this time. After dilution with water, extraction with chloroform, washing the chloroform with a saturated solution of sodium bicarbonate, drying and evaporation, an oil was obtained which, when triturated with ether, gave crystals. Subsequent recrystallization from methylene chloride–ether yielded 30 mg. of analytically pure 9α-chloro-11α-methyl-17α,20;20,21-bismethylenedioxy-4-pregnene-11β-ol-3-one (XI), m.p. 260–265° dec.; λ_{max}^{Nujol} 2.8, 6.05, 6.2(sh), 9.2–9.4 μ. *Anal.* Calcd. for $C_{24}H_{32}O_6Cl$: C, 63.77; H, 7.13; Cl, 7.84. Found: C, 63.94; H, 7.34; Cl, 7.94.

11α-Methyl-9,11β-oxido-17α,20;20,21-bismethylenedioxy-4-pregnene-3-one (X) from **9α-Chloro-11α-methyl-17α,20;20,21-bismethylenedioxy-4-pregnene-11β-ol-3-one (XI).**—Twenty milligrams of 9α-chloro-11α-methyl-17α,20;20,21-bismethylenedioxy-4-pregnene-11β-ol-3-one (XI) was heated at reflux for two hours in 5 ml. of methanol with 20 mg. of potassium carbonate in 2 ml. of water. After evaporation to dryness *in vacuo*, the product was extracted with methylene chloride, dried and evaporated to yield crystals which gave a negative Beilstein test. Recrystallization from methanol yielded 10 mg. of 11α-methyl-9,11β-oxido-17α,20;20,21-bismethylenedioxy-4-pregnene-3-one (X), m.p. 235–240°. Admixture with an authentic sample of the oxide did not depress the melting point and the infrared spectra of the two compounds were identical.

11α-Methyl-9,11β-oxido-4-pregnene-17α,21-diol-3,20-dione 21-Acetate (XII).—One hundred milligrams of 11α-methyl-9,11β-oxido-17α,20;20,21-bismethylenedioxy-3-ethylenedioxy-5-pregnene (IX) was heated at steam-bath temperature for 5 minutes with 12 ml. of glacial acetic acid, 12 ml. of water and 2 ml. of concentrated hydrochloric acid. It was cooled, poured into 10% sodium hydroxide, extracted well with ethyl acetate, washed with water, dried and evaporated *in vacuo*. Acetylation of the total crude was accomplished by heating for 10 minutes on the steam-bath with 1 ml. of pyridine and 1 ml. of acetic anhydride. It was worked up in the usual manner and chromatographed on 4 g. of acid-washed alumina. Elution of the column with ether–chloroform (1:4) and chloroform gave 20 mg. of the desired 11α-methyl-9,11β-oxido-4-pregnene-17α,21-diol-3,-20-dione-21-acetate (XII) as a non-crystalline solid, suitable for use in subsequent transformations; $\lambda_{max}^{CHCl_3}$ 2.8, 5.70–5.79, 6.0, 6.15(sh), 7.90 μ.

9α-Chloro-11α-methyl-4-pregnene-11β,17α,21-triol-3,20-dione 21-Acetate (XIII).—One hundred twenty milligrams of 11α-methyl-9,11β-oxido-4-pregnene-17α,21-diol-3,20-dione 21-acetate (XII) was dissolved in 5 ml. of chloroform. It was cooled to ice-bath temperature and 5 ml. of 0.45 *N* hydrogen chloride in chloroform was added. The reaction mixture was allowed to stir at ice-bath temperature for a half-hour and at room temperature for a half-hour. Water and chloroform were added and the chloroform phase was washed with a saturated solution of sodium bicarbonate, dried, evaporated and the resulting oil chromatographed on 5 g. of acid-washed alumina. Elution of the column with ether–chloroform (1:4) and chloroform gave crystals which upon recrystallization from methylene chloride–ether gave 50 mg. of analytically pure 9α-chloro-11α-methyl-4-pregnene-11β,17α,21-triol-3,20-dione 21-acetate (XIII), m.p. 230–235° dec.; λ_{max}^{MeOH} 242 mμ, *E* 16,400; λ_{max}^{Nujol} 2.75, 3.0, 5.70, 5.80, 6.1, 6.2(sh), 8.1 μ. *Anal.* Calcd. for $C_{24}H_{33}O_6Cl$: C, 63.63; H, 7.34; Cl, 7.83. Found: C, 63.64; H, 7.40; Cl, 8.36.

