City, who made the microanalyses for carbon and hydrogen, which are reported in this paper.

Summary

1. A series of new 5,5-dialkyl-hydantoins has been prepared.
2. A report of a preliminary pharmacological study is included.
3. Several of these hydantoins, 5-methyl-5-β-phenylethylhydantoin, and its 5-ethyl analog, have marked hypnotic properties, and are being subjected to clinical study to determine whether they possess any therapeutic value in the treatment of nervous diseases.
4. Two new α-amino acids related to the hydantoins have been prepared.

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[Contribution from the Chemical Laboratory of the University of Illinois]

THE DIRECTIVE INFLUENCE OF THE ALKYLSULFONAMIDO AND DIALKYLSULFONAMIDO GROUPS

By R. L. Shriner, M. T. Goebel and C. S. Marvel

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There have been numerous attempts to formulate rules which will allow one to predict the position which a group will take when it enters a monosubstituted benzene ring. Interest in this general problem has been revived by the appearance of two papers[1] which set forth new empirical rules which are apparently less subject to exceptions than are the previous generalizations. It is obvious, however, that a general rule based on theoretical considerations cannot be formulated until all of the common substituents in the ring have been considered. The present work concerns the sulfonamido and disulfonamido groups, which have not been fully considered in the earlier papers.

Hammick and Illingworth[1b] have stated the following orientation rule: "If in the benzene derivative C_6H_5XY, Y is to the right of X in the periodic table, or if, being in the same group, Y is of a lower atomic weight than X, a second atom or group will enter the nucleus in the meta position. In all other cases including that in which XY is a single atom, a second entering group or atom goes to the ortho and para positions." The effect of ionic charges on XY is also discussed and it is pointed out that positive charges direct meta and negative charges direct ortho and para. In the application of their rule they do not clearly indicate what may be expected from a group such as CH_2Cl or $CHCl_2$ where X is C and Y may be H or Cl. In such a case it is obvious that following the rule alone one would predict mixtures of ortho, meta and para isomers. This agrees

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[1] (a) Latimer and Porter, This Journal, **52**, 206 (1930); (b) Hammick and Illingworth, *J. Chem. Soc.*, 2358 (1930). A review of the earlier literature can be found in these articles.

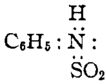
fairly well with the facts which have been established by experiment. A group such as the sulfonamido $—N\langle\begin{smallmatrix}SO_2R\\ H\end{smallmatrix}$ is another of this doubtful type, for the hydrogen atom is to the left of the nitrogen in most arrangements of the periodic table and sulfur is to the right of nitrogen. Hence, according to the above rule, a mixture of all three isomers would be predicted. Another factor which must be considered is the acidic properties of the monosulfonamides. This property would lead one to expect a behavior similar to that of the aci-nitro compounds which, as Baker[2] has shown, direct the entering group meta.

However, the aryl sulfonamido group is known to be a group which directs mainly to the ortho and the para positions. Without attempting to cite all of the literature references it can be stated that many aryl sulfonanilides have been halogenated and nitrated and that the products formed were ortho and para substituted derivatives. Quite recently Bell[3] has studied carefully the nitration and halogenation of certain aryl sulfonanilides and has compared the directive effect of the aryl sulfonamido group with that of the acetamido group. His results indicate clearly that the aryl sulfonamido group is an ortho–para directing group.

The disulfonamido group $—N—(SO_2R)_2$ has been less thoroughly examined and the only information concerning its effect is the statement by Bell[3b] that it is more difficult to nitrate a diaryl sulfonanilide than an aryl sulfonanilide and that under vigorous conditions of nitration nitro groups are introduced in both the aryl sulfonyl and the aniline residues. The rule of Hammick and Illingworth[1b] would lead one to predict that the disulfonamido group would direct an entering group to the meta position only.

