coholic ammonia gave the succinamide derivative, with admixture of the ethyl ester V.

Compound I (14.4 g.), finely powdered, was allowed to stand in saturated alcoholic ammonia for six days, with occasional shaking. The appearance changed while the heavy crystalline powder became more voluminous. When all heavy material had disappeared, the product was filtered off and washed with alcohol. It melted at 228–232°. After recrystallization from a mixture of pyridine and acetone it melted at 240°. The admixture of the ester was detected only after reduction (see below).

A pure preparation was obtained by ammonolysis with concentrated aqueous ammonium hydroxide. Compound I was warmed with 28% ammonium hydroxide in a stoppered bottle at 60° for two days. The product was washed with water and crystallized from pyridine. To remove pyridine of crystallization, the crystals were suspended in warm alcohol; the volume of the material increased considerably. After washing with alcohol and drying, the m. p. was 242°.

The compound was not soluble in alcohol or acetone, sparingly soluble in dioxane or glacial acetic acid, soluble in hot pyridine.

4-Amino-4′-β-carbamylpropionylaminodiphenylsulfone (IX).—Compound VIII, obtained by alcoholic ammonolysis, was reduced with Raney nickel catalyst and hydrogen in alcoholic suspension. The crude reduction product melted at 135°. Most of it was soluble in hot water. When recrystallized from hot water, containing a little ammonia, colorless fine needles were obtained of m. p. 140°. The solubility in water at 26° was 0.4%. The water-insoluble material was identified with VII by melting point and analysis.

4-Nitro-4′-β-phenylcarbamylpropionylaminodiphenylsulfone (X).—Compound I (13.5 g.) was refluxed with aniline for fourteen hours. After dilution with alcohol, 10.5 g. of material m. p. 205–210° was isolated. From hot acetone (charcoal) cream crystals of m. p. 225–226° were obtained. It is sparingly soluble in hot alcohol.

4-Amino-4′-β-phenylcarbamylpropionylaminodiphenylsulfone (XI) was prepared from X using the procedure II 2.

4-Nitro-4′-β-cyclohexylcarbamylpropionylaminodiphenylsulfone (XII).—Compound I (7.2 g.) was refluxed with cyclohexylamine for five hours. The yield was 8.7 g., the m. p. 276°. Recrystallized from glacial acetic acid, the cream needles melted at 275–276°. The compound was not soluble in alcohol or acetone, soluble in hot pyridine and hot glacial acetic acid.

4-Amino-4′-β-cyclohexylcarbamylpropionylaminodiphenylsulfone (XIII) was prepared from XII using the procedure II 2.

Summary

The preparation of succinic acid derivatives of 4-nitro-4′-aminodiphenylsulfone and of 4,4′-diaminodiphenylsulfone has been described. 4-Amino-4′-succinimidodiphenylsulfone (II) and 4′-amino-4′-β-carboethoxypropionylaminodiphenylsulfone (VII) were tested in experimental pneumonia and tuberculosis and found to be active. 4-Amino-4′-β-carboxypropionylaminodiphenylsulfone (IV) and 4-amino-4′-β-carbamylpropionylaminodiphenylsulfone (IX) were also active in experimental pneumococcus infections in mice.

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Kinetic Analysis of Irreversible Consecutive Reactions

BY JEN-YUAN CHIEN

The kinetics of consecutive reactions have been of considerable interest since even simple chemical change may go through a number of intermediate steps. When the rate constants of each step are comparable in magnitude, the integration of the kinetic equations presents considerable difficulties. Especially when reactions of high order in the intermediate steps are involved, the resulting system of non-linear differential equations can only be solved by successive approximations. Hill[1] has recently outlined a general scheme of such methods, but the amount of labor required would be tremendous because of the fact that the rate constants themselves are the unknown parameters sought. In this paper, certain types of two step irreversible consecutive reactions are considered, where the solution in closed form has been found. These solutions serve as an extension to the summary of formulas compiled by Moelwyn-Hughes.[2]

Integration of the Kinetic Equations

I. Uni-unimolecular Reaction.—The general solution for a unimolecular reaction chain of any number of steps has been found.[3] For the particular case of a two-step reaction

$$\mathrm{A} \xrightarrow{k_1} \mathrm{B} \xrightarrow{k_2} \mathrm{C} \qquad \text{(I)}$$

starting with a_0 mole of A, the solution may be expressed in terms of a dimensionless variable τ and a dimensionless parameter κ in the following form, where A, B and C are concentrations of A, B and C, respectively, at t.

$$\left.\begin{aligned} A &= a_0\tau \\ B &= a_0\left(\frac{\tau^\kappa - \tau}{1-\kappa}\right) \\ C &= a_0 - A - B \\ &\text{where} \\ \tau &= e^{-k_1t} \text{ and } \kappa = k_2/k_1 \end{aligned}\right\} \quad (1)$$

II. Uni-bimolecular reaction.—Two separate cases are to be considered, one with a single

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[1] T. L. Hill, THIS JOURNAL, 64, 465 (1942).

