1,2,3,4-tetrahydroquinazoline, II. That the formation of II probably proceeds through I was shown by the fact that I reacts with carbon monoxide to give II in quantitative yield at 230°. Similar conversions to analogs of I and II were carried out with 4-chloroazobenzene and 4-dimethylaminoazobenzene.

These reactions constitute the first examples of the formation of the indazolone ring system and its conversion to the tetrahydroquinazoline ring system by the use of carbon monoxide. In the case of the substituted azobenzenes ring closure occurred on the ring containing the substituent, as shown by alkaline hydrolysis to form the 5-substituted-2-aminobenzoic acids. Further studies on the reaction of carbon monoxide with other ring systems are under way.

Experimental.—A solution of 5 g. of azobenzene and 1 g. of dicobalt octacarbonyl in 50 ml. of benzene was heated at 230° under 150 atmospheres pressure of carbon monoxide for two hours to give 3 - phenyl - 2,4 - dioxo - 1,2,3,4 - tetrahydroquinazoline, II, m.p. 277°, in 80% yield. The structure was established by comparison (mixed m.p. and infrared spectra) with an authentic sample prepared from anthranilic acid and phenylurea.[2] The same product was obtained in smaller yield when iron pentacarbonyl was used, but was not obtained with nickel carbonyl.

In a similar experiment with dicobalt octacarbonyl (190°, 150 atmosphere of carbon monoxide) a 55% yield of 2-phenylindazoline, I, m.p. 204°, was obtained together with a smaller amount of II and diphenylurea. The identity of I was established by comparison (mixed m.p. and infrared spectra) with an authentic sample prepared from the amide of anthranilic acid.[3]

With dicobalt octacarbonyl and carbon monoxide at 230° 4-chloroazobenzene gave 23.8% of 2-phenyl-5-chloroindazolone, m.p. 233° (*Anal.* Calcd. for $C_{13}H_9ClN_2O$: C, 63.9; H, 3.7; N, 11.5. Found: C, 63.6; H, 3.8; N, 10.6) and 45% of 3-phenyl-6-chloro-2,4-dioxo-1,2,3,4-tetrahydroquinazoline, m.p. 264° (*Anal.* Calcd. for $C_{14}H_9ClN_2O_2$: C, 61.8; H, 3.3; N, 10.3. Found: C, 61.1; H, 3.4; N, 9.6). Similarly with 4-dimethylaminoazobenzene there were obtained 80% of 2-phenyl-5-dimethylaminoindazolone, m.p. 217° (*Anal.* Calcd. for $C_{15}H_5N_3O$: C, 71.1; H, 5.9; N, 16.6. Found: C, 71.5; H, 5.7; N, 16.9) and 18% of 3-phenyl-6-dimethylamino-2,4-dioxo-1,2,3,4-tetrahydroquinazoline, m.p. 281° (*Anal.* Calcd. for $C_{16}H_{15}N_3O_2$: C, 68.3; H, 5.3; N, 14.9. Found: C, 67.7; H, 5.1; N, 14.7).

---

(2) F. Kunckell, *Ber.*, **43**, 1234 (1910).

(3) K. von Auwers and K. Hüttenes, *ibid.*, **55**, 1112 (1922).

FACULTY OF SCIENCE
OSAKA UNIVERSITY (OSAKA) AND
INSTITUTE OF SCIENTIFIC AND
INDUSTRIAL RESEARCH (SAKAI)
JAPAN

SHUNSUKE MURAHASHI
SHIGEKI HORIIE

RECEIVED JUNE 27, 1956

STRUCTURE OF THE AMINOSUGAR DERIVED FROM STREPTOTHRICIN AND STREPTOLIN B

Sir:

On acid hydrolysis, the *streptomyces* antibiotics streptothricin[1] and streptolin B[2] yield, *inter alia*, carbon dioxide, ammonia, L-β-lysine,[3,4] streptolidine,[5] and a strongly reducing substance, the structure of which has now been elucidated.

Through chromatography of the hydrolysates, Compound 2 was obtained as a crystalline hydrochloride, m.p. 152–162° dec., $[\alpha]^{21}\text{D}$ +5.6° (5 min.) → −18.7° (4 hr. and final) (*c* 2.9, water) (Calcd. for $C_6H_{13}NO_5 \cdot HCl$: C, 33.42; H, 6.54; N, 6.49; Cl, 16.45. Found: C, 33.54; H, 6.64; N, 6.50; Cl, 16.71). Compound 2 gave positive ninhydrin, Tollens, and Elson–Morgan reactions; it reduced five moles of sodium periodate, yielding ammonia, one mole of formaldehyde, and five moles of formic acid. Degradation by means of ninhydrin yielded xylose, which was identified by paper chromatography. Compound 2 phenylosazone displayed an X-ray diffraction pattern indistinguishable from that of L-gulose phenylosazone, and was identified on the basis of its rotation as D-gulose phenylosazone. These data limit the possible structures to two: 2-amino-2-deoxy-α-D-gulose and 2-amino-2-deoxy-α,D-idose.

