with $KMnO_4$ in dilute NaOH[13] gave the diketo acid V, m.p. 280–290° (dec.); λ^{alc}_{max} 293 mμ (ϵ = 9,000); *anal.* Calcd. for $C_{12}H_8O_6N_2S_2$: C, 42.3; H, 2.37; S, 18.8. Found: C, 42.4; H, 2.19; S, 18.5, in addition to a small amount of 4-thiazolecarboxylic acid. The above data permit the assignment of structure IV to thiostreptoic acid. Unambiguous proof was provided by a synthesis of V.

Succindialdehyde was treated with potassium cyanide and the resulting cyanhydrin benzoylated *in situ.*[13,14] As expected, two isomers, the meso form and the racemate of α,δ-dibenzoyloxyadipic acid dinitrile were isolated, m.p. 135–137°; and m.p. 212–216°; *anal.* Calcd. for $C_{20}H_{16}O_4N_2$: C, 69.0; H, 4.63; N, 8.04. Found: C, 68.9; H, 4.60; N, 7.93 for the lower melting and C, 69.0; H, 4.81; N, 8.10 for the higher melting isomer. The lower melting isomer was used in the subsequent steps. Treatment with hydrogen sulfide in dimethylformamide in the presence of triethanolamine[13,14] furnished α,δ-dibenzoyloxyadipic acid dithioamide, m.p. 203–205°; *anal.* Calcd. for $C_{20}H_{20}O_4N_2S_2$: N, 6.73; S, 15.4. Found: N, 6.94; S, 15.4, which was condensed with ethyl bromopyruvate to give the diethyl ester of 2,2′-(1,4-dibenzoyloxytetramethylene) - bis - [4-thiazolecarboxylic acid], m.p. 144–145°; *anal.* Calcd. for $C_{30}H_{28}O_8N_2S_2$: N, 4.60; S, 10.5. Found: N, 4.68; S, 10.6. Hydrolysis with potash in ethanol yielded the corresponding dihydroxy acid, m.p. 240–242°; *Anal.* Calcd. for $C_{12}H_{12}O_6N_2S_2$: C, 41.9; H, 3.51; N, 8.23. Found: C, 42.0; H, 3.95; N, 8.35, which on oxidation with $Na_2Cr_2O_7$ gave 2,2′-succinylbis-(4-thiazolecarboxylic acid), m.p. 284–286° (dec.); λ^{Nujol}_{max} 5.84 sh, 5.90; *anal.* Found: C, 42.5; H, 2.90, identical in all respects with the diketo acid V derived from thiostreptoic acid.

The sulfur content of the antibiotic (9.4%) considered in conjunction with the four sulfur-containing fragments isolated so far require for thiostrepton a minimum molecular weight of 1700.[15]

[13] P. Brookes, A. T. Fuller and J. Walker, *J. Chem. Soc.* 689 (1957).

[14] J. F. Olin and T. B. Johnson, *Rec. Trav. Chim.*, **50**, 72 (1931).

[15] Ether extraction of acid hydrolysates (1 *N* HCl, 24 hours, at 105°) furnished a yellow volatile crystalline compound. *Anal.* $C_{12}H_9O_4N$: C, 62.6; H, 4.3; N, 6.14; λ_{max} 265 mμ (ϵ, 25,000), 375 mμ (ϵ, 2,000). An additional fragment from the same hydrolysate contains alanine acylated by the yellow chromophore.

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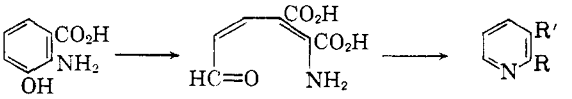
RECEIVED JULY 28, 1960

CONVERSION OF 3-AMINOCATECHOLS TO 6-HYDROXYPICOLINIC ACIDS[1]

Sir:

In the enzymatic conversion of 3-hydroxyanthranilic acid (I) to quinolinic (III, R = R′ = CO_2H), nicotinic (III, R = H, R′ = CO_2H) and picolinic acid (III, R = CO_2H, R′ = H), α-amino-β-carboxymuconic acid semialdehyde (II), an established intermediate produced by a ring cleavage, undergoes decarboxylation and/or intramolecular cyclization.[2] Chemical conversions of benzene derivatives to pyridine derivatives by cleavage of the carbocyclic ring and recyclization have not been developed.[3]



