Reactions of Anthranilium Salts with Nucleophiles: Adduct Formation and Rearrangement

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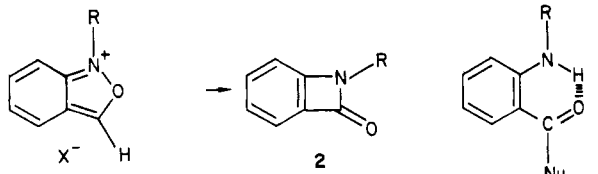
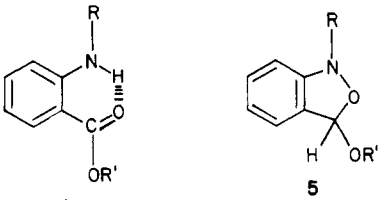
3-Unsubstituted anthranilium salts **1** react with alcohols in the presence of bases to yield adducts **5** which rearrange to the esters **4** when refluxed in xylene. Similar processes involving **1** and cyanide or azide also have been observed. Evidence favoring benzoazetinones **2** as rearrangement intermediates is presented. The chemistry of **1** with phosphines and phosphites also is described. For example, treatment of **1c** with trimethyl phosphite yields the rearranged adduct salt **14** which cleaves to the acyl phosphonate **15** when treated with triethylamine.

In the preceding paper,[1] the titration of anthranilium salts **1** with triethylamine in CH_2Cl_2 to generate benzoazetinones **2** is reported. The ring-opening of **2** with



1a, R = methyl; X = BF_4
1b, R = ethyl; X = BF_4
1c, R = *tert*-butyl; X = ClO_4

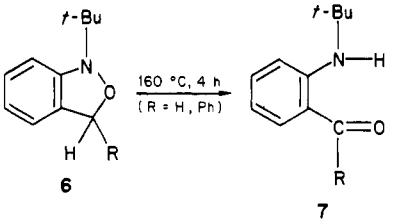
nucleophiles (:Nu) to give **3** also is discussed. This latter process is illustrated by the formation of the mixed anhydride **3**, (R = *t*-Bu, Nu = $OC(=O)C_6H_5$) on treatment of **2** (R = *t*-Bu) with benzoic acid. Examples of the synthesis of anthranilate esters **4** from reaction of **2** with alcohols also are presented. By reacting **1c** with aqueous sodium benzoate **3** (R = *t*-Bu, Nu = $OC(=O)C_6H_5$) can be obtained in one step. However, similar treatment of **1** with R'ONa in R'OH only yields small amounts of **4**. The main product is the isomeric adduct **5**.



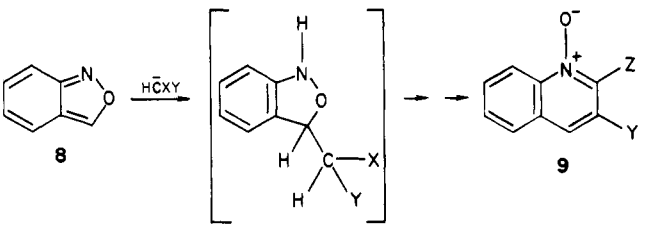
4 **5**

a, R = R' = methyl
b, R = ethyl; R' = methyl
c, R = R' = ethyl
d, R = *tert*-butyl; R' = methyl
e, R = *tert*-butyl; R' = ethyl

The discovery[2] that **5** rearranges to **4** when heated prompted the investigations reported here. The pathway we first proposed for this isomerization requires initial reversion of **5** to the anthranilium cation plus alkoxide followed by proton removal to give **2** and R'OH which then could react normally to produce **4** ($5 \rightleftharpoons 1^+ + R'O^- \rightarrow 2 + R'OH \rightarrow 4$). However, Coombs and Hardtmann[3] have described a similar isomerization, **6** → **7**, for which our suggested mechanism seems unlikely.[4] In both rearrangements, a radical or base-initiated elimination would yield the product directly. Also, in the anthranil series, Taylor and Bartulin[5] have questioned the acidity of C_3H in discussing the novel transformation, **8** → **9**.