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RAHWAY, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF FOREST CHEMISTRY, COLLEGE OF FORESTRY, STATE UNIVERSITY OF NEW YORK, AND THE POLYMER RESEARCH LABORATORY, THE DOW CHEMICAL CO.]

Distribution of Methoxyl Groups in the Methylation of the Monosodio Derivatives of Methyl α-D-Glucopyranoside and Cellulose[1,2]

BY ROBERT W. LENZ

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The monosodio derivatives of methyl α-D-glucopyranoside and cellulose were prepared and methylated, and the products were analyzed by hydrolysis and quantitative paper chromatography. The methylated derivatives of both contained unsubstituted, mono-, di- and tri-O-methylglucoses and the mono-O-methyl fraction contained the three principal isomers. In both cases, 2-O-methyl-D-glucose was the sugar present in the highest percentage of the hydrolyzate. Application of Spurlin's statistical treatment gave the relative rate constants: $k_2 = 5$, $k_3 = 1$, $k_6 = 2.5$, $k_a = 8$, $k_b = 6.7$.

The relative reactivities of the three hydroxyl groups in cellulose remains a fundamental problem in the chemistry of this polymer. This problem has gained an increasing amount of attention in recent years for a number of reasons. For one, a correlation appears to exist between the chemical and physical properties of cellulose derivatives and the relative distribution of the substituent groups on the primary and secondary hydroxyls.[3-6] For another, knowledge of the mode of distribution is important for elucidating the structure of addition compounds formed as intermediates[7-9] and in interpreting the mechanism of the substitution reactions used for the preparation of derived polymers of cellulose.[10-14]

Through the years a considerable weight of experimental evidence has been amassed which indicates that the C-2 hydroxyl group is the most acidic hydroxyl group of the three in the glucopyranoside repeating unit of cellulose. As a result, both equilibrium and rate-controlled reactions which involve the alkoxide anion appear to occur preferentially

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(2) Presented at the Symposium on Chemical Reactions of Polymers, Division of Polymer Chemistry, 136th Meeting of the American Chemical Society, Atlantic City, N. J., September 15, 1959.

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(10) J. E. Mahoney and C. B. Purves, THIS JOURNAL, **64**, 15 (1942).

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at this position. The principal exceptions to this generalization are the reactions in which steric effects are important as in the formation of trityl ethers and tosyl esters.[15] The preferential reactivity of the C-2 hydroxyl appears to be particularly evident in the methylation of glucosides and di- and polysaccharides by the Williamson synthesis. This preference has been reported in both the homogeneous and heterogeneous methylations of cellulose[8,9,16–28] but does not appear to hold in other etherification reactions. Even in the closely related ethylation reaction, a preference for the less sterically hindered primary hydroxyl has been observed,[6,22,29,30] and increasing the size of the etherifying agent to the hydroxyethyl,[31] cyanoethyl,[32] benzyl[33] or carboxymethyl[6,14,34] group appears to magnify this effect considerably, indicating a marked steric control in these reactions.

Under certain conditions the preferential reactivity of the C-2 hydroxyl groups in methyl α-D-glucopyranoside, starch and cellulose has been reported to be complete; that is substitution was believed to occur only at this position.[15] This selectivity has been reported for the methylation of the monopotassio derivatives of amylose and cellulose,[20,21] the monosodio derivative of starch,[35] and the monosodio derivatives of methyl α-D-glucopyranoside[36] and cellulose.[37,38] The purpose of the present investigation was to verify or disprove the reported extreme selectivity of these monoalkali glucosides to methylation. In almost all previous investigations the distribution of substituents on the three hydroxyl groups has been determined either by fractional crystallization or distillation of the methylglucoses obtained on hydrolysis of the methylcellulose, or by a series of substitution and degradation reactions carried out directly on the derived polymer.[9] Neither of these procedures, however, gives a complete and unequivocal accounting of all substituents. In fact, most of the reactions employed quantitatively in the chemical methods of analysis have been criticized in the literature including the tosylation–iodination,[11,39] tritylation[5] and periodate oxidation[40–43] procedures. In the present investigation, quantitative paper chromatography of the hydrolyzate was employed to determine the distribution of methoxyl groups in the methylation of the monosodio derivatives of methyl α-D-glucopyranoside and cellulose.

