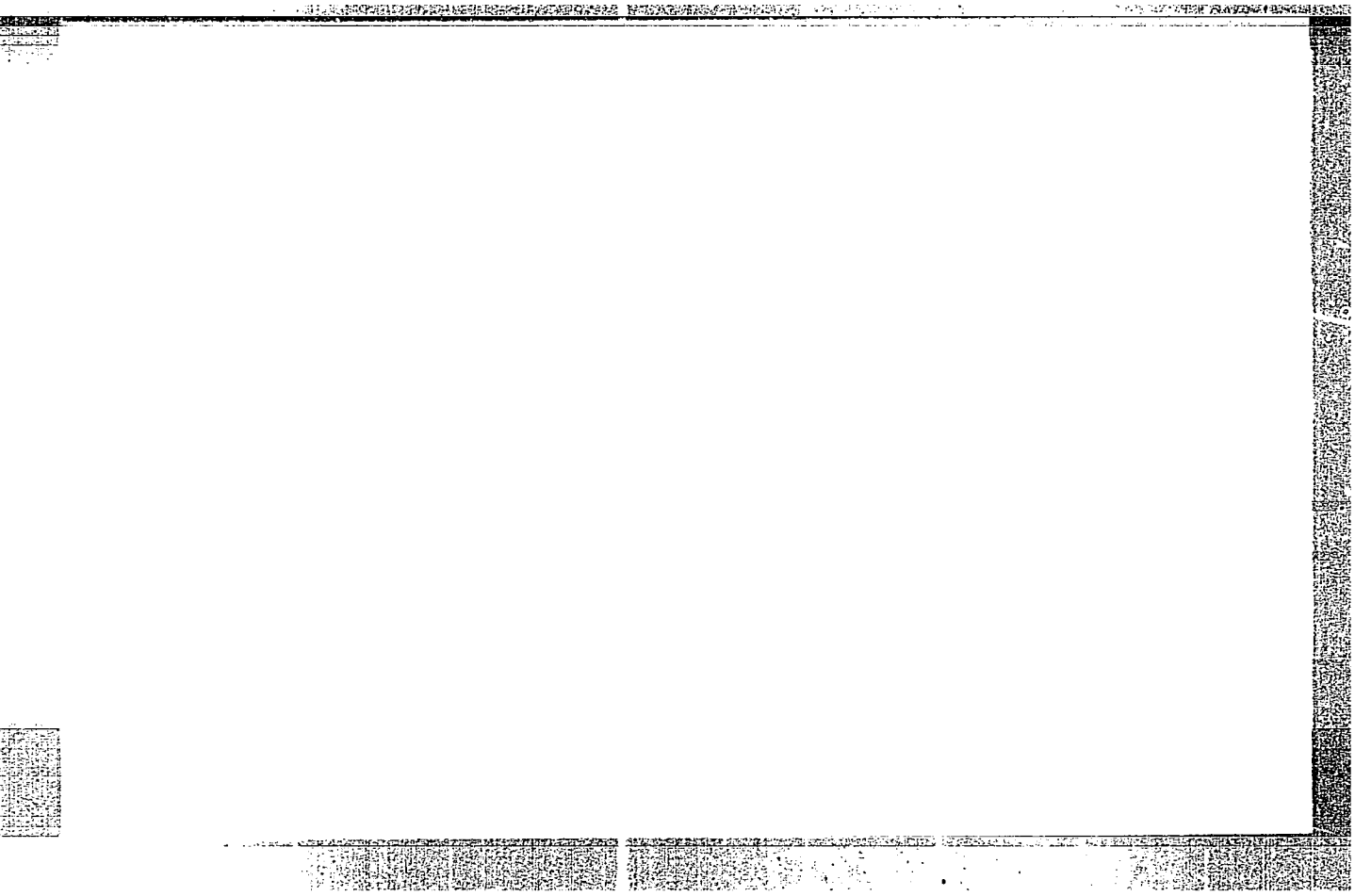

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FODOR, E.; MARAZAN, N.; MERCEA, V.; OLARIU, A.

Nitrogen influence on the reaction of isotopic exchange between hydrogen and watery vapors. Studii cerc fiz 14 no.1:7-23 '63.

1. Institutul de fizica atomica, Sectia Cluj, Universitatea "Babes-Bolyai" Facultatea de fizica, Cluj.

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Separation in a column with steam distillation depending on the medium concentration of the mixture. Studia Univ B-B S. Math-Phys 7 no.1:137-147 '62.

UNGUREANU, C.; FODOR, E.

Spectral analysis of poor alloyed steels. Rev chimie Min petr 14 no.8:467-469 Ag '63.

1. Institutul de fizica atomica, Sectia Cluj (for Ungureanu).
2. "Industria sirmei"- Cimpia Turzii, Laboratorul central (for Fodor).

FODOR, FERENC

Balla Antal; elete es muszaki munkassaga (1739-1815). Budapest. Tankonyvkiado (1953) 59 p. (Budapesti Muszaki Egyetem Kozponti Konyvtara. Muszaki tudomanytorteneti kiadvanyok, 2. szam) (Antal Balla; his life and technical activities (1739-1915). English and Russian summaries. maps) CtY Not in DLC

SOURCE: Monthly list of East European Accessions, (EEAL), LC, Vol. 5, No. 3, March, 1956

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"Geographical Positions of Bratislava, Buda, and Cluj on Our Oldest Maps (To be Cont'd)", P. 225, (FOLDRAJZI KOZLEMENYEK, Vol. 6, No. 4, 1954, Budapest, Hungary)

SC: Monthly List of East European Accessions (EEAL), LC, Vol. 4, No. 3, March 1955, Uncl.

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Balla Antal elete es muszaki munkassaga (1739-1815). Budapest, Tankonyvkiado (1953) p. 59. (Budapest. Muszaki Egyetem. Kozponti Konyvtara. Muszaki tudomanytorteneti kiadvanyok, 2. sz.) (Antal Balla's life and technical activities 1739-1815) English and Russian summaries. maps. bibl., facsim.
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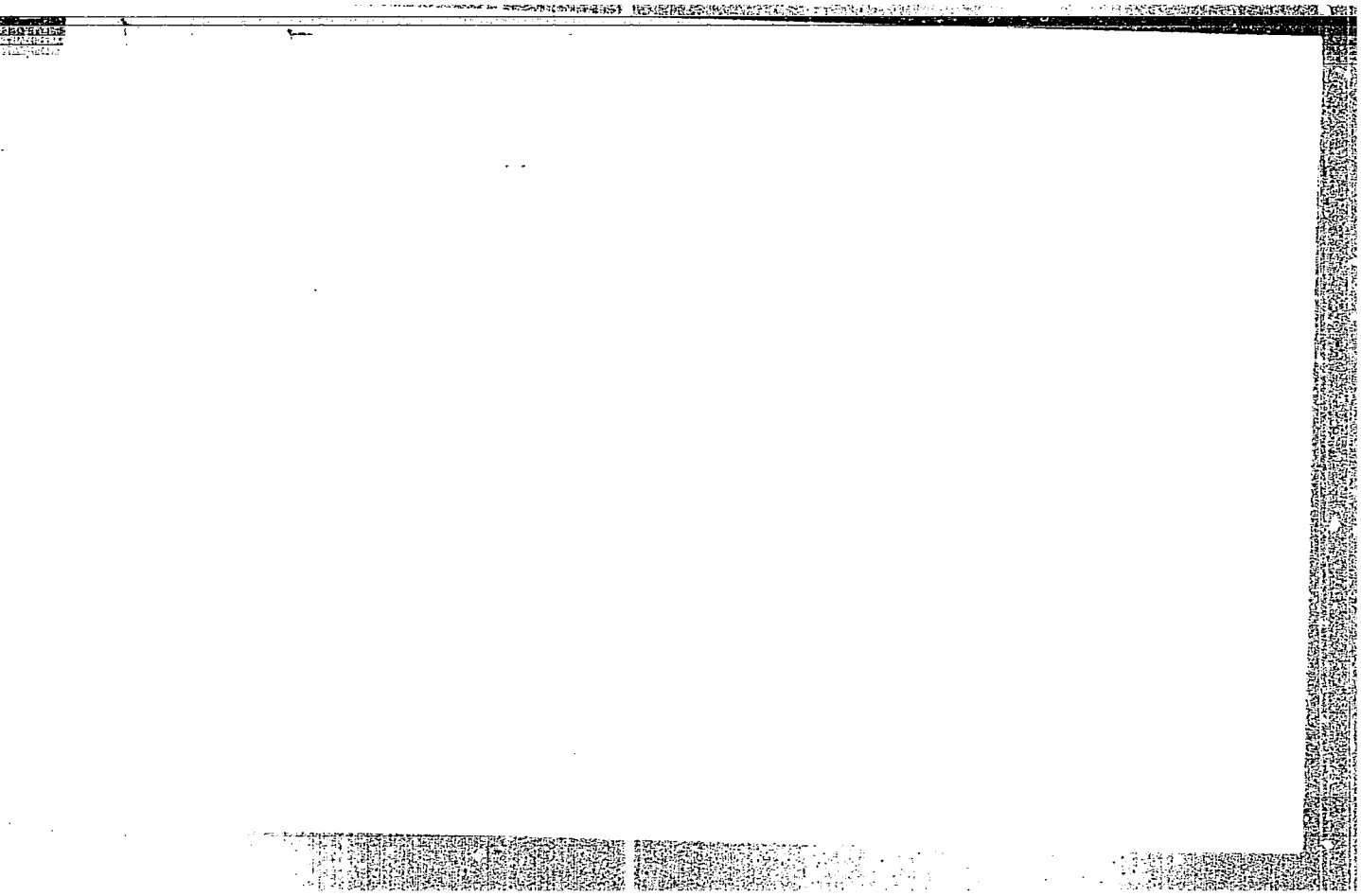
SO: Monthly List of East European Accessions (EEAL) LC, Vol. 6, no. 6, June 1957. Uncl.



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FODOR-F

67. **Antal Balla, Hungarian hydraulic engineer of the 18th century.** F. Fodor. *Mérnéplétudományi Szemle.* Vol. 5, 1955, No. 8, pp. 372–374

Among the hydraulic engineers of his time Antal Balla (1739–1815) was one of the most prominent representatives of his profession. At a time when the civilian training of engineers was practically non-existent in Europe Antal Balla had a scientific erudition which surpassed by far that of his contemporaries. In the eighties of the 18th century he was one of Hungary's most excellent and best educated technicians with a wide intellectual horizon who at the same time was a most exact and highly talented cartographer as well. Several excellent maps and designs for a stone bridge connecting Pest and Buda were also found among his papers. His work on theory of measurement proved him an outstanding physicist, his classical-humanist education was also on a high level. He wrote papers on archaeology, theory of music and history. His chief works however concerned hydraulics. He was the first to design a canal connecting the Danube and the *Tisza* rivers for which he had drawn with remarkably fine technique a comprehensive map including ample astronomical, geographical and hydrographical explanations and notes on agriculture and communication.

Geophy 1

BANHIDY, Ferenc, dr.,; FODOR, Ferenc, dr.

Postoperative results in the therapy of chronic purulent infection of the middle ear. Ful orr gegegyogy. no.4:112-116 Nov. 55

1. Baja Varosi Tanacs Korhaza Ful-, Orr-, Gegeosztalyanak (foorvos: Banhidy Ferenc dr.) kozlemenye.
(OTITIS MEDIA, surgery
radical, results in chronic)

FODOR, Ferenc, dr.

About the cleanness campaign. Nepegaszsegugy 37 no.4:109-110 Apr 56.

1. Kozlemeny a Hajdu-Bihar megyei kozegeszsegugyi-jarvanyugyi allomasrol (igazgato-foorvos: Fodor, Ferenc dr.)
(PUBLIC HEALTH
in Hungary, campaign for promotion of hygiene in public institutions, schools & industry, standards (Hun))

BANHIDY, Ferenc. dr.,; FODOR, Ferenc, dr.

Tuberculosis of the tonsils in pulmonary tuberculosis. Orv. hetil. 97 no.4:100-103 22 Jan 56.

1. A Baja Varosi Tanacs Korhaza (igazgato: Burg Ete dr. kandidatus) Ful-orr-gege Osztalyanak (foorvos: Banhidy Ferenc dr.) kozlemenye.

(TONSILS, dis.
tuberc. with pulm. tuberc., tonsillectomy & pathol. (Hun))
(TUBERCULOSIS, PULMONARY, compl.
tuberc. of tonsils, tonsillectomy & pathol. (Hun))

FODOR Ference

KOTAY, Pal, Dr.; GREPALY, Andras, Dr.; BALOGH, Erno; FODOR, Ferenc

Problems of renal tuberculosis in children and in puberty. Magy. sebeszet 10 no.2-3:183-188 Apr-June 57.

1. Tirgu-Mures--Marosvansarhely (Rumania)
(TUBERCULOSIS, RENAL, in inf. & child
in child. & in puberty (Hun))

FODOR, Ferents, [Fodor, Ferenc] (Vengerskaya Narodnaya Respublika)

Public health organization in Hajdu-Bihar region. Sov.zdrav. 17 no.10:47-51 O '58 (MIRA 11:11)

(PUBLIC HEALTH, in Hungary (Rus))

FODOR, Ferenc, dr.

Medical ethics and basic problems of medical legislation. Orv. hetil. 100 no.50:1800-1803 D '59.
(ETHICS, MEDICAL)
(LEGISLATION, MEDICAL)

GYERGYAY, E., Assist. Prof.; FODOR, FERENC; ANTALFFY, A.; STROMPEL, E.

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Rumanian M. Rev. 4 no.1:3-6 Ja-Mr '60.
(DIABETES INSIPIDUS etiol.)
(PITUITARY GLAND dis.)

MONOKI, St., dr.; HORVATH, Eva, dr.; WIENER, Fr., dr.; FODOR, Fr., dr.

Heart diseases in collagen diseases. Med. inter., Bucur 13 no.2: 195-199 F '61.

1. Lucrare efectuata in Clinica a II-a medicala, Catedra de anatomie patologica si Catedra de biologie, Tg. Mures.

(COLLAGEN DISEASES complications)
(HEART DISEASES etiology)

FODOR, Ferenc, dr.; EGYEDI, Laszlo, dr.

Morbidity structure changes observed by district physicians in a central area of Budapest. Nepegeszsegugy 42 no.9:268-271 S '61.

1. Kozlemeny a Budapesti Orvostudomanyi Egyetem Kozegeszsegtani Intezetebol (tanszekvezeto professzor: Melly Jozsef dr. egyetemi tanar) es a fovarosi tanacs Trefort utcai rendelointezetebol)

(MORBIDITY statist)

FODOR, Ferenc, dr.; SZAKKAY, Antal, dr.

Some epidemiological data on tuberculosis obtained during contact preventive examinations. Nepegesszegugy 43 no.1:12-14 Ja '62.

(TUBERCULOSIS epidemiol)

FODOR, Ferenc, dr.

Morbidity in various regions of Budapest according to data on the turnover of patients. Nepegeszsegugy 43 no.6:166-171 Je '62.

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(MORBIDITY)

FODOR, Ferenc, dr.; MADAI, Lajos, dr.

Emergency hospitalizations in Budapest, with special reference to internal medicine wards. Nepegeszsegugy 43 no.11:337-344 N '62.

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FODOR, Ferenc, dr.; SZAKKAY, Antal, dr.

Epidemiological significance of a pathological form of tuberculosis based on contact morbidity within the family. Tuberkulozis 16 no.1: 7-12 Ja '63.

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FODOR, Forents [Fodor, Ferenc], doktor; MADAI, Layosh [Madai, Lajos] doktor (Budapesht)

Hospitalization of therapeutic patients for emergency causes in Budapest. Sov. zdrav. 22 no.7:68-71 '63 (MIRA 16:12)

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1. Kozlemeny a Budapesti Orvostudomanyi Egyetem Kozegeszsegtani Intezetebol es a Fovarosi Tanacs VB Egeszsegugyi Osztalyarol.

*

FODOR, G. (Szeged)

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1. Institute of Atomic Physics of the Rumanian Academy, Magurele.

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SCIENCE

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FODOR GABORNE VARGA, Eva

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Study of the way in which the road systems in the central control station of the Institute of Transports and Telecommunications meet the requirements imposed by heavy traffic. Rev transport 11 no.10:452-461 O '64.

FODOR, Gabor

Some questions relating to socialist morality. Munka 14 no.4:22 Ap '64.

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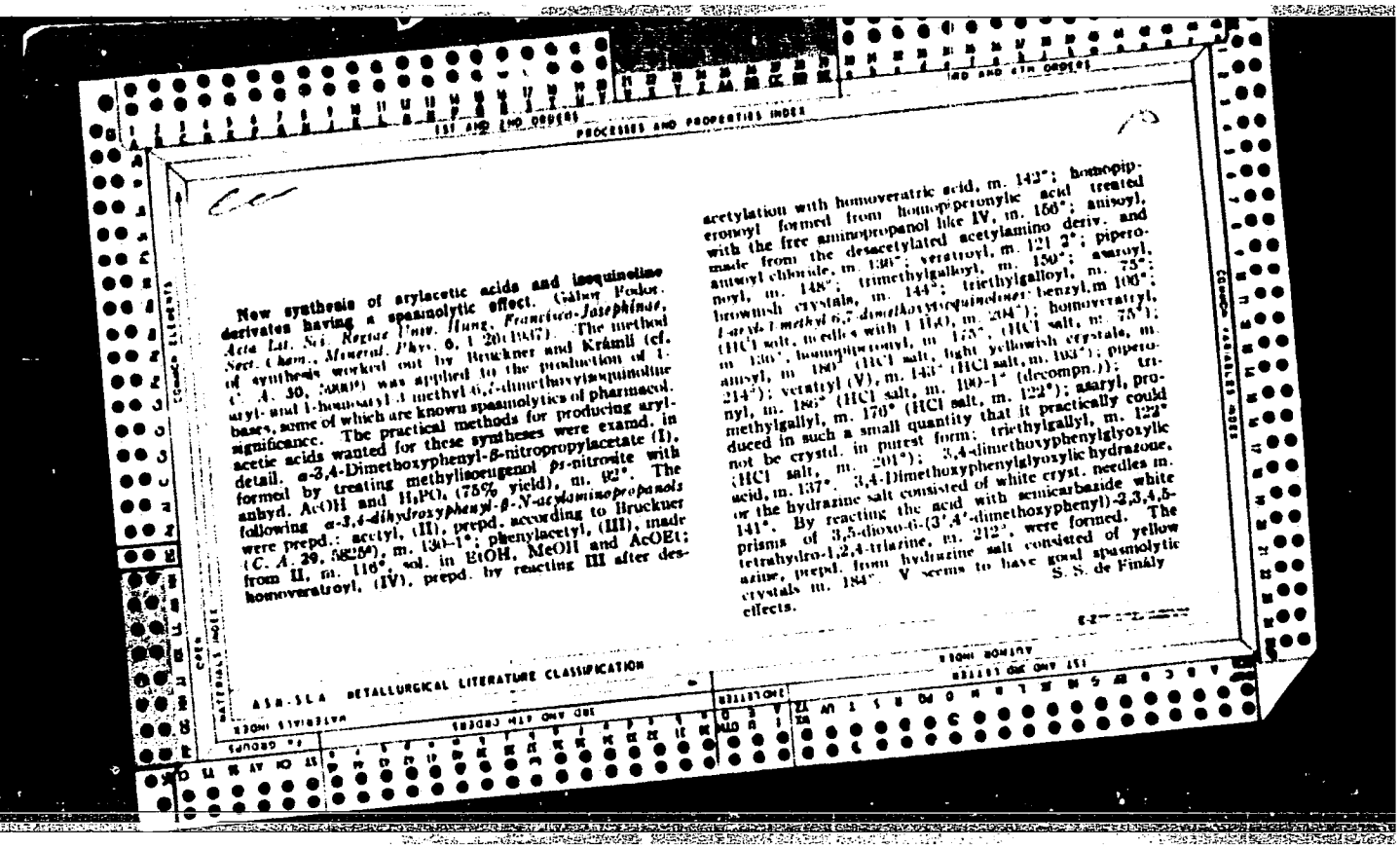
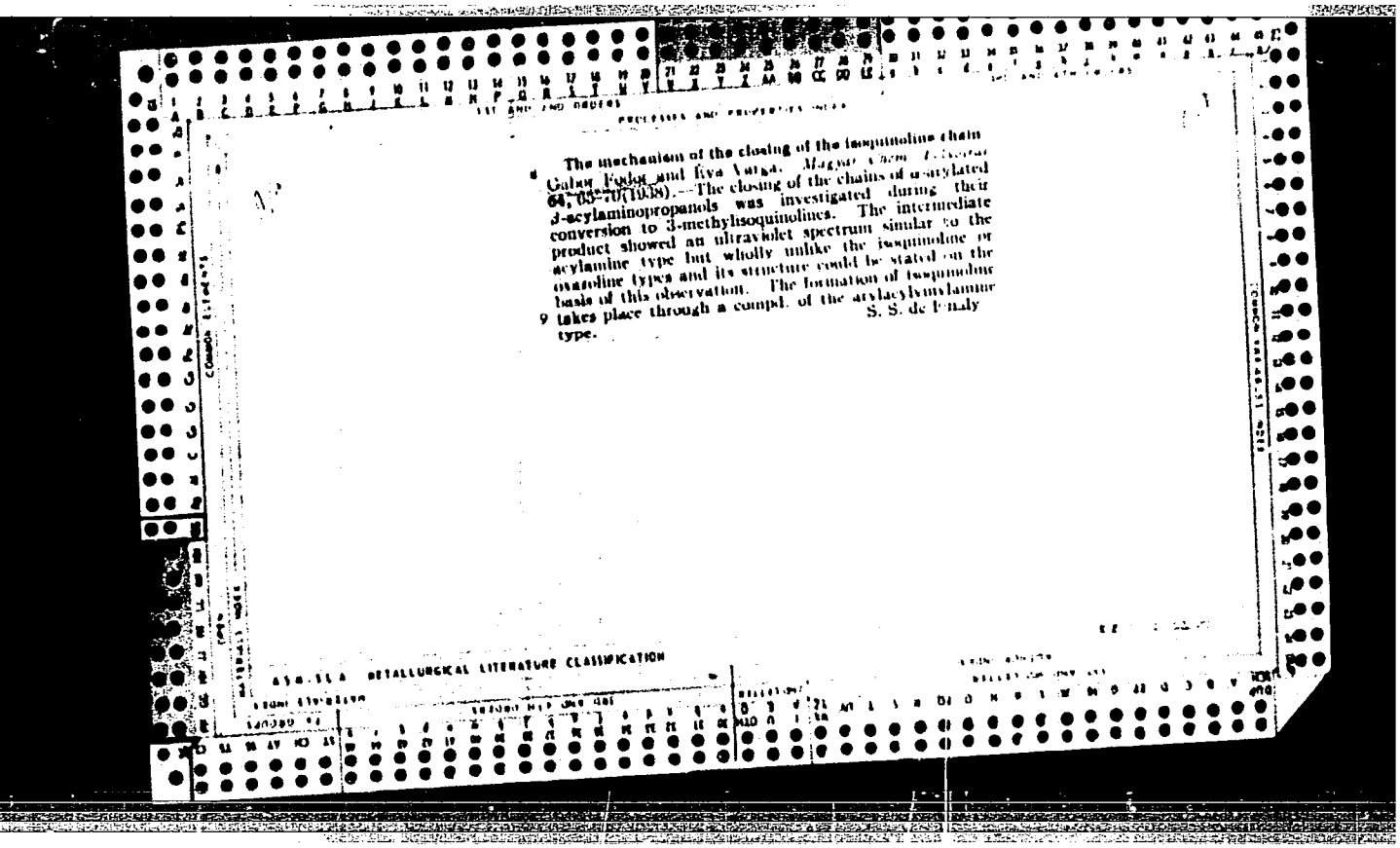


New synthesis of arylacetic acids and isoquinoline derivatives having a spasmolytic effect. (Gábor Fodor. *Acta Lit. Sci. Regiae Univ. Hung. Francisco-Josephinae, Sect. Chem., Mineral. Phys.* 6, 1 20(1933). The method of synthesis worked out by Bruckner and Krámli (cf. *C. A.* 30, 3881[9]) was applied to the production of 1-aryl- and 1-homoaryl-3-methyl-6,7-dimethoxyisoquinoline bases, some of which are known spasmolytics of pharmacol. significance. The practical methods for producing arylacetic acids wanted for these syntheses were examd. in detail. α-3,4-Dimethoxyphenyl-β-nitropropylacetate (I), formed by treating methylisoeugenol *ps*-nitrosite with anhyd. AcOH and H_3PO_4 (75% yield), m. 92°. The following α-3,4-dihydroxyphenyl-β-*N*-acylaminopropanols were prepd.: acetyl, (II), prepd. according to Bruckner (*C. A.* 29, 5856), m. 130–1°; phenylacetyl, (III), made from II, m. 116°, sol. in EtOH, MeOH and AcOEt; homoveratroyl, (IV), prepd. by reacting III after desacetylation with homoveratric acid, m. 142°; homopiperonoyl formed from homopiperonylic acid treated with the free aminopropanol like IV, m. 160°; anisoyl, made from the desacetylated acetylamino deriv. and anisoyl chloride, m. 130°; veratroyl, m. 150°; asaroyl, m. 148°; trimethylgalloyl, m. 144°; triethylgalloyl, m. 75°; brownish crystals, m. 144°; 1-aryl-1-methyl-6,7-dimethoxyisoquinolines: benzyl, m. 100°; (HCl salt, needles with 1 H₂O, m. 175°, (HCl salt, m. 75°); anisyl, m. 180° (HCl salt, light yellowish crystals, m. 214°); veratryl (V), m. 143° (HCl salt, m. 183°); piperonyl, m. 186° (HCl salt, m. 122°); asaryl, prodused in such a small quantity that it practically could not be crystd. in purest form; trimethylgallyl, m. 170° (HCl salt, m. 201°); 3,4-dimethoxyphenylglyoxylic acid, m. 137°. 3,4-Dimethoxyphenylglyoxylic hydrazone, or the hydrazine salt consisted of white cryst. needles m. 141°. By reacting the acid with semicarbazide white prisms of 3,5-dioxo-6-(3',4'-dimethoxyphenyl)-2,3,4,5-tetrahydro-1,2,4-triazine, m. 212°, were formed. The azine, prepd. from hydrazine salt consisted of yellow crystals m. 184°. V seems to have good spasmolytic effects.

