X-ray analysis of 3,3-bis(4-hydroxyphenyl)-1(3*H*)-isobenzofuranone, better known as phenolphthalein, was undertaken. The pH dependent color change of phenolphthalein has been ascribed to a structure change from the lactone (I) to the dianionic resonating form (II), as shown in Fig. 1. Phenolphthalein shows vibrational bands characteristic of the structure (I) in the solid state. The OH stretching bands are observed at 3383, 3329 and 3291 cm^{-1} in the IR spectrum. The intense band at 1737 cm^{-1} with a shoulder peak at 1718 cm^{-1} is assigned to the C=O stretching of the lactone group. The corresponding Raman bands are observed at 1737 and 1719 cm^{-1}.

Crystals suitable for X-ray analysis were grown from an aqueous ethanol solution at room temperature. A colorless prism with dimensions 0.6×0.3×0.4 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC-5R diffractometer with a graphite monochromated Mo K_α radiation (λ=0.71069 Å). The detailed measurement conditions and crystal data are listed in Table 1. The intensity data were collected at 23°C using the ω-2θ scan technique to a maximum 2θ of value of 55.0°. A total of 4195 reflections were collected. The intensities of three representative reflections which were measured after every 150 reflections declined by 0.49%. A linear correction was applied to the data to account for this phenomenon. The linear absorption coefficient for Mo K_α is 0.8 cm^{-1}. An empirical absorption correction, based on azimuthal scans of several reflections, was applied, which resulted in transmission factors ranging from 0.98 to 1.00. The data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods.[2] The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located from a difference Fourier map and included in the full-matrix least squares refinement. The atomic scattering factors and anomalous dispersion terms were taken from the International Tables for X-ray Crystallography, Vol. IV.[3] All calculations were performed using the program TEXSAN crystallographic software package.[3] Selected positional parameters are listed in Table 2. The molecular structure is shown in Fig. 2, together with the atomic labeling scheme. Selected bond distances and angles are listed in Table 3.

There are two independent molecules in the asymmetric unit (Molecule 1 and Molecule 2). The molecules consist essentially of three groups: an isobenzofu-

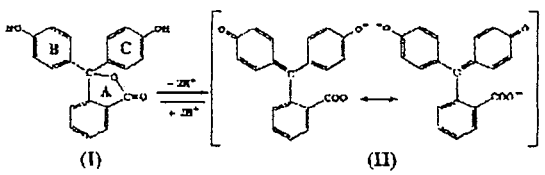

Fig. 1 Dissociation equilibrium of phenolphthalein

Table 1 Crystal and experimental data

Formula: $C_{20}H_{14}O_4$
Formula weight: 318.33
Crystal system: orthorhombic
Space group: $Pna2_1$ Z= 8
a= 19.276(3)Å
b= 14.822(2)Å
c= 11.3884(9)Å
V= 3254(1)Å^3
D_{calc}= 1.299 g/cm^3
No. of reflections used= 2970 ($I>1.20\sigma(I)$)
No. of parameters = 542
R=0.038
R_w=0.037
Goodness-of-fit = 1.25
$(\Delta\rho)_{max}$ = 0.18 eÅ^{-3}
$(\Delta\rho)_{min}$ = −0.18 eÅ^{-3}
Measurement: Rigaku AFC-5R
Program system: TEXSAN
Structure determination: direct method
Refinement: full-matrix least-squares

† To whom correspondence should be addressed.

Table 2 Fractional coordinates and equivalent isotropic thermal parameters of non-hydrogen atoms

