CHEMICAL & PHARMACEUTICAL BULLETIN

Vol. 25, No. 7 July 1977

Regular Articles

Chem. Pharm. Bull. 25(7)1493—1496(1977)

UDC 547.74.04.08 : 546.142.13.04

Microdetermination of Pyrrole Derivatives using Bromine Monochloride in Acetic Acid Medium

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(Received August 12, 1976)

A micromethod for determination of pyrrole derivatives using bromine monochloride in acetic acid as the reagent is described. The results obtained show the maximum error of 1.06% on the average.

Keywords——bromine monochloride; pyrrole derivatives; iodometry; acetic acid; stoichiometry

Numerous methods[2–4)] have been developed for the determination of pyrrole derivatives. Emil[5)] developed a photocolorimetric method for the determination of 3-indole acetic acid. Kupfer and coworker[6)] described a method for the determination of indole, tryptophan and anthranilic acid in a mixture. Rosselli[7)] described a method for the determination of carbazole and phenanthrene in anthracene. Lopatinskii[8)] described a titrimetric procedure for the determination of 9-acyl carbazole. Hennart and coworker[9)] developed a titrimetric method for the determination of benzimidazoles, using perchloric acid as a titrant and methyl violet as an indicator. Starkova and coworkers[10)] evolved a vapor-phase oxidation method for the determination of pyrrole, furfuryl alcohol and thiophene using bromate-bromide as a reagent for bromination. In the present work a rapid and convenient method for the determination of certain pyrrole derivatives, based upon the reaction with bromine monochloride and titration of the excess reagent by iodometry, is described.

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Experimental

Reagents and Solutions——Bromine monochloride solution, 0.1N; 1.3917 g (A.R., B.D.H.) potassium bromate and 1.9835 g (A.R., B.D.H.) potassium bromide were dissolved in 125 ml of distilled water in a 500 ml volumetric flask. The solution was cooled in an ice-bath, 100 ml of concentrated hydrochloric acid (M.A.R. grade) added and the solution diluted to the mark. Potassium iodide solution, 15% (w/v), (Baker Analytical Reagent). Glacial Acetic acid (A.R., B.D.H.). Starch solution, 1% (w/v). Sodium thiosulfate standard solution, 0.04N.

Sample Solution: 1) The sample solutions of indole, isatin, indole-3-acetic acid, indole-3-propionic acid and indole-3-butyric acid were prepared by dissolving accurately weighed amounts of the materials around 50 mg in about 10 ml glacial acetic acid in a 50 ml volumetric flask and the solutions were diluted by distilled water to the mark. 2) The sample solution of carbazole was prepared by dissolving accurately weighed amount (*ca.* 50 mg) in 10 ml glacial acetic acid in a 50 ml volumetric flask. The solution was warmed slightly to dissolve the sample completely and the solution made up to the mark with glacial acetic acid (water precipitates out carbazole). Different aliquotes of the solutions were used in determination.

Procedure——An aliquot volume of the sample solution containing 2—10 mg of the sample was taken in a 100 ml iodine flask. A 2 ml of glacial acetic acid and 10 ml of bromine monochloride solution were added and the flask was stoppered and shaken well. The flask was kept in an ice-bath and the reaction mixture allowed to cool well for 5—8 minutes (time required for completion of the reaction). After the reaction was over, the stopper was washed with 5 ml of distilled water and 5 ml of potassium iodide, the liberated iodine was then titrated by standard sodium-thiosulfate solution using starch as an indicator. A blank test was always run under the identical conditions except using the sample.

Calculation

$$\text{Recovery (mg)} = \frac{\text{mol. wt}}{2n} \cdot N_{\mathrm{Na_2S_2O_3}} (V_{\mathrm{Blank}} - V_{\mathrm{Sample}})$$

where:

Mol. wt = Molecular weight of the sample
$N_{\mathrm{Na_2S_2O_3}}$ = Normality of the sodium thiosulfate solution
V_{Blank} = Volume of sodium thiosulfate required to titrate blank (ml)
V_{Sample} = Volume of sodium thiosulfate required to titrate sample (ml)
n = Number of moles of bromine monochloride required per mole of the sample for complete reaction (Isatin; $n=2$, other pyrrole derivatives; $n=3$)

Results and Discussion

Stoichiometry of the Reaction

Before applying the reaction for the determination of pyrrole derivatives, the stoichiometry of the reaction was established as follows: 2—6 ml of the sample solutions of known concentration made up with glacial acetic acid and water media were reacted with a known

TABLE I. Determination of the Stoichiometry of the Reaction

Compound	Aliquot taken (mg)	Sample taken (mg)	Number of moles of BrCl consumed per mole of the compound
Indole	2	2.070	3.002
	4	4.140	3.100
Carbazole	2	2.120	3.110
	4	4.240	3.011
Isatin	2	2.058	1.994
	6	6.174	2.014
Indole-3-acetic acid	2	2.018	3.005
	6	6.054	2.956
Indole-3-propionic acid	1	1.406	3.102
	4	5.624	3.002
Indole-3-butyric acid	2	2.086	3.102
	6	6.258	3.001

excess of bromine monochloride solution. The reaction was allowed to proceed in ice-bath for 8 minutes in case of indole and 5 minutes in case of other compounds, and the excess of the reagent was back-titrated iodometrically. Results obtained are presented in Table I.