S. S. de Finály



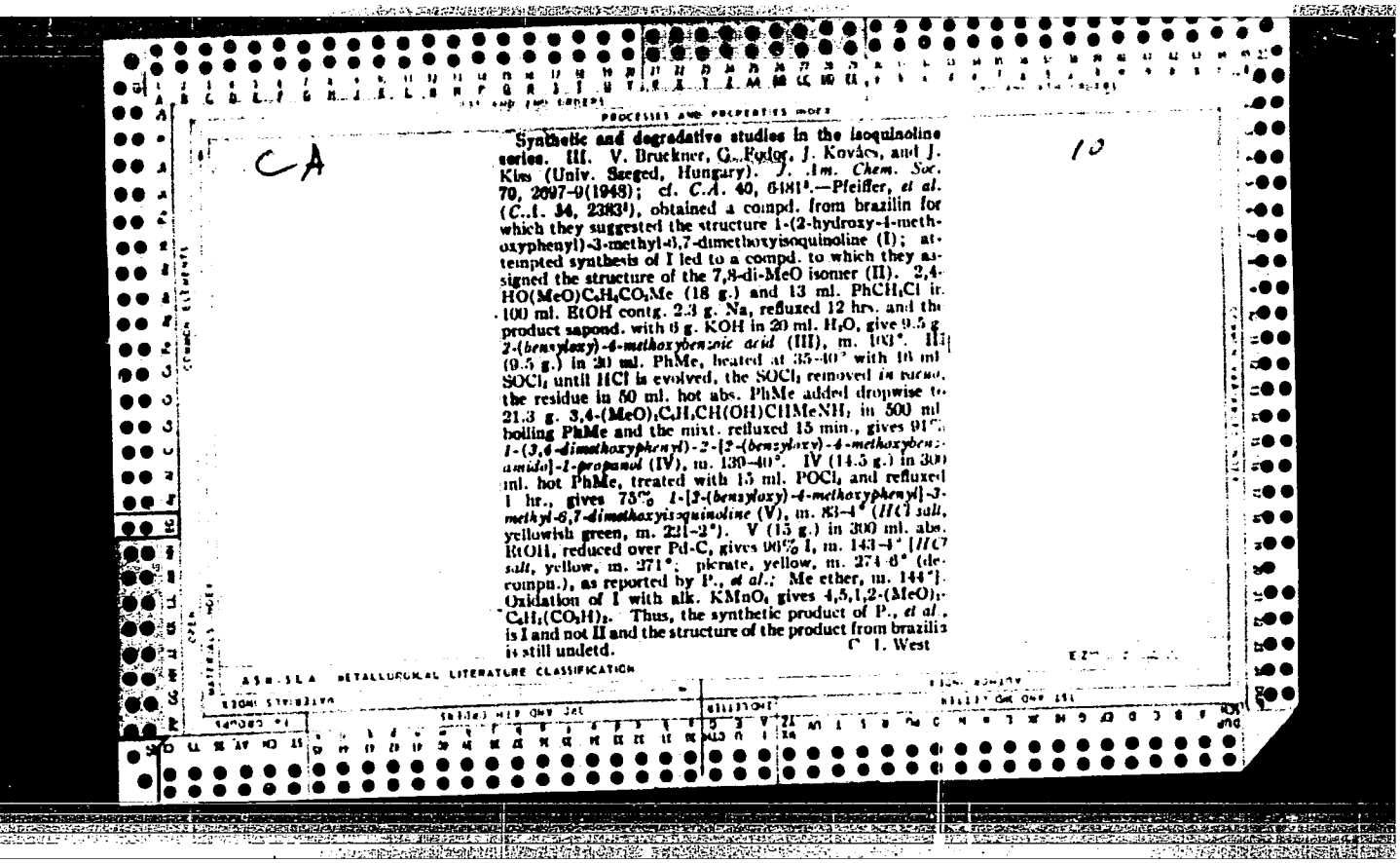
The mechanism of the closing of the isoquinoline chain
Gabor Fodor and Eva Vargha. *Magyar Kém. Folyóirat* 64, 65–70 (1958).—The closing of the chains of α-acylated β-acylaminopropanols was investigated during their conversion to 3-methylisoquinolines. The intermediate product showed an ultraviolet spectrum similar to the acylamine type but wholly unlike the isoquinoline or oxazoline types and its structure could be stated on the basis of this observation. The formation of isoquinoline takes place through a compd. of the acylacylvinylamine type.
S. S. de Finaly

FODOR, G. 1948

(Res. Labs. Chinoin Chem. & Pharmaceut. Works Ltd. Ujpest, Hungary.)

"Investigations Relating to the Synthesis of Patulin."

Jour. of the Chemical Society 1948 (Sept.) pp. 1295-1299
Abst: Exc. Med. 11, Vol. 11, No. 10. p. 1360



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Synthetic and degradative studies in the isoquinoline series. III. V. Bruckner, G. Fodor, J. Kovács, and J. Kiss (Univ. Szeged, Hungary). *J. Am. Chem. Soc.* 70, 2697-9(1948); cf. *C.A.* 40, 6481[8].—Pfeiffer, *et al.* (*C.A.* 34, 2383[3]), obtained a compd. from brazilin for which they suggested the structure 1-(2-hydroxy-4-methoxyphenyl)-3-methyl-6,7-dimethoxyisoquinoline (I); attempted synthesis of I led to a compd. to which they assigned the structure of the 7,8-di-MeO isomer (II). 2,4-HO(MeO)$C_6H_3CO_2Me$ (18 g.) and 13 ml. $PhCH_2Cl$ in 100 ml. EtOH contg. 2.3 g. Na, refluxed 12 hrs. and the product sapond. with 6 g. KOH in 20 ml. H_2O, give 9.5 g. *2-(benzyloxy)-4-methoxybenzoic acid* (III), m. 161°. III (9.5 g.) in 20 ml. PhMe, heated at 35–40° with 16 ml. $SOCl_2$ until HCl is evolved, the $SOCl_2$ removed *in vacuo*, the residue in 50 ml. hot abs. PhMe added dropwise to 21.3 g. 3,4-$(MeO)_2C_6H_3CH(OH)CHMeNH_2$ in 500 ml. boiling PhMe and the mixt. refluxed 15 min., gives 91% *1-(3,4-dimethoxyphenyl)-2-[2-(benzyloxy)-4-methoxybenzamido]-1-propanol* (IV), m. 130–40°. IV (14.5 g.) in 300 ml. hot PhMe, treated with 15 ml. $POCl_3$ and refluxed 1 hr., gives 75% *1-[2-(benzyloxy)-4-methoxyphenyl]-3-methyl-6,7-dimethoxyisoquinoline* (V), m. 83–4° (*HCl salt*, yellowish green, m. 231–2°). V (15 g.) in 300 ml. abs. EtOH, reduced over Pd-C, gives 90% I, m. 143–4° [*HCl salt*, yellow, m. 271°; picrate, yellow, m. 274–6° (decompn.), as reported by P., *et al.*; Me ether, m. 144°]. Oxidation of I with alk. $KMnO_4$ gives 4,5,1,2-$(MeO)_2C_6H_1(CO_2H)_3$. Thus, the synthetic product of P., *et al.*, is I and not II and the structure of the product from brazilin is still undetd.

C. L. West

CA

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Synthesis of some new hydrazine derivatives of thiazole. Gábor Fodor. *Acta Univ. Szeged. Chem. et Phys.* 2, 167-74(1949)(in English).—Efforts were made to synthesize (sulfanilylhydrazino)methylthiazoles in a search for more active therapeutics. The synthesis was made in the following steps: $PhCH_2NHNH_2.HCl$, m. 148°, prepd. from $(PhCH:N)_2$ and $N_2H_4.H_2O$, was transformed through $PhCH_2NHNHCSNH_2$, m. 175°, into *2-(Benzylhydrazino)-4-methylthiazole*, m. 44°. $(PhCH_2)_2NNH_2$ (I), m. 65°, prepd. according to Busch and Weiss [*Ber.* 33, 2702(1900)], was converted into $(PhCH_2)_2NNHCSNH_2$ (II), best prepd. (67.6% yield) by rearrangement of I.HSCN in aq. alc. From II and $ClCH_2COMe$ in EtOH was obtained *2-(2,2-dibenzylhydrazino)-4-methylthiazole*, m. 158-9°, which with Ac_2O in dry pyridine gave *2-(1-acetyl-2,2-dibenzylhydrazino)-4-methylthiazole*, m. 90°. $PhCH:NNHCSNH_2$ in Me_2CO refluxed with $ClCH_2COMe$ gave *2-(2-benzylidenehydrazino)-4-methylthiazole* (III), m. 190°; *HCl salt*, m. 195°. Pure III in hot pyridine with *p*-$AcNHC_6H_4SO_2Cl$ yielded *2-[1-(N-acetylsulfanilyl)-2-benzylidenehydrazino]-4-methylthiazole*, m. 171-2°, converted into *2-(2-sulfanilylhydrazino)-4-methylthiazole*, m. 153-5° (decompn.), which showed *antibacterial effects*, especially a *tuberculostatic activity*. Details of the syntheses and analytical data are given.

István Finály

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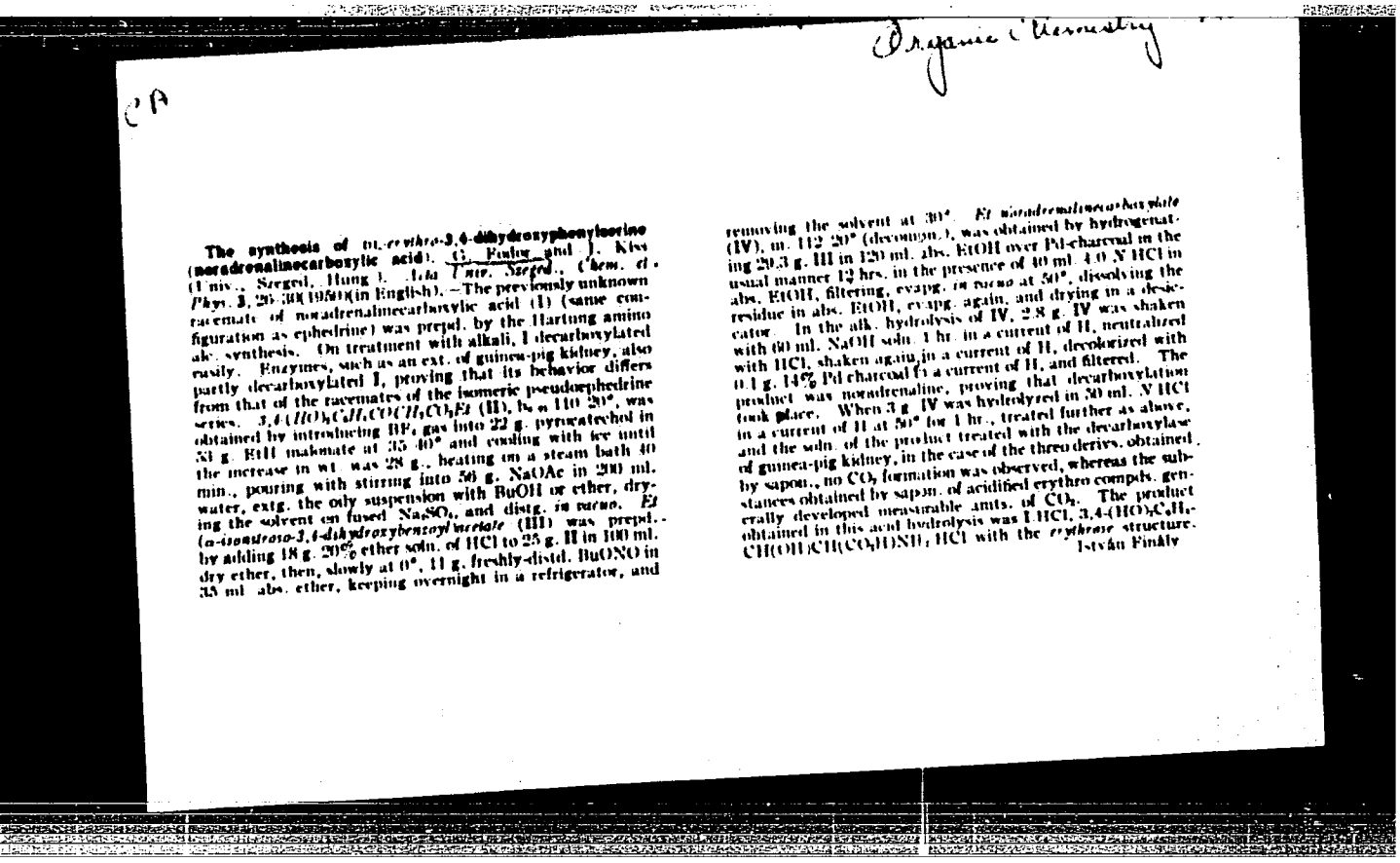
The mesomerism of propenylbenzene and of allylbenzene derivatives. Árpád Kiss, Gábor Fodor, and I Molnár. *Acta Univ. Szeged, Chem. et Phys.* 2, 189-91 (1949)(in English).—The ultraviolet absorption curves of allyl and propenyl phenols and their ethers showed that the mesomeric effect of the substituents was in all cases larger than their inductive effect. The curves of allylbenzene derivs. corresponded closely to those of the resp phenols and phenol ethers, slight differences being due only to the inductive effect of the allyl chain. The extinction of the allyl chain could be observed only in the ascending part of the curves. The absorption spectra of all propenyl derivs., i.e., *p*-anol, anethole, isoeugenol, isohomogenol, isosafrole, isomyristicin, and isochavicetol, revealed a close resemblance to that of PhCH:CHMe. This indicates that the π-electrons of the propenyl chain play an important part in the mesomerism of propenylbenzene derivs István Finály

CA

Configurations of alicylic amino alcohols. G. Fodor and J. Kiss (Univ. Szeged, Hung.). *Nature* 164, 917-18 (1949).—Investigations of the acyl migration reaction N → O (cf. *C.A.* 43, 4238b) were extended to diastereoisomeric alicyclic amino alcs. to establish steric positions. When 2-benzamidocyclohexanols m. 189° and 174° were treated separately with alc. HCl at room temp., the 189° material rearranged more rapidly (by a factor of 10 or 20) and was considered to be cis; it gave *O*-benzoyl 2-aminocyclohexanol-HCl, m. 228°, also thought to be cis. The 174° material, considered to be trans, gave *O*-benzoyl 2-aminocyclohexanol-HCl (trans), m. 284°. Both HCl salts were rearranged to the original amides by alkali. At 100° the rates of rearrangement of the 2 amides were more nearly alike, but the same products as before were obtained. The studies are to be extended to the aminoisomeols.

H. H. Voge



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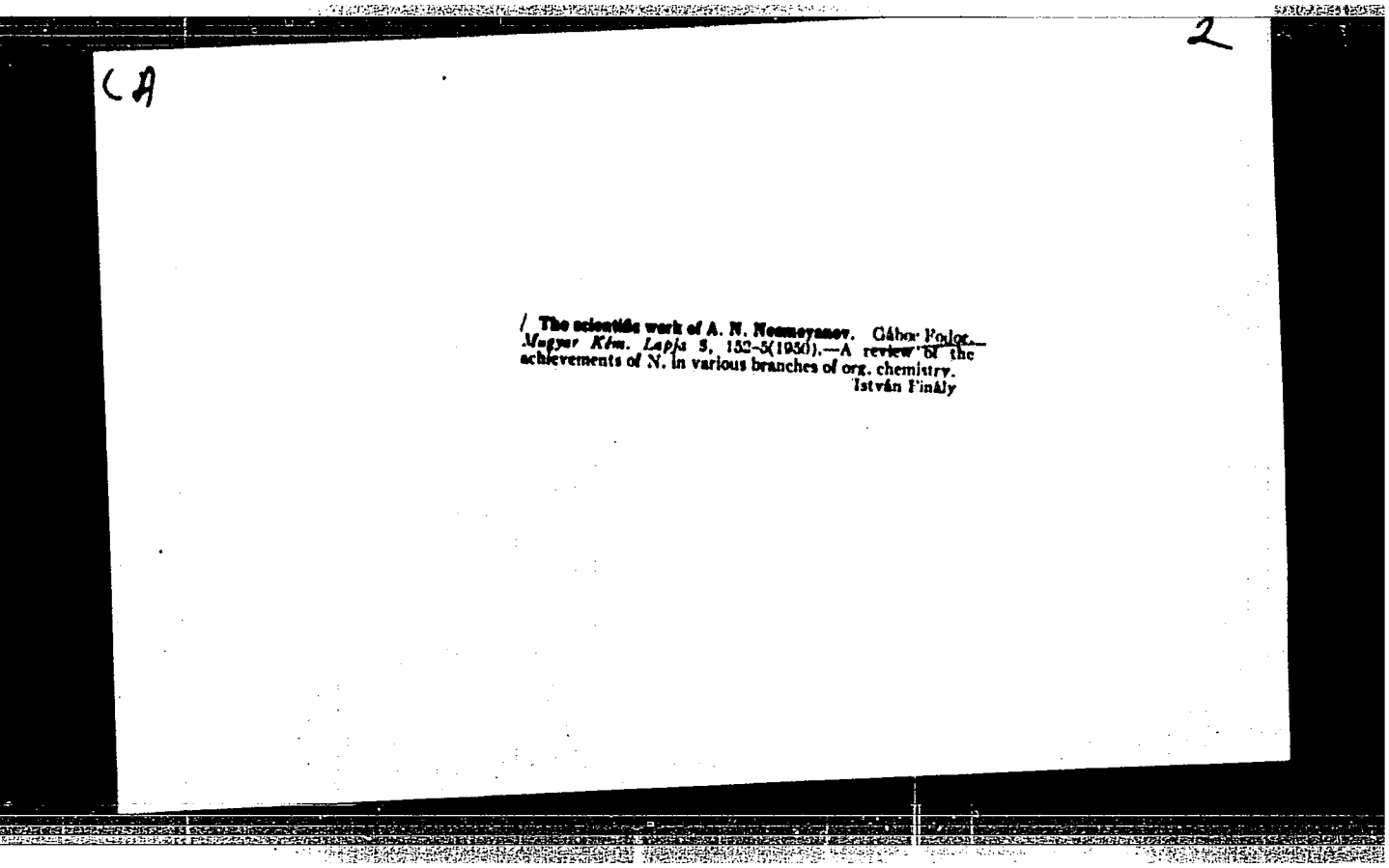
Organic Chemistry

The synthesis of DL-*erythro*-**3,4-dihydroxyphenylserine (noradrenalinecarboxylic acid).** G. Finkly and I. Kiss (Univ., Szeged, Hung.). *Acta Univ. Szeged., Chem. et Phys.* **3**, 25-30(1958)(in English).—The previously unknown racemate of noradrenalinecarboxylic acid (I) (same configuration as ephedrine) was prepd. by the Hartung amino alc. synthesis. On treatment with alkali, I decarboxylated easily. Enzymes, such as an ext. of guinea-pig kidney, also partly decarboxylated I, proving that its behavior differs from that of the racemates of the isomeric pseudoephedrine series. *3,4-(HO)$_2$C$_6$H$_3$COCH$_2$CO$_2$Et* (II), b$_{10}$ 110-20°, was obtained by introducing BF$_3$ gas into 22 g. pyrocatechol in 53 g. EtII malonate at 35-40° and cooling with ice until the increase in wt. was 28 g., heating on a steam bath 40 min., pouring with stirring into 50 g. NaOAc in 200 ml. water, extg. the oily suspension with BuOH or ether, drying the solvent on fused Na$_2$SO$_4$, and distg. *in vacuo*. *Et (o-isonitroso-3,4-dihydroxybenzoyl)acetate* (III) was prepd. by adding 18 g. 20% ether soln. of HCl to 25 g. II in 100 ml. dry ether, then, slowly at 0°, 11 g. freshly-distd. BuONO in 35 ml. abs. ether, keeping overnight in a refrigerator, and removing the solvent at 30°. *Et noradrenalinecarboxylate* (IV), m. 112-20° (decompn.), was obtained by hydrogenating 20.3 g. III in 120 ml. abs. EtOH over Pd-charcoal in the usual manner 12 hrs. in the presence of 40 ml. 4.0 *N* HCl in abs. EtOH, filtering, evapg. *in vacuo* at 50°, dissolving the residue in abs. EtOH, evapg. again, and drying in a desiccator. In the alk. hydrolysis of IV, 2.8 g. IV was shaken with 60 ml. NaOH soln. 1 hr. in a current of H, neutralized with HCl, shaken again in a current of H, and filtered. The 0.1 g. 14% Pd charcoal in a current of H, decolorized with product was noradrenaline, proving that decarboxylation took place. When 3 g. IV was hydrolyzed in 50 ml. *N* HCl in a current of H at 50° for 1 hr., treated further as above, and the soln. of the product treated with the decarboxylase of guinea-pig kidney, in the case of the threo derivs. obtained by sapon., no CO_2 formation was observed, whereas the substances obtained by sapon. of acidified erythro compds. generally developed measurable amts. of CO_2. The product obtained in this acid hydrolysis was I.HCl, 3,4-(HO)$_2$C$_6$H$_3$CH(OH)CH(CO$_2$H)NH$_2$.HCl with the *erythro* structure.