Latimer and Porter[1a] base their predictions of the position taken by a group entering a monosubstituted benzene ring on values obtained by calculating in a semi-quantitative manner the residual charge on the atom attached to the ring. By a study of most of the known groups they show that if the residual charge on this atom has a high positive value ($> +0.6$), the new group enters the meta position; whereas if the value of the residual charge is negative, zero or slightly positive ($< +0.1$), ortho and para substitution occur. Mixtures result in the case where the residual charge is between $+0.1$ and $+0.6$. If Latimer and Porter's method of calculating residual atomic charges is applied to the sulfonamido and disulfonamido groups the results are as follows

Residual charge on nitrogen equals



$$C_6H_5:\overset{\displaystyle H}{\underset{\displaystyle SO_2R}{\ddot{N}}}:\quad +5-2-(2\times{}^1/_2)-(2\times{}^5/_9)-(2\times{}^5/_{11}) = -0.02$$

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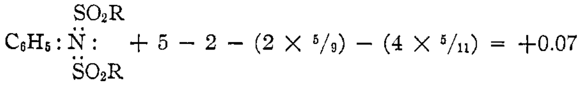
[2] Baker, *J. Chem. Soc.*, 2257 (1929).

[3] Bell (a), *ibid.*, 2770 (1928); (b) 2787 (1929); (c) 2338 (1931).

Residual charge on nitrogen equals



$$C_6H_5:\overset{\mathrm{SO_2R}}{\underset{\mathrm{SO_2R}}{\ddot{\mathrm{N}}}}:\quad +5-2-(2\times {}^5/_9)-(4\times {}^5/_{11}) = +0.07$$

It will be noted that the charge on the nitrogen atom is negative in the monosulfonanilide, and slightly positive but less than +0.1 in the disulfonanilide. Hence, both of these groups would fall in the ortho and para directing class.

The present work was undertaken to confirm the previously reported directive effects of the sulfonamido group and to determine that of the disulfonamido group. Methanesulfonanilide and dimethanesulfonanilide were selected for study because each contains only one aromatic nucleus and the alkyl sulfonyl group is small so that steric effects should be of less consequence. Nitration was selected as a suitable reaction for introducing a new group since it is a characteristic reaction and usually gives crystalline derivatives. The nitration of methanesulfonanilide proceeded smoothly and the crystalline product isolated from the nitration mixture in yields of over 80% of the theoretical amount was 2,4-dinitro-methanesulfonanilide. Some hydrolysis occurred during nitration. Hydrolysis and mechanical losses account for the difference between the actual yield and the theoretical yield. No other isomer could be detected.

The nitration of dimethanesulfonanilide was more difficult to bring about. The fact that nitration proceeded more slowly was in agreement with the statement of Bell[3b] concerning substitution in diaryl sulfonanilides. In addition to the well-defined crystalline *p*-nitro derivative, a mixture of lower-melting products, including a resinous impurity, was obtained. The lower-melting fractions were hydrolyzed and by steam distillation some *o*- and *m*-nitroanilines were carried over. A further quantity of *p*-nitroaniline was recovered in the non-volatile portion. By repeated distillation with steam and recrystallization, rather pure *m*-nitroaniline was obtained. A very small amount of crystalline *o*-nitroaniline was obtained by sublimation. With this evidence of its presence further estimation of the amounts of the ortho and meta isomers which were present in the material could be made by use of Tingle and Roelker's[4] data on the melting points of mixtures of these compounds.

The results of this separation of products indicate that the nitration of dimethanesulfonanilide gave over 61% of the para isomer, and approximately 13% of meta and 6% of the ortho isomers. This estimation of the ortho isomer is the least satisfactory and probably the portion unaccounted for was the ortho isomer. It is thus established that the di-methanesulfonamido group is essentially an ortho–para directing group.

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[4] Tingle and Roelker, THIS JOURNAL, **30**, 822 (1908).

Experimental Part

Methanesulfonyl chloride and methanesulfonanilide were prepared by the procedures previously described.[5]

Dimethanesulfonanilide.—A solution of 27 g. of methanesulfonanilide and 20 g. of methanesulfonyl chloride in 100 cc. of dry benzene was refluxed for two hours. The solvent was then removed by distillation under reduced pressure and the sirupy residue was treated with about 200 cc. of cold 10% aqueous sodium hydroxide solution to extract the unreacted methanesulfonanilide. The insoluble residue was collected on a Büchner funnel and washed repeatedly with hot alcohol. The white crystalline material thus obtained weighed 29 g. (71% of the theoretical amount); m. p. 201–202°.

Anal. (Kjeldahl) Subs., 0.5032, 0.4420: 20.2, 17.6 cc. of 0.101 *N* HCl. Calcd. for $C_8H_{11}O_4NS_2$: N, 5.62. Found: N, 5.68, 5.64. (Parr Bomb) Subs., 0.6355, 0.3370: $BaSO_4$, 1.1969, 0.6317. Calcd. for $C_8H_{11}O_4NS_2$: S, 25.7. Found: S, 25.80, 25.67.