The monosodio derivatives of these two glucosides were prepared according to the procedures described by Wolfrom and co-workers[36,37] in which the glucoside is refluxed with sodium hydroxide in 1-butanol and the water formed is removed by azeotropic distillation. The sample of methyl monosodio-α-D-glucopyranoside obtained had a ratio of 0.94 equivalent of base per equivalent of glucoside unit as compared to 0.92 observed by Wolfrom and El-Taraboulsi.[36] This derivative was methylated with methyl iodide at 100° and the products were hydrolyzed and chromatographed. The monosodio cellulose prepared was methylated by the same procedure to a product having a degree of substitution of 0.96 as compared to 1.03 obtained by Sugihara and Wolfrom.[37] This methylcellulose was also hydrolyzed and chromatographed. In the analysis of the methylated products, of both the mono- and polysaccharide, the unsubstituted, mono-, di- and tri-O-methylglucoses obtained were first separated,[28] and then the eluted mono-O-methylglucose fraction was resolved into the three principal isomers. In both cases quantitative paper chromatography was used.[28,44] The results are presented in Tables I and II.

TABLE I

SUBSTITUTION DISTRIBUTION OBTAINED IN THE METHYLATION OF THE MONOSODIO DERIVATIVES

Sugar present in hydrolyzate	Mole per cent. Methyl α-D-glucopyranoside	Mole per cent. Cellulose
Glucose	30	38
Mono-O-methyl-D-glucose	36	34
Di-O-methyl-D-glucose	22	22
Tri-O-methyl-D-glucose	12	6
D. S.	1.16	0.96

TABLE II

DISTRIBUTION OF MONO-O-METHYL-D-GLUCOSES OBTAINED IN THE METHYLATION OF THE MONOSODIO DERIVATIVES

Sugar present in hydrolyzate	Mole per cent. Methyl α-D-glucopyranoside	Mole per cent. Cellulose
2-O-Methyl-D-glucose	52	49
3-O-Methyl-D-glucose	12[a]	10
6-O-Methyl-D-glucose	36	41

[a] Probably also includes the 4-O-methyl-D-glucose present in the hydrolyzate as the spot obtained was more diffuse than normal.

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(29) J. E. Mahoney and C. B. Purves, THIS JOURNAL, **64**, 9 (1942).
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(41) C. S. Hudson and E. L. Jackson, THIS JOURNAL, **59**, 944, 2049 (1937).
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The exclusive selectivity proposed by the previous workers for the methylation of these monosodio derivatives is apparently contradicted by the results of Tables I and II. The hydrolyzates of the methylated products of the monosodio derivatives of both methyl α-D-glucopyranoside and cellulose were found to contain mono-, di- and tri-O-methylglucoses, and the mono-O-methylglucose fractions contained at least the three principal isomers. In addition, a tetra-O-methylglucose fraction may have also been present, but, if so, this fraction was either included in the tri-O-methyl spot or carried off of the filter paper as no other spot was observed. Furthermore, the 3-O-methyl spot obtained from the chromatographic separation of the monosubstituted fraction from methyl α-D-glucopyranoside was observed to be more diffuse at the front end than in the control separations. This elongation was believed to be caused by the presence of 4-O-methyl-D-glucose in the hydrolyzate.

The relative amounts of the various methylglucoses obtained may explain the erroneous conclusions of the previous workers on the exclusive formation of the C-2 substituted derivatives. Wolfrom and El-Taraboulsi, using a fractional crystallization procedure on the products of the methylation of methyl monosodio-α-D-glucopyranoside, were able to isolate only the 2-O-methyl-D-glucose as the triacetate after the removal of unsubstituted methyl α-D-glucopyranoside.[34] This mono-O-methylglucose derivative, however, was obtained in only 12.5% yield. In the present investigation, the 2-O-methyl-D-glucose present amounted to 18.2% of the products in the hydrolyzate. Obviously, the 2-O-methyl derivative is present to largest extent of all substituted glucoses and it is the only methylglucose representing more than 13% of the product. Therefore, the fact that no other sugar could be made to crystallize out is not surprising. These results and conclusions have been fully corroborated by Hess and coworkers who, however, worked only with monosodio cellulose and were able to separate quantitatively only the methyl glucoses of different degrees of substitution.[45]