[2] E. A. Moelwyn-Hughes, "Physical Chemistry," Cambridge University Press, Appendix 9, 1940, pp. 633–641.

[3] H. Bateman, *Proc. Camb. Phil. Soc.*, 15, 423 (1910).

starting material and the other with two starting materials.

$$\begin{array}{lllll} \text{(a)} & \mathrm{A} & \xrightarrow{k_1} \mathrm{B} & & \\ & & \mathrm{2B} & \xrightarrow{k_2} & \mathrm{C} \\ t = 0: & a_0 & 0 & & 0 \\ t\quad : & x_1 & x_2 & & x_3 \end{array} \qquad \text{(IIa)}$$

These kinetic equations describe the processes:

$$\begin{cases} \mathrm{d}x_1/\mathrm{d}t = -k_1x_1 & \text{(2i)} \\ \mathrm{d}x_2/\mathrm{d}t = k_1x_1 - k_2x_2^2 & \text{(2ii)} \\ \mathrm{d}x_3/\mathrm{d}t = {}^1/_2k_2x_2^2 & \text{(2iii)} \end{cases}$$

Integration of (2i) gives

$$x_1 = a_0e^{-k_1t} \qquad (3)$$

and then the Riccati equation (2ii) becomes

$$\mathrm{d}x_2/\mathrm{d}t = a_0k_1e^{-k_1t} - k_2x_2^2 \qquad (4)$$

On using the transformation

$$x_2(t) = \frac{1}{k_2u(t)}\frac{\mathrm{d}u(t)}{\mathrm{d}t} \qquad (5)$$

which transforms the non-linear first order equation (4) in x_2 into a linear second order equation in $u(t)$

$$\mathrm{d}^2u/\mathrm{d}t^2 - a_0k_1k_2e^{-k_1t}\,u = 0$$

A further change of the independent variable t to $\tau = e^{-k_1t}$ yields an equation of the Bessel type[4]

$$\frac{\mathrm{d}}{\mathrm{d}\tau}\left(\tau\frac{\mathrm{d}u}{\mathrm{d}\tau}\right) - \kappa u = 0,\ \kappa = a_0k_2/k_1 \qquad (6)$$

The solution of (6) is

$$u = \alpha J_0(2i\sqrt{\kappa\tau}) + \beta' iH_0^{(1)}(2i\sqrt{\kappa\tau})$$

where α,β' are arbitrary constants, $i = \sqrt{-1}$, and J_0, $H_0^{(1)}$ are Bessel functions of the first and third kind of order zero respectively. Then, by the recurrence relations of Bessel functions[5]

$$\frac{\mathrm{d}J_0(2i\sqrt{\kappa\tau})}{\mathrm{d}\tau} = -\sqrt{\frac{\kappa}{\tau}}\,iJ_1(2i\sqrt{\kappa\tau})$$

$$i\,\frac{\mathrm{d}H_0^{(1)}(2i\sqrt{\kappa\tau})}{\mathrm{d}\tau} = \sqrt{\frac{\kappa}{\tau}}\,H_1^{(1)}(2i\sqrt{\kappa\tau})$$

and hence the solution[6] for x_2 is, by (5)

$$x_2 = a_0\sqrt{\frac{\tau}{\kappa}}\,\frac{iJ_1(2i\sqrt{\kappa\tau}) - \beta H_1^{(1)}(2i\sqrt{\kappa\tau})}{J_0(2i\sqrt{\kappa\tau}) + \beta iH_0^{(1)}(2i\sqrt{\kappa\tau})} \qquad \text{(7i)}$$

where the arbitrary constant β is determined by the initial condition $x_2(0) = 0$, which gives

$$\beta = \frac{iJ_1(2i\sqrt{\kappa})}{H_1^{(1)}(2i\sqrt{\kappa})} \qquad \text{(7ii)}$$

For $x_3(t)$, use is made of (2ii) and (2iii), *i. e.*

$$x_3 = \frac{k_1}{2}\int_0^t x_1\mathrm{d}t - \frac{x_2}{2} = \frac{a_0}{2}(1 - \tau) - \frac{x_2}{2}$$