6 **7**

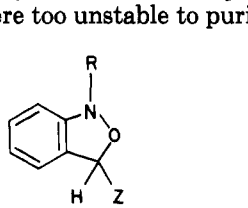


8 **9**

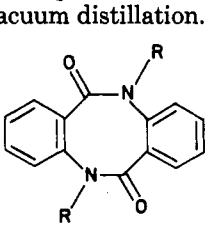
Results and Discussion

The adducts **5** were obtained most cleanly by adding triethylamine to a solution of **1** in the desired alcohol. Distilled yields of **5a–d** ranged from 60% to 78%. Vacuum distilled products **5a,b,d** contained 3–5% of the isomeric amino esters **4** not present before distillation. Spectral and analytical data were in accord with the proposed structures. Moreover, the NMR spectrum of **5d** in CF_3CO_2H was the sum of the separate NMR spectra of *N*-*tert*-butylanthranilium cation and methanol in this medium, indicating that reversion to these precursors had occurred and ruling out any unusual addition–rearrangement. This result was confirmed by the isolation of **1c** (84% yield) by adding ether to a solution of **5d** in $HClO_4$–acetone.

The analogous cyano and azido adducts **10a–d** could be made easily (75–86% yields) just by adding the salts **1** to aqueous solutions of sodium cyanide or sodium azide followed by an extraction–evaporation workup. The azides **10c,d** were too unstable to purify by vacuum distillation.



10a, R = ethyl; Z = C≡N
10b, R = *tert*-butyl; Z = C≡N
10c, R = ethyl; Z = N=N⁺=N⁻
10d, R = *tert*-butyl; Z = N=N⁺=N⁻



11a, R = methyl
11b, R = ethyl

(1) Olofson, R. A.; Vander Meer, R. K.; Hoskin, D. H.; Bernheim, M. Y.; Stournas, S.; Morrison, D. S. *J. Org. Chem.*, first in a series in this issue.
(2) Olofson, R. A.; Vander Meer, R. K.; Stournas, S. *J. Am. Chem. Soc.* **1971**, *93*, 1543.
(3) Coombs, R. V.; Hardtmann, G. E. *J. Org. Chem.* **1970**, *35*, 2440. For other data explained here, see: Coombs, R. V. *Ibid.* **1977**, *42*, 1812.
(4) For discussion of the chemistry of *N*-ethyl-1,2-benzisoxazoline, see: Kemp, D. S. *Tetrahedron* **1967**, *23*, 2001.
(5) Taylor, E. C.; Bartulin, J. *Tetrahedron Lett.* **1967**, 2337.

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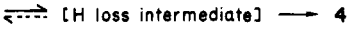
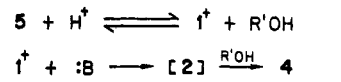
Scheme I



Scheme II



When the *O*-methyl adduct **5a** was refluxed in xylene, two products were obtained, the amino ester **4a** in 49% yield and the known[6] *N,N'*-dimethyldianthranilide (**11a**, 43% yield). Similarly, **5b** afforded **4b** (53%) and **11b** (44%). The dimer **11b** also was isolated (33%) from thermolysis of **5c** along with the ester **4c** (30%). Dianthranilide **11b** was the only compound identified from thermolysis of cyanobenzisoxazoline **10a**. No acyl cyanide was found. Finally, the *N-tert*-butyl amino ester **4d** (45%) but no dianthranilide (steric factors?) was obtained when **5d** was refluxed in xylene. Since the amino ester **4b** was stable in refluxing xylene, it cannot be the source of *both* halves of the dimeric **11b**.

The azido adducts **10c,d** readily rearranged to acyl azides (90+% yields) just by refluxing in ether or CH_2Cl_2. At higher temperatures, these latter compounds underwent Curtius rearrangement and cyclization to benzimidazolones as already described.[1]

Two classes of mechanisms have been considered for the thermal **5** → **4** rearrangement. In Scheme I **4** is formed directly from **5** by β-elimination with ring-opening. This scission could be catalyzed by base (proton abstraction) or by acid (H^+ addition to N to increase its effectiveness as a leaving group). The analogous radical-induced process also is possible. A concerted elimination is unlikely since the optimum geometry for such a process requires the C–H and O–N bonds in **5** to be in the same plane (actual dihedral angle probably ca. 55°). In Scheme II the key step is the initial acid-catalyzed elimination of R'OH from **5** to give the anthranilium cation 1^+. This then is converted to the benzoazetinone **2** which finally reacts with the previously released R'OH to give the ester **4**.

The second mechanism is preferred for the following reasons.

First, all steps separately have been shown to occur (see above).

Second, the rearrangement **5b** → **4b** is not accelerated by NaOMe; this would be required for the base-catalyzed version of Scheme I to be operative. Also, the cleavage of the cyano adduct **10a**—in which C_3H should be several orders of magnitude more acidic than in **5**—is not catalyzed by diisopropylethylamine. A Scheme II reaction would be inhibited by added base since the initial equilibrium would be suppressed. This has been demonstrated for the isomerization **5b** → **4b** with diisopropylethylamine as the added base (see below).

