been discontinued, there will be no further meetings of the Committee on Grants-in-Aid.

A limited fund is still available, however, for the making of grants in the medical sciences only. The next meeting of the Council's Division of Medical Sciences for the awarding of grants will be held in November, 1936. Applications should be addressed to the Secretary, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C. Applications to be considered at the November meeting must be on file on or before October 1, 1936.

FRANK R. LILLIE,
Chairman, National Research Council

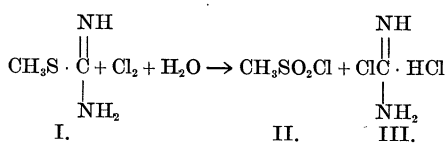
SPECIAL ARTICLES

THIOUREA AS A KEY REAGENT FOR THE PREPARATION OF ALIPHATIC SULPHONYL CHLORIDES AND BROMIDES[1]

A CLASS of organic compounds which has not received its proper share of attention by organic chemists is that comprising the aliphatic sulphonyl halides, ($R \cdot SO_2Cl$ and $R \cdot SO_2Br$) and their derivatives. They represent one of the forgotten groups in our rapid development of the chemistry of aliphatic compounds. The introduction of the sulphonic acid radical ($—SO_2OH$) into aliphatic compounds by direct treatment with sulphuric acid is extremely limited in its application and is not of practical utility. The method of synthesis which has proven most serviceable is one involving direct replacement of a halogen atom in an aliphatic compound with the sulphonic acid group by interaction with sodium sulphite. The standard procedure for conversion of sulphonic acids into their corresponding halides is by treatment with the required phosphorus halide (PCl_5 or PBr_5). In many cases, however, this method is not practical, and furthermore the use of phosphorus halides has serious objections in both industrial and laboratory operations.

Professor Karrer in the revised edition[2] of his well-known book, "Lehrbuch der Organischen Chemie," introduces the chapter on sulphonic acids as follows: "In der aliphatischen Reihe spielen Sulfonsauren eine untergeordnete Rolle (s.d.); sie sind für allgemeinere Verwendbarkeit zu schwer zuganglich."

The authors desire to report in this preliminary note that aliphatic sulphonyl chlorides and bromides can be prepared with ease without the use of phosphorus halides in any form. In place of the common phosphorus halides used in organic synthesis for preparing such halides the authors substitute thiourea. Starting with this cheap sulphur reagent and an aliphatic halide or alcohol we have developed a method of synthesis which makes the sulphonyl halides available in any quantity desired. The reaction applied, for example, for the synthesis of methyl sulphonyl chloride II is expressed below:



I. II. III.

The s-methylisothiourea I, which is obtained in quantitative yield in the form of its sulphate by interaction of dimethyl sulphate with thiourea, reacts with nascent chlorine in cold aqueous solution to form the sulphonyl chloride II in a yield of 76 per cent. of theory. Marvel, Helfrick and Belsley[3] report that the yield of this same sulphonyl chloride II when prepared by treatment of the sodium salt of methyl sulphonic acid (CH_3SO_2ONa) with phosphorus pentachloride is 21–27 per cent. of theory. If bromine is substituted for chlorine in the authors' process an excellent yield of methyl sulphonyl bromide (CH_3SO_2Br) is obtained. A paper describing this new method of preparing aliphatic sulphonyl halides has been presented by the authors for publication in a future number of the *Journal of the American Chemical Society*.

TREAT B. JOHNSON
JAMES M. SPRAGUE

[1] From the Sterling Chemistry Laboratory of Yale University, New Haven, Connecticut.

[2] "Lehrbuch der Organischen Chemie," Vierte Auflage, Georg Thieme, Verlag, Leipzig (1936).

[3] *Jour. Amer. Chem. Soc.*, 51: 1272, 1929.

BAR DUPLICATION

IN connection with the article "Bar as a Duplication,"[1] published in the February 28 issue of SCIENCE, and signed by C. B. Bridges in Pasadena on February 21, the attention of American readers is called to the fact that essentially the same findings and interpretation as here given by Bridges had already been set forth by the undersigned in co-authorship with Prokofyeva and Kossikov in a preliminary article without figures, entitled "Unequal Crossing over in the Bar Mutant as a Result of Duplication of a Minute Chromosome Section."[2] This article was sent in on December 15, 1935, to the bi-monthly journal, *Comptes Rendus of the Academy of Sciences of the USSR*, and was published in the second number of that journal for 1936, issued on January 25. This issue probably did not

[1] C. B. Bridges, SCIENCE, 83: 210–211, 1936.