The complete solution of the problem is summarized as

$$\left.\begin{aligned} A &= a_0\tau \\ B &= a_0\sqrt{\frac{\tau}{\kappa}}\,\frac{iJ_1(2i\sqrt{\kappa\tau}) - \beta H_1^{(1)}(2i\sqrt{\kappa\tau})}{J_0(2i\sqrt{\kappa\tau}) + \beta iH_0^{(1)}(2i\sqrt{\kappa\tau})} \\ C &= {}^1/_2(a_1 - A - B) \end{aligned}\right\} \quad (8)$$

where

$$\tau = e^{-k_1t},\ \kappa = a_0k_2/k_1,\ \beta = iJ_1(2i\sqrt{\kappa})/H_1^{(1)}(2i\sqrt{\kappa})$$

$$\begin{array}{llllll} \text{(b)} & \mathrm{A} & \xrightarrow{k_1} & \mathrm{B} & & \\ & & & \mathrm{B} + \mathrm{D} & \xrightarrow{k_2} & \mathrm{C} \\ t = 0: & a_0 & 0 & d_0 & & 0 \\ t\quad : & a_0 - x & x - y & d_0 - y & & y \end{array} \qquad \text{(IIb)}$$

The kinetic equations are

$$\begin{cases} \mathrm{d}(a_0 - x)/\mathrm{d}t = -k_1(a_0 - x) & \text{(9i)} \\ \mathrm{d}y/\mathrm{d}t = k_2(x - y)(d_0 - y) & \text{(9ii)} \end{cases}$$

Integration of (9i) gives

$$x = a_0(1 - e^{-k_1t})$$

then (9ii) becomes

$$\mathrm{d}y/\mathrm{d}t = k_2(a_0 - a_0e^{-k_1t} - y)(d_0 - y)$$

This is also a Riccati equation which in general cannot be solved. However, it is known that if one particular solution y_1 is found, the equation can be reduced to linear form by the transformation $y = y_1 \pm 1/v$. Following Bruins[7] $y_1 = d_0$ is obviously a solution, and

$$y = d_0 - 1/v(t)$$

leads to an equation for $v(t)$

$$\frac{\mathrm{d}v}{\mathrm{d}t} - a_0k_2(\lambda_0 - e^{-k_1t})\,v = k_2$$

where $\lambda_0 = (a_0 - d_0)/a_0$ The solution of this linear differential equation in v is

$$v = \tau^{-\lambda_0\kappa}\,e^{\kappa\tau}\left[-\frac{\kappa^{(1-\lambda_0\kappa)}}{a_0}\,\Gamma(\lambda_0\kappa,\kappa\tau) + \gamma\right] \qquad \text{(10i)}$$

where

$$\tau = e^{-k_1t},\quad \kappa = a_0k_2/k_1$$

and

$$\Gamma(n,x) = \int_0^x \xi^{n-1}\,e^{-\xi}\,\mathrm{d}\xi \qquad \text{(10ii)}$$

is the incomplete Γ-function.[8] Evaluation of the arbitrary constant γ by the initial condition gives

$$y = d_0\left[1 - \frac{\tau^{\lambda_0\kappa}\,e^{-\kappa\tau}}{e^{-\kappa} - (1 - \lambda_0)\kappa^{(1-\lambda_0\kappa)}\{\Gamma(\lambda_0\kappa,\kappa\tau) - \Gamma(\lambda_0\kappa,\kappa)\}}\right] \qquad (11)$$

Hence

$$\left.\begin{aligned} A &= a_0\tau \\ D &= d_0\frac{\tau^{\lambda_0\kappa}\,e^{-\kappa\tau}}{e^{-\kappa} - (1 - \lambda_0)\kappa^{(1-\lambda_0\kappa)}\{\Gamma(\lambda_0\kappa,\kappa\tau) - \Gamma(\lambda_0\kappa,\kappa)\}} \\ C &= d_0 - D \\ B &= a_0 - A - C \end{aligned}\right\} \quad (12)$$

where

$$\tau = e^{-k_1t},\ \kappa = a_0k_2/k_1,\ \lambda_0 = (a_0 - d_0)/d_0$$

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(4) *Cf.* T. v. Kármán and M. A. Biot, "Mathematical Methods in Engineering," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter II, p. 66.

(5) *Cf.* G. N. Watson, "A Treatise on the Theory of Bessel Functions," Cambridge University Press, Second Edition, 1944, pp. 45, 74.

(6) Tables of $J_0(ix)$, $-iJ_1(ix)$, $iH_0^{(1)}(ix)$ and $-H_1^{(1)}(ix)$ are given in E. Jahnke and F. Emde, "Tables of Functions," Dover Publications, New York, N. Y., 1943, pp. 224–229, 236–243.

(7) E. M. Bruins, *Rec. trav. chim.*, **59**, 739 (1940).

(8) Values of $I(x,n) = \Gamma(n,x)/\Gamma(n)$ have been tabulated by K. Pearson, "Tables of the Incomplete Γ-function," His Majesty's Stationery Office, London, 1922.

