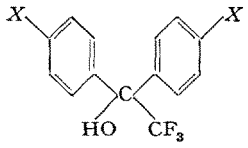
Summary

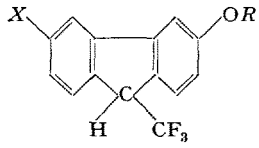
Several compounds belonging to the group of *para*-substituted N-arylglycines have been found to exhibit pronounced tuberculostatic activity *in vitro*, but are too toxic for practical application. The relationship between chemical structure and activity is similar to that observed in the group of thiocarbanilides.

A Cycloisomerization Reaction of Di-(*p*-halogenophenyl)-trifluoromethyl-carbinols

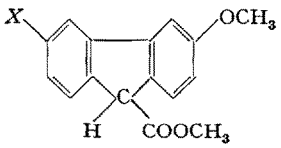
Di-(*p*-halogenophenyl)-trifluoromethyl-carbinols (I, X = halogen)[1] dissolve in concentrated sulphuric acid with an intensely purple colour (λ_{max} = 570–580 mμ) which changes rapidly to orange (λ_{max} = 495 mμ); this change is accompanied by formation of the corresponding hydrohalogenic acid, HX. When the orange solution is poured into water, III (X = halogen, R = H; m.p. 192–193°) is formed. When methyl alcohol is employed instead of water, the methyl ether II is obtained. In a similar cyclodehydration reaction benzilic acid is converted by aluminium chloride into fluorene-9-carboxylic acid[2].



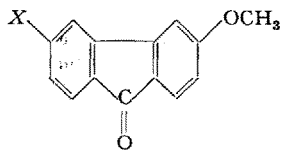
I



II $R = CH_3$
III $R = H$

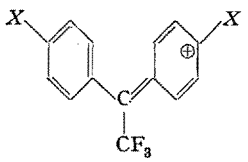


IV

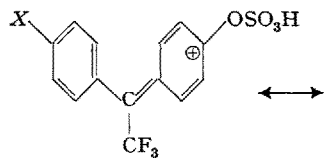


V

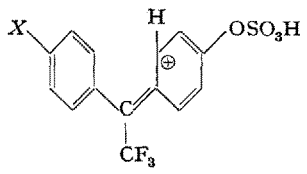
The structure of II was proven as follows: the trifluoromethyl group is converted easily by methanolic alkali to a carbomethoxy group (IV; m.p.129–130°). Oxidation of IV with alkaline hydrogen peroxide gave a yellow ketone $C_{14}H_9ClO_2$ (m.p. 181–182°), which was shown to be 3-methoxy-6-chlorofluorenone (V) by an unambiguous synthesis, starting from 4-chloro-anthranilic acid and anisole.



VI



VII



VIII

The following mechanism for the formation of II from I (X = Cl) appears reasonable. In the carbonium ion VI which is formed when I is dissolved in concentrated sulphuric acid, one of the halogen atoms is non-aromatic and reacts with the acid to VII⟷VIII. This is cyclized with elimination of a proton; the product reacts with methanol or water to give II or III, respectively.

S. COHEN and A. KALUSZYNER

Research Laboratories, Medical Corps, Israel Defence Forces, January 22, 1957.

Résumé

Une solution de di-(*p*-chlorophényl)-trifluorométhyl-carbinol dans l'acide sulfurique concentré, diluée à l'eau ou au méthanol, donne naissance à du chloro-3-hydroxy-(ou méthoxy-)-6-trifluorométhyl-9 fluorène. Le composé méthoxylé, après l'alcoolyse alcaline du groupement $-CF_3$, a été dégradé au fluorénone correspondant, dont la synthèse a été realisée indépendamment.

Quantitative Determination of Bone Minerals from Roentgenograms

Densitometric measurements of radiograms have been much used to estimate the mineral content of bones[1] However, the apparatus required is expensive and complicated and the technique is tedious. Moreover, because the materials which absorb roentgen rays are not randomly distributed, subjective judgement plays an important role in the selection of the areas to be measured. Besides the danger of subjective bias, the uneven distribution of minerals renders the interpretation of the data obtained by density measurements rather difficult, as has been shown in connection with histological sections[2].

For obviating the distribution error, ORNSTEIN[3] described a new photographic method. A specimen to be examined was photographed. The emulsion was developed to produce a γ value = 1. A positive print was then made using a photographic enlarger. The positive image was developed to produce a γ value = 1. The images of individual nuclei were cut out of the film, and the amount of silver per image was determined. ORNSTEIN stated that the use of silver estimation method in film blackening measurements might be at least as accurate as the densitometric scanning methods. Moreover, it is faster and requires fairly simple and inexpensive apparatus.

Theoretically the same method could be expected to apply equally well to quantitative roentgenological studies of bones[4]. ORNSTEIN's method has been modified

[1] E. D. BERGMANN, A. S. TAHORI, A. KALUSZYNER, and S. REUTER, Nature *176*, 266 (1955). – A. KALUSZYNER, S. REUTER, and E. D. BERGMANN, J. Amer. chem. Soc. *77*, 4146 (1955).

[2] D. VORLAENDER, Ber. dtsch. chem. Ges. *44*, 2467 (1911).

[1] W. Mc FARLAND, Science *119*, 810 (1954).

[2] D. GLICK, A. ENGSTRÖM, and B. G. MALMSTRÖM, Science *114*, 253 (1951). – O. ERÄNKÖ and J. KIHLBERG, *Quantitative methods in histology and microscopy histochemistry* (S. Karger, Basel and New York; Little, Brown & Co., Boston and Toronto 1955).

