Solid–Solid Reaction Between Sulfacetamide and Phthalic Anhydride

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Received May 23, 1983, from the *College of Pharmacy, The University of Iowa, Iowa City, IA 52240.* Accepted for publication September 30, 1983.

Abstract □ Thermal and kinetic data for the solid-state addition reaction of sulfacetamide and phthalic anhydride are presented. A compaction method was used so that the influence of some pharmaceutical parameters (compressional pressure, particle size, concentration, and temperature) on the reaction kinetics could be observed.

Keyphrases □ Sulfacetamide—solid-solid reaction with phthalic anhydride □ Phthalic anhydride—solid-solid reaction with sulfacetamide □ Solid-solid reactions—sulfacetamide and phthalic anhydride, thermal and kinetic analyses

The stability of a medicinal compound in a solid dosage form is routinely investigated in terms of the percentage of the medicinal compound that is unchanged after exposure to various temperatures (1–4). Although thermal decomposition is an important consideration in the processing, testing, and storage of solid dosage forms, only a limited number of reports in the pharmaceutical literature have been concerned with the physicochemical mechanism and kinetics of solid-state reactions (5–13). In general, the chemistry of solids has been presented in several texts (14–18). This study was initiated to present a simple model of a solid-state addition reaction so that some pharmaceutical factors (compressional pressure, concentration, particle size, and temperature) could be viewed in relation to their influence on the reaction.

EXPERIMENTAL SECTION

Samples of sulfacetamide[1] and phthalic anhydride[2] were individually separated into a 100/140-mesh-size fraction by means of U.S. standard sieves and a shaker[3]. Blends of the sulfacetamide and phthalic anhydride were prepared at 2:1, 1:1, and 1:2 molar ratios and were passed through a 200-mesh sieve. The thermal analytical data of the components and the blends were determined with a thermogravimetric analyzer[4] and a differential thermal analyzer[5]. Typical thermograms are given in Figs. 1 and 2.

For the study concerned with the effect of molar ratio on the reaction kinetics of sulfacetamide and phthalic anhydride, compacts with molar ratios of 1:1, 1:2, and 1:3 were used. An appropriate weight (400 mg) of a 100/140-mesh fraction of the blend was compressed for 1 min at a pressure of 3580 kg/cm^2 with an hydraulic press[6] fitted with a 1.27-cm punch and die set. Each compact was sealed under nitrogen in a glass vial and then immersed in a thermostated oil bath at 95 ± 0.5°C. At a given time, the reaction was quenched by immersion of the vial in ice, and the compact was then assayed. The reaction was conducted in triplicate. Typical data of the percent conversion of sulfacetamide to phthalylsulfacetamide are given in Table I.

For the study of the effect of particle size on the reaction kinetics, sulfacetamide was recrystallized from distilled water and then dried in a vacuum oven at 60°C. The purity of the sulfacetamide, as analyzed by differential scanning calorimetry[7], was 99.63%. With sieves and a shaker, the sulfacetamide was classified into 40/45-, 45/60-, 60/80-, 80/100-, and 100/140-mesh fractions. Blends with a 1:2 molar ratio of sulfacetamide and phthalic anhydride were prepared with phthalic anhydride of a 100–140-mesh fraction and the five sizes of sulfacetamide. An appropriate weight (2025 mg) of the blends was compressed for 1 min at a pressure of 35 kg/cm^2 with a hydraulic press fitted with a 2.857-cm punch and die set. Each compact, which corresponded to a specific particle size of sulfacetamide, was manually divided diametrically into six parts with a razor blade. Three parts were assayed for initial content, and the other parts were used for the kinetic study at 95°C. The percent conversion of sulfacetamide to phthalylsulfacetamide is shown in Table II.

For the study concerned with the effect of compressional pressure on reaction kinetics, a blend of an equimolar ratio of sulfacetamide and phthalic anhydride with a 100/140-mesh fraction was compressed for 1 min with a hydraulic press fitted with a 2.857-cm punch and die set at 35, 106, 283, 601, 1003, 2005, 3580, and 5371 kg/cm^2. The percent conversion is shown in Table III.

For the study concerned with the influence of temperature on the reaction kinetics, a blend of an equimolar ratio of sulfacetamide and phthalic anhydride with a 100/140-mesh fraction was compressed for 1 min in an hydraulic press fitted with a 1.27-cm punch and die set at a pressure of 3580 kg/cm^2. Each compact weighed 400 mg. The reaction was conducted at 85°C, 90°C, 95°C, 100°C, 105°C, and 110°C. Typical data are given in Table IV.