The stoichiometry of the reaction between bromine monochloride and pyrrole derivatives indicated in Table I can not be explained on the basis of either electrophilic substitution or addition alone for all the compounds studied. It seems likely that different mechanisms operate for different types of compounds. For indole (I) in Chart 1 and its 3-substituted acids, a mixed mechanism of addition and substitution is more likely. Addition of two moles of bromine monochloride to two C=C bonds in five membered ring and substitution at position 6 in the six membered ring will require three moles of bromine monochloride for the complete reaction. Isatin (II) can easily tautomerise in acid medium which will help in substitution at the hetero atom in the manner as indicated in the same table. Second mole of bromine monochloride would likely attack position 6 in benzene ring to give an overall dibromoproduct.

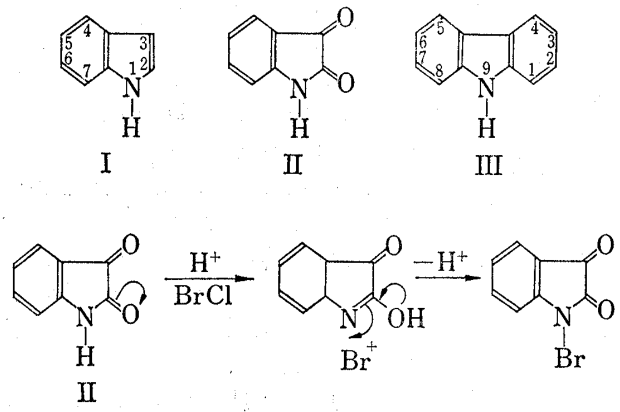

Chart 1

Carbazole (III), which has two benzene rings, will consume three moles of bromine monochloride to give a 2,7 and 9 substituted tribromo derivative. Position 2 and 7 in carbazole and position 6 in indole and 3- substituted indoles are known to be sufficiently reactive to undergo electrophilic substitution. The substitution at the nitrogen atom would only take place when N-H bond is sufficiently polar. Very strong electron-attracting

Table II. Microdetermination of Pyrrole Derivatives Using Bromine Monochloride in Acetic Acid Medium

Sample	Sample taken (mg)	Recovery (mg)			Mean (mg)	Error (% recovery)
Indole	2.070	2.093	2.087	2.090	2.090	+0.97
	4.140	4.130	4.110	4.120	4.120	−0.48
	6.210	6.200	6.170	6.200	6.190	−0.32
	8.280	8.290	8.270	8.190	8.250	−0.36
Carbazole	2.120	2.110	2.180	2.130	2.140	+0.94
	4.240	4.280	4.260	4.180	4.240	0.00
	6.360	6.420	6.460	6.320	6.400	+0.62
	8.480	8.480	8.420	8.510	8.470	+0.11
Isatin	2.058	2.072	2.084	2.090	2.082	+1.06
	4.116	4.090	4.096	4.096	4.094	−0.53
	6.174	6.178	6.172	6.178	6.176	−0.03
	8.232	8.190	8.192	8.185	8.189	−0.52
Indole-3-acetic acid	2.018	2.006	2.000	2.000	2.002	−0.79
	4.036	4.042	4.048	4.045	4.045	+0.22
	6.054	6.048	6.046	6.047	6.047	−0.11
	8.072	7.980	7.962	7.956	7.966	−0.07
Indole-3-propionic acid	1.406	1.398	1.394	1.396	1.396	−0.71
	2.813	2.790	2.798	2.788	2.792	−0.74
	5.627	5.634	5.622	5.634	5.630	+0.05
	8.440	8.380	8.382	8.369	8.377	−0.77
Indole-3-butyric acid	2.086	2.082	2.078	2.047	2.069	−0.81
	4.172	4.180	4.200	4.211	4.197	+0.59
	6.258	6.260	6.250	6.252	6.254	+0.06
	8.344	8.290	8.260	8.287	8.279	−0.78

carbonyl groups in isatin make N-H bond sufficiently polar. A similar elecron attracting role is also played by two benzene rings in carbazole making the N-H bond polar and thus facilitating the substitution at nitrogen atom.

Results of Analysis

The proposed method has been applied for the determination of indole and its derivatives and the results are presented in Table II. The results show the maximum error of 1.06% as the average percentage recovery. Acetic acid has already been used[11,12] as a solvent in the various reactions of bromine monochloride. Variation of acetic acid concentration has been studied and it has been found that the recoveries of the samples were unaffected. However, when the reaction was carried out in a large excess of acetic acid (10—15 ml), the accurate detection of end point was difficult.

The reaction of bromine monochloride with pyrrole derivatives is not instantaneous and bromine monochloride consumption was almost negligible when the titration was carried out immediately after the addition of bromine monochloride. It was found that 8 minutes were required for completion of the reaction in case of indole, while in case of other compounds studied only 5 minutes were required. For the determination usually 0.1 N bromine monochloride has been used, but the rate of the reaction was independent of the concentration of bromine monochloride.

It has been found that the compounds such as nitrobenzene, *m*-dinitrobenzene, glycerol, aliphatic aldehyde do not react with bromine monochloride and do not interfere with the reaction while presence of compounds such as amines, hydrazines, hydrazones which react with bromine monochloride interfere with the reaction.

Acknowledgement The authors wish to express their thanks to Professor R.D. Tewari for his interest in the investigation and supply of materials.

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