It is interesting to compare the distribution of methylated glucoses of different degrees of substitution obtained in this investigation with distributions reported for other methylcelluloses. Rebenfeld and Pacsu analyzed a commercial methyl cellulose prepared by a very similar procedure, *viz.* gaseous methyl chloride on alkali cellulose.[28] The analysis is given in Table III along with the theoretical distribution calculated by Spurlin for a homogeneous, rate-controlled reaction.[4] The close agreement between the products from the methylation of the monosodio cellulose and alkali cellulose leaves no doubt about the close similarity of the two types of substrates. On the other hand, comparison of the observed distribution of methyl glucoses with that calculated for homogeneous methylation in Table III assuming complete accessibility of all repeating units and equal reactivity of all hydroxyl groups emphasizes the dissimilarity between these reaction types. Two important

(45) K. Hess, E. E. Heumann and R. Leipold, *Ann.*, **594**, 119 (1955).

TABLE III

SUBSTITUTION DISTRIBUTIONS FOR METHYLCELLULOSE

Sugar present in hydrolyzate	Methylcellulose: From monosodio cellulose	Methylcellulose: From commercial methylation[a]	Theoretical for homogeneous methylation[b]
Glucose	38	36	34
Mono-O-methyl-D-glucose	34	36	44
Di-O-methyl-D-glucose	22	21	19
Tri-O-methyl-D-glucose	6	7	3
D.S.	0.96	0.99	0.91

[a] Prepared by reacting alkali cellulose with gaseous methyl chloride. [b] Assuming a ratio of rate constants $k_2:k_3:k_6$ of 1:1:1.[4]

conclusions can be drawn from this comparison. First, the higher than theoretical percentage of unsubstituted glucose can be attributed to the presence of inaccessible regions in the cellulose sample reacted. The second, and more tenuous conclusion, is that the higher than theoretical percentage of di- and trisubstituted glucoses can be attributed to an enhancement of the reactivity of one hydroxyl group when another on the same repeating unit was substituted. Of course the alternate and more popular conclusion would be to attribute this high degree of polysubstitution to the operation of a micellar heterogeneous reaction[18,28,46] in which the more accessible repeating units were doubly and triply methylated because of diffusion control of the reaction. However, when the results in Tables I and II were applied to Spurlin's treatment in which the relative rate constant of one secondary hydroxyl group was increased by substitution of the adjacent group, good agreement between the observed and calculated distributions was obtained.[47] From the distribution of monosubstituted glucoses in the methylation of methyl monosodio-α-D-glucopyranoside, the relative rate constants for substitution at the C-2, C-3 and C-6 hydroxyl groups, k_2, k_3 and k_6, were calculated to be 5, 1 and 2.5, respectively. By inserting these values in the equations derived by Spurlin[47] and solving for the two modified rate constants by trial and error, it was found that when substitution occurred on the adjacent secondary hydroxyl group the modified relative rate constant for the C-2 hydroxyl, k_a, was 8 and that for the C-3 hydroxyl, k_b, was 6.7. The results of this analysis are given in Table IV in which it can be seen that very good agreement was realized. In these calculations the rate constant, k_3, for substitution on the C-3 hydroxyl is probably a sum value for the rate constants of the C-3 and C-4 hydroxyls, because it was believed that the spot attributed to the 3-O-methyl derivative also contained both 3- and 4-O-methyl-D-glucose. In subsequent calculations on cellulose this apparent sum value was taken as the rate constant for the C-3 hydroxyl alone. The agreement obtained between observed and calculated distributions for cellulose indicates that this assumption was a reasonable one.

The constants obtained for methyl α-D-glucopyranoside were then applied directly to the

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TABLE IV

CALCULATED AND OBSERVED DISTRIBUTIONS IN THE METHYLATION OF METHYL MONOSODIO-α-D-GLUCOPYRANOSIDE FOR $k_2 = 5$, $k_3 = 1$, $k_6 = 2.5$, $k_a = 8$, $k_b = 6.7$

Component	Mole per cent. Observed	Calculated
C_0[a]	30	31
C_1	36	36
C_2	22	25
C_3	12	8
S_2[b]	19	19
S_3	4	4
S_6	13	13
D.S.	1.16	1.10

[a] C_m represents the mole fraction of the glucose methyl ethers having a D.S. = m. [b] S_n represents the mole fraction of a particular glucose methyl ether substituted at position n.

methylation of monosodio cellulose by assuming that the reaction was homogeneous in the accessible regions. The fraction of inaccessible repeating units was readily calculated from the observed and theoretical percentages of glucose in the hydrolyzate, 38 and 30%, respectively. These quantities indicated that 10% of the cellulose was inaccessible, and applying the relative rate constants above to the accessible 90% gave the calculated values of Table V. The correlation is again very good.