The unreacted sulfacetamide was colorimetrically analyzed by diazotization and a coupling reaction with *N*-naphthylethylenediamine dihydrochloride (19, 20). A standard concentration–absorbance curve was determined by transferring 0.5-, 1.0-, 2.0-, 3.0-, and 4.0-mL aliquots of a stock solution

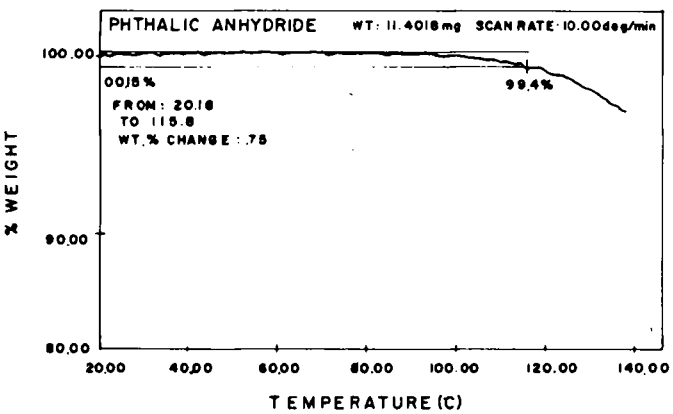

Figure 1—*Thermogram of phthalic anhydride showing its sublimation characteristics.*

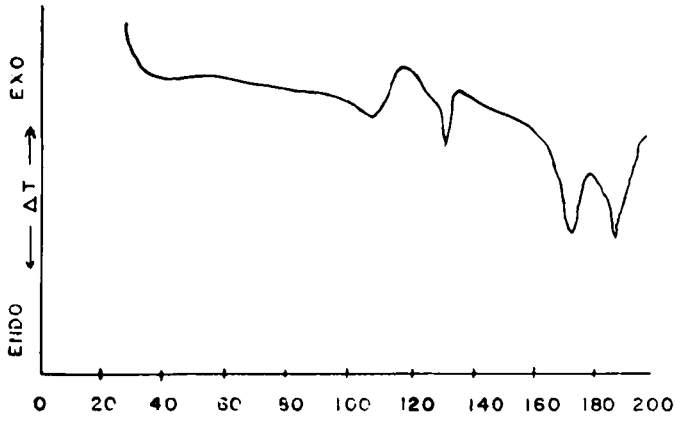

Figure 2—*DTA thermogram of a 2:1 molar ratio of sulfacetamide and phthalic anhydride. Reference, glass beads; heating rate, 20°C/min; atmosphere, N_2 (1 atm); sensitivity of* y*-axis, 0.2°C/cm.*

[1] Lot 59C-0276; Sigma Chemical Co.
[2] Reagent grade, lot 88C-0525; Fisher Scientific Co.
[3] Central Scientific Co.
[4] Model TGS-2; Perkin-Elmer.
[5] Model 900; E.I. duPont de Nemours & Co.
[6] Model C; Carver Press.
[7] Model DSC-2 differential scanning calorimeter; Perkin-Elmer.

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Table I—Conversion of Sulfacetamide to Phthalylsulfacetamide [a]

Time, min	Conversion, %	Mean Conversion ± SD, %
0	0	0
10	6.68	
	6.71	5.90 ± 1.38
	4.31	
20	8.19	
	5.45	6.05 ± 1.91
	4.52	
30	7.03	
	6.61	5.89 ± 1.62
	4.04	
60	9.14	7.33 ± 2.57
	5.51	
180	10.24[b]	
	8.28[b]	10.07 ± 0.72
	10.68[b]	
300	13.66[b]	
	16.00[b]	14.85 ± 1.17
	14.88[b]	

[a] At 95°C as a function of time for a 1:2 molar ratio of sulfacetamide and phthalic anhydride. [b] Corrected to include sublimed phthalic anhydride (0.51 and 1.10% of total compact weight for 180 and 300 min, respectively).

(prepared by dissolving 125.6 mg of sulfacetamide in 50 mL of 0.5 M NaOH and adjusting with distilled water to 250 mL in a volumetric flask) into sufficient distilled water to make 50 mL. From each dilution, 5.0 mL was transferred into a 50-mL volumetric flask and neutralized with 0.02 M HCl. Then, 5.0 mL of 0.5 M HCl and 5.0 mL of a 0.1% aqueous sodium nitrite solution were added to the flask. After 3 min, 5.0 mL of 0.5% ammonium sulfamate solution was added, and the volume was adjusted to 50 mL by the addition of distilled water. The absorbance was measured against a blank at 536 nm. A plot of absorbance against concentration showed a Beer's law relationship.

