

Quantitative Analysis of Indole Compounds Via Electron-Acceptor Complexes

A. QAZI NAWAB MANZAR*

Faculty of Chemistry, Moscow State University, Moscow, U.S.S.R.

(Received 5th November, 1980)

Summary: The formation of electron-donor acceptor complexes of some carbethoxy derivatives of indoles with a strong electron acceptor 2,6-dichloroquinone-4-chlorimide has been investigated quantitatively by photometric method. This is rather a simple, less time consuming and accurate technique for routine analysis of the samples.

Introduction

The indole compounds act as a good electron donor in charge transfer complexes (1, 2, 3). Intense colour produced in several reactions of indole compounds (4, 5) are usually associated with the charge transfer complexing particularly in the solid state and this property has been used as a detection method for indoles in paper and thin layer chromatography (6, 7). The information about the identification of complexes has come from many different experimental methods like ultraviolet and visible spectrophotometry (8, 9). The charge transfer complexes have not been used in quantitative determination of indoles by spectrophotometric method, while 2,6-dichloroquinone-4-chlorimide can be used as complexing agent for indole drug estimation (10). In this investigation, quantitative estimations, their characterisation by H_{NMR} studies have been carried out on a series of complex between 2,6-dichloroquinone-4-chlorimide and various methyl and methoxy substituted derivatives of 3-carbethoxy indole.

Results and Discussion

A new photometric method was developed for the quantitative analysis of 3-carbethoxy indole compounds having CH_3 and CH_3O - group attached in benzene ring or in pyrrole ring. Results show that the method is suitable for all indole compounds which form stable coloured complexes with a good acceptor like 2,6-dichloroquinone-4-chlorimide. Indole compounds and 2,6-dichloroquinone-4-chlorimide were taken in the ratio of 1:1 either in isopropyl alcohol or ethyl alcohol. Charge

transfer complexes are formed in various colour as shown in table 1.

Results of table-1 indicate that the solution of coloured complexes of indole compounds with 2,4-dichloroquinone-4-chlorimide are stable. The stability of the coloured solution lasts for 20 minutes. Thus all colours are ascribed to charge transfer transitions (11) between the acceptor and donor compounds. The absorption spectra of 1,2-dimethyl-3-carbethoxyindole complex with 2,6-dichloroquinone-4-chlorimide was found between the wavelength from 460-490 nm (Fig. 1). In case of 1,2-dimethyl-3-carbethoxy-5-oxyindole and 1,2-dimethyl-3-carbethoxy-5-methoxyindole, where the CH_3 - group was changed into OH- group and CH_3O -group, the absorption spectra were marked increased and a bathchromic shift occurred from 490-560 nm (Fig. 2).

There is no marked change in absorption spectra in 1,2,6-trimethyl-3-carbethoxy-5-methoxyindole (Fig. 2). Thus complexes are characterized by an intense absorption spectra in the visible region. The intense absorption in the visible or UV region of the spectrum is in fact the most prominent feature of 1:1 molar ratio complexes (12). A satisfactory explanation of this properties is given by Mulliken's Charge Transfer theory (13). The decay of the absorption spectra at 550m μ , is characteristic of the charge transfer complex (14). Complex composition of indole compounds with 2,6-dichloroquinone-4-chlorimide was determined by isomolecular series method and was found in the ratio 1:1. For this purpose 1,2-dimethyl-3-carbethoxy-5-oxyindole was taken as an

*Present address: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Karachi, Karachi, Pakistan.

TABLE I.

Characteristics of Coloured Indole Complexes with 2,6-dichloroquinone-4-chlorimide.