Third, Scheme I does not satisfactorily account for the formation of dianthranilide **11**. It has already been stated that the only probable precursor, the amino ester **4**, is not the source of both halves of the dimer **11**. In contrast, generation of **11** is easily rationalized with the aid of Scheme II. It is only necessary to postulate that the amine function of a molecule of **4** reacts with a molecule of the highly electrophilic benzoazetinone **2** to give the dimeric monoamide which then cyclizes to **11** with the expulsion of R'OH. An acyl cyanide from isomerization of **10a,b** could similarly serve as a precursor to **11** (loss of HCN on cyclization).

(6) Schroeter, G.; Eisleb, O. *Liebigs Ann. Chem.* **1909**, *367*, 101.

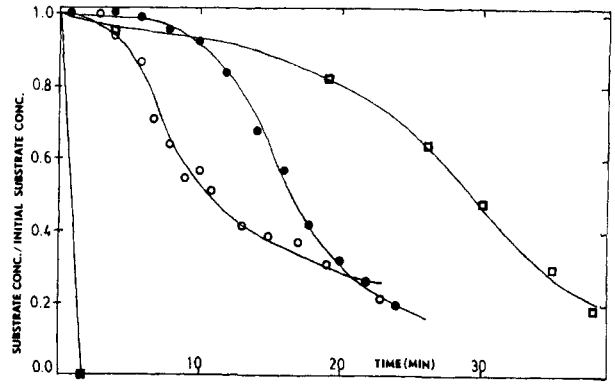


Figure 1. Rate of thermal decomposition of *N*-ethyl-3-methoxy-2,1-benzisoxazoline (**5b**) to methyl *N*-ethylanthranilate (**4b**) at 139 °C in CCl_4–CH_2Cl_2. (●) Reaction of 2.8 M **5b**. (□) Same with 0.2 equiv of *i*-Pr_2NEt added. (○) First reaction with 0.18 equiv of MeOH added. (■) Reaction of 2.8 M **5b** in 1,2-dichloroethane–CH_2Cl_2 with 0.18 equiv of $Et_3NH^+BF_4^-$ added.

Fourth, when an equimolar mixture of the *N*-ethyl 3-ethoxy adduct **5c** and the *N-tert*-butyl 3-methoxy adduct **5d** was refluxed in xylene and the product amino ester fraction isolated, it contained all four possible amino esters: **4b**, **4c**, **4d**, and **4e**; ratio 36:14:18:31.[7] Thus, the scrambling required by the first step in Scheme II does take place under the experimental conditions. Therefore, even if Scheme I is operative, the first step of Scheme II must be included as a side equilibrium.

Fifth, rearrangement **5b** → **4b** is catalyzed by acid. Some crude rate curves using 2.8 M solutions of **5b** are depicted in Figure 1. Significant conclusions based on Figure 1 are (1) addition of 0.2 equiv of diisopropylethylamine slightly reduced the reaction rate; (2) 0.18 equiv of methanol added to the medium decreased the induction period; and (3) 0.18 equiv of added $Et_3NH^+BF_4^-$ increased the rate spectacularly. In another experiment with 0.3 equiv of $BF_3{\cdot}Et_2O$ as the added catalyst, the rate was almost as fast (solid formed so quantitative data not available). All the results are easily accommodated by Scheme II but do not rigorously exclude an unusual acid-catalyzed variant of Scheme I. If Scheme II is correct, C_3H of anthranilium cations must be very acidic or a concerted base-induced elimination with simultaneous cleavage of C_3H and N–O in **1** must be extremely facile.[8]

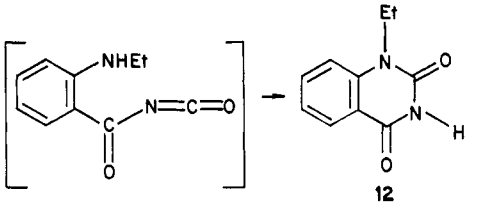
Sixth, the facility of isomerization of the benzisoxazoline adducts to **3** should generally reflect the leaving group power of :Nu and similarly the pK_a's of the conjugate acids (H:Nu). The data are in accord with this correlation: benzoate adducts rearrange faster than azides **10c,d** (at 35–45 °C, pK_a HN_3 is 4.7) which in turn are more reactive than cyanides **10a,b** (pK_a HCN is 9.3) which are followed by **5**. As ionization becomes more difficult, Scheme I may take over. Thus, adduct **6** in which :Nu is hydride may thermally isomerize by a free-radical chain mechanism in which some radical species initiates the reaction by abstracting H· from **6**.