István Finkly



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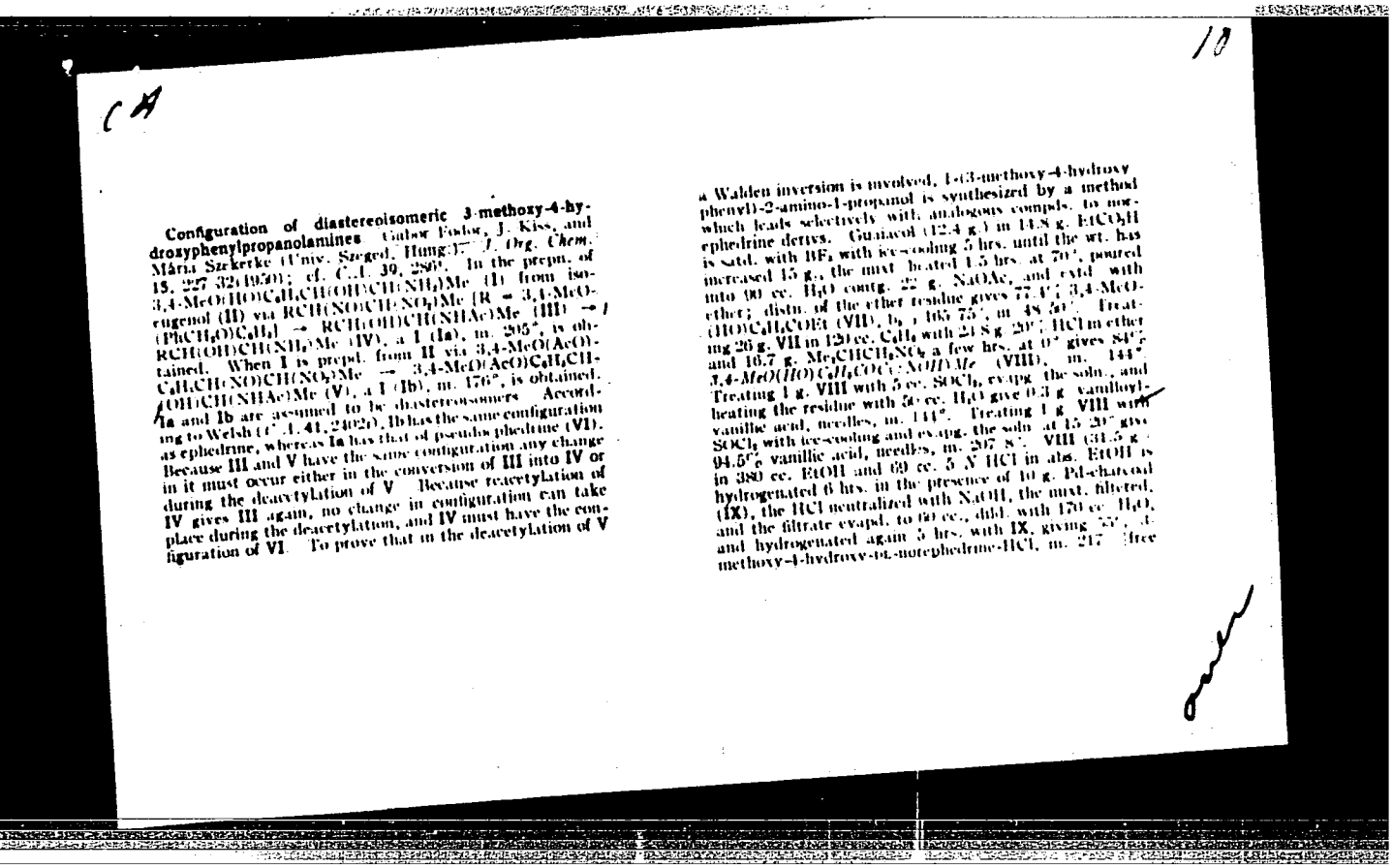
The scientific work of A. N. Nesmeyanov. Gábor Pulay. *Magyar Kém. Lapja* 5, 152–5(1950).—A review of the achievements of N. in various branches of org. chemistry.
István Finály



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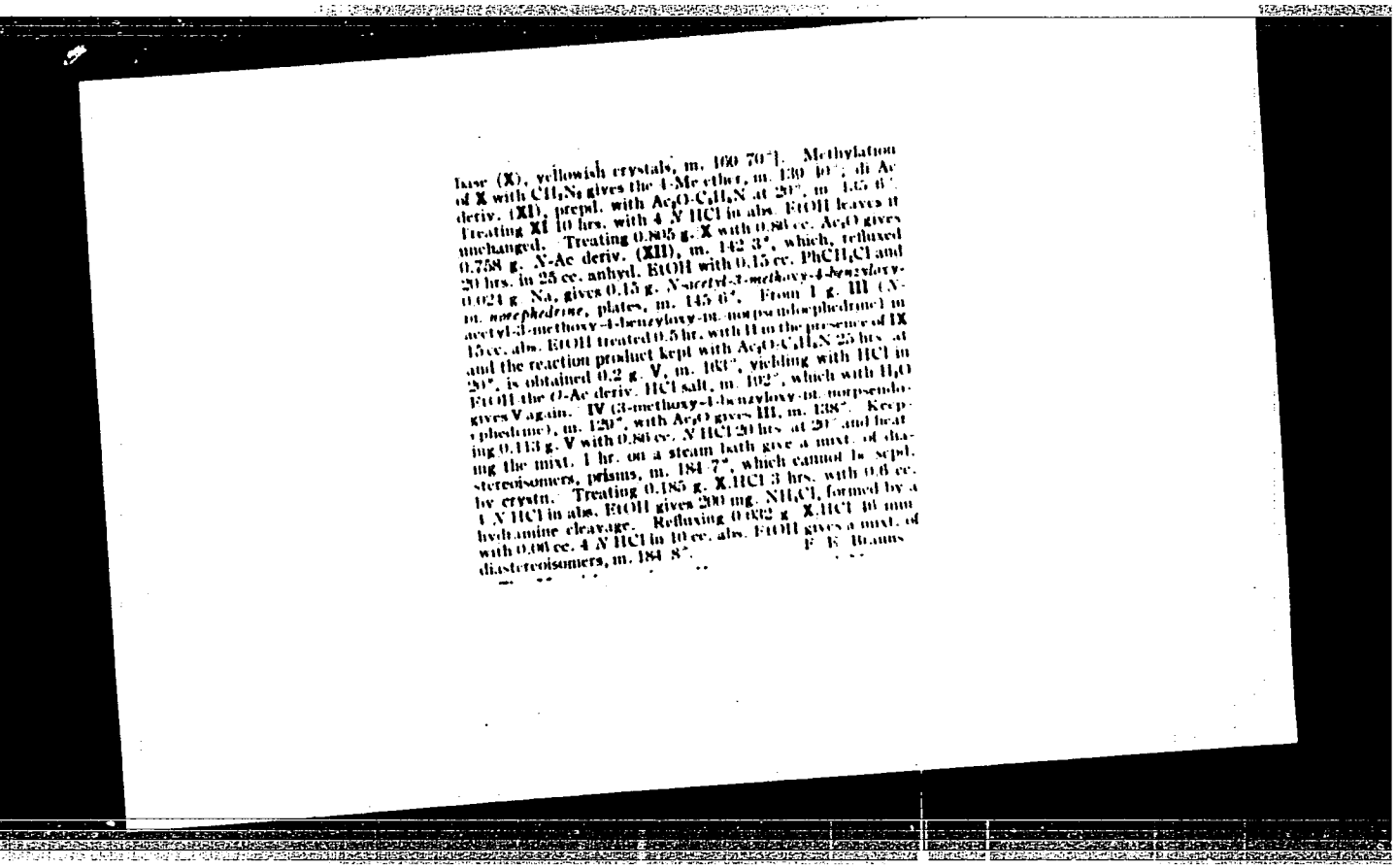
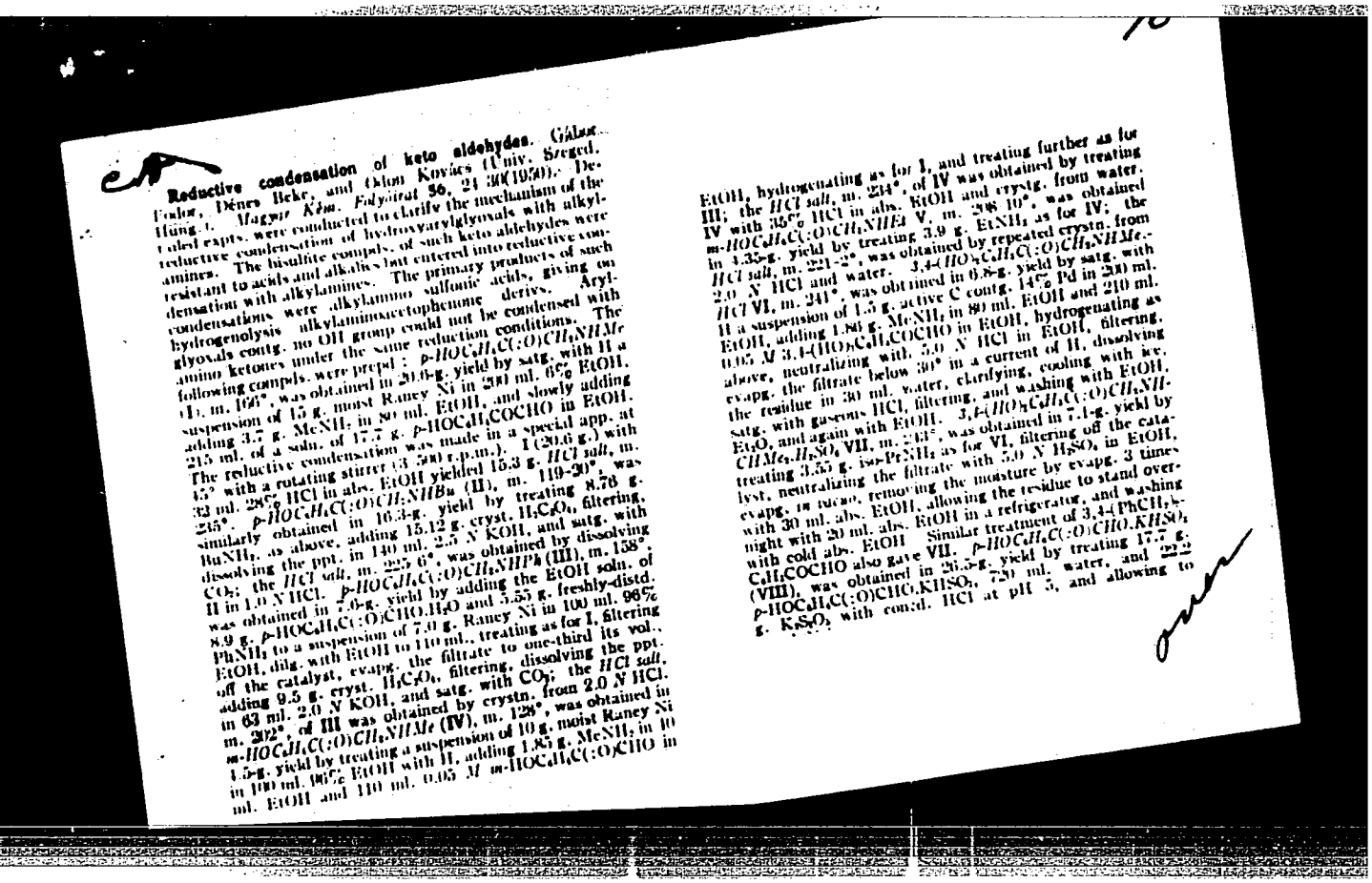
Configuration of diastereoisomeric 3-methoxy-4-hydroxyphenylpropanolamines. Gabor Fodor, J. Kiss, and Mária Szekerke (Univ. Szeged, Hung.). *J. Org. Chem.* 15, 227-32 (1950); cf. *C.A.* 39, 2805. In the prepn. of 3,4-MeO(HO)C_6H_3CH(OH)CH(NH_2)Me (I) from isoeugenol (II) via RCH(NO)CH:NO_2)Me (R = 3,4-MeO(PhCH$_2$O)C_6H_3 → RCH(OH)CH(NHAc)Me (III) → RCH(OH)CH(NH_2)Me (IV), a I (Ia), m. 205°, is obtained. When I is prepd. from II via 3,4-MeO(AcO)C_6H_3CH:NO)CH(NO_2)Me → 3,4-MeO(AcO)C_6H_3CH(OH)CH(NHAc)Me (V), a I (Ib), m. 176°, is obtained. Ia and Ib are assumed to be diastereoisomers. According to Welsh (*C.A.* 41, 2402*e*), Ib has the same configuration as ephedrine, whereas Ia has that of pseudoephedrine (VI). Because III and V have the same configuration any change in it must occur either in the conversion of III into IV or during the deacetylation of V. Because reacetylation of IV gives III again, no change in configuration can take place during the deacetylation, and IV must have the configuration of VI. To prove that in the deacetylation of V a Walden inversion is involved, l-(3-methoxy-4-hydroxyphenyl)-2-amino-1-propanol is synthesized by a method which leads selectively with analogous compds. to normal ephedrine derivs. Guaiacol (12.4 g.) in 14.8 g. EtCO$_2$H is satd. with BF_3 with ice-cooling 5 hrs. until the wt. has increased 15 g., the mixt. heated 1.5 hrs. at 70°, poured into 90 cc. H_2O contg. 22 g. NaOAc, and extd. with ether; distn. of the ether residue gives 77.4% 3,4-MeO(HO)C_6H_3COEt (VII), b$_{15}$ 165-75°, m. 48.5°. Treating 26 g. VII in 120 cc. C_6H_6 with 24.8 g. Br_2 at 0° and 16.7 g. $Me_2CHCH_2NO_2$ a few hrs. at 0° gives 84% *3,4-MeO(HO)*C_6H_3*COC(NO)Me* (VIII), m. 144°. Treating 1 g. VIII with 5 cc. $SOCl_2$ evapg. the soln., and heating the residue with 5 cc. H_2O give 0.3 g. vanilloylvanillic acid, needles, m. 141°. Treating 1 g. VIII with $SOCl_2$ with ice-cooling and evapg. the soln. at 15-20° gives 94.5% vanillic acid, needles, m. 207-8°. VIII (31.5 g.) in 380 cc. EtOH and 69 cc. 5 *N* HCl in abs. EtOH is hydrogenated 6 hrs. in the presence of 10 g. Pd-charcoal (IX), the HCl neutralized with NaOH, the mixt. filtered, and the filtrate evapd. to 90 cc., dild. with 170 cc. H_2O, and hydrogenated again 5 hrs. with IX, giving 55% dl-methoxy-4-hydroxy-α-norephedrine-HCl, m. 217°. Free



base (X), yellowish crystals, m. 160–70°]. Methylation of X with CH_2N_2 gives the 4-Me ether, m. 130–40°; di Ac deriv. (XI), prepd. with Ac_2O-C_5H_5N at 20°, m. 145–6°. Treating XI 10 hrs. with 4 *N* HCl in abs. EtOH leaves it unchanged. Treating 0.815 g. X with 0.81 cc. Ac_2O gives 0.758 g. *N*-Ac deriv. (XII), m. 142–3°, which, refluxed 20 hrs. in 25 cc. anhyd. EtOH with 0.15 cc. $PhCH_2Cl$ and 0.024 g. Na, gives 0.15 g. *N-acetyl-3-methoxy-4-benzyloxy-*m. *norephedrine*, plates, m. 145–6°. From 1 g. III (*N*-acetyl-3-methoxy-4-benzyloxy-m.-norpseudoephedrine) in 15 cc. abs. EtOH treated 0.5 hr. with H in the presence of IX and the reaction product kept with Ac_2O-C_5H_5N 25 hrs. at 20°, is obtained 0.2 g. V, m. 181°, yielding with HCl in EtOH the O-Ac deriv. HCl salt, m. 192°, which with H_2O gives V again. IV (3-methoxy-4-benzyloxy-m. norpseudoephedrine), m. 120°, with Ac_2O gives III, m. 138°. Keeping 0.113 g. V with 0.86 cc. *N* HCl 20 hrs. at 20° and heating the mixt. 1 hr. on a steam bath give a mixt. of diastereoisomers, prisms, m. 184–7°, which cannot be sepd. by crystn. Treating 0.185 g. X.HCl 3 hrs. with 0.6 cc. 1 *N* HCl in abs. EtOH gives 200 mg. NH_4Cl, formed by a hydramine cleavage. Refluxing 0.082 g. X.HCl 40 min. with 0.00 cc. 4 *N* HCl in 10 cc. abs. EtOH gives a mixt. of diastereoisomers, m. 184–8°.

F. E. Braams



Reductive condensation of keto aldehydes. Gábor Fodor, Dénes Ilcke, and Ákos Kovács (Univ. Szeged, Hung.). *Magyar Kém. Folyóirat* **56**, 21–30(1950). Detailed expts. were conducted to clarify the mechanism of the reductive condensation of hydroxyarylglyoxals with alkylamines. The bisulfite compds. of such keto aldehydes were resistant to acids and alkalies but entered into reductive condensation with alkylamines. The primary products of such condensations were alkylammo sulfonic acids, giving on hydrogenolysis alkylaminoacetophenone derivs. Arylglyoxals contg. no OH group could not be condensed with amino ketones under the same reduction conditions. The following compds. were prepd.: *p*-$HOC_6H_4C(:O)CH_2NHMe$ (I), m. 166°, was obtained in 20.6-g. yield by satg. with H a suspension of 15 g. moist Raney Ni in 200 ml. 6% EtOH, adding 3.7 g. $MeNH_2$ in 80 ml. EtOH, and slowly adding 215 ml. of a soln. of 17.7 g. *p*-HOC_6H_4COCHO in EtOH. The reductive condensation was made in a special app. at 45° with a rotating stirrer (3 500 r.p.m.). I (20.6 g.) with 33 ml. 28% HCl in abs. EtOH yielded 15.3 g. *HCl salt*, m. 245°. *p*-$HOC_6H_4C(:O)CH_2NHBu$ (II), m. 119–20°, was similarly obtained in 16.3-g. yield by treating 8.76 g. $BuNH_2$, as above, adding 15.12 g. cryst. $H_2C_2O_4$, filtering, dissolving the ppt. in 140 ml. 2.5 *N* KOH, and satg. with CO_2; the *HCl salt*, m. 225.6°, was obtained by dissolving II in 1.0 *N* HCl. *p*-$HOC_6H_4C(:O)CH_2NHPh$ (III), m. 158°, was obtained in 7.0-g. yield by adding the EtOH soln. of 8.9 g. *p*-$HOC_6H_4C(:O)CHO.H_2O$ and 5.55 g. freshly-distd. $PhNH_2$ to a suspension of 7.0 g. Raney Ni in 100 ml. 96% EtOH, dilg. with EtOH to 110 ml., treating as for I, filtering off the catalyst, evapg. the filtrate to one-third its vol., adding 9.5 g. cryst. $H_2C_2O_4$, filtering, dissolving the ppt. in 63 ml. 2.0 *N* KOH, and satg. with CO_2; the *HCl salt*, m. 202°, of III was obtained by crystn. from 2.0 *N* HCl. *m*-$HOC_6H_4C(:O)CH_2NHMe$ (IV), m. 128°, was obtained in 1.5-g. yield by treating a suspension of 10 g. moist Raney Ni in 100 ml. 96% EtOH with H, adding 1.85 g. $MeNH_2$ in 10 ml. EtOH and 110 ml. 0.05 *M* *m*-$HOC_6H_4C(:O)CHO$ in EtOH, hydrogenating as for I, and treating further as for III; the *HCl salt*, m. 234°, of IV was obtained by treating IV with 35% HCl in abs. EtOH and crystg. from water. *m*-$HOC_6H_4C(:O)CH_2NHEt$ V, m. 208.10°, was obtained in 3.35-g. yield by treating 3.9 g. $EtNH_2$ as for IV; the *HCl salt*, m. 221–2°, was obtained by repeated crystn. from 2.0 *N* HCl and water. 3,4-$(HO)_2C_6H_3C(:O)CH_2NHMe$.*HCl* VI, m. 241°, was obtained in 0.8-g. yield by satg. with H a suspension of 1.5 g. active C contg. 14% Pd in 200 ml. EtOH, adding 1.86 g. $MeNH_2$ in 80 ml. EtOH and 210 ml. 0.05 *M* 3,4-$(HO)_2C_6H_3COCHO$ in EtOH, hydrogenating as above, neutralizing with 5.0 *N* HCl in EtOH, filtering, evapg. the filtrate below 30° in a current of H, dissolving the residue in 30 ml. water, clarifying, cooling with ice, satg. with gaseous HCl, filtering, and washing with EtOH, Et_2O, and again with EtOH. 3,4-$(HO)_2C_6H_3C(:O)CH_2NH$-$CHMe_2.H_2SO_4$ VII, m. 241°, was obtained in 7.1-g. yield by treating 3.55 g. iso-$PrNH_2$ as for VI, filtering off the catalyst, neutralizing the filtrate with 5.0 *N* H_2SO_4 in EtOH, evapg. in vacuo, removing the moisture by evapg. 3 times with 30 ml. abs. EtOH, allowing the residue to stand overnight with 20 ml. abs. EtOH in a refrigerator, and washing with cold abs. EtOH. Similar treatment of 3,4-$PhCH_2$-C_6H_3COCHO also gave VII. *p*-$HOC_6H_4C(:O)CHO.KHSO_3$ (VIII), was obtained in 26.5-g. yield by treating 17.7 g. *p*-$HOC_6H_4C(:O)CHO.KHSO_3$, 750 ml. water, and 22.2 g. $K_2S_2O_5$ with concd. HCl at pH 5, and allowing to

stand 24 hrs. VIII was also obtained in 22.6-g. yield by refluxing 24.15 g. cryst. *p*-$HOC_6H_4CH(OH)CCl_3$ and 720 ml. water with 15 g. coarse $CaCO_3$, allowing to stand a day, filtering, adding 22.2 g. $K_2S_2O_5$, and allowing to stand 24 hrs. A 3rd method consists of clarifying with active C an aq. soln. of *p*-$HOC_6H_4C(:O)CHO$ (obtained by oxidizing *p*-HOC_6H_4Ac with SeO_2 as described in *C.A.* **43**, 4240*b*), adding 44.4 g. $K_2S_2O_5$, then concd. HCl to pH 5, allowing to stand 24 hrs., and crystg. from water in the presence of 10% $K_2S_2O_5$. *3-(p-Hydroxyphenyl)-quinoxaline* (**IX**), m. 201°, was obtained in 3.4-g. yield by boiling 5.4 g. VIII in 65 ml. hot water with 2.38 g. *o*-$C_6H_4(NH_2)_2$ 15 min., allowing to stand a day, filtering, and crystg. from dil. MeOH. IX was resistant to mineral and org. acids, alkalies, and acid carbonates. *m-HOC₆H₄C(:O)CHO.KHSO₃* (**X**) (5.6 g.) of 96% purity was obtained by evapg. the aq. soln. of *m*-$HOC_6H_4C(:O)CHO$ [produced from *m*-HOC_6H_4Ac by oxidizing with SeO_2 (*loc. cit.*)] to 35 ml., adding 22.2 g. $K_2S_2O_5$ in 70 ml. hot water, adding concd. HCl to pH 5, allowing to stand, and crystg. from water. *p-HOC₆H₄C(:O)CH(NHMe)SO₃K* (**XI**), was obtained in 75% yield by dissolving 27 g. VIII in 36 ml. 18.6% $MeNH_2$ soln., adding 194 ml. 84% EtOH, allowing to stand overnight, filtering, and washing with 20 ml. $MeNH_2$ in EtOH. *p-HOC₆H₄C(:O)CH(NHPh)SO₃K* (**XII**), m. 239-41° (decompn.), was obtained in 88% yield by refluxing 27 g. VIII, 10.2 g. freshly-distd. $PhNH_2$, and 150 ml. water 30 min., allowing to stand overnight, clarifying with 1% active C, filtering, evapg. the mother liquor, filtering, and combining both ppts. *p-HOC₆H₄C(:O)CH₂NHMe* (**XIII**), m. 146°, was obtained in 10.7-g. yield by satg. a suspension of 25 g. Raney Ni in 300 ml. 84% EtOH, with H, dissolving 28.4 g. XI in 140 ml. water, dilg. to 215 ml. with 84% EtOH, reducing as described above, filtering off the catalyst, treating the filtrate with 11.5 g. 87% H_3PO_4, allowing to stand overnight, filtering, dissolving the ppt. in 120 ml. water, clarifying with 2% active C, filtering, and adding 28% NH_4OH to pH 9.5. *p-HOC₆H₄C(:O)CH₂NHPh.HCl* (**XIV**), m. 199°, was obtained in 6.8-g. yield by satg. with H a suspension of 25 g. Raney Ni in 300 ml. 80% EtOH, dissolving 34.5 g. XII in 140 ml. lukewarm water, dilg. with 80% EtOH to 215 ml., reducing as above, filtering off the catalyst, evapg. the filtrate *in vacuo* to 200 ml., adding 36.9 g. cryst. $H_2C_2O_4$, allowing to stand several days, filtering, and satg. the soln. of the crystals in 200 ml. 2.0 *N* KOH with CO_2. The reductive condensation of VIII without sepn. of the intermediate product gave I, m. 147° (this sample was shown to be "identical" (mixed m.p.) with the previously prepd. sample of I, m. 166°) in 11.7-g. yield by satg. with H a suspension of 17 g. moist Raney Ni in 310 ml. 84% EtOH, dissolving separately 27 g. VIII in 110 ml. water with cooling, adding 7.75 g. $MeNH_2$ as a 40% aq. soln., dilg. with 84% EtOH to 215 ml., adding to the catalyst until 1 mol. H is absorbed, filtering off the catalyst, adding 36 g. 87% H_3PO_4 to the filtrate, chilling 24 hrs. in the refrigerator, filtering, dissolving the residue in 240 ml.

