C H A P T E R - I

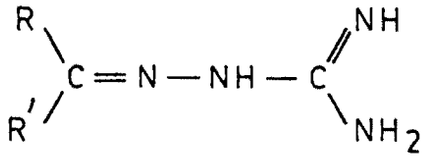
SYNTHESIS AND CHARACTERISATION OF SALICYLALDEHYDE GUANYLHYDRAZONE

1.1 INTRODUCTION

Metal complexes of schiff bases have occupied a central role in the development of coordination chemistry. This situation is manifested by the number of publications of synthetic and modern physicochemical studies of these metal complexes. A tremendous variety of stable chemical species have been synthesized containing both transition and non-transition metals and various ligand systems. Many of these complexes are of only incidental importance in modern coordination chemistry. However, a significant number of groups of complexes, defined by the basic structure of their ligand systems, have assumed significance in this field. According to this, we have reported the physicochemical studies of the complexes of transition metals with salicylaldehyde and aminoguanidine.

As analytical reagents, Schiff's bases have more importance in analytical chemistry. Thiosemicarbazones, hydrazones and oximes have been most widely studied, but guanylhydrazones have not previously been studied as analytical reagents. As chelating ligands, guanylhydrazones react and form complexes with transition metal ions. Aldehydes and ketones give easily crystallizable guanylhydrazone derivatives and this property is used for identification of

the compounds with C = O function. Guanylhydrazones were first synthesized by Thiele and Dralle.[1] Their general structure is

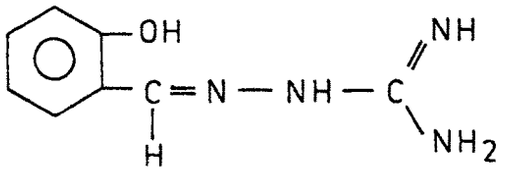


where R and R' are H or any organic radical. The analytical properties of the guanylhydrazone depend on the structural features of both R and R'.

Guanylhydrazones have a structure similar to thiosemicarbazones. The great affinity to sulphur for coordination of metal ions poses a serious hindrance in the use of thiosemicarbazones as analytical reagents, since it makes selective methods difficult to establish. The replacement of the sulphur atom of the thiosemicarbazones by the imine group of the guanylhydrazones can increase the selectivity.

The reactivity of Schiff's bases is also dependent on the structural characteristics of the aldehyde or ketone which is condensed with the amine. Salicylaldehyde has been used extensively.

The structure of salicylalehyde guanylhydrazone (SAG) is



The number of compounds were prepared with guanylhydrazones and are useful as bactericides and insecticides,[2-4] in treating heart insufficiency and hypersensitivity,[5] in normal leukemia bearing mice as growth inhibitors. Some of these compounds have extremely high bacterial activity and are suitable as internal, external and oral disinfectants[6] and are used as antiseptics for foods.[7]

Guanylhydrazone compounds are cardioactive substances[8,9] and also used as new pharmaceuticals.[10]

Several steroid guanylhydrazones were prepared[11,12] Inhibitory effect of these compounds are shown on invitro growth of some dermatophytes. They are also useful in waste water purification, precipitation of organic anions especially dyes from waste water.

Several guanylhydrazone complexes have antifungal activity[13] and act as anticancer and antiinflammatory agents.[14] Some compounds possess antileukemic activity, antihistamine activity,[15] antiviral activity[16] and also antimalarial activity.

Some aminoguanidine derivatives are used in photographic materials and for paper treatment,[17] useful as cationic agents for retention of dyes and pigments on cellulose fibres and provides dry and wet strength in paper.

These studies have been useful in the chemistry of complexes of guanylhydrazones. Most of the chemical research is directed towards the structure and bonding in metal complexes in solid state. A very few work is done about the physicochemical properties of metal complexes in solutions and almost nothing is known of the reactions of the ligands and complexes. Therefore, the present authors have chosen this topic.

Salicylaldehyde guanylhydrazone (SAG) can be used for the determination of cobalt, manganese, nickel and iron. The reagent is useful for the determination of single elements.