TABLE V

CALCULATED AND OBSERVED DISTRIBUTIONS IN THE METHYLATION OF MONOSODIO CELLULOSE FOR $k_2 = 5$, $k_3 = 1$, $k_6 = 2.5$, $k_a = 8$, $k_b = 6.7$, 90% ACCESSIBLE

Component	Mole per cent. Observed	Calculated
C_0	38	38
C_1	34	32
C_2	22	23
C_3	6	7
S_2	17	17
S_3	3	4
S_6	14	11
D.S.	0.96	0.99

Croon and Lindberg treated the results obtained from a homogeneous methylation of cellulose in a similar manner.[48] These workers, however, used relative rate constants for k_2, k_3, k_6 of 3.5, 1, 2 and assumed that k_3 would increase to 2 when the C-2 hydroxyl group is substituted but that k_2 would remain unchanged by substitution at the C-3 position. The correlation between observed and calculated values was fair. Application of the relative rate constants derived in the present investigation for the degrees of substitution obtained by Croon and Lindberg gave approximately the same agreement as these authors obtained but with the deviations in the opposite direction of the observed values. This less satisfactory correlation for the homogeneous methylation using the relative rate constants derived for the methylation of the monosodio derivatives does not necessarily compromise the present results as the two reactions almost certainly differ in the variation of individual alkoxide ion concentrations with conversion which will determine the product ratio and may even differ in mechanism.

In the methylation of the monosodio derivatives the reaction of the alkoxide ions apparently went to completion because the degrees of substitution of the initial alkoxides and methylated products were essentially identical. However, even if these reactions proceeded by an SN2 attack of alkoxide ion on methyl iodide, the distribution of methoxyl groups was not necessarily identical with the initial distribution of alkoxide groups. For the two distributions to have been identical the observed high proportion of di- and trimethylated products would have required an identically high proportion of di- and triionized glucoside units at the start. Such a high concentration of polyionized units would be very unlikely as the ionization of one of the hydroxyls on the ring would undoubtedly reduce the acidity of the others by several orders of magnitude. This effect would certainly be true for the two secondary hydroxyls and probably hold to a significant although somewhat less extent for the interaction between the primary and secondary hydroxyls.

If the distributions of methoxyl groups and alkoxide ions were not identical then two possible mechanisms are suggested for the methylation reaction, *viz.*, either (1) methylation occurred on unionized hydroxyl groups or (2) the distribution of ionized hydroxyl groups changed continually during the course of the reaction. The first mechanism would be analogous to SN reactions between polar molecules generally referred to as solvolysis when run in a large excess of the nucleophile.[49] A similar type of dipole–dipole reaction, *i.e.*, the formation of ammonium salts from amines and alkyl halides, has been observed to go with finite rates in non-polar solvents including hexane, benzene and carbon tetrachloride and even in gaseous reactions,[50,51] although the latter was believed to be almost entirely a surface reaction.[52] This mechanism would favor polysubstitution because the partially substituted products would be much more compatible with the methyl iodide reaction medium. Nevertheless, postulation of this mechanism would not explain the identity between the D.S. of the initial alkoxide and the final methylated derivative. If this mechanism was operative, excessive methylation would have been expected. Furthermore, it is well known that neutral carbohydrates will not react to any significant extent with methyl iodide and that the reaction of methyl bromide with methanol in dry benzene is several powers of ten slower than with pyridine.[51] One possibility is that the hydroxyl group reaction has a very unfavorable equilibrium, and for the reaction to go to any extent, the hydrogen iodide formed must be taken up in a subsequent step as in the reaction with an alkoxide.

The alternate possibility involving the continuous equilibration of alkoxide units during the course

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of the reaction may be more acceptable except that the absence of a polar solvent makes this proposed equilibration difficult to accept. Consistent with this mechanism, however, is the observation recently reported that methylation of one secondary hydroxyl in simple glucosides increases the acidity of the adjacent group.[53] Whatever the explanation may be, the mechanism of the reaction reported in this work would not be expected to be identical to that of the reaction occurring in a homogeneous methylation in a solution of a quaternary ammonium hydroxide or in a heterogeneous methylation of alkali cellulose using a comparatively highly polar, high boiling reagent like dimethyl sulfate. In these polar solvents the reaction would almost certainly occur exclusively at equilibrated alkoxide ions as predicted by solvent effects[54] in bimolecular ion–molecule reactions. For these reasons, and the steric effects discussed earlier, the results obtained in this investigation and relative rate constants derived therefrom are not expected to be directly applicable to other alkylations of cellulose.

