Proceeding Bromometric Phenol Assay without Starch Indicator[#]

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Abstract

In this research, we exclude starch indicator preparation,that is used in official phenol assay method. The liberated iodine, in presence of chloroform, was acting as indicator and titrated with sodium thiosulfate until getting a sharp colorless end point. Similarly, starch was cancelled during both blank and standardization of bromine water solution experiments needed in phenol assay. The results obtained were the same volumes and weights as that achieved using starch with just about 0.03% difference in sample procedure. Finally, this work will enable us to save time, effort, fuel and materials spended in laboratory.

Key word:- Phenol, assay, starch indicator

الخلاصة

هذا البحث يقوم على الغاء تحضير محلول النشا المستعمل كدليل عند تحليل الفينول رسمياً حيث نقوم بتسحيح اليود بوجود الكلوروفورم والذي يعطينا لوناً احمر غامق مع محلول الثايوسلفات الصوديوم لنحصل في النهاية على محلول شفاف ونقطة نهاية واضحة بدون استعمال محلول النشا وينطبق هذا ايضاً على تجربتي ايجاد البلانك وتقييس محلول البروم اللتين نحتاجهما خلال عملية التحليل. ولقد اعطتنا هذه الطريقة المختصرةنتائج دقيقة بالنسبة لتجربة التقييس والبلانك مع فارق ضئيل يقدر بحوالي 0.03% لتجربة التحليل وبهذا العمل نستطيع توفير الوقت، الجهد، الطاقة والمواد المصروفة في المختبر.

Introduction

Phenol or so-called carbolic acid is a colorless to pale pink crystalline material with a characteristic medicinal odour. It is slightly soluble in water but freely soluble in some organic solvents and can be present as liquefied phenol. It is still used occasionally as an antipruritic in phenolated calamine lotion exerting local anesthetic effects. It remains the standard to which the activity of most germicidal substances is compared with phenol coefficient of 1.0 [(1)] Phenol is preserved in tight and light-resistant containers with suitable stabilizer [(2a)]. It is identified with ferric chloride or bromine solution [(3a)].Phenol can be thought of as hydroxy derivative of benzene. It occurs widely throughout nature mainly obtained from coal tar. It is a general disinfectant and it serves as intermediate in the industrial synthesis of products as diverse as adhesives and antiseptics. It was used for manufacturing the explosive picric acid. It can be used as Bakelite resin and adhesives for binding plywood. It is also the starting material for the synthesis of chlorinated phenols and the food preservative BHT (Butylated Hydroxytoluene) & BHA (Butylated Hydroxyanisole). Pentachlorophenol is widely used as wood preservative. The herbicide 2, 4-D(2, 4- dichlorophenoxy acetic acid and hospital antiseptic hexachlorophene are derivatives of phenol.Phenol is oxidized with strong oxidizing agents (like Fremy's salt) yielding a cyclohexa-2, 5-diene -1, 4-Dione (Quinone) [(4)].This oxidative dearomatization to quinones also known as the Teuber reaction using oxone as oxidizing reagent [(5)].phenol is also used in the preparation of cosmetics including sunscreens [(6)].Phenol can be made also by fusing sodium benzene sulfonate with NaOH or by heating mono chlorobenzene with aqueous NaOH under high pressure [(7)].Phenol may be formed endogenously from metabolism of other xenobiotics,notably benzene,and by catabolism of protein and other compounds by gut bacteria[(8)].Under laboratory conditions mimicking hydrothermal circulation (water,200^{o}C,1.9 GPa),phenol is found to form from sodium hydrogen carbonate and iron powder [(9)].The most striking chemical property of phenol is as extremely high reactivity of its ring toward electrophilic substitution as a strong ortho-and para-director potentiated with its acidity [(10)],and it has been recently shown that only about 1\3 of the increased acidity of phenol is due to inductive effects,with resonance accounting for the rest [(11)]. Phenol,as oily injection,is used to inject haemorrhoids particularly when unprolapsed [(12)].Simply heating a mixture of phenol and formaldehyde with aqueous acid leads Bakelite which was the first commercially available cross-linked three dimensional network polymer molecule that is very resistant to solvents, heat and electricity and widely used in household products [(13)].