Compound	Colour	Appearance of colour (minutes)	Stability of colour (minutes)	ϵ
1,2-dimethyl-3-carbethoxyindole.	Orange	At once	120	47
1,2,5-trimethyl-3-carbethoxyindole.	Pink	At once	30	76
1,2,7-trimethyl-3-carbethoxyindole.	Orange	At once	20	44
1,2-dimethyl-3-carbethoxy-5-oxyindole.	Reddish - Pink	At once	20	55
1,2-dimethyl-3-carbethoxy-5-methoxyindole.	Light - Pink	At once	from 5-25	50
1,2,6-trimethyl-3-carbethoxy-5-methoxyindole.	Violet	At once	from 5-60	125

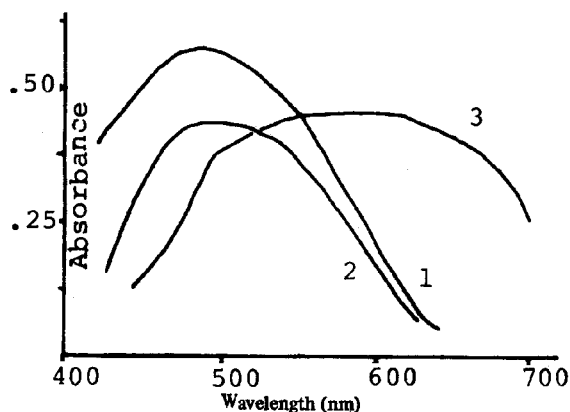


Fig. 1. 1. 1,2-dimethyl-3-carbethoxyindole.
 2. 1,2,5-trimethyl-3-carbethoxyindole.
 3. 1,2,7-trimethyl-3-carbethoxyindole.
 Determination of λ_{\max} of various indoles compounds used in present investigation.

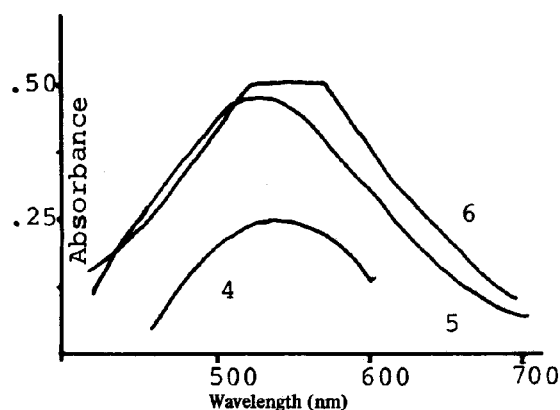


Fig. 2. 1,2-dimethyl-3-carbethoxy-5-methoxyindole.
 1,2-dimethyl-3-carbethoxy-5-oxyindole.
 1,2,6-trimethyl-3-carbethoxy-5-methoxy.
 Determination of λ_{\max} of various indoles compounds used in present investigation.

example to show 1:1 ratio (Fig. 3) of the complex solution. The ratio 1:1 is generally suitable for quantitative analysis. This ratio, for the first time, allowed a complete quantitation of indole compounds with 2,6-dichloroquinone-4-chlorimide in the form of charge transfer complex (CTC).

1,2-dimethyl-3-carbethoxyindole was studied in H_{NMR} spectra-1,2-dimethyl-3-carbethoxyindole and 2,6-dichloroquinone-4-chlorimide were taken in carbon tetra chloride (CCl_4) solution and the replacement of the signal leads to a characteristic feature of charge transfer complex. CH_3 -group signal of indole nucleus

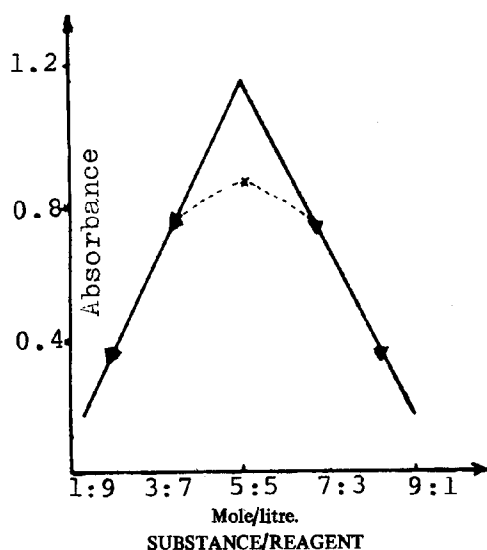


Fig. 3. Determination of complex composition of 1,2-dimethyl-3-carbethoxy-5-oxyindole with 2,6-dichloroquinone-4-chlorimide by isomolecular series method.

