Wenig Erfolg hatten die, die direkte Herstellung der Verbindung bezweckenden Versuche. Im Wasser erwärmt reagierte ein stöchiometrisches Gemisch von $PbJ_2 + 2CaO + PbO$ nur sehr träge. Nach gewisser Zeit erstarrt das Gemisch. Ebenso führte zu keinen Resultaten das Kochen von den folgenden Gemischen:

$$3PbSO_4 + 2KJ + 4CaO, \quad \text{bzw.} \quad 3PbCl_2 + 2KJ + 4CaO$$

Zusammenfassung.

Zur Bestimmung des Cyangehaltes der $PbSO_4$ haltigen gerösteten Erzen wurde die Liebig-Deniges Methode gewählt. Bei der Zugabe von H_4NOH zu den $Ca(OH)_2$ haltigen Filtrat entsteht mit KJ ein hellgelber kristalliger Niederschlag mit der Zusammensetzung: $Pb_3Ca_2J_2O_4 . 7H_2O$. Dieser entsteht wahrscheinlich aus dem in der Lösung befindlichen $CaPbO_2$ nach der Gleichung:

$$3CaPbO_2 + 2KJ + xH_2O = \\ = PbJ_2(CaPbO_2)_2 . 7H_2O + Ca(OH)_2 + 2KOH + (x-9)H_2O$$

In Alkaliplumbit Lösung entsteht mit KJ kein Niederschlag.

Institute of Organic Chemistry of the University of Szeged. Director: Prof. G. Fodor

The Synthesis of dl-erythro-3,4-dihydroxyphenylserin (nor-adrenaline carboxylic acid)

G. Fodor and J. Kiss

Received Aug. 1949

Rosenmund and Dornsaft (1) prepared dl-3,4-dihydroxyphenyl--serin-ethylester by addition of protocatechualdehyde and glycocoll-ethylester and subsequently hydrolised it to 3,4-dihydroxyphenyl--serin. Later Dalgliesh and Mann (2) improving this route facilated the preparation of the compound.

Lately the biological interest centering on 3,4-dihydroxyphenyl 2-amino ethanol has increased through Blaschko's recent investigations (3) proving that in the human organism the adrenaline synthesis proceeds through nor-adrenaline. In pathologic cases as observed by Tullar (4) — whose observations were also supported by Holton (5) and Goldenberg (6) — e.g. in the case of adrenal tumors, the equilibrium of nor-adrenaline and adrenaline has practically completely shifted in the direction of the formation of nor-adrenaline. Consequently the next chain-link to investigate is the elucidation of the formation of nor-adrenaline.

Blaschko assumed that nor-adrenaline forms through decarboxylation of dl-3,4-dihydroxyphenyl-serin. To control this suggestion Blaschko, Holton and Stanley (7) performed different enzymatic decarboxylation experiments with kidney and adrenal gland extracts of guinea-pigs, they could, however, not observe carbon

dioxide formation. Although it is true that they succeeded in the presence of Streptococcus faecalis R, in decarboxylating 3,4-dihydroxyphenyl-serin into dl-nor-adrenaline, however, the occurence of this conversion can of course not be directly applied to the human organism. On the base of these experiments the formation of nor-adrenaline from the so called nor-adrenaline-carboxylic-acid was discarded.

On the base of our most recent investigations (8) concerning diastereoisomeric amino alcohol chemistry we were of the opinion that the synthesis of Dalgliesh and Rosenmund (1) had to lead to the respective diastereoisomeric amino-hydroxycarboxylic-acid agreeing in spatial structure to that of the pseudo-ephedrine one. Thus knowing the extremely specific functioning of ferments the supposition arose as to whether it would be possible that the enzymes of the adrenal gland and the kidneys are only capable of decomposing one of the racemates of 3,4-dihydroxy-phenyl-serin and exert no effect on the other one. To decide this question we had first to prepare the as yet not synthesized diastereoisomer of 3,4-dihydroxyphenyl-serin possessing an identical configuration to ephedrine. The fact of their also being a great difference between the physiological effect of ephedrine and pseudo-ephedrine in favour of the former seemed to support our suggestion.