For the particular case when $a_0 = d_0$, it is necessary to return to (10i) and in this case

$$v = e^{\kappa\tau}\left[\frac{\kappa}{a_0}\{-Ei(-\kappa\tau) + Ei(-\alpha)\} + \gamma'\right]$$

where

$$-Ei\,(-x) = \int_x^\infty \frac{e^{-\xi}}{\xi}\,\mathrm{d}\xi$$

is the exponential integral,[9] and α is some positive number.[10] Evaluation of γ' by the initial condition gives

$$D = a_0\frac{e^{-\kappa\tau}}{e^{-\kappa} + \kappa\{-Ei(-\kappa\tau) + Ei(-\kappa)\}} \qquad (12')$$

III. Bi-unimolecular Reaction.—One of the two possible cases of consecutive bi-unimolecular reactions is

$$\begin{array}{lccc} & 2\mathrm{A} \xrightarrow{k_1} & \mathrm{B} \xrightarrow{k_2} & \mathrm{C} \\ t = 0: & a_0 & 0 & 0 \\ t\ \ : & a_0 - 2x & x - y & y \end{array} \qquad \text{(III)}$$

The kinetic equations are

$$\begin{cases} \dfrac{\mathrm{d}(a_0 - 2x)}{\mathrm{d}t} = -k_1(a_0 - 2x)^2 & \text{(13i)} \\ \mathrm{d}y/\mathrm{d}t = k_2(x - y) & \text{(13ii)} \end{cases}$$

Integration of (13i) gives

$$a_0 - 2x = a_0/(1 + a_0k_1t) \qquad (14)$$

Then (13ii) becomes

$$\frac{\mathrm{d}y}{\mathrm{d}t} + k_2y = \frac{a_0{}^2}{2}\frac{k_1k_2}{1 + a_0k_1t}\,t \qquad (15)$$

This linear equation has the solution

$$y = e^{-k_2t}\left[\frac{a_0{}^2}{2}\,k_1k_2\int^t \frac{te^{k_2t}}{1 + a_0k_1t}\,\mathrm{d}t + \gamma\right]$$

The indefinite integral in the above expression for y can be evaluated by a change of variable. Let

$$\tau = 1 + a_0k_1t, \text{ and } \kappa = k_2/a_0k_1$$

then

$$\frac{a_0{}^2}{2}\,k_1k_2\int^t \frac{te^{k_2t}}{1 + a_0k_1t}\,\mathrm{d}t = \frac{a_0}{2}\,\kappa e^{-\kappa}\left[\int^\tau e^{\kappa\tau}\,\mathrm{d}\tau - \int^\tau \frac{e^{\kappa\tau}}{\tau}\,\mathrm{d}\tau\right]$$
$$= \frac{a_0}{2}\,[e^{\kappa(\tau-1)} - \kappa e^{-\kappa}\,Ei(\kappa\tau) + \text{const.}]$$

where the exponential integral[11]

$$Ei(x) = \int_{-\infty}^x \frac{e^\xi}{\xi}\,\mathrm{d}\xi$$

And therefore

$$y = \frac{a_0}{2}\,[1 - \kappa e^{-\kappa\tau}\,Ei(\kappa\tau) + \gamma' e\kappa(1 - \tau)]$$

Evaluation of the constant γ' by the initial condition $y(0) = 0$ gives

$$y = \frac{a_0}{2}\,[1 - e^{-\kappa(\tau-1)} - \kappa e^{-\kappa\tau}\{Ei(\kappa\tau) - Ei(\kappa)\}] \qquad (16)$$

Thus the complete solution[12] is

$$\left.\begin{aligned} A &= a_0/\tau \\ B &= \frac{a_0}{2}\,[e^{-\kappa(\tau-1)} + J] - \frac{A}{2} \\ C &= \frac{a_0}{2}[1 - e^{-\kappa(\tau-1)} - J] \\ &\text{where} \\ \tau &= 1 + a_0k_1t,\ \kappa = k_2/a_0k_1 \\ &\text{and} \\ J &= \kappa e^{-\kappa\tau}\{Ei(\kappa\tau) - Ei(\kappa)\} \end{aligned}\right\} \qquad (17)$$

IV. Bi-bimolecular Reaction.—Two particular cases of reactions of this type where solutions to the kinetic equations have been found are

$$\begin{array}{lcccc} \text{(a)} & 2\mathrm{A} \xrightarrow{k_1} & \mathrm{B} & & \\ & & 2\mathrm{B} \xrightarrow{k_2} & \mathrm{C} & \text{(IVa)} \\ t = 0: & a_0 & 0 & 0 & \\ t\ \ : & x_1 & x_2 & x_3 & \end{array}$$

The kinetic equations are

$$\begin{cases} \mathrm{d}x_1/\mathrm{d}t = -k_1x_1^2 & \text{(18i)} \\ \dfrac{\mathrm{d}x_2}{\mathrm{d}t} = \dfrac{k_1}{2}\,x_1^2 - k_2x_2^2 & \text{(18ii)} \\ \dfrac{\mathrm{d}x_3}{\mathrm{d}t} = \dfrac{k_2}{2}\,x_2^2 & \text{(18iii)} \end{cases}$$