Atom	x	y	z	B_{eq}/Å^2
O1	0.2304(1)	0.4152(2)	0.0982	4.2(1)
O2	0.4595(1)	-0.0192(2)	0.4275	4.9(1)
O3	0.3255(1)	0.7606(3)	-0.0469(2)	3.4(1)
O4	0.3484(1)	0.0333(2)	-0.2235	5.7(1)
O5	0.4156(1)	0.1361(2)	0.3963(3)	4.7(1)
O6	0.3495(1)	0.4153(2)	-0.4315(2)	4.4(1)
O7	0.2562(1)	0.6293(1)	0.0143(2)	3.22(9)
O8	0.1923(1)	0.7456(2)	0.0692(3)	5.4(1)
C1	0.3497(1)	0.1644(2)	0.0020(3)	3.0(1)
C2	0.2582(1)	0.2268(2)	0.0546(3)	2.9(1)
C3	0.2879(2)	0.2832(2)	0.1519(3)	3.6(1)
C4	0.2351(2)	0.3456(2)	0.1687(3)	3.5(1)
C5	0.1826(1)	0.3527(2)	0.0874(3)	3.1(1)
C6	0.1818(2)	0.2968(2)	-0.0054(4)	3.8(1)
C7	0.2343(2)	0.2350(2)	-0.0253(3)	3.5(1)
C8	0.3794(1)	0.1191(2)	0.1403(3)	2.7(1)
C9	0.3349(2)	0.0814(2)	0.2225(3)	3.7(2)
C10	0.3606(2)	0.0241(2)	0.3176(3)	3.9(2)
C11	0.4312(2)	0.0245(2)	0.3329(3)	3.4(1)
C12	0.4754(2)	0.0612(2)	0.2512(3)	3.9(2)
C13	0.4500(2)	0.1083(2)	0.1564(3)	3.4(1)
C14	0.4029(1)	0.2105(2)	-0.0426(3)	2.7(1)
C15	0.4402(2)	0.2868(2)	-0.0215(4)	4.2(2)
C16	0.4887(2)	0.3152(3)	-0.1065(5)	5.9(2)
C17	0.4935(3)	0.2698(4)	-0.2123(5)	6.9(3)
C18	0.4542(2)	0.1963(4)	-0.2368(4)	5.8(2)
C19	0.4088(2)	0.1662(2)	-0.1498(3)	3.7(1)
C20	0.3604(2)	0.0908(2)	-0.1487(3)	3.3(2)
C21	0.3339(1)	0.6169(2)	-0.0054(2)	2.7(1)
C22	0.3603(1)	0.5603(2)	0.1022(3)	2.6(1)
C23	0.4250(2)	0.5222(2)	0.1004(3)	3.2(1)
C24	0.4534(2)	0.4814(2)	0.1988(3)	3.5(1)
C25	0.4151(2)	0.4772(2)	0.3012(3)	3.2(1)
C26	0.3456(2)	0.5145(2)	0.3042(3)	3.6(2)
C27	0.3229(2)	0.5561(2)	0.2055(3)	3.3(1)
C28	0.3396(1)	0.5590(2)	-0.1191(3)	2.7(1)
C29	0.3254(2)	0.4664(2)	-0.1211(3)	3.1(1)
C30	0.3281(2)	0.4178(2)	-0.2231(3)	3.5(1)
C31	0.3449(2)	0.4604(2)	-0.3271(3)	3.0(1)
C32	0.3550(2)	0.5521(2)	0.3280(3)	3.2(1)
C33	0.3550(2)	0.6005(2)	-0.2244(3)	2.9(1)
C34	0.3655(2)	0.7046(2)	-0.0175(3)	2.9(1)
C35	0.4231(2)	0.7309(2)	-0.0254(3)	3.6(1)
C36	0.4488(2)	0.8210(2)	-0.0136(4)	4.5(2)
C37	0.3977(2)	0.8838(2)	0.0158(4)	5.4(2)
C38	0.3301(2)	0.8584(2)	0.0322(4)	5.3(2)
C39	0.3147(2)	0.7667(2)	0.0202(3)	3.8(1)
C40	0.2456(2)	0.7185(2)	0.0342(3)	3.8(1)

$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}a_i^*a_j^*(a_i \cdot a_j)$.

ran ring (A) and two *para*-hydroxyphenyl rings (B and C) attached to the tetrahedral carbon atom in the five-membered lactone ring. Each of the three moieties is almost planar. The two *para*-hydroxyphenyl groups lie on opposite sides of the isobenzofuran plane. The geometry differences between the two molecules are found in the orientations of the planes. The rings B and C are inclined with respect to each other at 71.40° for Molecule 1 and 74.63° for Molecule 2. The rings B and C are also oriented with respect to the isobenzofuran ring A at 76.65° and 73.63°, respectively, for Molecule 1 and 75.18° and 70.16°, respectively, for Molecule 2. The C-O bonds in the five-membered lactone rings, which cleave at alkaline pH, are 1.490(3) and 1.484(3)Å, respectively, for Molecule 1 and Molecule 2. They are longer than the normal lactone C-O single bond value (1.462(2)Å)[4] and shorter than the value of 1.525(3)Å found for fluorescein.[5] Fitzgerald and Gerkin[6] have recently reported the crystal structure of phenolphthalein obtained from ethanol solution (R=0.045, Rw=0.097). Differences between the present work and the reported result were observed mainly in the molecular geometries of the lactone moieties.

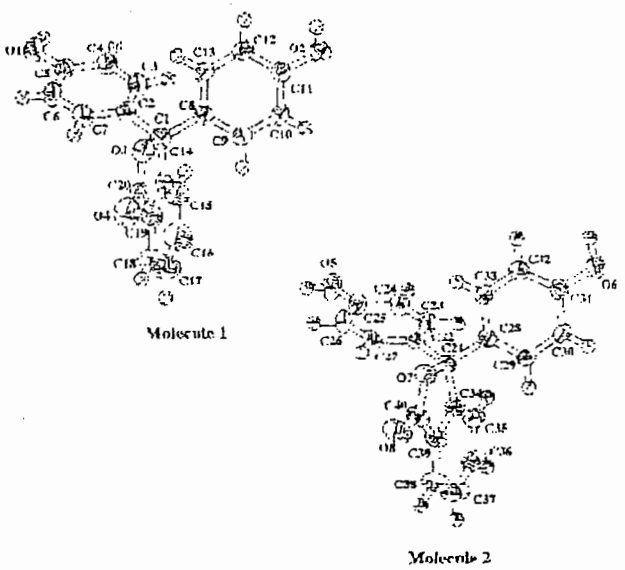

Fig. 2 Molecular structure with the numbering of the atoms. Thermal ellipsoids of the non-hydrogen atoms are scaled to enclose 50% probability. The spheres of the hydrogen atoms are drawn in an arbitrary scale.

