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(10 mL). After a few minutes, the solvent was evaporated in vacuo and the residue triturated with ether. The oil (6.11 g, 82% yield) from evaporation of the ether extract decomposed on vacuum distillation. Chromatographic efforts to obtain analytically pure **15** also failed: IR (CCl_4) 6.06μm (s); ^{1}H NMR (CCl_4) δ 7.1–7.7 (m, 4 H), 3.73 (d, 6 H, J = 11 Hz, checked at 100 MHz), 2.80 (s, 3 H), 1.05 (s, 9 H).

When concentrated *N-tert*-butylbenzoazetinone[1] and $(MeO)_3P$ in CH_2Cl_2 were refluxed, no reaction occurred (tars obtained in refluxing xylene).

Reaction of 15 wtih Methanol. **15** (6.00 g, 0.02 mol) was refluxed in MeOH (30 mL) overnight and then vacuum evaporated, and the residue was triturated with pentanes. The insoluble oil was distilled and identified as dimethyl phosphite (0.76 g, 30%, comparison with commercial sample). The pentanes soluble methyl *N-tert*-butyl-*N*-methylanthranilate (**16**) was vacuum distilled; 4.0 g (90% yield) of bp 78–79 °C (0.5 mm). **16** was contaminated by 5% **4a** which could not be removed by distillation because **16** was thermally unstable and decomposed to **4a** and isobutene on attempted distillation. **16** was obtained pure by preparative VPC: IR (CCl_4) 5.77μm (s); ^{1}H NMR (CCl_4) δ 6.9–7.5 (m, 4 H), 3.76 (s, 3 H), 2.67 (s, 3 H), 1.09 (s, 9 H).

When **16** was heated at 170 °C overnight, the IR and NMR spectra of the oily residue (quantitative yield) were identical with data for **4a**.[1]

Acknowledgment. We thank the National Institutes of Health for the grant which supported this research.

Registry No. **1a**, 31767-66-5; **1b**, 31767-67-6; **1c**, 31562-01-3; **5a**, 91157-23-2; **5b**, 31562-02-4; **5c**, 91157-24-3; **5d**, 61752-05-4; **10a**, 31562-03-5; **10b**, 91157-25-4; **10c**, 91157-26-5; **10d**, 91157-27-6; **11a**, 22292-42-8; **11b**, 31562-04-6; **12**, 2217-25-6; **13a**, 91157-29-8; **13b**, 91157-31-2; **14**, 91157-33-4; **15**, 91157-34-5.

Supplementary Material Available: Additional spectral (MS) and analytical data plus details of the kinetic measurements for Figure 1 (3 pages). Ordering information is given on any current masthead page.

Mechanisms of the Reactions of Benzoazetinones with Nucleophiles: Evidence for an Imino Ketene Intermediate

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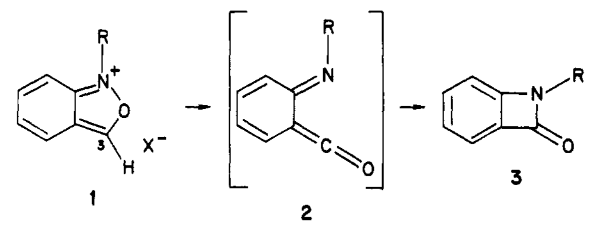
From studies of the kinetics of the reactions of *N-tert*-butylbenzoazetinone (**3a**) with diethylamine and with alcohols to give the ring-opened adducts **4**, the presence of a trace equilibrium component, the more electrophilic imino ketene **2a**, has been inferred. The transformation **3a** → **2a** can be catalyzed by light. The adduct, 1-*tert*-butyl-3-phenyl-2,4(1*H*,3*H*)-quinazolinedione (**5**), has been isolated in 80% yield from reaction of **3a** with phenyl isocyanate.