Integration of (18i) gives

$$x_1 = \frac{a_0}{1 + a_0k_1t} \qquad (19)$$

Then

$$\frac{\mathrm{d}x_2}{\mathrm{d}t} = \frac{k_1}{2}\,\frac{a_0^2}{(1 + a_0k_1t)^2} - k_2x_2^2 \qquad (20)$$

This is also a Riccati equation[13] and inspection shows that

$$X_2 = \frac{\alpha a_0}{1 + a_0k_1t}$$

is a particular solution, where α is a constant so chosen as to satisfy the equation. Thus

$$\alpha = \frac{1}{2\kappa}\,(1 + \sqrt{1 + 2\kappa}),\quad \kappa = k_2/k_1$$

Let the general solution be

$$x_2 = X_2 + 1/v(t)$$

then the equation for v will be

$$\mathrm{d}v/\mathrm{d}t - 2k_2X_2v = k_2 \qquad (21)$$

The solution to this equation is

$$v = \tau^{\mu+1}\left[-\frac{\kappa}{a_0\mu}\,\tau^{-\mu} + \gamma\right]$$

where $\tau = 1 + a_0k_1t$ and $\mu = 2\alpha\kappa - 1 = \sqrt{1 + 2\kappa}$.

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[9] "Tables of Sine Cosine and Exponential Integrals," Federal Works Agency, New York, 1940; or E. Jahnke and F. Emde, "Tables of Functions," *loc. cit.*, pp. 6–9.

[10] Here the indefinite integral is changed to a definite integral with a lower limit α by changing the additive constant γ' to avoid the difficulty of infinite Ei(0).

[11] In Jahnke and Emde, *loc. cit.*, this function is tabulated under the notation $\overline{\mathrm{Ei}}(x)$.

[12] The solution of this type of reaction has been previously reported by A. A. Balandin and L. S. Leebenson, *Comp. rend. URSS.*, **39**, 22 (1943), but apparently they gave a wrong sign on J for both B and C.

[13] The equation (20) can also be solved by the following transformation

$$x_2 = \frac{1}{k_2u}\,\frac{\mathrm{d}u}{\mathrm{d}t},\quad 1 + a_0k_1t = e^s$$

which leads to a second order linear equation in u with constant coefficients:

$$\frac{\mathrm{d}^2u}{\mathrm{d}s^2} - \frac{\mathrm{d}u}{\mathrm{d}s} - \kappa u = 0,\quad \kappa = k_2/k_1$$

Determination of the arbitrary constant γ from the initial condition $x_2(0) = 0$ leads to

$$v = -\frac{\kappa\tau}{a_0\mu}\left[1 + \frac{\mu - 1}{\mu + 1}\tau^\mu\right] \qquad (22)$$

Therefore

$$x_2 = \frac{a_0}{2}\frac{1}{\kappa\tau}\left[\mu + 1 - \frac{2\mu}{1 + \frac{\mu - 1}{\mu + 1}\tau^\mu}\right] \qquad (23)$$

Integration of (18iii) by using (18ii) gives

$$x_3 = \frac{a_0}{4}\left(1 - \frac{1}{\tau}\right) - \frac{x_2}{2}$$

Thus the complete solution[14] is

$$\left.\begin{aligned} A &= a_0/\tau \\ B &= \frac{a_0}{2}\frac{1}{\kappa\tau}\left[\mu + 1 - \frac{2\mu}{1 + \frac{\mu - 1}{\mu + 1}\tau^\mu}\right] \\ C &= \frac{1}{2}\left[\frac{a_0}{2} - \frac{A}{2} - B\right] \\ &\text{where} \\ \tau &= 1 + a_0k_1t, \quad \kappa = k_2/k_1, \quad \mu = \sqrt{1 + 2\kappa} \end{aligned}\right\} \qquad (24)$$

(b) $2\mathrm{A} \xrightarrow{k_1} \mathrm{B}$

$$\begin{array}{lcccc} & & \mathrm{B} & + \mathrm{D} \xrightarrow{k_2} & \mathrm{C} \qquad \text{(IVb)} \\ t = 0: & a_0 & 0 & d_0 & 0 \\ t\ \ : & a_0 - 2x & x - y & d_0 - y & y \end{array}$$

The kinetic equations are

$$\begin{cases} \mathrm{d}(a_0 - 2x)/\mathrm{d}t = -k_1(a_0 - 2x) & (25\text{i}) \\ \mathrm{d}y/\mathrm{d}t = k_2(x - y)(d_0 - y) & (25\text{ii}) \end{cases}$$

Integrating (25i) gives

$$a_0 - 2x = \frac{a_0}{1 + a_0k_1t}$$

Then (25ii) becomes

$$\frac{\mathrm{d}y}{\mathrm{d}t} = k_2\left(\frac{1}{2}\frac{a_0^2k_1t}{1 + a_0k_1t} - y\right)(d_0 - y) \qquad (26)$$