[2] H. J. Muller, A. A. Prokofyeva-Belgovskaya and K. V. Kossikov, *C.R. Acad. Sci. USSR.*, 2: 78, 1936.

reach the United States in February, but our results had been publicly announced at a meeting of geneticists in Moscow on December 26, and privately communicated to a number of American and English colleagues in December and January. We should, of course, in our original article, have called the attention of the readers to Bridges' independent or confirmatory work, had we known of it, but we must here explain that our first information concerning it was contained in the above-mentioned issue of SCIENCE. On the other hand, we did in our article mention the partially parallel work of Volotoff, of the Institute of Experimental Biology, Moscow (announced at the same meeting but as yet unpublished), in which the presence of an "inserted section," of unidentified origin, had been observed in the case of double Bar.

Our own finding came as the result of a long and deliberate search for the very structure finally found; in this we had long been hampered by certain technical difficulties. The idea that Bar may represent a duplication *in situ* had been proposed by the present author some years ago,[3] in consideration of its furnishing an explanation of the phenomenon of unequal crossing over and of certain other peculiarities of the Bar case. It may be noted that Bridges' more refined optical technique has allowed him, in this case as in others, to observe a greater degree of detail in the banding of the chromosomes than has been directly visible to us. The same principles concerning the construction of the duplication were, however, noted in both cases—the immediate juxtaposition of the two identical sections, their identical direction (not mirror-image-wise), the greater degree of transverse expansion of each section when they were duplicated than otherwise, and the greater obscurement or zigzagging tendency of their bands when duplicated. The latter two phenomena were interpreted by us both as effects of that tendency to synapsis between the anterior and posterior twin sections which, when occurring in the germ cells, results in the unequal crossing over.

We would take issue, however, with Bridges' designation of the duplication as an "inserted" piece, the point of "insertion" of which (to right or left of the original single section) is uncertain. Not only the cytological evidence, but, with much more exactitude, the fact that normals derived from Bar by unequal crossing over are never deficient, prove that the two twin sections follow immediately upon one another, without any intervening section whatever. This in turn shows that if there had been an actual insertion of a piece from one X chromosome into a sister or homologous X chromosome, one of the two points of breakage giving rise to the small fragment of the first chromosome must have been in exactly the same position as the point of breakage of the second chromosome, into which the piece from the first became inserted. Such a coincidence could be plausibly explained only on the hypothesis that a single X chromosome had become broken at the two points in question first, and then, before reattachment occurred, had doubled, forming two parallel chromatids; after that, attachments of the broken ends occurred in such a way as to result in the inclusion of both of the interstitial fragments, one after the other, into the same chromosome, while the other chromosome (if it rejoined at all) was left deficient. On this view *both* twin pieces would really have been both deleted and inserted. The simpler and more probable explanation for this case, however, is that the two sister or homologous X chromosomes were already separate at the time of breakage, that only the left-hand break occurred in one of them, and only the right-hand break in the other, and that in the subsequent process of attachment, the left-hand piece of the chromosome having the breakage further to the right became attached to the right-hand piece of the chromosome having the breakage further to the left. On this more probable view, then, the duplication did not originate as an insertion at all, and the original mutual breakage point is the point where one twin section now joins the other one. If the remaining pieces also reunited, they must have formed a complementary, deficient chromosome, which was later lost. It is evident that, on this view, the Bar duplication itself has originated by a process which may be termed "unequal crossing over." The unequal crossing over ordinarily observed in Bar is, then, only a kind of secondary unequal crossing over, resulting indirectly from the primary unequal crossing over which established the duplication in the first place.

We would also take issue with Bridges' opinion that the phenotypic effect, Bar eye, may, according to "taste," be considered either as a result of the relative dosage change of genes in the duplicated section, or as a "position effect." For evidence has been found (see discussion by the author,[3,4] chiefly based on evidence by Offermann), that Bar behaves as a neomorph. That is, the mere addition of extra doses of the general region in question (when these contain genes of normal arrangement and composition) does not increase the Bar effect; only extra doses of the Bar genetic complex itself increase the Bar effect. On the other hand, other rearrangements of genes in the Bar region, which we have no reason to suppose involve duplications, do cause phenotypic effects similar to those of the Bar duplication (the first case known to us being

[3] H. J. Muller, *Proc. 6th Int. Cong. Gen.*, 1: 213–255 (see p. 247), 1932.

[4] H. J. Muller, B. B. League and C. A. Offermann, *Anat. Rec.*, 51, 1931.

that of Stone's "Super-Bar," 1930, then Dobzhansky's "Baroid," 1931, then two "moderate-Bar" inversions of the author and many rearrangements recently reported by Volotoff). The phenotypic change is therefore solely a result of the "position effect," and this effect must be sharply distinguished from the effect of dosage change, even though in many individual cases in genetics it has not yet been possible to judge with which class of effect we are dealing.