Our synthesis proceeded in the manner usually leading to amino alcohols the configuration of which agree with that of ephedrine. Just for this reason we chose as key intermediate (III) α-isonitroso-3,4-dihydroxy-benzoyl-acetate.

We synthesised ethyl 3,4-dihydroxybenzoylacetate from pyrocatechol (I) and ethyl hydrogen malonate using boron trifluoride (8). We succeeded in obtaining with isobutylnitrite (II) in absolute ether the suitable oximino ketone (III) which separated as an amorphous powder. As the purifying of the substance caused difficulties we had to employ direct catalytical hydrogenation e. g. in the presence of Pd-charcoal in alcoholic hydrogenchloride, after taking up 3 moles of hydrogen we obtained the 3,4-dihydroxyphenyl-serin--ethylester hydrochloride; the m. p. of which differs from that of the nor-adrenaline-carboxylic acid-ethylester hydrochloride prepared by Rosenmund and Dalgliesh, its analytical data, however, agree with the calculated values. The obtained ethylester (IV) was hydrolysed according to Rosenmund and Dalgliesh using dilute sodium hydroxide in a hydrogen atmosphere.

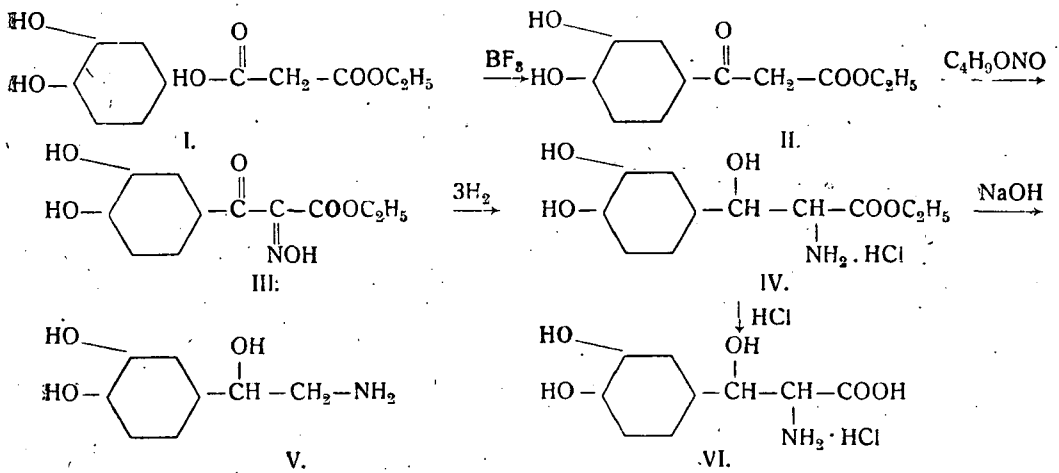
The m. p. of the obtained product and its nitrogen content indicated that during the alkaline saponification the serin derivative was decarboxylated and nor-adrenaline (V) formed. The strong blood pressure increasing effect of the product supports this view. Subsequently we carried out the hydrolysis in dilute hydrochloric acid at 50° in a H_2 current. The analytical data of the nor-adrenaline-carboxylic-acid-hydrochloride (VI) obtained in this way agreed with the calculated values. At our request decarboxylation experiments were carried out with the diastereoisomers of both nor-adrenaline-carboxylic-acids at the Pharmacological Institute and the Neurological Clinic of the University of Szeged. According to the experiments, on the action of decarboxylase ferment prepared from

the kidney of the guinea-pig, the isomer of pseudo-ephedrine configuration does not decarboxylate at all, the recently prepared isomer nor-adrenaline carboxylic-acid on the other hand, partly undergoes decarboxylation. The further investigation of the biochemical side of the question extends over the frame of this paper and necessitates very thorough studies on ferments. The results of these further examinations will be reported elsewhere.

Authors are indebted to Jenő Domonkos and Tibor Stürzer assistants at the University of Szeged, who aided us in performing the biological tests.