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Phenol is incompatible with alkaline salts and nonionic surfactants. The antimicrobial activity of phenol may be diminished through increasing pH or through combination with blood and other organic matters. It should not be used to preserve preparations that are to be freeze-dried [14].A ten-day,nose-only,phenol inhalation toxicity study in Fischer 344 rats did not find evidence of adverse effects [15],in addition ,phenol has been evaluated in vivo studies using specialized protocols [16].The aromatic C-O bond is difficult to break in phenol using strong acids like HBr to form bromobenzene. Thus HBr can protonate phenol, but no further reaction occurs [17].Spore proteins of Aspergillus versicolor, as an indoor mould, can be purified using phenol extraction with subsequent solvent precipitation and washing steps. This protein was prepared for two-dimensional (2D)-gel electrophoresis with sera from patients to study about indoor exposure of moulds and their influence on the development of allergies by screeing sera for IgE antibodies specific for A. versicolor and others [18].Hydroquinone,as a member in phenols family,is assayed with volumetric titration unlike the bromometric method used for phenol [2b] while resorcinol assay followes the later one [3b].Phenol showes a characteristic broad IR absorption at 3500 Cm^{-1} due to the-OH group, as well as the usual 1500 and 1600 Cm^{-1} aromatic bands in addition to monosubstituted aromatic ring peaks at 690 and 760 Cm^{-1} while it possesses H NMR absorptions near 7-8 S of aromatic ring protons. Phenol-OH protons absorb at 3-8 S [4].These spectroscopies are used for identification of phenol together with ferric chloride or bromine solution chemical tests mentioned previously. Accordingly, phenol reaction with bromine gives 2, 4, 6-tribromophenol [19] as a white chloroform soluble precipitate and this is the principle of quantitative phenol assay that is officially followed in USP and B-P using starch as indicator. Therefore we are going to proceed the same procedure for assaying phenol with the exception of no need to add starch.

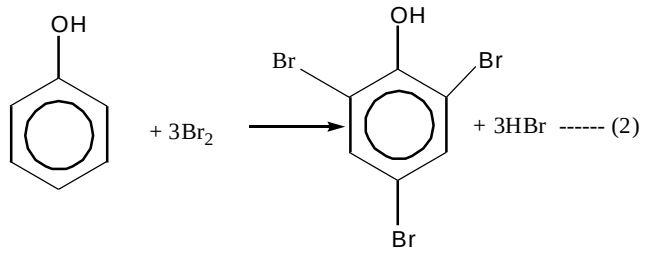
Materials and method

Potassium bromate from BD; Potassium bromide, M&B; Phenol, BDH; Sodium Thiosulfate, Hopkin & Williams Synchemica, England. And Chlorofrom, GCC, United Kingdom. England; Potassium iodide, Merck; hydro chloric acid, Riedel-De Haen; Starch, Merch, Germany;25 ml-bulb pipette,Din,West Germany;50 ml- Burette,Permagold,Exelo;500 ml-volumetric flask,pyrex,USA;500 ml-iodine flask,Schott(Witeg),West Germany.The method used for assaying phenol here is the same as that mentioned in USP or BP and it depends on oxidation-reduction reaction steps.First of all, we did standardization for bromine (bromide and bromate) solution by taking 25 ml into 500ml- iodine flask and 120 ml distilled water was added followed by 5 ml concentrated HCL, the flask was then stoppered and shaken gently, we added 5 ml of 20% potassium iodide solution and restoppered the flask. The mixture was shaken, allowed to stand for 5 min. and then titrated with 0.1N sodium thiosulfate using starch indicator which gave deep blue colour with liberated iodine. The end point is indicated with colorless solution. We repeated the standardization procedure but without starch indicator (here we can also add 5ml of chloroform to act as co-indicator with iodine) and recorded the volumes of sodium thiosulfate of both experiments. The equation $N_1V_1=N_2V_2$ is used to find the normality of bromine solution and the results are shown in table 1. These events are represented with equations 1, 3 & 4 [2c].At second stage, we did bromometric phenol assay which includes addition of excess (50 ml of 0.1N) bromine solution to 25 ml-phenol solution (sample1, which was prepared by dissolving 1.1gm phenol in 500 ml water to get 0.055gm /25 ml) and then liberation of bromine by addition of 5 ml concentrated HCl. Bromine reacts readily with phenol through electrophilic aromatic substitution yielding 2, 4, 6-tribromophenol as a white precipitate. Stoppering well the iodine flask is necessary to prevent escape of bromine vapour. The flask was shaken repeatedly for 30 min., leave to stand for 15min.and 5 ml of 20% potassium iodide solution was added with contineous shaking and the flask and stopper was washed with water and 5 ml chloroform was then added to dissolve the precipitate. Iodine, released due to potassium iodide reaction with bromine, was titrated against 0.1N sodium thiosulfate solution until pale yellow occurred. 1-2 ml starch solution was added giving deep blue colored complex with iodine and we continued the titration until discharging the colour to a clear colorless end point. Again, we repeated the same experiment above but without adding starch indicator and, here, the solution became brown-deep red colour due to the presence of iodine itself which was then titrated versus sodium thiosulfate solution until sharp colorless end point. In the same way, we repeated the same experiments (with and without starch) on second amount of phenol (sample 2), recorded the volumes of sodium thiosulfate needed for

each pair of samples knowing that each 1ml of 0.1 N bromine solution is equivalent to 0.001569 gm of phenol (the chemical factor, which is number of gm weight equivalent to 1 ml of standard solution) and the resultant weights were shown on tables 3 and 4. equations 1-4 are the principle of phenol assay.Finally, we had to do blank without phenol twicely (with and without starch too) and the volumes of titrant were recorded to be employed mathematically. The results were shown in table 2 . Equations 1,3 and 4 represented these reactions.