Experimental

Monosodio Cellulose.—Holocellulose, prepared from yellow birch screenings by chlorination and extraction with monoethanolamine,[55] was extracted with 17.5% alkali to obtain the α-cellulose fraction. A 20-g. sample of α-cellulose was dissolved in 600 ml. of cuprammonium hydroxide solution and regenerated by precipitation in 1.5 l. of 6 *N* sulfuric acid. The activated cellulose was treated with sodium hydroxide in boiling butanol-1 by the procedure described by Sugihara and Wolfrom[37] for the preparation of monosodio cellulose. Identical procedures were also used to analyze and methylate the monosodio derivative.

Methyl Monosodio-α-D-glucopyranoside.—The preparation and methylation of methyl monosodio-α-D-glucopyranoside was performed as described by Wolfrom and El-Taraboulsi.[36]

Hydrolysis of Methylcellulose.—A 100 mg. sample of methyl cellulose was stirred into 3 g. of 72% sulfuric acid and allowed to hydrolyze for 15 hours at room temperature. The acid was diluted to approximately 1 *N* by adding 27 ml. of distilled water, and the mixture was refluxed on the steam-bath for 4 hours. After cooling, the solution was transferred to a beaker and Amberlite IR4B was added portionwise under constant stirring at such a rate as to bring the *p*H of the solution up to approximately 4.0 in 30 minutes. The solution was decanted off and reduced in a vacuum oven at 50°.[28]

Hydrolysis of Methylated Methyl α-D-Glucopyranoside.—The sirup obtained on methylating methyl monosodio-α-D-glucopyranoside was refluxed on a steam-bath with 20 ml. of 1 *N* sulfuric acid for 4 hours. The solution was neutralized with Amberlite IR-4B and concentrated as above.

Paper Chromatography.—Quantitative paper chromatography of the neutralized hydrolyzates were performed as described by Lenz and Holmberg.[44] The glucose methyl ethers of different degrees of substitution (*i.e.*, D-glucose, mono-, di- and tri-O-methyl-D-glucose) were separated with the top layer of a 5:1:4 mixture of butanol-1–ethanol–water. The mono-O-methyl-D-glucose isomers were separated with the top layer of a 2:5:5 mixture of 2,4,6-collidine–ethyl acetate–water.

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[CONTRIBUTION FROM THE BIOMEDICAL RESEARCH GROUP OF THE LOS ALAMOS SCIENTIFIC LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Quaternary Salt Formation of Substituted Oxazoles and Thiazoles[1]

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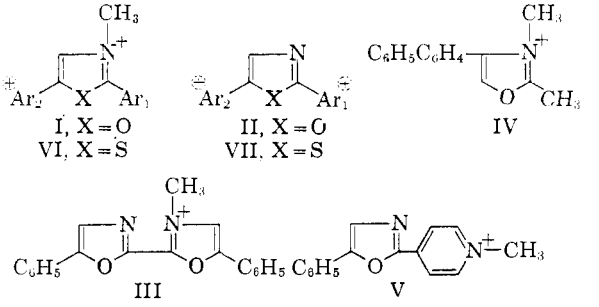
The course of quaternization of a number of oxazoles and thiazoles and various dimethylaminophenyl, pyridyl and quinolyl derivatives has been investigated. The salts have been screened for hypotensive activity.

Until recently, there has been little pharmacological interest in oxazole compounds. After the discovery that certain oxazole quaternary salts produced poikilothermia in mice,[2] there have followed some investigations of other pharmacological properties of these compounds. They have been screened for anti-cancer activity,[3] and they have been found to be active hypotensive agents.[4–7]

In an effort to determine what relationship existed between chemical structure and hypotensive activity, a number of new oxazole quaternary salts and related compounds were synthesized.



Preliminary screening for hypotensive activity has been carried out,[7] both for the compounds reported here (Table I) and those in an earlier paper.[8] The activity of these salts is very de-

(1) Work performed under the auspices of the U. S. Atomic Energy Commission.

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