Summary.

We synthesised according to the principle of Hartung's amino-alcohol synthesis the hitherto unknown racemate of nor-adrenaline-carboxylic-acid (its configuration agrees with that of ephedrine). We experienced that on treating it with alkali it decarboxylated easily. Fermentatively — e. g. in the presence of guinea pig kidney extract — it also decarboxylates partly thus strongly diverging from the behaviour of the racemate of the isomeric pseudo-ephedrine series. Further enzymatic decarboxylation experiments are in progress.



Experimental.

Ethyl-3, 4-dihydroxy-benzoylacetate.

22 g (0.2 mole) pyrocatechol is dissolved in 53 g (0.4 mole) ethyl-hydrogen-malonate subsequently boron fluoride gas is introduced into the system.

The temperature of the reaction mixture is kept between 35—40°. The pyrocatechol dissolves in 12—15 minutes. Under cooling with iced water the boronfluoride is introduced until the increase in weight reaches 28 g. Subsequently it is heated on a hot steam bath for 40 minutes and then poured under stirring into 56 g of sodium acetate which has been diluted with 200 ml water. A fine red oily suspension is obtained. It is extracted with 2 x 80 ml of n-butanol and the butanol solution is washed with a 5% $NaHCO_3$ solution till the formation of CO_2 can be observed. Instead of butanol 250 ml ether can be used for the

extraction. The butanol or ether solution is dried on fused Na_2SO_4. After distillation in vacuo of the solvent the residue was submitted to molecular distillation. At 0.01 mm a viscous pale yellow oil distillating between 110—120° is obtained.

Analysis. Calculated for $C_{11}H_{12}O_5$: OC_2H_5, 20.1. Found: OC_2H_5, 22.8%.

Ethyl-α-oximino-3,4-dihydroxy-benzoylacetate.

25 g of the preceeding ester is dissolved in 100 ml. dry-ether and then 18 g 20% abs. ethereal hydrogen-chloride is added. Subsequently we add under stirring dropwise during an hour at a temprature of about 0°, 11 g of freshly distilled n-butylnitrite in 35 ml of abs. ether. The dark red reaction mixture is kept overnight in the refrigerator and the solvent removed at 30°. It yields a dark red viscous oil, which was submitted to catalytical hidrogenation.

Nor-Adrenaline-carboxylic-acid-ethylester.

The oil, 29.3 g, obtained by the evaporation of the above mentioned ethereal solution is dissolved in 120 ml abs. ethanol, and subsequently hydrogenated over Pd-charcoal in the usual manner in the presence of 40 ml of 4 N abs. ethanolic hydrogen chloride. During 12 hours it absorbed 7.7 l of hydrogen. The alcoholic solution is filtered off from the catalyst it has a pale yellow colour and is evaporated at 50° in vacuo. It yields a viscous oil which is still twice dissolved in abs. ethanol (80 ml) and then evaporated again. The residue, a thick oil was rubbed with 120 ml of abs. ether. It solidifies into a pale drab crystalline powder.

The ether is decanted a few times and then quickly filtered and dried in a desiccator over phosphorus-pentixede. It yields a pale drab powder resembling „corbasil" hydrochloride (10) M. p. 112—120 (decomposition).

Analysis. Calculated for $C_{11}H_{16}O_5NCl$:	Cl, 12.77%.	Found	Cl, 11.2%
	N, 5.00 „		N, 4.5 „
	OC_2H_5, 16.21 „		OC_2H_5, 20.7 „

Alkaline hydrolysis of ethyl nor-adrenaline-carboxylate.