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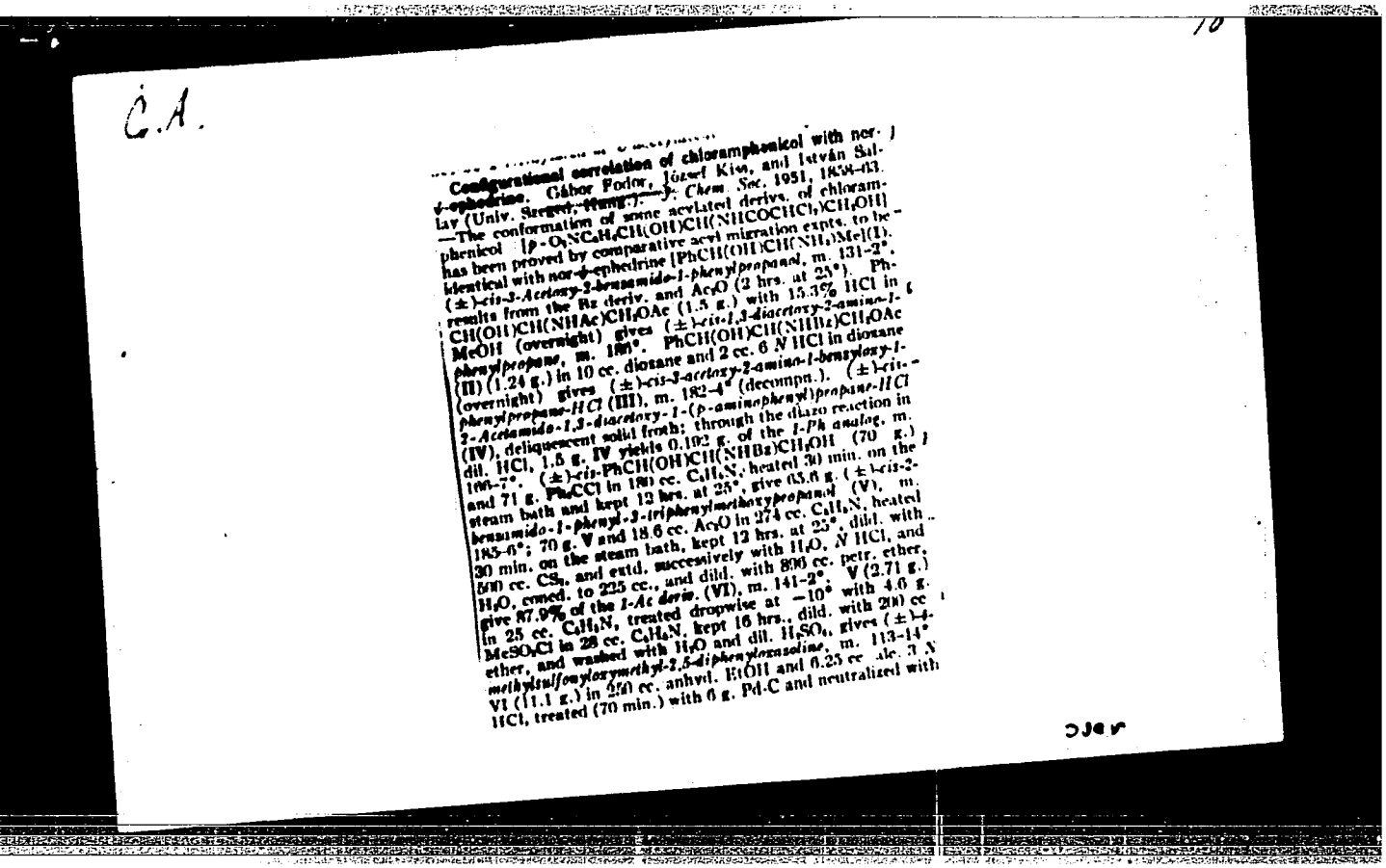
Acyl migration O → N in the diastereomeric 2-aminocyclohexyl benzoates. Gábor Fodor and J. Kiss (Univ., Szeged, Hung.). *J. Am. Chem. Soc.* 72, 3495-7(1950).—*cis*-2-Benzamidocyclohexanol (I) (2.5 g.) in 8.7 cc. abs. EtOH and 5 cc. 5 *N* abs. EtOH-HCl, heated 2 hrs. at 100°, gives 46% unchanged I and 45% *cis*-2-*aminocyclohexyl benzoate*·HCl (II), m. 228°. The *trans*-isomer (III) of I similarly gives 43% recovered III and 40% of the *trans-isomer* (IV) of II, m. 274°. II (0.280 g.) in 20 cc. H_2O, treated with 0.85 cc. *N* NaOH, gives an oil which, on scratching and addn. of excess alkali, yields 0.173 g. I; 0.220 g. IV with 0.9 cc. NaOH gave an oil which did not crystallize until the further addn. of 0.6 cc. alkali, when it yielded 0.120 g. III. The intermediate oil from II is *cis*-2-aminocyclohexyl benzoate, which can be isolated by immediate tosylation in C_5H_5N to the *N-tosyl deriv.* (V), m. 180°. *cis*-2-Aminocyclohexanol·HCl (0.691 g.) in 10 cc. H_2O and 0.8 g. *p*-$MeC_6H_4SO_2H$ in 3 cc. C_5H_5N, stirred with excess alkali, give 0.786 g. of the *N-tosyl deriv.* (VI), m. 152-4°; with BzCl in C_5H_5N it yields V. Similarly 1.125 g. IV yields 0.9 g. of the *trans-isomer* (VII) of V, m. 168-70°. The *trans-isomer* of VI, m. 128°, gives VII with BzCl in C_5H_5N. A mechanism of the O → N acyl migration is presented.

C. J. West



C.A.

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Configurational correlation of chloramphenicol with nor-ψ-ephedrine. Gábor Fodor, József Kiss, and István Salay (Univ. Szeged, Hung.). *J. Chem. Soc.* 1951, 1850–63.—The conformation of some acylated derivs. of chloramphenicol [*p*-$O_2NC_6H_4CH(OH)CH(NHCOCHCl_2)CH_2OH$] has been proved by comparative acyl migration expts. to be identical with nor-ψ-ephedrine [$PhCH(OH)CH(NH_2)Me$] (I). (±)-*cis*-3-*Acetoxy*-2-*benzamido*-1-*phenylpropanol*, m. 131–2°, results from the Bz deriv. and Ac_2O (2 hrs. at 25°). Ph-$CH(OH)CH(NHAc)CH_2OAc$ (1.5 g.) with 15.3% HCl in MeOH (overnight) gives (±)-*cis*-1,3-*diacetoxy*-2-*amino*-1-*phenylpropane*, m. 180°. $PhCH(OH)CH(NH_2)CH_2OAc$ (II) (1.24 g.) in 10 cc. dioxane and 2 cc. 6 *N* HCl in dioxane (overnight) gives (±)-*cis*-3-*acetoxy*-2-*amino*-1-*benzyloxy*-1-*phenylpropane*-*HCl* (III), m. 182–4° (decompn.). (±)-*cis*-2-*Acetamido*-1,3-*diacetoxy*-1-(*p*-*aminophenyl*)*propane*-*HCl* (IV), deliquescent solid froth; through the diazo reaction in dil. HCl, 1.5 g. IV yields 0.102 g. of the 1-*Ph analog*, m. 100–7°. (±)-*cis*-$PhCH(OH)CH(NHBz)CH_2OH$ (70 g.) and 71 g. Ph_3CCl in 180 cc. C_5H_5N, heated 30 min. on the steam bath and kept 12 hrs. at 25°, give 65.6 g. (±)-*cis*-2-*benzamido*-1-*phenyl*-3-*triphenylmethoxypropanol* (V), m. 185–6°; 70 g. V and 18.6 cc. Ac_2O in 274 cc. C_5H_5N, heated 30 min. on the steam bath, kept 12 hrs. at 25°, dild. with 500 cc. CS_2, and extd. successively with H_2O, *N* HCl, and H_2O, concd. to 225 cc., and dild. with 800 cc. petr. ether, give 87.9% of the 1-*Ac deriv.* (VI), m. 141–2°. V (2.71 g.) in 25 cc. C_5H_5N, treated dropwise at −10° with 4.6 g. $MeSO_2Cl$ in 28 cc. C_5H_5N, kept 16 hrs., dild. with 200 cc. ether, and washed with H_2O and dil. H_2SO_4, gives (±)-4-*methylsulfonyloxymethyl*-2,5-*diphenyloxazoline*, m. 113–14°. VI (11.1 g.) in 250 cc. anhyd. EtOH and 6.25 cc. alc. 7 *N* HCl, treated (70 min.) with 6 g. Pd-C and neutralized with

C.A

Configuration of diastereoisomeric 2-aminocyclohexanols and a suggested mechanism for acyl migration N→O. Gábor. Fodor and I. Kiss (Univ. Szeged, Hung.). *Acta Chim. Hung.* 1, 130-6 (1951) (in English). *2-Acetamidocyclohexanol* (I), m. 112-4°, was obtained in 18-g. yield by treating a suspension of 40 g. o-AcNHC$_6$H$_{11}$OH in 400 ml. EtOH with 50 g. wet Raney Ni in an autoclave 30-50 min. with H under 70-80 kg. sq. cm. pressure at 180° with continuous shaking, allowing to stand 2 hrs. at this temp. and pressure, filtering, evapg. the filtrate in vacuo at 35-40°, and boiling the residue with 100 ml. MeCO a few min. *dl-cis-2-Benzamidocyclohexanol* (II), m. 180°, was obtained in 17.2-g. yield by refluxing 18 g. I with 100 ml. 18% HCl 2 hrs., evapg. the soln., dilg. with water to 500 ml., and benzoylating by the Schotten-Baumann reaction. *dl-trans-2-Benzamidocyclohexanol* (III) was obtained by ammonolysis of 2-chlorocyclohexanol, followed by a Schotten-Baumann benzoylation of the amino alc. produced (cf. MacCasland, *et al.*, C. A. 43, 3372g). When II was treated with 2 moles HCl, 95% *dl-cis-O-benzoyl-2-aminocyclohexanol-HCl*, m. 228°, was obtained. If the amt. of HCl added was increased to 10 or 35 moles, the yields were 32 and 50%, resp. Similar treatment of III gave yields below 4.4%. When II or III was treated 2 hrs. in a sealed tube at 100°, 2 moles HCl was sufficient to reach a yield of 50%. These results are interpreted by assuming that the acyl shift N→O occurs in 2 steps. First an unstable N-acylamide-HCl is formed easily in nonpolar solvents, such as CeH$_6$. This product is decompd. or rearranged in polar solvents or by heating. In alc. the equil. between amide and amide salt is shifted toward the amide, and an excess of HCl shifts it toward the amide salt. The 2nd step of the acyl shift is a rearrangement to an O-acylamide salt, the rate of which is detd. by the distance between the rearranging groups. The varying distance between the substituents may also explain the occurrence of an incomplete acyl migration even for the cis form. The marked difference between the rates of N→O acyl migration of the stereoisomeric 2-benzamidocyclohexanols at room temp. is evidence of their steric structure.

István Finály

Configurational correlation of pharmacologically active alcohols. I. Conversion of *N*-methyl-DL-ephedrine into DL-ephedrine and *d*-ephedrine. Gábor Fodor, Károly Kocka, and László Szekeres (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 1, 377-84(1951).—Pharmacologically active DL-*N*-methylephedrine (I) was converted *via N*-cyano-O-benzoyl-DL-ephedrine (II) into DL-ephedrine (III) and *d*-ephedrine (IV) providing proof of the respective configurational correlation. BzCl (15 g.) was added to 1 in $CHCl_3$ and refluxed to give O-Bz deriv. (V), m. 75° after crystn. *N*-cyanoderiv. of V (VI), m. 78-9°, was obtained from V and BrCN at room temp. Alkaline hydrolysis of VI (10 g.) gave II (4 g.), m. 72-8°, from petr. ether. Refluxing I (5 g.) with *p*-NO_2BzCl gave I·HCl (2.6 g.), m. 203-8°, and 1,4-nitrobenzoate, m. 78-81°. Evapn. of II *in vacuo* followed by cooling in petr. ether gave O-(*p*-NO_2Bz) deriv. of I, m. 81°. Thermal degradation of I followed by addn. of NaOH liberated Me_2NH as proved by a mixed m.p. detn. of its *p*-$CH_3C_6H_4SO_3$ deriv. II was refluxed with HCl and treated with NaOH to give an oily base convertible by HCl-EtOH to 3,4-dimethyl-5-phenyl-2-imino-oxazolidinium chloride (VII), m. 235° from $MeCO$-MeOH. IV, m. 117-8° was prepd. by boiling VII with 17% NaOH. III. Conversion of DL-norephedrine into 4-hydroxy- and 4-methoxy-DL-norephedrine. Gábor Fodor, József Kiss, Éva Feher, and Dezső Bánfi. *Ibid.* 385-9.—This paper deals with the correlation of the configuration of *p*-hydroxynorephedrine (I) with that of DL-norephedrine (II) and, therefore, with that of DL-ephedrine. II nitrate (10.6 g.) was added with stirring to cold HNO_3-H_2SO_4 to give *p*-nitronorephedrine nitrate (1.65 g.), m. 207° (from MeOH-$CHCl_3$), free base (III), m. 159°. Bz deriv. of III, m. 160°, was washed with dil. acid and H_2O, and reduced with Pd-C to *p*-amino-*N*-benzoyl-DL-norephedrine (IV), m. 176°. *p*-Hydroxy-*N*-benzoyl-DL-norephedrine (V), m. 176°, was prepd. from IV with HNO_2 and from *p*-$HOC_6H_4CH_2CH(NH_2)CH_3OH$ with BzCl. V and CH_2N_2 gave the corresponding Me ether (VI), m. 145-50° (from 95% EtOH). *N*-Acetyl-DL-norephedrine in HNO_3-H_2SO_4 gave the *p*-NO_2 deriv., m. 140° (from EtOH-Et_2O then from CH_3-EtOH). VI showed no depression in m.p. when mixed with the product from the benzoylation of DL-1-(4-CH_3O-$C_6H_4CH_2CH(NH_2)CH_3OH$. W. T. Somerford

FODOR, GABOR

Anomalous nitration of *p*-methoxypropiophenone. László Szekeres and Gábor Fodor (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 1, 201–4 (1951)(in English).—Dropwise addn. in 100 min. of 100 g. *p*-$MeOC_6H_4COEt$ (I) to 500 g. HNO_3 (d. 1.5) below 1°, stirring 15 min., and pouring on ice gave an oil which crystd. to give 75 g. crude *2,4-dinitroanisole* (II), m. about 60°; 1 recrysta. from MeOH and 1 from C_6H_6 gave 20–5 g. yellow needles, m. 95–7°. II with $Na_2Cr_2O_7$ and H_2SO_4 gave *2,4-dinitrophenol*, m. 114–16°. II hydrogenated over Pd-C in MeOH contg. HCl absorbed 102% H (calcd. for reduction of 2 nitro groups). II (8.8 g.) in 24 ml. hot AcOH added to 20.8 g. Sn dissolved by heating in 108 ml. concd. HCl and 24 ml. H_2O, the mixt. heated 1 hr. at 100°, cooled, made alk., extd. 6 times with C_6H_6, and the exts. evapd., gave 5.3 g. black oil, which crystd. from MeOH to 1.2 g. *2-amino-4-nitroanisole* (III), orange crystals, m. 115–17°; acetylated by Ac_2O at room temp. to the *N-Ac deriv.*, m. 178°. II (20 g.) in 100 ml. EtOH treated dropwise at 100° with 5 ml. $N_2H_4.H_2O$ and 8 ml. AcOH in 50 ml. EtOH and heated 30 min. more, gave 19.2 g. $2,4\text{-}(O_2N)_2C_6H_3NHNH_2$, m. 198–9° (from C_6H_6); 2,4-$(O_2N)_2C_6H_3NHN{:}CMe_2$, m. 126–8°. Nitration of I as above at −5° gave almost entirely 3,4-$O_2N(MeO)C_6H_3COEt$ (IV). The mechanism of conversion of I to II is believed to involve nitration of I to IV, oxidation to 3,4-$(O_2N)(MeO)C_6H_3CO_2H$, decarboxylation to *o*-$MeOC_6H_4NO_2$, and nitration to II.

Richard I. Akawie

Synthesis of DL-noradrenaline and of related amino alcohols with a primary amino group. Gábor Fodor, Odon Kovács, and Tibor Mecher (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 1, 395-402(1951)(in English).--A new synthesis of Adrenaline and of related *N*-substituted amino alcs. starting with hydroxyaryl glyoxals was extended to noradrenaline and similar compds. *p*-$HOC_6H_4COCH_2NHCH_2Ph$ (I), m. 131-2°, was prepd. by reducing *p*-HOC_6H_4COCHO hydrate or its $KHSO_3$ addn. product with Raney Ni in the presence of $PhCH_2NH_2$. The products were identical and the yields were 82 and 70%, resp. Reduction of I with Raney Ni gave $PhCH_2NHCH_2CH(C_6H_3OH\text{-}p)OH$ (II), m. 126-9°. Norsynephrine, m. 177-8°, was obtained in excellent yields by reducing (Pd-C) the HCl salts of I or II. A mixt. of $PhCH_2NH_2$ (0.075 mole) and 3,4-$(HO)_2C_6H_3COCHO$ (0.05 mole) was reduced over prehydrogenated Raney Ni to give a 73% yield of 3,4-$(HO)_2C_6H_3COCH_2NHCH_2Ph$, m. 147-8°; HCl salt (III), m. 220-1°. Reduction of II over Pd-C gave noradrenaline (82% yield), m. 188-9°. A mixt. of 3,4-MeO(HO)$C_6H_3COCHO.KHSO_3$ and $PhCH_2NH_2$ was reduced (Raney Ni) to give 75% 3,4-MeO(HO)$C_6H_3COCH_2NHCH_2Ph.HCl$ (IV), m. 221-2°. Reduction (Pd-C) of IV gave $H_2NCH_2CH(OH)C_6H_2(OH)$-OMe-4,3.HCl, m. 192-3°. 3,4-HO(MeO)C_6H_3COCHO (V), m. 120°, was prepd. by refluxing 3,4-AcO(MeO)-C_6H_3COMe with SeO_2. 2-(3-Hydroxy-4-methoxyphenyl)-quinoxaline, m. 142-3° (from dil. EtOH), was prepd. from V and *o*-$C_6H_4(NH_2)_2$ in hot aq. soln. Reduction (Raney Ni) of V with $PhCH_2NH_2$ gave 3,4-HO(MeO)$C_6H_3COCH_2$-$NHCH_2Ph$ (VI), m. 226° (from EtOH). Lower yields were obtained with the glyoxal in stock soln. H_2NCH_2CH-$(OH)C_6H_2(OMe)OH$-4,3.HCl, m. 170-1° (from MeOH-Et_2O) was prepd. by reducing (Pd-C) VI in EtOH. A mixt. of *p*-$HOC_6H_4COCHO.KHSO_3$ and Et_2NH absorbed 1 mole of H (Raney Ni), but only a hydroxy ketone, presumably *p*-$HOC_6H_4COCH_2OH$, was obtained. W. T. S.

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10

Modified synthesis of 2-methyl-4-amino-5-(ethoxymethyl)pyrimidine. G. Fodor, A. Gerecs, I. Kiss, Ya. Kolbuich, Ya. Vein, and E. Kovach (Szeged State Univ., Hung.). *Zhur. Obshchei Khim.* (J. Gen. Chem.) 21, 1897-1902(1951).—The pyrimidine synthesis from esters of enols has been extended to enol ethers. To 23 g. Na wire in 500 ml. C_6H_6 was added 83 g. $EtOCH_2CH_2CN$ and 90 g. HCO_2Et at 8–10°; after 5 hrs. the pptn. of the Na enolate was complete; this was allowed to stand 3 days at 15°, the mixt. treated with 125 g. Me_2SO_4, kept 3 hrs. at 55°, filtered, and the filtrate distd., yielding 32.3 g. *α-methoxymethylene-β-ethoxypropionitrile* (I), b_1 92–5°, b_1 64–71°, b_1 71–92° (the above are the b.ps. of the 3 fractions, all of which gave analyses corresponding to the above and were apparently composed of the 2 geometrical isomeric structures possible for the product). The above Na salt sepd. by centrifuging and treated with $HC(OEt)_3$ in the presence of $PhSO_3H$ in dry Et_2O readily formed the *α-ethoxymethylene analog* (II), an oil which was not purified further. The Na salt with p-$O_2NC_6H_4COCl$ gave 60% *α-p-nitrobenzoxymethylene-β-ethoxypropionitrile*, m. 109–10° (from C_6H_6). I (2.82 g.) and 1.16 g. acetamidine in EtOH let stand 24 hrs. give 66% *2-methyl-4-amino-5-(ethoxymethyl)pyrimidine*, isolated as the *picrate*, m. 181–3°; *free base*, m. 90°. A similar result is obtained from I and acetamidine-HCl treated with an equimol. amt. of EtONa in abs. EtOH; the product may be isolated as the *HCl salt*, m. 209° (from BuOH). The latter procedure with $EtOCH_2C(:CHOAc)CN$ and acetamidine-HCl in C_6H_6 gave *acetamidine acetate*, m. 162–5°, and a good yield of *2-methyl-4-amino-5-(ethoxymethylene)pyrimidine*, after sublimation *in vacuo*. Bromoacetal (21 g.) kept 12 hrs. at room temp. with 4.1 g. NaCN in aq. EtOH in the presence of NaI apparently did not react; heating bromoacetal with KCN and NaI in aq. EtOH to 75° gave only traces of N-contg. products; neither did bromoacetal react with CuCN on heating. Dichromate oxidation of $(EtOCH_2)_2CHOH$ gave *1,3-diethoxy-2-propanone*, b_{20} 95–100°; this (14 g.) shaken with fresh $NaHSO_3$ soln. and extd. with Et_2O gave an oil described as the cyanohydrin(?), which treated in the Et_2O soln. without purification with Ac_2O gave *1,3-diethoxy-2-acetoxy-2-cyanopropane*, b_6 104–6°. No satisfactory method of cleavage of the Ac group was found; even heating with P_2O_5 and $POCl_3$ in pyridine gave only polymeric products so that pure $(EtOCH_2)_2C(OH)CN$ could not be prepd.