At each time period, the compact was triturated in a mortar, and the appropriate amount of powdered compact corresponding to 125 mg of sulfacetamide was accurately weighed and transferred to a 250-mL volumetric flask. The subsequent addition of reagents and the procedure have been described above. By means of the standard curve, the measured absorbance was used to determine the concentration of unreacted sulfacetamide. When sublimation occurred, a correction was made in the calculation of the percent conversion.

RESULTS AND DISCUSSION

Physicochemical Characteristics—As reports (14–18) have been published for single-solid decompositions, the reaction of sulfacetamide and phthalic anhydride was selected as an example of a solid–solid addition reaction for the simple model: A + B → AB. Samples of sulfacetamide maintained at 50°C, 90°C, and 110°C for 24 and 16 d and 5 h, respectively, showed no degradation within the variability (0.6%) of the analytical method.

Table II—Influence of Particle Size on Conversion of Sulfacetamide [a]

Particle Size[b] of Sulfacetamide, μm	Conversion, %[c]	Mean Conversion ± SD, %
128	22.45	
	18.47	21.54 ± 2.74
	23.71	
164	15.80	
	22.08	19.43 ± 3.25
	20.42	
214	14.49	
	20.23	17.25 ± 2.88
	17.03	
302	18.31	
	6.81	15.69 ± 7.90
	21.95	
387	11.90	
	4.25	9.34 ± 4.41
	11.88	

[a] After 3 h at 95°C. [b] Mean of U.S. Standard Sieve opening passed and retained. [c] Corrected to include sublimed phthalic anhydride.

Table III—Influence of Compression Pressure on Conversion of Sulfacetamide in an Equimolar Blend of Sulfacetamide and Phthalic Anhydride [a]

Compressional Pressure, kg/cm²	Conversion, %[b]	Mean Conversion ± SD, %
0	7.01	
	9.87	8.19 ± 1.49
	7.69	
35	19.92	
	23.78	19.40 ± 4.66
	14.51	
106	18.54	
	15.88	16.48 ± 1.84
	15.02	
283	17.83	
	17.98	17.28 ± 1.08
	16.04	
601	14.98	
	9.95	12.26 ± 2.54
	11.86	
1003	11.18	
	11.13	11.26 ± 0.19
	11.48	
2005	11.43	
	9.89	10.45 ± 0.85
	10.04	
3581	8.67	
	12.07	
	9.39	9.61 ± 1.76
	11.36	
	8.70	
	7.45	
5381	8.51	
	7.81	8.50 ± 0.69
	9.19	

[a] After 3 h at 95°C. [b] Corrected to include sublimed phthalic anhydride.

It has been demonstrated that the solid-state reaction of sulfathiazole and phthalic anhydride is an addition reaction with a 1:1 stoichiometry (21). Preliminary differential thermal analysis (DTA) of an equimolar ratio of sulfacetamide and phthalic anhydride showed that (*a*) the stoichiometry was 1:1, (*b*) the reaction product melted at 195°C [lit. mp of phthalylsulfacetamide (22) 196°C] and (*c*) decomposition occurred as the temperature exceeded 196°C. The anhydrous state of each reactant was determined by thermogravimetry. The weight loss of phthalic anhydride is due to sublimation, as the slope (*dW/dT*) (Fig. 1) is negatively increasing without discontinuity. The melting points of sulfacetamide and phthalic anhydride, as shown on the thermograms, were 185°C and 132.1°C, respectively [lit. mp (22) 182–184°C and 130.8°C, respectively].

Figure 2 is a typical thermogram of those determined on the blends of various molar ratios. The endothermic peak at 107°C is probably caused by fusion of the sulfacetamide and phthalic anhydride eutectic because a large exothermic peak ensues immediately. The exothermic peak at 117°C is due to the liquid-state addition reaction. At 131°C, the unreacted anhydride is completely melted and penetrates into the surface fissures of any solid sulfacetamide undergoing the addition reaction, as indicated by the broad exothermic peak between 135°C and 156°C. The endothermic peak at 172.5°C is likely caused by the melting of the sulfacetamide-phthalylsulfacetamide eutectic. After melting, a small exothermic peak occurs at 178.5°C and may be due to the liquid-state addition between sulfacetamide and the residual anhydride. Finally, the endothermic peak at 187°C may be caused by fusion of phthalylsulfacetamide (depressed by impurity).