2.8 g of the nor-adrenaline carboxylic acid ethylester described above is introduced into a flask (150 ml) for hydrolysis and shaken for an hour in a current of hydrogen with 60 ml NaOH. The yellowish-red coloured aqueous solution is neutralised with 51 ml N-HCl and again shaken in a current of hydrogen. The solution does not decolorise. It is then decolorised with 0.1 g 14% Pd, charcoal in a hydrogen atmosphere. It had still taken up 105 ml hydrogen gas. It was filtered. The solution is as clear as water. At 20° the water is removed and a pale drab amorphous powder is obtained, which is again evaporated with 60 ml abs. ethanol. Subsequently it is still twice dissolved in abs. ethanol the undissolved NaCl is filtered off it is evaporated and finally dried over P_2O_5 in vacum dessicator. Yield pale drab hygroscopic powder. Analysis, calculated for $C_8H_{11}O_3N$: N, 8.3 Foud: N, 8.7%. The result of the analysis indicates that the substance has undergone decarboxylation under saponification with sodium hydroxide and nor-adrenaline has formed. The same fact is supported by the strong blood pressure accelerating effect it exerts on the experimentally decapitated cat. The other diastereoisomeric ethylester (threo) obtained by similar saponificaton with alkali causes hardly any rise in blood pressure.

Acid hydrolysis of nor-adrenaline carboxylic acid ethylester.

3 g of the preceeding ester hydrochloride is dissolved in 50 ml N. HCL, and heated at 50° for an hour in a current of hydrogen. Subsequently the solu-

tion is purfied with charcoal it has a red colour, then it is hydrogenated in the usual manner with 0.1 g Pd-charcoal. It absorbed 65 ml hydrogen. The catalyst is filtered off ond the colourless solution is freed from the solvent at 30°, a graish-drab solid foam is obtained, which is dried over phosphorus-pentoxide and solid sodium hydroxide in a vacuum desiccator.

Analysis. Calculated for $C_9H_{11}O_5N.HCl$: N. 5.6%. Found: N. 5.00%.

For the investigation relating to the blood pressure enhancing effect a 1/1000 solution was used. The decarboxylation experiments were accomplished in a 1/100 molar solution under the conditions laid down by Blaschko and co-workers. The aqueous nor-adrenaline-carboxylic-acid solution was fixed with a phosphate buffer at pH 7.5. The decarboxylase ferment was extracted with water from the kidney of a guinea-pig. In the case of the threo-derivatives obtained by saponification we did not experience CO_2 formation, whereas the substance obtained by saponification of acidified erythro series evolved on the average (0.4 m) 12.5 min CO_2.

References.

1. *Rosenmund, K. W.* and *Dornsaft, H.* Ber. dtsch. chem. Ges. 52. (1919) 1734.
2. *Dalgliesh, C. E., and Mann, F. G. J.* Chem. Soc. (1947) 658.
3. *Blashko, H.*, J. Physiol., 101. (1942) 337.
4. *Tullar*, Science 109, 536 (1949).
5. *Holton, P.* Nature, London, 163. (1949) 534.
6. *Goldenberg, M., et al.* Science 109, (1949) 534.
7. *Blashko, H., Holton, R., Stanley*, S., British Journ. Pharm. and Chemother. (1948) 3.
8. *Fodor, Bruckner, Kiss* and *Ohegyi*, Journ. Org. Chem. 14. (1949) 337; *Fodor* and *Kiss*, Nature, London, 163. (1949) 287.
9. One of us (J. Kiss) carried out the preparation of many polyhydroxy-ary, alkyl ketones with boronfluoride as catalyst; these results are still unpublished.
10. *Bruckner* and *Fodor*, Ber. dtsch. Chem. Ges. 76. (1943) 466.

Institute of General and Physical Chemistry of the University of Szeged (Hungary)
Director: Prof Á. Kiss

Examination of layer inhibiting the corrosion of Aluminium on the base of the differential-effect

Preliminary Report

BY GY. BÁCSKAI AND K. KOVÁCS

The interpretation of the protecting power of natural and artificial coating layers covering the metal surface may be attempted on the base of the general theory of corrosion.

On corrosion of metal anode places are formed, which are in conducting correlation on the surface, on the action of the local current inducted by the polyelektrode-systeme evolved in this manner, the ground metal goes into solution. The local current is determined by the general equation of the polyelektrode-corrosion theory:

$$i_L = \Sigma i_1 \frac{E - E_p}{\Sigma f (w_1 + w_2 + \ldots + w_n)} \qquad (1)$$