G. M. Kosolapoff

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The synthesis of tetrahydroisoquinoline alkaloids under physiological conditions. Ödön Kovács and Gábor Fodor (Univ. Szeged, Hung.). *Chem. Ber.* **84**, 795-801(1951).—Because salsoline (I) always occurs in the plant as a racemate and is therefore probably formed without the action of enzymes, an attempt is made to synthesize I from *3,4-HO-(MeO)*$C_6H_3CH_2CH_2NH_2$ (II) under physiol. conditions. Adding 40 g. $PhCH_2NH_2$ to 45 g. 3,4-MeO(HO)C_6H_3CO-$CHO.KHSO_3$ in 180 cc. H_2O, making up the soln. to 330 cc. with 83% EtOH, adding this soln., dropwise and with vigorous stirring in such a way that 1 mol. H is consumed, to 75 g. Raney Ni in 300 cc. 83% EtOH previously satd. with H at 45°, acidifying the filtered soln. with 0.52 mol. alc. HCl, concg. the soln. *in vacuo* at 50° to 150 cc., and keeping it 24 hrs. give 76% *3,4-MeO(HO)*$C_6H_3COCH_2NHCH_2Ph$.*HCl* (III), m. 230°. Hydrogenating 15.4 g. III in 300 cc. 97.5% AcOH in the presence of 5 g. 10.5% Pd-charcoal until 2 mols. H are absorbed (18 hrs.), adding 3 cc. 70% $HClO_4$ in 30 cc. AcOH, and continuing the hydrogenation at 85° cause the absorption of a 3rd mol. H in 6 min. KOAc in AcOH equiv. to the amt. of $HClO_4$ used is added to the hot filtered soln., which is filtered again, acidified with 5 cc. concd. HCl, and evapd. *in vacuo*, giving 94% *3,4-MeO-(HO)*$C_6H_3CH_2CH_2NH_2$.*HCl* (IV), m. 203-4° (*picrate*, orange-yellow crystals, m. 197-8°). Adding 104 g. 3,4-AcO(MeO)C_6H_3COMe [prepd. in 36% yield according to a slightly modified form of the method of Schneider and Kraft (*C.A.* 17, 85)] to 55 g. SeO_2 dissolved in 300 cc. dioxane and 10 cc. H_2O at 60°, refluxing the mixt. 6 hrs., evapg. the filtered soln. *in vacuo*, stirring the residue 10 hrs. with 800 cc. H_2O on the water bath, and concg. the soln. give a sirup contg. 60.5% 3,4-HO(MeO)C_6H_3COCHO (V), lemon-yellow needles, m. 126°. Adding 1.2 g. o-$C_6H_4(NH_2)_2$ in 10 cc. hot H_2O to 1.8 g. V in 10 cc. H_2O gives 2.18 g. 2-(3-*hydroxy-4-methoxyphenyl)quinoxaline*, m. 142-3°. Reductive condensation of 16 g. $PhCH_2NH_2$ and 18 g. V in 520 cc. EtOH in the presence of 25 g. Raney Ni 45 min. at 45° as described above gives 54% *3,4-HO(MeO)*$C_6H_3COCH_2NH$-CH_2Ph.*HCl*, m. 218°, which (15.4 g.), on further hydrogenation, is converted into 92% II.HCl, m. 196-7° (*picrate*, golden-yellow leaflets, m. 202-3°). II.HCl, IV, 3,4-(MeO)$_2$-$C_6H_3CH_2CH_2NH_2$.HCl (VI), 4-HO$C_6H_4CH_2CH_2NH_2$.HCl (VII), and 3,4-(HO)$_2C_6H_3CH_2CH_2NH_2$.HCl (VIII) are condensed with AcH under conditions used by Schöpf and Bayerle (*C.A.* 29, 1420). A soln. of 0.0125 mol. amine in 20 cc. H_2O and 25 cc. N AcH is made up to 50 cc., kept 72 hrs. at 20° with the AcH content detd. every 24 hrs., evapd. *in vacuo* at 50°, and a part converted into the picrate and the other part recrystd. Whereas VIII gives 70% *dl*-6,7-dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (norsalsoline), m. 181-3° (picrate, m. 204.5-5.5°), and II gives 89% I.HCl, m. 147-9° (picrate, m. 189-91°), IV, VI, and VII give no condensation products. F. E. Brauns

Fodor, G.

2

547-435 : 541.63

No. Stereospecificity in the chemistry of amino alcohols. — *Sztereospecifitás az aminoalkoholok kémiájában* — G. Fodor. (Proceedings of the Chemical Science Department of the Hungarian Academy of Sciences — *A Magyar Tudományos Akadémia Kémiai Osztályának Közleményei* — Vol. I, No. 3—4, 1952, pp. 1—9, 4 figs.)

The study of the stereospecific reactions in the chemistry of amino alcohols has led to the positive result of gaining an insight into the configuration of molecules. Proof could be established by simultaneous research of configurative correlations and the mechanism of reactions that configurations were also identical when the respective compounds were of identical conformation. The problem of the stereo-conformity of amino propanol derivatives has been elucidated and the author has succeeded in recognizing a new transformation bywhich configurations in this group can be easily retained or changed through the recognition of a new stereospecific reaction. *I. Findly*

Hungarian Technical Abst.
Vol. 5 No. 2
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FODOR, GABOR

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V Preparation of nitrosaryl ketones from aminoaryl ketones. István Sallay and Gábor Fodor (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 2, 57–60(1952)(in English).—Adding 1020 g. AcCl to a stirred suspension of 4200 g. $AlCl_3$ and 1200 g. $AcNHPh$ in 5500 ml. CS_2 and working up the mixt. by the procedure of Kunckell [*Ber.* 33, 2641(1900)] yielded 1342 g. (85.3%), *p*-$AcNHC_6H_4Ac$ (I), m. 162–4°. *p*-$H_2NC_6H_4Ac$ (II) (7.18 g.), prepd. from I by K.'s procedure, was diazotized in 20 ml. concd. HCl and 100 ml. H_2O by adding 3.7 g. $NaNO_2$ in 15 ml. H_2O at 0°, the Ca diazotate (III) formed by pouring the soln. onto 10 g. $CaCO_3$ with vigorous stirring, and the III added over 4 min. to an intensively stirred aq. suspension (100 ml.) contg. 75 g. $NaNO_2$, 15 g. $CuSO_4$, giving 10 g. crude *p*-$O_2NC_6H_4Ac$ (IV), m. 68–77°; distn. at 1 mm. pressure yielded pure IV, m. 78–80°. Crude IV was formed in 38% yield by adding III to a soln. of $NaNO_2$, $CuSO_4$ and Na_2SO_3, and in 34% yield by prepg. the diazonium borofluoride from II and treating it with $NaNO_2$, $CuSO_4$ and Cu_2O. IV thiosemicarbazone, m. 229°. M. O. Armstrong

GABOR, Fodor –

Chemical Abst.
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Organic Chemistry

Chem (3)

Decomposition of *N*1-acetylsulfanilyl thiosemicarbazide and hydrazide into 4,4'-diacetamidodiphenyl disulfide. Gábor Fodor and Gyorgy Wilhelm (Univ. Szeged, Hung.). *Acta Chim. Acad. Sci. Hung.* 2, 183–7(1953)(in English).—(*p*-$AcNHC_6H_4)_2S_2$ (I), m. 216°, is obtained in 1.5-g. (55%) yield by heating 4.6 g. *p*-$AcNHC_6H_4SO_2NHNHCSNH_2$ (II) with 8 ml. dry pyridine and 1.84 g. freshly distd. $MeCOCH_2Cl$ in a sealed flask 1 hr. on the steam bath, pouring the liquid into 150 ml. water acidified with a few ml. H_2SO_4, and recrystg. the product repeatedly from 80% Me_2CO, and drying it at 100°. It seems that II undergoes in pyridine disproportionation into I, thus withdrawing it from the reaction with $MeCOCH_2Cl$. This appears to be confirmed by the facts that (a) II yields I in the same expt. at room temp., (b) 1-acetonylpyridinium chloride is isolated from the reaction mixt., (c) II affords I in pyridine soln. (slowly at room temp., readily on heating 24 hrs. to 40°). No N evolution was observed when the latter expt. was conducted in a sealed vessel in a stream of CO_2. It was surprising that II, a deriv. of $NH_2CSNHNH_2$, should almost spontaneously undergo an intramol. oxidation-reduction process. It appears that both the NHNH and the CSH groups confer instability upon the $NH_2CSNH-NH_2$ mol. and the decompn. is probably very complex.

István Finály

11-27-54

FODOR, G.

Chemical Abst.
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Organic Chemistry

Synthesis and structure of 2-hydrazino-4-methylthiazole. Gábor Fodor and György Wittmann (Univ. Szeged, Hung.). *Acta Chimica* [illegible] — 2-Hydrazino-4-methylthiazole (I) [illegible] a 19.8% yield by shaking [illegible] in 300 ml. $CHCl_3$ with 48 ml. $MeCOCH_2Cl$, filtering, and recrystg. the product from 2[illegible] ml. abs. EtOH. I is also prepd. in 31% yield (5.2 g.) by shaking 6 hrs. 12 g. Me_2C:$NNHCSNH_2$, 72 ml. $CHCl_3$, and 2 ml. 5*N* HCl in abs. dioxane and recrystg. the product from 100 ml. abs. EtOH. To prove the structure of I various expts. were carried out. The mercaptotriazine or mercaptoimidazole structure was excluded since the test with $2,4-(O_2N)_2C_6H_3Cl$ gave no evidence of the presence of an SH group in I. The thiazine deriv. described in the literature has properties differing from those of I. I with PhCOCHO gave a S-free deriv. with a high N content, the empirical formula of which agreed with that for a monohydrazone of PhCOCHO (II), but the compd. was not identical with a modification of II described in the literature. A mol. wt. according to Rast yielded the value 171. The existence of this compd. proved that 2 N atoms can be readily liberated from the original compd., corroborating thus the hydrazinothiazole structure as against the theoretically possible 3-amino-2-imino-4-methyl-4-thiazoline. An unexpected mode of conversion of I was also examd. where PhCOCHO reacts as N_2H_4 acceptor.

István Finály

FODOR, G.; KOVACH, E.

No. 1

New synthesis of salsoline. Doklady Akad. Nauk S.S.S.R. 82, 71-4 '52.
(CA 47 no.14:6958 '53) (MLRA 5:2)

1. Szeged Univ., Hung.

Salsoline produces a very high tension on smooth muscle tissue. It has therefore been adopted as a medicinal and included in the Soviet pharmacopeia. The synthesis consists of oxidizing acetoisovanillone into 4-methoxy-3-oxyphenylglyoxal with SeO_2. This in turn is transformed into alpha-benzylaminoacetoisovanillone by reductive condensation with benzylamine and then by hydrogenation; the benzyl radical is removed and the keto group exchanged for a methyl group. This product is treated with acetaldehyde and yields dl-salsolinephydrochloride. A detailed description of the lab method of prepn is given in the exptl part. Presented by Acad V.M.Rodionow 24 Oct 51.

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FODOR, GABOR

Chemical Abst.
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Organic Chemistry

The stereochemistry of the tropine alkaloids. I. The configuration of tropine and pseudotropine. Gábor Fodor and Károly Nádor (Univ. Szeged, Hung.). *J. Chem. Soc.* 1953, 721–3.—Comparison of the rates of N → O acyl migrations has shown that the relative positions of the nitrogen bridge and the C-3 HO group in nortropine and in norpseudotropine are trans and cis resp. The stereochemical notation for these being fashioned after the steroids and triterpenes, therefore nortropine and norpseudotropine are nortropan-3α-ol and -3β-ol respectively. *N*-Acetylnortropan-3β-ol (I) and 5.15*N* HCl in dioxane yield I.HCl, m. 155°. *N-Benzoylnortropan-3β-ol* (II), m. 160°, is obtained by Schotten-Baumann benzoylation of the nortropan-3β-ol carbamate (III). *O-Benzoylnortropan-3β-ol-HCl* (IV), m. 212°, is obtained from III, *N* HCl, and BzCl heated on a steam bath for 5 hrs. *O-Acetylnortropan-3β-ol-HCl* (V), m. 213–14°, is prepd. by refluxing nortropan-3β-ol-HCl with AcCl for 1 hr. *O-Benzoylnortropan-3α-ol-HCl* (VI), m. 214–16°, is prepd. by refluxing nortropan-3α-ol-HCl with excess BzCl for 5 hrs. *N-Acetylnortropan-3α-ol-HCl* (VII), m. 160–3°, is prepd. from *N*-acetylnortropan-3α-ol and 5*N* HCl in dioxane. *O-Acetylnortropan-3α-ol-HCl* (VIII), m. 192–4°, is obtained from tropan-3α-yl carbamate with 5*N* HCl and AcCl. II on standing for 24 hrs. at 25° with 5*N* HCl in

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dioxane yields IV. IV rearranges to II on treatment with 2*N* NaOH. *N-Benzoylnortropan-3α-ol* is recovered unchanged by treatment with HCl. VI, when treated with *N* NaOH, apparently does not react. I on heating to 160° melts and then solidifies, yielding V. V, when neutralized with 0.1*N* NaOH, gives I.HCl. VII on heating to 160° for 10 min. gives VIII. II. **The configuration of the cocaines.** Gábor Fodor and Odón Kovács. *Ibid.* 724–7.—The configurations of the epimers, ecgonine and pseudoecgonine and cocaine and pseudococaine, have been established by acyl migrations and other stereospecific reactions. The C-3 HO group proved to be in the α-position in ecgonine. *N*-Acetylnor-3β-ecgonine Et ester, m. 112°, gives *O*-acetyl-3β-ecgonine Et ester-HCl on treatment with HCl on the steam bath for 4 hrs. The reverse reaction is observed by treatment of the *O*-Ac HCl salt with NaOEt. *N*-acetyl-3α-ecgonine Et ester, m. 150°, $[\alpha]^{25}_{D}$ −19.4° (*c* 2, EtOH) does not rearrange with HCl in dioxane. 2-α-Benzamidotropan-3-α-ol-HCl (I), m. 228°, $[\alpha]^{25}_{D}$ −40.5°, is obtained by Curtius degradation of (−)-benzoyl-3α-ecgonine and treatment with HCl. I refluxed with MeOH contg. 3.5*N* anhyd. HCl gave 2α-amino-3α-benzoyloxytropane-2HCl, m. 214–15°, $[\alpha]^{25}_{D}$ −21.9° (*c* 2, H_2O). Reverse reaction occurs in *N* NaOH. As a by-product in the prepn. of I, 2-α-aminotropan-3α-ol-2HCl was obtained. Curtius degradation of (−)-*O*-benzoyl-3β-ecgonine yields 2α-benzamidotropan-3β-ol, m. 203°, $[\alpha]^{25}_{D}$ 82° (*c* 2, H_2O), which does not rearrange on heating with HCl in MeOH. Cocaine on reduction with $LiAlH_4$ gives, after treatment with HCl, (−)-3α-ecgoninol (II) HCl salt, m. 270–2°, $[\alpha]^{25}_{D}$ −37.3°; while $LiAlH_4$ reduction of (+)-3β-ecgonine Me ester gives (+)-3β-ecgoninol m. 131–3°, $[\alpha]^{25}_{D}$ 58.3° (*c* 3, H_2O) [HCl salt, m. 232–3°, $[\alpha]^{25}_{D}$ 46.3°)]. When II is treated with PhCHO and $PhSO_3H$ there is obtained *O,O'*-benzylidene-3α-ecgoninol, m. 192–4°, $[\alpha]^{25}_{D}$ −9.43. No benzylidene deriv. is obtained from the 3β-compd. II dehydrates when treated with chloral hydrate and concd. H_2SO_4 at 20°, however the 3β-compd. does not react. K. C. Schreiber

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FODOR, G.

USSR

Condensation of *meso*-halo-1,3-dioxo compounds with ureas. L. Szekeres and G. Fodor (Inst. Org. Chem., Univ. Szeged, Hung.). *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk* 1953, 996–1002.—Refluxing 12 g. BzCHBrCHO in 200 ml. Me_2CO and 8 g. $CO(NH_2)_2$ 40 min., followed by concn. and dild. with H_2O gave 8.3 g. *2-amino-5-benzoyloxazole* (I), m. 180–202° (from EtOH), sol. in dil. HCl and warm 2*N* NaOH; purified by addn. of NH_4OH to its soln. in HCl, it m. 208–10°; evapn. with 20% HCl gave the *HCl salt*, m. 198–200° (from EtOH), while refluxing 1 hr. with Ac_2O gave the *N-Ac deriv.* (Ia), m. 189–91°. The latter treated with hot alc. KOH gave on cooling a ppt. of the K enolate, which with dil. HCl gave the original Ia. Hydrogenation of I over C-Pd in EtOH gave a *compd.* $C_{16}H_{14}N_2O_3$, m. 146–8° (from EtOAc), also formed on similar hydrogenation of $BzCOCH_2NHCONHAc$ (Ib), and unchanged after prolonged boiling with 20% HCl or 20% KOH; it was either *2-amino-5-benzyloxazolidine* or $Ph(CH_2)_2NHCONH_2$. I dissolved in warm 5% NaOH, then cooled, gave the yellow *Na enolate of 1-phenyl-3-ureido-1,2-propanedione* (II). A filtered hot soln. of 1.5 g. I in 25 ml. 2*N* KOH gave with 15 ml. concd. HCl 1.5 g. yellow ppt., decomp. 250°, yielding after purification with AcOH 0.7 g. pure *2,5-dioxo-6-phenylpyrimidine*, decomp. 320°, which, refluxed 2 hrs. in Ac_2O, then dild., gave the *di-Ac deriv.*, m. 83–4° (from dil. Me_2CO). $PhCH_2Cl$ (2 ml.) in dry xylene and 1.5 g. powd. II boiled 8 hrs., and the solid filtered, and washed with C_6H_6, and extd. with boiling H_2O yielded 1 g. crude (0.3 g. pure) *2,5-dioxo-6-phenyl-5-pyrimidine* (III), while the mother liquor gave 0.35 g. *monobenzyl ether*, m. 198–200°, insol. in HCl, sol. in alkalies, thus indicating readily enolization of the oxo group. The ether refluxed 5 hrs. with AcOH-HBr gave the original III. Ia in warm EtOH treated with concd. aq. KOH, and the soln. dild. with much H_2O and acidified with concd. HCl, yielded after several hrs. Ib, decomp. 230° (from MeOH); with *o*-$C_6H_4(NH_2)_2$ it gave *2-phenyl-3-(acetylureidomethyl)-quinoxaline*, m. 268–7[illegible]°. Ib with HIO_4 in aq. dioxane gave *hydantoin*, m. 218–21[illegible], and BzOH. Cf. *C.A.* 48, 12361f.

G. M. Kosolapoff

FODOR, GABOR
~~ABOT, Fodor~~

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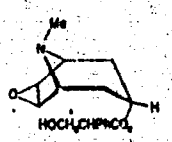
The stereochemistry of the tropane alkaloids. III. The configuration of scopolamine and of valeroidine. Gábor Fodor and Orion Kovács (Univ. Szeged, Hung.). *J. Chem. Soc.* 1953, 2341–4; cf. *C.A.* 48, 2060h.—Scopolamine (I) was converted by hydrogenolysis with Raney Ni at 150 atm. and 25° and hydrolysis of the ester-HBr mixt. into (+)-3,6-dihydroxy *tropane* (II), m. 179–80° [HCl salt, m. 295°; HBr salt, m. 257° (decompn.)], and (−)-tropic acid, m. 126–7°, $[\alpha]_D^{25}$ −7° (*c* 2, H_2O). This hydrolysis was carried out by refluxing 16 hrs. with 10% HBr or 10% HCl or 2 hrs. with $Ba(OH)_2$. The dibenzoate of II, m. 268°, could not be resolved by use of α-bromo-(+)-camphor-π-sulfonic acid or (+)-tartaric acid. II was resolved with (+)-tartaric acid [II (+)-tartrate hydrate, m. 150–1°, $[\alpha]_D^{25}$ 14.23°], giving (+)-II, m. 209–10°, $[\alpha]_D^{25}$ 24.14° (*c* 1.988, EtOH) (picrate, m. 251–2°), as well as the (−)-isomer from the mother liquors, m. 209°, $[\alpha]_D^{25}$ −23.31° (*c* 2.036, EtOH). Resolution of II was also achieved with (levorotatory) *O,O'*-dibenzoyl-(+)-tartaric acid, thus yielding (−)-II, m. 210°, $[\alpha]_D^{25}$ −24.33° (*c* 2.014 EtOH), identical with the alkamine from valeroidine (III) (*C.A.* 47, 8757c). I and III are both β-oriented at C-6 since III forms a cyclic urethan and, since scopoline (IV) can be formed from I by $LiAlH_4$ reduction only if the OH group at C-3 group in the latter is α-oriented with respect to the N bridge.



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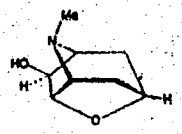

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K. C. Schreiber

FODOR, G.

The stereochemistry of organically bound nitrogen. Gábor Fodor. *Magyar Tudományos Akad. Kém. Tudományok Osztályának Közleményei*, 3, 311–23(1953).—Although previous work showed that the configuration of tropine was anti with respect to the NMe and OH groups, and that of pseudotropine was syn, no decision had been made on the possible boat or chair form of the piperidine portion of the compd. Derivs. of 4-piperidinol probably exist in the chair form since they undergo transacetylation only with great difficulty. Since in the tropines the acetyl group readily shifts from the N to the O, presumably with intermediate ring formation, it is assumed that the piperidine group in the tropines must readily shift to the boat form, even if the chair form is the favored one. Reduction of tropanone by $LiAlH_4$ should give the less hindered product. Pseudotropine, which is actually formed, can be this only if it is both *syn* and in the chair form with the OH group in an equatorial position. Hydrolysis rates of the esters also confirm this interpretation. *Syn*-tropine on treatment with Et iodoacetate gave a compd. which differed from that obtained by first treating *nor-syn*-tropine with this reagent and then methylating. The former, after hydrolysis, was stable to heat; the latter decompd. with loss of water to form a lactone. This showed that in the first case the NCH_3 group was oriented in toward the piperidine ring; in the second, the NCH_2CO_2H group had this configuration.

C. L. Pribram

FODOR, G.

Hungarian Technical Abst.
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1954

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14. The trans-ethylenic configuration of sphingosine — *A szfingozin transz-etilén szerkezete* — G. Fodor and I. Kiss. (Hungarian Journal of Chemistry — *Magyar Kémiai Folyóirat* — Vol. 59, 1953, No. 1, pp. 29–31, 6 figs.)

Triacetyl sphingosine and triacetyl dihydrosphingosine do not give a m p depression in the mixture but form mixed crystals. The case is the same with tribenzoyl derivatives. Considering the *Bruni* rule the conclusion can be drawn that natural sphingosine is of a trans-ethylenic configuration.

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16. Condensation of meso-halogen 1,3-dicarbonyl compounds with urea — *Meso-halogén-1,3-dioxovegyületek kondenzációja karbamiddal* — L. Szekeres and G. Fodor (Hungarian Joutnal of Chemistry — *Magyar Kémiai Folyóirat* — Vol. 59. 1953. No. 7. pp. 193—195)

Investigations were carried out concerning the structure of the condensation product of the reaction between μ-bromo-benzoyl acetaldehyde and urea. Based on the experimental results oxazole structure was attributed to the condensation product which, by the addition of 1 mol sodium hydroxide, yields the sodium enolate of 2-amino-5-benzoyl-oxazole which, in turn, is converted by the action of hydrochloric acid to 2,5-dihydroxy-6-phenylpyrimidine. The monoacetyl derivative of the condensation product is converted by the action of alcoholic alkaline hydroxide solutions into its enol form, thus the cleavage of the keto-ring takes place. The free enol compound is liberated by the hydrochloric acid treatment of the enol-alkaline salt and it proved to be a dicarbonyl compound. This compound with orthophenylene diamine yields a quinoxaline derivative and when oxidized with periodic acid yields benzoic acid and hydantoin. The dicarbonyl compound is identical with 1-phenyl-3-(acetyl-ureido)-propane-1,2-dione. Hence it was established that the original condensation product is identical with the compound 2-amino-5-benzoyl-oxazole. The possible mechanism of the reaction between μ-bromo-benzoyl-acetaldehyde and urea is that the cleavage of the bromine anion takes place whereas the imino-nitrogen attacks the carbon atom of the hydroxy-group of the aldo-enol system.

Fodor, Gabor

The configuration of scopolamine. Gábor Fodor and Odon Kovács (Univ. Szeged, Hung.). *Helv. Chim. Acta* 59, 230–240(1953).—Scopolamine was converted by hydrogenolysis into *dl*-3,6-dihydroxytropane and then resolved into the *d*- and *l*-forms. The latter proved to be identical with the alk. component of valeroidine. Scopolamine and valeroidine are both considered as having the *syn* (β) configuration in respect to C-7, since norvaleroidine forms a cyclic urethan with the C-7 HO and the ring N. Since oscine can be formed from scopolamine only if the latter's C-3 HO is *anti* (α) to the ring N, the C-configuration of valeroidine must be the same as in scopolamine and tropine.

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Fodor, Gabor

The conformation of the piperidine ring. Gábor Fodor and János Lestyán (Univ. Szeged, Hung.). [illegible] *Felsmad* 57, 240-2(1951): cf. preceding abstr. [illegible] Acyl migration expts. with [illegible] [illegible] acyl migration [illegible] 100° in dioxane under the effect [illegible] benzoyl-4-piperidinol-HCl. At lower temps. only unchanged amide was recovered. Attempts to carry out the reversed $O \rightarrow N$-acyl migration failed, confirming the probability of the chair form of the piperidine ring against the tub form. The values derived from calcns. of dipole moments on 4-piperidinol approximated those obtained for conformations with far-lying N and O atoms. Scopolamine can be converted into scopoline under very mild conditions, indicating that the C-4 O atom and the C-6 C atom are close to each other; thus the chair form seems to occur more often than the tub form in piperidine rings in the [illegible] and [illegible]

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3

The stereochemistry of the pyrrolizidine alkaloids. G. Fodor (Univ. Szeged, Hung.). *Chemistry & Industry* 1955, 1431-5.—The structures 7-*anti*-hydroxy-1-*anti*-hydroxymethylpyrrolizidine, 1,2-dehydro-7-*syn*-hydroxy-1-hydroxymethylpyrrolizidine, and 1,2-dehydro-7-*anti*-hydroxy-1-hydroxymethylpyrrolizidine are proposed for platynecine (I), heliotridine (II), and retronecine (III), resp. Previously reported reactions are employed in arriving at these structures. II and III are known to be stereoisomers and III is converted into I by hydrogenation. Since I forms an internal ether when treated with H_2SO_4 or $SOCl_2$ and subsequently with alk., it is assumed that the two OH groups are cis to each other and anti to N. A mechanism is proposed for the etherification reaction as well as a possible route to a rigorous proof of the proposed structures. D. Hamm.