At molar ratios of 1:1 and 1:2 sulfacetamide and phthalic anhydride, the thermograms (not shown to conserve space) are essentially the same as those for the 2:1 molar ratio at temperatures <160°C. The relatively small quantity of sulfacetamide in the 1:2 molar ratio has undergone addition, so there is no endothermic peak corresponding to the melting of sulfacetamide at 172.5°C. The final endothermic peaks are caused by the melting of impure phthalysulfacetamide; however, the quantity of impurity is different in the three ratios.

Influence of Concentration on Reaction Kinetics—Molar ratios of sulfacetamide to phthalic anhydride from 1:1 to 1:3 provide excess phthalic anhydride so that the initial contact area between the reactants is varied as the concentration of sulfacetamide is changed. The conversion (milligrams sulfacetamide per gram of anhydride) is shown as a function of time in Fig. 3.

Table IV—Conversion of Sulfacetamide to Phthalylsulfacetamide at 90°C as a Function of Time for an Equimolar Ratio of Sulfacetamide and Phthalic Anhydride

Time, min	Conversion, %[a]	Mean Conversion ± *SD*, %
0	0	0
10	1.53	
	1.94	
	2.28	
	4.85	2.62 ± 1.08
	2.79	
	2.23	
	2.73	
20	3.61	
	3.18	
	3.01	3.32 ± 0.74
	3.74	
	4.06	
30	4.58	
	3.19	
	3.66	3.81 ± 0.51
	3.92	
	3.69	
60	4.77	
	4.23	
	6.04	5.20 ± 0.46
	5.24	
	5.70	
180	5.63	
	8.18	
	7.07	7.84 ± 1.31
	9.34	
	8.98	
300	11.20[a]	
	8.87[a]	
	9.07[a]	10.64 ± 1.74
	10.97[a]	
	13.10[a]	

[a] Corrected to include sublimed phthalic anhydride (0.53% of weight of compact).

The conversion (milligrams of sulfacetamide per gram of anhydride) is greater for a high concentration of sulfacetamide than for a lower concentration as the reaction time is increased (Fig. 4). For example, a comparison of the 60- and 180-min curves shows that for the 1:1 molar ratio, an additional 33.7 mg of sulfacetamide/g of anhydride was converted during the 120-min interval, whereas for the same interval of time, only an additional 16.5 mg of sulfacetamide/g of anhydride was converted at the 1:3 molar ratio.

Influence of Particle Size on Reaction Kinetics—By using a 1:2 molar ratio of sulfacetamide to phthalic anhydride, compacts were prepared with several sizes of sulfacetamide. A low compressional pressure (35 kg/cm²) was used to retain the integrity of the particles. The percent conversion of sulfacetamide after 3 h at 95°C is given for the various sizes in Table II. It appears that a reduction of particle size increases the percent conversion.

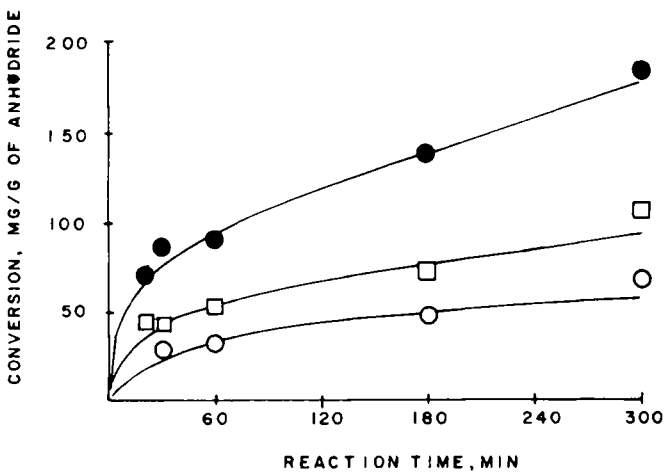

Figure 3—*Influence of concentration on the reaction at 95°C of sulfacetamide and phthalic anhydride prepared from 100/140-mesh fraction compressed at 3581 kg/cm². Key: (○) 1:3; (□) 1:2; (●) 1:1.*

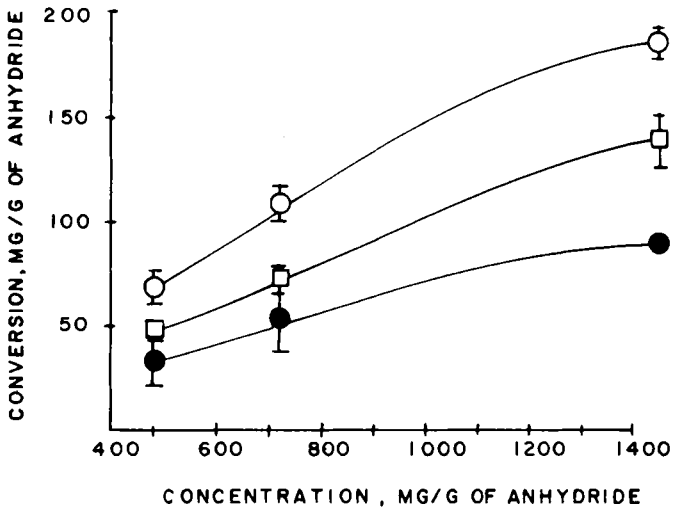

Figure 4—*Influence of concentration of sulfacetamide on weight conversion at various times at 95°C. Key: (●) 60 min; (□) 180 min; (○) 300 min. Bars represent* SD.