1.2 EXPERIMENTAL

1.2.1 Apparatus :

The absorbance measurements were done on a spectronic-20-Bausch and Lomb equipped with matched pair of glass test-tubes.

For pH measurements, Digital pH meter ELICO, Model L1-120 having glass-calomel combination electrode was used. The pH meter was standardized by using 0.05 M potassium hydrogen phthalate (pH = 4.01) and 0.01 M borax (pH = 9.18) buffers.

All the measurements were done at room temperature $\sim$ 25 to 30°C.

1.2.2 Reagents :

All solvents and reagents were of analytical reagent grade.

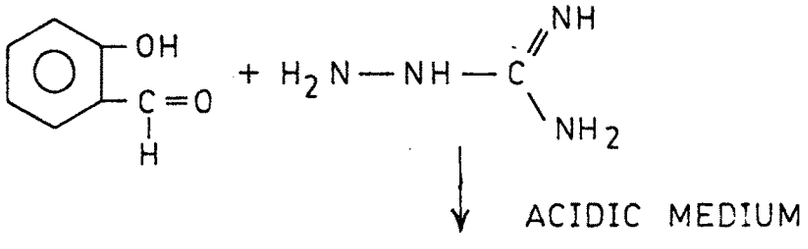
Glass distilled conductivity water was used throughout the work.

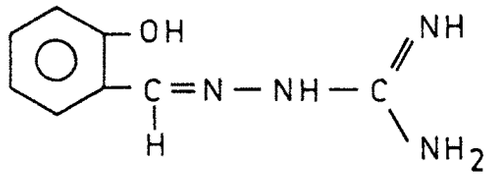
1.2.3 Synthesis of SAG :

For the synthesis of salicylaldehyde guanylhydrazone (SAG), aminoguanidine bicarbonate was used instead of aminoguanidine dihydrochloride, which simplified the synthesis and gave much better yield.

2.0 g of aminoguanidine bicarbonate was completely dissolved in concentrated nitric acid (till evolution of carbon dioxide was completely stopped). 1.793 g (1.54 ml) salicylaldehyde was diluted with 10.0 ml ethanol and the two solutions were mixed together. The mixture was kept as such for about 1/2 hour. The white coloured product was formed which was filtered and crystallised from ethanol to give shining white crystals of salicylaldehyde guanylhydrazone (~1.8 g). M.P. = 209-210°C. The compound is quite stable for months.

The reaction is





1.2.4 Solubility :

The reagent is soluble in water, ethanol, methanol and acetone but insoluble in chloroform, carbon tetrachloride and benzene.

The solution of the reagent in water was stable for months without any deterioration.

1.2.5 Characterisation of SAG :

SAG is stable in air. There is no action of light on the reagent. So, no special care is required to protect it from light.

The microelemental analysis of the chromatographically purified reagent confirmed the formula to be $C_8H_{10}N_4O$. Calculated percentage of elements are C = 53.94 %, H = 5.61 %, N = 31.47 % and O = 8.98 %. Experimentally found percentage of elements are C = 53.69 %, H = 5.87 %, N = 30.96 % and O = 9.48 %.

1.2.6 Absorption spectra of the reagent (SAG) :

Figure 1.1 shows the absorption spectra of the reagent (SAG) in water (1.0×10^{-4}M) at different pH values.