I II III

We wish to report a new and general method for the chemical conversion of 3-aminocatechols (IV) to 6-hydroxypicolinic acids (VII). Unstable 3-aminocatechol (IVa),[4] 3,4-dihydroxyanthranilic acid (IVb),[5] m.p. 175° (dec.), unstable 2,3-diamino-4,5-dihydroxytoluene (IVc),[6] 1,2-dihydroxy-3-aminonaphthalene (IVd), m.p. 164° (dec.), and unstable 1,2-dihydroxy-3-amino-4-anilinonaphthalene (IVe)[7] are transformed respectively to 6-hydroxypicolinic acid (VIIa), m.p. 261–263°, 6-hydroxyquinolinic acid (VIIb), m.p. 253–254.5°, 3-amino-4-methyl-6-hydroxypicolinic acid (VIIc), m.p. 285–288° (dec.), isocarbostyril-3-carboxylic acid (VIId), m.p. 318–320° and 4-anilinoisocarbostyril-3-carboxylic acid (VIIe), m.p. 250–256° (dec.).[8]

Silver oxide in anhydrous ethyl acetate oxidizes each dihydroxyamine (IV) to a blue-black unstable aminoquinone (V).[9] In an extension of the application of the Baeyer–Villiger reaction to *o*-quinones,[10] each aminoquinone, after separation from inorganic material, is oxidized without isolation from solvent with a peroxy organic acid apparently to an unisolated derivative of muconic acid anhydride (VI). On treatment of the anhydride with water a substituted muconic acid presumably is formed. Hydrolysis of monocyclic muconic acid anhydrides in the presence of strong ultraviolet light gives only intractable tars. Apparently *cis-cis* muconic acid derivatives are produced initially and isomerize to *trans–trans* modifications.[11] In the absence of

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[1] Financial assistance from National Institutes of Health Grants Nos. H-2295 and CY-2895 is gratefully acknowledged.

[2] H. S. Mason, "Mechanisms of Oxygen Metabolism" in "Advances in Enzymology," Vol. 19, Interscience Publishers, Inc., New York, N. Y., 1957, p. 92.

[3] Ozonolysis of a substituted aminomethylcatechol ether and then cyclization accounts for the construction of ring III as a pyridone in the synthesis of strychnine (R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daenker and K. Scheinker, THIS JOURNAL **76**, 4749 (1954)). Pyridine is reported to be one of the products from benzene and active nitrogen (P. M. Aronovich, N. K. Bel′skii, and B. M. Mikhailov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 696 (1956), *C.A.* **51**, 1893 (1957)).

[4] Identified as its hydrochloride, m.p. 196–202° (dec.).

[5] At one time this compound was considered to be an enzymatic intermediate in the conversion of I to III (K. Makino, F. Itoh and K. Nishi, *Nature*, **167**, 115 (1951)).

[6] Isolated as its dihydrobromide salt, m.p. 162–176° (dec.).

[7] Identified as its hydrochloride salt, m.p. 211–213° (dec.).

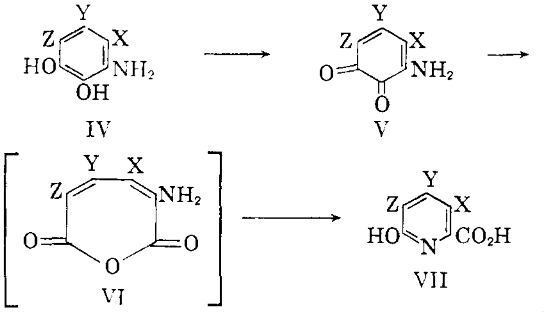
[8] Satisfactory analytical data have been obtained for all compounds and/or their derivatives reported in this Communication.

[9] Through condensation with o-phenylenediamine each aminoquinone is transformed into the corresponding derivative of 1-aminophenazine which was analyzed. Aminoquinones, tautomeric hydroxyquinone-monoimines and imino dihydroquinones are regarded as equivalent structures for the present purpose.

[10] P. Karrer, R. Schwyzer and A. Neuwirth, *Helv. Chim. Acta*, **31**, 1210 (1948).

[11] In boiling water exposed to an ultraviolet lamp, *cis,cis*-muconic acid is changed quantitatively to the *trans,trans*-isomer (J. A. Elvidge, R. P. Linstead, B. H. Orkin, P. Sims, H. Baer and D. B. Pattison, *J. Chem. Soc.* 2228 (1950)).

strong ultraviolet light hydrolysis of each anhydride (VI) brings about isomerization to a hydroxypicolinic or an isocarbostyrilcarboxylic acid (VII). Percentage yields for the transformations of IV to VII are: a, 16; b, 11; c, 16; d, 65; e, 31.

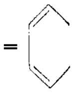


a, X = Y = Z = H

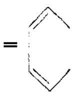
b, X = CO_2H, Y = Z = H

c, X = NH_2, Y = CH_3, Z = H

d, X = H, XZ =



e, X = C_6H_5NH, YZ =



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(12) This investigation was carried out during the tenure of a Predoctoral Fellowship from the National Heart Institute, United States Public Health Service, 1959–1960.