Although the conversion rate of sulfacetamide has been shown to be proportional to its concentration, it may be more meaningful to describe the kinetics of solid-solid reactions in terms of interfacial area of contact between the reactants (18, 23); however, the determination of actual area of contact is questionable. Since the actual area of contact is unknown but is probably proportional to the total surface area, reaction kinetics of a solid-solid system could be considered in terms of the total surface area of the sulfacetamide, because phthalic anhydride is the only mobile phase (21, 24) and is transported to the surface of the sulfacetamide by surface migration (21) and/or sublimation. Assuming that the particles of sulfacetamide are spherical, the total surface area per gram of blend was calculated and plotted against the percent conversion (Fig. 5).

Influence of Pressure on Reaction Kinetics—Compacts of an equimolar blend of sulfacetamide and phthalic anhydride were prepared at pressures up to 5380 kg/cm² and were maintained for 3 h at 95°C. The percent conversion of sulfacetamide increases to a maximum value (17%) as the compressional pressure is increased to 283 kg/cm² (Fig. 6), and then, with further increases in compressional pressure, the percent conversion decreases.

As the compressional pressure is increased, packing of the particles is more dense, and as bonding occurs, the porosity is decreased (25, 26). As consolidation occurs, the area of contact between the reactants is increased by fragmentation or deformation (27) until a maximum specific surface area, which provides more reaction sites between the sulfacetamide and phthalic anhydride, is attained. Additional increases in compressional pressure result in consolidation with a progressive decrease in specific surface area, which

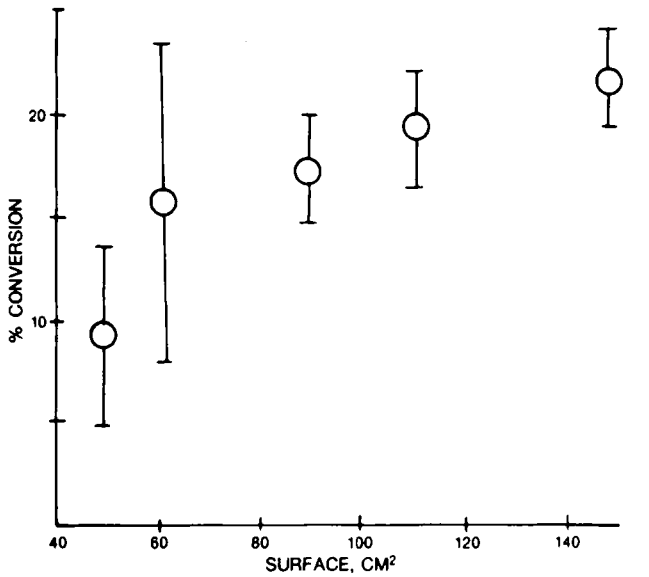

Figure 5—*Influence of total surface area of sulfacetamide on conversion after 3 h at 95°C. Bars represent* SD.

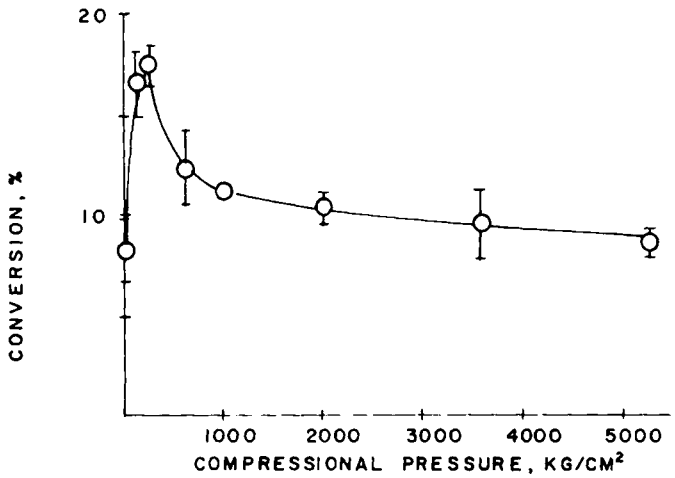

Figure 6—*Influence of compressional pressure on the conversion of sulfacetamide after 3 h at 95°C. Bars represent* SD.

provides fewer reaction sites. In addition, the transport rate of the anhydride by diffusion through the phthalylsulfacetamide layer (24), surface migration (21), and/or sublimation will be decreased. Both effects operate to decrease the percent conversion.

