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Derivation of Kinetic Expression for Enantioselectivity. Monomeric 1.

For a reversible equilibrium between **1** and **3** as shown in Scheme 1, there will exist two different catalytic species, **1** and **1•3**, both of which catalyze the formation of product **3** with different rates and enantioselectivities. As it is known that there is no appreciable background rate for the reaction of aldehydes with HCN in toluene,¹ the rate of production of each cyanohydrin isomer can be written as:

$$\frac{d[\mathbf{3}_R]}{dt} = k_{1R} [\text{HCN}][\mathbf{2}][\mathbf{1}] + k_{13R} [\text{HCN}][\mathbf{2}][\mathbf{1}\cdot\mathbf{3}]$$

$$\frac{d[\mathbf{3}_S]}{dt} = k_{1S} [\text{HCN}][\mathbf{2}][\mathbf{1}] + k_{13S} [\text{HCN}][\mathbf{2}][\mathbf{1}\cdot\mathbf{3}]$$

where k_{1R} , k_{13R} , k_{1S} and k_{13S} are fundamental rate constants for the production of the two cyanohydrin isomers **3_R** and **3_S** as catalyzed by the two species **1** and **1•3**, respectively. Assuming a simple, two-state equilibrium between **1** and **1•3** with equilibrium constant $K_A = [\mathbf{1}\cdot\mathbf{3}]/[\mathbf{1}][\mathbf{3}]$, one can replace **1•3** with $K_A[\mathbf{1}][\mathbf{3}]$ to give:

$$\frac{d[\mathbf{3}_R]}{dt} = [\text{HCN}][\mathbf{2}][\mathbf{1}](k_{1R} + k_{13R} K_A [\mathbf{3}])$$

$$\frac{d[\mathbf{3}_S]}{dt} = [\text{HCN}][\mathbf{2}][\mathbf{1}](k_{1S} + k_{13S} K_A [\mathbf{3}])$$

Using the relationships $[\mathbf{1}] + [\mathbf{1}\cdot\mathbf{3}] = [\mathbf{1}]_{\text{tot}}$ and $[\mathbf{1}\cdot\mathbf{3}] = K_A[\mathbf{1}][\mathbf{3}]$ allows one to make the substitution $[\mathbf{1}] = \frac{[\mathbf{1}]_{\text{tot}}}{1 + K_A [\mathbf{3}]}$ and yield:

$$\frac{d[\mathbf{3}_R]}{dt} = \frac{[\text{HCN}][\mathbf{2}][\mathbf{1}]_{\text{tot}}(k_{1R} + k_{13R} K_A [\mathbf{3}])}{1 + K_A [\mathbf{3}]}$$

$$\frac{d[\mathbf{3}_S]}{dt} = \frac{[\text{HCN}][\mathbf{2}][\mathbf{1}]_{\text{tot}}(k_{1S} + k_{13S} K_A [\mathbf{3}])}{1 + K_A [\mathbf{3}]}$$

Using the definition of enantiomeric excess, one can construct an equation relating an "instantaneous" enantiomeric excess $ee'(t)$ to the rates of production of each isomer as:

$$ee'(t) = \frac{\frac{d[\mathbf{3}_S]}{dt} - \frac{d[\mathbf{3}_R]}{dt}}{\frac{d[\mathbf{3}_S]}{dt} + \frac{d[\mathbf{3}_R]}{dt}} = \frac{(k_{1S} + k_{13S} K_A [\mathbf{3}]) - (k_{1R} + k_{13R} K_A [\mathbf{3}])}{(k_{1S} + k_{13S} K_A [\mathbf{3}]) + (k_{1R} + k_{13R} K_A [\mathbf{3}])}$$

To convert this time-dependent function to a function of degree of conversion, one must relate the time-dependent variable **[3]** to degree of conversion (X) using the definition $X = [\mathbf{3}]/[\mathbf{2}]_0$, where **[2]₀** is the initial concentration of aldehyde **2**. Doing so gives the following equation:

$$ee'(X) = \frac{(k_{1S} - k_{1R}) + (k_{13S} - k_{13R})K_A [\mathbf{2}]_0 X}{(k_{1S} + k_{1R}) + (k_{13S} + k_{13R})K_A [\mathbf{2}]_0 X}$$