As in the case IIb, $y_1 = d_0$ is obviously a solution of this Riccati equation, so

$$y = d_0 - 1/v(t)$$

leads to a linear equation in v

$$\frac{\mathrm{d}v}{\mathrm{d}t} - k_2\left(\frac{1}{2}\frac{a_0^2k_1t}{1 + a_0k_1t} - d_0\right)v = k_2$$

The solution for v is

$$v = e^{\lambda_0\kappa\tau}\tau^{-\kappa}\left[\frac{2\kappa}{a_0}\int^\tau e^{-\lambda_0\kappa\tau}\tau^\kappa\,\mathrm{d}\tau + \gamma\right]$$

or

$$v = e^{\lambda_0\kappa\tau}\tau^{-\kappa}\left[\frac{2}{a_0\lambda_0}(\lambda_0\kappa)^{-\kappa}\,\Gamma(\kappa + 1, \lambda_0\kappa\tau) + \gamma'\right] \qquad (27)$$

where

$$\tau = 1 + a_0k_1t, \quad \kappa = k_2/2k_1, \quad \lambda_0 = (a_0 - 2d_0)/a_0$$

and $\Gamma(n,x)$ is the incomplete Γ-function defined previously by (10ii). By the initial condition $y(0) = 0$, the constant γ' is evaluated and then

$$y = d_0\left[1 - \frac{\tau^\kappa e^{-\tau}}{1 - \left(\frac{1 - \lambda_0}{\lambda_0}\right)(\lambda_0\kappa)^\kappa e^{\lambda_0\kappa}\{\Gamma(\kappa + 1, \lambda_0\kappa\tau) - \Gamma(\kappa + 1, \lambda_0\kappa)\}}\right] \qquad (28)$$

Therefore the complete solution is

$$\left.\begin{aligned} A &= a_0/\tau \\ D &= d_0\frac{\tau^\kappa e^{-\tau}}{1 - \left(\frac{1 - \lambda_0}{\lambda}\right)(\lambda_0\kappa)^\kappa e^{\lambda_0\kappa}\{\Gamma(\kappa + 1, \lambda_0\kappa\tau) - \Gamma(\kappa + 1, \lambda_0\kappa)\}} \\ C &= d_0 - D \\ B &= {}^1/_2(a_0 - A) - C \\ &\text{where} \\ \tau &= 1 + a_0k_1t, \quad \kappa = k_2/2k_1, \quad \lambda_0 = (a_0 - 2d_0)/a_0 \end{aligned}\right\} \qquad (29)$$

For the special case when $\lambda_0 = 0$, *i. e.*, $c_0 = 2d_0$, equation (28) becomes indeterminate, but the solution is easily obtained from (27) where the integral gives an algebraic function of τ, and the particularly simple result

$$D = \frac{a_0}{2}\frac{(\kappa + 1)\tau^\kappa}{1 + \kappa\tau^{\kappa+1}} \qquad (29')$$

is obtained.

Discussion

All the solutions obtained for the two step irreversible consecutive reactions considered above have been expressed in terms of a dimensionless variable τ and some dimensionless parameters defined for each type of reaction in question. The general behavior of these solutions is shown in Figs. 1 and 2 for hypothetical reactions with $\kappa = 0.5$. For the reaction type IIb and IVb, equal initial concentrations for A and D are assumed. In these plots, $1/1 + a_0k_1t$ is chosen as abscissa. This particular choice appears to be most suitable to show the different characters of the reaction mechanism. It is obvious that if the first step is bimolecular, the decay curve for A will be linear. A unimolecular step will result in a change of the direction of curvature in the formation curve of both B and C, while no inflection point will be found on the curve if the steps involved are bimolecular. Therefore, such a plot will give directly an insight into the reaction mechanism. A linear time scale is also attached on the top of each curve.

Experimentally the aim is always the evaluation of the rate constants of each step and thus an assignment of possible reaction mechanism. In view of the difficulties involved in a simultaneous evaluation of the two rate constants, it appears desirable to follow the decay of the initial compound A. This will give the rate constant k_1 immediately. The evaluation of κ can then be made, by comparing the experimental formation curve of either the product C or the intermediate B, or the decay curve of the other starting compound D, to

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(14) The solution of this problem has been considered by J. Hirniak, *Acta Physico-chimica URSS*, **14**, 613 (1941). He arrived at essentially the same result as (24) but through an entirely different and lengthy derivation. However, his *b* differs from μ of this paper, which should be identical, because he overlooked the fact that four molecules not two of A are consumed to give one molecule of C.