(characteristic cation radical in CTC) replaced in the region of 0.1-0.2 mg. Spectra of the aromatic part of the molecule remain unchanged. In charge transfer complex, the pyrrole nucleus is active due to the high electron density (2, 15, 16). Accordingly, signals of aromatic protons and dichloroquinone chlorimide moved in the region of weak field (initial substance-7.40 and 7.83mg, complex -7.00 and 7.43mg) (Fig. 4). The ratio 1:1 is generally suitable for quantitative analysis. This ratio, for the first time, allowed a complete quantitation of indole compounds with 2,6-dichloroquinone-4-chlorimide in the form of charge transfer complex (CTC).

Using the Beer-Lambert's law the concentration of each indole complex solution with the reagent, 2,6-dichloroquinone-4-chlorimide in a cuvette of 2cm under the following wavelength has been calculated 1,2-dimethyl-3-carbethoxyindole=440nm; 1,2,5-trimethyl-3-carbethoxy-indole=490nm; 1,2,7-trimethyl-3-carbethoxyindole=490nm; 1,2-dimethyl-3-carbethoxy-5-oxyindole=490nm; 1,2-dimethyl-3-carbethoxy-5-methoxyindole=490nm; 1, 2, 6-trimethyl-3-carbethoyl-5-methoxy-indole=540nm.

At the time of analysis each indole compound was characterised by m.p. and TLC. Results of the analysis of each substance are given in the table-II.

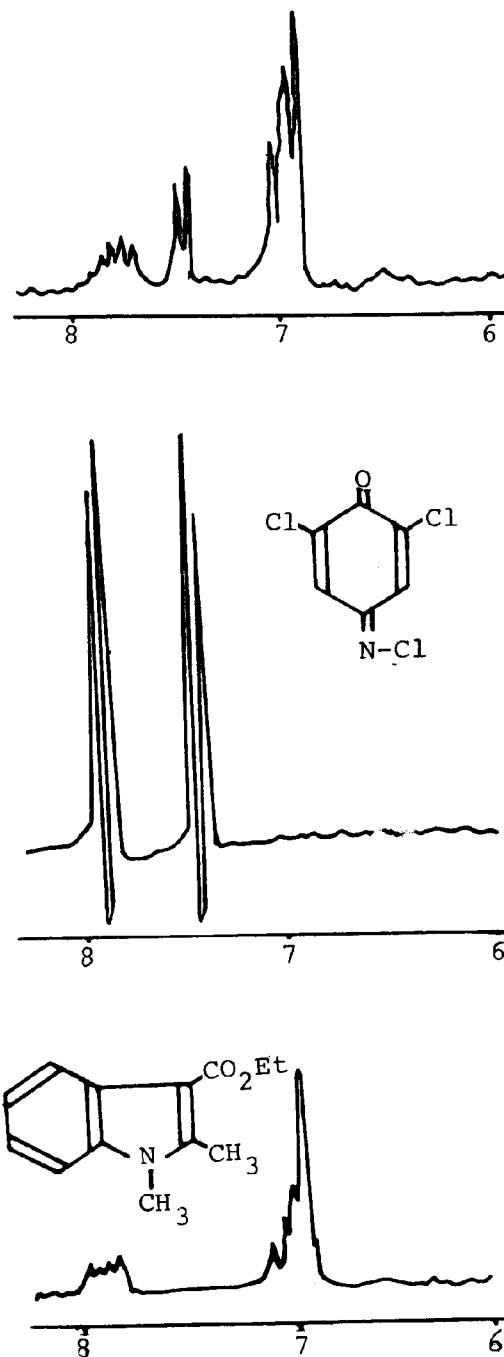


Fig. 4. $^1\text{H-NMR}$ Spectra (Aromatic region) of 1,2-dimethyl-3-carbethoxyindole, 2,6-dichloroquinone-4-chlorimide and their complex in CCl_4 .

TABLE II.

Determination of indole compounds with 2,6-dichloroquinone-4-chlorimide.