Useful predictions in preparative chemistry can be extrapolated from these observations. For example, very decomposition-prone benzoazetinones **2**, too unstable to isolate, still can be efficient synthetic precursors by taking advantage of the "holding tank" equilibrium between **1** and adduct. This can limit the amount of **2** present in a medium preventing several kinds of unwanted side reactions. The point is illustrated here by heating the *N*-ethyl salt

(7) Since **5c** and **5d** ionize at different rates and reaction (→ **11**) has different intermediates, product ratios should not be statistical.

(8) Elimination is concerted for benzisoxazolium cations; see ref 4.

1b with sodium cyanate in acetonitrile. The known diketotetrahydroquinazoline **12**[9] was obtained in 81% yield. Solutions of both *N*-ethylbenzoazetinone[1] and HNCO are very unstable and any standard attempt to react these two would give more side products than **12**.



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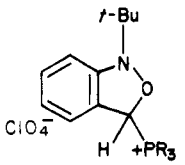
Other predictions are made. With some nucleophiles which in addition are very weak bases, a rapid equilibrium between adduct and 1 plus :Nu should be observable and by experimental manipulation also displaceable. Finally, because of the presence of other reaction sites, adduct chemistry should not be limited to reversion to **1**. These hypotheses have been explored with phosphines and phosphites as the added nucleophiles.

The product obtained in 81% yield from reaction of **1c** with tri-*n*-butylphosphine was the simple C_3 adduct **13a**.

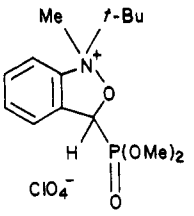


13a, R = *n*-butyl
13b, R = phenyl
13c, R = O-phenyl
13d, R = O-methyl

The NMR C_3H resonance of **13a** was found as a doublet at δ 6.53 in CD_3CN. The peak position is in accord with the data for other C_3 adducts (**5a–d** at δ 6.1–6.25, **10a,b** at 5.9–6.2, and **10c,d** at 6.3–6.4 vs. 9.9–10.0 for **1a–c**) and the 12.5-Hz coupling constant is consistent with J_{PCH} values for other heteroatom-substituted phosphonium salts.[10] In contrast, though a substance which analyzed as the adduct **13b** (70% yield) also was precipitated from reaction of **1c** with the weaker nucleophile, triphenylphosphine, the NMR C_3H of this compound was found at δ 8.48 in CD_3CN. Also, although this peak was broadened, no coupling to phosphorus was observed. In solution, **13b** must be in rapid equilibrium with **1c** and free Ph_3P with an equilibrium constant near unity. The NMR peak then is the time average of the C_3H resonance of **1c** and the absorption required by **13b**. In accord with this explanation, the peak position was much more solvent dependent than that of **13a**: shifted δ 0.4 downfield in CD_3NO_2 vs. <0.1 δ downfield for **13a** (minor solvent polarity change effected equilibrium displacement). Also, the presumed **13b** was immediately converted to Ph_3P and *N-tert*-butylbenzoazetinone on treatment with Et_3N. When **13a** was similarly reacted, complete conversion to benzoazetinone took at least 2 h.

No adduct **13c** was isolated from reaction of **1c** with triphenyl phosphite and the NMR spectrum of a mixture indicated that trace addition had taken place (C_3H at δ 9.69). The result was similar with Me_2S as the added nucleophile (C_3H at δ 9.79).

With trimethyl phosphite, reaction did occur but the product (80% yield) was not the simple adduct **13d**. The compound was assigned structure **14** from combustion and



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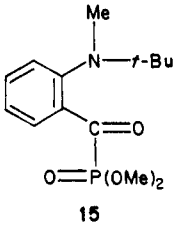

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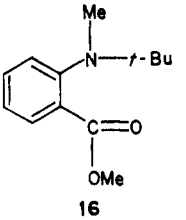

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spectral data (^1H NMR δ C_3H at 6.31, NMe at 3.95, OMe at 3.93 and 3.76, J_{HCP} = 11 Hz; no IR C=O or NH stretch) and further chemical transformations. The salt **14** formally is the product from Arbuzov demethylation by an amino function of a precursor phosphonium salt **13d**. Other examples of Arbuzov reactions in which a nucleophilic site in the same molecule has been alkylated by the methyl lost have been documented.[10] If the amine alkylation is intermolecular as predicted, the question of the stereochemistry of **14** is not resolved. The compound with H and methyl in the trans relationship would probably be favored thermodynamically but attack of the methylating agent on the nitrogen of *O*-demethyl-**13d** should occur most readily on the side of the ring plane opposite the phosphonate group (one isomer by NMR).