In the first paper of this sequence, the facile conversion of 3-unsubstituted anthranilium salts **1** to *N*-alkylbenzoazetinones **3** on treatment with triethylamine is described.[1] Despite intensive efforts, no spectral evidence for the presumed imino ketene intermediate **2** could be obtained. An equilibrium between **2** and **3**, though possible, seemed unlikely from the spectral data and could be excluded in the solid state where an X-ray crystal structure determination guaranteed the antiaromatic benzoazetinone formulation given for **3b**.[1]



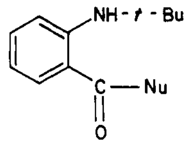
a, R = *tert*-butyl; b, R = 1-adamantyl

In this paper, we present indirect evidence (a) for the existence of the ring–chain tautomer equilibrium, **2** ⇌ **3**, even at room temperature, (b) that this equilibrium can be displaced photochemically to increase the concentration of **2**, and (c) that the imino ketene **2** is more electrophilic than **3**.

Results and Discussion

The kinetics of the reactions of *N-tert*-butylbenzoazetinone (**3a**) with Et_2NH and with alcohols to give the ring-opened products **4** have been studied. The effect of light on reaction rate also was investigated in experiments motivated by the observations of Burgess and Ege.[2]

Reaction of **3a** (0.057 M) with Et_2NH (0.057 M) in anhydrous *n*-pentane proceeded cleanly in the dark at 25.0 ± 0.2 °C to give **4a**. A good straight line was obtained in a plot of log [**3a**] vs. time: $k = 5.3 \times 10^{-6}\ s^{-1}$ ($t_{1/2}$ = 36 h).[3] When [Et_2NH] initial was doubled, k was 8.4×10^{-6} s^{-1} ($t_{1/2}$ = 23 h). Amide **4a** also was cleanly the product of the light-catalyzed reaction of **3a** with Et_2NH when a



4a, Nu = NEt_2
4b, Nu = O-methyl
4c, Nu = O-ethyl
4d, Nu = O-isopropyl
4e, Nu = O-*tert*-butyl

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(1) Olofson, R. A.; Vander Meer, R. K.; Hoskin, D. H.; Bernheim, M. Y.; Stournas, S.; Morrison, D. S. *J. Org. Chem.*, first paper in a series in this issue.

(2) For discussion, see ref 1. Burgess, E. M.; Milne, G. *Tetrahedron Lett.* **1966**, 93. Ege, G. *Chem. Ber.* **1968**, *101*, 3079. Ege, G.; Pasedach, F. *Ibid.* **1968**, 3089.

(3) The rate of product formation paralleled the rate of disappearance of **3a**; see experimental section.

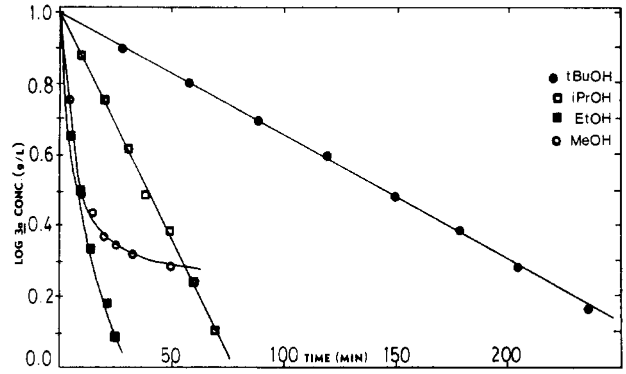

Figure 1. Light-accelerated reaction of **3a** with alcohols in *n*-pentane at 25 °C (both at 0.057 M, Pyrex filter).