Table 3 Selected bond lenghts (Å) and angles (°)

Atom	Atom	Distance	Atom	Atom	Distance
O3	C1	1.440(3)	O7	C21	1.484(3)
O8	C20	1.241(4)	O7	C40	1.343(3)
O1	C20	1.216(4)	O8	C40	1.208(4)
C19	C20	1.493(5)	C39	C40	1.466(5)

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C20	O8	C1	111.3(2)	C40	O7	C21	111.3(2)
O3	C1	C14	101.7(2)	O7	C21	C34	102.4(2)
O3	C1	C8	106.5(2)	O7	C21	C28	107.4(2)
O3	C1	C2	107.7(3)	O7	C21	C22	107.4(2)
O4	C20	O8	121.1(3)	O8	C40	O7	120.2(3)
O4	C20	C19	129.7(3)	O8	C40	C39	131.0(3)
O8	C20	C19	109.2(3)	O7	C40	C39	108.8(3)

Estimated standard deviations in the least significant figure are given in parentheses.

References

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ANALYTICAL SCIENCES APRIL 1999, VOL. 15

Features of Phenolsulfonphthalein and Phenolphthalein Substituted at All *Ortho*-Positions of Phenols with Bromine

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The influence of bromination at all the *ortho*-positions of phenols on the features of phenolsulfonphtalein and phenolphtalein was investigated. The absorption spectra of Bromphenol Blue (H_2BPS) in phosphate buffers demonstrated the complete opening of the lactone ring to form yellow $HBPS^-$ at pH 1 where pK_2=3.8. The reaction of hydroxide ion with blue BPS^{2-} was found to produce colorless $BPS(OH)^{3-}$ required heating where pK_3≒9. On the contrary, the spectra of 3′,3″,5′,5″-tetrabromophenolphtalein (H_2BPP) demonstrated that the lactone ring was very stable. More than 99.5% of BPP^{2-} species consisted of a colorless lactone possessing two isolated phenol groups where pK_1'=6.0 and pK_2'=6.8; the reaction of hydroxide ion with BPP^{2-} to produce $BPP(OH)^{3-}$ was slow where pK_3=10.3. These results indicate the increased acidity of phenols and the greater tendency of the central carbon atom to act as an electron acceptor.

Keywords Bromphenol Blue, 3′,3″,5′,5″-tetrabromophenolphtalein, structural formula and color, dissociation exponent

Different from the widely accepted γ-lactone form, the molecular structure of red crystalline phenolsulfonphthalein ($H_2^+PS^-$) was identified by X-ray crystallography with a zwitter ion.[1] Only such a structure was able to explain the successive changes with pH in color and absorption spectrum of the aqueous solution of $H_2^+PS^-$.[2] On the other hand, the γ-lactone was proved to be rather stable in phenolphthalein (H_2PP). Hence, the monovalent anion HPP^- was colorless, and even the divalent anion PP^{2-} was the mixture of a red quinoid species and a colorless lactone. Further, the slow addition of OH^- to PP^{2-} to produce colorless trivalent anion $PP(OH)^{3-}$ was observed.[2]

Contrary to $H_2^+PS^-$, the molecular structure of colorless crystalline Bromphenol Blue (H_2BPS) was identified with a γ-lactone using X-ray crystallography.[3] This discrepancy led us to investigate the features of the dissociation and coloration of H_2BPS, 3′,3″,5′,5″-tetrabromophenolphthalein (H_2BPP) and its ethyl ester (HBPE) in their aqueous solutions using spectrophotometric analysis.

Experimental

Materials

3′,3″,5′,5″-Tetrabromophenolphthalein (Tokyo Chemical Industry Co., Ltd.) was recrystallized from ethanol with water. The elemental analytical data were agreeable. Bromphenol Blue (Wako Pure Chemical Industries, Ltd.), 3′,3″,5′,5″-tetrabromophenolphthalein ethyl ester potassium salt (KBPE, Tokyo Chemical Industry Co., Ltd.) and other chemicals were of analytical reagent grade.

Buffers

Phosphate buffer of 0.2 M were prepared with sodium dihydrogenphosphate, hydrochloric acid, sodium hydroxide and redistilled water, and ethanol was added if required for dissolving the pigments.

Preparation of sample solutions

After 6.7 mg of H_2BPS was dissolved in 1 ml of ethanol and diluted to 10 ml with water, the resulting 10^{-3} M solution was diluted 200 times with the buffers to obtain 5×10^{-6} M sample solutions of H_2BPS.

A 10^{-2} M solution of H_2BPP in ethanol (63.4 mg in 10 ml) was diluted 100 times with the buffers of pH 8 to 12 to obtain the 10^{-4} M sample solutions and this diluted form was used for the measurement of visible absorption spectra. Similarly 10^{-5} M solutions of H_2BPP in the buffers of pH 8 to 12 were prepared for the measurement of pK_3 of the compound. A 10^{-3} M solution of H_2BPP in ethanol was diluted 100 times with the buffers of pH 2 to 9 containing 30% ethanol to obtain the 10^{-5} M sample solutions for the measurement of pK_1 and pK_2 of the compound.

After 7.0 mg of KBPE was mixed with 1 ml of water and diluted to 10 ml with ethanol, the resulting 10^{-3} M solution was diluted 200 times with the buffers containing 15% ethanol to obtain 5×10^{-6} M solutions of HBPE.