Note:- all the volumes, except that of standardization, of sodium thiosulfate must be corrected to 0.1 N.

$5KBr+KBrO_3+6HCl \rightarrow 3Br_2+6KCl+3H_2O$ --------- (1)



Phenol

2,4,6-tribromophenol(White ppt.)

$Br_2 + 2KI \rightarrow I_2 + 2KBr$ -------- (3)

excess (unreacted)

$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$ ------ (4)

Equation (4) represents the end point.

Scheme I: Sequential equations of phenol assay

Results and Discussion

As shown in tables 1,2, 3 and 4 we see the followings:-

- The volume of sodium thiosulfate solution for standardization of bromine solution with starch experiment was as exact as that without starch experiment and therefore the normalities of bromine solution for both experiments will be exactly the same.
- Therefore, total bromine solution that must be added is the same for blank and assay experiments with and without starch procedure.
- The volume of $Na_2S_2O_3$ of blank experiment with starch was nearly exact to that without starch experiment and therefore the blank, that must be used mathematically, was also nearly the same for both experiment (after correction).
- For sample 1 , the volume of $Na_2S_2O_3$ of assay experiment with starch was closely related to that of without starch procedure and, as a result, the weight of phenol with starch was closely the same as that of without starch experiment.
- For sample 2 , on the other hand, the volume of $Na_2S_2O_3$ for assaying phenol with starch was also approximately equal to that without starch and the corresponding weights of phenol were approximating too.

Therefore, we see a small difference ranging from 0.03-0.04% (as shown on table 5) between the resultant weights of phenol assay with and without starch procedure possibly due to simple error in technique (may occur in measuring phenol samples since capacity of bulb pipette is 25±0.03 ml). Starch makes a deep blue color complex with iodine and should be added when iodine is in a low concentration (near the end point) and when all iodine is depleted, the solution becomes colorless[19a]. While in our new experiment, this disadvantage will be abolished since there is no starch present but, instead, iodine in the presence of chloroform will act as indicator exhibiting a deep red colour and, at the end point, the mixture will be colorless too. This resembles ascorbic acid assay procedure that runs using chloroform-iodine as indicator[19b].At last, starch preparation needs weighing, adding water, boiling the solution, cooling and then filtration to be ready for use. So, our modified experiment will have the advantage of saving time, fuel, effort and materials owing to similarity in quantitative and qualitative results that were obtained.

Table (1):- The results of standardization experiment with and without starch.

Experiments	Method with starch	Method without starch
N. of $Na_2S_2O_3$ must be 0.1N. N. of $Na_2S_2O_3$ prepared & used was	0.131 N	The same
V. of $Na_2S_2O_3$ for standardization of bromine solution prepared and used was	21 ml	The same

Table (2):- The results of blank experiment with and without starch.

Experiments	Method with starch	Method without starch
N. of bromine solution prepared and used was	0.11 N	The same
Total bromine must be used was	45.45 ml of 0.11 N	The same
V. of $Na_2S_2O_3$ 0.131 N needed for blank was	39.2 ml	39.15 ml
V. of $Na_2S_2O_3$ 0.1 N (after correction) needed for blank experiment was	(V blank) 51.352 ml	(V blank) 51.287 ml

Table (3) :- The results of sample 1 experiment with and without starch.

Experiments	Method with starch	Method without starch
Sample 1:- V. of $Na_2S_2O_3$ 0.131 N react with excess bromine solution was	13.45 ml	13.6 ml
Sample 1:- V. of 0.1 N of $Na_2S_2O_3$ react with excess bromine solution (after correction)	17.620 ml (Vexcess)	17.816ml (Vexcess)
V blank – Vexcess=Vreact with phenol=	33.732 ml	33.471ml
Vreactwith phenol X Chemical factor = weight of phenol in sample1	0.0529 gm	0.0525 gm

Table (4) :- The results of sample 2 experiment with and without starch.