This equation is the familiar sigmoidal, binding isotherm relationship exhibited by any two-state equilibrium, where the instantaneous enantioselectivity is the variable responding to changes in concentration of cyanohydrin. To derive an expression for the enantiomeric excess of accumulated product, one must integrate the expression for "instantaneous" enantiomeric excess with respect to the variable X from X=0 to X= χ . Doing so affords the expression:

$$ee(\chi) = \frac{k_{13S} - k_{13R}}{k_{13R} + k_{13S}} \chi + \frac{(k_{1S} - k_{1R})(k_{13R} + k_{13S}) - (k_{1R} + k_{1S})(k_{13S} - k_{13R})}{(k_{13S} + k_{13R})^2 K_A [2]_0} \ln \left[1 + \frac{k_{13R} + k_{13S}}{k_{1R} + k_{1S}} [2]_0 K_A \chi \right]$$

This expression must be normalized for the degree of conversion by division by χ to afford equation 2.

Derivation of Kinetic Expression for Enantioselectivity. Dimeric 1.

If one assumes that the catalytic species in Scheme 1 are dimeric, the rate of production of cyanohydrin isomers will depend on $[1]^2$ and $[1 \bullet 3]^2$ and the expression for instantaneous enantioselectivity will be given as:

$$ee'(X) = \frac{(k_{1S} - k_{1R}) + (k_{13S} - k_{13R}) K_A^2 [2]_0^2 X^2}{(k_{1S} + k_{1R}) + (k_{13S} + k_{13R}) K_A^2 [2]_0^2 X^2}$$

Integrating this expression with respect to X from X=0 to X= χ affords the following relation:

$$ee(\chi) = \frac{k_{13S} - k_{13R}}{k_{13R} + k_{13S}} \chi + \frac{(k_{1S} - k_{1R})(k_{13R} + k_{13S}) - (k_{1R} + k_{1S})(k_{13S} - k_{13R})}{(k_{13S} + k_{13R})^2 \sqrt{(k_{1R} + k_{1S}) K_A [2]_0}} \tan^{-1} \left[\sqrt{\frac{k_{13R} + k_{13S}}{k_{1S} + k_{1R}}} K_A [2]_0 \chi \right]$$

Normalizing this expression for the degree of completion affords equation 3.