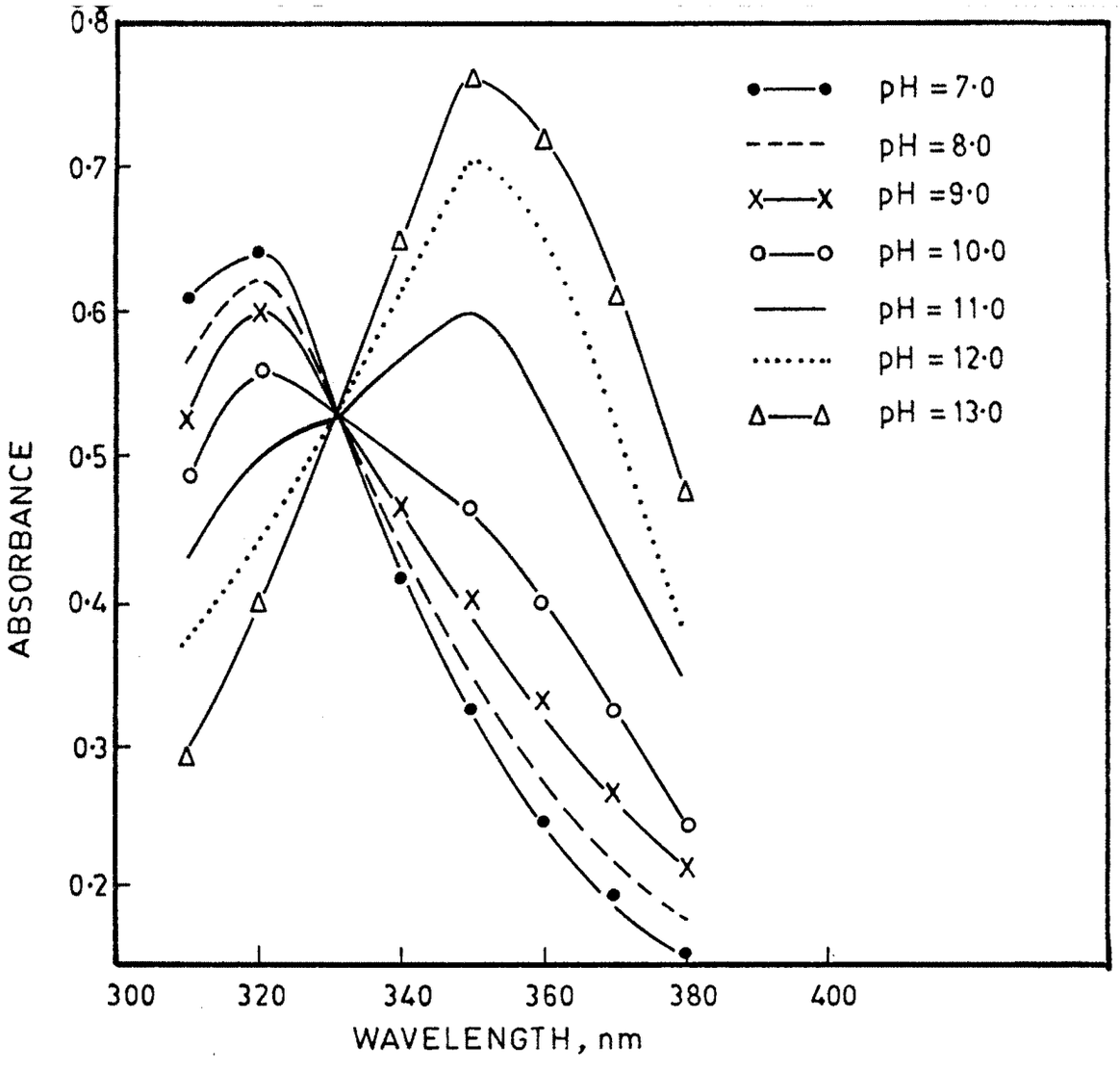


FIG. 1·1 ABSORPTION SPECTRA OF REAGENT (SAG).