Instruments and measurements

A Hitachi U-3210 spectrophotometer with a scan speed of 120 nm/min and a band path of 2 nm, and a pair of matching cells of 1 cm light pass were used to measure the absorption spectra at 25±2°C with the wavelengths longer than 240 nm where water was able to be used as a reference. A Toa-HM-20E glass electrode pH meter was used at 25±2°C and calibrated with

standard solutions of pH 6.86 and 4.01.

A Macintosh Quadra 840 AV Personal Computer of Apple Co., Ltd. was used to analyze the absorption spectra.

Results and Discussion

By dissolving the colorless H_2BPS in water, a yellow colored solution was obtained. The absorption spectra in Fig. 1 showed the complete opening of the lactone ring to form a quinoid $HBPS^-$ at pH 1. The spectra having absorption maxima at 591.8 nm, 437 nm *etc.* and three isosbestic points demonstrated the presence of $HBPS^-$ and BPS^{2-} in the range of pH 1 to 8. The molar fractions of BPS^{2-} estimated from the absorbances at 591.8 nm coincided well with a theoretical curve for a monobasic acid as in Fig. 2, and hence pK_2 of H_2BPS was determined as 3.8.

The addition of OH^- to BPS^{2-} was very slow at room temperature, however, after heating the solution at pH 12 and 100°C for 2 h, the visible absorption completely disappeared, this was almost completely recovered by heating at pH 6 and 100°C for 2 h. Therefore the pK_3 was estimated to be about 9. The recovery became incomplete with a more concentrated solution, perhaps due to the occurrence of an intermolecular reaction of $BPS(OH)^{3-}$.

From these observations, the structural formulas of existent molecular species in aqueous solutions of H_2BPS were estimated as shown in Fig. 3.

Since the neutral molecule of H_2BPP was almost insoluble in water, the alkaline aqueous solutions were first analyzed. The blue color of BPP^{2-} was very light and the molar extinction coefficient at λ_{max} (585.0 nm) and pH 8 in Fig. 4 (314) was 0.38% of that of BPS^{2-} in Fig. 1 (83,120). Since the molar extinction coeffi-

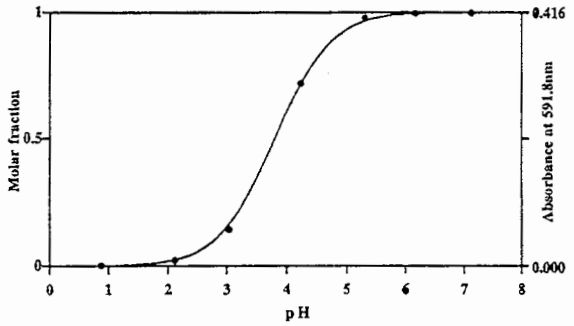

Fig. 2 Graphic plotting of the molar fraction of BPS^{2-} (●) together with the theoretical curve (—) for a monobasic acid of pK=3.8

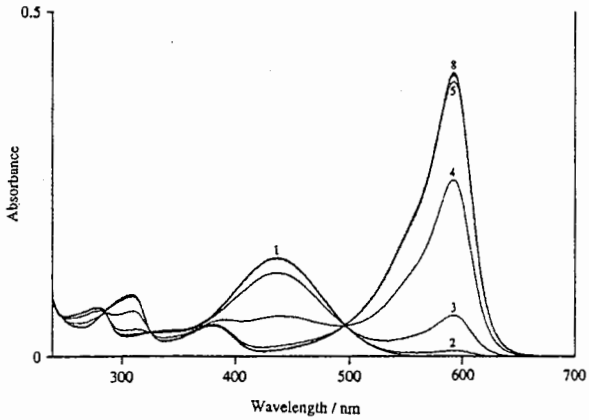

Fig. 1 Absorption spectra of Bromphenol Blue (H_2BPS). The concentration was 5×10^{-6} M. The rough pH values of solutions are given on the spectra.

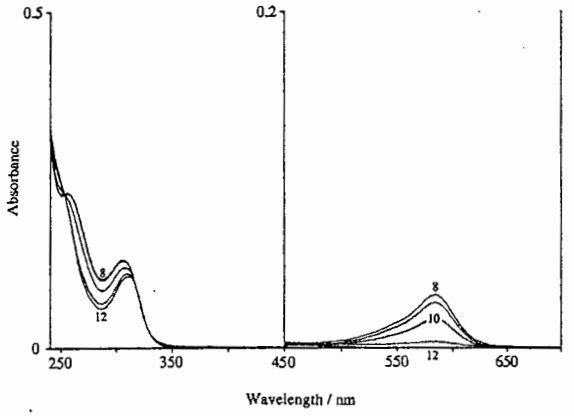

Fig. 4 Absorption spectra of 3′,3″,5′,5″-tetrabromophenolphtarein (H_2BPP) in the alkaline solutions after standing for four days. The concentrations were 10^{-5} M (left) and 10^{-4} M (right).