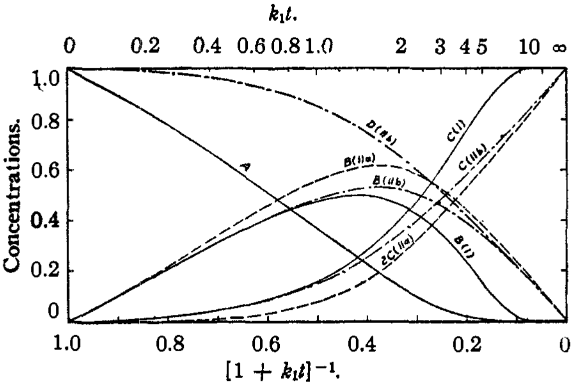

Fig. 1.—Uni-uni- and uni-bi-molecular reactions, $a_0 = 1$, $k = 0.5$.

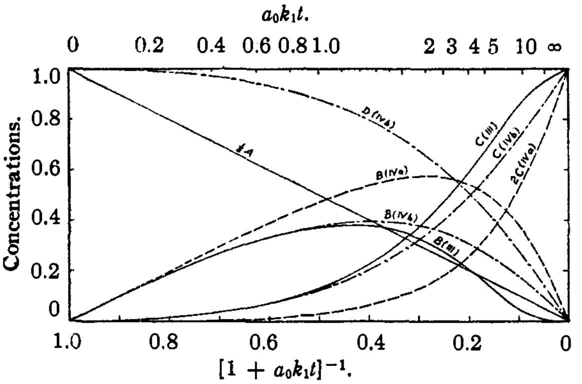

Fig. 2.—Bi-uni- and bi-bi-molecular reactions, $a_0 = 2$, $k = 0.5$.

a set of computed curves. It might be mentioned here that for the special case of reaction type I, Swain[15] has devised a graphical method of evaluating k_1 and k_2 from a single experimental curve of $(a_0 - A + C)$.

Experimental studies on the kinetics of consecutive reactions have been handicapped by their complexity. The present analysis shows definitely that a separate determination of the kinetic behavior of the initial step leads to an essential simplication of the problem. With the value of a_0 chosen as 1 or 2, depending on the reaction mechanism of the first step of the reaction, the graphs shown in Figs. 1 and 2, with different values of κ can be constructed and can then be used to analyze all experimental data in any given case. This procedure amounts to plotting all experimental values of concentrations relative to the concentration of the initial compound A and on a time scale of $(1 + a_0k_1t)^{-1}$. A similar procedure has been used for the study of concurrent consecutive reactions.[16]

It is interesting to note here that for the reaction type III, the formation curve of C as computed from equation (17) could well be represented by an empirical unimolecular equation with an apparent induction period. For example, for $a_0 = 2$ and $\kappa = 0.5$, the theoretical curve and an empirical equation like

$$C' = 1 - e^{-0.253(\tau - 1.50)} \tag{30}$$

agree very well from 15 to 90% completion of the reaction as shown in Table I. This case corresponds to an apparent unimolecular rate constant of approximately half the true value of k_2. As κ decreases the agreement will be better, and finally when $a_0k_1 \rightarrow \infty$

$$\lim_{a_0k_1 \rightarrow \infty} J = k_2e^{-k_2t} \lim_{a_0k_1 \rightarrow \infty} \frac{\int_{k_2/a_0k_1}^{k_2t} \frac{e^{\xi}}{\xi}\, d\xi}{a_0k_1} =$$

$$k_2e^{-k_2t} \lim_{a_0k_1 \rightarrow \infty} \frac{e^{k_2/a_0k_1}}{a_0k_1} = 0$$

Therefore

$$C \xrightarrow[a_0k_1 \rightarrow \infty]{} \frac{a_0}{2}(1 - e^{-k_2t})$$

which is the unimolecular formation of C from B as would be expected.

TABLE I

COMPARISON OF EQUATIONS (17) AND (30) FOR $a_0 = 2$ AND $\kappa = 0.5$

τ	C	C'	Δ%
1.0	0		
1.4	0.029		
1.8	.092	0.073	−21
2.2	.166	.162	−3.0
2.6	.242	.243	+0.4
3.0	.314	.316	+0.6
3.5	.398	.398	±0.0
4.0	.473	.468	−1.1
5.0	.593	.588	−0.8
6.0	.682	.680	−0.3
8.0	.794	.807	+1.6
10.0	.855	.884	+3.4
20.0	.943	.991	+5.1

In conclusion, it is hoped that the solutions of irreversible consecutive reactions here presented will be useful for the study of many organic reactions. Some of the results appear to be particularly simple to apply. The only limitation will lie in the reversibility of the reactions. For such cases the kinetic equations have not been integrated at the present moment.

Acknowledgment.—The author is indebted to Professor R. E. Langer of the Mathematics Department, University of Wisconsin, for valuable suggestions and to Professor G. Glockler for a discussion of the topic involved.

Summary

1. Solutions in closed form for some two step irreversible consecutive reactions are presented, with the results expressed in terms of a dimension-

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[15] C. G. Swain, THIS JOURNAL, 66, 1696 (1944).