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RECEIVED JULY 1, 1960

CHEMISTRY OF THE METAL CARBONYLS. V. THE DESULFURIZATION OF THIOPHENE[1]

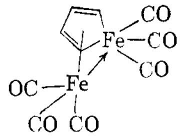
Sir:

At elevated temperatures, thiophene and iron carbonyls undergo a novel reaction resulting in removal of the sulfur atom from the thiophene ring and its substitution by the iron atom of an iron tricarbonyl group.

A 250-ml. flask was fitted with a Soxhlet extractor and a reflux condenser to the top of which was attached a tube for the introduction of prepurified nitrogen. After the apparatus had been flushed with nitrogen, a 150 ml. (1.9 moles) sample of thiophene, in which no impurities could be detected by vapor phase chromatography, was placed in the flask and a 10 g. (20 mmoles) sample of triiron dodecacarbonyl was placed in the thimble of the Soxhlet. The flask and its contents were heated for 15 hr., during which time the iron carbonyl was extracted continuously. Black solid formed in the flask and the green color due to triiron dodecacarbonyl eventually disappeared. After the flask and its contents cooled to room temperature, filtration afforded a pale red or orange filtrate, from which excess of thiophene was removed (25°, 15 mm.) leaving an orange solid and a red oil. The residue was dissolved in 10 ml. of pentane and chromatographed on a 2 × 50 cm. column of Merck alumina, thereby giving a yellow band preceded by a small red band. Elution with pentane and removal of solvent afforded a trace of a red oil from the first eluate and an orange solid from the later eluate. The orange solid (450 mg., 5% yield) obtained (m.p. 52–54°), as well as that formed in a repeat experiment, was found to have the composition $C_{10}H_4O_6Fe_2$.

Anal. Calcd. for $C_{10}H_4O_6Fe_2$: C, 36.1; H, 1.2; Fe, 33.7; S, 0.00; mol. wt., 332. Found: C, 36.2, 35.6; H, 1.3, 1.4; Fe, 32.9, 33.1; S, 0.00, 0.00; mol. wt., 348 (determined from vapor pressure of a dichloromethane solution).

The orange solid, pale red when impure, shows carbonyl bands in its infrared spectrum (tetrachloroethylene solution, Perkin Elmer Model 21 spectrophotometer fitted with CaF_2 prism) at 2079 (s), 2042 (vs), 2006 (vs.), 1998 (vs) and 1962 (vw) cm^{-1}. Since it has been reported[2] that under certain conditions acetylene and iron carbonyls react to give an orange solid (m.p. 54–55°,[2a] 53°[2b]) of composition $C_{10}H_4O_6Fe_2$, it seemed possible that this compound, which has been assigned[2a,b] structure (I), was identical with the compound formed from thiophene and iron carbonyls. Accordingly, the preparation of I from acetylene was repeated by the method described elsewhere.[2a] The orange solid thus obtained had an infrared spectrum (3500–800 cm.$^{-1}$) exactly coincident with that of the orange solid obtained from thiophene and iron carbonyls; the identity of the two solids also was shown by the identity of their individual and mixed melting points.



I

In our hands the reaction between thiophene and iron pentacarbonyl or triiron dodecacarbonyl carried out in a flask without use of a Soxhlet gave products similar to those described above, but in poorer yield. Solid black residues from the reactions afforded hydrogen sulfide on treatment with dilute hydrochloric acid. The red oil mentioned above and formed in very small amounts appears to be a mixture worthy of further investigation. One component, sulfur and iron containing, shows in its infrared spectrum (tetrachloroethylene solution, CaF_2 prism) carbonyl bands at 2072 (s), 2035 (vs), 2000 (vs), 1989 (vs) and 1956 (vw) cm.$^{-1}$. This infrared band pattern in the carbonyl region also is shown by products obtained from reactions, at present under study, between a number of organosulfur compounds and iron carbonyls.

Formation of I from an iron carbonyl and thiophene may not be unrelated to the mechanism of certain metal-desulfurization processes in organic chemistry. Moreover, the reaction described here suggests that derivatives of thiophene might function as intermediates for the synthesis of new heterocyclic iron compounds having covalent iron-iron bonds. It is of further interest to note that

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[1] Previous article in this series, R. B. King and F G. A. Stone, THIS JOURNAL, **82**, 4557 (1960).

[2] (a) W. Hübel and E. Weiss, *Chemistry and Industry*, 703 (1959); (b) W. Hübel and E. H. Braye, *J. Inorg. Nucl. Chem.*, **10**, 250 (1959); (c) M. L. H. Green, L. Pratt and G. Wilkinson, *J. Chem. Soc.*, 989 (1960).