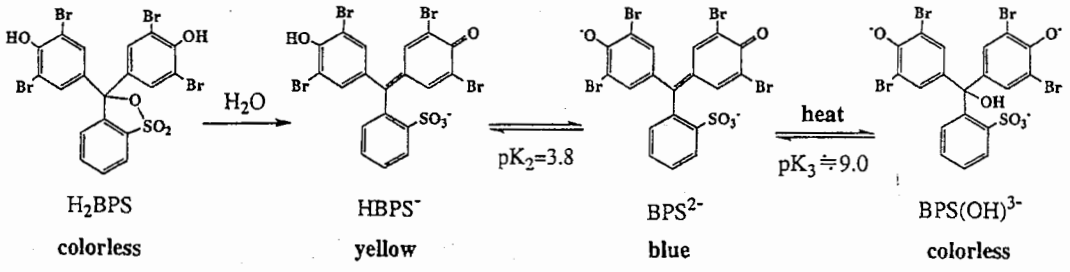

Fig. 3 Structural formulas, colors and pK values of the existent molecular species in aqueous solutions of H_2BPS.

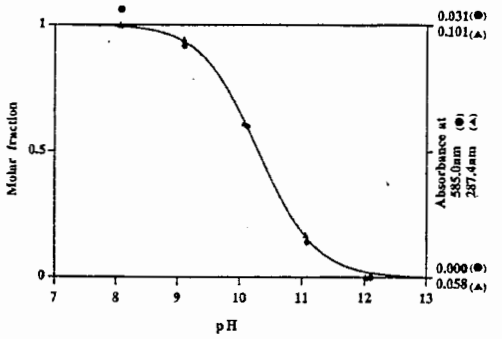

Fig. 5 Graphic plotting of the molar fraction of BPP^{2-} by the use of absorbances at 585.0 nm (●) and 287.4 nm (▲); and the theoretical curve (—) for a monobasic acid of spectra of pK=10.3. The higher absorbance at pH 8 (●) was probably due to turbidity.

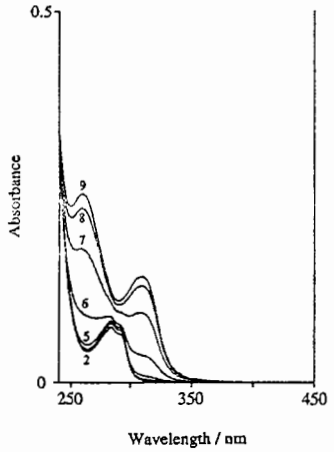

Fig. 6 Absorption spectra of H_2BPP in the solutions containing 30% ethanol with apparent pH 2 to 9. The concentration was 10^{-5} M.

cient of quinoid form of BPP^{2-} was thought to be similar to that of BPS^{2-}, the result demonstrated that more than 99.5% of the species BPP^{2-} consisted of a lactone.

Similarly to phenolphthalein, the slow addition of OH^- to BPP^{2-} was observed at 25°C, and after standing for four days, pK_3 of H_2BPP was determined to be 10.3 by the analysis of absorbances at 585.0 nm, as shown in Figs. 4 and 5. The figures also demonstrated that a similar result was obtained by the analysis of absorbances at 287.4 nm.

Secondly, the solutions of 10^{-5} M H_2BPP in the buffers containing 30% ethanol with apparent pH values of 2 to 9 were investigated to obtain Fig. 6. The spectrum at pH 2 was assigned to H_2BPP species since its shape was quite similar to that of phenolphthalein H_2PP, while the spectrum at pH 9 was assigned to BPP^{2-} species having blue color, as mentioned above. Therefore two steps of dissociation should occur between pH 2 and 9. From the fact that more than 99.5% of BPP^{2-} species maintained the lactone ring, the

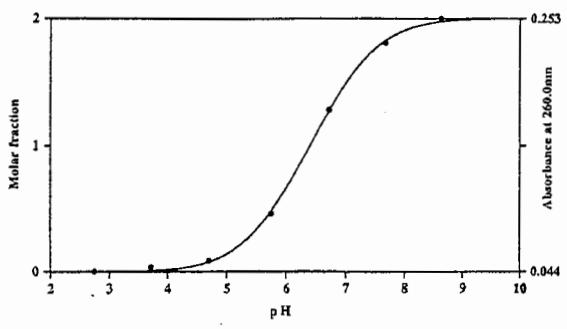

Fig. 7 Graphic plotting of the molar fraction of the phenolate moiety in the molecule of H_2BPP (●) together with the theoretical curve (—) for a dibasic acid of pK_1=6.0 and pK_2=6.8

central carbon atom of triphenylmethane structure should be mostly used for the lactone formation. Hence the double bond formation through this carbon atom became negligible and the phenol moieties attached to the atom became independent in the conjugation system contributive to the light absorption. So the spectral change from pH 2 to 9 was thought to mostly depend on the structural change from phenol to phenolate. Thus the molar fraction of the phenolate moiety ($\sum\phi O^-/\sum A$) was calculated from the following equations using the assumed apparent pK values, pK_1' and pK_2', and the trial-and-error method, to coincide with the observed absorbances (●) at 260.0 nm shown in Fig. 7.