Influence of Temperature on Reaction Kinetics—Compacts compressed at a pressure of 3581 kg/cm² from an equimolar blend of sulfacetamide and phthalic anhydride of a 100/140-mesh fraction were exposed to six temperatures from 85°C to 110°C. The percent conversion of sulfacetamide at these temperatures is shown as a function of time in Fig. 7. At 100°C, 105°C, and 110°C, the curve attains a plateau in a very brief time because of the fast reaction. Based on the thermogram (Fig. 2), it is likely that the initial phase-boundary reaction proceeds mainly in the liquid state, in which a more vigorous chemical reaction would be expected according to the lever rule (28), which infers that the fraction of the melt at the interface between the reactants is approximately proportional to the reaction temperature. At 85°C, 90°C, and 95°C, there is a slowing of the reaction rate, possibly due to the fact that the reaction occurs primarily in the solid state, which requires more energy and is more restrictive of molecular movement than in the liquid-solid reaction.

In addition to the solid-solid interaction at the phase boundary, mass transport of the anhydride to the free sulfacetamide surface occurs simultaneously (21). Diffusion through a solid is slow, and after the phase-boundary reaction is completed, the conversion curve asymptotically approaches a plateau. Since the percent conversion at 85°C, 90°C, and 95°C significantly increases, although at a slower rate, it could be considered as phase-boundary reaction and treated mathematically (see *Appendix*). The reaction rate constants for given conditions at 85°C, 90°C, and 95°C were calculated by starting with an A value, which was set equal to the percent conversion at 300 min, and then sequentially, reaction rate constants were calculated by continuous increments of 0.5 to the previous A value. The value of the derived constant, A, was selected which best fit the experimental data.

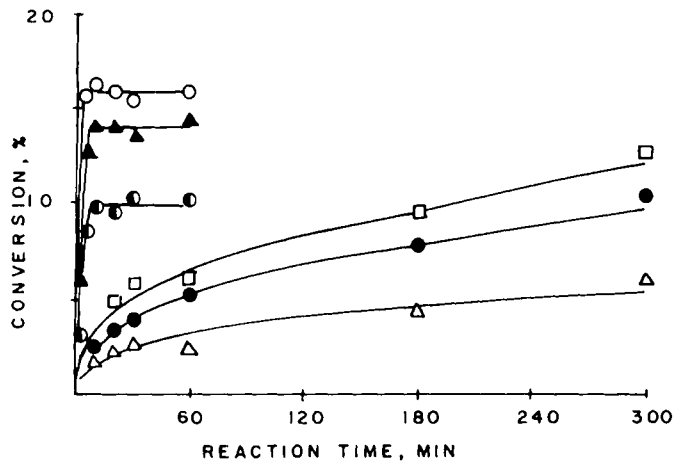

Figure 7—*Influence of temperature on the reaction kinetics of equimolar sulfacetamide and phthalic anhydride compacts prepared at 3581 kg/cm². Key: (△) 85°C; (●) 90°C; (□) 95°C; (◐) 100°C; (▲) 105°C; (○) 110°C.*

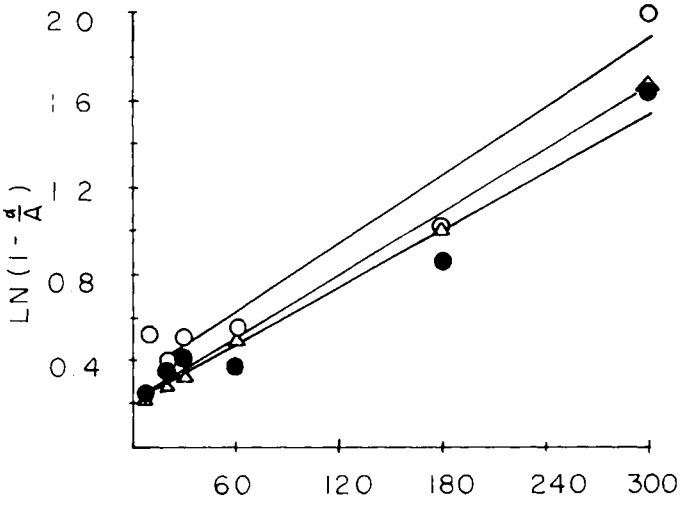

Figure 8—*Linear plot of $-\ln(1 - \alpha/A)$ against reaction time at various temperatures. Key: (●) 85°C; (△) 90°C; (○) 95°C.*