Nitration of Methanesulfonanilide.—To a well-stirred mixture of 100 cc. of concentrated nitric acid (sp. gr. 1.42) and 50 cc. of concentrated sulfuric acid (sp. gr. 1.84) maintained at 30–40° was slowly added 20 g. of methanesulfonanilide. The addition required an hour and the mixture was allowed to stand for three hours longer. It was then poured into 400 cc. of ice and water in order to precipitate the nitration product. By filtering this solution and air drying the precipitate, there was obtained 27 g. of light yellow product, m. p. 120–170°. This product was washed four times with 50-cc. portions of hot alcohol. The insoluble residue weighed 23 g. and melted sharply at 171–172°.

The alcoholic solution was evaporated and yielded 4 g. of a product melting at 130–160°. This was renitrated with 50 cc. of red fuming nitric acid at 40°. On working up this mixture as before 1.5 g. of product melting at 170–172° was obtained. From the alcoholic mother liquors about 1 g. of low melting material was again recovered.

Further recrystallization of the nitration product gave pure 2,4-dinitromethanesulfonanilide which melted at 173.5–174.5°.

Anal. (Parr Bomb). Subs., 0.6625, 0.6588: $BaSO_4$, 0.6000, 0.5945. Calcd. for $C_7H_7O_2SN(NO_2)_2$: S, 12.25. Found: S, 12.41, 12.36.

The total yield of dinitro compound (m. p. 170–172°) was 24.5 g. (80.6% of the theoretical amount). The fact that the low-melting compound could be further nitrated to yield the higher-melting compound indicated that the first product was a mixture of ortho- and para-mononitro derivatives.

Identification of the Dinitromethanesulfonanilide.—Five grams of the dinitromethanesulfonanilide (m. p. 170–172°) obtained as described above was hydrolyzed by refluxing it for six hours with a mixture of 30 cc. of concentrated sulfuric acid and 30 cc. of water. The reaction mixture was poured into a large volume of ice water and the precipitate of 2,4-dinitroaniline was filtered. After washing with water and alcohol and air drying, the yellow crystalline material melted at 176.5–178° and weighed 3.5 g. (practically a quantitative yield). A mixture of this product with known 2,4-dinitroaniline (m. p. 180°) melted at 179–180°.

The 2,4-dinitroaniline from the hydrolysis mixture was further characterized by treating a sample (0.5 g.) with excess acetyl chloride. The 2,4-dinitroacetanilide thus obtained melted at 119–120°. The melting point recorded for this product is 120–121°.

The same dinitromethanesulfonanilide was obtained by nitrating *p*-nitromethanesulfonanilide prepared by the method of Morgan and Pickard.[6]

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[5] Marvel, Helfrick and Belsley, THIS JOURNAL, **51**, 1272 (1929).

[6] Morgan and Pickard, *J. Chem. Soc.*, **97**, 61 (1910).

Nitration of Dimethanesulfonanilide.—Preliminary experiments showed that nitration did not take place when dimethanesulfonanilide was treated with a mixture of concentrated nitric and sulfuric acid at 30–40°, or at 60–70°. The use of fuming nitric acid gave satisfactory results.

To a mixture of 100 cc. of red fuming nitric acid (sp. gr. 1.60) and 50 cc. of concentrated sulfuric acid (sp. gr. 1.84) was added slowly 30 g. of dimethanesulfonanilide. The mixture was stirred and the temperature maintained at about 20°. The mixture was stirred for two hours after the addition of the anilide was complete, diluted with ice water, and filtered. The crude air-dried nitration product weighed 30 g. (85% of the theoretical yield of mononitro compound).

Repeated extraction with hot alcohol and subsequent recrystallization yielded, from 24 g. of the crude product, the following fractions: (I) m. p. 215–225°, 12 g.; (II) m. p. 160-195°, 3 g.; (III) m. p. 140–150°, 5 g.; (IV) m. p. 110–135°, 1.5 g.; (V) resinous material, 1 g.

Fraction (I), which was almost insoluble in hot alcohol, was further washed, and finally recrystallized from benzene. The pure product melted at 230-231°. It was analyzed for sulfur and results of the analysis show that it is a mononitro derivative.

Anal. (Parr Bomb). Subs., 0.3985: $BaSO_4$, 0.6379. Calcd. for $C_8H_{10}O_4NS_2$-(NO_2); S, 21.77. Found: S, 21.91.