Accompanying the hexosamine in the hydrolysates was a related substance, Compound 1, which was isolated as a crystalline hydrochloride, m.p. 235–240° dec. (monohydrate), $[\alpha]^{25}\text{D}$ +44.8° (anhydrous) (*c* 3.5, water) (calcd. for $C_6H_{11}NO_4 \cdot HCl$: C, 36.46; H, 6.12; N, 7.09; Cl, 17.94. Found: C, 36.36; H, 5.75; N, 7.67; Cl, 17.89). A mixture of Compounds 1 and 2 was produced, as evidenced by paper chromatography, when either pure component was treated with hot, dilute hydrochloric acid. Compound 1 gave a positive ninhydrin reaction, but negative Tollens and Elson–Morgan reactions. Two moles of sodium periodate was reduced, affording ammonia, one mole of formic acid, but no formaldehyde. The major periodate oxidation product yielded a crystalline dimedone derivative, m.p. 135.6–136.2° $[\alpha]^{25}\text{D}$ −13.3° (*c* 0.8, ethanol), which, by virtue of rotational, infrared spectral, and mixed melting point comparison, was identified as the dimedone derivative of *cis*-1,3-dioxolane-2,4-carboxaldehyde, secured by periodate oxidation of 1,6-anhydro-β-D-gulopyranose.[6] Compound 1 is therefore the 1,6-anhydrosugar derived from Compound 2.

Comparison of the molecular rotations of various α- and β-sugars with the rotations of the corresponding aminosugar anomers reveals that replacement of a hydroxyl by an amino group does not result in any significant numerical change.[7] Since

---

[1] H. E. Carter, R. K. Clark, Jr., P. Kohn, J. W. Rothrock, W. R. Taylor, C. A. West, G. B. Whitfield and W. G. Jackson, THIS JOURNAL, **76**, 566 (1954).

[2] E. E. Smissman, R. W. Sharpe, B. F. Aycock, E. E. van Tamelen, and W. H. Peterson, *ibid.*, **75**, 2029 (1953).

[3] H. E. Carter, W. R. Hearn, E. M. Lansford, Jr., A. C. Page, Jr., N. P. Salzman, D. Shapiro and W. R. Taylor, *ibid.*, **74**, 3704 (1952).

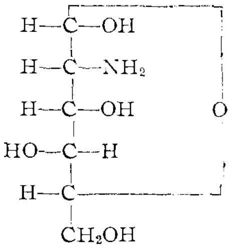
[4] E. E. van Tamelen and E. E. Smissman, *ibid.*, **74**, 3713 (1952).

[5] Streptolidine is the trivial name we have assigned to the aminoimidazoline amino acid[1] present in the acid hydrolysis of both antibiotics. Details relating to the structure of streptolidine will be submitted in a separate contribution.

[6] Kindly supplied by Dr. N. K. Richtmyer, National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland.

[7] This relationship also holds for the pair 1,6-anhydro-β-D-altropyranose, [M] +345, and 3-amino-3-deoxy-1,6-anhydro-β-D-altropyranose, [M] +340.

the molecular rotation of Compound 1 (+88)[8] approximates that of 1,6-anhydro-β-D-gulopyranose (+82) but contrasts with that of 1,6-anhydro-β-D-idopyranose (−103), we regard Compound 2 as 2-amino-2-deoxy-α-D-gulose (α-D-gulosamine) (I). This case apparently constitutes the first example of a naturally occurring sugar with the gulose configuration.



I

The weakly reducing Compound C,[1] (crystalline hydrochloride, m.p. 215–220° dec.) (found: C, 34.57; H, 6.17; N, 16.20; Cl, 16.70) obtained from both streptothricin and streptolin B, is regarded as an intermediate hydrolysis product, since it yields, on prolonged treatment with aqueous acid, streptolidine and Compounds 1 and 2. Structural investigations of Compound C are in progress.