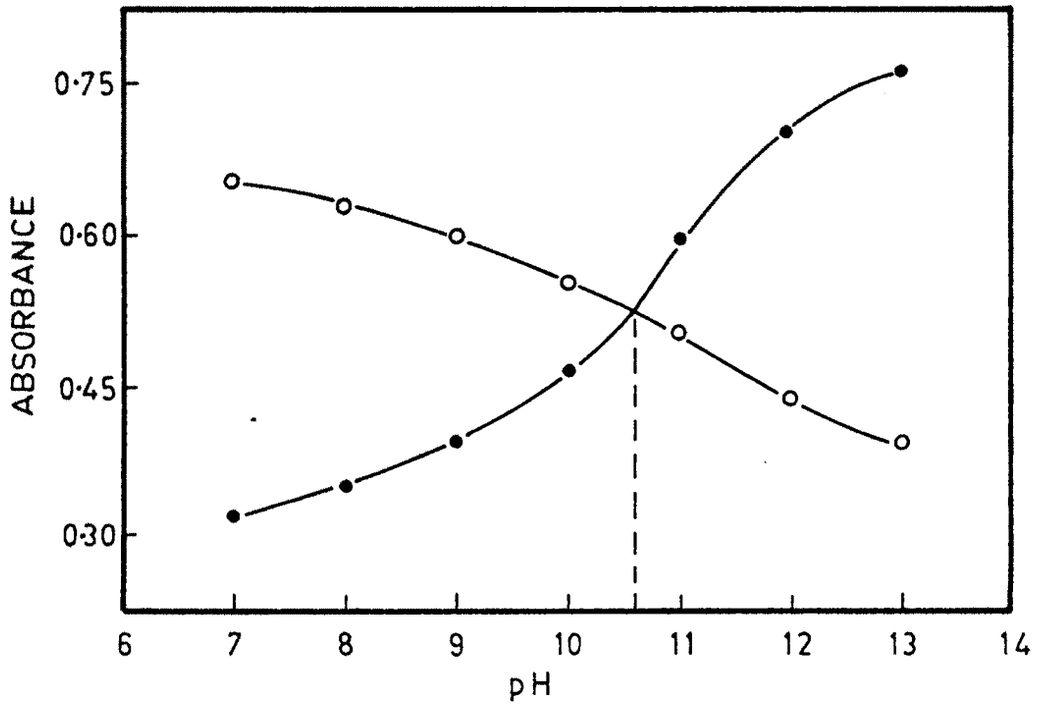


FIG. 1·2 DETERMINATION OF pK

o——o 320 nm, ●——● 350 nm

Absorption maxima and molar extinction coefficients of the reagent at different pH values are given in table 1.1.

Table 1.1 : Spectral characteristics of the reagent (SAG)

pH	Absorbances at λ		Molar extinction coefficients, ε l mole^{-1} cm^{-1} at λ	
	320 nm	350 nm	320 nm	350 nm
7.0	0.64	0.32	0.64×10^4	0.32×10^4
8.0	0.62	0.35	0.62×10^4	0.35×10^4
9.0	0.60	0.40	0.60×10^4	0.40×10^4
10.0	0.56	0.46	0.56×10^4	0.46×10^4
11.0	0.50	0.60	0.50×10^4	0.60×10^4
12.0	0.44	0.70	0.44×10^4	0.70×10^4
13.0	0.40	0.76	0.40×10^4	0.76×10^4

1.2.7 Infrared spectrum of the reagent (SAG) :

Infrared absorption spectrum in the range 4000 to 200 cm^{-1} was run on Perkin Elmer 221 IR spectrophotometer in KBr (Fig.1.3). The characteristic absorption bands were observed as follows :