The best plot ($r = 0.9758$) of $-\ln[1 - (\alpha/A)]$ against time at 85°C is shown in Fig. 8 ($A = 7.75\%$; $k = 0.004704\ \text{min}^{-1}$). The experimental percent conversion at 85°C is compared in Fig. 9 with that calculated with the best set of values of A and k and Eq. 14 (see *Appendix*). The greatest deviation in the plot occurs at short reaction times and is obviously due to the omission in case 2 (see *Appendix*) of the second term of Eq. 12. Similar results occur if the data at 90°C ($A = 13.14\%$; $k = 0.004912\ \text{min}^{-1}$; $r = 0.9875$) and at 95°C ($A = 14.72\%$; $k = 0.005272\ \text{min}^{-1}$, $r = 0.9437$) are plotted.

As shown in Fig. 10, a plot of ln k against reciprocal temperature is linear with a slope of $-1502\ \text{K}^{-1}$. From the plot of ln k against reciprocal temperature over the range from 85°C to 95°C, it could be inferred that the reaction rate constants could be estimated at various temperatures; however, this concept has its limitations and may not be extended to other temperatures at which different physical parameters and mechanisms of transport and reaction occur (18).

APPENDIX

By assuming that the solid-solid reaction rate, $d\alpha/dt$, is proportional to the area of contact, X, between the reactants at time, t:

$$\frac{d\alpha}{dt} = \frac{k}{c}X \qquad \text{(Eq. 1)}$$

where k is the reaction rate constant and c is the proportionality constant. If the rate of generation of new contact area between the reactants is proportional to the free sulfacetamide surface, X_f, at time, t:

$$\frac{dX}{dt} = -kX + k_1X_f \qquad \text{(Eq. 2)}$$

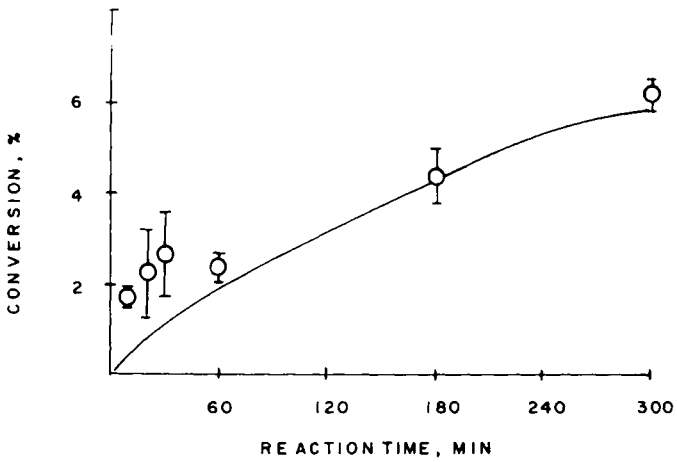

Figure 9—*Conversion curve at 85°C of equimolar sulfacetamide and phthalic anhydride compacts compressed at 3581 kg/cm². Solid curve represents theoretical values according to Eq. 14. Points are experimental values; bars represent* SD.

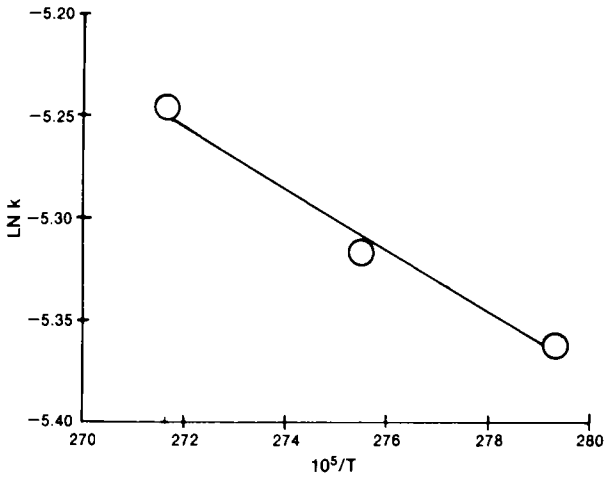

Figure 10—*Arrhenius plot of reaction rate constants and temperatures (T).*

where k_1 is the rate constant for the generation of new area of contact and is related to the mass transport of the anhydride. The changing rate of free sulfacetamide surface may be expressed as:

$$\frac{dX_f}{dt} = -k_1 X_f \qquad \text{(Eq. 3)}$$

The Laplace transformations of Eqs. 1–3 are:

$$s\bar{\alpha} = (k/c)\bar{X} \qquad \text{(Eq. 4)}$$

$$s\bar{X} - k_2X_0 = -k\bar{X} + k_1\bar{X}_f \qquad \text{(Eq. 5)}$$

$$s\bar{X}_f - k_2k_3X_{f,0} = -k_1\bar{X}_f \qquad \text{(Eq. 6)}$$

where s is the Laplace parameter, X_0 is the initial contact area between the reactants, $X_{f,0}$ is the initial free sulfacetamide area of contact, k_2 is the fraction of ultimately reacted area of contact, k_3 is the fraction of ultimately covered free sulfacetamide surface area, and $\bar{\alpha}$ is the Laplace transform of α. After combining the same terms in Eqs. 5 and 6:

$$\bar{X} = \frac{k_2X_0 + k_1\bar{X}_f}{s + k} \qquad \text{(Eq. 7)}$$

$$\bar{X}_f = \frac{k_4X_{f,0}}{s + k_1} \qquad \text{(Eq. 8)}$$

where $k_4 = k_2k_3$. By combining Eqs. 7 and 8 and substituting $\bar{X}$ into Eq. 4:

$$\bar{\alpha} = \frac{(k/c)k_2X_0s + (k/c)k_1k_2X_0 + (k/c)k_1k_4X_{f,0}}{s(s + k)(s + k_1)} \qquad \text{(Eq. 9)}$$

In Case 1, assume that $k \gg k_1$, and then the anti-Laplace transformation of $\bar{\alpha}$ in Eq. 4 would be:

$$\alpha = \frac{(kk_1k_2X_0 + kk_1k_4X_{f,0})/c}{kk_1} - \frac{(k^2k_2X_0 - kk_1k_2X_0 - kk_1k_4X_{f,0})/c}{k(k - k_1)} \cdot \exp(-kt) - \frac{(kk_1k_2X_0 - kk_1k_2X_0 - kk_1k_4X_{f,0})/c}{k_1(k - k_1)} \cdot \exp(-k_1t) \qquad \text{(Eq. 10)}$$

Because $k \gg k_1$, the second term on the right side of the equation rapidly becomes negligible, and in a short reaction time, Eq. 10 reduces to:

$$\alpha = (k_2X_0 + k_4X_{f,0})/c - (k_4X_{f,0}/c) \cdot \exp(-k_1t) \qquad \text{(Eq. 11)}$$

and at $t = 0$ and $\alpha = 0$, $k_2X_0/c = 0$. Since X_0 and c cannot be zero, the inference is that $k_2 = 0$ (no reaction occurred). Thus, the simplified form (Eq. 11) does not meet the initial condition, although it may apply when the reaction time is long enough to neglect the second term of Eq. 10. In addition, at a molar ratio of 1:3 sulfacetamide to phthalic anhydride, the sulfacetamide would be completely covered by the anhydride, and the third term of Eq. 10 would be operative. As shown in Fig. 9, the conversion is continuing. The value of k is relatively small, so the second term in Eq. 10 is not negligible throughout the 5-h reaction time.

In Case 2, assume that $k_1 \gg k$ and then:

$$\alpha = \frac{(kk_1k_2X_0 + kk_1k_4X_{f,0})/c}{kk_1} - \frac{(kk_1k_2X_0 - kk_1k_4X_{f,0} - kk_1k_2X_0)/c}{k_1(k_1 - k)} \cdot \exp(-k_1t) - \frac{(k^2k_2X_0 - kk_1k_2X_0 - kk_1k_4X_{f,0})/c}{k(k_1 - k)} \cdot \exp(-kt) \qquad \text{(Eq. 12)}$$

Because $k_1 \gg k$, the second term on the right side of the equation rapidly becomes negligible, so in a very short reaction time:

$$\alpha = (1/c)(k_2X_0 + k_4X_{f,0})[1 - \exp(-kt)] \qquad \text{(Eq. 13)}$$

or:

$$\alpha = A[1 - \exp(-kt)] \qquad \text{(Eq. 14)}$$

$$A = (1/c)(k_2X_0 + k_4X_{f,0}) \qquad \text{(Eq. 15)}$$

Thus, a plot of $-\ln[1 - (\alpha/A)]$ against time will produce a straight line with the slope equal to k.

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ACKNOWLEDGMENTS

This study was abstracted in part from a dissertation submitted by Ho-Lun Weng to the Graduate College, University of Iowa, in partial fulfillment of the Doctor of Philosophy degree requirement.