[8] Neither the α- nor β-forms of gulose or idose are reported in the literature.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN
NOYES LABORATORY OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

EUGENE E. VAN TAMELEN
JOHN R. DYER
HERBERT E. CARTER
JACK V. PIERCE
EDWARD E. DANIELS

RECEIVED JULY 30, 1956

AN UNUSUAL FLUORINE MAGNETIC RESONANCE MULTIPLET[1]

Sir:

The nuclear magnetic resonance multiplets[2] which arise from the indirect coupling of nuclear spins[2,3] *via* their interactions with the electrons[2,4] in a molecule are of interest in relation to molecular and electronic structures. In those cases reported thus far, the magnitude of the coupling constant, A_{ij}, decreases monotonically with the number of chemical bonds separating nuclei i and j. However, we have found a molecule, $(CF_3)_2NCF_2CF_3$, in which the fluorine nuclei separated by four and five chemical bonds have considerably larger coupling constants (16 and 6 c.p.s.) than those separated by only three bonds (<1 c.p.s.).

The fluorine spectrum of the liquid has three main lines with chemical shifts, $10^5\,(H_r - H_c)/H_r$ referred to trifluoroacetic acid, of -1.99,[2] -0.84[3] and $+2.31$.[6] From the relative intensities, given in parentheses, the three lines are assigned to the $N{-}CF_2{-}$, $C{-}CF_3$ and $(CF_3)_2N$ groups. The spectra were obtained with a modified version[5] of our high resolution spectrometer.[6] The samples were provided by Dr. R. D. Dresdner of the University of Florida.

Under higher resolution, the three lines exhibit the multiplet structures reproduced in Figs. 1A, B and C, respectively. Figures 1A and B are septets, with relative intensities of 1:6:15:20:15:6:1, characteristic of coupling with six equivalent nuclei of spin 1/2. From this we conclude that the $(CF_3)_2N$ fluorine nuclei are coupled to both the $N{-}CF_2{-}$ and the $C{-}CF_3$ fluorine nuclei; the coupling constants are 16 and 6 c.p.s., respectively. On the other hand, there are no resonance components attributable to coupling between the fluorines in the $N{-}CF_2{-}$ and $C{-}CF_3$ groups. Any coupling between them is less than the line widths, which give an upper limit of about 1 c.p.s.

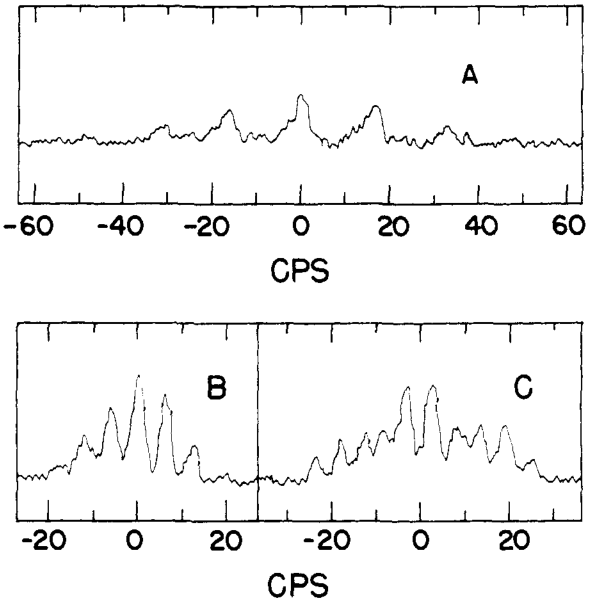


Fig. 1.—The high resolution fluorine magnetic resonance absorption spectrum of $(CF_3)_2NCF_2CF_3$, observed at a fixed frequency of 16.685 Mc. A, B and C are the absorption of the $N{-}CF_2{-}$, $C{-}CF_3$ and $(CF_3)_2N$ groups, centered at δ values of −1.99, −0.85 and +2.31, respectively.

These results show that there are two or more contributions to the F–F coupling, of comparable magnitude, with opposing signs, and attenuating at considerably different rates with the number of bonds between the fluorines. This interpretation is supported by the molecular orbital estimates made by McConnell[7] of the various interactions coupling the fluorine spins in fluoroethylenes.

A related though not as striking a case is that of the fluorobenzenes for which the dependence of the F–F coupling constant on orientation is $A_o >$

---

[1] Assisted by the U. S. Office of Naval Research and by Grants-in-Aid from the E. I. du Pont de Nemours and Co. and from the Upjohn Co.

[2] H. S. Gutowsky, D. W. McCall and C. P. Slichter, *J. Chem. Phys.*, **21**, 279 (1953).

[3] E. L. Hahn and D. E. Maxwell, *Phys. Rev.*, **88**, 1070 (1952).

[4] N. F. Ramsey, *ibid.*, **91**, 303 (1953).

[5] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, in press (1956).

[6] H. S. Gutowsky, L. M. Meyer and R. E. McClure, *Rev. Sci. Instr.*, **24**, 644 (1953).

[7] H. M. McConnell, *J. Chem. Phys.*, **24**, 460 (1956).