Solution for Kinetic Parameters k_{1S} , k_{1R} , k_{13S} , k_{13R} and K_A

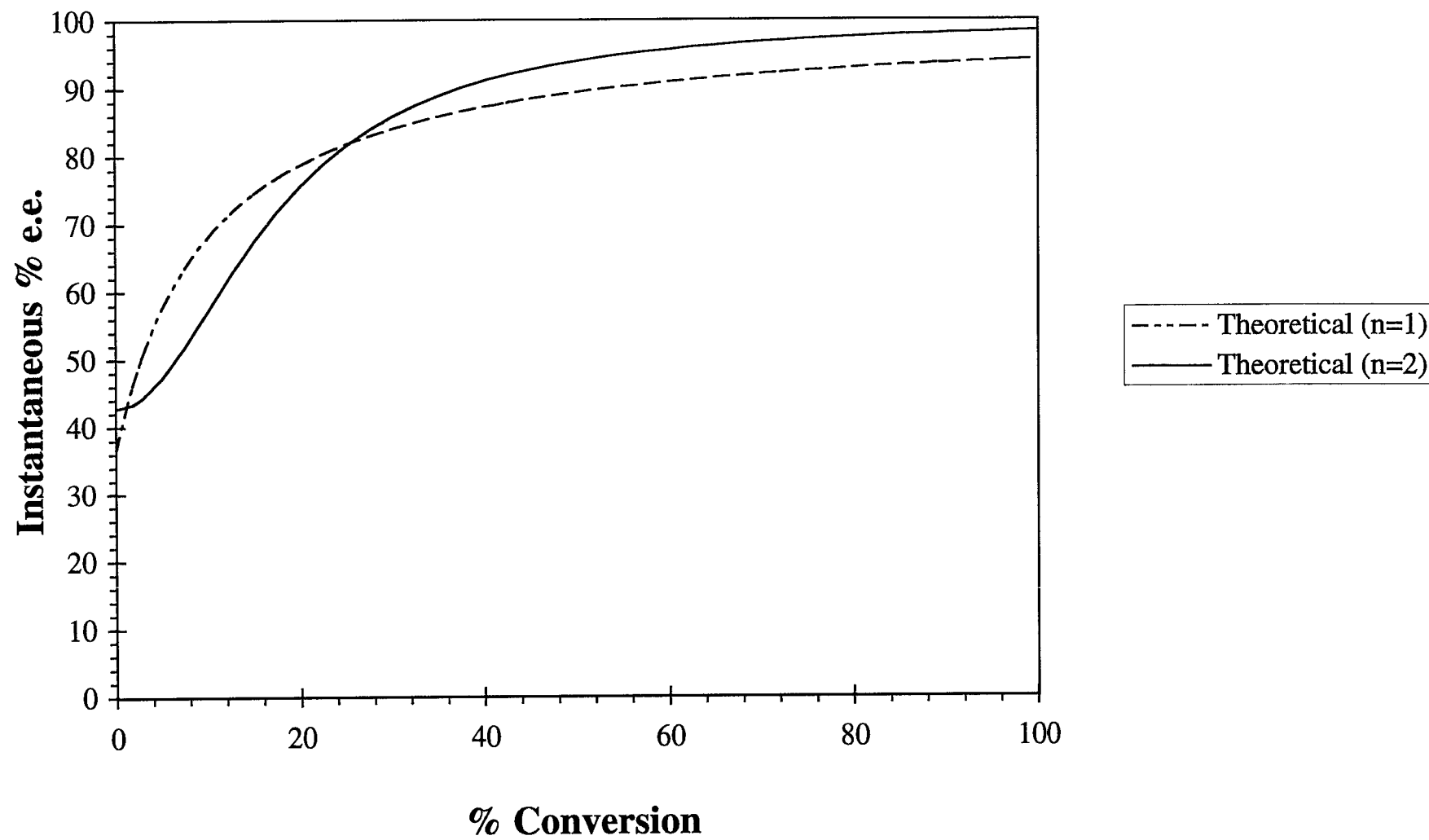
The data shown in Fig. 1 were fit to equations 2-3 using the non-linear regression function of Microsoft Excel 5.0. From the fit, the four rate constants k_{1R} , k_{1S} , k_{13R} and k_{13S} were obtained. To obtain the equilibrium constant K_A , the sigmoidal equations for $ee'(X)$ were solved for K_A using the rate constants previously obtained. The parameters obtained, along with the residual error from each fit, are given below:

aldehyde	equation	k_{1R}	k_{1S}	k_{13R}	k_{13S}	K_A	residual
2a	2	1686.9	785.1	2476.4	-0.0	9.91	0.02614
2a	3	5.19E6	2.58E6	3.53E6	-0.0	5.80	0.01380
2b	2	57.4	57.4	115.0	-0.0	9.69	0.02760
2b	3	8.82E7	3.54E7	5.79E8	3.54	7.19	0.01523
2c	2	106.2	58.0	1057.0	-0.0	2.91	0.01979
2c	3	2.19E6	5.44E5	2.30E7	1.93E5	1.94	0.02136
2d	2	11.0	7.72	18.7	-0.0	2.22	0.00649
2d	3	1.64E5	9.16E4	2.55E5	-0.0	1.84	0.00503
2e	2	208.2	191.8	134.8	87.7	27.47	0.00136
2e	3	1.08E6	8.33E5	1.91E6	0.02	7.19	0.00136

