developed for testing and interpreting kinetic data, and for determining dissociation constants of enzyme-substrate and enzyme-inhibitor compounds and other related constants when the data are found to be consistent with an assigned mechanism.

2. Representative analyses are given for invertase, raffinase, amylase, citric dehydrogenase, catalase, oxygenase, esterase and lipase, involving substrate activation, substrate inhibition, general competitive and non-competitive inhibition, steady states and reactions of various orders.

3. A plot of the reciprocal of the observed velocity v against the reciprocal of the substrate concentration (S) yields in the simplest case (*e. g.*, invertase, amylase) a straight line whose slope and ordinate intercept yield K_S (Michaelis dissociation constant) and V_{max} (theoretical maximum velocity). In the presence of competitive inhibitors the slope is increased but the intercept is unchanged. With non-competitive inhibitors the intercept also is raised. When the active intermediate contains n molecules of S a straight line is obtained upon plotting the reciprocal of $(S)^n$, instead of the reciprocal of (S), which would yield a curve concave upward. A steady-state occurring before the formation of the active intermediate, to whose concentration v is proportional, will yield a curve with two limiting slopes. Curves of v plotted directly against (S), passing through an optimum and approaching a zero value, indicate the existence of an additional inactive intermediate (catalase), whereas approaching a constant value indicates two or more active intermediates (*l*-ethyl mandelic esterase). The constants involved in the three latter cases are determined from limiting slopes and intercepts of various plots.

4. The various methods described are applicable to general chemical catalysis, homogeneous or heterogeneous, and possess many advantages of usefulness and convenience over less extensively developed methods employed heretofore. They are capable of eliminating certain postulated mechanisms, and indicating what mechanism or mechanisms *may* be involved, though not necessarily proving what mechanism *is* involved, in a given case.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Orientation in the Furan Nucleus. VIII. β-Acylaminofurans

BY ROBERT R. BURTNER

This report is concerned with the synthesis of one of the more promising precursors of simple β-aminofurans, namely, the β-acylaminofurans. The increased availability of 3-furoic acid[1] opens an attractive avenue of approach to 3-acylaminofuran. The following sequence of reactions illustrates the synthesis of 3-benzoylaminofuran

$$3\text{-}C_4H_3OCOOH \longrightarrow 3\text{-}C_4H_3OCOOC_2H_5 \xrightarrow{NH_2NH_2}$$

$$3\text{-}C_4H_3OCONHNH_2 \xrightarrow{HNO_2} 3\text{-}C_4H_3OCON_3 \longrightarrow$$

$$3\text{-}C_4H_3ONCO \xrightarrow{C_6H_5MgBr} 3\text{-}C_4H_3ONHCOC_6H_5$$

In like manner, 2-methyl-3-benzoylaminofuran was prepared from 2-methyl-3-furoic acid, and the corresponding 2-methyl-3-acetaminofuran was obtained by the use of methylmagnesium iodide instead of phenylmagnesium bromide.

Experimental Part

3-Furoyl Hydrazide.—This hydrazide was prepared from ethyl 3-furoate and hydrazine hydrate in a customary manner. The yield was 75% and the compound melted at 124–124.5° after crystallization from a benzene–methanol mixture.

Anal. Calcd. for $C_5H_6O_2N_2$: C, 47.61; H, 4.76. Found: C, 47.37; H, 5.01.

3-Furyl Isocyanate.—A solution of 12 g. (0.1 mole) of 3-furoyl hydrazide in 300 cc. of water was mixed with 75 cc. of 2 *N* sulfuric acid and the resulting solution chilled to 0°. To this was added dropwise and with shaking a solution of 7 g. (0.11 mole) of sodium nitrite in 30 cc. of water. The azide was removed by extraction with ether, and this extract was washed with water and then dried over sodium sulfate. Approximately three-fourths of the ether was removed by distillation; then 90 cc. of dry benzene was added; and, finally, the remaining ether was removed by distillation. The benzene solution of 3-furoyl azide was then carefully heated until the calculated volume of nitrogen was evolved for con-

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[1] Gilman and Burtner, THIS JOURNAL, **55**, 2905 (1933).

version to 3-furyl isocyanate, which was not isolated, particularly because of its pronouncedly offensive properties.