$$[2\phi OH] \overset{pK_1}{\rightleftharpoons} [\phi O^-, \phi OH] \overset{pK_2}{\rightleftharpoons} [2\phi O^-]$$

$$[2\phi OH]+[\phi O^-, \phi OH]+[2\phi O^-]=\sum A$$

$$a_{H^+}^2+a_{H^+}\times 10^{-pK_1}+10^{-pK_1-pK_2}=\Sigma$$

$$[2\phi OH]/\sum A=a_{H^+}^2/\Sigma$$

$$[\phi O^-, \phi OH]/\sum A=a_{H^+}\times 10^{-pK_1}/\Sigma$$

$$[2\phi O^-]/\sum A=10^{-pK_1-pK_2}/\Sigma$$

$$\sum\phi O^-=[\phi O^-, \phi OH]+2[2\phi O^-]$$

$$\sum\phi OH=2[2\phi OH]+[\phi O^-, \phi OH]$$

$$\sum\phi OH+\sum\phi O^-=2\sum A$$

$$Abs._{obs}=l\varepsilon_{\phi O^-}\sum\phi O^-+l\varepsilon_{\phi OH}\sum\phi OH+B(\text{constant})$$

$$Abs._{pH>9}=l\varepsilon_{\phi O^-}\times 2\sum A+B,\ Abs._{pH<3}=l\varepsilon_{\phi OH}\times 2\sum A+B$$

$$\therefore Abs._{obs}-Abs._{pH<3}=l(\varepsilon_{\phi O^-}\sum\phi O^-+\varepsilon_{\phi OH}\sum\phi OH-2\varepsilon_{\phi OH}\sum A)$$
$$=l\sum\phi O^-(\varepsilon_{\phi O^-}-\varepsilon_{\phi OH})$$

$$\frac{2(Abs._{obs}-Abs._{pH<3})}{Abs._{pH>9}-Abs._{pH<3}}=\frac{2l\sum\phi O^-(\varepsilon_{\phi O^-}-\varepsilon_{\phi OH})}{2l\sum A(\varepsilon_{\phi O^-}-\varepsilon_{\phi OH})}=\frac{\sum\phi O^-}{\sum A}$$

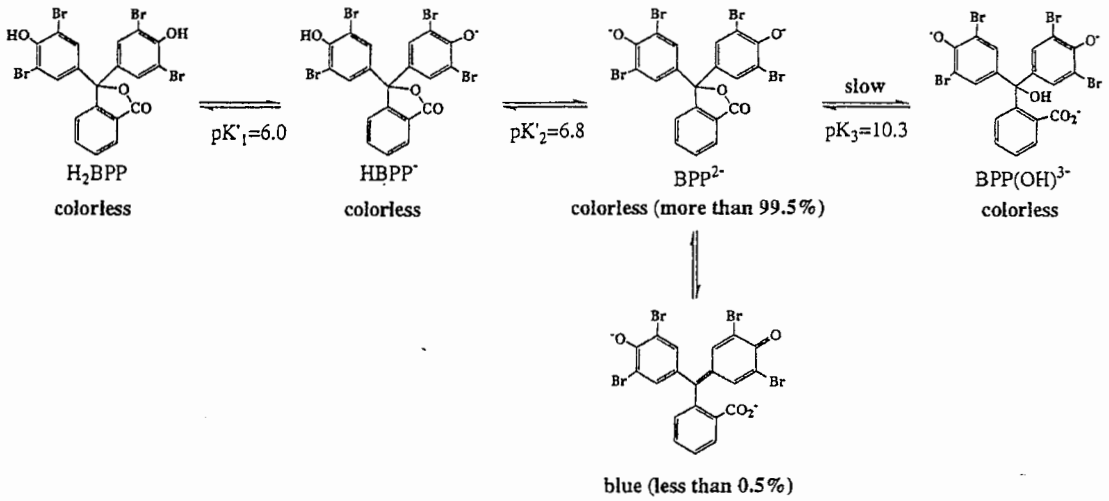

Fig. 8 Structural formulas, colors and pK values of the existent molecular species in aqueous solutions of H_2BPP. pK' was the apparent pK with the solutions containing ethanol.

Table 1 Comparison of the pK values

	H_2BPS	$H_2^+PS^-$	H_2BPP	H_2PP
pK_1	n.o.[a]	1.2	6.0[c]	9.05
pK_2	3.8	7.7	6.8[c]	9.5
pK_3[b]	9	n.o.[a]	10.3	12

a. Not observed.
b. Obtained with the OH^- addition reaction.
c. These value were obserbed in 30% ethanol.

As the result, the values of pK_1' and pK_2' were estimated to be 6.0 and 6.8, respectively.

The absorption spectra of HBPE, in which the lactone formation was inhibited, were thought to be essentially similar to those of $HBPS^-$; however, because of easy hydrolysis of the ethyl ester, HBPE was gradually converted to H_2BPP during the spectral measurement of the solutions containing 15% ethanol. Therefore, the exact analysis was not achieved.

From the data obtained above, the structured formulas of existent molecular species in solutions of H_2BPP were estimated as shown in Fig. 8.

In Table 1, the pK values of H_2BPS and H_2BPP are compared with the corresponding pK values of the mother compounds: $H_2^+PS^-$ and H_2PP.

The values of pK_1 and pK_2 in the table clearly demonstrate the increased acidity of phenols by the bromination at *ortho*-positions.

Further, the pK_3 value of H_2BPP concerning OH^- addition reaction, revised with the quinoid form, which is less than 0.5% of BPP^{2-}, is about 8. The value is much lower than that of H_2PP similarly treated (11.7) indicating the greater tendency of the central carbon atom to act as an electron acceptor together with the increased stability of the lactone ring in H_2BPS (Fig. 3) and H_2BPP (Fig. 8).