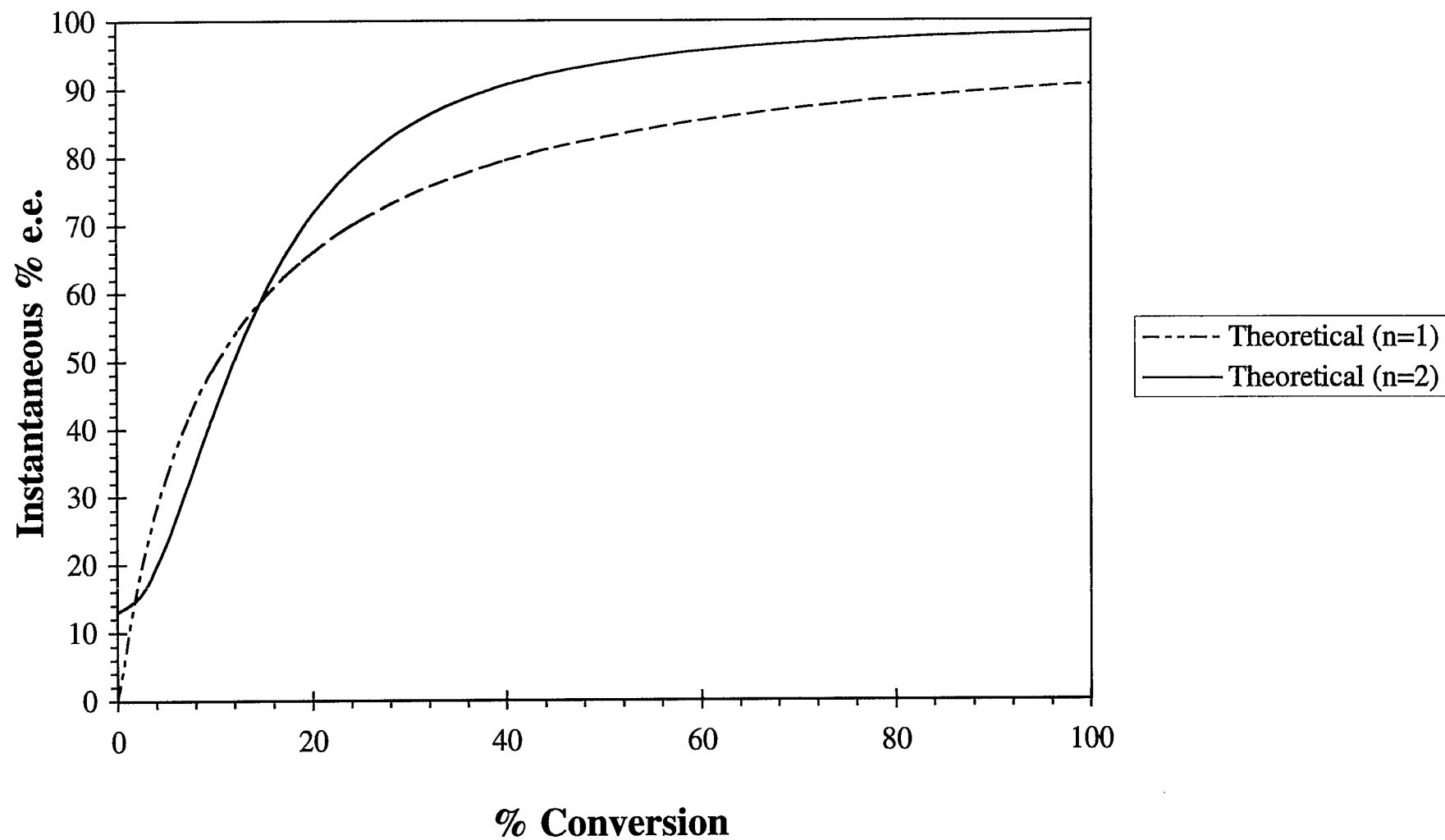
From these parameters, the values of ee_1 , ee_{13} and k_{rel} were derived