On treatment with triethylamine, **14** was converted in 82% yield to a substance too unstable to obtain analytically pure but whose spectral characteristics (IR C=O stretch at 6.06μm;[11] NMR δ NMe at 2.80, OMe at 3.73, J = 11 Hz,[11] MS M^+ at m/e 229) were in accord with structure **15**. When refluxed in methanol overnight, **15** underwent methanolysis to give dimethyl phosphite (compared with commercial sample) and methyl *N-tert*-butyl-*N*-methylanthranilate (**16**, 90% yield). The tertiary amine **16** thermally de-*tert*-butylated to **4a**.[1] The Et_3N-induced elimination (→ **15**) would be facilitated by both the adjacent P=O and the plus charge. From the $(PhO)_3P$ data, **13d** should be a minor equilibrium component. Subsequent irreversible N-methylation would drive the process to conclusion. In a control experiment, no reaction occurred when a concentrated solution of *N-tert*-butylbenzoazetinone and $(MeO)_3P$ in CH_2Cl_2 was refluxed for a prolonged period.

Experimental Section[12]

***N*-Ethyl-3-methoxy-2,1-benzisoxazoline (5b).** Et_3N (8.10 g, 0.08 mol) was slowly added to a stirred, cooled (0 °C) solution of *N*-ethylanthranilium fluoborate (**1b**[1]) (4.70 g, 0.02 mol) in MeOH (40 mL). Stirring was continued at 25 °C overnight, excess MeOH and Et_3N were removed at reduced pressure, and the residue was extracted with ether (2 × 30 mL). Distillation of the ether extract afforded **5b**: 2.45 g (68% yield) of bp 84–85 °C (0.7 mm); IR (CCl_4) 6.2 (m), 6.75 μm (m); ^1H NMR (CCl_4) δ 6.6–7.4 (m, 4 H), 6.20 (s, 1 H), 3.30 and 3.28 and 3.25 (s and q, J = 7 Hz, and q, J = 7 Hz, 5 H), 1.19 (t, 3 H, J = 7 Hz). NMR analysis indicated that distilled **5b** contained 5% of methyl *N*-ethylanthranilate (**4b**[1]) not present before distillation.

***N*-Methyl-3-methoxy-2,1-benzisoxazoline (5a).** Reaction of *N*-methylanthranilium fluoborate (**1a**[1]) with MeOH as above gave **5a** in 66% yield; bp 78–80 °C (0.4 mm); ^1H NMR (CCl_4) δ 6.6–7.4 (m, 4 H), 6.23 (s, 1 H), 3.32 (s, 3 H), 3.03 (s, 3 H). Distilled

(9) Lange, N. A.; Sheibley, F. E. *J. Am. Chem. Soc.* **1933**, *55*, 2113.
(10) Walinsky, S. W.; Ph.D. Thesis, The Pennsylvania State University, 1971.
(11) The IR C=O stretch of p-$MeOC_6H_4C(=O)P(=O)(OMe)_2$ occurs at 6.07 μm: Berlin, K. D.; Taylor, H. A. *J. Am. Chem. Soc.* **1964**, *86*, 3862. In $CH_2=CHOC(=O)P(=O)(OMe)_2$, J_{MeOP} is 11.5 Hz and OMe is found at δ 3.90: Yamamoto, Y. S.; Ph.D. Thesis, The Pennsylvania State University, 1971.
(12) For data on physical and spectral apparatus used, see ref 1.

5a contained 3% of the isomeric ester **4a**.[1]

***N*-Ethyl-3-ethoxy-2,1-benzisoxazoline (5c).** Similar attack of **1b** by EtOH afforded pure **5c** in 60% yield: bp 77.5–78.5 °C (0.5 mm); ^{1}H NMR (CCl_4) δ 6.6–7.4 (m, 4 H), 6.25 (s, 1 H), 3.66 and 3.25 (q, J = 7 Hz, and q, J = 6.5 Hz, 4 H), 1.19 and 1.16 (t, J = 7 Hz, and t, J = 7 Hz, 6 H).