Pyrex sleeve was used to shield the reaction from short wavelength light (Hanovia 450-W Hg vapor lamp inserted in a quartz well condenser immersed in reaction solution; ±2 °C). In duplicate runs with a 1:1 ratio of **3a** to Et_2NH, $k = 1.02 \pm 0.02 \times 10^{-4}$ s^{-1} ($t_{1/2} = 112$ min). With a 1:2 initial ratio of **3a** to Et_2NH, k increased to 1.25×10^{-4} s^{-1} ($t_{1/2} = 93$ min) and under the same conditions but with shorter wavelength light (Vycor sleeve instead of Pyrex), a further rate increase was observed: $k = 2.3 \times 10^{-4}$ s^{-1} ($t_{1/2} = 51$ min). In this latter system, however, the reaction was not as clean (solution discolored and small new IR peaks appeared). The rate enhancement of ca. 20 with 1:1 **3a**:Et_2NH found with Pyrex-filtered light requires light catalysis of the aminolysis, **3a** → **4a**. However, the magnitude of the catalytic effect is uncertain since the data are not only a function of light intensity but also of apparatus design (Pyrex thickness, vessel shape, etc.[4]).

In contrast to the Et_2NH results, no reaction was observed between the more hindered diisopropylamine and **3a**. In the photocatalyzed experiment, decomposition of **3a** occurred over a prolonged period but also was found in the absence of added nucleophile. No IR peaks attributable to imino ketene **2a** were generated on simple photolysis of **3a** in pentane.

The photocatalyzed reaction of *i*-PrOH with **3a** to give amino ester **4d** was somewhat faster than the related reaction of Et_2NH: with 1 equiv of *i*-PrOH, $k = 4.8 \times 10^{-4}$ s^{-1} ($t_{1/2} = 24$ min) and with 2 equiv of *i*-PrOH, $k = 8.9 \times 10^{-4}$ s^{-1} ($t_{1/2} = 13$ min). The first rate was unaffected by the inclusion of 0.1 equiv of Et_3N in the reaction mixture ($t_{1/2} = 23$ min). A comparison of the rates of photoinduced addition of *t*-BuOH, *i*-PrOH, EtOH, and MeOH is given in Figure 1. *t*-BuOH reacted slower than *i*-PrOH as anticipated from steric considerations: $k = 1.31 \times 10^{-4}$ s^{-1} ($t_{1/2} = 89$ min). The reactions of EtOH and MeOH both were faster than the *i*-PrOH reaction but did not follow first-order kinetics. The MeOH curve in Figure 1 was reproducible. While the EtOH and MeOH runs in Figure 1 curve up, a much smaller curvature in the 2 equiv of *i*-PrOH run was down. The amino esters **4b–e** were the sole products from reaction of all alcohols with **3a** so the kinetic variation does not reflect a change in product composition.

The dark or thermal addition of *i*-PrOH and *t*-BuOH to **3a** (0.057 M) to give the amino esters **4d,e** also was investigated. The comparative half-lives vs. the photo processes are 1 equiv of *i*-PrOH, 14 h dark and 24 min light; 2 equiv of *i*-PrOH, 10 h and 13 min; 1 equiv of *t*-BuOH, 59 h and 89 min; 1 equiv of Et_2NH, 36 h and 112 min; 2 equiv of Et_2NH, 23 h and 93 min. While *t*-BuOH reacted slower than *i*-PrOH both in the dark and in the light, the same uniformity in a comparison of the ROH and Et_2NH data was not found. However, this latter contrast is misleading since there is a crucial difference between the mechanisms of the dark alcohol and dark amine reactions. While amine addition follows mainly first-order kinetics, the dark alcohol reactions follow mainly second-order kinetics as is seen in Figure 2, rate = k_2[**3a**][ROH]; k_2's are *i*-PrOH, 1 equiv, 3.4×10^{-4}; 2 equiv,[5] 2.8×10^{-4}; *t*-BuOH, 1 equiv, 8.1×10^{-5}, 2 equiv, 5.8×10^{-5} (all M^{-1} s^{-1}).