Indole Compound	Given $10^{-4}M$	Observed* $10^{-4}M$	S**	S _r ***
1,2-dimethyl-3-carbethoxyindole.	6.00	6.28	0.178	0.0280
1,2,5-trimethyl-3-carbethoxyindole.	2.50	2.51	0.075	0.0301
1,2,7-trimethyl-3-carbethoxyindole.	4.00	4.10	0.070	0.0170
1,2-dimethyl-3-carbethoxy-5-oxyindole.	3.43	3.38	0.044	0.0190
1,2-dimethyl-3-carbethoxy-5-methoxyindole.	4.00	4.06	0.098	0.0242
1,2,6-trimethyl-3-carbethoxy-5-methoxyindole.	1.20	1.22	0.050	0.0411

* = Mean value of six readings ** = S = Standard deviation

*** = S_r = Relative standard deviation.

Statistical values clearly show that the result of the analysis of indole compounds with 2,6-dichloroquinone-4-chlorimide in the form of charge transfer complex are quite satisfactory. The proposed method of analysis may be recommended for the quantitative determination of indole compounds which form charge transfer complexes with a good acceptor like 2,6-dichloroquinone-4-chlorimide.

Experimental

The following pure samples have been used in this investigation 2,4-dichloroquinone-4-chlorimide, 1,2-dimethyl-3-carbethoxyindole, 1,2,5-trimethyl-3-carbethoxyindole, 1,2,7-trimethyl-3-carbethoxyindole, 1,2-dimethyl-3-carbethoxy-5-oxyindole, 1,2-dimethyl-3-carbethoxy-5-methoxyindole, 1,2,6-trimethyl-3-carbethoxy-5-methoxyindole. The condition for the formation of coloured charge transfer complexes is shown in table III.

Solution of individual indole compound were made by weighing (x) mg of the compound in 50 ml. Volumetric flask. Six samples of 1,2,3,4,5,6 ml are drawn from the flask and placed in 10 ml capacity volumetric flask. To each flask 4.00 ml freshly prepared reagent solution is dropped in. After keeping the solution for a minute at room temperature and brought to 10 ml volume by

adding isopropyl or ethylalcohol. The optical densities of the above solutions are recorded on FEK-56-2 photoelectric colourimeter.

Using filter No.	4 ($\lambda = 440$ nm)
filter No.	5 ($\lambda = 490$ nm)
filter No.	6 ($\lambda = 540$ nm)

in a cuvette of 2cm. Reagent solution is used as a reference. Calibration curves are made and each indole complex solution concentration is determined. Absorbance spectra of each coloured complex solution is recorded on spectrophotometer CF-10 and molar extinction coefficient (ϵ) is determined as follows:

$$\epsilon = \frac{A}{Cl}$$

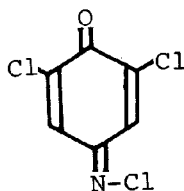
where A = Optical density
C = Concentration of the solution, mole/lit
l = Cuvette layer thickness in cm.

Method of Job (17) and its modification by Vosburoch and Cooper (18) was used to determine the complex composition of indole compounds with the reagent 2,6-dichloroquinone-4-chlorimide. The result of 1,2-dimethyl-3-carbethoxy-5-oxyindole is given in the table-IV.

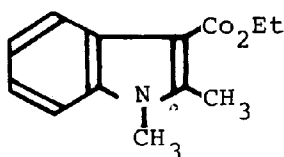
TABLE III.

Condition for the formation of indole complexes with 2,6-dichloroquinone-4-chlorimide.

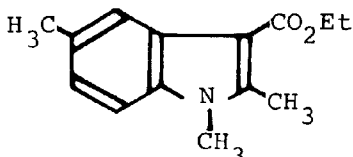
Indole Compound	Wt. of the substance (x) mg	Access of reagent M	Concentration of the substance $10^{-3}M/l$
1,2-dimethyl-3-carbethoxyindole.	217.00	2	2.00
1,2,5-trimethyl-3-carbethoxyindole.	115.50	7	1.00
1,2,7-trimethyl-3-carbethoxyindole.	115.50	3	1.00
1,2-dimethyl-3-carbethoxyl-5-oxyindole.	100.00	6	0.86
1,2-dimethyl-3-carbethoxy-5-methoxyindole.	123.50	13	1.00
1,2,6-trimethyl-3-carbethoxy-5-methoxyindole.	052.20	12	0.40



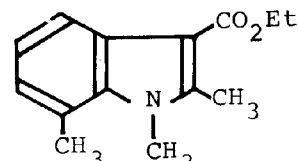
2,6-dichloroquinone-4-chlorimide.