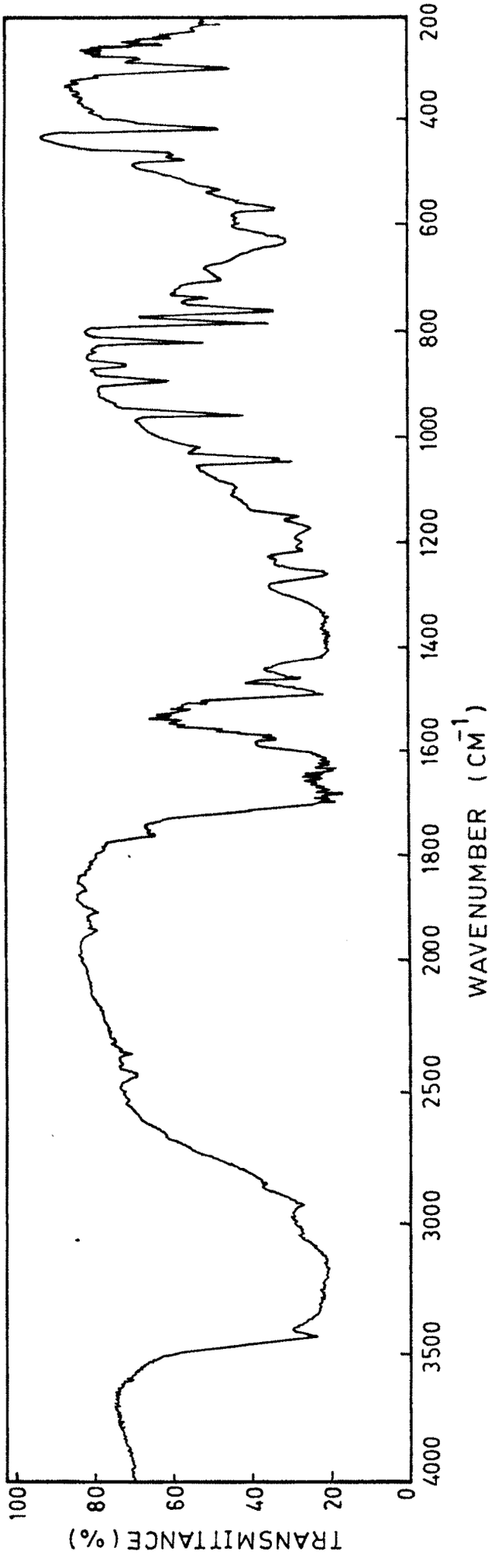


FIG. 1·3 INFRARED SPECTRUM OF REAGENT (SAG).

3400 cm^{-1} ⟶	NH stretch
3200 cm^{-1}(broad) ⟶	OH-N internally bonded
3200-3100 cm^{-1}(broad) ⟶	NH_2 stretching
2920 cm^{-1} ⟶	= N-vibrations
1680-1600 cm^{-1} ⟶	NH_2 deformation, complicated pattern
1670-1500 cm^{-1} ⟶	N_2C= N absorption due to guanidines and due to NH deformation and CN stretching vibrations.
1490, 1460 cm^{-1} ⟶	Aromatic band-phenyl ring
1145, 1045, 780 cm^{-1} ⟶	Ortho substitution patterns
760, 735, 725 cm^{-1} ⟶	4 adjacent H wag.

1.2.8 Determination of ionization constant of SAG :

The ionization constant of the reagent (SAG) was obtained both by spectrophotometric method and by pH-metric method.

a) By Spectrophotometric Method :

The absorption spectra of the reagent are shown in fig. 1.1. At pH 7.0, the reagent shows the absorption band with λmax at 320 nm, which lowers in intensity as pH increases.

With increasing value of pH, the absorbance at longer wavelength increases, and at pH 13.0, highest intensity band with λmax at 350 nm appears. All the spectral curves pass through the isosbestic point at 331 nm, thereby indicating a dynamic equilibrium between ligand and its deprotonated species, assuming that at pH 7.0, the molecular form of the ligand is exclusively present and the deprotonated species is absent and that at pH 13.0, the deprotonated species is present exclusively and the molecular form is absent. By using Henderson equation and also from the half height[18] of the sigmoid curve (Fig.1.2), the pK value for the deprotonation of the ligand is found to be 10.7.

b) By pH-metric Method :

5.0 ml of 0.01 M SAG was taken in a thermostated titration vessel at 30 ± 1°C containing 20.0 ml distilled water. The solution was titrated with 0.1 M NaOH. An ELICO Digital pH meter with pH readable to ± 0.01 was used. The pH meter was calibrated with pH 4.01 and 9.18 by phthalate and borax buffers respectively. The ionization constants were calculated from the pH values. The pK was determined by using the formula

$$pK = pH + \log \frac{[HA]}{[A^-]}$$

HA represents the reagent, SAG. The log $[H^+]$ values were read from the pH-meter.

The titration was repeated until two sets of values differing within ± 0.01 pH units were obtained. The results of study are summarised in table 1.2 which show that the pK is 10.704 for salicylaldehyde guanylhydrazone (SAG).

Table 1.2 : Determination of ionization constant of SAG at 30 ± 1°C.
[SAG] = 0.01 M; NaOH = 0.1 M.