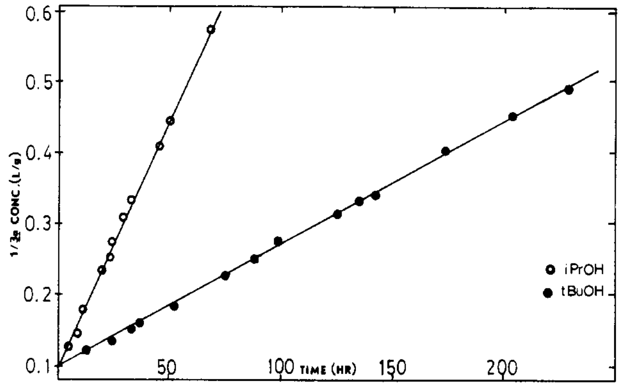

Figure 2. Second-order rate plot of thermal reaction of **3a** with *i*-PrOH and *t*-BuOH in *n*-pentane at 25 °C (1:1 ratio of **3a** to ROH).

The kinetic data do not rigorously define the pathways utilized for the thermal and photocatalyzed addition of ROH and Et_2NH to **3a**. However, the following rationalization, compatible with the results, is favored.

Let A be the concentration of **3a** and B be a very small amount of imino ketene **2a** in equilibrium with **3a**. Also let N stand for the concentration of the nucleophilic reactant (ROH or amine) and P be the ring-opened product. Finally, let C be some adduct intermediate generated on reaction of A with N. Then assume the following pathways account completely for the production of P:

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$$

$$A + N \underset{k_4}{\overset{k_3}{\rightleftharpoons}} C \xrightarrow{k_5} P$$

$$B + N \xrightarrow{k_6} P$$

If both B and C can be treated as steady-state intermediates, then,

$$\frac{-\mathrm{d}A}{\mathrm{d}t} = \left[\frac{k_1 A}{k_2 + k_6 N}\right] k_6 N + \left[\frac{k_3 k_5}{k_4 + k_5}\right] AN \qquad (1)$$

However, $k_1 A/(k_2 + k_6 N) = B$, which under steady-state conditions should be approximately constant so it is possible to write $-(\mathrm{d}A/\mathrm{d}t) = k_b N + k_a AN$.

In the thermal ROH reaction, it is suggested that the nucleophilic alcohol is activated enough to react directly with **3a** to give product. The last term in the rate equation predominates and second-order kinetics are observed. By increasing the concentration of the much more electrophilic imino ketene **2a**, the effect of light is to increase the first

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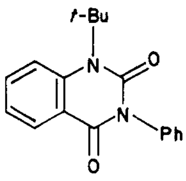
[4] By repeating runs at various times, it was shown that the output of the UV lamp remained constant throughout the kinetic studies, thus validating the relative rate comparisons presented here.

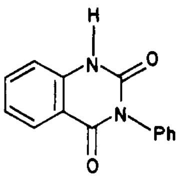
[5] When **3a** and [ROH] are not equal, k_2's are calculated as described by Laidler, K. J. "Chemical Kinetics", 2nd ed; McGraw-Hill: New York, 1965.

kinetic term (presumably both k_1 and k_2 are increased though to different extents[6]) and convert the reaction to a first-order process ($k_b > k_aA$). Presumably, Et_2NH, in contrast to ROH, reacts mostly with **2a** in the dark and may even be a more reactive trap than ROH for this species. Light then would just accelerate the amine reaction without changing kinetic order. The likelihood that Et_2NH is less active than ROH toward direct attack on **3a** may have steric causes or may reflect some special role for the labile hydroxyl protons in the reaction mechanism. The variation of the raw experimental rate constants with nucleophile concentration is accommodated by the competition (including the first- to second-order flexibility in the first term) encompassed in eq 1. The complications in the photolytic MeOH and EtOH kinetics may be due to the presence of agglomerates of ROH (or ROH + **3a**) in pentane.