References

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3. K. Yamaguchi, Z. Tamura and M. Maeda, *Anal. Sci.*, **13**, 1057 (1997).

(Received November 9, 1998)
(Accepted February 17, 1999)

NTP CHEMICAL REPOSITORY
[redacted]

-IDENTIFIERS
==========

*CATALOG ID NUMBER: 000461

*CAS NUMBER: 85-44-9

*BASE CHEMICAL NAME: PHTHALICANHYDRIDE

*PRIMARY NAME: PHTHALIC ANHYDRIDE

*CHEMICAL FORMULA: C8H4O3

*STRUCTURAL FORMULA: Not printable

*WLN: T56 BVOVJ

*SYNONYMS:
1,2-BENZENEDICARBOXYLIC ACID ANHYDRIDE
1,3-DIOXOPHTHALAN
ESEN
1,3-DIHYDRO-1,3-DIOXOISOBENZOFURAN
1,3-ISOBENZOFURANDIONE
NCI-C03601
PHTHALANDIONE
1,3-PHTHALANDIONE
PHTHALIC ACID ANHYDRIDE
RETARDER AK
RETARDER ESEN
RETARDER PD
RCRA WASTE NUMBER U190
UN 2214

-PHYSICAL CHEMICAL DATA
=====================

*PHYSICAL DESCRIPTION: LITERATURE: White to pale cream powder or flakes
REPOSITORY: White solid

*MOLECULAR WEIGHT: 148.12

*SPECIFIC GRAVITY: 1.527 @ 4 C [043,055,062]

*DENSITY: Not available

*MP (DEG C): 130.8 C [031,038,055,205]

*BP (DEG C): 295 C (sublimes) [017,031,043,047]

*SOLUBILITIES:
WATER : Decomposes

DMSO : >=100 mg/mL @ 19 C (RAD)

95% ETHANOL : <1 mg/mL @ 19 C (RAD)

METHANOL : Not available

ACETONE : >=100 mg/mL @ 19 C (RAD)

TOLUENE : Not available

OTHER SOLVENTS:

Carbon disulfide: Soluble [031,062]
Ether: Sparingly soluble [025,031,043,205]
Alcohol: Soluble [043]

*VOLATILITY:
Vapor pressure: 0.0002 mm Hg @ 20 C [055]; 0.001 mm Hg @ 30 C [055,058]
Vapor density : 5.10 [043,055,058,102]

*FLAMMABILITY(FLASH POINT):
This chemical has a flash point of 151.6 C (305 F) [043,062,102,275]. It is combustible. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. A water spray may also be used [058]. The autoignition temperature is 570 C (1058 F) [043,102,371,451]. It may form explosive mixtures with air [058].

*UEL: 10.4% [043,058,102] LEL: 1.7% [043,058,102,451]

*REACTIVITY:
This chemical is incompatible with strong oxidizers [043,058,102,269]. It is also incompatible with strong acids, strong bases and strong reducing agents [269]. It may react violently with copper oxide or sodium nitrite [036,043, 269]. It may also react with nitric acid [036,043]. Nitration with sulfuric acid may also present a danger [036]. It is incompatible with water, alkalis, nitrating mixtures and amines [058].

*STABILITY:
This chemical is sensitive to moisture [269,275]. It may also be sensitive to heat. UV spectrophotometric stability screening indicates that solutions of this chemical in 95% ethanol are stable for less than two hours but solutions in acetone are stable for at least 24 hours (RAD).

*OTHER PHYSICAL DATA:
Choking odor [102,371]
Vapor pressure: 1 mm Hg @ 96.5 C [038,043]
Freezing point: 131 C [371]
Saturation concentration: 0.0016 g/m3 @ 20 C; 0.0078 g/m3 @ 30 C [055]
Acidic pH [058]
Percent volatile (in water): 0.5% max [058]

-TOXICITY

*NIOSH REGISTRY NUMBER: TI3150000

*TOXICITY: (abbreviations)

typ. dose	mode	specie	amount	units	other
LD50	orl	rat	4020	mg/kg	
LDLo	orl	gpg	100	mg/kg	
LD50	orl	mus	1500	mg/kg	
LD50	orl	cat	800	mg/kg	

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR: Poison by ingestion. Experimental teratogenic effects. A common air contaminant. Moderate explosion hazard in the form of dust when exposed to flame. The production of this material has caused many industrial explosions.

*CARCINOGENICITY:
Status: NCI Carcinogenesis Bioassay (Feed); Negative: Male and Female Rat, Male and Female Mouse [620]

*MUTATION DATA:

test	lowest dose	test	lowest dose
Not available			

*TERATOGENICITY:
Reproductive Effects Data:
TDLo: ipr-mus 203 mg/kg (8-10D preg)

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: Federal Register (1/19/89) and 29 CFR 1910.1000 Subpart Z
Transitional Limit: PEL-TWA 2 ppm [015,326,545,610]
Final Limit: PEL-TWA 1 ppm [015,545,610]
ACGIH: TLV-TWA 1 ppm [015,415,421,610]
NIOSH Criteria Document: None
NFPA Hazard Rating: Health (H): 2
Flammability (F): 1
Reactivity (R): 0
H2: Materials hazardous to health, but areas may be entered freely with full-faced mask self-contained breathing apparatus which provides eye protection (see NFPA for details).
F1: Materials that must be preheated before ignition can occur (see NFPA for details).
R0: Materials which are normally stable even under fire exposure conditions and which are not reactive with water (see NFPA for details).