***p*-Nitrodimethanesulfonanilide.**—The structure of the compound constituting Fraction I was established by synthesis from *p*-nitromethanesulfonanilide and by hydrolysis to *p*-nitroaniline. One gram of *p*-nitromethanesulfonanilide was refluxed with 2 cc. of methanesulfonyl chloride and 2 cc. of tributylamine in toluene solution. The toluene was distilled under reduced pressure and the residue was washed with sodium carbonate solution and dilute hydrochloric acid. The insoluble residue (0.5 g.) was recrystallized from an excess of hot alcohol. The product melted at 225–228°. A mixture with the product obtained in fraction I above melted at 228–230°.

Hydrolysis of Nitration Products.—Five grams of fraction (I) was refluxed for six hours with a mixture of 30 cc. of concentrated sulfuric acid and 30 cc. of water. The reaction mixture was cooled, diluted with water to 200 cc., made slightly alkaline by the addition of 20% sodium hydroxide solution, cooled and extracted with three 200-cc. portions of ether. The residue after evaporating the ether from the extract weighed 2.2 g. and melted at 141–145°. A mixed melting point with known *p*-nitroaniline showed no depression.

One gram of this product was refluxed with a slight excess of acetic anhydride for fifteen minutes. The *p*-nitroacetanilide, recovered by dilution with water, melted at 203–207°. The melting point of *p*-nitroacetanilide is given as 207–210°.

The lower melting fractions which remained after separating the pure *p*-nitrodimethanesulfonanilide could not be separated into pure substances by further crystallizations. No simple or accurate method of analysis was available but by the following methods it was possible to show that some meta- and some ortho-nitrodimethanesulfonanilide were formed in the nitration.

Two grams of fraction (II) was hydrolyzed with 50% sulfuric acid. This reaction mixture was then diluted, neutralized with sodium hydroxide solution, and steam distilled. Two liters of distillate were collected. Each portion of distillate was extracted with ether. Fraction (VI), recovered from the first liter of distillate as a residue when the ether was evaporated, weighed 0.1 g. and melted at 80–90°. Fraction (VII), recovered in the same manner from the second liter, weighed 0.2 g. and melted at 90–110°. The residue remaining in the distilling flask was also extracted with ether to yield fraction (VIII) which weighed 0.4 g. and melted at 135–141°. Fraction (VIII) when mixed with known *p*-nitroaniline melted at 140–145°.

Three grams of fraction (III) was hydrolyzed and the products of hydrolysis were separated as above. Fraction (IX) weighed 0.2 g. and melted at 55–80°. Fraction (X) weighed 0.2 g. and melted at 85–100°. Fraction (XI), recovered from the residue, melted at about 90°. It was recrystallized from alcohol and yielded 0.4 g. of material (fraction (XII)) melting at 127–139°. This was mainly *p*-nitroaniline. Fraction (XIII), recovered from the alcoholic mother liquors, weighed 0.2 g. and melted at 85–95°.

One gram of fraction (IV) was hydrolyzed as described above. It was then extracted with ether. The material recovered from this extract weighed 0.4 g. and melted at 48–80°. This residue was not entirely soluble in dry ether, however. About 0.05 g. was recovered as an insoluble residue, melting above 260°, which burned explosively when held over the Bunsen flame. This product was isolated in only one experiment, and so could not be investigated further. The ether-soluble portion now melted at 48–70°.

Fractions (VI), (VII), (X), and (XIII) were combined and dissolved in 10 cc. of dilute hydrochloric acid. This solution was made slightly alkaline. On long standing, and cooling in an ice-bath, 0.4 g. of material precipitated out as yellow needle-like crystals, melting at 108–112°. A mixed melting point with known *m*-nitroaniline (m. p. 114°) showed no depression.

The *m*-nitroacetanilide was prepared by treatment with acetic anhydride and melted at 147–149°. This checks the melting point reported for *m*-nitroacetanilide.

Fraction (IX) was combined with the low melting product recovered by hydrolysis of fraction (IV). This was placed in a porcelain dish, covered with a watch-glass, and allowed to stand for several days. At the end of this time, 0.1 g. of sublimate was recovered from the watch-glass. This material melted at 65–68°, and melted at 67–70° when mixed with known *o*-nitroaniline.