NaOH ml	pH	Stoichiometric concentration		$\log \frac{[HA]}{[A^-]}$	pK
		HA	A^-		
0.5	9.07	0.018	0.002	0.954	10.024
1.0	10.06	0.016	0.004	0.602	10.662
1.5	10.58	0.014	0.006	0.367	10.947
2.0	10.82	0.012	0.008	0.176	10.996
2.5	10.99	0.010	0.010	0.000	10.990
3.0	11.09	0.008	0.012	-0.176	10.914
3.5	11.17	0.006	0.014	-0.367	10.803
4.0	11.25	0.004	0.016	-0.602	10.648
4.5	11.31	0.002	0.018	-0.954	10.356
				Mean pK =	10.704

1.2.9 Complex formation :

The reagent (SAG) forms complexes with Co(II), Mn(II), Ni(II) and Fe(II). A detailed account of the complex formation with these four metals is discussed in the following chapters.

1.3 REFERENCES

1. Thiele, J. and Dralle, E., Annalen, 302, 278 (1898).

2. Farbenfabriken Bayer Akt. Ges. (by Fritz Mietzsch) Ger. 958, 832, Feb. 28, 1957.

3. Farbenfabriken Bayer Akt. Ges. (Siegfried Peterson and Gerhard Domagk, inventors) Ger. 963, 513, May 9, 1957 (Cl 120, 25).

4 Farbenfabriken Bayer Akt. Ges. (Siegfried Peterson and Gerhard Domagk, inventors) Ger. 942, 627, May 3, 1956 (Cl 120, 22).

5 Adrian Marxer (CIBA Ltd.) Ger-offen. 1914, 999 (Cl.C 07c A 61 k) 06 Nov. 1969 Swiss Appl. 04 April 1968 - 21 Feb, 1969, 50 pp.

6 Farbenfabriken Bayer A.G., Brit. 768, 089 Feb. 13, 1957.

7 Fujikawa, F., Tokuoka, A., Takimura, M. and Miura, K. (Kyoto Coll. Pharm.) J. Pharm. Sec. Japan, 72, 518 (1952) c.f. CA 46 1714c X.

8 Farbenfabriken Bayer A.G. Brit. 1, -036, 987 (Cl. G 07c, d) July 20, 1966. Ger. Appl. April 30, 1964 3 pp.

9 Farbenfabriken Bayer A.G. Brit., 1, -024, 490 (Cl. C 07c) March 30, 1966, Ger. Appl. April 10, 1963 3 pp.

10. Farbenfabriken Bayer A.G. Brit., 1, 042, 857 (Cl.C 07c), Sept. 14, 1966. Ger. Appl. Jan. 29, 1964, 3 pp.

11. Farbenfabriken Bayer A.G. Brit., 1, 018, 803 (Cl.C 07c), Feb. 2, 1966, Ger. Appl. Jan. 23, 1963, 4 pp.

12. Farbenfabriken Bayer A.G. Brit., 1, 005, 650 (Cl.C 07c), Sept. 22, 1965, Ger. Appl. Jan. 23, 1963, 4 pp.

13. Tamio, N., Harashige, T., Yasuo, S., Masao, K., Harumi, F., Yuzo,K., Ysuharu,S. (Sch. Hyg. Sci. Kitasato Univ. Sagamihara, Japan), Bokin Bobi 9(4), 173 (1981).

14. Ikuo,M., Kanji,N. (Banju Pharmaceutical Co. Ltd.) Japan 68, 12, 356. (Cl.16E 431) 24 May 1968, Appl. 03 Dec. 1965, 3 pp.

15. Hans,K., Lothar,H., Ines,W., Karl,K. and Angela,H. (Akademie der Wissenschaften der DDR, Institut Fuer Werkstofferschmy) Ger. (East) 139, 259 (Cl.C 07 D 215/12) 19 Dec. 1979. Appl. 208, 532, 19 Oct. 1978, 10 pp.

16. Garuti,L., Ferranti,A., Giovanninetti,G., Baserga,M., Palenzona Mannini,A. (Ist. Chim. Farm. Tossicol. Univ. Bologna. Italy) Farmaco. Ed. Sci. 36(6), 393 (1981).

17. Charles, L.M. (to United States Dept. of Agriculture) U.S. 3, 230, 213 (Cl. 260-233-3) Jan,18,1966, Appl. July 19, 1962, 2 pp.

18. Stenstrom,W. and Goldsmith,N., J. Phys. Chem., 30, 1683 (1926,.