3-Benzoylaminofuran.—The benzene solution of 3-furyl isocyanate was added dropwise to an ether solution of phenylmagnesium bromide, observing customary precautions for interaction of isocyanates with Grignard reagents. Hydrolysis with a 10% solution of ammonium chloride gave 3-benzoylaminofuran, which after crystallization from benzene melted at 142°.

Anal. Calcd. for $C_{11}H_9O_2N$: C, 70.58; H, 4.81. Found: C, 70.40; H, 5.26.

2-Methyl-3-furoyl Hydrazide.—This hydrazide was prepared from ethyl 2-methyl-3-furoate in a 91% yield; and after crystallization from aqueous methanol it melted at 148°.

Anal. Calcd. for $C_6H_8O_2N_2$: C, 51.43; H, 5.71. Found: C, 51.11; H, 6.11.

The hydrazide was transformed as usual to the azide and this, in turn, to the isocyanate. The 2-methyl-3-furyl isocyanate was converted by the addition of water to the corresponding urea, *sym*-di-(2-methyl-3-furyl) urea, which melted at 226° after crystallization from alcohol.

2-Methyl-3-benzoylaminofuran.[2]—The same sequence of reactions was used here as with the 3-benzoylaminofuran, and the 2-methyl-3-benzoylaminofuran melted at 135° after crystallization from water.

Anal. Calcd. for $C_{12}H_{11}O_2N$: C, 71.14; H, 5.47. Found: C, 71.02; H, 5.93.

Hydrolysis of 2-Methyl-3-benzoylaminofuran.—The benzoylamino compound is rather resistant to hydrolysis both by aqueous or alcoholic potassium hydroxide. However, hydrolysis is promptly effected by sulfuric acid. In an orienting experiment with 1 g. of compound, the acid hydrolysate was made slightly alkaline with potassium hydroxide and the resulting mixture was steam distilled at once and in an inert atmosphere. The clear distillate had an odor remindful of naphthylamine and gave a carbylamine test. An aliquot of the steam distillate was diazotized, and the resulting solution was treated with β-naphthol to give a yellow-greenish precipitate. The diazotized solution with dimethylaniline gave a bright red solid which gradually darkened on long standing in the light.

The residue from steam distillation was acidified and then extracted to give a quantitative yield of benzoic acid.

2-Methyl-3-acetaminofuran, $2\text{-}CH_3C_4H_2ONHCOCH_3\text{-}3$.—This acetaminofuran was prepared in a manner essentially identical with that in the synthesis of 2-methyl-3-benzoylaminofuran. The amide melts at 148°, and alkaline hydrolysis gives the corresponding amine, the hydrochloride of which has been diazotized.

Anal. Calcd. for $C_7H_9O_2N$: C, 60.43; H, 6.61. Found: C, 60.48; H, 6.61.

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Summary

Incidental to the use of β-furandiazonium salts for purposes of orientation, 3-benzoylaminofuran, 2-methyl-3-benzoylaminofuran and 2-methyl-3-acetaminofuran have been prepared from the furyl isocyanates and the appropriate Grignard reagents.

AMES, IOWA

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[2] This compound was described recently by Blomquist and Stevenson [THIS JOURNAL, 56, 146 (1934)].

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

An Optical Method for the Study of Reversible Organic Oxidation–Reduction Systems. II. Halogenated Benzoquinones

BY D. E. KVALNES[1]

It has been shown[2] that the relative potentials of various oxidation–reduction systems can be measured without recourse to the potentiometric method by the use of an optically active quinone–hydroquinone pair (Q^* and H_2Q^*) as a reference system, and by observing the rotation of equilibrium mixtures such as that resulting from the interaction in a suitable solvent of a quinone, Q', with the optically active hydroquinone

$$H_2Q^* + Q' \rightleftharpoons Q^* + H_2Q' \qquad \text{(I)}$$

The particular value of the new method is in the fact that it permits a study of the organic systems in non-polar solvents, where potentiometric measurement is impossible. It should, of course, be equally applicable to solutions in polar solvents, and a series of measurements in aqueous or in alcoholic solution would indeed be of great value in affording a means of testing the reliability and the accuracy of the new method by comparison with the results obtained by the electrical method. Unfortunately experiments in this direction so far have met with no success; the hydroxylic solvents

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[1] National Research Fellow in Chemistry.

[2] Hunter and Kvalnes, THIS JOURNAL, 54, 2869 (1932).