We consider the point of chief interest in the Bar case to be its illustration of the manner of origination of extra genes in evolution. Bar had for a long time offered the best case yet known for the idea that genes could arise *de novo*. Its interpretation as some sort of duplication met with difficulties, in our ignorance of the real existence of a "position effect" of non-allelomorphic genes upon one another. Now these difficulties are resolved and there remains no reason to doubt the application of the dictum "all life from pre-existing life" and "every cell from a pre-existing cell," to the gene: "every gene from a pre-existing gene." We need at present make an exception here only of those very special conditions under which life itself, as a naked gene, originates.

That the addition of genes by duplicational processes, such as the insertion of small pieces and primary unequal crossing over, is still a factor in evolution, has previously been urged by us. We have discussed the matter recently in connection with the case of achaete and scute, in which the functional similarity found to exist between these neighboring genes suggested that a duplication had occurred in the ancestry of the normal form,[5] and we have discussed it again in the case of a small insertion (scute 19) produced by x-rays, in which a stock of individuals homozygous for the extra section is viable and fertile.[6] It was pointed out in the latter paper that the twin regions would more commonly lie near to one another, in the same chromosome, rather than far apart, as they did in this case. These papers were independent of the recent paper of Bridges[7] on "Salivary Chromosome Maps," which gives cytological evidence of the repetition of at least two sections in the normal second chromosome, and which, on the basis of these, arrives at the same general conclusions. Another case of this kind (that of the "bulb" in the normal X chromosome) has, independently of the cases of Bridges, been discovered by Offermann,[8] who again draws similar conclusions. And most recently Kossikov has found still another case, as yet unpublished. The Bar case fits in with all this convergent evidence and constitutes the first case actually observed in Drosophila of the spontaneous origination of a minute duplication capable of maintaining itself in the homozygous condition.

H. J. MULLER

[5] H. J. Muller, *Jour. Hered.*, 26: 469–478 (see p. 476), 1935.
[6] H. J. Muller, *Genetica*, xvii, 237–252 (see p. 249–250), 1935.
[7] C. B. Bridges, *Jour. Hered.*, 26: 60–64, 1935.
[8] C. O. Offermann, *Jour. Genet.*, 32: 103–116, 1936.

LIVER AS A SOURCE OF VITAMIN G

IN studies relating to the effects of diet on coccidian infections, one of the problems is that of determining the rôle of vitamins. Our previous published results[1] showed that "vitamin G" in autoclaved yeast favored the multiplication of *Eimeria miyairii* in the white rat, as indicated by oocyst counts. In a report now in press,[2] we have shown that when dried powdered liver or liver extract were employed as the sole source of vitamin G, the numbers of oocysts passed by the rats were still only a fraction of those passed by the controls, which received a basal diet plus 10 per cent. yeast. Since the growth of the rats receiving liver was considerably less than that of the reference series receiving yeast, further study on the relation of the amount of liver fed to the growth of the host and the numerical increase of the coccidium was indicated.

Nine rats having a mean weight of 76 gm were fed the basal diet made up to 10 per cent. with powdered dried liver prepared by us as a source of vitamin G and to 4 per cent. with rice polish as a source of vitamin B. Nine rats with a mean weight of 78 gm received the basal diet made up to 10 per cent. with powdered yeast (unautoclaved). During the 22 succeeding days, the test rats gained 70 gm each; the reference rats, 72 gm. It is evident that the animals receiving liver made "normal" growth. All were infected with 1,500 oocysts of *Eimeria miyairii* on the eleventh, thirteenth and fifteenth days on the diets. Subsequently, the test series eliminated a mean of 39.5 million oocysts; the reference series, 137.6 million. It is evident that the addition of liver and rice polish conditioned normal growth, but did not favor the parasite to the extent that yeast did. Furthermore, all the rats were immune to reinfection.

Nine two-week chicks were fed the growing ration we feed rats (Steenbock's), and nine the liver ration described in the preceding paragraph. After twelve days on these diets, each chicken was given 40,000 oocysts of *Eimeria tenella* from a four-month-old culture kept in a refrigerator. During the subsequent infections, the birds on the growing ration for rats eliminated a mean of 67.75 million oocysts; those on the liver diet, a mean of 4.55 million oocysts. In this case also the addition of liver to the diet as the sole source of vitamin G resulted in a much lower oocyst count. These data, however, are not so reliable as

[1] E. R. Becker and N. F. Morehouse, *Proc. Soc. Exp. Biol. and Med.*, 33: 487, 1936.
[2] *Ibid.*, in press.