Attempts to trap the elusive imino ketene **2a** by cycloaddition to maleic anhydride failed. However, **3a** did react with PhN=C=O in refluxing dichloroethane to give a white solid which analyzed as a 1:1 adduct (80% yield). Spectral data[7] are in accord with the N=C addition structure **5**. While **5** would be the expected product from a Diels–Alder reaction of **2a**, a pathway involving nucleophilic attack of the isocyanate on **3a** is not excluded. When heated to its melting point (209 °C) or at lower temperature in solution, **5** released isobutylene and was converted to the known 3-phenyl-2,4(1*H*,3*H*)-quinazolinedione[8] (**6**). Efforts to achieve a photocatalyzed reaction between **3a** and PhN=C=O were unsuccessful.



5



6

Experimental Section[9]

Reactions of *N-tert*-Butylbenzoazetinone (3a) with Alcohols and Amines: Kinetic Studies. In all kinetic runs, sodium-dried *n*-pentane was the solvent and the concentration of **3a** was 0.057 M (1.00 g/100 mL). The following nucleophiles at either the same or twice the **3a** concentration were the other reactants: MeOH, EtOH, *i*-PrOH, *t*-BuOH, Et_2NH, and *i*-Pr_2NH. Reactions were monitored by following the decrease in intensity of the IR 5.48-μm C=O stretch of **3a**. Measurements were made directly on samples taken at various times from the reaction solution. **3a** concentrations were determined from this data with the aid of a calibration curve. The rate of formation of the ester or amide paralleled the decrease in **3a** concentration with the exceptions noted, and at the end of the reaction the IR spectrum was essentially that of a sample of the expected product[1] (when reactants 1:1). To minimize error from instrument fluctuations in slow runs, the spectrophotometer was recalibrated with standard solutions of **3a**. In practice, there was little variation over periods as long as 4 days. In a normal run, 10 points over 2 or more half-lives were taken.

Thermal kinetics were performed at 25 ± 0.2 °C with light excluded by using aluminum foil to shield the constant-temperature bath and by painting the reaction vessel black.

A Hanovia 450-W medium-pressure Hg vapor lamp was utilized for photocatalyzed reactions. This was inserted into the reaction solution (separated by quartz well water condenser). Reactions without filters were very rapid but decomposition also was important. When solutions were shielded from the light by a Vycor filter, rates were slower but reactions were somewhat cleaner. Except for the *i*-Pr_2NH reaction, only slight decomposition was found with the Pyrex filter used for almost all kinetic runs. An attempt to study the photocatalyzed addition of *i*-Pr_2NH to **3a** failed. **3a** slowly decomposed without the appearance of amide absorption. Since the photochemical reaction failed, the thermal process was not studied. Because of the nature of the apparatus, temperature could be maintained only ±2 °C. **3a** alone decomposed slowly in the presence of light in dried pentane. No IR peaks appeared in the 4–5-μm region during this process and the product was an intractable gum.

1-*tert*-Butyl-3-phenyl-2,4(1*H*,3*H*)-quinazolinedione (5). **3a** (1.50 g, 0.0086 mol) and phenyl isocyanate (1.07 g, 0.0086 mol) in 1,2-dichloroethane (15 mL) were refluxed 16 h. After solvent removal in vacuo, the residue was washed with a little hexane and then filtered; yield 2.20 g (80%); mp 200 °C with dec to a solid of mp 278–280 °C. Several recrystallizations from CH_3NO_2 furnished analytically pure **5**: mp 209 °C dec; IR (CH_2Cl_2) 5.84 (s), 5.98 (s), 6.75 (m), 6.82 μm (s) (C=O also at 5.84 and 5.98 in Nujol); ^1H NMR (CD_3NO_2) δ 7.8–8.1 (m, 1 H), 7.1–7.8 (m, 8 H), 1.77 (s, 9 H); ^{13}C NMR (1:1 $CDCl_3$:CH_2Cl_2) 162.5 (amide C=O[10]), 151.5 (urea C=O), 128.9 and 128.4 (o,m-CH of N-Ph), 132.3, 128.2, 128.2, 122.5, and 119.3 (CH of Ar), 140.5, 135.7, and 119.1 (quaternary C of Ar), 61.2 (CMe_3), 30.0 ppm (Me); high-resolution mass spectrum, *m/e* (relative intensity) 294.1372 (2, M^+) ($C_{18}H_{18}N_2O_2$ requires 294.1369), 238.0719 (75, $M^+ - C_4H_8$), 194 (10), 146 (75), 119 (100, $[C_6H_5NCO]^+$), 92 (25), 77 (13, $[C_6H_5]^+$). Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.17; H, 6.19; N, 9.45.