Benzaldehyde

Instantaneous % ee vs. % Conversion

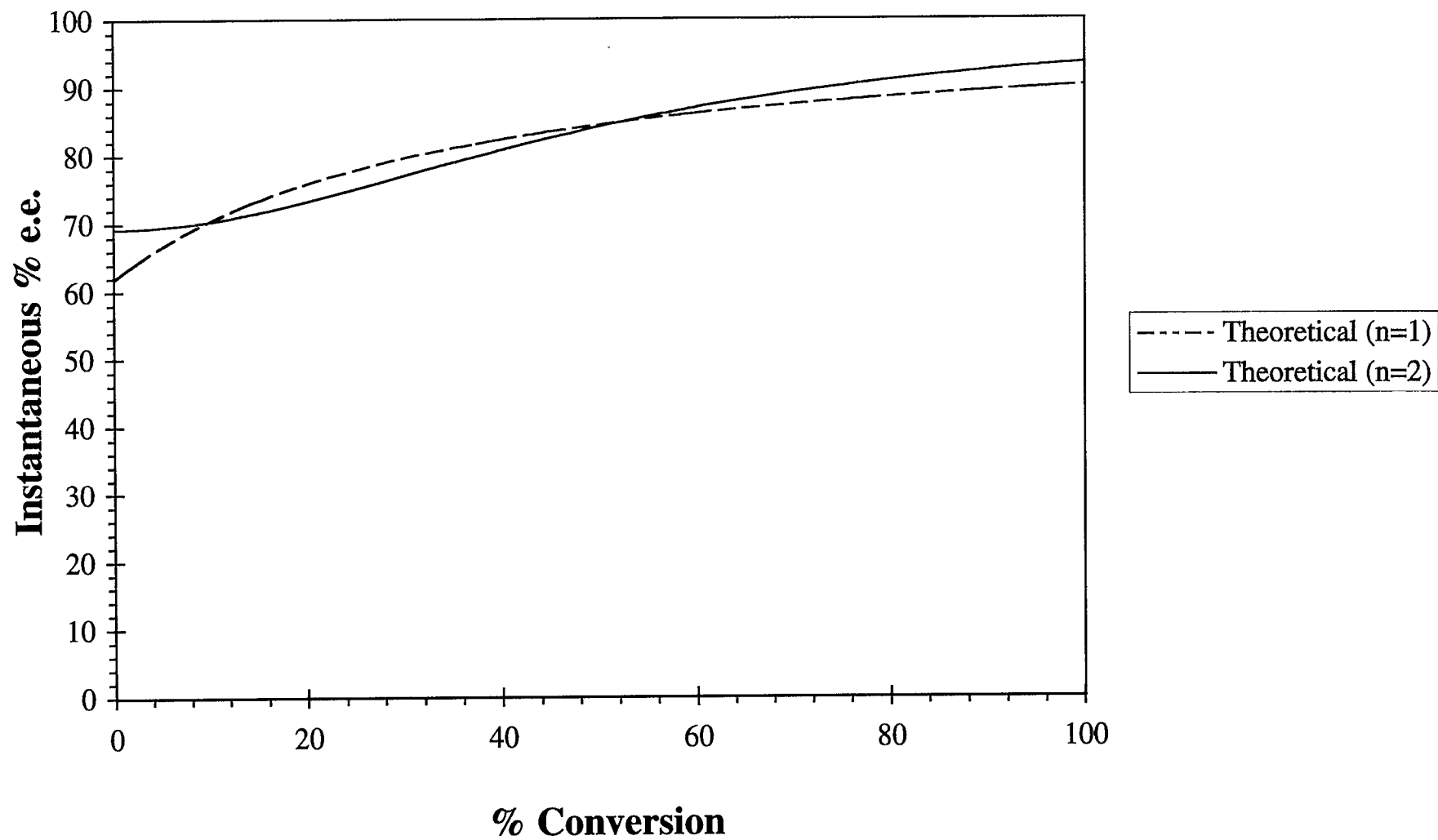


***m* -Phenoxybenzaldehyde**
Instantaneous % ee vs. % Conversion