***N-tert*-Butyl-3-methoxy-2,1-benzisoxazoline (5d).** This analogue from *N-tert*-butylanthranilium perchlorate (**1c**[1]) and MeOH was obtained in 78% yield: bp 77 °C (0.3 mm); ^{1}H NMR (CCl_4) δ 6.8–7.3 (m, 4 H), 6.10 (s, 1 H), 3.32 (s, 3 H), 1.25 (s, 9 H). Distilled **5d** was contaminated with 5% of **4d**.[1]

The NMR spectrum of **5d** in CF_3CO_2H was the sum of the spectra of *N-tert*-butylanthranilium cation and MeOH [δ 3.98 (s, 1.3 H, from CF_3CO_2Me), 3.48 (s, 1.7 H)] in the same solvent.

5d. NaOMe Method. **1c** (8.3 g, 0.03 mol) was slowly added to stirred, cooled NaOMe (from 0.03 mol Na) in MeOH. The mixture was stirred 2 h at 25 °C and evaporated in vacuo, and the residue was triturated with ether. Distillation of the ether extract gave a mixture of **4d** and **5d** in a 19:81 ratio (NMR, 16:84 before distillation); 5.70 g (91% yield) of bp 94–95 °C (1 mm). When NaOMe–MeOH was added to **1c** in MeOH, the ratio was 10:90.

Reaction of 5d with $HClO_4$. 5d (2.07 g, 0.01 mol) in acetone (5 mL) was stirred as concentrated $HClO_4$ (4.5 g, 0.03 mol) was slowly added. The precipitated solid was identified as **1c**: 2.32 g (84% yield) of mp 147–148 °C.[1]

***N*-Ethyl-3-cyano-2,1-benzisoxazoline (10a). 1b** (4.7 g, 0.02 mol) was slowly added to a stirred solution of NaCN (10 g, 0.2 mol) in 100 mL of water. The mixture immediately was extracted with CH_2Cl_2 (3 × 40 mL). The combined extracts were dried (Na_2SO_4) and crude **10a** (3.16 g, 91%) obtained after evaporation was distilled: 2.62 g (75% yield), bp 96–97 °C (0.4 mm); IR (CCl_4) 4.50μm (vw); ^{1}H NMR (CD_3NO_2) δ 6.8–7.6 (m, 4 H), 6.23 (s, 1 H), 3.48 and 3.43 (2q's, 2 H, J = 7 Hz), 1.25 (t, 3 H, J = 7 Hz).

***N-tert*-Butyl-3-cyano-2,1-benzisoxazoline (10b).** Reaction as above of **1c** gave **10b** in 82% yield; bp 107 °C (0.5 mm); ^{1}H NMR (CCl_4) δ 6.8–7.4 (m, 4 H), 5.94 (s, 1 H), 1.23 (s, 9 H).

Thermolyses of 5a–d. 5d (1.75 g, 0.01 mol) in xylene (50 mL) was refluxed overnight and then the solvent was removed by distillation. **4b**[1] (0.93 g, 53% yield) was extracted from the residue by trituration with pentanes and isolated by distillation. The insoluble fraction consisted mostly of *N,N'*-diethyldianthranilide (**11b**, 0.64 g, 44% yield), crystallized from EtOH: mp 192–193 °C; IR (CH_2Cl_2) 6.09μm (s); ^{1}H NMR (CD_3CN) δ 7.34 (s, 8 H), 4.2–5.0 (m, 2 H), 3.1–3.8 (m, 2 H), 1.15 (t, 6 H, J = 7 Hz). **4b** was recovered (86%) after refluxing in xylene for 18 h.

Reaction of **5a** and workup as above gave **4a**[1] (49% yield) and *N,N'*-dimethyldianthranilide (**11a**, 43% yield); recrystallized from MeOH, mp 205–206 °C (lit.[6] mp 207 °C); IR (CH_2Cl_2) 6.09μm (s); ^{1}H NMR (CD_3NO_2) δ 7.30 (s, 8 H), 3.40 (s, 6 H). Similarly **5c** produced **4c**[1] (30% yield) and **11b** (33% yield). When **5d** was refluxed in xylene for 4 days, only **4d**[1] (45% yield after vacuum distillation) was found after solvent rotoevaporation.

Thermolysis of 10a. When **10a** (1.74 g, 0.01 mol) in xylene (20 mL) was refluxed 3 days, the black viscous residue obtained after vacuum evaporation was chromatographed on silica (2:1:1 CH_3CN–CH_2Cl_2–$CHCl_3$). The only product identified was **11b**, 0.39 g (27% yield). When **10a** was heated neat at 120 °C (20 h), the **11b** yield was 14%.