FODOR, G.

The conformation of D-glucosamine. G. Fodor and I. Otvos (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 5, 211-205-7 (1954) (in English).—Evidence is presented to show that the functional groups at C-2 and C-3 of Me 2-amino-3,4,6-triacetyl-β-D-glucopyranoside (I), m. 152°, $[\alpha]_D^{\psi}$ 17° (H_2O), 10° (MeOH), 32° (C_5H_5N), are near each other in space. This requires that these groups be bound in equatorial positions in a C-1 conformation. The evidence for this lies in the fact that $[\alpha]_D^{\psi}$ of I changes on standing in Me_2CO or CH_3OH from +10.8° to −30.5°, the rate rising with pH. This indicates a migration of an Ac group from C-3 OH to C-2 NH_2, yielding Me 2-amino-3,4,6-triacetyl-β-D-glucopyranoside (II), a reaction known to be intramol. (Fodor and Kiss, *C.A.* 46, 2511*d*). The presence of II in the levorotatory soln. (III) is shown by treating the mixt. with $PhNCO$, yielding the 3-*N*-phenylcarbamate of II, m. 75–9°, $[\alpha]_D^{\psi}$ 42° (Me_2CO). The acyl migration is readily reversed by adding HCl in Me_2CO to III, I.HCl, m. 233° (decompn.), $[\alpha]_D$ 17° (MeOH), being produced. A figure of the steric structures is included as well as physical constants for the following compds.: [compd., m.p., and $[\alpha]_D^{\psi}$ (solvent) given]: Et 2-amino-3,4,6-triacetyl-β-D-glucopyranoside (IV), 134°, 8° (MeOH); IV.*HBr*, 270° (sinter), 13.5° (MeOH); IV 2-*N*-*phenylcarbamate*, 223°, 7° (Me_2CO); I 3-*N*-*phenylcarbamate*, 183°, 7.8° (Me_2CO). M. A. S.

FODOR, G.

V Spacial configufation of the Tropane alkaloids. Gábor Fodor. *Magyar Tudományos Akad. Kém. Tudományok Osztályának Közleményei* 5, 351–407(1954).—An extremely detailed review with 95 references. A. Halasz

FODOR, G.

AID P - 267

Subject : USSR/Chemistry

Card : 1/1

Author : Fodor, G. (Seged, Hungary)

Title : Stereochemistry of the tropane alkaloids.

Periodical : Usp. khim. 23, No. 2, 264-272, 1954

Abstract : The structure of some tropane alkaloids is reviewed. 22 references (6 Russian): 1906-1952.

Institution : None

Submitted : No date

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Sphingosin and sphingolipides. XI. Simple preparation of the *erythro*-2-amino-1,3-octadecanediols. L. Sallay, I. Dutka, and G. Fodor (Univ. Szeged, Hung.). *Helv. Chim. Acta*, 37 [1954]. (10.4 in German).—H_2SO_4-dried Br (71.7 g.) was added (3 hrs.) to 512.5 g. palmitic acid (I), m. 62–4°, previously ground with red P; the mixt. kept 6 days (55–65° and room temp. at nights), then warmed slowly *in vacuo* to 75–80° (5 hrs.), and a soln. of the residue in 600 ml. petr. ether at −18° washed with three 100-ml. portions of ice H_2O. Attempted distn. (at 0.01 mm.) of 700 gm. dried ($MgSO_4$) and C treated, crude $C_{15}H_{31}CHBrCOBr$ (II) caused decompn. II (515.2 g.) was added (3.5–4 hrs.) to 627 g. N_2CHCO_2Et (III) and the mixt. kept overnight at 20°, then warmed at 30–5° until N evolution ceased (4–5 hrs.), giving 616 g. crude $C_{15}H_{31}CHBrCOC(:N_2)CO_2Et$ (IV), m. 43–52°, crystd. from EtOH, m. 58–9°. Crude IV in 1500 ml. alc. treated with 30.5 (sic) ml. 8.98% alc. HCl (0.9 moles) was hydrogenated with 40 g. 11.1% Pd-C prereduced in 500 ml. alc., concd. 1/3, and chilled, giving 77.5 g. ppt.; further concn. gave an addnl. 32.3 g. Two crystns. from EtOAc (10 g./30 ml.) gave DL-$C_{15}H_{31}COCH(NH_2)$-CO_2Et (V) HCl salt, m. 114–16° (from alc.); V HBr, m. 111–12.5°. IV in hexane with Pd-C was hydrogenated to Et 2,5-dipentadecyldihydro-3,6-pyrasinedicarboxylate (VI), m. 73–4° (from alc.). V.HBr (0.34 g.) and 0.16 g. NaOAc in 15 ml. H_2O treated 10 min. with 2.04 g. Ac_2O gave VI. A mixt. of 37 ml. Ac_2O, 35 g. AgOAc, 75.57 g. V.HCl, and 600 ml. MeOH shaken 5 hrs. in the dark, boiled 5–10 min., filtered hot, and the filtrate chilled gave 62.2 g. crude DL-$C_{15}H_{31}COCH$ [illegible] Et (VII), m. 63–9°; crystn. from

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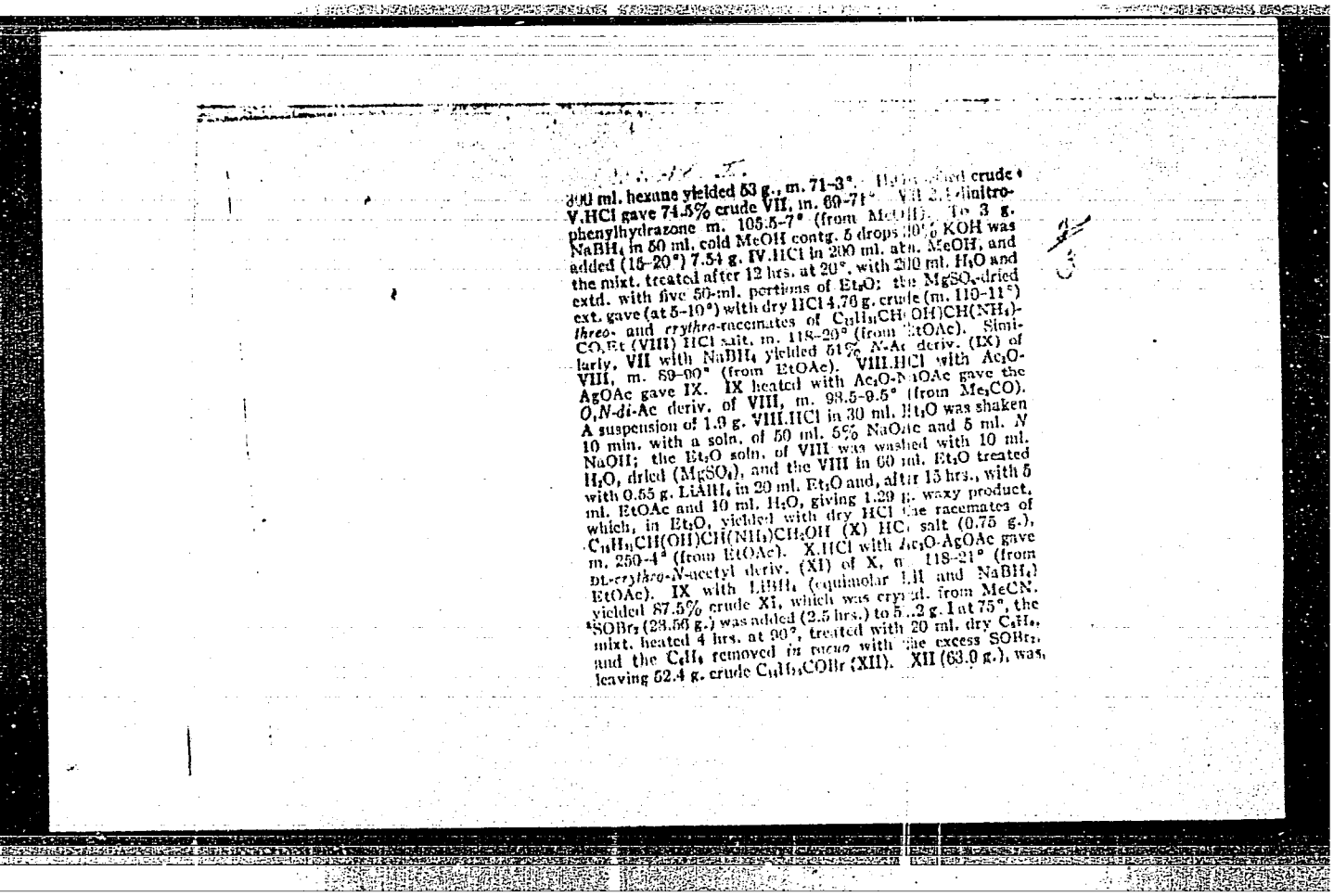
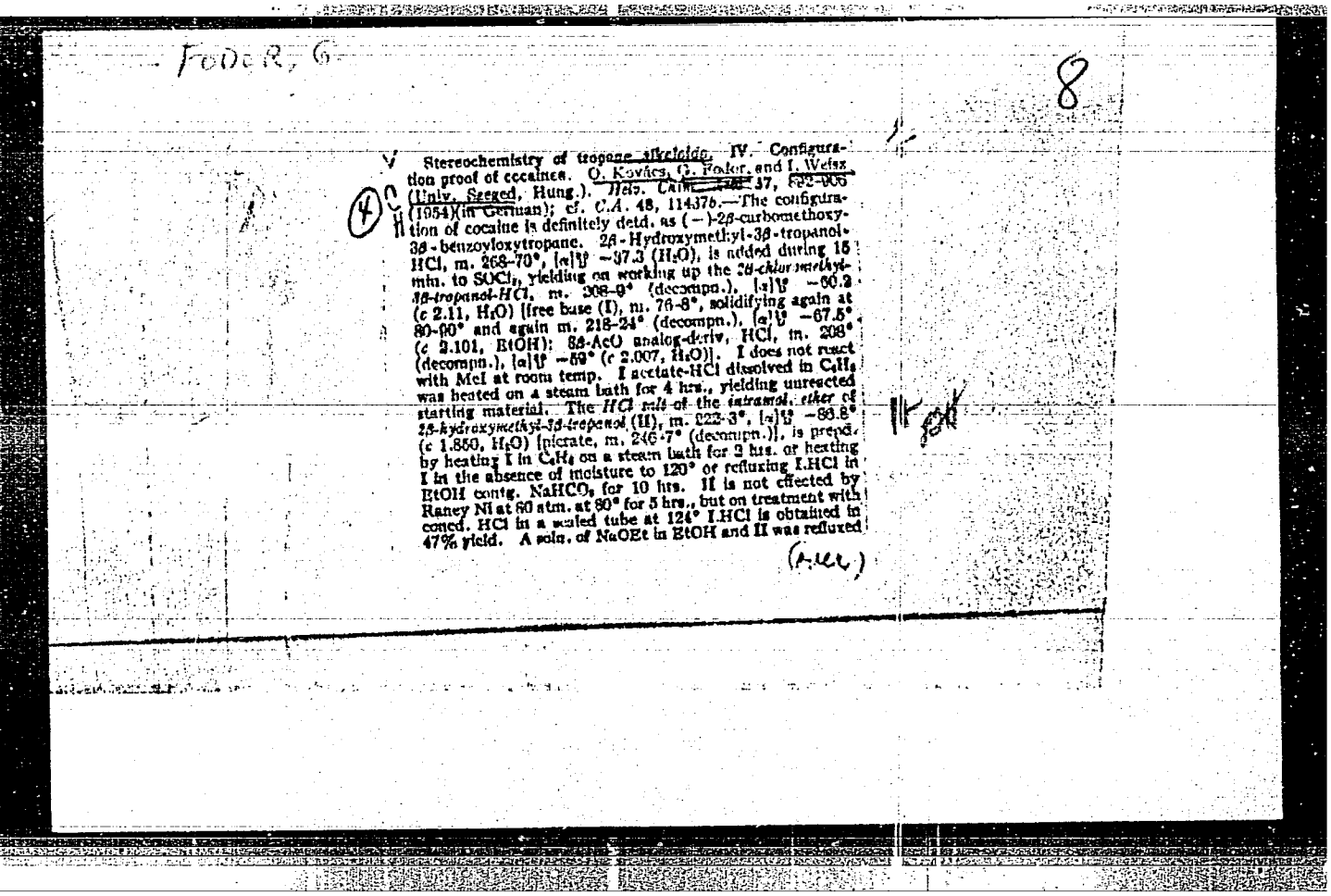


400 ml. hexane yielded 53 g., m. 71–3°. Hydrolyzed crude V.HCl gave 74.5% crude VII, m. 69–71°. VII 2,4-dinitrophenylhydrazone m. 105.5–7° (from MeOH). To 3 g. $NaBH_4$ in 60 ml. cold MeOH contg. 5 drops 30% KOH was added (15–20°) 7.54 g. IV.HCl in 200 ml. abs. MeOH, and the mixt. treated after 12 hrs. at 20°, with 200 ml. H_2O and extd. with five 50-ml. portions of Et_2O; the $MgSO_4$-dried ext. gave (at 5–10°) with dry HCl 4.76 g. crude (m. 110–11°) *threo*- and *erythro*-racemates of $C_6H_5CH(OH)CH(NH_2)CO_2Et$ (VIII).HCl salt, m. 118–20° (from EtOAc). Similarly, VII with $NaBH_4$ yielded 51% N-Ac deriv. (IX) of VIII, m. 89–90° (from EtOAc). VIII.HCl with Ac_2O-AgOAc gave IX. IX heated with Ac_2O-NaOAc gave the *O,N-di*-Ac deriv. of VIII, m. 98.5–9.5° (from Me_2CO). A suspension of 1.9 g. VIII.HCl in 30 ml. H_2O was shaken 10 min. with a soln. of 50 ml. 5% NaOAc and 5 ml. *N* NaOH; the Et_2O soln. of VIII was washed with 10 ml. H_2O, dried ($MgSO_4$), and the VIII in 60 ml. Et_2O treated with 0.55 g. $LiAlH_4$ in 20 ml. Et_2O and, after 15 hrs., with 5 ml. EtOAc and 10 ml. H_2O, giving 1.29 g. waxy product, which, in Et_2O, yielded with dry HCl the racemates of $C_6H_5CH(OH)CH(NH_2)CH_2OH$ (X) HCl salt (0.75 g.), m. 250–4° (from EtOAc). X.HCl with Ac_2O-AgOAc gave DL-*erythro*-*N*-acetyl deriv. (XI) of X, m. 118–21° (from EtOAc). IX with $LiBH_4$ (equimolar LiH and $NaBH_4$) yielded 87.5% crude XI, which was crystd. from MeCN. $SOBr_2$ (28.56 g.) was added (2.5 hrs.) to 5.2 g. I at 75°, the mixt. heated 4 hrs. at 90°, treated with 20 ml. dry C_6H_6, and the C_6H_6 removed *in vacuo* with the excess $SOBr_2$, leaving 52.4 g. crude C_6H_5COBr (XII). XII (63.0 g.), was,

added (10–15°) to 45.6 g. III in 40 ml. petr. ether, and the mixt. kept 1 day at 0° and 2 days at 20°, then treated with 10.7 g. pyridine in 50 ml. petr. ether; the 1-carbethoxymethylpyridinium bromide (41.3 g.) which pptd. m. 112–15° (from $CHCl_3$). The filtrate, washed with three 30-ml. portions of H_2O, five 30-ml. portions of 10% HCl, and three 30-ml. portions of *N* KOH, dried ($MgSO_4$), concd. *in vacuo*, and the residue (65.5 g.) crystd. at 0° and dried on a cold clay plate gave 44.8 g. $C_6H_5COCH_2CO_2Et$ (XIII), m. 35–8° (from EtOH). XIII hydrogenated in HBr-EtOH gave V.HBr.

George L. Sutherland



Foder, G.

8

Stereochemistry of tropane alkaloids. IV. Configuration proof of cocaines. O. Kovács, G. Fodor, and I. Weisz (Univ. Szeged, Hung.). *Helv. Chim. Acta* 37, 922-906 (1954)(in German); cf. *C.A.* 48, 11437b.—The configuration of cocaine is definitely detd. as (−)-2β-carbomethoxy-3β-benzoyloxytropane. 2β-Hydroxymethyl-3β-tropanol·HCl, m. 268–70°, $[\alpha]^{25}_D$ −37.3 (H_2O), is added during 15 min. to $SOCl_2$, yielding on working up the *2β-chlormethyl-3β-tropanol-HCl*, m. 308–9° (decompn.), $[\alpha]^{25}_D$ −60.2 (*c* 2.11, H_2O) [free base (I), m. 76–8°, solidifying again at 80–90° and again m. 218–24° (decompn.), $[\alpha]^{25}_D$ −67.5° (*c* 2.101, EtOH); 3β-AcO analog-deriv, HCl, m. 208° (decompn.), $[\alpha]^{25}_D$ −59° (*c* 2.007, H_2O)]. I does not react with MeI at room temp. I acetate-HCl dissolved in C_6H_6 was heated on a steam bath for 4 hrs., yielding unreacted starting material. The *HCl salt* of the *intramol. ether* of *2β-hydroxymethyl-3β-tropanol* (II), m. 222–3°, $[\alpha]^{25}_D$ −86.8° (*c* 1.850, H_2O) [picrate, m. 246–7° (decompn.)], is prepd. by heating I in C_6H_6 on a steam bath for 2 hrs. or heating I in the absence of moisture to 120° or refluxing I.HCl in EtOH contg. $NaHCO_3$ for 10 hrs. II is not effected by Raney Ni at 60 atm. at 80° for 5 hrs., but on treatment with concd. HCl in a sealed tube at 124° I.HCl is obtained in 47% yield. A soln. of NaOEt in EtOH and II was refluxed

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for 2 hrs., yielding a compd., b$_{4.5}$ 143–4°, $[\alpha]_D^{25}$ −28.7° (*c* 2.197, EtOH), probably a mixt. of 2 isomers of the mono-Et ethers of ecgonimol. Reaction of II with NaOH gave a mixt. of C-3 epimers of 2-hydroxy-3-tropanol. I.HCl in MeOH was treated with NaOMe, hydrogenated with Pd-C at 15°, yielding *2β-methyl-3β-tropanol-HCl* (III.HCl) (98%), m. 265–6° (decompn.), $[\alpha]_D^{25}$ −36.5° (*c* 2.787, H_2O) [free base, m. 56°, $[\alpha]_D^{25}$ −58.2° (*c* 2.154, EtOH); 3β-AcO analog deriv., oil; 3β-AcO analog-HBr, m. 203–4°, $[\alpha]_D^{25}$ −39° (*c* 2.338, EtOH); *N*-methiodide, m. 300° (decompn.), $[\alpha]_D^{25}$ 2.5° (*c* 2.002, H_2O)]. To a soln. of redistd. BrCN in C_6H_6 is added 2β-methyl-3β-acetoxytropane at 60° and kept at that temp. for 3 hrs., concd. yielding cryst. *2β-methyl-3β-acetoxytropan-HBr* and an oil, which after hydrolysis with NaOH at 100° and working up gave *nor-2β-methyl-3β-tropanol* (IV), m. 105–6°, $[\alpha]_D^{25}$ −57.0° (*c* 2.002, EtOH) [HCl deriv., m. 265–6° (decompn.), $[\alpha]_D^{25}$ −43.5° (*c* 2.182, H_2O), *N*-Bz deriv., m. 177–8°, $[\alpha]_D^{25}$ 19.2° (*c* 2.14, dioxane)]. IV in PhCl, satd. with CO_2 is treated with *p*-nitrobenzaldehyde, heated in oil bath to 142°, PhCl distd., dried with $MgSO_4$ and put back into reaction flask, heated for 2 hrs. at 100°, PhCl distd., and the residue crystd. yielding *p-nitrophenyltetrahydro-m-oxazine deriv.* of IV, m. 77–9°, $[\alpha]_D^{25}$ 3.5° (*c* 2.003, C_6H_6), which on treat-

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ment with HCl in EtOH gave back IV. Oxidation of III with (iso-PrO)$_3$Al and cyclohexanone gave 2β-methyl-3-tropanone, b_{16} 125–6°, $[\alpha]_D^{25}$ −25.5° (*c* 2.041, abs. EtOH) [HCl salt, m. 200–1°, $[\alpha]_D^{25}$ −12.5° (*c* 2.003, H_2O); oxime (V), m. 150–1°, $[\alpha]_D^{25}$ −41.5° (*c* 2.005, abs. EtOH)]. V in H_2O brought to pH 1.0 was heated on a steam bath and then treated with a soln. of picric acid in 96% EtOH, yielding on concn. *2α-methyl-3-tropanone picrate*, m. 213–14°, from which the parent compd., m. 190–1°, $[\alpha]_D^{25}$ 6.15° (*c* 1.234, H_2O), was obtained. Treatment of 2α-hydroxymethyl-3β-tropanol-HCl with $SOCl_2$ for 15 min. at 25°, yielding *2α-chloromethyl-3β-tropanol-HCl*, m. 283–4° (decompn.), $[\alpha]_D^{25}$ 56.5° [free base (VI), m. 95–6°, $[\alpha]_D^{25}$ 67.7° (*c* 2.074, abs. EtOH); methiodide, m. 239° (decompn.), $[\alpha]_D^{25}$ 4–5° (*c* 2.002, H_2O)], which on reduction with Raney Ni in MeOH at 50 atm. pressure and 90° for 5 hrs. gave *2α-methyl-3β-tropanol-HCl*, m. 251–2° (decompn.), $[\alpha]_D^{25}$ 33.5° (*c* 1.703, H_2O) [free base, $[\alpha]_D^{25}$ 38.5° (*c* 2.205, abs. EtOH); methiodide, m. 294°, $[\alpha]_D^{25}$ 27° (*c* 2.004, H_2O); acetate-HBr, m. 192–4°, $[\alpha]_D^{25}$ 49.3° (*c* 1.943, abs. EtOH)]. VI on refluxing in C_6H_6 for 4 hrs. gave unchanged VI. When 2α-methyl-3β-acetoxytropane was treated with BrCN, *N-cyannor-2α-methyl-3β-acetoxytropane*, m. 79–81°, $[\alpha]_D^{25}$ 52° (*c* 2.001, abs. EtOH), was obtained, which on hydrolysis with aq. NaOH at 100° for 12 hrs. gave *nor-2α-methyl-3β-tropanol* (VII), m. 124–5°, $[\alpha]_D^{25}$ 50.5° (*c* 2.003,

abs. alc.) [*p*-nitrophenyl-*m*-oxazine deriv. (VIII), m. 90–101°, $[\alpha]_D^{25}$ 70.5° (*c* 2.010, abs. C_2H_5OH); *N*-Bz *deriv.*, m. 141–2°, $[\alpha]_D^{25}$ −8.45° (*c* 1.42, dioxane)]. Treatment of VIII with 2% HCl gave VII. Oxidation of 2α-methyl-3β-tropanol with CrO_3 in glacial HOAc gave *2α-methyl-N-tropanone* [HCl deriv., m. 191–3°, $[\alpha]_D^{25}$ 8.25° (*c* 2.430, H_2O); *oxime*, m. 151–2°, $[\alpha]_D^{25}$ −38.2° (*c* 1.050, abs. alc.)]. The *N*-Bz derivs. of IV and VII each underwent acyl migration when treated with 3*N* HCl in dioxane to give the amino ester salt, m. 270° (decompn.), $[\alpha]_D^{25}$ −47.5° (*c* 0.89, H_2O), and m. 235° (decompn.), $[\alpha]_D^{25}$ 53.4° (*c* 1, H_2O), resp. *N*-Benzoylnorecgonine also gave acyl migration in HCl-dioxane to yield *O*-benzoylnorecgonine-HCl, m. 128–9°, $[\alpha]_D^{25}$ −42° (H_2O). *N*-Cyanonorcocaine in glacial HOAc was treated with concd. H_2SO_4 for 4 hrs., at room temp., Et_2O added and the solid treated with aq. 3*N* K_2CO_3 to yield *N-carbamylnorcocaine*, m. 179–80°, $[\alpha]_D^{25}$ −27.5° (MeOH), which was reacted with NaOMe in MeOH at −15° for 84 hrs. to yield the *Me ester*, m. 212°, $[\alpha]_D^{25}$ −93.5° (70% MeOH), and the *cyclic ureide* m. 198°, $[\alpha]_D^{25}$ −1.5°. V. **The determination of the configuration of the tropane-alkaloids containing oxygen functions attached to the pyrrolidine ring.** G. Fodor, J. Tóth, and I. Vincze *ibid.* 907–13.—A new method for establishing the configurations of amino alcs. with a tertiary N atom is outlined. Tropidine (I), *dl*-oscine (II), and *dl*-3,6-dihydroxytropane [(3) for-

nished by reaction with ICH_2CO_2Et (IV) the salts of the corresponding lactones of the *N*-carboxymethyl deriv., involving OH groups at C-6 and(or) -7. The syn (β) position of these groups is therefore proved. II dissolved in C_6H_6 and treated with IV gave the *lactone* of *N-carboxymethylhyoscinium iodide* (V), m. 246°, which on shaking with aq. Ag_2O gave the *betaine* of *N-carboxymethylhyoscine*, m. 260° (decompn.), reconverted to the lactone with HI. Scopolamine-$HBr.3H_2O$ in H_2O treated with $NaHCO_3$, extd. with $CHCl_3$, and dried over $MgSO_4$, yielded amorphous scopolamine, which on treatment with IV gave *N-carboxymethylscopolaminium iodide*, m. 155°, which on refluxing with 10% HCl gave V. III with IV gave the *iodide* of *dl-N-carboxymethyl-3α,6β-dihydroxytropane*, m. 259° (decompn.), which on treatment with $AgNO_3$ gives the *betaine* of *N-carboxymethyl-3α,6β-dihydroxytropane*, m. 280° (decompn.). I with IV gave *N-carbethoxymethylteloidinium iodide*, m. 204°, and a fraction, m. 255–66°, which on treatment with Ag_2O gave the betaine, m. 252°, which on treatment with HI gave the *iodide* of *dl-N-carboxymethylteloidine lactone*, m. 259° (decompn.). Teloidinone in water oxidized with periodic acid utilized one mole of HIO_4 while the lactone did not react with HIO_4.