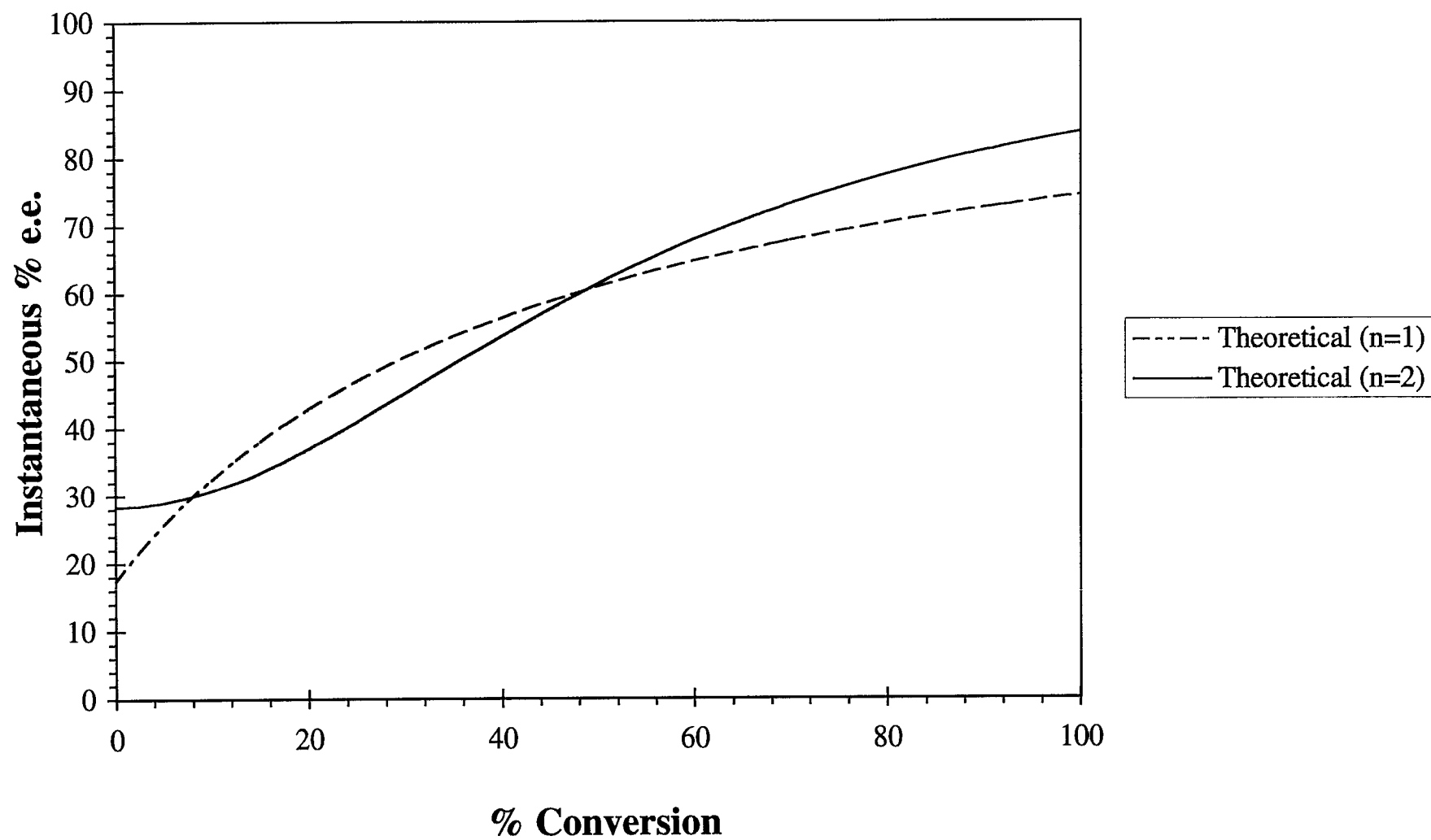
Naphthaldehyde

Instantaneous % ee vs. % Conversion



Furfural

Instantaneous % ee vs. % Conversion



Pivaldehyde

Instantaneous % ee vs. % Conversion