[16] C. Potter and R. R. McLaughlin, Can. J. Research, B25, 405 (1947).

less variable and dimensionless parameters. Uni-bi-, bi-uni- and bi-bi-molecular reactions are the cases considered.

2. Experimental evaluation of the rate constants is discussed. A separate determination of the rate of decay of the initial substance is desirable for the interpretation of the mechanism and the evaluation of rate constants.

3. Practical applications of the results are limited only by the possible reversibility of the reaction steps involved.

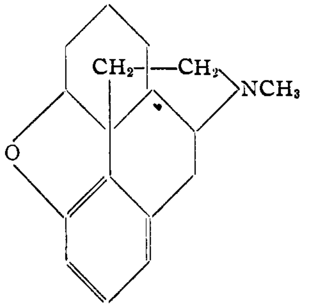
Iowa City, Iowa Received December 9, 1947

[Contribution from the Marion Edwards Park Laboratory of Bryn Mawr College]

The Synthesis of Ring Systems Related to Morphine. I. 9,10-Dioxo-13-cyanomethyl-5,8,9,10,13,14-hexahydrophenanthrene

By Marshall Gates and William F. Newhall

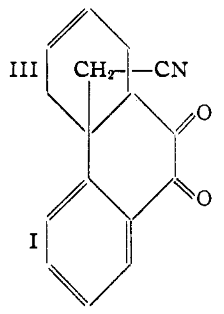
A synthesis of the ring system (I) present in morphine and its close relatives has not yet been achieved although a number of interesting attempts have been reported.[1] We have been engaged for some time in an attempt to synthesize derivatives of such a ring system which might be compared with certain degradation products of the morphine alkaloids. Such a synthesis would offer a rigorous solution to the question of the point of attachment of the ethanamine side chain of morphine. The appearance in recent months of several publications[1a,c,d] bearing on this general problem has prompted us to offer our results for publication.



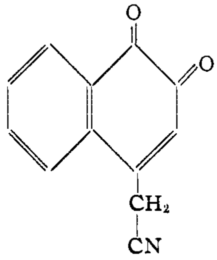
I

We have developed a convenient synthesis for 9,10 - dioxo - 13 - cyanomethyl - 5,8,9,10,13,14-hexahydrophenanthrene (II) which appears to be flexible enough to allow the introduction of substituents into rings I and III by suitable choice of starting materials.

The starting point for the preparation of this substance is the 4-(carbethoxycyanomethyl)-1,2-naphthoquinone of Sachs and Craveri,[2] which is available from ammonium 1,2-naphthoquinone-4-sulfonate by an improved procedure in 91% yield. This material is reduced, hydrolyzed and decarboxylated in one step giving 4-cyanomethyl-1,2-naphthohydroquinone in 91% yield. Dichromate oxidation of this hydroquinone in glacial acetic acid affords 4-cyanomethyl-1,2-naphthoquinone (III)[3] in 83% yield.



II



III

The quinone III condenses readily with butadiene in acetic acid to give the diketone II. Excellent quality adduct is readily obtained in 56% yield.[4] Its formulation as II appears to be required by the fact that its azine IV, easily prepared by condensation with *o*-phenylenediamine, yields 1,2,3,4-dibenzophenazine (9,10-phenanthrenequinone azine) (V) on distillation with zinc dust.

Experiments are in progress on the reduction of II by a variety of methods. We hope to effect a

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(1) See, for example, (a) Holmes' recent [This Journal, **69**, 2000 (1947)] extension of (b) Fieser and Holmes' [*ibid.*, **60**, 2548 (1938)] work; also the recent papers of (c) Horning, *ibid.*, **69**, 2929 (1947); (d) Newman, *ibid.*, **69**, 942 (1947), (e) Grewe, *Ber.*, **76**, 1072, 1076 (1943); (f) Ghosh and Robinson, *J. Chem. Soc.*, 506 (1944); (g) Ganguly, *Science and Culture*, **7**, 319 (1941); (h) Koelsch, This Journal, **67**, 569 (1945), and others.

(2) Sachs and Craveri, *Ber.*, **38**, 3685 (1905).

(3) The position of the cyanomethyl group in this substance has been conclusively demonstrated by Miss Elizabeth R. Carmichael, working in this laboratory on another problem, by hydrolyzing and decarboxylating the azine of this substance to 4-methyl-1,2-naphthophenazine [Fieser and Bradsher, This Journal, **61**, 417 (1939)] which was compared with an authentic sample kindly furnished us by Professor Louis F. Fieser of Harvard University.

(4) Compare the work of Fieser and Bradsher, This Journal, **61**, 417 (1939), in which 2,3-dimethylbutadiene was shown to add slowly to 4-benzyl- and 4-dicarbethoxymethyl-1,2-naphthoquinones.