A mixture of both reactants also was photoirradiated at 25 °C in pentane for 28 h. At the end of this time, the **3a** absorption (IR) had decreased significantly but the isocyanate peak had not. A little uncharacterized orange solid had deposited on the quartz insert.

When **3a** was refluxed with maleic anhydride in CCl_4, no reaction occurred. A neat 1:1 mixture heated at 130 °C overnight turned dark brown; IR contained C=O of maleic anhydride but the **3a** C=O was not present. Similar failures were recorded on attempted reaction of **3a** with benzyl isocyanide and ethyl diazoacetate.

3-Phenyl-2,4(1*H*,3*H*)-quinazolinedione (6). A neat mixture of **3a** (1.75 g, 0.01 mol) and phenyl isocyanate (1.19 g, 0.01 mol) was placed in a hot bath at 145 °C. A vigorous exothermic reaction with gas evolution ensued. The next day, the mixture was cooled, and the product was chipped out and recrystallized from CH_3NO_2 to give pure **6**: 2.56 g (87% yield); mp 279–280 °C (lit.[8] mp 280 °C); IR (CH_2Cl_2) 5.81 (s), 5.96 (s), 6.22 (w), 6.24 μm (m) (C=O stretches at 5.77, 6.01, and 6.06 in Nujol and 5.78 and 6.06 in KBr); ^1H NMR (Me_2SO-d_6) δ 11.47 (br s, 1 H), 7.0–8.1 (m, 9 H); ^{13}C NMR (Me_2SO-d_6) 162.1 (amide C=O[10]), 150.1 (urea C=O), 129.0 and 128.7 (o,m-CH of N-Ph), 135.0, 128.0, 127.5, 122.4, and 115.2 (CH of Ar), 139.8, 135.7, and 114.3 ppm (quaternary C of Ar); high-resolution mass spectrum, *m/e* (relative intensity) 238.0737 (80, M^+) ($C_{14}H_{10}N_2O_2$ requires 238.0742), 146.0241 (40, $M^+ - C_6H_5NH$), 119.0371 (100, $[C_6H_5NCO]^+$), 92 (30), 77 (5, $[C_6H_5]^+$).

6 also was produced (75% yield) by refluxing a xylene solution of equimolar **3a** and PhN=C=O for 2 days. **6** was isolated in quantitative yield by heating **5** at 205 °C for 5 min.

Acknowledgment. We are grateful to the NIH for supporting this research. We also thank Mr. D. S. Morrison for experimental assistance.

Registry No. **3a**, 31562-07-9; **5**, 91238-43-6; **6**, 603-23-6.

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(6) Because of the multiplicity of electronic systems which can be included in the transformation, the $\mathbf{2a} \rightleftharpoons \mathbf{3a}$ interconversion is formally Woodward–Hoffmann allowed both thermally and photochemically.

(7) For IR comparison data, see: Kurihara, M.; Yoda, N. *Tetrahedron Lett.* **1965**, 2597. Culbertson, H.; Decius, J. C.; Christensen, B. E. *J. Am. Chem. Soc.* **1952**, *74*, 4834.

(8) Taub, B.; Hino, J. B. *J. Org. Chem.* **1961**, *26*, 5238.

(9) For data on physical and spectral apparatus used, see ref 1.

(10) Assignment of amide and urea C=O shifts is based on data for thymine; Tarpley, A. R.; Goldstein, J. H. *J. Am. Chem. Soc.* **1971**, *93*, 3573.