[3] L. ORNSTEIN, J. Lab. Invest. *1*, 250 (1952).

[4] I am grateful to Prof. O. ERÄNKÖ from the Department of Anatomy, University of Helsinki, for suggesting the use of silver analysis.

by me and the results hitherto obtained with the modified method seem promising.

Basal phalanges of human fingers were found convenient for this kind of study. The hand was radiographed in a perspex tray with a layer of water, as JACKSON[5] has proposed. JACKSON's method was modified by using only a 3·5 cm thick layer of water and placing a 1–2 cm thick plate made of a modified Columbian paste under the basal phalanges to be examined. The thickness of the plate used depended on the thickness of the basal phalanx to be examined, because the distance between the upper surface of the finger and the bottom of the perspex tray was kept constant. The modified Columbian paste contained following agents:

Paraffin wax	90·0 g
Beeswax	110·0 g
Birch saw dust	28·0 g

This paste corresponded to the absorption qualities of the soft parts surrounding finger phalanges.

The roentgenograms were developed to produce a γ value around 3. Two reference systems were used for

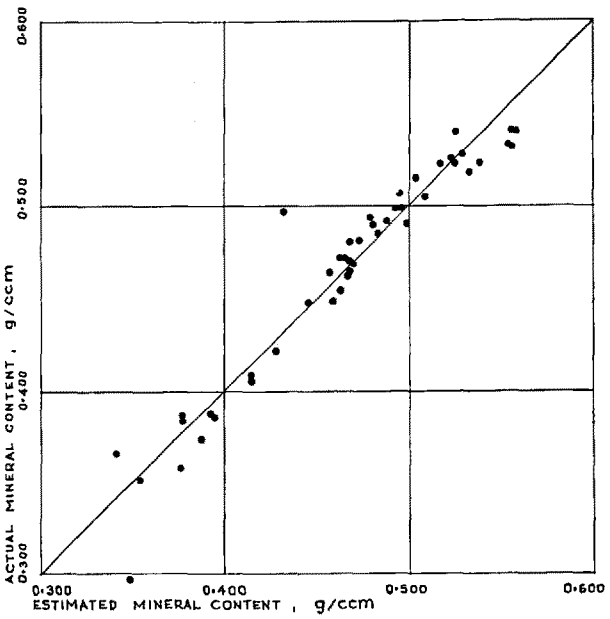


Fig. 1.

the density control of films. The other consisted of perspex boxes containing various amounts of bone powder made of beef bones. The other reference system was a set of standard bones, i.e. basal phalanges with varying mineral contents of fingers obtained from autopsied subjects. These basal phalanges were embedded into a layer of the modified Columbian paste corresponding to the soft parts and a 1–2 cm thick layer of the modified Columbian paste was placed under them to make their distances to the bottom of the perspex tray constant. Both reference systems were usually radiographed together with the hand to be examined. The tube distance was fixed at 1·6 m, and the exposure was 40 mAs at 60 kVp with a standard X-ray machine, Siemens Roentgenkugel. The films were developed with continuous agitation for 5 min at 20°C with Kodak's D-19b developer. The fixation, washing and drying were made under strictly standardized conditions. Kodirex non-screen roentgen film was used. The images of the phalanges to be examined and those of the standard bones and the perspex boxes were cut out of the radiograms. The areas of these images were then measured and the silver contents determined. Instead of the various methods mentioned by MEES[6], VOLHARD's indirect titration[7] was used taking into account the common principles of accuracy for volumetric methods stated by CONWAY[8]. This determination proved to be fast and inexpensive and the error of method proved to be moderate, within the range used about 0·3%.

To check the accuracy of this roentgenological method, left hands of 86 autopsy subjects were radiographed as described. Every hand was exposed twice on two pieces of Kodirex non-screen film placed on another. Thus, four roentgenograms were obtained in every case. Curve was prepared in which the silver content was plotted against the thickness of bone powder layer in the perspex boxes. Only such films, from which a good curve was obtained and the silver contents of the images of the standard bones were within previously determined limits, were used in analyses. These conditions were fulfilled in 46 cases. In these cases the basal phalanges were removed and their volume and mineral contents were determined. The Figure shows the estimated mineral content as plotted against the actual content found. The error of method of such an estimate was calculated by regression analysis (ERÄNKÖ *et al.*[2]) to be about 3·6%, and the statistical possibility to obtain an error greater than about 7·2% is 5 times in 100 analyses[9].

This method has also been used in a study on the mineral contents of the phalanges of the fingers in living subjects suffering from rheumatoid arthritis (to be published).

P. VIRTAMA

Department of Anatomy, University of Helsinki, December 5, 1956.

Zusammenfassung

Eine neue röntgenologische Methode für die Bestimmung des Mineralgehaltes im Knochen wird beschrieben. Die Genauigkeit konnte durch Vermeidung der Fehler, die wegen der unregelmässigen Verteilung des absorbierenden Materials entstehen, erhöht werden.

[5] H. JACKSON, Brit. J. Radiol. *24*, 613 (1951).

[6] C. E. K. MEES, *The theory of the photographic process* (The Macmillan Company, New York 1954).

[7] A. J. VOGEL, *A text-bock of quantitative inorganic analysis. Theory and practice* (Green and Co., London, New York, and Toronto 1953).

[8] E. J. CONWAY, *Microdiffusion analysis* and *volumetric error* (Crosby Lockwood & Son, London 1950).

[9] Mr. J. KIHLBERG has calculated by multiregression analysis the optimum equation necessary for obtaining the estimates. I am very grateful to him.