Kurt C. Schreiber

HUNG.

Sphingosine and sphingolipides. XII. Correlation of the configuration of (natural) sphingosine with that of *erythro*-2-amino-3,4-dihydroxybutyric acid. T. Kiss, G. Lodor, and H. Bauti (Univ. Szeged, Hung.). *Helv. Chim. Acta* 37, 1471–81(1954)(in German); cf. C.A. 49, 10958b.—Triacetylsphingosine (I), 5 g. in 80 ml. abs. $CHCl_3$, was treated 90 min. with 5% ozone. The $CHCl_3$-insol. ozonide (oil) was heated (80–100°) with 80 ml. H_2O, then was chilled and the H_2O was decanted. The dried (desiccator with $CaCl_2$) residue (3.1 g.), crystd. from petr. ether, gave 0.42 g. myristic acid (II), m. 51.3°. The petr. ether soln. gave a residue yielding 0.7 g. myristaldehyde 2,4-dinitrophenylhydrazone, m. 106–7° (from EtOH). Ozonolysis of 6 g. I (contg. fat-sol. material) gave a product which treated in 50 ml. alc. with 4.5 ml. 2*N* NaOH and 3.7 g. *S*-benzylisothiuronium chloride in 50 ml. alc. added gave 2.5 g. of the salt of II, m. 138° (from EtOH). The H_2O-sol. ozonolysis product was decolorized with C and evapd. *in vacuo* to give 2.52 g. residue; this in 15 ml. dioxane mixed with 8 ml. EtSH and 6 ml. 6*N* HCl in dioxane and shaken 4–5 days in a bomb tube, gave 2.36 g. crude product, which in turn gave 0.143 g. 2-amino-3-hydroxybutyrolactone-HCl (III), m. 219–21° (decompn.), $[\alpha]_D^{25}$ 47.2° (*c* 0.554, H_2O). Evapg. the $CHCl_3$

from 8 g. ozonized I gave an oil which was warmed 30 min. at 80–90° (bath) with 50 ml. 30% H_2O_2. Evapn. of the aq. soln. gave 1.5 g. oil; this on standing 1 week in 25 ml. 3*N* HCl, concg., adding alc. and CaH_2, evapg., and crystg. the residue from 10 ml. alc. gave 0.04 g. III. Evapn. of the filtrate and 2 extns. of the residue (0.54 g.) with alc. gave serine. III (0.28 g.) in 15 ml. H_2O was shaken 3 days with H and 0.4 g. Pd-C (12% PdO), the combined filtrate and washings evapd. *in vacuo*, and the residue treated with two 20-ml. portions EtOH and EtOH-Et_2O to give 0.142 g. 3-amino-2,4-dihydroxybutyraldehyde-HCl (IV), m. 207–8° (decompn.), $[\alpha]_D^{25}$ 22.5° (*c* 0.4, H_2O). IV (0.11 g.) in 15 ml. H hydrogenated 4 weeks with 0.5 g. Pd-C, the filtrate and washings evapd. *in vacuo*, and the residue, crystd. from MeOH-Et_2O, gave 0.035 g. hygroscopic D(−)-*erythro*-2-amino-1,3,4-butanetriol-HCl (V), m. 202–4°, $[\alpha]_D^{25}$ −1.78° (*c* 0.554, H_2O). IV could also be hydrogenated with

Raney Ni at 120 atm. and 90°. D-*three*-2-Benzamido-3,4-dihydroxy-γ-butyrolactone (2 g.) and 10 ml. SOCl₂ gave L-(+)-*erythro*-2-amino-3-hydroxy-γ-butyrolactone-HCl (VI) by the method of Hauret and Painter (*C.A.* 48, 3908e). A by-product (0.8 g.), m. 100–1° (from alc.), is putative 2-benzamido-3-chloro-4-hydroxy-γ-butyrolactone (VII), $[\alpha]_D^{25}$ −120° (*c* 0.3, EtOH). An aq. suspension of 1.2 g. VII treated with 10 ml. *N* NaOH gave 0.7 g. 2-phenyl-5-hydroxymethyl-4-carboxyoxazole lactone (VIII), m. 159–61° (from 1:1 EtOH-petr. ether). Heating (160–5°) 2-phenyl-5-hydroxymethyl-4-carboxyoxazoline lactone-HCl also gave VIII. VIII was optically inactive and could not be hydrogenated at 100 atm. with Raney Ni. VI (2.5 g.) (H. and P., *loc. cit.*) in 150 ml. H_2O with 15 g. Raney Ni hydrogenated 12 hrs. at 90° and 120 atm., 0.1 g. Mg powder added, hydrogenation continued 4 hrs. at 100–3° and 130 atm. (when the Fehling test was neg.), the combined filtrate and washings concd. *in vacuo* and evapd. with alc. C_6H_6, and the residue (2.1 g.) crystd. from MeOH-Et_2O gave L-(+)-*erythro*-2-amino-1,3,4-butanetriol-HCl (IX), m. 201–3° (foaming), $[\alpha]_D^{25}$ 1.07° (*c* 3, H_2O). IX is the antipode of V. Similar reduction of 2.5 g. of the D-isomer of VI (H. and P., *loc. cit.*) gave 0.8 g. V, $[\alpha]_D^{25}$ −1.03° (*c* 0.8, H_2O), m. 203° (decompn.), which did not depress the m.p. of V from I. Thus sphingosine is D-*erythro*-2-amino-1,3-dihydroxy-4-*trans*-octadecene.

George H. Sutherland

HUNG.

V Stereochemistry of cocaine. G. Fodor, O. Kovács, and I. Weisz (Univ. Szeged, Hung.). [illegible] 174, 131–3 (1961).—A brief review is presented of the evidence concerning the stereochemistry of cocaine (I). The following new evidence is advanced in support of the syn position of the CO_2H group and the N atom in I. N-cyanonorcocaine, m. 180°, $[\alpha]_D^{20}$ −31° (MeOH). It gave N-carbamylnorecgonine Me ester (III), m. 213°, $[\alpha]_D^{20}$ −63° (70% MeOH in H_2O), and the neutral cyclic imide of N-carbamylnorecgonine, m. 195°, on treatment with NaOMe at −15°. This evidence in combination with that obtained previously is considered to establish that I is (−)-2β-carbomethoxy-3β-benzoyloxytropane. Donald Hanna

4

Footer, Cl.

/ Synthesis of chloramphenicol. G. Fodor, I. Tóth, K. Kovacs, and J. Kiss (Univ. Szeged, Hung.). *Invest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk* 1955, 441–51; *Bull. Acad. Sci. U.S.S.R. Div. Chem. Sci.* 1955, 391–9(Engl. translation); cf. Fodor, *et al.*, *C.A.* 44, 7273g.—PhCH:CHCH$_2$OAc (90 g.) in 450 ml. PhMe added to 400 g. $NaNO_2$ in 250 ml. H_2O in a dark vessel, the stirred mixt. treated 7 hrs. at 0° with 1.4 l. 20% H_2SO_4 with occasional bubbling of CO_2 to break the foam, and the MePh layer filtered gave the crude product, which, washed with EtOH and EtOH-Et_2O, yielded 89 g. DL-*erythro-PhCH(NO)CH(NO$_2$)CH$_2$OAc*, m. 124°, discoloring after several weeks' storage. This (56 g.) treated with stirring in 224 ml. Ac_2O at 25–9° over 40 min. under CO_2 with 24 g. concd. H_2SO_4 and 72 ml. Ac_2O, stirred 50 min. longer, dild. with 1 l. ice water, and kept 3–4 days in a refrigerator gave 69% DL-*threo-PhCH(OAc)CH(NO$_2$)CH$_2$OAc* (I), m. 72° (from EtOH). (Cl_3CHCO_2O in the above reaction similarly gave, after treatment of the quenched product with Na_2CO_3 and NaOAc, 40% DL-*threo-PhCH(O$_2$CCHCl$_2$)CH(NO$_2$)CH$_2$OAc* (II), m. 74° (crude), m. 82° (from EtOH). I (64 g.) in 960 ml. Me_2CO treated over 10 min. with 1.150 l. *N* HCl, then refluxed 3.5 hrs., concd., treated with 130 g. $NaHCO_3$, extd. with Et_2O, and the ext. shaken with $KHSO_4$ gave 68.5% DL-*threo-PhCH(OH)CH(NO$_2$)CH$_2$OH*, m. 82.5° (from Et_2O-petr. ether). Hydrogenation of I in AcOH over Pd-C at 40 atm. gave 40% DL-*threo-PhCH(OH)CH(NHAc)CH$_2$OAc* (III), m. 168–9° (cf. U.S. 2,483,885, *C.A.* 45, 06[illegible]a), which (1 g.), kept 24 hrs. with 5 ml. quinoline and 1.5 g. Ac_2O, gave 1.1 g. DL-*threo-PhCH(OAc)CH(NHAc)CH$_2$OH*, m. 79–80°. III refluxed 2 hrs. with 5% HCl gave 82% DL-*threo-PhCH(OH)CH(NH$_2$)CH$_2$OH.HCl*, m. 192 (cf. U.S. 2,513,346, *C.A.* 45, 179d). I hydrogenated in AcOH-$(CO_2H)_2$ over Pd-C at atm. pressure gave 49.5% DL-*threo-PhCH(OH)CH(NH$_2$)CH$_2$OH oxalate*, m. 139–40° (from EtOH), which yielded the *free base*, m. 82–3°. Electrolytic reduction of I in 100 ml. AcOH and 200 ml. 96% EtOH with a Hg-pool electrode and 20% HNO_3 catholyte in a porous cup at 0.07 amp./sq. cm. and 44–5°, the catholyte being acidified with HCl, gave in 3 hrs., from 14 g. I, 2.4 g. DL-*threo-PhCH(OH)CH(NHAc)CH$_2$OAc*, m. 169–70° (from AcOH). II similarly treated in alc. HCl at 35–7° gave 28% Cl-free product, m. 168°. PhCH(OH)-CH(NH_2)CH_2OH (16.7 g.) in 100 ml. H_2O and 200 ml. EtOAc treated with stirring in 50 min. with 30 ml. 40% NaOH at 30°, with the pH kept at 6–8, the aq. phase extd. with EtOAc, the combined org. solns. evapd., and the residue treated with abs. EtOH-HCl gave 50.5% DL-*threo-PhCH(OH)CH(NH$_2$)CH$_2$OAc.HCl*, m. 178°, which with K_2CO_3 gave the *free base*, m. 136–8°, identified as DL-*threo-PhCH(OH)CH(NHAc)CH$_2$OH*. Cl_3CHCO_2Me instead of EtOAc in the above gave 64.8% DL-*threo-PhCH(O$_2$CCHCl$_2$)CH(NH$_2$)CH$_2$OH.HCl*, m. 195°. The latter (15.75 g.) treated with 15 ml. H_2O and 90 ml. EtOAc, then at 25° with 3.45 g. K_2CO_3, stirred 5 min., and extd. with EtOAc gave 78% DL-*threo-PhCH(OH)CH(NHCOCHCl$_2$)CH$_2$OH* (IIIA), m. 94–5° (from 50% EtOH), which stirred with pyridine-Ac_2O 0.5 hr. at 100°, yielded 83% DL-*threo-PhCH(OAc)CH(NHCOCHCl$_2$)CH$_2$OAc* (IIIB), m. 93–5° (from 60% EtOH); IIIA kept 15 min. at 70° with Ac_2O gave 72% DL-*threo-PhCH(OH)CH(NHCOCHCl$_2$)CH$_2$OAc* (IV), m. 100–1° (from EtOAc-petr. ether), which with abs. Et_2O-EtOH-HCl at 0° yielded in 24 hrs. 74% DL-*threo-PhCH(O$_2$CCHCl$_2$)CH(NH$_2$)CH$_2$OAc.HCl* (IVA), m. 167° (from EtOH-Et_2O). IV (3.2 g.) in 10 ml. dioxane treated with 5 ml. dioxane contg. 0.94 g. HNO_3 at 0° and kept several days at 0° gave 75.5% *HNO_3 analog* (IVB) of IVA, $C_{11}H_{13}O_7N_3Cl_2$.

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Fodor, G.

Synthesis of 6-tropen-3-ol, a suggested intermediate for scopolamine. G. Fodor, J. Tóth, I. Koczor, and I. Vincze (Inst. of Org. Chem., Szeged, Hung.). *Chemistry & Industry*, 1955, 1290–1.—The title compd. was prepd. via the reactions: (±)-6β-hydroxytropan-3-one was converted to its phenylurethan, m. 127–9°, which was hydrogenated to (±)-6β-phenylcarbamoyloxy-3α-hydroxytropane (I), m. 182–3°. I was acetylated and distd. *in vacuo*, resulting in the reversal of urethan formation, yielding (±)-3α-acetoxy-6β-hydroxytropane (II), m. 121°. II (2 moles) was treated with one mole tosyl chloride to give the *p*-toluenesulfonate, which was cleaved by collidine at 180° in a N atm. in a sealed tube into 6-tropen-3-yl acetate (III), b_2 85°. 6-Tropen-3α-ol [picrate, m. 278° (decompn.)] was prepd. by the Kunz hydrolysis of III.

Susan I. Wright

FODOR, G.

Stereochemical and synthetic studies in the sphingosine field. IX. Ozonolysis of natural sphingosine. J. Kiss, G. Fodor, and D. Bánó (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 5, 341–8(1955)(in English); cf. *C.A.* 49, 4521e.—To correct a literature discrepancy (Klenk and Diebold, *C.A.* 25, 4278; Niemann and Nichols, *C.A.* 36, 3784[9]), the ozonolysis of sphingosine (I) and its derivs. was reinvestigated. The crude sulfate of I (87 g.), obtained by the acid hydrolysis of sphingolipides from the brain and spinal cord of cattle according to Carter, *et al.* (*C.A.* 41, 6503g), suspended in 1 l. 0.5*N* NaOH, extd. 3 times with 1 l. ether, the solid residue from the evapn. of the combined ether exts. dissolved in 150 ml. dry C_5H_5N, treated at 0° with 120 ml. Ac_2O, and heated 15 min. yielded, after standing a day in the cold, 20.3 g. tri-Ac deriv. (II) of I, m. 102–4°, $[\alpha]_D^{20}$ −9.7° (*c* 1.1, $CHCl_3$). Alk. hydrolysis of II gave crude I, m. 60–78°, which (1.1 g.) was reacetylated to yield 1.1 g. II, identical with the preceding sample. Thus, no Walden inversion had occurred during the prepn. of II from lipides by their acid hydrolysis, followed by the alk. hydrolysis of II (cf. Jeany and Grob, *C.A.* 49, 8576). Partial alk. hydrolysis of 6.4 g. II in 200 ml. MeOH by letting it stand 12 hrs. at 18° with 40 ml. *N* KOH in MeOH, evapg. the mixt. to 100–20 ml. at 30°, adding 200 ml. H_2O, and extg. with ether yielded from the ether ext. 3 g. *N*-Ac deriv. (III) of I, m. 60–5°, $[\alpha]_D^{20}$ −5.5° (*c* 2, $CHCl_3$); mixed m.p. with the dihydro deriv. of III, 62–111°. The mother liquor from the prepn. of pure II freed from the solvent *in vacuo* and the residue dissolved in $CHCl_3$ and neutralized gave an oil, $b_{0.001}$ 170–90° (bath temp.), $[\alpha]_D^{20}$ −6° (*c* 2, $CHCl_3$), probably $C_{13}H_{27}CH{:}CHCH(OR')CH(NHR)CH_2OR'$ (R = R' = Ac, R'' = Me). I (1.3 g.) from the alk. hydrolysis of 2 g. II in 10 ml. dry C_5H_5N treated with 4 g. *p*-$O_2NC_6H_4COCl$, heated 15 min. on a steam bath, allowed to stand 1 day at room temp., 20 ml. H_2O added, and the mixt. extd. with $CHCl_3$ yielded 1.14 g. tris-(*p*-nitrobenzoyl) deriv. (IV) of I, m. 136–9° (from 90% Me_2CO-H_2O). Similar treatment of 2 g. dihydrosphingosine (V) gave 2.5 g. tris-(*p*-nitrobenzoyl) deriv. (VI) of V, m. 144–5° (from abs. EtOH); mixed m.p. with IV, 138–42°. Alk. hydrolysis of VI gave the *N*-*p*-O_2N-C_6H_4CO deriv. (VII) of V, m. 124–8° (from dil. EtOH). The stability and crystn. properties of IV, VI, and VII

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J. Kiss

6 2/4

were not appropriate for ozonolysis, and only I and II were used. O_3 (5%) bubbled through 6 g. II in 100 ml. $CHCl_3$ 1.5 hrs. at room temp. pptd. the ozonide, and evapg. the $CHCl_3$ *in vacuo*, shaking the residue 60 min. with 100 ml. H_2O, and cooling in ice yielded 4 g. H_2O-insol. oil (VIII), sepd. by petr. ether into (*1*) 0.6 g. petr. ether-sol. myristic acid, m. and mixed m.p. 51–2° (*S*-benzylisothiuronium salt, m. 138° (cf. Donleavy, *C.A.* 30, 5102⁸), and (*2*) glacial AcOH-sol. myristaldehyde (IX), which reduced Fehling soln. and yielded 0.7 g. 2,4-dinitrophenylhydrazone (X) of IX, m. 104–5° (from EtOH). The aq. layer sepd. from VIII also reduced Fehling soln., and after evapn. of the solvent, the residual (2.28 g.) sirup was acetylated to 0.52 g. $AcOCH_2CH(NHAc)CH(OAc)CHO$, noncryst. but characterized by its compd. with 2,4-$(O_2N)_2C_6H_3NHNH_2$, probably the osazone of $AcOCH_2CH(NHAc)COCHO$, m. 175–8° (decompn., softening at 160°). Also from the combined aq. mother liquors of the preceding ozonolysis products, acidified, evapd. to dryness, and the residue extd. with hot abs. EtOH, was obtained 0.3 g. *3-amino-2-hydroxy-4-butyrolactone HCl salt*, m. 218–20°, $[\alpha]_D^{25}$ 47.2° (c 0.554, H_2O), which fails to give ninhydrin and Fehling soln. tests. Similar ozonolysis of I gave no isolatable products except X. The splitting at the double bond was attempted also through the epoxide: 5.1 g. II in 12 ml. $CHCl_3$ treated with 0.35 g. BzO_2H in 51 ml. $CHCl_3$, allowed to stand 2 days at 0°, and evapd. *in vacuo* gave a yellow oil, whose ether-insol. portion yielded 1.55 g. epoxide (XI) of II, m. 134–6° (from Me_2CO), $[\alpha]_D^{25}$ 16.6° (c 0.6, $CHCl_3$) (*C.A.* 47, 8641h). Hydrolysis of 0.6 g. XI by heating 6 hrs. at 120–30° in a sealed tube with 10 ml. H_2O gave a tri-Ac deriv. of an amino tetraol, but periodic oxidation failed, probably because of the migration of an Ac group so that no vicinal OH groups remained. X. **Preparation of several long-chain aliphatic ketones.** I. Sallay. *Ibid.* 549–55 (in German) (English summary).—As a step toward complete synthesis of sphingosine, the key compd., *n*-$C_{11}H_{23}CH{:}CHAc$ (I), was prepd., after preliminary expts. on model compds.: *n*-$C_{16}H_{33}OH$ (484.8 g.), warmed 7 hrs. on a steam bath with 306.7 g. $POCl_3$ according to Plimmer and Burch (*C.A.* 23, 2417), gave 646 g. crude $C_{16}H_{33}OPO_2H_2$ (II), m. 73–82° (sample recrystd. from $CHCl_3$). Distn. and redistn. of 106 g. II *in vacuo* gave the fractions (g., b.p., n_D^{25}): 126.5, b_{15} 147–70°, —; 15, b_{15} 146–53°, 1.4424; 76, b_{15} 155–7°, 1.4437 (III); 20, b_{15} 155–7°, 1.4445. Ozonolysis of III according to Asinger and Eckoldt (*C.A.* 38, 57⁹) yielded 8.8 g. mixed acids, sepd. by vacuum distn. into 0.6 g. lauric, b_{12} 9)–172°, and 5.1 g. myristic acid, m. 34–40°, characterized by their *S*-benzylisothiuronium salts, m. 140–1° and 139°, resp. A shift of the double bond had obviously occurred during the thermal