Attempted Deprotonation of 5b and 10a. 5b (0.90 g, 0.005 mol, contaminated by 5% **4b**) in NaOMe–MeOH (25 mL, from 0.02 mol Na) was stirred at 25 °C overnight. After workup, unchanged **5b** was isolated (same isomer ratio) in 86% yield (0.78 g). Similarly, **10a** was recovered almost quantitatively after refluxing overnight with 0.2 M i-Pr_2NEt in CCl_4.

Crossover Reaction. A solution of **5c** (2.25 g, 0.0116 mol) and **5d** (2.25 g, 0.011 mol) in xylene (40 mL) was refluxed overnight. The mixture of four amino esters was isolated as one distillation fraction; 3.25 g (72% yield) of bp 78–84 °C (0.4 mm). The two methyl esters **4b,d** then were separated from the two ethyl esters **4c,e** by preparative VPC. Both VPC peaks were of ca. equal area. The methyl ester fraction contained (NMR) 28% **4b** and 72% **4d** and the ethyl esters consisted of 61% **4c** and 39% **4e**.

***N*-Ethyl-3-azido-2,1-benzisoxazoline (10c). 1b** (2.25 g, 0.01 mol) was slowly added to a solution of NaN_3 (13 g, 0.2 mol) in 75 mL water and the mixture then extracted with CH_2Cl_2 (3 × 30 mL). The dried (Na_2SO_4) extract was evaporated in vacuo, giving **10c** as a thermally unstable oil: 1.53 g (80% yield); IR (CCl_4) 4.77μm (s); ^{1}H NMR (CCl_4) δ 6.4–7.4 (m, 4 H), 6.33 (s, 1 H), 3.27 (q, 2 H, J = 7 Hz), 1.20 (t, 3 H, J = 7 Hz).

N-Ethylanthraniloyl azide[1] (93% yield) obtained after refluxing **10c** in CH_2Cl_2 overnight contained 5% of *N*-ethylbenzimidazolone.[1] This was made in 74% yield by refluxing **10c** in CCl_4 overnight, mp 119–120 °C.[1]

***N-tert*-Butyl-3-azido-2,1-benzisoxazoline (10d).** Reaction as above of **1c** afforded **10d**, unstable oil, 86% yield: IR (CCl_4) 4.77μm (s); ^{1}H NMR (CCl_4) δ 6.7–7.4 (m, 4 H), 6.39 (s, 1 H), 1.29 (s, 9 H). When **10d** was refluxed in ether overnight, it rearranged to *N-tert*-butylanthraniloyl azide (90% yield).

1-Ethyl-2,4-diketotetrahydroquinazoline (12). A solution of **1b** (5.88 g, 0.025 mol) in CH_3CN (40 mL) was refluxed overnight with 1.95 g (0.03 mol) of sodium cyanate. The mixture was filtered and the filtrate concentrated, yielding crude **12**: 3.95 g (81%), mp 205–210 °C; recrystallized from MeOH; 2.88 g (60%), mp 213–215 °C (lit.[9] mp 215–217 °C); IR (CH_2Cl_2) 2.97 (w), 5.90 (s), 6.23μm (m); ^{1}H NMR (Me_2SO-d_6) δ 11.43 (br s, 1 H), 6.9–8.1 (m, 4 H), 4.03 (q, 2 H, J = 7 Hz), 1.14 (t, 3 H, J = 7 Hz).

3-(*N-tert*-Butyl-2,1-benzisoxazolinyl)tri-*n*-butylphosphonium Perchlorate (13a). (n-Bu)$_3$P (redistilled, 4.04 g, 0.02 mol) in CH_3CN (20 mL) was dripped into stirred, cooled **1c** (5.50 g, 0.02 mol) in CH_3CN (60 mL). After the exothermic reaction had subsided, the ice bath was removed and the solution stirred overnight at room temperature. The oil obtained after evaporation was dissolved in EtOAc and **13a** was precipitated with ether: 7.75 g (81% yield), mp 118–119 °C; analysis sample reprecipitated from 1:1 CH_2Cl_2–EtOAc with ether, same mp; ^{1}H NMR (CD_3CN) δ 7.0–7.5 (m, 4 H), 6.53 (d, 1 H, J = 12.5 Hz), 1.8–2.5 (m, 6 H), 1.28 and 1.1–1.8 (s and m, 21 H), 0.7–1.1 (m, 9 H). In CD_3NO_2 the C_3H doublet was found at δ 6.60 and in $CDCl_3$ at δ 6.68 (12.5 Hz shown to be J value by NMR at 100 MHz).