Experiments	Method with starch	Method without starch
Sample 2 :- V. of 0.131 N $Na_2S_2O_3$ react with excess bromine solution was	26.7 ml	26.5 ml
V. of 0.1 N $Na_2S_2O_3$ react with excess bromine solution (after correction) Vexcess was	34.977 ml (Vexcess)	34.715 ml (Vexcess)
Vblank – Vexcess= V react with phenol=	16.375 ml	16.572ml
Vreact with phenol X chemical factor (0.001569) = weight of phenol in sample 2	0.0257 gm	0.0260 gm

Table (5) :- Weight (gm) difference between the weight of phenol assayed with and that assayed without starch for the two phenol samples.

Phenol sample	Obtained phenol concentration (gm/25ml)		Gm weight difference between with and without starch results
	With starch	Without starch	
Sample 1	0.0529	0.0525	0.0004 (0.04%)
Sample 2	0.0257	0.0260	0.0003 (0.03%)

Note:- Chemical factor:- 1 ml 0.1 N bromine=~ 0.001569 gm phenol

Conclusion

From this research we conclude that starch indicator preparation and addition can be no further continued whether at bromometric assay of phenol or at any iodometric titration with sodium thiosulfate as in ferric chloride colorimetric solution [2d].

References

1. *Wilson and Gisvold's textbook of organic medicinal and pharmaceutical chemistry* 11th edition, John H. Block and John M. Beale, 2004, Lippincott Williams and Willkins p.221.
2. *United Sates Pharmacopiea* 27th edition and National formulary 22nd edition,2004, united States pharmacopeial Convention, Inc; Rock Ville, MD, a. p. 1464, b. p. 937, c. p. 2733, d. p.2725.
3. *British Pharmacopoeia*, vol. II, 2008, Britishpharmacopoeia Commission Office, Satationery Office,a. P. 1701,b.1881.
4. *John McMurrry Organic Chemistry*, 7th edition, Thomson Learning, Inc; David Harris, 2008, Sandra Kiselica, p.599.
5. C.Carmen;G-L.Marcos and U.A.Antonio:Oxidative dearomatization of para-alkyl phenols into para-peroxyquinols and para-quinols mediated by oxone as a source of singlet oxygen M.;*Chemie International Edition* ,2006, 45(17):2737-2741.
6. A.Svobodova;J.Psotova and D.Walterova:Natural phenolics in the prevention of UV-induced skin damage.A review;*Biomed.Papers*,2003,147(2):137-145.
7. *Merck Index* 14th edition, Merck Research laboratories, 2006, Merck and C0., Inc. White House Station, NJ, USA, phenol 7241, p. 1250.
8. T.McDonald;N.Holland;C.Skibola;P.Duramad;M.Smith:Hypothesis:Phenol and hydroquinone derived mainly from diet and gastrointestinal flora activity are causal factors in leukemia;*Leukemia*,2001, 15:10-20.
9. T.Ge;Y.Hongming;M.Ying;H.Chao and F.Shouhua:Hydrothermal reactions from sodium hydrogen carbonate to phenol;*Org.Lett.*,2007,9(10):2019-2021.
10. *Morrison and Boyd organic chemistry* 6th edition, prentice Hall International, Inc; 1992, Dan Joranstad, p. 899.
11. J.S.Pedro:Inductive and resonance effects on the acidities of phenol,enols and carbonyl alpha-hydrogens;*J.Org.Chem*.,2009,74:914-916.
12. *British National Formulary*, 51 edition, BMJ Publishing Group Ltd, 2006, p. 65.
13. Richard F. Daley and Sally J. Daley, *organic chemistry* 1st edition, Wm. C. Brown publishers, 1996, John Berns, p. 1153.
14. *Martindale the complete drug reference*, 33 edition, Sean C. Sweetman, pharmaceutical press, 2002, p. 1152.
15. G.Hoffman;B.Dunn;C.Morris;J.Butala;S. Dimond;R.Gingell et al:Two-week(ten-day) inhalation toxicity and two-week recovery study of phenol vapor in the rat;*Inter.J.Toxico*.,2001,20:45-52.
16. B.Ryan;R.Selby;R.Gingell;JJ.Waechter;J. Butala;S.Dimond et al:Two-generation reproduction study and immunotoxicity screen in rats dosed with phenol via the drinking water ; *Inter J. Toxico*. ,2001 , 20:121-142.
17. Schmid George, *organic chemistry*, Mosby (James M. Smith), 1996, Lioyd W. black, p. 1026.

18. D. Benndorf, A. Muller, K Bock, O. Manuwald, O. Herbarth, M. von Bergen, identification of spore allergens from the indoor mould Aspergillus versicolor, *Allergy* 2008; 63: 454-460.

19. Beckett and Stenlake, *Practical pharmaceutical chemistry*, second edition, part one, the Athlone press, 1968, a. p. 174, b. p.184-185.