*OTHER TOXICITY DATA:
Skin and Eye Irritation Data:
skn-rbt 500 mg/24H MLD
eye-rbt 100 mg SEV
Review: Toxicology Review-3
Standards and Regulations: DOT-IMO: Corrosive material; Label: None
Status: EPA Genetox Program 1988, Negative: Carcinogenicity-mouse/rat
EPA TSCA Chemical Inventory, 1986
EPA TSCA Test Submission (TSCATS) Data Base, June 1988
Meets criteria for proposed OSHA Medical Records Rule

-OTHER DATA (Regulatory)

*PROPER SHIPPING NAME (IATA): Phthalic anhydride

*UN/ID NUMBER: UN2214

*HAZARD CLASS: 8 SUBSIDIARY RISK: None PACKING GROUP: III

*LABELS REQUIRED: Corrosive

*PACKAGING: PASSENGER: PKG. INSTR.: 822, Y822 MAXIMUM QUANTITY: 25 kg, 5 kg
CARGO : PKG. INSTR.: 823 MAXIMUM QUANTITY: 100 kg

*SPECIAL PROVISIONS: A74

*USES:
This compound is used in alkyd resins, plasticizers, hardeners for resins, polyesters and synthesis of phenolphthalein and other phthaleins, dyes, chlorinated products, pharmaceutical intermediates, insecticides, diethyl phthalate, dimethyl phthalate and laboratory reagents. It is also used in the manufacture of specialty chemicals, synthetic fibers, pigments, synthetic indigo, artificial resins (glyptal), phthalates and benzoic acid. It is used as a dehydrating agent for alcohols, protecting reagent for amino acids, fire retardant for use in components of polyester resins and in the manufacture of metallic and acid salts.

*COMMENTS: Not available

-HANDLING PROCEDURES

*ACUTE/CHRONIC HAZARDS:
This chemical is a severe irritant of the skin, eyes and respiratory system [036,058,401]. These irritating effects are worse on moist surfaces

[102,275]. When heated to decomposition it emits toxic fumes of carbon monoxide and carbon dioxide [102,269]. It is readily absorbed through the skin [269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
GlovES+ Expert System Glove Types For The Neat (Undiluted) Chemical:
This chemical has not been tested for permeation by Radian Corporation; however, the GlovES+ expert system was used to extrapolate permeation test information from compounds in the same chemical class. The GlovES+ system uses permeation data from literature sources; therefore, extra safety margins should be used with the estimated protection time(s). If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

The GlovES+ expert system is a tool that can help people better manage protection from chemicals, however this tool cannot replace sound judgment nor make technical decisions. Our GlovES+ expert system is designed to offer initial advice and assistance in glove selection while the final glove selection should be made by knowledgeable individuals based on the specific circumstances involved.

Glove Type	Model Number	Thickness	Estimated Protection Time
Nitrile	Edmont 32-155	0.38 mm	480 min
Neoprene	Edmont 29-870	0.50 mm	480 min
Butyl rubber	North B-161	0.60 mm	480 min
PE/EVOH/PE	Broste 4H Glove	0.07 mm	240 min

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical under refrigerated temperatures and protect it from moisture. Keep it away from mineral acids and bases. If possible, it would be prudent to store this compound under inert atmosphere.

*SPILLS AND LEAKAGE:
If a spill of this chemical occurs, FIRST REMOVE ALL SOURCES OF IGNITION, then you should dampen the solid spill material with acetone and transfer the dampened material to a suitable container. Use absorbent paper dampened with acetone to pick up any remaining material. Seal your contaminated clothing and the absorbent paper in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with acetone followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.

If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.

Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:

First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.

Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.

IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:

DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.

If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:

Symptoms of exposure to this compound may include moderate to severe irritation of the eyes and skin [058,102,371,421]. It may also cause irritation of the mucous membranes and upper respiratory tract [036,058,421]. Inhalation of the dust or vapors of this compound may cause coughing or sneezing [102, 371]. It may also cause nosebleeds and asthma attacks in persons who have previously had asthma [102]. It may also cause bronchitis [102,421]. Repeated or prolonged exposure can cause skin burns [058,102,371]. It may also cause skin rash, dermatitis, conjunctivitis and chronic eye irritation. Absorption into the body leads to formation of methemoglobin which in sufficient concentration causes cyanosis. Onset may be delayed 2-4 hours or longer. Exposure may also damage the liver and kidneys [102]. It may possibly cause pulmonary sensitization [421]. Other symptoms include chronic congestion and ulceration of the nose, eye burns, allergic respiratory reaction, a burning sensation in the nose and throat and gastrointestinal disturbances [058]. Consumption of alcohol may increase toxic effects [269]. It will cause internal irritation if taken by mouth [036]. It may also cause smarting of the skin [371]. Skin sensitization may occur [401].

-SOURCES

*SOURCES:

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