13a (2.40 g, 0.005 mol) and Et_3N (4.0 g, 0.04 mol) in CH_2Cl_2 (35 mL) were stirred under N_2 at 25 °C. From periodic IR spectra, it was found that *N-tert-butylbenzoazetinone*[1] first formed (at least 2 h) and this slowly was converted to *N-tert*-butylanthranilic anhydride (trace water?). After 12 h, volatiles were removed in vacuo and the residue was triturated with ether. (n-Bu)$_3$P (0.58 g, 58%) was isolated by vacuum distillation of the ether extract and the distillation residue was comprised mainly of anhydride.

3-(*N-tert*-Butyl-2,1-benzisoxazolinyl)triphenylphosphonium Perchlorate (13b). 1c (2.75 g, 0.01 mol) and Ph_3P (2.62 g, 0.01 mol) in acetone (75 mL) was left at 25 °C overnight. The precipitated white solid was filtered and combined with more **13b** from filtrate concentration: 3.72 g (70% yield) of mp 146 °C dec; recrystallized from acetone, same mp; ^{1}H NMR (CD_3CN) δ 8.48 (broadened s, 1 H), 7.15–7.9 (m, 19 H), 1.50 (s, 9 H). The NMR s at δ 8.48 shifted to 8.86 in CD_3NO_2 and to 8.75 in dilute $CDCl_3$.

13b (5.40 g, 0.01 mol) and Et_3N (5.0 g, 0.05 mol) in CH_2Cl_2 (60 mL) were evaporated after 10 min and the residue was triturated with ether. *tert*-Butylbenzoazetinone (0.78 g, 45%) was distilled from the ether extract. The distillation residue contained mostly Ph_3P with some *tert*-butylanthranilic anhydride. **1c** precipitated quantitatively with ether from a solution in CH_2Cl_2 containing 2 equiv of Me_2S after stirring overnight at 25 °C. In the NMR (CD_3NO_2) spectrum of a solution of **1c** and Me_2S, C_3H was found as a sharp s at δ 9.79. **1c** also was recovered from a solution with triphenyl phosphite and the NMR C_3H peak of the mixture occurred at δ 9.69.

***N-tert*-Butyl-*N*-methyl-3-(dimethoxyphosphinyl)-2,1-benzisoxazolinium Perchlorate (14).** A mixture of **1c** (11.0 g, 0.04 mol) and $(MeO)_3P$ (7.44 g, 0.06 mol) in CH_3CN (75 mL) was kept at 0 °C overnight. Then ether was added to precipitate **14**, which was filtered and vacuum dried: 14.7 g (80% yield) of mp 109 °C dec; analysis sample from acetone–ether, mp 114 °C dec; ^{1}H NMR (CD_3CN) δ 7.82 (br s, 4 H), 6.31 (s, 1 H), 3.95 and 3.93 and 3.76 (s and d, J = 11 Hz, and d, J = 11 Hz, 9 H [ca. 3:3:3], J at 100 MHz), 1.60 (s, 9 H) (the δ values shifted <2 Hz when solution diluted in half).

Dimethyl *N-tert*-Butyl-*N*-methylanthraniloylphosphonate (15). **14** (10.0 g, 0.025 mol) in CH_2Cl_2 (70 mL) was slowly added to stirred, cooled Et_3N (5.0 g, 0.05 mol) in CH_2Cl_2

(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); ^1H 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); ^1H 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]

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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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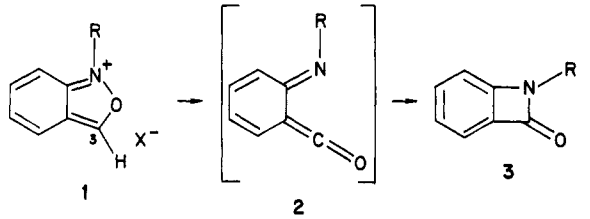
From studies of the kinetics of the reactions of *N-tert*-butylbenzoazetinone (**3a**) with diethylamine and with alcohols to give the ring-opened adducts **4**, the presence of a trace equilibrium component, the more electrophilic imino ketene **2a**, has been inferred. The transformation **3a** → **2a** 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]



1 **2** **3**

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

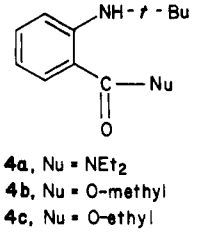
In this paper, we present indirect evidence (a) for the existence of the ring–chain tautomer equilibrium, **2** ⇌ **3**, even at room temperature, (b) that this equilibrium can be displaced photochemically to increase the concentration of **2**, and (c) that the imino ketene **2** is more electrophilic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

(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.

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



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

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

(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.

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