J. Kiss 6 74

decompn. of II. The desired pure 1-C_6H_{11} (IV) was prepd. from $C_6H_{11}O_2CC_6H_{11}$ (V) according to Waterman, *et al.* (*C.A.* 24, 823) by heating 1300 g. V under N 4 hrs. from b_{18} 330° to b_{20} 360°, giving 651 g. distillate (332 g. $C_6H_{11}CO_2H$ as residue). The oily distillate in 1 l. petr. ether (b. 30–50°) washed with 3% NaOH and then EtOH, dried, treated with Na wire, refluxed 5 hrs., filtered, neutralized, and dried again gave 448 g. crude IV, fractionally d'std. *in vacuo* to yield 236 g. pure IV, b_{14} 153–7°, n_D^{20} 1.4415. Ozonolysis of 30 g. IV yielded the expected $C_6H_{11}CHO$ (25 g. crude), m. 23–5° (from EtOH); 2,4-dinitrophenylhydrazone, m. 102–3° (cf. Landa, *C.A.* 20, 362). IV (22.4 g.) in 50 ml. CS_2 and 14.4 ml. AcCl in 20 ml. CS_2 at −20° treated during 30 min. with rapid stirring with 13.3 g. $AlCl_3$ yielded, after the usual decompn. and purification, 7.25 g. (only 27.2%) crude $C_6H_{11}CH{:}CHAc$ (VI), b., and, after drain *in vacuo*, 2.1 g. (only 7.9%) pure VI, b_2 158–63° [semicarbazone, m. 115–16° (from EtOH)]. This small yield led to the improved method for analogs of VI [$CdMe_2$ (VII) with α,β-unsatd. acid chlorides] previously used for the synthesis of satd. ketones (Gilman and Nelson, *C.A.* 30, 5951⁴). As preliminary model expts., 0.1 mole VII, prepd. according to Cason (*C.A.* 41, 397g), in dry C_6H_6 was treated with ice cooling during 10 min. with 0.1 mole $C_6H_{11}COCl$ (VIII) in 20 ml. dry C_6H_6, and the mixt. refluxed 1 hr., cooled to 0°, and poured onto 200 ml. 10% ice-cold H_2SO_4; from the C_6H_6 layer was obtained 75% $C_6H_{11}Ac$, m. 53–5° (semicarbazone, m. 119°). Similar treatment of $C_6H_{11}COCl$ in place of VIII yielded 70% $C_6H_{11}Ac$ (IX), m. 40–8°; semicarbazone (X), m. 121–2°. These 2 good yields encouraged the use of VII in the prepn. of the desired I. $C_6H_{11}CH{:}CHCO_2H$ was prepd. according to Myers (*C.A.* 46, 1438g), and its acid chloride (XI), m. 166–8°, with $SOCl_2$ in the usual way. Treatment of 0.1 mole XI with 0.1 mole VII as above yielded 60% crude and 69% pure I, b_3 150–60°, n_D^{20} 1.4450 (semicarbazone, m. 110–12°; mixed m.p. with X, 118–20°), taken as evidence for a *trans*-ethylenic configuration in I (cf. Fodor and Kiss, *C.A.* 48, 3252e). Ozonolysis of I, followed by H_2O_2 oxidation, gave 80% myristic acid, and reduction of I by Pd-C gave IX, both results being confirmations of the structure of I. The attempted condensation of I with Et_2CO_3 in the presence of NaH (cf. Soloway and La Forge, *C.A.* 42, 1204h) gave unexpectedly 3-C_6H_{11}-, with perhaps a small amt. of $C_6H_{11}CH{:}CHCOCH_2CO_2Et$; this reaction will be further investigated. XIII Preparation of DL-*threo*-2-acetamido-1,3-diacetoxyoctadecane. I. Sallay and F. Duthaler *Ibid.* 359–63(in English); cf. *C.A.* 49, 6024c.—The previously reported synthesis (*C.A.* 49, 5008b) of *n*-$C_6H_{11}CH(OH)CH(NHAc)CH_2OH$ (I) is modified by the use of the Japp-Klingemann reaction [*Ann.* 247, 216 (1888)] on Et palmitoylacetoacetate (II). Fused $C_6H_{11}CO_2H$, treated with $SOCl_2$ according to Ralston and Selby (*C.A.* 33, 5358⁷), yielded 70% pure $C_6H_{11}COCl$ (III), $b_{3.4}$ 155.2–8.0°. Adding 55.2 g. $AcCH_2CO_2Et$ in 400 ml. ether dropwise to 9.36 g. powd. Na in 400 ml. ether, stirring, refluxing 2 addnl. hrs., adding dropwise 97.7 g. III to the ice-cold mixt., refluxing 1 hr., and pouring into 150 ml. 10%

(NOT)

J. Kiss

HCl yielded from the ether layer 129.1 g. (99%) II, b$_{4-6}$ 175° (cf. Visconti and Merckling, *C.A.* 47, 12223e); *p*-O$_2$NC$_6$H$_4$N$_2$Cl (*from* 2.07 g. *p*-O$_2$NC$_6$H$_4$NH$_2$) in 10 ml. ice-cooled H$_2$O added to 7.36 g. II in 12 ml. EtOH and 0.46 g. Na in 15 ml. EtOH and the resulting emulsion stirred 30 min. at room temp. yielded from the ether ext. 1.6 g. (10.9%) *p*-O$_2$NC$_6$H$_4$NHN:C(CO$_2$Et)COC$_6$H$_5$ (IV), m. 73–4° (from EtOH). On hydrogenation over Pd-C in 25 ml. abs. EtOH acidified with 2.4 ml. 20.7% HCl in dry ether, 0.05 g. IV absorbed 220 ml. H (theoretical, 224 ml.) to yield inactive C$_6$H$_5$COCH(CO$_2$Et)NH$_2$Cl (V), m. and mixed m.p. 114–16° (from AcOEt) (yield not given). Previously reported procedures (*loc. cit.*) changed V by means of Ac$_2$O and AcOAg to 67% inactive C$_6$H$_5$COCH-(CO$_2$Et)NHAc, m. 71–3° (2,4-dinitrophenylhydrazone, m. 105–7°), and thence by means of LiBH$_4$ (Kollonitsch, *et al.*, *C.A.* 49, 2295*h*) to 90% mixed *threo*- and *erythro*-racemates of I, m. 90–107°, sepd. by fractional crystn. of the tri-Ac derivs. (VI). The mixed racemates (1.815 g.) in 60 ml. dry C$_5$H$_5$N and 6.3 ml. Ac$_2$O kept 48 hrs. at 20°, evapd. *in vacuo* at 40°, and the residue taken up in ether yielded 2.05 g. (91%) crude VI, m. 50–70°. Fractional recrystn. from petr. ether (b. 25–40°) sepd. 2 compds., m. 80–2° and 66–8°, resp. [cf. for the *threo*-racemate of I, m. 67–8° and 65–6°, found by Grob, *et al.* (*C.A.* 46, 6590*a*), and Carter, *et al.* (*C.A.* 48, 9937*g*). Insp.]. XIV. Structure of sphingoglycosides. J. Kiss and I. Jurcsik. *Ibid.* 477–80 (in English).—A preliminary communication. The only unsolved structural problem for the 3 sphingoglycosides (I) is the question of α- or β-linkage of the galactose. Cerebron, kerasin, and nervon were separately hydrolyzed and [α]$_D^{25}$ values detd. for the liberated sugars, together with those for the hydrolysis product of α-Et galactose. Curves for [α]$_D^{25}$ values vs. time are similar for all 4 sugars, and the α-linkage is therefore probable for all. This conclusion is confirmed by the slow (72 hrs.) rate of mercaptolysis at room temp. of I (cf. Lemieux, *C.A.* 48, 1346) and by enzymic tests. Exptl. details are to be reported later.

H. S. French

FODOR-G.

Hydrogenation of cyanamides to *N*-mono- and *N,N*-di-substituted formamidines. G. Fodor (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 5, 375–8(1955)(in English).—Hydrogenating 1.56 g. *N*-cyano-2β-methoxycarbonyl-3β-benzoxynortropane in 50 ml. anhyd. EtOH over 1 g. of Pd-C contg. 9% PdO, adding 3 ml. 3.4*N* HCl in anhyd. EtOH, filtering, and evapg. the filtrate to dryness *in vacuo* gave 0.65 g. *N*-formimidoylnorcocaine-HCl (I), colorless needles, m. 214° (from EtOH-petr. ether). Similarly were prepd.: *N*-phenyl-*N*-methylformamidine (II) picrate, m. 145°, and picrocolate, m. 198°; *N*-phenylformamidine picrate, m. 191°; *N*-benzylformamidine (III) picrate, m. 172°, and picrocolate, m. 210°; *N*-(imidoformyl)morpholine, m. 150°; *N*-benzoyl I, m. 174°. Joseph B. P. Apelbaum

FODOR, G.

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Steric structure of tropane alkaloids. G. Fodor (Univ. Szeged). *Acta Chim. Acad. Sci. Hung.* 5, 47–112 (1955) (in English); cf. *C.A.* 49, 3989*e*.—A review with emphasis on the contributions of F., 112 references. H. S. F.

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Situation of organic chemistry in Europe. p. 193. MAGYAR KEMIKUSOK LAPJA. (Magyar Kemikusok Egyesulete) Budapest. Vol. 10, No. 7, July 1955

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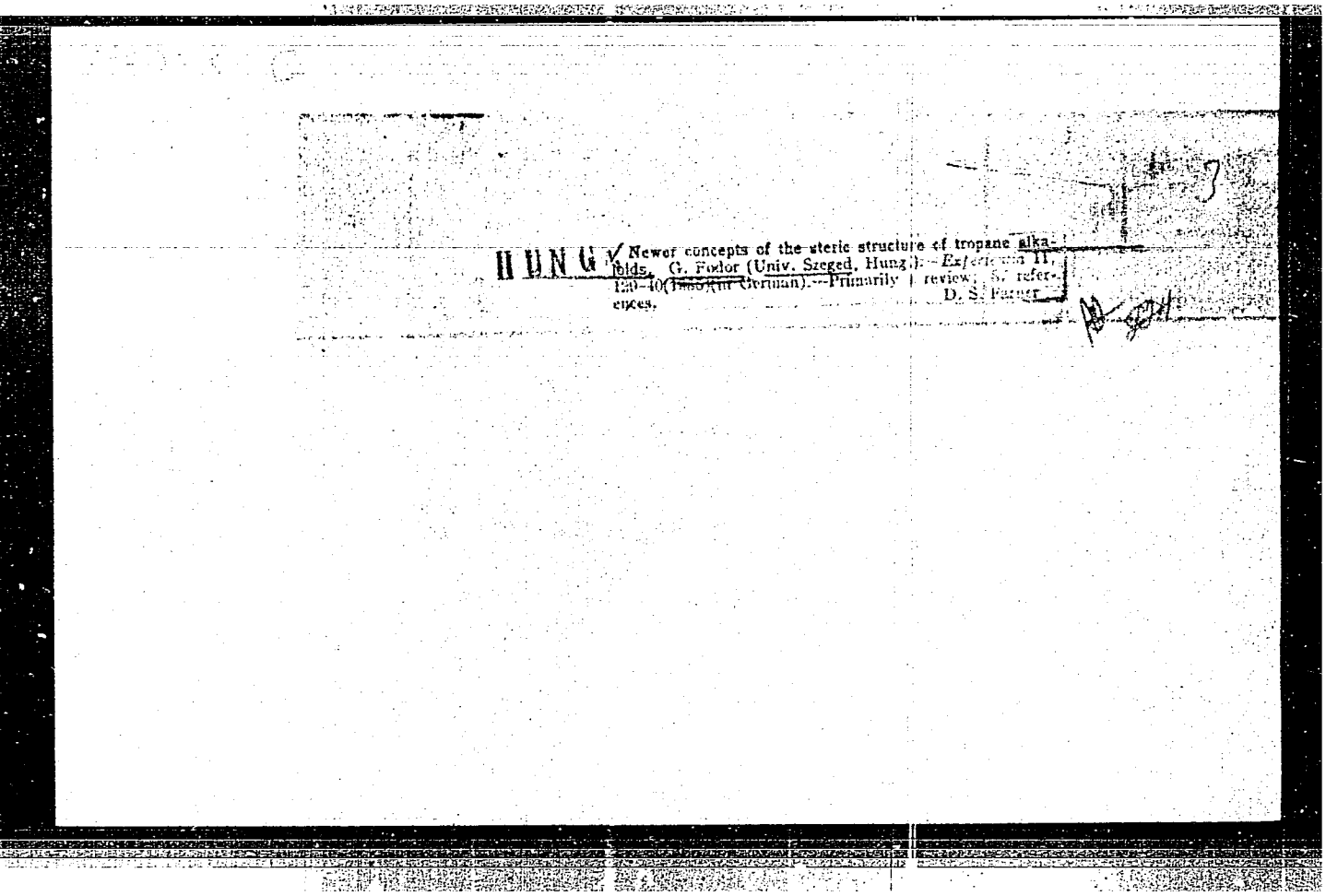

HUNG ✓ Newer concepts of the steric structure of tropane alkaloids. G. Fodor (Univ. Szeged, Hung.). *Experientia* 11, 120–40(1955)(in German).—Primarily a review, with 57 references. D. S. Farner

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Annual meeting of the Chemical Society in the German Democratic Republic from 19-22 October 1955.

"Synthese von 6-Tropen-3-ol, ein vermutetes gemeinsames Zwischenprodukt saemtlicher Tropanalkaloide"

SO: Chemische Technik, Feb 1956, Unclassified.

FODOR, G.

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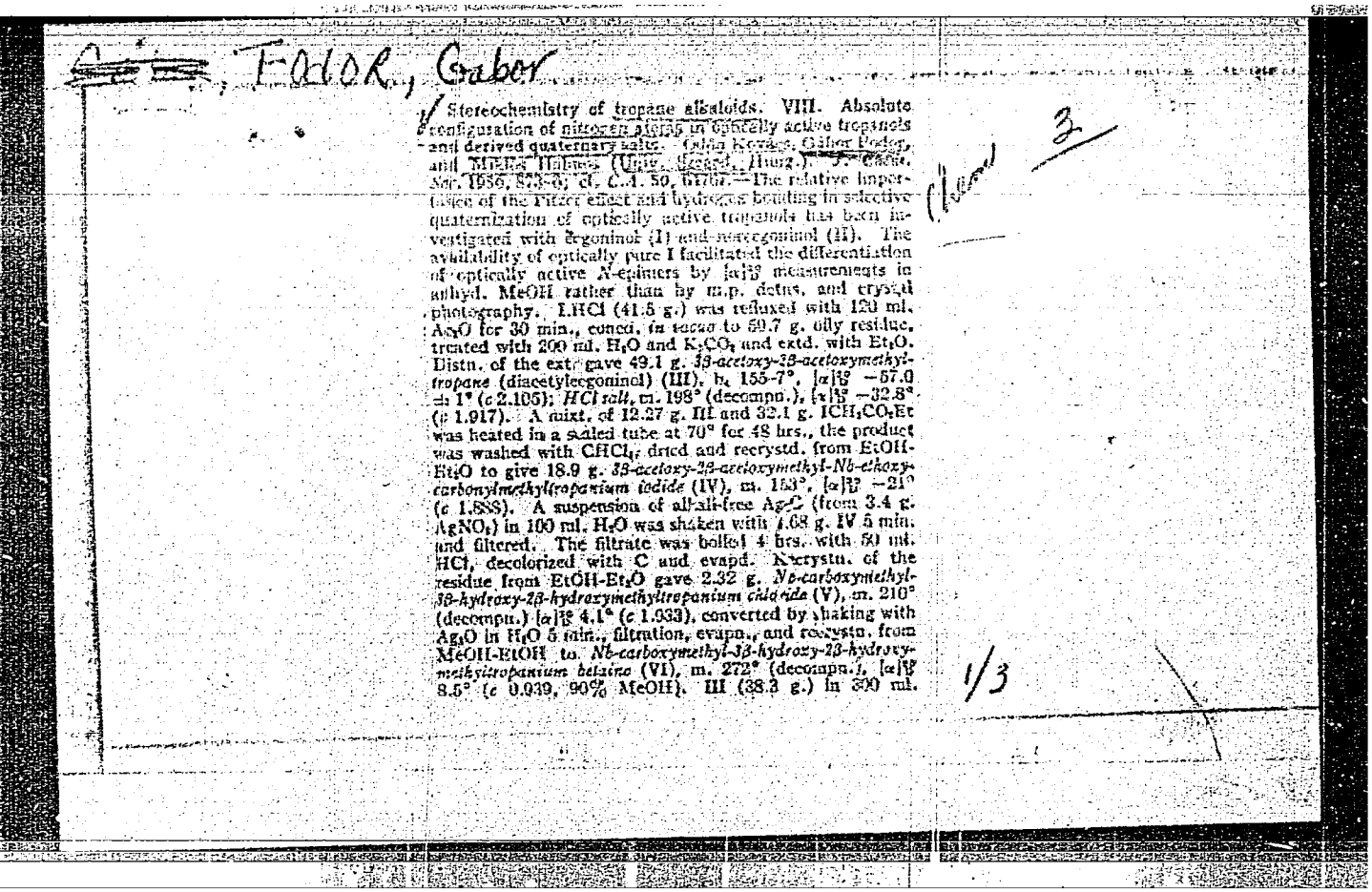
Total synthesis of scopolamine. G. Fodor, J. Toth, I. Koczor, P. Dohó, and I. Vincze (Inst. Organic Chem. Univ., Szeged, Hung.). *Chemistry & Industry* 1956, 784.—The 1st total synthesis of scopine (I) and scopolamine (II) is reported. Oxidation of the *trifluoroacetate* of *3α-acetoxytrop-6-ene* in MeCN with F_3CCO_3H in CH_2Cl_2 gave *scopyl acetate* (III); *picrate*, m. 222°; HCl salt, m. 231°. III *N*-oxide on hydrogenation gave 3α-acetoxy-6β-hydroxytropane, m. 121°. III was converted to I, m. 76°, and oscine by hydrolysis in acetone-NaOH at 20° for 2 days. I and *acetyltropsyl chloride* (IV) gave *aposcopolamine* (*picrate*, m. 216°), and *acetyloscine* (picrate, m. 161°). *Acetylscopylamine* (V) was obtained by heating IV and I.HCl 4 days at 60° in $PhNO_2$. Deacetylation of V gave II.HCl. II *picrate* m. 175.5–6.5°. Chas. Burkhard



Fodor, Gabor

Stereochemistry of tropane alkaloids. VIII. Absolute configuration of nitrogen atom in optically active tropanols and derived quaternary salts. Gábor Fodor, Gábor Bodor, and Mária Halmos (Univ. Szeged, Hung.). *J. Chem. Soc.* 1956, 3133-6; cf. *C.A.* 50, 6778d.—The relative importance of the Pfeiffer effect and hydrogen bonding in selective quaternization of optically active tropanols has been investigated with ψ-tropinol (I) and -pseudotropinol (II). The availability of optically pure I facilitated the differentiation of optically active *N*-epimers by $[\alpha]_D^{25}$ measurements in anhyd. MeOH rather than by m.p. data, and crystal photography. I.HCl (41.5 g.) was refluxed with 120 ml. Ac_2O for 30 min., concd. *in vacuo* to 59.7 g. oily residue, treated with 200 ml. H_2O and K_2CO_3 and extd. with Et_2O. Distn. of the ext. gave 49.1 g. *3β-acetoxy-2β-acetoxymethyltropane* (diacetylecgoninol) (III), b_4 155-7°, $[\alpha]_D^{25}$ −57.0 ± 1° (*c* 2.105); *HCl salt*, m. 198° (decompn.), $[\alpha]_D^{25}$ −32.8° (*c* 1.917). A mixt. of 12.27 g. III and 32.1 g. ICH_2CO_2Et was heated in a sealed tube at 70° for 48 hrs., the product was washed with $CHCl_3$, dried and recrystd. from EtOH-Et_2O to give 18.9 g. *3β-acetoxy-2β-acetoxymethyl-Nb-ethoxycarbonylmethyltropanium iodide* (IV), m. 153°, $[\alpha]_D^{25}$ −21° (*c* 1.888). A suspension of alkali-free AgCl (from 3.4 g. $AgNO_3$) in 100 ml. H_2O was shaken with 4.68 g. IV 5 min. and filtered. The filtrate was boiled 4 hrs. with 50 ml. HCl, decolorized with C and evapd. Recrystn. of the residue from EtOH-Et_2O gave 2.32 g. *Nb-carboxymethyl-3β-hydroxy-2β-hydroxymethyltropanium chloride* (V), m. 210° (decompn.) $[\alpha]_D^{25}$ 4.1° (*c* 1.933), converted by shaking with Ag_2O in H_2O 5 min., filtration, evapn., and recrystn. from MeOH-EtOH to *Nb-carboxymethyl-3β-hydroxy-2β-hydroxymethyltropanium betaine* (VI), m. 272° (decompn.), $[\alpha]_D^{25}$ 8.5° (*c* 0.939, 90% MeOH). III (38.3 g.) in 300 ml.

KOVACS, O., FODOR, G., HALMOS, M.

C_6H_6 was added dropwise in 4 hrs. to 35 g. freshly distd. BrCN in 350 ml. anhyd. C_6H_6. The mixt. was refluxed 5 hrs. and evapd. to give 25.65 yellow crystals, purified by washing and extg. with Et_2O 18 hrs. to yield 21.5 g. *3β-acetoxy-2β-acetoxymethyl-N-cyanonortropane* (VII), m. 104°, $[\alpha]_D^{25}$ −72.4° (*c* 2.015), together with 8 g. III. A mixt. of 30 g. VII, 36 g. NaOH, and 350 ml. H_2O was refluxed for 8 hrs., acidified to Congo red with HCl and evapd. The residue was extd. with 8 portions of 100 ml. anhyd. alc., and the ext. concd. to 60 ml. and treated with the calc. amt. of NaOMe. Evapn., extn. with 200 ml. $CHCl_3$ and distn. gave *3β-hydroxy-2β-hydroxymethylnortropane* (II), b. 150° *fclerate*, m. 180° (from EtOH). II [illegible] ICH_2CO_2Et, and 30 ml. anhyd. EtOH was kept at room temp. 36 hrs., evapd. *in vacuo* to a syrup and taken up in 150 ml. $CHCl_3$. The soln. was washed with H_2O, the washings were extd. with $CHCl_3$ and the combined $CHCl_3$ solns. were dried over $MgSO_4$, acidified with dry alc. HCl and evapd. Crystn. of the residue from EtOH-Et_2O yielded 12 g. *N-ethoxycarbonylmethyl-3β-hydroxy-2β-hydroxymethylnortropanium chloride* (VIII), m. 165–6° (decompn.), $[\alpha]_D^{25}$ −42.0° (*c* 3.015), converted to *N-carboxymethyl-3β-hydroxy-2β-hydroxymethylnortropanium chloride* (VIIIa), m. 131° (decompn.), $[\alpha]_D^{25}$ −45° (*c* 1.96). [illegible] 3 hrs. in 8 parts H_2O and 4 parts concd. HCl. VIIa (2.23 g.) in 20 ml. H_2O was shaken 5 min. with 3.4 g. freshly prepd. Ag_2O, filtered over C and evapd. *in vacuo* to give the betaine (VIIIb), m. 247° (decompn.), $[\alpha]_D^{25}$ −41.3° (*c* 0.932). VIII (2.78 g.) and 25 ml. Ac_2O were heated 4 hrs. on the steam bath, kept overnight at room temp. and concd. *in vacuo*. Crystn. of the residue from MeOH-Et_2O gave 2.09 g. *3β-acetoxy-2β-acetoxymethyl-N-ethoxycarbonylmethylnortropanium chloride* (VIIIc), m. 84°, $[\alpha]_D^{25}$ −38.4° (*c* 1.071). A mixt. of 1.810 g. VIIIc in 40

2/3

Kovács O., Fodor, G., Halmos, M.

ml. Me_2CO and 2.13 ml. of 5.42% NaOEt in EtOH was centrifuged, the Me_2CO-free ppt. was heated at 120-5° with 5 ml. PhMe and 4 ml. MeI and filtered. The red cryst. residue was washed with Me_2CO and recrystd. from EtOH-Et_2O yielding 0.422 g. *Na-carboxymethyl-3β-hydroxy-2β-hydroxymethyltropanium iodide lactone* (IX), m. 203° (decompn.), $[\alpha]_D^{25}$ 0° (*c* 1.030). A mixt. of 0.727 g. IX in 30 ml. 50% aq. MeOH and 0.43 g. Ag_2O in 10 ml. H_2O was shaken for 6 hrs. and filtered. The filtrate was refluxed with 20 ml. concd. HCl for 2 hrs., filtered, decolorized with C and evapd. *in vacuo* to give 0.320 g. *Na-carboxymethyl-3β-hydroxy-2β-hydroxymethyltropanium chloride* (X), m. 205° (decompn.), $[\alpha]_D^{25}$ −38.6° (*c* 0.983). Evapn. of the Me_2CO-PhMe mother liquor from IX gave a red sirup which was treated with Ag_2O (from 1.7 g. $AgNO_3$) and 20 ml. H_2O and filtered. The residue on evapn. of the filtrate was refluxed 3 hrs. with concd. HCl and evapd. Crystn. of the residue from MeOH-Et_2O yielded 0.795 g. X, converted by shaking with Ag_2O, working up and recrystg. from MeOH-Et_2O to the *betaine* (Xa), m. 238° (decompn.), $[\alpha]_D^{25}$ −60.8° (*c* 2.20, 90% MeOH). The carboxymethyl derivs. and betaines from the two reaction sequences show striking differences in rotational values. Quaternization of I produces strong pos. shift in rotation whereas the reverse sequence gives compds. in which the original levo rotation is maintained or increased. It is concluded that the lactone IX is derived from *Na*-carboxymethyl-3*β*-hydroxy-2*β*-hydroxymethyltropanium iodide and that identical configurations at the N atom can be deduced for the salts VIII, VIIIa, VIIIc, and X, the opposite configuration occurring in the quaternary salts IV and V. Thus, the *N*-Me groups in I and III and the ethoxycarbonylmethyl group in the free base related to VIII appear to be predominantly oriented towards the piperidine ring, indicating the predominating importance of the Pitzer effect. C. R. Addinall

3/3