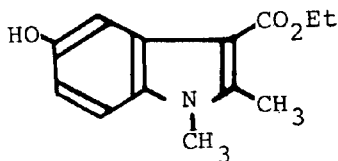
1,2-dimethyl-3-carbethoxyindole.



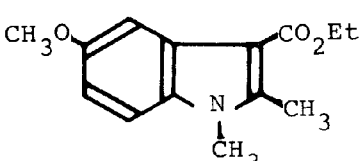
1,2,5-trimethyl-3-carbethoxyindole.



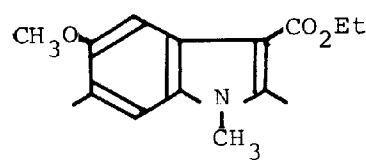
1,2,7-trimethyl-3-carbethoxyindole.



1,2-dimethyl-3-carbethoxy-5-oxyindole.



1,2-dimethyl-3-carbethoxy-5-methoxyindole.



1,2,6-trimethyl-3-carbethoxy-5-methoxyindole.

TABLE IV.

Determination of complex composition of 1,2-dimethyl-3-carbethoxy-5-oxyindole by isomolecular series method.

Molecular ratio substance/reagent.	1:9	3:7	5:5	7:3	9:1
Optical density	0.36	0.76	0.78	0.75	0.41
$\lambda_{\max} = 490 \text{ nm.}$					

Acknowledgement

I would like to thank my Director of Research A.N. Kost and Co-Director S.I. Obtemperanskya for guidance and supervision of the work.

References

- O. Hutzinger, *J. Chromatogr.*, **40**, 117 (1969).
- P. Millie, J.P. Malrien, J. Benaim, J. Y. Lallemond and M. Jullia, *J. Med. Chem.*, **11**, 207 (1968).
- O. Hutzinger, W.D. Jamieson, J.D. MacNeil, and R.W. Frei, *Anal. Chem.*, **54**, 1100 (1971).
- K. David, *Analyt. Biochem.*, **8**, 75 (1964).
- A. Anthony and H.E. Street, *New Phytologist*, **69**, 47 (1970).
- R.A. Heacock, and O. Hutzinger, *Canad. J. Chem.*, **42**, 514 (1964).
- O. Hutzinger, R.A. Heacock, J.D. MacNeil and R.W. Frei, *J. Chromatogr.*, **68**, 173 (1972).
- G. Briegleb, "Electronen-Donator-Acceptor Komplex". Springer, Berlin, 1961.
- L.J. Andrews and R.M. Keefer, *Molecular Complexes in Organic Chemistry*, Holden-Day Inc. San Francisco, 1964.
- A. Qazi Nawab Manzar and A.N. Kost, *Die Pharmazie*, Berlin, Under Press (1980).
- P.R. Hammond and L.A. Burkardt, *J. Phys. Chem.*, **74**, 639 (1970).
- David Both, *Science Progress*, **48**, 435 (1960).
- R.S. Mulliken, *J. Am. Chem. Soc.*, **72**, 600 (1950); **74**, 84 (1952) *ibid.*, *J. Phys. Chem.*, **59**, 801 (1952).
- R. Foster and P. Hanson, *Tetrahedron*, **21**, 255 (1965).
- B. Sabourault, and Bourdais, *Comptes Rendus Acad. Sci.*, **274**, 813 (1972).
- R. Foster and C.A. Fyfe, *J. Chem. Soc. (B)*, 1966, 926.
- P. Job, *Analyt. Chem.*, **9**, 113 (1928).
- W.G. Vosburoch and G.R. Cooper, *J. Amer. Chem. Soc.*, **63**, 437 (1941).