By this rather complicated method, from 24 g. of nitration product there was recovered 12 g. of substantially pure *p*-nitrodimethanesulfonanilide and 1.25 g.[7] of *p*-nitroaniline. This corresponds to 61% of the theoretical amount of *p*-nitro isomer.

There was also isolated 1.1 g. of impure *m*-nitroaniline which melted 87–104°. Tingle and Roelker[4] have found that a mixture of nitroanilines containing 20–22% of the ortho isomer and 80–78% of the meta isomer melts in this range. In calculating the approximate yields of the isomers formed in our experiments, this mixture was assumed to contain 20% of the ortho isomer.

A further fraction of 0.95 g. of a mixture of *o*- and *m*-nitroanilines melting from 60–80° was obtained. The melting point curves indicate that the mixtures of the ortho and meta isomers which melt in this range contain about 40% of the ortho compound. This figure was used in calculating the composition of this fraction.

This indicates that the original nitro derivative contained approximately 13% of meta and 6% of the ortho isomer. These figures represent the minimum amounts of each which must have been formed during the nitration of dimethanesulfonanilide.

Summary

1. The nitration of methanesulfonanilide results in an 80% yield of 2,4-dinitromethanesulfonanilide.

2. The nitration of dimethanesulfonanilide yields a mixture of mononitro derivatives which have been shown to contain at least 61% para, 13% meta and 6% ortho. The estimation of the ortho isomer is the least satisfactory.

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[7] This figure is calculated as the total amount of *p*-nitroaniline and is based on the results of the hydrolysis of an aliquot part of fraction (VI).

3. These results indicate that the directive effect of the monosulfonamido and disulfonamido groups in the benzene ring is predominantly ortho-para.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

THE PREPARATION OF CERTAIN KETO-CHLORIMINES BY THE ACTION OF CHLORINE ON COMPOUNDS OF THE TYPE $R'R''C{=}NMgX$[1]

BY C. R. HAUSER, H. A. HUMBLE AND G. J. HAUS

RECEIVED FEBRUARY 1, 1932 PUBLISHED JUNE 6, 1932

In connection with a study of ald-chlorimines[2] we were desirous of obtaining certain keto-chlorimines in order to make a comparative study of these compounds. Several keto-chlorimines previously have been prepared by Peterson[3] by a method which involves several steps. Thus, benzophenone was converted into benzophenone dichloride, which in turn was converted, by means of urethan, into the imine hydrochloride. The latter was treated with hypochlorous acid, yielding the chlorimine according to equation (1).

$$(C_6H_5)_2C{=}NH + HOCl \longrightarrow (C_6H_5)_2C{=}NCl + H_2O \qquad (1)$$

In the hope of developing a shorter method for the preparation of certain keto-chlorimines, it seemed worth while to attempt the chlorination of nitrogen-magnesium compounds of the type $R'R''C{=}NMgX$,[4] which may readily be obtained from Grignard reagents and nitriles,[5] by means of chlorine (2), and of alkyl hypochlorites (3).

$$-R'R''C{=}NMgX + Cl_2 \longrightarrow R'R''C{=}NCl + MgXCl \qquad (2)$$

$$-R'R''C{=}NMgX + R'''OCl \longrightarrow R'R''C{=}NCl + MgXOR''' \qquad (3)$$

Since Durand and Naves[6] have shown previously that ethyl hypochlorite reacts with the nitrogen-magnesium compound obtained from aniline and ethylmagnesium bromide to yield presumably a chloramine (4), it might

$$-C_6H_5NHMgBr + C_2H_5OCl \longrightarrow C_6H_5NHCl + C_2H_5OMgBr \qquad (4)$$

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[1] This paper is in part constructed from portions of a thesis presented by G. J. Haus in partial fulfilment of the requirements for the degree of Master of Arts in the Graduate School of Arts and Sciences, Duke University.

[2] Hauser and Gillaspie, THIS JOURNAL, **52,** 4158, 4517 (1930).

[3] Peterson, *Am. Chem. J.*, **46,** 325 (1911).

[4] Since compounds of the type $R'R''C{=}NMgX$ might be considered as salts of imines ($R'R''C{=}NH$) and $MgX(OH)$, chlorine might be expected to react with the nitrogen-magnesium linkage under certain conditions. Doubtless other reactions also occur. A discussion of these reactions is withheld pending further investigation.

[5] Blaise, *Compt. rend.*, **132,** 40 (1901).

[6] Durand and Naves, *Bull. soc. chim.*, **37,** 717 (1925).